Can International Organizations Shape Scientific Development?

Zoe Xincheng Ge*

Mengfan Cheng†

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Abstract

Scientific development is not neutral. One underlying source of the biased development is innovators' lack of information about the market demand for the new technology. We argue that IOs can provide information about the priority of technology to convince innovators of a credible market demand for ignored technologies, which facilitates the R&D investment. We focus on the influence of the World Health Organization (WHO) on medical research on infectious diseases. Using disease characteristics to explore the informativeness of the market demand, we find that diseases with unequal geographic distribution receive a higher priority from the WHO, while severe diseases are not listed as a high priority, confirming that the WHO's information provision substitutes for the lack of information about the market demand. Using a difference-in-differences specification to examine the effect of WHO priority on R&D investment, we find that WHO priority may have increased R&D investment in ignored diseases but discouraged clinical trials on these diseases.

*Assistant Professor, School of Politics, Economic & Global Affairs, IE University. Email: xincheng.ge@ie.edu.

†PhD Candidate, Department of Politics, New York University. Email: m.cheng@nyu.edu.

1 Introduction

Scientific development is biased in favor of the interest of capital. Knowledge that contributes to a higher market return tends to receive more attention and funding for research and development (R&D), while areas lacking market profitability tend to undergo a slower process of scientific development, which often overlook the welfare of the less privileged population. For example, in the field of infectious diseases, despite the fact that malaria is deadlier than COVID-19 in Africa, malaria vaccine takes much longer to be developed than COVID-19 due to the concentration of malaria in poor regions (Wilkins and Paquette, 2021). Given their active role in promoting development, especially in middle- and low-income countries, can international organizations (IOs) facilitate the overlooked area of scientific development?

This paper shows that, by using its agenda-setting power to set the priority of technologies, IOs can provide information to facilitate the market demand for the technology, which incentivizes more investment in the overlooked technologies.

We focus on the role of the World Health Organization's (WHO) in global health research. Studies on infectious diseases contributes to the efficient control of disease outbreaks. The development of vaccine technology and treatment medicine can greatly alleviate the severity of disease outbreaks. Yet, not all infectious diseases receive the same attention and resources. One example is the development of an Ebola vaccine called rVSV-ZEBOV (Branswell, 2020). The vaccine delivery technology is called vesicular stomatitis virus (VSV) and has been available since 1994. Yet, even though the testing in animals proved to be effective against the virus and showed no sign of negative consequences, the vaccine did not receive any grants until 2014, which was given by a Canadian defense program as a tool to combat bioterrorism. Despite the great promise, there was a lack of funding for this vaccine candidate to enter the clinical trial stage, leading to another 5 years of delay before the vaccine was finally approved. During this prolonged period of Ebola vaccine development, there were two declarations of the Public Health Emergency of International Concern (PHEIC) related to Ebola, one in West Africa in 2014 and another in the Democratic Republic of the Congo in 2019, causing

an estimation of more than 13,000 deaths. Considering the consequence of such unequal scientific development and the WHO's role of facilitating disease control as a global public good, how can the WHO facilitate the R&D investment in diseases that are ignored?

One of the key reasons for the unequal R&D investment in different infectious diseases is a lack of information. The market of medical products targeting infectious diseases is highly unpredictable, especially for those concentrated in low-income countries where the government's purchasing power is limited. Without the information on the market demand for specific medical products, pharmaceutical firms lower the expected return for their R&D investment in these diseases, discouraging such investment. In addition, as pharmaceutical firms tend to have multiple lines of R&D investment on different health issues, there is a high opportunity cost for firms to divert resources from a more stable and profitable market—such as seasonal flu—to ignored infectious diseases (Branswell, 2020). As a result, the unpredictability of the market demand is a big obstacle to R&D investment in diseases concentrated in low-income countries.

We argue that the WHO can leverage its influence on the market of medical products and provide information to convince pharmaceutical firms of a credible market for ignored diseases. To do so, the WHO publishes information about the priority of diseases and medical products to reduce the uncertainty in the demand for medical products. In addition, the WHO collaborates with other procurement agencies such as the United Nations International Children's Emergency Fund (UNICEF) and Gavi, the Vaccine Alliance (Gavi) to build a market for medical products targeting low-income countries. By pooling their financial resources together, these procurement agencies can create a large enough market, which addresses the problem of fragmented small markets that low-income countries have. Altogether, these efforts help facilitate the R&D investments in these ignored diseases.

To examine this argument, we look into one important agenda-setting tool of the WHO: the priority of vaccine prequalification. Vaccine is one of the most cost-effective interventions (World Health Organization, 2009). However, the efficacy and safety of vaccines require

constant regulation. Equipped with its expertise in public health, the WHO was delegated the authority of vaccine quality control by other United Nations (UN) procurement agencies. This procedure is called vaccine prequalification, which is a necessary condition for a vaccine to enter the UN procurement process. Hence, the WHO has the authority to give market access to vaccine products to a bigger market. By setting a higher priority for certain types of vaccines, the WHO can signal to pharmaceutical firms a higher probability that the product will enjoy a big market, which increases the marginal benefits of investing in the vaccine for firms.

Given the information problem of market demand, we examine how disease characteristics affect the credibility of market demand and, as a result, the vaccine priority set by the WHO. We hypothesize that the WHO sets a higher priority for diseases that are unequally distributed around the world because pharmaceutical firms may have more difficulty in predicting the outbreak trend and the market demand for such diseases. On the other hand, we hypothesize that diseases with greater severity may not necessarily receive a higher priority because it is more visible to the public when a disease outbreak affects multiple countries. The descriptive analysis confirms these hypotheses.

To examine the effect of vaccine priority on R&D investment, we employ a difference-in-differences specification. We use the publication of the vaccine priority list as the treatment and examine the treatment uptake by exploring the variation in the level of priority. To measure R&D investment in different diseases, we use the research funding data on the Research, Condition, and Disease Categorization (RCDC) provided by the National Institutes of Health (NIH) and an online database of clinical research studies around the world. Using regular expressions to detect diseases and the corresponding viruses, we categorize the funding and clinical trials into 38 types of vaccine-preventable diseases.[1] The results show that a higher priority set by the WHO may have increased the research funding but discouraged the investment in clinical trials.

[1]Website: https://www.who.int/teams/immunization-vaccines-and-biologicals/diseases

This paper contributes to the literature on the international determinants of scientific development. While existing work has shown the importance of economic factors (Acemoglu, 2002; Acemoglu et al., 2015) and domestic politics (Drezner, 2001) in the development of science and technology, an emerging literature is focusing on the role of international politics. Milner and Solstad (2021) shows that international competition accelerates the speed for states to adopt new technology, while Drezner (2019) highlights the importance of power distribution. Most closely related to this paper, Hai (2023) studies how states influence IOs' interpretation of scientific information to set the agenda in international negotiation. This paper reveals how international institutions can channel the direction of investment in scientific development.

This paper also speaks to the literature on IOs' strategic provision of information. Existing studies show that IOs' information provision is shaped by the need to persuade domestic policymakers (Fang and Stone, 2012), to influence the bargaining dynamics (Johns, 2007), and to compete with other IOs (Miyano, 2024). We show that IOs may also provide information to make up for the market failure.

This paper also contributes to the understanding of the source of agenda-setting power in IOs. Existing studies have identified the influence of expertise (Haas, 1992; Pollack, 1997; Heinzel and Koenig-Archibugi, 2024), domestic audience (Bisbee et al., 2019; Kelley and Simmons, 2020), and bureaucrats (Arias, 2024) as the source for IOs' agenda-setting power. This paper adds to these studies by highlighting IOs' influence on the market as a new source for their ability to set the agenda.

2 Argument

2.1 Information Problem in Scientific Development

Scientific development is biased. While the direction of scientific development can be determined by the profitability of the price effect and the market size effect in the production

output assisted by the technology (Acemoglu, 2002), we argue that one of the reasons for the biased directed technological change can be informational.

To illustrate the information problem, imagine a simple model with an innovator (F) and two states (G_h and G_l) planning to purchase F's products with G_h more well-resourced than G_l.

F can invest in two directions of the technology (d_1 and d_2) that targets the solution to a problem. The investment is costly. d_1 targets the market of G_h, while d_2 targets the market of G_l. By optimizing its investments in d_1 and d_2, F aims to maximize its profits.

G_h and G_l purchases the product from F to solve their problem. Assume that G_h always buys d_1 because it has a big budget, while G_l is constrained by its budget, and its probability of purchasing d_2 is ϵ. To make it simple, assume that G_h and G_l can purchase 1 unit of d_1 and d_2, respectively, with the same price.

We assume that F faces an opportunity cost of investing in d_1 and d_2. For example, if F invests in d_2, but G_l fails to purchase d_2, F will lose its investment in d_2, which could have been invested in the other product.

In this extremely simple model, due to the uncertainty that F faces in the market demand in G_l, F will only invest in d_2 if the probably for G_l to purchase d_2 is greater than the investment. Considering the high cost of R&D investment, F only invests in d_1 to avoid the sunk cost in investing in d_2.

This simple model suggests that market uncertainty can prevent scientific development, especially for technologies targeting low-income countries.

We focus on the biased development of medical technology that addresses infectious diseases. While pharmaceutical firms can develop medicines targeting all infectious diseases around the world, the opportunity cost of focusing on any disease can be high if there is not a healthy market demand for that disease. Hence, pharmaceutical firms have to be strategic in their investment choice in infectious diseases. As most pharmaceutical firms are located in rich countries with well-developed health systems, the product profiles of these firms mainly

target the market in rich countries. In addition, due to the disparity of infectious disease distribution between rich and low-income countries, as is shown in Figure 1, some of the outbreaks of infectious diseases that are common in low-income countries, such as Dengue and Cholera, are rare events in high-income countries. Due to such geographic mismatch, it is difficult for pharmaceutical firms to predict the trend of disease outbreaks in low-income countries and to focus on specific features of vaccines and treatment medicines to address the disease outbreaks, leading to more resources allocated to health research on diseases concentrated in rich countries (Adam et al., 2023).

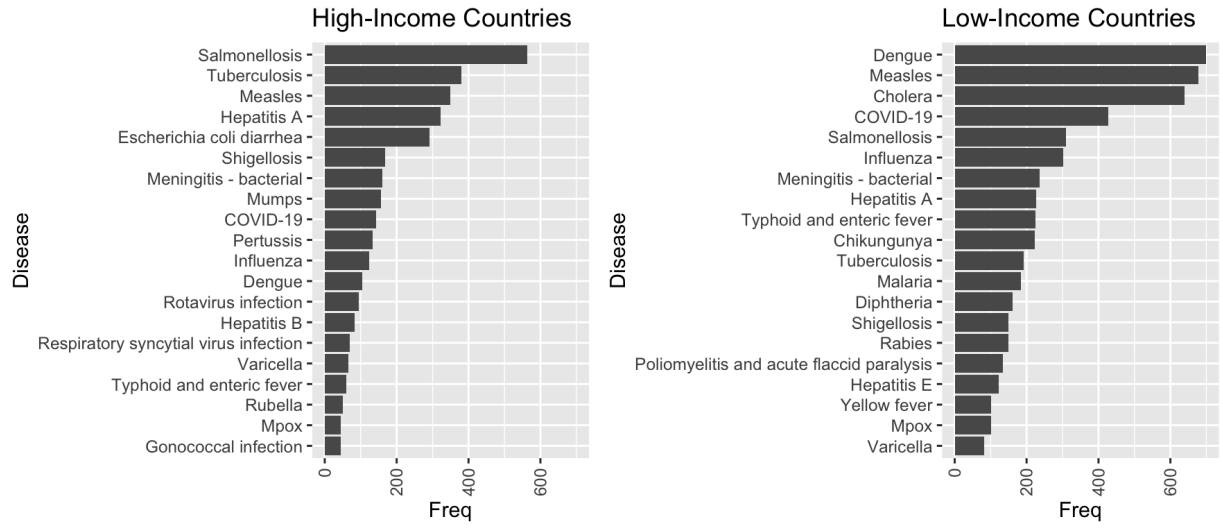

Figure 1: Top Disease Outbreaks in High and Low-Income Countries (1990-2023)
Note: High and low-income countries are defined based on whether a country is in the first and last quantile based on GDP per capita.

2.2 How Can the WHO Shape R&D investment?

We argue that the WHO can provide information about the priority of diseases and medical products to shape R&D investment in infectious diseases. Such priority information can serve as an agenda-setting tool and increase the salience of certain technologies. Bisbee et al. (2019) show that, as an international assessment mechanism of government performance, global performance indicators (GPIs) induced governments to shift the investment in social

development that is not calculated in GPIs to targets that are measured in GPIs. The same logic may apply to firms' investment decisions. Once IOs categorize certain technologies as of higher priority than other related technologies, profit-driven firms speculate a higher probability of credible market demand for the product, which increases firms' expected return from investment and motivates firms to channel investment in other technologies to the more salient ones.

In addition, to enhance the credibility of its information provision, the WHO can connect the technology of higher priority to market access. With its close connection to other IOs and non-governmental organizations (NGOs), the WHO can create a sizable market that pools resources from these organizations. Figure 2 shows a pathway through which the WHO can shape R&D investment.

Figure 2: How Does the WHO Shape R&D Investment?

3 World Health Organization and Scientific Development

The WHO is a specialized agency of the United Nations (UN) in charge of promoting international public health. Prior to the creation of the WHO, the first effort of international cooperation on global health started from the International Sanitary Conference in 1851. The priorities of the International Sanitary Conference in the late nineteenth and early twentieth centuries focused on preventing the spread of a limited list of diseases—cholera, plague, and yellow fever—from Asia and the Middle East to Europe and North America (Fidler, 2005). The establishment of the WHO expanded the narrow scope in this old regime and embraced new goals, policy orientation, and strategy to address global health. More specif-

ically, the WHO embraced the goal of Health for All, which covers not only the eradication and containment of infectious diseases, but also the improvement of overall health outcomes, especially in the developing world. Meanwhile, the WHO's policy orientation transformed from old regimes' focus on balancing economic interests of great powers with health risks to the pure focus on improving health outcomes through disease eradication and universal primary health care. Lastly, the WHO's strategy compared to the old regime involves active application and dissemination of scientific advancements, such as antibiotics and vaccines.

In terms of its relationship with scientific development, the WHO engages in three aspects of activities: to guide, develop, and deliver health policies based on scientific evidence. The first is to set the agenda to guide the research focus to gaps and priorities that are responsive to local contexts. The second is to evaluate the quality of new scientific advancements by developing and disseminating the appropriate norms and standards for practice. The last is to translate the latest data, research, and evidence into real-world adoption. Therefore, the WHO plays a critical role in connecting the scientific community to real-world practitioners for the promotion of health for all populations around the world.

3.1 How Does the WHO Influence Vaccine Technology?

We focus on the case of vaccine technology, which is one of the most successful and cost-effective health interventions (World Health Organization, 2009).

One of the WHO's most important programs related to vaccine technology is the vaccine prequalification program. Different from chemical pharmaceuticals, vaccines are biological products and are derived from living organisms. Due to the inherent variability of living organisms, vaccines could be damaged from the contamination of materials or changing environments. Constant quality control and assessment are necessary to ensure the safety and efficacy of vaccine products. In response to such quality-control demand, the vaccine prequalification program was initiated in 1987 as a quality-control service provided to the United Nations Children's Fund (UNICEF) and other UN procurement agencies to ensure

the safety and efficacy of the procured products. The program started as a temporary and modest project which involved the testing of vaccine lots, review of summary lot protocols, and the inspection of manufacturing sites. As the demand, diversity, and complexity of vaccine products submitted for prequalification continued to grow, the prequalification procedure gradually became a long-term program, which become a necessary condition for any vaccine products to enter the UN procurement.[2] The program has also gone through multiple reforms to increase its efficiency. Since 2002, the WHO has required the national regulatory authority (NRA) of the vaccine producing country to be functional—defined as the establishment of appropriate capacity for vaccine regulation—as a prerequisite for accepting submissions of vaccine prequalification by manufacturers from that country. This requirement has a great impact on strengthening vaccine regulation capacity in developing countries. In 2012, in response to the increased volume and cost of new vaccines, the WHO developed a streamlined prequalification procedure to reduce the timeline and resources for assessment. For example, the assessment reports by certain NRAs are recognized to avoid duplicative regulatory efforts.[3]

In addition to the quality evaluation of vaccine products, the WHO's work related to vaccine technology also involves guidance and market maintenance. To guide the direction of the development of vaccine products, the WHO publishes priority lists of vaccines eligible for prequalification.[4] This means a vaccine product must be on the list to be eligible for prequalification and to get access to UN procurement. The list categorizes vaccine types into high, medium, low and no priority, which is updated by the WHO in consultation with the UNICEF and the Revolving Fund of the Pan American Health Organization, a mechanism that provide technical support to national immunization programs through overcoming the barriers of price and access. Four criteria determine the priority of a vaccine: market demand, programmatic needs of the WHO, recommendation by the WHO's Strategic Advisory Group

[2]Appendix A describes the procedure for a vaccine product to obtain the prequalification status.

[3]The recognized NRAs include Australia, Belgium, Canada, France, Italy, the United States, and the European Medicines Agency.

[4]Website: https://extranet.who.int/prequal/vaccines/vaccines-eligible-who-prequalification

of Experts on immunization (SAGE), and supply security due to shortage.

In terms of market maintenance, the WHO collaborates with the UNICEF and Global Alliance for Vaccines and Immunization (GAVI) to predict, maintain, and create the market for vaccines. The vaccine market is small and concentrated from both the supply and demand perspective. More specifically, on the supply side, manufacturers of vaccines are mainly located in developed countries. On the demand side, however, many diseases are concentrated in low- and middle-income countries (LMICs). While vaccine sales to high-income countries generate more revenue, sales to LMICs are of much larger volume. Due to the geographic mismatch in the demand and supply of vaccines, it is challenging for manufacturers to predict which vaccine product to prioritize. Moreover, given that each vaccine product—even for the same type of disease—has its specificities, individual vaccines or vaccine types have their own individual markets, making the prediction of the pricing and procurement a complex task. Given the complex nature of vaccine market, the WHO's function of connecting vaccine manufacturers with the procurement agencies and donors in these agencies plays a critical role in ensuring a healthy vaccine market.

4 Hypotheses

To test the argument of how the WHO uses information provision to shape R&D investment, we propose the following testable hypotheses, which examines the determinants and effect of the WHO's agenda-setting on the priority of scientific development.

The key function that the WHO serves to shape the R&D investment in infectious diseases is its ability to convince pharmaceutical firms of a credible market demand. This suggests that the information provision on the priority of vaccines should substitute for the lack of information about the market demand for pharmaceutical firms.

To explore the variation in the information environment that pharmaceutical firms face, we investigate disease characteristics. One of the key factors for the lack of information

for firms is the geographic mismatch between where disease outbreaks occur and where the technology owner is located. Hence, if a disease is more concentrated in low-income countries, it may be more challenging for firms to predict the market demand for products targeting that disease. However, if a disease is equally likely to occur in many countries, it becomes easier to understand the market demand for firms. Hence, the inequality in disease distribution creates a more opaque market demand for firms, which motivates the WHO to set a higher priority for these diseases.

Another important disease characteristic is disease severity. The market demand is more observable if a disease outbreak influences multiple countries and large populations. In that case, it is not necessary for the WHO to provide more information about the market demand for products targeting the disease. Hence, the severity of a disease may not necessarily increase the priority set by the WHO.

The following two hypotheses summarize the determinants of the WHO's priority-setting.

Hypothesis 1. *Diseases with more unequal distribution receive a higher priority.*

Hypothesis 2. *Disease severity does not necessarily affect WHO priority.*

Lastly, to examine the effect of the WHO's priority-setting on R&D investment, the following hypothesis lays out the theoretical prediction.

Hypothesis 3. *Diseases with a higher priority receive more research funding and have more clinical trials.*

5 How Does the WHO Set the Priority?

5.1 WHO Priority on Vaccines

The WHO published two priorty lists for vaccine prequalification in 2017 and 2023, respectively. The lists categorize vaccine types into high, medium, low, and no priority. As the

treatment in our theoretical prediction is at the disease level, we need to aggregate and convert these categories from the vaccine level into the disease level. One empirical complexity in this process is the case of combination vaccines, which combine vaccines targeting different diseases into one shot. Examples include DTap for diphtheria, tetanus, and pertussis and MMR for measles, mumps, rubella. For these vaccines, one priority category apply to multiple diseases, leading to some diseases to receive different priority categories and making it less straightforward to create a measure of priority at the disease level. To address this complexity, we create two disease-level priority measures. First, we create the priority score by assigning points to each category at the vaccine level[5] and taking the average of these points at the disease level. The second measure uses the share of vaccines that are categorized as high and medium priority. Figure 3 shows the priority measures for each disease in the 2017 and 2023 priority list.

5.2 Disease Inequality and Severity

To create measures of disease distribution, we use the Global Infectious Diseases and Epidemiology Network (GIDEON) database, which monitors and collects data on outbreak events of infectious diseases. We use vaccine-preventable diseases as the sample[6] and construct two variables at the disease-year level. First, to measure the unequal distribution of disease outbreaks, we use the GINI index approach, where we replace the income variable in traditional GINI index with the outbreak occurrence related to a certain disease in a year. The index ranges between 0 and 1, which higher number indicating more unequal distribution.[7] To measure disease severity, we use the total number outbreaks a disease have in a certain year.

Figure 4 shows the annual average of these two measures in the period from 2015 to 2021.

[5]High priority has 3 points. Medium priority has 2 points. Low priority receives 1 point. No priority is 0 point.

[6]https://www.who.int/teams/immunization-vaccines-and-biologicals/diseases

[7]For diseases with zero outbreaks in a year, the GINI index does not apply. We code the index as zero because the lack of outbreaks indicates the perfect equality of disease distribution.

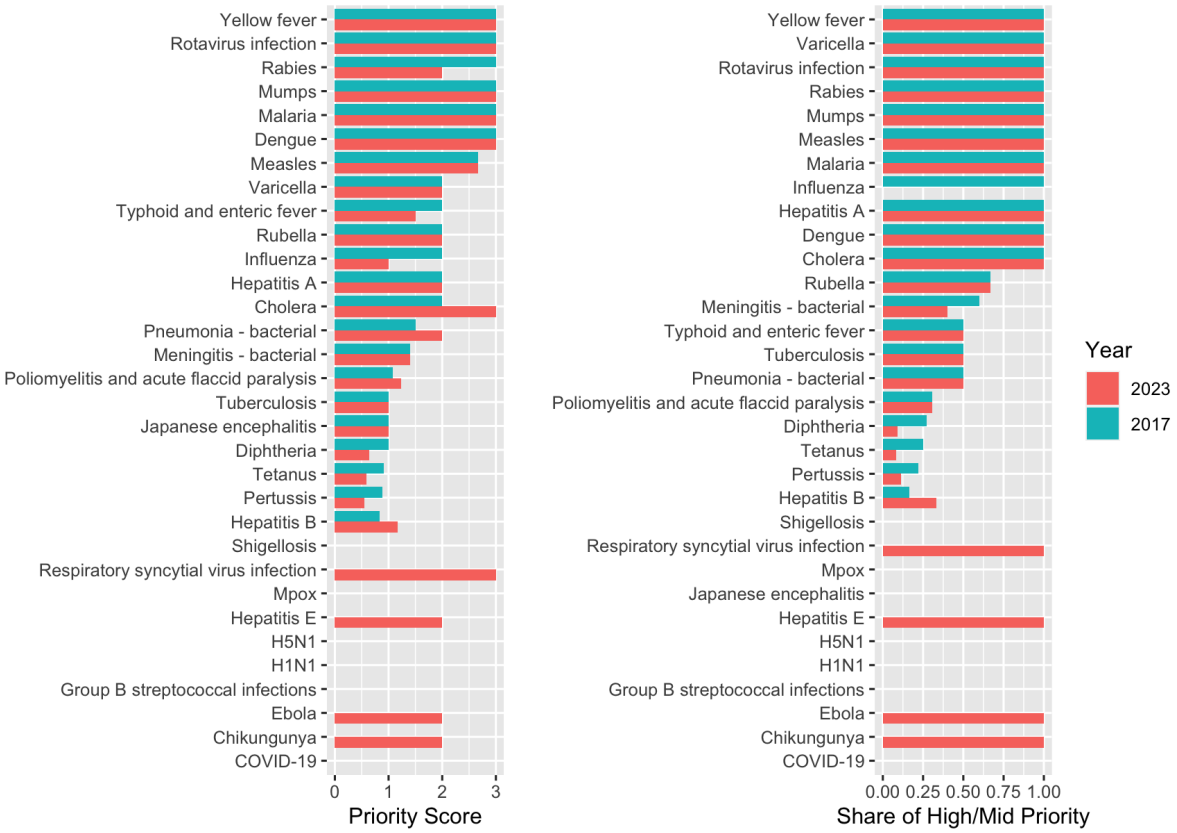

Figure 3: Disease Priority: 2017 vs. 2023

We can see that while Ebola is the most unequally distributed disease, it is not so severe based on the number of annual occurance. In contract, COVID-19 is the most severe disease and has high equality given its wide spread.

5.3 Results

After mapping the disease priority to disease distribution data,[8] we regress disease priority on disease characteristics. Table 1 presents the results. All disease distribution variables are standardized to allow for coefficient comparison, and these variables are lagged for one year to avoid simulneity bias. Columns (1) and (5) shows the coefficient estimates of disease inequality. For both measurements of disease priority, we find statistically significant and

[8]We treat vaccine-preventable diseases without a match in the priority list as no priority.

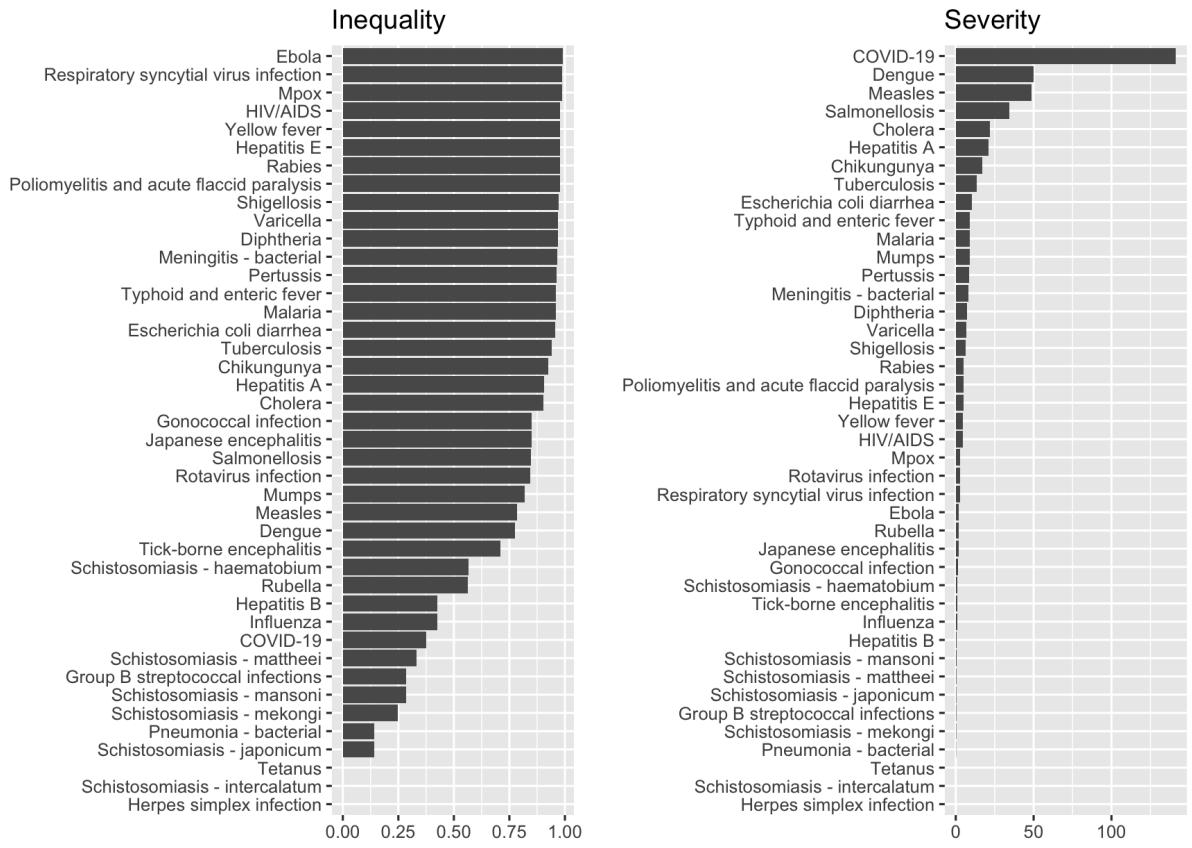

Figure 4: Disease Distribution: Annual Average (2015-2021)

positive correlation between disease inequality and disease priority, suggesting that balancing out the lack on attention on unequal diseases is an important concern for the WHO's priority-setting. This provides support for Hypothesis 1.

Columns (2) and (6) shows the coefficient estimates for disease severity. We do not find any statistically significant relationship between disease severity and priority. In Column (3) and (7), we break down the outbreak events based on whether the oubreaks occur in developing countries or developed countries.[9] More outbreak events in developing countries increase the WHO priority, while more outbreaks in developed countries reduce the WHO priority. These results suggest that disease severity alone is not an important consideration

[9]Using the World Bank classification of countries based on income levels (https://datahelpdesk.worldbank.org/knowledgebase/articles/906519-world-bank-country-and-lending-groups), we treat high- and upper-middle-income economies as developed countries. We treat low- and lower-middle-income economies as developing countries.

Table 1: Disease Distribution and Priority

	Dependent variable:							
	Priority Index				Share of High and Medium Priority			
	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)
Inequality (GINI index)	0.317*				0.133**			
	(0.178)				(0.063)			
Severity: N. of outbreaks		−0.078				−0.026		
		(0.067)				(0.025)		
N. of outbreaks in developing countries			0.268***				0.101**	
			(0.099)				(0.044)	
N. of outbreaks in developed countries			−0.302***				−0.111***	
			(0.071)				(0.036)	
Share of outbreaks in developing countries				0.156				0.055
				(0.154)				(0.059)
Year FE	Y	Y	Y	Y	Y	Y	Y	Y
Observations	59	59	59	59	59	59	59	59
R^2	0.072	0.031	0.127	0.029	0.075	0.021	0.104	0.022
Adjusted R^2	0.039	−0.004	0.079	−0.006	0.041	−0.014	0.055	−0.013

Note: *p<0.1; **p<0.05; ***p<0.01
Standard errors clustered at the disease level in parentheses

in the WHO's priority-setting. What matters more is where the outbreak is, which is consistent with the developmental consideration in the WHO's decision-making process. Last, in Column (4) and (8), we examine the effect of the share of outbreaks in developing coutries. The coefficient estimates are positive but not statistically significant.

6 Can the WHO Priority Shape R&D Investment?

6.1 R&D Investment in Infectious Diseases

We collect two sets of data to measure R&D investment in infectious diseses. First, we use funding issuance records published on the Research, Condition, and Disease Categorization (RCDC) system[10] by National Institute of Health (NIH) to measure research funding. This dataset is available from 2008 to 2023. As the NIH awards grants to organizations mostly within the US with a small proportion of foreign awardees, this dataset allows us to observe government support for different infectious diseases with a focus on the US, where a big portion of pharmaceutical firms are located.

Second, we collect the clinical research trials data from ClinicalTrials.gov, a website maintained by the National Library of Medicine (NLM) in the US. The website publishes self-reported clinical trials from over 200 countries. The NLM does not approve or review

[10]Website:https://report.nih.gov/funding/categorical-spending/rcdc

any of the registered trials. Investigators may choose to publish their studies for different reasons. They may be required by domestic law and academic journal submission rules to publish their clinical studies on a public database. Also, the WHO stated in 2006 that clinical trials happening anywhere around the world must have some information available on ClinicalTrials.gov or other similar databases. Researchers are further incentivized to publish their information to attact subjects because patients who have no access to fully grown treatment may actively search and sign up for on-going clinical trials on this website. The registration reports date and location of trials as well as the conditions under study. We leverage these information and matched 24,073 trials from 2000 to 2023 to vaccine-preventable diseases in our analysis.

One empirical challenge with both datasets is that they do not report records based on disease categories.[11] To overcome this challenge, we use regular expression to identify disease names and the corresponding virus related to each disease from the title of the project that are granted the funding and the conditions of the clinical trial. This allows us to match 38 vaccine-preventable diseases.

Table 2: Disease Distribution and R&D Investment

	Dependent variable:							
	log(1+NIH Funding)				log(1+Clinical Trials)			
	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)
Inequality (GINI index)	−0.018				−0.025			
	(0.030)				(0.035)			
Severity: N. of outbreaks		0.036				0.062**		
		(0.022)				(0.029)		
N. of outbreaks in developing countries			−0.052				−0.057	
			(0.071)				(0.054)	
N. of outbreaks in developed countries			0.081				0.116*	
			(0.069)				(0.061)	
Share of outbreaks in developing countries				−0.058				−0.058
				(0.070)				(0.041)
Year FE	N	N	N	N	N	N	N	N
Disease FE	Y	Y	Y	Y	Y	Y	Y	Y
Disease-Specific Trend	Y	Y	Y	Y	Y	Y	Y	Y
Observations	485	485	485	485	793	793	793	793
R^2	0.958	0.958	0.958	0.958	0.902	0.903	0.904	0.903
Adjusted R^2	0.949	0.950	0.950	0.950	0.890	0.891	0.891	0.890

Note: *p<0.1; **p<0.05; ***p<0.01
Standard errors clustered at the disease level in parentheses

After identifying the relevant grants and trials, we aggregate the grant amount and trials

[11] For the RCDC data, some of the grants are reported at the disease level, while others are reported in more general categories, such as vaccine related, infectious diseases, and emerging infectious disease. In these cases, we look into project titles to identify the relevant diseases.

to the disease-year level. Table 2 examines the correlation between disease distribution and R&D investment. The dependent variables are in logarithm. Consistent with the specification in Table 1, all disease distribution variables are standardized and lagged for one year. We can see that more unequal diseases tend to receive less R&D investment. Diseases with more outbreaks events tend to receive more R&D investment, suggesting that the potential of a big market demand incentivizes investment. In terms of outbreak locations, more outbreaks in developed countries encourage more investment, while outbreaks in developing countries do not. A great proportion of outbreaks in developing countries discourages investment. Overall, despite the low statistical siganicance, the pattern presented in Table 2 confirms that scientific development is biased in favor of the interest of capital.

6.2 Empirical Specification

To examine how the WHO priority shape R&D investment in infectious diseases, we use a difference-in-differences specification, which is shown in the following equation.

$$Investment_{it} = \gamma_i + \lambda_t + \beta_2 Priority_i \times Post_t + X_{i,t-1}\beta + \epsilon$$

$Investment_{it}$ refers two measures of the R&D investment. One is the annual total amount of grants invested in disease i in year t. The other is the total number of clinical trials on disease i in year t. $Post_t$ indicates whether a year is after 2017, which is the year when the first Vaccine Prequalification Priority List was published.[12] $Priority_i$ is the disease-level priority index as is discussed in Section 5.1. γ_i is the disease fixed effect, which captures the disease-specific characteristics that may affect the overall level of R&D investment. λ_t is the year fixed effects and captures the time-specific factors that contributes to the R&D

[12]There have been two published list of Vaccine Prequalification Priority. One was published in 2017 after the First Annual review of diseases prioritized under the Research and Development Blueprint. It covers the period from 2018 to 2020. The other one was published in 2023 after the WHO launched a global scientific process to update the list of priority pathogens and covers the period from 2024 to 2026. As the R&D investment may have a delay in the response to the publication of the priority list, we can only examine the effect of the first list.

investment. For example, due to the American Recovery and Reinvestment Act of 2009 (ARRA), there were extra funding for health research in year 2009 and 2010. The year fixed effects can control for such changes in funding. $X_{i,t-1}$ are control variables related to disease distribution characteristics, which are all standardized and lagged for one year.

6.3 Results

Table 3 presents the regression results using the share of high and medium priority as the disease priority measure.[13] The first four columns examine the effect of the WHO priority on research funding, while the last four columns look into the WHO priority's effect on clinical trials. Columns (1) and (5) only control for the year fixed effect. Columns (2) and (6) control for the disease fixed effect. Columns (3) and (7) further add the disease-specific time trend to control for the time-dependency in R&D investment over time. In Columns (4) and (8), disease distribution characteristics are controlled for.

Table 3: WHO Priority and Disease Investment

	Dependent variable:							
	log(1+NIH Funding)				log(1+Clinical Trials)			
	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)
Priority (High & Medium)	−0.395				0.533			
	(0.818)				(0.445)			
Priority (High & Medium) * Post	0.213	0.362	0.269	0.321	−0.522*	−0.522*	−0.397*	−0.320*
	(0.318)	(0.244)	(0.188)	(0.194)	(0.307)	(0.303)	(0.230)	(0.174)
Inequality (GINI index)				−0.008				−0.013
				(0.035)				(0.039)
N. of outbreaks in developing countries				−0.073				−0.063
				(0.067)				(0.060)
N. of outbreaks in developed countries				0.086				0.118**
				(0.069)				(0.057)
Year FE	Y	Y	N	N	Y	Y	N	N
Disease FE	N	Y	Y	Y	N	Y	Y	Y
Disease-Specific Trend	N	N	Y	Y	N	N	Y	Y
Observations	440	440	440	389	798	798	798	691
R^2	0.009	0.933	0.959	0.971	0.120	0.819	0.874	0.904
Adjusted R^2	−0.024	0.925	0.949	0.963	0.095	0.805	0.857	0.890

Note: *p<0.1; **p<0.05; ***p<0.01
Standard errors clustered at the disease level in parentheses

Throughout different specifications, WHO priority increases research fundings, but the effect is not statistically significant. Interestingly, opposite to Hypothesis 3, we find statistically significant negative effect of WHO priority on clinical trials.

[13]Table B.1 presents the results using the priority score.

7 Discussion

Can IOs use its agenda-setting power to shape scientific development? We argue that IOs can provide information to substitute for the lack of market demand for ignored technologies to induce R&D investment in these technologies.

Empirically, we examine how the WHO's agenda-setting on vaccine technology can shape R&D investment in infectious diseases. The empirical test supports the argument that the WHO's information provision aims to substitute for the lack of market information. However, we find mixed evidence on the relationship between the WHO priority and R&D investment. While we find some empirical support for the boosting effect of the WHO priority on research funding for ignored diseases, we also find that the WHO priority can depress clinical trials in these diseases.

Two potential explanations may explain these mixed findings. First, as the WHO priority on vaccines focuses on the application and end product of vaccine technology, the WHO priority may have shifted the R&D investment in basic research to investment focusing on bringing the product to the market. Further evidence on the increased investment on vaccine end products is necessary to support this explanation.

Another explanation is that due to the mismatch between the goal of vaccine priority and other WHO practice to shape R&D investment. One of the key determinants of the vaccine priority is the supply security, which aims to monitor and respond to factors that may lead to vaccine shortages. Since many of the vaccine types listed in the priority list are routine and well-established vaccines targeting disease like diphtheria, tetanus, measles, and mumps among others, there is not much need to further develop these vaccines. To address this mismatch, we will examine the other priority lists published by the WHO, which include the Bacterial Priority Pathogens List and the list of Diseases Prioritized Under the R&D Blueprint.

References

Acemoglu, D. (2002). Directed Technical Change. *Review of Economic Studies*, 69(4):781–809.

Acemoglu, D., Gancia, G., and Zilibotti, F. (2015). Offshoring and directed technical change. *American Economic Journal: Macroeconomics*, 7(3):84–122.

Adam, T., Ralaidovy, A. H., Ross, A. L., Reeder, J. C., and Swaminathan, S. (2023). Tracking global resources and capacity for health research: time to reassess strategies and investment decisions. *Health Research Policy and Systems*, 21(1).

Arias, S. B. (2024). Who Sets the Agenda? Diplomatic Capital and Small State Influence in the United Nations. *Working Paper*.

Bisbee, J. H., Hollyer, J. R., Peter Rosendorff, B., and Vreeland, J. R. (2019). *The Millennium Development Goals and Education: Accountability and Substitution in Global Assessment*, volume 73.

Branswell, H. (2020). 'Against all odds': The inside story of how scientists across three continents produced an Ebola vaccine. *STAT*, (April 2014):1–17.

Drezner, D. (2001). State structure, technological leadership and the maintenance of hegemony. *Review of International Studies*, 27(1):3–25.

Drezner, D. W. (2019). Technological change and international relations. *International Relations*, 33(2):286–303.

Fang, S. and Stone, R. W. (2012). International organizations as policy advisors. *International Organization*, 66(4):537–569.

Fidler, D. P. (2005). From International Sanitary Conventions to Global Health Security: The New International Health Regulations. *Chinese Journal of International Law*, 4(2):325–392.

Haas, P. M. (1992). Introduction: Epistemic communities and international policy coordination. *International Organization*, 46(1):1–35.

Hai, Z. (2023). The Global Politics of Scientific Consensus : Evidence from the Intergovern-

mental Panel on Climate Change. *Working Paper*, pages 1–36.

Heinzel, M. and Koenig-Archibugi, M. (2024). Global epistemic authority and its limits: Evidence from the WHO's efforts to preserve antibiotic efficacy. *Working Paper*, pages 1–51.

Johns, L. (2007). A servant of two masters: Communication and the selection of international bureaucrats. *International Organization*, 61(2):245–275.

Kelley, J. G. and Simmons, B. A. (2020). *The Power of Global Performance Indicators*. Cambridge University Press.

Milner, H. V. and Solstad, S. U. (2021). Technological Change and the International System. *World Politics*, 73(3):545–589.

Miyano, S. (2024). Regime Complexity and Overlapping Information : The Case of Energy Forecasts. *Working Paper*.

Pollack, M. A. (1997). Delegation, agency, and agenda setting in the European Community. *International Organization*, 51(1):99–134.

Wilkins, B. H. and Paquette, D. (2021). Malaria is far deadlier in Africa than the coronavirus . Why is the vaccine taking so. *Washington Post*.

World Health Organization (2009). *State of the world' s vaccines and immunization*. World Health Organization.

World Health Organization (2014). Assessing the programmatic suitability of vaccine candidates for WHO prequalification. (Revision).

A Procedure of Vaccine Prequalication

To start the prequalification process, manufacturers have to initiating the process by submitting an application to the WHO. However, for a manufacturer to be eligible, the corresponding NRA of the manufacturer must be classified as a functional NRA or WHO-listed authority operating at maturity level 3. This is to ensure the regulatory oversight of the product. After the submission, the WHO will screen the application based on the programmatic suitability (World Health Organization, 2014), which evaluates the characteristics of the vaccine candidate, such as heat stability, presentation, labeling, and shipping conditions. Only when the vaccine candidate is compliant with the compulsory characteristics can the product start the prequalification assessment.[14] The assessment includes a scientific evaluation of evidence, sample testing, and inspection of the manufacturing site. Once a vaccine product is considered to meet all the requirements, it will be included in the WHO List of Prequalified Vaccines.[15]

After a vaccine product passes the prequalification requirements, there is an annual evaluation to ensure the quality and continued compliance with the required standards of the product. If a product fails to meet the post-prequalification testing and reporting requirements, the WHO can withdraw the product from its list of prequalified vaccines. Manufacturer can also withdraw their product from the list due to discontinued production or commercialization.

B Figures and Tables

[14]There are two categories of characteristics: mandatory and critical characteristics. Both categories are compulsory, but if a product deviates from the critical characteristics, the screening procedure will go through a review process involving the manufacturer and procurement agencies to determine whether to accept the application.

[15]Website: https://extranet.who.int/prequal/vaccines/prequalified-vaccines

Table B.1: WHO Priority and Disease Investment

	Dependent variable:							
	NIH Funding				Clinical Trials			
	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)
Priority Index	−0.290				0.180			
	(0.307)				(0.168)			
Priority Index * Post	0.083	0.144	0.062	0.074	−0.196	−0.196	−0.129	−0.098
	(0.120)	(0.095)	(0.069)	(0.069)	(0.119)	(0.118)	(0.089)	(0.063)
Inequality (GINI index)				−0.009				−0.015
				(0.035)				(0.040)
N. of outbreaks in developing countries				−0.069				−0.061
				(0.070)				(0.060)
N. of outbreaks in developed countries				0.083				0.118**
				(0.073)				(0.058)
Year FE	Y	Y	N	N	Y	Y	N	N
Disease FE	N	Y	Y	Y	N	Y	Y	Y
Disease-Specific Trend	N	N	Y	Y	N	N	Y	Y
Observations	440	440	440	389	798	798	798	691
R^2	0.023	0.933	0.959	0.970	0.116	0.819	0.874	0.904
Adjusted R^2	−0.009	0.925	0.948	0.963	0.091	0.805	0.857	0.890

Note: *p<0.1; **p<0.05; ***p<0.01
Standard errors clustered at the disease level in parentheses

Table B.2: WHO Priority and Clinical Trials: by Funder Type

	Dependent variable:							
	Funded by Industries				Funded by NIH			
	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)
Priority (High & Medium)	0.461				0.063			
	(0.363)				(0.258)			
Priority (High & Medium) * Post	−0.354	−0.354	−0.321	−0.181	−0.195*	−0.195*	−0.247	−0.229
	(0.248)	(0.245)	(0.244)	(0.186)	(0.115)	(0.113)	(0.168)	(0.141)
Inequality (GINI index)				−0.017				0.009
				(0.031)				(0.025)
N. of outbreaks in developing countries				−0.091				−0.007
				(0.056)				(0.041)
N. of outbreaks in developed countries				0.153***				0.075*
				(0.055)				(0.040)
Year FE	Y	Y	N	N	Y	Y	N	N
Disease FE	N	Y	Y	Y	N	Y	Y	Y
Disease-Specific Trend	N	N	Y	Y	N	N	Y	Y
Observations	798	798	798	691	798	798	798	691
R^2	0.087	0.765	0.825	0.857	0.025	0.719	0.760	0.815
Adjusted R^2	0.061	0.746	0.801	0.836	−0.002	0.697	0.727	0.788

Note: *p<0.1; **p<0.05; ***p<0.01
Standard errors clustered at the disease level in parentheses