# Innovation and Interdependence: The Case of Gene-Editing Technology*

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**Abstract**

Technological innovation has the potential to disrupt social, economic, and political systems, posing unique challenges for governments. In this paper, we examine how disruptive technologies shape patterns of interdependence between states. We argue that technological breakthroughs increase interdependence among national governments in two ways. First, they lower barriers to entry and create opportunities for forum-shopping by researchers, firms, and other actors. This facilitates regulatory arbitrage as actors evade national regulations by relocating to more permissive jurisdictions. Second, the misuse of new technologies in one jurisdiction risks generating public backlash elsewhere, undermining public support for research and commercial development. We examine these mechanisms in the case of gene editing, a field that has experienced rapid technological advancement and diffusion in recent years. We find empirical evidence for both processes in a novel survey experiment and an analysis of the geographic patterns of gene editing research. Our results demonstrate that technological disruption increases interdependence, undermining states' ability to regulate in isolation and strengthening the case for international policy coordination.

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# 1 Introduction

Technological innovation is a defining feature of contemporary social and economic life. Recent advances in fields like robotics, biotechnology, digital finance, and artificial intelligence promise improved welfare through enhanced health, productivity, and economic growth. They also pose significant risks: many emerging technologies can be misused to cause harm or violate ethical norms. The recent revolution in gene editing technology, for example, has been celebrated for facilitating new medical therapies and also criticized for enabling controversial modifications of human DNA.

Governments navigate this tradeoff by regulating the development and application of emerging technologies. Regulations seek to calibrate the pace of technological progress, balancing the economic and social potential of technological change against the risk of harm. Countries often make different choices in this environment – imposing more restrictive or permissive rules on the use of a particular technology – as governments align regulations with public preferences and social norms.

We argue that, in addition to provoking a regulatory choice *within* countries, technological disruption also shapes patterns of interdependence *between* them. Technological breakthroughs lower barriers to entry, erode incumbent advantages, and allow more actors in more jurisdictions to compete for status and profit. As the technology diffuses, countries' regulatory efforts become more closely linked in two ways.

First, the reduced entry barriers associated with new technologies create greater opportunities for forum-shopping by researchers and firms. This facilitates regulatory arbitrage as actors evade national regulations by relocating to more permissive jurisdictions. In some cases, governments will face pressure to weaken regulatory standards in order to stimulate domestic innovation and lure researchers, firms, and capital from other jurisdictions. While regulatory arbitrage and competition are well-established features of national governance

(Genschel & Plumper, 1997), we argue that technological shocks often exacerbate the problem by lowering costs of entry and increasing the cross-border mobility of production.

The second source of interdependence is rooted in public attitudes regarding emerging technologies. Because technological innovations involve risks of harm or misuse, they generate apprehension among citizens and potential consumers. Public controversies invite backlash and undermine support for research and commercial development. We argue that this backlash often spills across national boundaries, such that controversies in one state affect public attitudes in another. As a result, one government's decision to weaken regulation can damage confidence in the technology around the world. Unlike regulatory arbitrage, we are not aware of existing scholarship that examines the potential for spillovers in public backlash. Nonetheless, we argue that it is an important source of interdependence in the governance of new technologies.

Notably, these new patterns of interdependence weaken the power of national governments to regulate technology in isolation. Increased opportunities for arbitrage make it easier for targets of regulation to evade national rules. The potential for spillovers in public backlash mean that effective national governance cannot insulate a country from poor regulation in another jurisdiction. Both of these mechanisms increase the need for international policy coordination to manage interdependence.

We examine these processes in the case of gene editing, a field in the midst of a technological revolution. Gene editing, or genetic engineering, refers to the manipulation of an organism's genetic material. While researchers have been making targeted modifications to DNA for roughly fifty years, the emergence of CRISPR[1] and associated techniques in the last decade provides a dramatically more accurate, efficient, and economical method for editing genes. In the nine years since the method was introduced, CRISPR has become the

[1]The acronym CRISPR stands for clustered regularly interspaced short palindromic repeats. The term was coined by Ishino *et al.* (1987), who first noted the appearance of repeating DNA sequences in bacteria.

dominant technology in the field. In awarding the 2020 Nobel Prize in Chemistry to its chief architects, Emmanuelle Charpentier and Jennifer Doudna, the Royal Swedish Academy of Sciences celebrated CRISPR's revolutionary capability for "rewriting the code of life" (Royal Swedish Academy of Sciences, 2020).

In response to these technological advances, scientists in academia and industry are applying gene editing to an increasingly diverse set of objectives. Laboratory researchers routinely "knock out" genes in mice or other animals to study gene function and expression.[2] Therapeutic developers are creating new gene therapies to treat cancer and correct harmful genetic mutations (Khan *et al.*, 2016). Agricultural producers, who have long used genetic modification to improve crop yields, are applying CRISPR to both produce and livestock. Research teams have successfully altered the DNA of mosquitos to prevent the transmission of malaria (Gantz *et al.*, 2015). More recently, gene-editing technology has been used to develop diagnostic tests for COVID-19 (Straiton, 2020).

While many celebrate the promise of these applications, others are concerned about the rapid diffusion and unregulated use of gene-editing technology. Regulation of gene editing occurs via a patchwork of scientific, institutional, and national standards that have not matched the pace of technological change. The long-term biological effects of many gene-editing applications are unknown, as are the ethical, political, and social consequences of the technology's proliferation. As entry costs fall, many more researchers and laboratories are able to access and build upon these tools.

Concern about inappropriate genetic modification escalated sharply in 2018, when the Chinese scientist He Jiankui announced the birth of the world's first gene-edited infants. He's team used CRISPR to genetically alter two twin girls in-vitro to render them immune to HIV (Cyranoski, 2019). The revelation sparked international outcry, raising concerns about safety, consent of the participants, and the risks of modifying heritable germline cells

[2]See, for example, the Knockout Mouse Project: `https://www.komp.org`.

that will pass alterations to subsequent generations. Many questioned whether China had the institutional capacity or will to reign in potential ethical violations by its scientists. Still others worried that the experiment would usher in even more egregious applications of the technology (Regalado, 2018).

We argue that gene editing is an archetypal disruptive technology, and as a result it exhibits the two general forms of interdependence described above. First, it encourages regulatory arbitrage among actors in science and industry. As the capital and infrastructure needed to edit genes falls, countries with weaker regulatory environments become more attractive destinations for cutting-edge researchers. These countries can more easily capitalize on the scientific and economic potential of gene editing, in part by drawing human and financial capital away from countries with more stringent regulations.

Second, controversial applications of gene-editing technology generate public backlash that spans national borders. These controversies can undermine public support, reduce funding for related research, and constrain even responsible scientific activity. As a result, the field of gene-editing research has progressed in fits and starts, with periods of promising technological advancements interrupted by crises of public confidence. As clinical gene-editing applications are brought to market, lack of public trust could reduce demand for potentially life-saving technologies.[3] If lax regulation in one country can incentivize unethical or controversial research which has a negative impact on public support in other countries, a patchwork of uncoordinated national rules will have difficulty internalizing these spillovers.

We probe these arguments with two sets of empirical tests. We first analyze patterns of gene editing research and development to examine incentives for regulatory arbitrage. Specifically, we assess whether countries with weaker regulations outperform more stringent jurisdictions in the clinical development of gene therapies. We leverage the 2012 introduction

[3]Drezner (2008) argues that distrust of genetically-modified organisms in Europe, for example, led to increased regulations and low public support for GMO consumption despite its potential health and economic benefits.

of CRISPR as a temporal shock to examine how national regulatory environments affect the trajectory of gene-editing innovation. Our results are consistent with theoretical expectations: more regulatory rigor is associated with fewer gene-editing innovations in the CRISPR era. We also probe patterns of researcher relocation to establish evidence of forum shopping to weaker regulatory jurisdictions.

To test the potential for spillovers in public backlash, we implement a novel survey experiment that probes American respondents' reaction to a gene-editing controversy. The experiment varies information about the occurrence and location of inappropriate gene-editing activity. Respondents read about a controversial application of gene editing and then provide their opinion on the appropriate level of public funding and regulation of the field. We find that foreign gene-editing controversies negatively affect domestic public support for gene-editing research.

Our paper adds to a growing literature on international competition, cooperation, and technology (Milner & Solstad, 2020; Perlman, 2020b; Canfil, 2021). We develop a novel theory of technology regulation in a domain, gene editing, that has been largely neglected by scholarship in international relations and political science. While international relations scholars have paid close attention to the security implications of technological advancements (Buchanan & Keohane, 2015; Kreps & Wallace, 2016; Ayoub & Payne, 2016), we know less about governance of scientific issues in non-security sectors. We expect biotechnology to increase in salience for political science as governments and their citizens grapple with the unprecedented technological progress in this field.

More broadly, we identify two theoretical mechanisms — regulatory arbitrage and spillovers in public backlash — that link countries' fates as they govern emerging technologies. In doing so, we demonstrate how technological shocks interact with patterns of economic and political exchange to induce interdependence among countries. These mechanisms have clear implications for the design of international institutions, which are likely to be charged with

managing these interdependencies.

The rest of the paper is organized as follows. Section 2 summarizes the emergence and spread of gene-editing technology, with particular attention to recent advances. Section 3 presents our arguments regarding variation in national regulatory environments and cross-national spillovers in public backlash. Section 4 describes our empirical strategy and presents our findings, and section 5 concludes.

# 2 Gene Editing: Technological and Political Landscape

In this section, we review recent advances in gene-editing technology, summarize the existing rules that govern its use, and describe the political preferences of key states. We argue that new methods developed over the last decade have dramatically lowered the barriers to entry for researchers, firms, and individuals to engage in gene editing. This trend accelerated the diffusion of gene-editing technology around the globe. Efforts to govern genetic modification include a patchwork of national regulations, scientific norms, and nascent global initiatives, many of which have lagged behind the pace of technological advancement.

## 2.1 Innovation and Diffusion of Gene-Editing Technology

While ability to modify genetic material is not new, scientific advances have transformed the field over the past decade. The term "gene editing" (also referred to as genetic engineering, modification, or manipulation) refers to the direct alteration of an organism's DNA. The goal is typically to suppress or alter naturally-occurring biological traits of the organism. Historically, the field of gene editing evolved from splicing naturally-occurring genetic material together (producing "recombinant" DNA) in the 1970s to using cells' own DNA-repair technology to selectively edit specific genes (using "programmable nucleases") in the early

2000s.[4]

The emergence of the CRISPR method in the 2010s represented a particularly significant breakthrough in gene-editing technology. The name CRISPR (clustered regularly interspaced short palindromic repeats) refers to a series of repeating DNA sequences originally found in bacteria. These sequences provided bacteria with adaptive immunity, allowing them to recognize and destroy the DNA of harmful viruses. Scientists adapted this technique for programmable gene editing (Jinek *et al.*, 2012). CRISPR targets specific gene sequences and cleaves them with a nuclease, most commonly the Cas9 enzyme. This "CRISPR-Cas9" system is significantly more accurate, efficient, and economical than previous gene-editing methods.

In the years since its development, CRISPR has become the dominant technology in the field of gene editing (Carroll, 2018).[5] A recent report in Stanford Medicine notes that while "other gene-editing tools have emerged in recent years...none seems to match the precision, low cost and usability of CRISPR" (Shwartz, 2018). The cost savings are substantial: a CRISPR-Cas9 RNA template may cost $65 to design compared to $1000 for the same template using other technologies (Shwartz, 2018). Lower costs have facilitated the diffusion of CRISPR technology to laboratories around the world.[6]

Scientific norms regarding the accessibility and replicability of research are also a major force behind the diffusion of CRISPR technology. As a condition of publication, authors often must make their data and materials available to other researchers. Much of the biological material – including the plasmids used to edit genes – is handled by third-party

[4]For a general overview of scientific progress in gene-editing technology, see Gupta *et al.* (2014).

[5]Figure A1 in the appendix shows the number of patent applications utilizing three prominent gene-editing technologies: CRISPR, TALENs, and ZFNs. CRISPR has dominated technological development in the field, significantly outperforming other methods.

[6]However, as one expert noted, there continue to be barriers to entry for many laboratories. In particular, innovation using CRISPR technology requires financial resources and investment in learning how to adapt CRISPR tools to specific projects (Interview by authors, 11.13.2019).

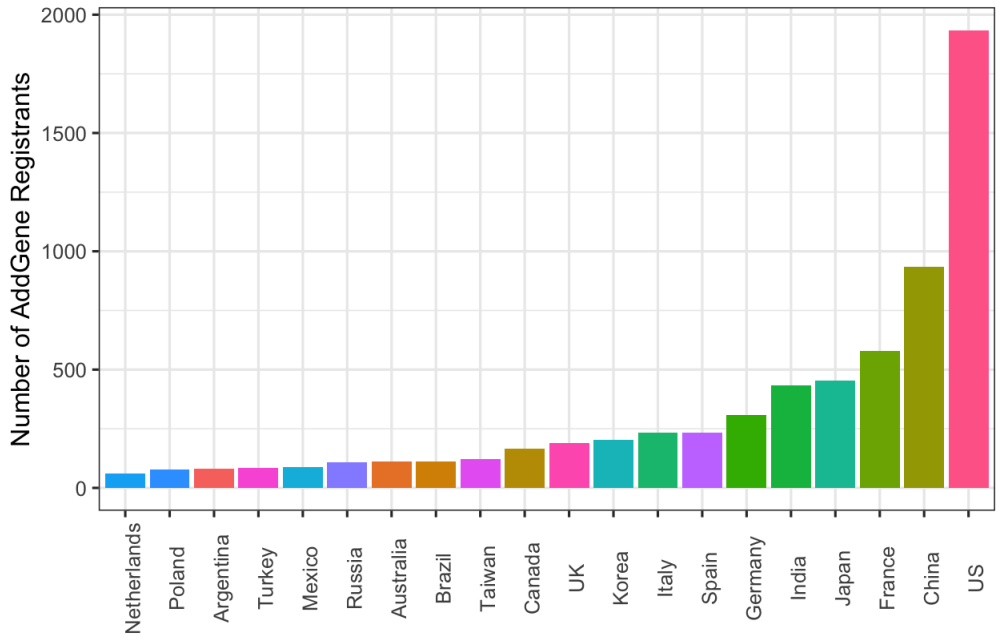


Figure 1: *AddGene Registered Researchers by Country of Origin*: The figure shows the number of researchers registered on the AddGene website, by country of origin. Data collected by authors.

distributors like AddGene, a global repository that stores and disseminates genetic material used in published studies.[7] Although CRISPR-related materials represent a small minority of AddGene's repository, they are among the most commonly requested plasmids from researchers.[8] Figure 1 shows the number of registered AddGene researchers by country of origin. American researchers are the largest group with nearly 2,000 registered users, followed by China, France, Japan, and India.[9]

[7]AddGene has served as a popular repository for CRISPR plasmids since Jinek *et al.* (2012) used the organization to store materials from their landmark paper. AddGene "is a global, nonprofit repository that was created to help scientists share plasmids;" the site allows scientists to register and deposit plasmids on the site and send a sample to the lab. Addgene then allows other scientists to request the material for their own research. Researchers who want to access these materials register on the AddGene website and pay a fee for the plasmid transfer. They are then free to replicate the parent study or alter the plasmids for their own research purposes. For more information, see `http://addgene.org`.

[8]An AddGene employee estimated that 25% of researcher requests are for CRISPR-related plasmids (Interview by authors, 11.25.2019).

[9]Researchers from the United States are overwhelmingly the most frequent depositors of CRISPR plasmids (see appendix Figure A2.)

Many have cheered the diffusion of gene-editing technology, which has stimulated a "biotechnological revolution" in clinical care, diagnostics, agriculture, and other fields (Knott & Doudna, 2018). As with other technologies, however, rapid progress has also been accompanied by ethical concerns and fears of potential misuse. Anxiety over gene editing varies based on the type of genetic material researchers seek to alter. *Somatic* gene editing, which targets non-heritable genes, is generally less contentious. This type of editing has been used to treat "a wide range of genetic diseases (including hematological, immunological, ocular, and neurodegenerative and metabolic disorders) and several types of cancer" (Kumar *et al.*, 2016). *Germline* gene editing targets heritable genes that are passed onto the offspring of the organism. There is a strong norm against editing germline cells in humans due to the unknown long-term effects of the changes, concerns about the ethics of editing heritable genes, and the difficulty of ensuring the safety of the procedure (Miller, 2015). The He Jiankui controversy, which altered germline cells in utero, is the most famous violation of this norm.

Other concerns are linked to the purposes that gene-editing technology can serve. The potential for genetic modifications to enhance socially-desirable traits in a human without conferring health benefits evoke the dark history of gene science. Following 19th century advances in genetics, the British scientist Francis Galton popularized the idea of "improving the human stock" by encouraging procreation based on desirable traits (Goering, 2014). The concept of "eugenics" took hold in the popular imagination and was weaponized to exclude immigrants to the US, sterilize disabled individuals, and justify racist laws and colonialism (Bouche & Rivard, 2014). The Nazi party and their campaign against Jews in Europe represented the height of eugenics thought and political power, though the ideology continues to persist in some quarters even today.

Finally, there are growing concerns that the increased accessibility and public profile of gene-editing technology encourage amateur scientists to experiment in unsafe conditions. Consumers can now make use of "DIY-CRISPR kits" that are ordered online and delivered

to one's home. Communities of self-proclaimed "bio-hackers" use gene-editing tools on test animals, livestock, or even themselves (Keulartz & van den Belt, 2016). In the absence of international or national laws, some U.S. states have begun mobilizing to address the health risks of amateurs performing experiments without proper training, equipment, or supervision.[10]

## 2.2 Governance of Gene-Editing Technology

Gene editing is governed by a fragmented patchwork of scientific norms, national laws, and international guidelines. When targeted gene editing first became feasible in the 1970s with the advent of recombinant DNA techniques, scientists attempted to construct self-governing arrangements with standards for appropriate gene-editing research. In 1973, leading geneticists announced a voluntary moratorium on gene-editing experiments involving certain viruses and toxins (Berg *et al.*, 1974). The moratorium was maintained for two years until it was replaced by formal guidelines adopted by the National Institutes of Health. Scientists involved in drafting the original guidelines argue that this decentralized approach was successful in constraining potentially inappropriate applications of gene-editing technology (Berg & Mertz, 2010).

In recent years, similar efforts have sought to establish new norms for the research community. A 2019 international conference of geneticists called for a global five-year ban on editing DNA in human eggs, sperm, or embyros that are brought to term (Lander *et al.*, 2019). However, there is dissent about this approach even among the most prominent genetic researchers (Cohen, 2019). The lack of consensus creates uncertainty about appropriate ap-

[10]California was credited with the "first CRISPR law" when the state legislature put into motion a ban the self-administration of CRISPR (see text of bill at `https://leginfo.legislature.ca.gov/faces/billCompareClient.xhtml?bill_id=201920200SB180&showamends=false`)

plications of gene-editing technology, potentially contributing to misuse.[11] In addition, there remain serious questions about whether voluntary, decentralized rules can succeed in a world where gene-editing technology is much cheaper and diffusely distributed than in the 1970s.[12]

As early gene-editing technology progressed, national regulations began to supplement scientific norms. The United States created national guidelines that built upon the partial gene-editing moratorium of 1973-4 (Baskin *et al.*, 2016). Other states followed suit as the practice became more widespread. Currently, there is significant variation in the structure and rigor of national rules. Some countries, for example, maintain a legal ban on the alteration of human germline cells.[13] Some have less formal "guidelines" prohibiting germline editing, while others are more permissive in the regulatory constraints they place on the technology (Araki & Ishii, 2014; Ishii, 2017). Figure 2 displays a recent measure of national gene-editing regulations developed by Baylis *et al.* (2020). Countries are shaded according to regulatory rigor, with darker shades indicating more restrictive national rules.

Inconsistent rules across countries stem, in part, from different national historical experiences and cultural expectations regarding the appropriate use of gene-editing technology. For example, Germany's experience with unethical human subjects experiments during the Nazi regime and their subsequent societal accounting with these human rights violations has conditioned the state's regulation of human subjects research.[14] South Korea developed strict biological research guidelines in response to a high-profile controversy regarding the falsification of data in a cloning experiment by Seoul University investigator Woo Suk Hwang

[11]Baylis (2019) states that He Jiankui likely believed his controversial research was in-line with existing ethical standards due to a lack of a clear scientific moratorium and conflicting recommendations from experts: "He [Jiankui] believed he had checked all the boxes."

[12]For example, despite efforts by academic journals to ensure published research meets strict ethical guidelines, norm-violating research can often be published in second-tier journals (Baylis, 2019).

[13]According to Ishii (2017), this group includes Canada, Brazil, Australia, and much of Western Europe.

[14]Bioethicist George Annas states ,"Germany has been very reluctant to get involved with anything that could lead to a re-introduction of eugenic practices in their society" (Begley, 2019).

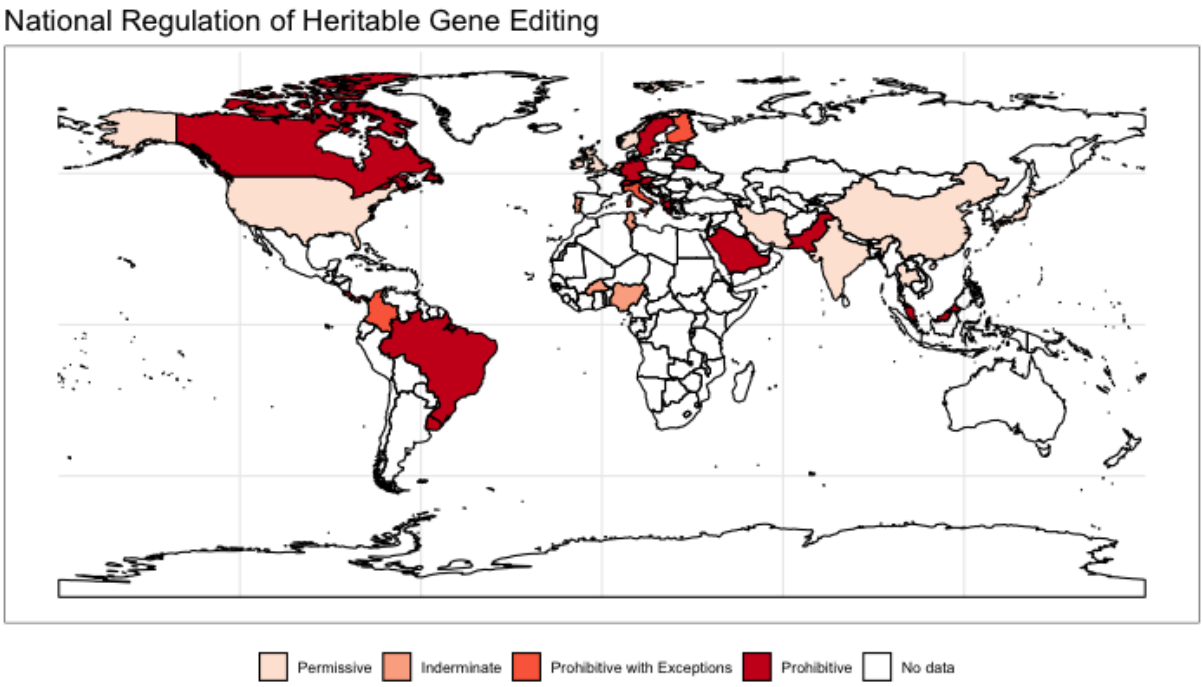


Figure 2: *National Gene-editing Regulations*. Countries are rated as "Permissive", "Indeterminate", "Prohibitive with exceptions," or "Prohibitive" according to national policy on the use of gene-editing technology in human subjects research. Data on national regulations are from Baylis *et al.* (2020).

(Resnik *et al.*, 2006). The United States developed comparatively weaker regulations for gene editing, consistent with a policy process that is more receptive to industry influence.[15] As described above, China also has come under criticism for lax ethical guidelines (Kleiderman & Ogbogu, 2019). In many cases, however, national regulations have simply not kept up with rapid advances in the field (Baylis, 2019).

At the global level, there is growing interest in international coordination. Notably, the prospects for multilateral cooperation have not been not plagued by the strong political cleavages common to other issue areas (e.g., geopolitical rivalry or North-South divisions). A set of legacy international agreements, negotiated in the 1990s in reaction to concerns

[15]One biotech investor referred to the regulation of gene-editing technology in the US as "the Wild West" (Interview by authors, 9/21/2020).

about cloning, provide a precedent for global governance of genetic research. The 1997 Oviedo Convention is a multilateral treaty that aims to prohibit the misuse of innovations in biomedicine (Oviedo, 1997). Its 34 signatories – all members of the Council of Europe – have agreed to ban the cloning of human beings and prohibit genetic screening for non-health purposes. In a similar declaration, members of the United Nations Educational, Scientific, and Cultural Organization (UNESCO) unanimously adopted the Universal Declaration on the Human Genome and Human Rights in 1997 (UNESCO, 1997). Subsequent UNESCO declarations articulated norms about genetic data and trade in genetic resources (UNESCO, 2003).

In recent years, formal international institutions have been slow to develop rules despite calls for new global standards. In 2016, environmental activists unsuccessfully pushed for the UN Convention on Biological Diversity to expand its mandate to regulate synthetic biology and gene drive organisms (Callaway, 2016). The World Health Organization is among the few international organizations explicitly addressing the issue, establishing an Advisory Committee on Human Genome Editing that remains in preliminary stages. The Committee's stated goal is to "advise and make recommendations on appropriate governance mechanisms for Human Genome editing."[16] More informally, a transnational network of National Academies of Science and Medicine are collaborating to evaluate social and ethical challenges in gene editing research and incorporate these issues into research protocols.

# 3 Interdependence & Technological Innovation

We argue that advances in gene editing, like many other disruptive technologies, increases international interdependence. We identify two specific sources of interdependence — regulatory arbitrage and spillovers from public controversies — through which policy decisions in

[16]The Committee is described at `https://www.who.int/ethics/topics/human-genome-editing/committee-members/en/`.

one country affect outcomes in another. In each case, we specify the underlying conditions that give rise to interdependence, draw analogies to other issue areas, and specify observable implications that are tested in Section 4. While our primary focus is gene editing, we argue that these linkages are likely to recur in other emerging fields such as artificial intelligence and cybersecurity.

## 3.1 Regulatory Arbitrage

Gene-editing technologies are inputs to an array of commercial applications that are expected to grow substantially over the next decade. In 2019, the gene-editing market was estimated to be worth $3.8 billion and is projected to exceed $10 billion in the next five years.[17] The most direct applications are in the pharmaceutical and healthcare industries, where firms are developing gene therapies to address a range of disorders and chronic illnesses. Among these are CRISPR Therapeutics, co-founded by Nobel laureate Emmanuelle Charpentier to develop gene-based medicines, which went public in 2016 and has since increased more than tenfold in market value.[18] Other sectors like agriculture, veterinary medicine, and industrial production processes also increasingly draw on gene-editing technology (Brinegar *et al.*, 2017).

The competition for these potential economic returns is fierce. Patent applications associated with gene-editing technologies have grown from less than 10,000 in 2000 to over 30,000 in 2019.[19] Firms are racing to develop commercial applications and successfully navigate regulatory hurdles to exploit the rapid market growth in gene editing. As in other emerging fields, pioneer firms may gain a first-mover advantage that endures even as competitors

[17]Projections are from Ugalmugle & Swain (2020). McKinsey estimates the broader biotechnology sector to have direct economic impact $2-4 trillion annually in the next 10-20 years (Chui *et al.*, 2020).

[18]CRISPR Therapeutics (CRSP) closed at $13.82 on its first day of trading in October 2016. Its closing price on February 8, 2021 was $169.23.

[19]Data on patent applications are from `lens.org`, a publicly available patent database, and reflect searches for "genetic editing" or "genetic engineering."

subsequently enter the market (Lieberman & Montgomery, 1988; Agarwal & Gort, 2001).

Consequently, researchers and firms are highly motivated to accelerate the development and commercialization of gene editing technology. One strategy for doing so is to seek out more permissive regulatory jurisdictions. While there are longstanding concerns about regulatory arbitrage in genetic research,[20] we argue that the recent revolution in gene-editing technology has substantially *increased* the potential for arbitrage. Reduced barriers to entry have expanded access to a more diverse set of actors in more jurisdictions. The ability to apply gene editing more easily and cheaply increases cross-border mobility, allowing human and financial capital to select into countries with less rigorous rules.

The ability of actors to opportunistically select into other jurisdictions creates several problems for governments as they regulate gene editing. First, it reduces a government's ability to restrict the use of the technology. Prior to recent technological breakthroughs – when altering genes was performed using difficult and expensive recombinant DNA techniques, for example – gene editing was constrained to a handful of institutions with the funding and infrastructure to support such methods. With few alternatives, researchers were largely forced to accept the regulations that governments imposed. The advent of programmable nucleases like CRISPR significantly increased the exit options available to scientists in academia and industry. This shift increased their ability evade unfavorable rules and weakened the hand of national governments.

A second problem is the emergence of regulatory competition among national governments. The economic returns associated with biotechnology, coupled with the potential relocation of researchers, firms, and investment flows into more permissive environments, creates strong pressure to lower regulatory barriers. For example, European plant breeders

[20]Notably, the potential for regulatory arbitrage by gene-editing researchers was raised by the geneticist Irving P. Crawford when scientists first developed recombinant DNA technology in the 1970s. Crawford argued that researchers would simply evade strict regulations, citing several clinical trials that had moved to Europe and South America to sidestep burdensome rules in the United States (Baskin *et al.*, 2016).

have pressed the EU to relax restrictions on gene editing, arguing that existing rules put them at a competitive disadvantage.[21] South Korea is reviewing its relatively onerous rules on gene therapy research in order to maintain its competitiveness in medical technology (Ji-young, 2017). In the United States, the agricultural industry successfully lobbied the government to weaken restrictions on gene-edited crops and livestock (Cancryn & Crampton, 2021; Stokstad, 2020). More broadly, commentators argue that China's progress in biotechnology and America's "eroding technological advantage" justify governance reforms and increased public investment (Darby & Sewall, 2021). Other countries have announced similar regulatory reviews or new public initiatives to capitalize on gene-editing technologies.[22] Since lax regulations can reap economic returns, governments have an incentive to undercut each other's rules. This can generate a "deregulatory spiral" in which governments collectively weaken standards in a race to the bottom.[23]

In international relations scholarship, regulatory competition is most closely associated with issues like tax policy, financial regulation, and environmental standards (Trachtman, 1993; Bretschger & Hettich, 2002; Angelini & Cetorelli, 2003; Konisky, 2007; Genschel & Schwarz, 2011). These are policy domains in which nations differ in their regulatory approach, economic output is responsive to rules, and assets have high cross-border mobility. We argue that these conditions increasingly characterize the field of gene editing. More broadly, the conditions are likely to develop in other fields undergoing rapid technological change. Technological advancement often lowers entry barriers and encourages diffusion to a

[21]The detailed position paper developed by European agricultural producers is available at `https://www.mpg.de/13748566/position-paper-crispr.pdf`.

[22]For example, policymakers in New Zealand are reviewing the country's gene-editing regulations, which some claim are outdated (Morton, 2019). In Russia, the government recently announced a collaboration with Rosneft, the country's largest oil producer, to develop gene-editing technology (Morton, 2020). For an overview of policy reforms regarding gene editing in agriculture, see Schmidt *et al.* (2020).

[23]In addition to lowering standards (race to the bottom), scholars have identified some cases where jurisdictions with sufficient market size can encourage higher standards (race to the top). See Genschel & Plumper (1997) and Barkin (2015).

wider set of regulatory jurisdictions. It frequently occurs in industries with enormous growth potential and where initial economic advantages can yield substantial returns. As a result, we should expect governance of emerging technologies to exhibit high levels of regulatory arbitrage and potential for regulatory competition.

In Section 4, we analyze arbitrage behavior in gene editing using data on gene therapy clinical trials and employment patterns of gene researchers. Before turning to this test, we describe the second source of interdependence that undermines decentralized governance of gene editing.

## 3.2 Spillovers in Public Controversies

The second source of interdependence is public attitudes about gene-editing technology. Like other emerging technologies, continued progress in the field of gene editing requires maintaining a high level of public confidence. Public attitudes affect the trajectory of the technology in at least three ways. First, beliefs about the safety and morality of gene editing shape consumer demand for gene therapies and other products. Aiyegbusi *et al.* (2020), for example, identify public perceptions of gene therapies as "central to their uptake and use." Second, public opinion affects the ability of firms to attract investors. Historically, controversies regarding one application of gene-editing technology have extinguished investor interest more broadly (Gardner, 2020). Finally, public attitudes influence regulation, which determines the permissible ends to which the technology may be applied.[24]

We argue that public attitudes about disruptive technologies are often fragile. By definition, rapid technological advances challenge existing systems of practice and thought. They do not nest neatly into existing ideological or political cleavages; instead, they frequently create unexpected coalitions and give rise to a mix of emerging public narratives. As a re-

[24]In the case of artificial intelligence, an overwhelming number of Americans (81%) "believe that robots and/or AI should be carefully managed," a statistic which Zhang & Dafoe (2019) suggest will shape governance outcomes for this and other technologies.

sult, we view emerging technologies as particularly vulnerable to backlash when controversies arise. If the technology intersects traditional political divides, elites may lack incentives to provide a narrative for individuals to anchor their own beliefs (Druckman *et al.*, 2013). With no pre-existing reference frame to "fix" individuals' views and moderate extreme reactions, high profile events can create quick and profound shifts in public opinion. Controversies can spark public backlash, lead to reductions in public funding, and engender knee-jerk regulatory responses that constrain even responsible scientific activity.

The recent history of gene therapy provides an example of public backlash. In 1999, 18-year old Jesse Gelsinger joined a clinical trial for a developmental gene therapy treatment run by the University of Pennsylvania. Unlike the previous seventeen participants, Gelsinger suffered a massive immune response that ultimately lead to his death. The tragic loss of the teenager led to an immediate and precipitous drop in public trust in clinical applications for gene-editing technology.As Jennifer Doudna recalls, the incident "made the whole field of gene therapy go away, mostly, for at least a decade. Even the term gene therapy became kind of a black label" (Rinde, 2019).

We do not argue that a reduction in trust for gene therapies after Gelsinger's death was unwarranted. Rather, the example illustrates how individuals update their beliefs in a highly uncertain environment with few consistent cues and even fewer data points. These features engender instability in public attitudes. As a result, emerging technologies that rely on public support often progress in fits and starts, with periods of promising technological advancements interrupted by crises of public confidence. There is evidence for this dynamic in the related field of genetically-modified organisms, where media exposure to controversies has been found to meaningfully affect public opinion (Prakash & Kollman, 2003; Drezner, 2008; Vigani *et al.*, 2012).

The recent gene-editing controversy surrounding He Jiankui similarly triggered public concern regarding the safety and propriety of gene-editing research. Unlike the Gelsinger

tragedy, however, it unleashed a response that spilled across national borders. Calls for a global moratorium on genetic editing research swiftly followed the revelation of He's experiment (Lander *et al.*, 2019). In contemporary scientific endeavors, norm violations in one country have the potential to undermine trust and support for the across the world.

We conceptualize backlash to gene-editing controversies as a negative externality that readily spills across national borders. In the absence of a robust global governance regime, each country sets its own regulatory policy. Countries receive several benefits from scientists who push the boundaries of gene-editing research. Successful innovation brings economic rewards in the form of marketable and profitable new technology and also enhances the prestige of the nation's scientific establishment. There are clear costs associated with lax regulation, including the potential for domestic public backlash, but these costs are not fully internalized by the home country. Like the technology itself, backlash diffuses across borders. Controversies may damage support for gene-editing research even in jurisdictions that are comparatively well-regulated.

While regulatory arbitrage has been studied and documented in other contexts, we are not aware of existing scholarship that examines the potential for spillovers in public backlash. Nonetheless, we expect that it is an important source of interdependence that occurs whenever a technology is associated with safety risks or ethical concerns. We argue that these are common traits of emerging technologies – from nuclear energy in the 1950s to artificial intelligence today – and expect public backlash to pose a recurring challenge for technology governance.

In the following section, we test for spillovers in public backlash using an original survey experiment on American respondents. We examine the effect of information about a hypothetical gene-editing controversy on public confidence and support for gene-editing research. The experiment varies whether the controversy occurs domestically or in a foreign country, allowing us to test whether foreign misuse of gene-editing technology affects public attitudes

in the United States.

We interpret evidence for both regulatory arbitrage and public backlash as support for international policy coordination. Each process represents a form of interdependence that undermines the efficiency of decentralized, national-level governance. This is precisely the class of governance problems appropriate for international coordination, which is designed to manage spillovers and resolve market failures among states (Keohane & Nye, 1977; Keohane, 1984; Farrell & Newman, 2015; Koremenos, 2016). The most straightforward way that international coordination can mitigate these spillovers is by harmonizing national rules via international standards. Even in the presence of enforcement problems, international rules can serve as a focal point to draw national regulations toward a single regulatory standard (Schelling, 1960; Perlman, 2020a). International institutions may also boost public confidence by monitoring for potential violations and certifying the responsible conduct of research. We discuss both mechanisms of global governance in Section 4.3.

# 4 Empirical Tests

We present two empirical tests of the theoretical logics described above. First, we leverage data on clinical trials to estimate the effect of national regulations on the gene therapy development. Because we expect the recent transformation of gene-editing technology to lower entry barriers and exacerbate forum shopping, we use the year in which CRISPR was introduced (2012) as a cutpoint in the analysis. We test whether countries with weaker gene-editing regulations benefited from this technological shock more than countries with strict regulations. We supplement this test with an analysis of the geographic movement of gene researchers across national jurisdictions.

For the second test, we fielded a survey experiment assessing the magnitude of public backlash from gene editing controversies. We experimentally manipulate the country in

which the unethical research took place to measure the extent to which foreign controversies shape domestic public attitudes. If public confidence and support for gene-editing research in the US decreases in response to misuse in other jurisdictions, this evidence would support our theory of public opinion spillover effects.

## 4.1 Regulatory Arbitrage

We argued above that actors can evade strict regulations by relocating to jurisdictions with weaker rules. To test this claim, we first examine patterns of clinical trials devoted to the development of gene therapies. While this test cannot definitively establish arbitrage behavior, it can demonstrate whether the recent breakthrough in gene-editing technology benefited countries with more permissive regulations, compared to their more stringent counterparts. To directly test whether researchers forum shop to weaker jurisdictions, we also analyze employment patterns of over 100,000 gene researchers.

### 4.1.1 Gene Therapy Clinical Trials

Gene therapy clinical trials test the safety and efficacy of clinical applications of gene-editing technology. They are a necessary step to gain market authorization for gene therapies, a growing industry with high consumer demand and significant profit potential (Macpherson & Rasko, 2014; Hirakawa *et al.*, 2020). Several high-profile gene therapies have been approved following successful clinical trials (June *et al.*, 2018; Gong *et al.*, 2018), and the race to develop new treatments has intensified in recent years.

We collect data on clinical trials from the Journal of Gene Medicine's "Gene Therapy Clinical Trials Worldwide" database. They capture all registered trials that perform gene therapy clinical interventions on human subjects. We structure the data at the level of the country-year, such that the outcome variable represents the number of new gene therapy trials registered in each country in each year. We restrict the sample to the 63 countries that

perform at least one gene therapy clinical trial in the time period covered by the study. The data include a total of 3,596 clinical trials. The average number of trials per country is 57.5.

The independent variable in our analysis is the rigor of national regulations governing the use of gene-editing technology. To measure regulations, we use a measure of national human genome editing policies developed by Baylis *et al.* (2020). Specifically, Baylis *et al.* (2020) identify regulations that "address the use of genetically modified in vitro embryos in laboratory research (germline genome editing)." These data serve as a proxy for general gene-editing regulations and correlate well with alternative regulatory proxies (see Appendix Figure A4 for correlation plots). The authors categorize countries' regulatory approach as *permissive*, *indeterminate*, *prohibitive with exceptions*, or *prohibitive* based on a review of national legislation, guidelines, and codes of conduct.[25] Cross-national variation in these regulations is visualized in Figure 2. In the analysis below, we transform the categories to a 4-point measure that increases with regulatory rigor, with (1) denoting *permissive* regulations and (4) denoting *prohibitive*.

Figure 3 displays temporal trends in gene therapy trials located in countries with different levels of regulatory rigor. The top left panel features countries with the weakest gene-editing regulations (*permissive*), followed by the top right (*indeterminate*), bottom left (*prohibitive with exceptions*), and bottom right (*prohibitive*).The figure provides some suggestive evidence that regulatory rigor is associated with clinical trial development. Countries with weak regulations (e.g., the United States and China) experience both higher overall numbers of clinical trialsand a sharper increase in later years compared to countries with strict policies (e.g., Germany).

To test the relationship between regulation and clinical trials more systematically, we employ a difference-in-differences specification. The analysis leverages the 2012 introduction

[25]Baylis *et al.* (2020) provide separate measures of gene-editing regulations regarding assisted human reproduction and those that focus on other applications. Since we are interested in rules regarding gene therapy development, we use the "not for reproduction" measure (see Table 4 of Baylis *et al.* (2020).

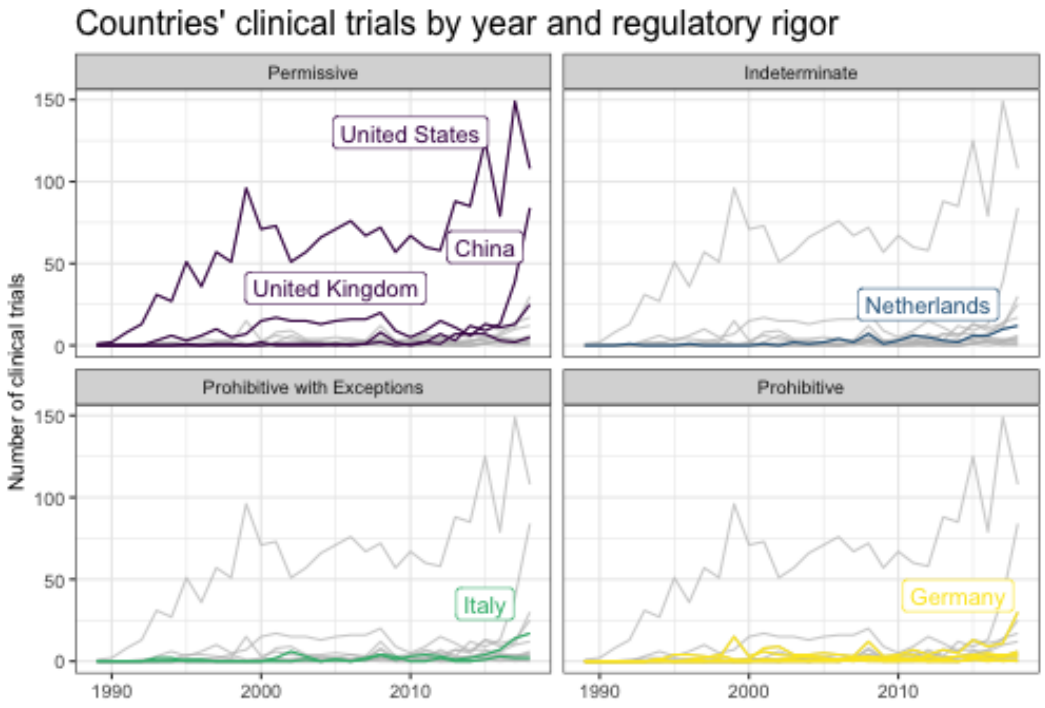


Figure 3: *Regulatory Rigor and Gene Therapy Clinical Trials* Each panel plots the number of clinical trials by countries that fall into a specific level of regulations: permissive, indeterminate, prohibitive with exceptions, or prohibitive. For interpretability, only countries with more than 50 total gene-editing trials are shown.

of CRISPR as a technological shock that should interact with countries' national regulations. We expect low-regulation countries to benefit more from this technology than countries with more exacting rules. After 2012, technological innovation lowers the human and financial capital needed to engage in gene-editing research. Cost and expertise recede as barriers to commercial development, while regulatory restrictions are more likely to become binding constraints. We therefore expect scientists in weaker regulatory jurisdictions to experience a larger increase in gene therapy trials after 2012 than those in more rigorous jurisdictions. We estimate the following equation to determine how regulatory rigor affects the quantity of a country's gene therapy trials.

$$\text{Trials}_{it} = \alpha + \beta_1 \text{Regulation}_i + \beta_2 \text{CRISPR}_t + \beta_3 (\text{Regulation}_i * \text{CRISPR}_t) + \beta_4 \text{X}_{it} + \epsilon_{it} \quad (1)$$

where $Trials_{it}$ are the number of gene therapy clinical trials conducted in country $i$ in year $t$, $Regulation_i$ is the 4-point measure of regulatory rigor, $CRISPR_t$ is an indicator for the post-2012 period, and $X_{it}$ is a vector of control variables. We expect $\beta_3$, the difference-in-differences coefficient, to be negative and statistically significant. This would signify that more rigorous jurisdictions "lose out" on gene editing development in the CRISPR era, compared to countries with weaker rules.

We include a set of control variables that reflect a country's national economic output and human capital, which are likely to shape gene therapy development. We include `GDP` to account for each country's economic capacity and `GDP per capita` for its level of development. We proxy scientific capital with a count of the number of patent applications in each country by residents `Patent Residents` and non-residents `Patent Non-Residents`.Data for all control variables are drawn from the World Bank's World Development Indicators (WDI) for the years 1989-2020. Each is measured at the country-year level and logged to account for skewed distributions.

Table 1 summarizes the results. Our core findings are consistent with theoretical expectations. In both the baseline (Column 1) and saturated (Column 2) models, the negative coefficient for `Regulation` reflects a general pattern of fewer gene therapy trials among countries with strict regulatory standards. The large and positive coefficient for `CRISPR` is consistent with an increase in the use of gene-editing technologies after 2012. Most importantly, the interaction term `Regulation`×`CRISPR` is negative and significant at the 0.1 level. This result confirms that the effect of `Regulation` on gene therapy development is greater following the technological shock of CRISPR. Substantively, a one-point reduction in regula-

| | *Dependent variable:* Gene therapy trials | |
|---|---|---|
| | (1) | (2) |
| Regulation | $-2.137^{***}$ | $-1.019^{***}$ |
| | (0.425) | (0.382) |
| CRISPR | $12.340^{**}$ | $10.855^{*}$ |
| | (6.178) | (5.887) |
| Regulation×CRISPR | $-3.035^{*}$ | $-3.029^{*}$ |
| | (1.728) | (1.649) |
| GDP (log) | | $4.460^{***}$ |
| | | (0.806) |
| GDP per capita (log) | | $2.160^{***}$ |
| | | (0.444) |
| Patent Resident (log) | | $-1.325^{***}$ |
| | | (0.442) |
| Patent Non-Resident (log) | | $1.326^{***}$ |
| | | (0.303) |
| Observations | 810 | 718 |
| Adjusted $R^2$ | 0.087 | 0.287 |

Table 1: *Effect of National Regulations on Gene Therapy Clinical Trials.* The table displays coefficient estimates and standard errors from a linear difference-in-differences model. Standard errors clustered at the country level. Statistical significance is denoted by: $^{*}$p<0.1; $^{**}$p<0.05; $^{***}$p<0.01.

tory rigor (e.g., moving from *prohibitive* to *prohibitive with exceptions*) increases the number of gene therapy trials by approximately two per year in the pre-CRISPR era and five per year thereafter. This shift is quite meaningful, representing a 284% increase over the mean value of 1.76 trials per country-year.

Other covariates perform largely as expected. Countries with greater GDP and higher levels of economic development conduct greater numbers of gene therapy trials. The two

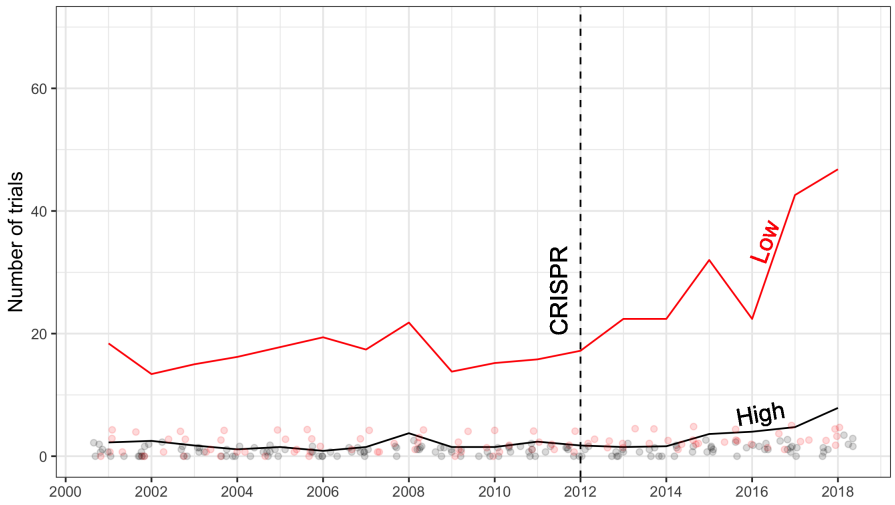


Figure 4: *Trends in Gene Therapy Trials, Low vs. High Regulation Countries.* The graph depicts the average number of clinical trials for high (black line) regulation countries and low (red) regulation countries. The vertical dashed line represents the introduction of CRISPR in 2012. Points on the graph are the (logged) number of gene-editing clinical trials in a given country in a given year.

patent measures produced mixed results: patent applications by non-residents has a positive association with gene therapy trials while the estimate for patent applications by residents is negative.

We summarize the trends for low- and high-regulation countries in Figure 4. To simplify the visualization, we classify countries as high-regulation (*prohibitive* and *prohibitive with exceptions*) and low-regulation (*indeterminate* and *permissive*). The 2012 technological shock is represented by the vertical dotted line. The figure provides some evidence in favor of the parallel trends assumption needed to causally identify the difference-in-differences test. In the pre-CRISPR period, the two groups move roughly in parallel over time. They begin to diverge after 2012, when low-regulation countries experience increasing numbers of gene therapy trials compared to their high-regulation peers.

Our analysis provides strong evidence that weaker regulatory environments "outperform" expectations in the conduct of gene therapy trials. This evidence is consistent with regulatory

arbitrage, since trials are concentrated in countries with lax national rules. However, it does not definitively establish arbitrage behavior. The same result could be obtained if low-regulation countries experienced increases in domestic clinical trial development, rather than attracting foreign researchers. We now examine arbitrage behavior directly by analyzing employment patterns among gene researchers.

### 4.1.2 Scientific Forum-Shopping

To test for forum-shopping behavior, we examine whether gene scientists relocate to institutions in low-regulation countries at higher rates after the invention of CRISPR. We posit that institutions located in countries with lower regulatory standards towards genetic editing will be more attractive destinations for scientists engaged in genetic editing research in the post-CRISPR era. States with the capacity to generate strict regulations for advanced technology may also be locations with high levels of scientific production and the know-how to develop clear rules. However, CRISPR should lower the barriers to entry for conducting high-quality research on an advanced topic even outside of established scientific hubs. If scientists choose to move to institutions in low-regulation countries at higher rates in the post-CRISPR period, this would constitute evidence of forum-shopping.

To test this claim, we examine patterns of employment among researchers who have published scientific papers in the field of genetic engineering. We collect these data from PubMed, a database of life sciences and biomedical publications maintained by the United States National Library of Medicine at the National Institutes of Health. To obtain the sample of gene researchers, we extract the names and institutional affiliations of all authors who have published papers on the topic "genetic engineering." The search yields approximately 150,000 papers and more than 400,000 unique gene researchers for the period 2002-2021.[26]

[26]We begin in the year 2002 because this is the first year PubMed records full author names for each publication.

To examine the potential for arbitrage in institutional affiliation, we first subset to the collection of 185,492 researchers who transfer institutions at least once during the time period. Since we are interested in the relocation patterns of these individuals, we create an indicator variable, `Change Institution Country`, that takes a value of 1 if the new institution is in a different country and 0 otherwise. We use the Baylis *et al.* (2020) data to code the rigor of gene-editing regulations in the destination country (`Regulation`). Finally, we use a logit model to predict `Change Institution Country` as a function of `Regulation`, an indicator for the post-CRISPR period (`CRISPR`), and the interaction of the two. We also include the vector of control variables described in the previous section.

Our theoretical expectations about forum shopping imply two results. First, we should observe more cross-border mobility in the post-2012 period. This would be reflected as a positive and statistically significant coefficient for `CRISPR`. Second, countries with lower `Regulation` scores should be more attractive destinations in this period, compared to the prior era. This should manifest as a negative coefficient on the `Regulation`× `CRISPR` interaction term.

We report the results of our main specifications with and without the inclusion of covariates in Table 2. In both models, the large and positive coefficient for `CRISPR` is consistent with an increase in the cross-border mobility after 2012. The interaction term `Regulation`×`CRISPR` is negative and statistically significant. This result confirms that the attractiveness of employment in permissive regulatory environments is greater following the technological shock of CRISPR. Notably, more stringent regulatory environments are still more attractive targets than their peers, as reflected in the positive coefficient for `Regulation`. This likely results from the greater resources and prestige associated with institutions in high-regulation countries. But the advantage of these jurisdictions is significantly diminished in the post-CRISPR era.

| | *Dependent variable:* | |
|---|---|---|
| | Cross-Border Employment Mobility | |
| | (1) | (2) |
| Regulation | $0.086^{***}$ | $0.030^{***}$ |
| | (0.006) | (0.008) |
| CRISPR | $0.062^{**}$ | $0.164^{***}$ |
| | (0.023) | (0.023) |
| Regulation×CRISPR | $-0.034^{**}$ | $-0.071^{***}$ |
| | (0.012) | (0.012) |
| GDP (log) | | $0.293^{***}$ |
| | | (0.019) |
| GDP per capita (log) | | $-0.122^{***}$ |
| | | (0.008) |
| Parent Resident (log) | | $-0.250^{***}$ |
| | | (0.008) |
| Patent Non-Resident (log) | | 0.001 |
| | | (0.007) |
| Observations | 185492 | 182935 |

Table 2: *Employment Relocation of Gene Researchers*: Logit estimates for the likelihood that a gene-editing scientist will move to an institution in another country, based on pre-post CRISPR eras and country-level regulations. Robust standard errors clustered at the country level are reported in parentheses. Statistical significance is denoted by: $^{*}$p<0.1; $^{**}$p<0.05; $^{***}$p<0.01.

These tests provide evidence consistent with forum-shopping behavior induced by low-cost, easy-to-use, disruptive technology. The advent of CRISPR increases the likelihood that scientists will move to an institution in a low-regulation country compared to a high-regulation country. The technology also increases institution-country-switching overall, consistent with CRISPR lowering institutional barriers to research. We now turn to the second

hypothesized mechanism related to spillovers in public backlash.

## 4.2 Survey Experiment on Public Backlash

We evaluate the spillover effects of controversial use of gene editing via a survey experiment. The survey examines backlash among the general public in response to a hypothetical, norm-violating application of gene-editing technology. We estimate the causal effect of information about the incident on public confidence and support for gene-editing research. To gauge the spillover effect, we examine both the effect of controversial activity in one's own country as well as activity in a foreign country.

The online survey was conducted in July 2020 on the survey platform Lucid on a sample of 1200 Americans quota-sampled to US census margins.[27] Table A1 in the appendix displays summary statistics of our survey sample. For our primary results, we use the full sample of survey respondents. To address concerns that changes in Lucid recruitment methods may depress respondent quality (Aronow *et al.*, 2020), we ensure our findings hold after removing those who do not successfully pass attention checks (see appendix Table A4).

We embed an experiment in the survey designed to address two questions. First, do controversies over the use of gene editing reduce public support for the technology and its potential applications? Second, does public backlash spill across national jurisdictions?

In the experiment, all respondents receive a basic summary of gene-editing technology. It reads:

> All organisms, from bacteria to lizards to humans, have molecules called DNA, or deoxyribonucleic acid. These DNA molecules contain the genetic code for each organism. DNA provides the instructions that determine an organism's physical characteristics and control how it develops, functions, and reproduces.

[27] In Appendix A.3, we list the full survey text and discuss its alignment with APSA Principles and Guidance for Human Subjects Research. Our pre-registration plan can be found under EGAP 20200505AA.

In recent years, scientists have developed new gene-editing technologies that can permanently alter an organism's DNA. These technologies allow scientists to make targeted changes to DNA molecules in plants and animals, modifying their biological traits. For example, scientists have edited the genes of wheat plants to make them easier to grow.

Following this introduction, some respondents are randomly assigned to a treatment condition where they are given additional information about a gene-editing controversy. Among treated respondents, we randomize whether the controversy occurs in the US, UK, or China. Appendix Table A2 summarizes covariate balance across the randomized treatment conditions. In the survey, the treatments are presented as a hypothetical news article set in the year 2021. To increase external validity, we model the experimental intervention on the real-world controversy surrounding He Jiankui. We present the text for the UK treatment condition here:

**Birth of Genetically Altered Babies in the UK Provokes Outcry**

January 25, 2021

[LONDON]– A British research team announced that they have used a new gene-editing technology to alter the DNA of a group of infants. In an unprecedented intervention, scientists on the research team deleted a set of genes believed to be linked to breast and prostate cancer. The deleted genes are not considered essential to basic biological functions in humans, but the long-term effects of their removal are unclear. The research team plans to periodically examine the infants throughout their lives to assess any side effects of the genetic alteration.

The disclosure this week of the research — carried out in the UK — has sparked urgent debate about the ethics of genetic alteration. The infants' birth represents a significant and controversial leap in the use of gene-editing technology. The

British study has also increased concerns about a future in which parents produce "designer babies" with selectively improved traits, such as height or intelligence.

After treatment assignment, respondents are asked to rate their agreement with four statements on a scale of 0 (no agreement) to 10 (complete agreement). The statements read as follows:

- Research in the US involving gene editing should be more strictly regulated.
- US patients should have access to medical treatments that involve gene editing.
- The US government should provide funding for gene editing research.
- Most US scientists conduct their research in a safe and responsible manner.

The statements estimate the extent of public confidence in the safety of gene-editing technology and support for continued development. Respondents' answers constitute our dependent variables in the analyses below.

Our theory of public backlash against emerging technologies implies two patterns of response. First, we expect that respondents who read about a controversy in their own country will be less supportive of gene-editing research. This "domestic public backlash" should heighten demand for strict regulation, depress calls for patient access to gene therapy, decrease support for funding gene-editing research, and decrease confidence in the safety of scientific research. Second, we expect foreign controversies to similarly reduce public support for gene editing among US respondents. A "public backlash spillover" occurs if the controversial use of gene editing generates a domestic backlash even when the scandal occurs in another country.

We report treatment effects for each outcome of interest in Figure 5. Coefficients in the figure represent the treatment effect of exposure to a gene-editing controversy, compared to the control (no controversy) condition.[28] Within each panel, we display the estimated treat-

[28]See Table A3 in the appendix for the full set of point estimates and standard errors.

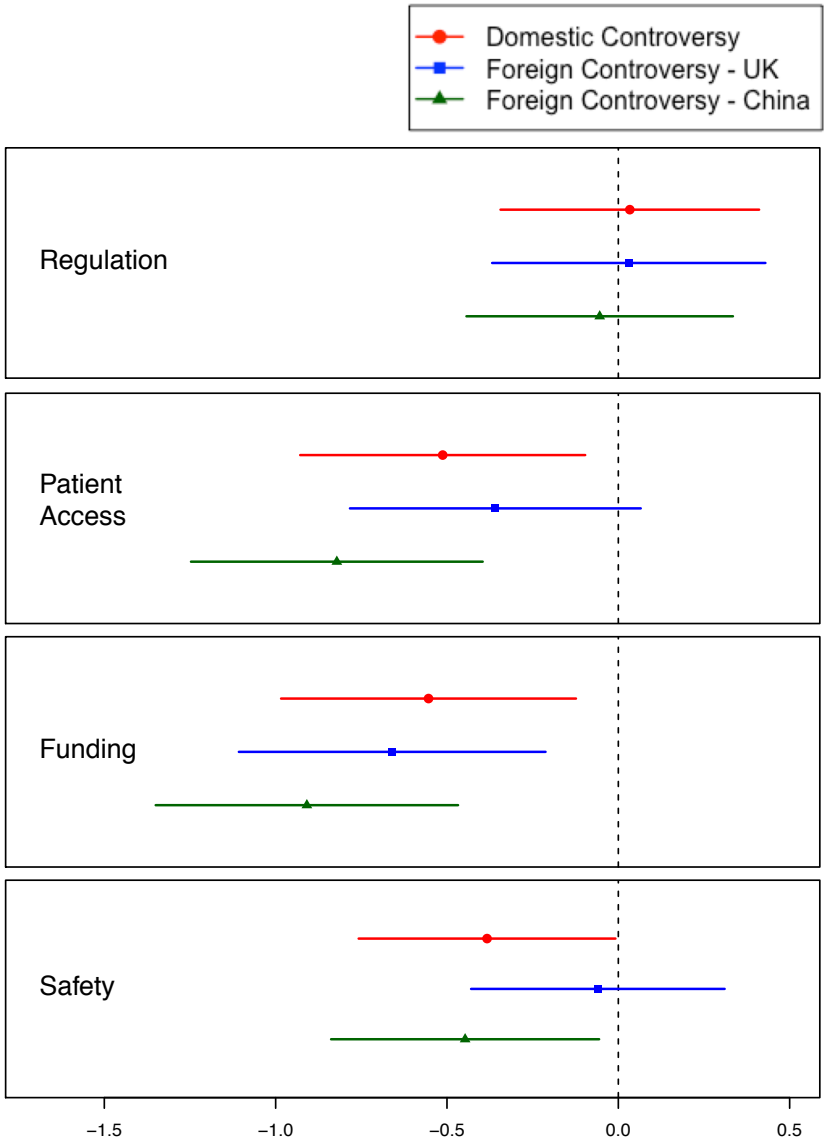


Figure 5: *Public Response to Gene-Editing Controversy.* The figure shows the treatment effect of learning about hypothetical, controversial gene-editing research in the United States, United Kingdom, and China. The four panels report effects on the four dimensions of public support listed above. 95% confidence intervals are reported.

ment effect of a purely domestic controversy, a foreign controversy in the United Kingdom, and a foreign controversy in China.

We find evidence of a domestic public backlash in three of four outcomes. When American respondents read about a hypothetical misuse of gene-editing technology by American

researchers, they significantly reduce support for patient access to gene therapies and public funding for gene-editing research. They also have diminished perceptions of the safety and responsibility of scientific research in the United States. On average, the domestic controversy treatment shifts opinion on each of these outcomes by approximately 0.5 points. Contrary to expectations, respondents do not increase demand for strict regulations in reaction to domestic gene-editing scandals. This null finding may reflect a ceiling effect, as even respondents in the control condition call for strict regulations in high numbers (see appendix Figure A3 for the distribution of responses across conditions).

There is clear evidence that backlash is not limited by national jurisdiction. As in the domestic scenario, neither of the foreign scandals significantly affects attitudes about gene-editing regulation. However, support for public funding of gene-editing research significantly decreases in response to foreign controversies in the UK and China. Additionally, both confidence in the responsibility of US scientists and support for expanded patient access to gene therapies decrease in the China and UK condition, though the UK treatment does not obtain conventional levels of statistical significance. Notably, the effects of domestic and foreign controversies are statistically indistinguishable across all four outcomes.

Together, these results suggest that the public does not discriminate between domestic and foreign research controversies. We find clear evidence that, for some public policy outcomes, the spillover effect of controversial research in one national jurisdiction negatively impacts domestic support for gene editing in another jurisdiction.

## 4.3 Discussion

Our findings provide evidence for two sources of interdependence that afflict national governance of gene-editing technology. We show that weaker national regulations boost gene therapy development, creating pressures for governments to engage in regulatory competition. We also demonstrate that the risks of weak national rules are not fully internalized

by the home country. If a government's lax regulation increases the risk of inappropriate behavior, the resulting backlash spills across national boundaries.

Taken together, our results suggest that governments have compelling incentives to lower regulatory barriers beyond the level they would otherwise prefer. Each country can obtain individual economic benefits from weakening rules, while the risks of doing so are diffusely spread across multiple jurisdictions. If governments respond rationally to these incentives, effective regulation will be under-produced and the systemic risk of misuse will rise.

By illuminating patterns of interdependence among states, our arguments examine the *functional* case for global governance of gene-editing technology. Functionalists argue that states build international institutions to manage transnational spillovers, resolve information problems, and reduce transaction costs (Keohane, 1982, 1984; Haggard & Simmons, 1987). They view global governance bodies as a rational response to "political market failures" among states with fixed preferences (Keohane, 1984). Though we adopt a functional framework in this paper, we acknowledge that other perspectives may generate valid arguments for or against a global gene-editing regime.[29]

There are at least two functions an international institution could provide to improve governance of gene editing. First, it can encourage partial harmonization of the disparate national and subnational rules governing the technology. While it is politically-infeasible to expect countries to delegate regulatory power to a supranational body, a global gene-editing regime could establish a floor of basic ethical and safety protections that all countries are expected to follow. This would limit the scope for regulatory competition and reduce the risk of scandalous applications of gene-editing technology.

Second, an international institution could assuage public anxiety by establishing clear

[29]For example, Buchanan & Keohane (2015) adopt a primarily normative lens in arguing for a drone accountability regime. Johnston (2001) argues that international institutions can be used as vehicles for persuasion and social influence, changing state preferences. Bioethicists working in the field of gene editing have explicitly called for ethically-based global standards informed by public discussion and attention to local cultures and environments (Kofler *et al.*, 2018).

norms of appropriate use and monitoring gene-editing applications to human subjects. As we argued above, one reason technological scandals generate wild fluctuations in public support is that citizens lack a coherent frame of reference for understanding the risks and benefits associated with disruptive technologies. International institutions can help fill this void by articulating norms that reflect a broad-based global consensus.

If public anxiety is rooted in the belief that existing governance efforts are insufficient, rigorous monitoring by international bodies may increase public confidence and support. To probe this idea, we added a corollary condition to our public backlash experiment in which the hypothetical news article alerts readers to monitoring by the World Health Organization (WHO).[30] We found that this treatment failed to improve respondent confidence, suggesting the mere existence of monitoring does not substantially reduce public concern.[31]

Finally, our findings have institutional design implications for a potential global governance regime. Scholars argue that international regimes are designed to address the unique cooperation problems states confront in an issue area (Martin, 1992; Koremenos *et al.*, 2001). By theorizing and testing two patterns of state interdependence distinctive to gene-editing technology, we specify a set of important issues that international institutions should address. Given the widespread diffusion of gene-editing technology, an effective regime would need to be broad-based in membership and participation. This could be achieved by nesting the institution within an existing global body like the WHO. Our analysis of public backlash also suggests the regime should prioritize building resilience in public confidence. This requires investing in features that increase the legitimacy of the institution in the eyes of the public, including transparency and political impartiality.

[30]In these conditions, we add the following language to the news article: "Gene-editing research is closely monitored by the World Health Organization (WHO), which has established guidelines to ensure scientific activities are conducted safely and carefully. The study is currently under review by the WHO to assess its compliance with these guidelines."

[31]See Appendix A.4 for full results from this treatment arm.

# 5 Conclusion

This paper demonstrates that gene-editing technology is subject to at least two sources of interdependence that undermine governance at the national level. As in other issue areas, we argue that governments face economic pressures to weaken standards, generating regulatory competition. We analyze patterns of gene therapy clinical trials to show that lower-regulation jurisdictions can more easily capitalize on recent advances in genetic technology than their more stringent peers.

Secondly, we argue that controversial applications of gene-editing technology creates public backlash that can spill across national boundaries. As far as we are aware, we are the first to identify this theoretical mechanism that links public attitudes in one country to policy decisions in another. The effect of these controversies can be dramatic: in the history of gene editing, high-profile scandals led to collapsed public support, the abandonment of commercial applications, and harsh regulatory responses. We demonstrate the mechanism in an original survey experiment on American respondents. Our findings support the existence of a public backlash spillover that can undermine confidence in gene-editing technology.

While our tests focus on the field of gene editing, we argue these dynamics recur in the governance of disruptive technological innovations more generally. Our theory illustrates how rapid technological change interacts with existing processes in ways that increase interdependence among states. For example, pressure for regulatory competition increases with potential economic gains and the cross-border mobility of production. Technological innovations act as positive shocks to these latter variables, creating a race for commercialization while reducing costs and other barriers to production. Similarly, emerging technologies frequently trigger public anxiety and therefore increase the potential for public backlash spillovers.

Future work can assess the generalizability of our theory by expanding empirical tests to

other fields. In addition to contemporary emerging technologies like artificial intelligence, historical disruptions such as the nuclear energy and computer revolutions may shed light on whether international coordination was motivated in part by these mechanisms. We also hope our paper will inspire studies of other relatively "ungoverned" issue areas in world politics. While examining long-standing issues of global governance like trade and arms control are undoubtedly important, scholars of international cooperation should not neglect important policy domains that are not yet subject to multilateral regimes.

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# Appendix

## A.1: Tables

| Variable | Sample Proportion |
|---|---|
| Party ID | |
| Democrat | 0.36 |
| Republican | 0.36 |
| Independent | 0.28 |
| Age | |
| 18-30 | 0.15 |
| 31-45 | 0.36 |
| 46-60 | 0.30 |
| over 60 | 0.19 |
| Education | |
| High School or Less | 0.30 |
| Some College | 0.32 |
| Bachelor's Degree | 0.22 |
| Post-Graduate | 0.17 |
| Gender | |
| Female | 0.51 |
| Male | 0.49 |
| Ethnicity | |
| White | 0.83 |
| Black or African American | 0.14 |
| Asian | 0.01 |
| Other | 0.02 |
| Hispanic | |
| Yes | 0.13 |
| No | 0.87 |
| Household Income | |
| $< \$25{,}000$ | 0.55 |
| \$25-50,000 | 0.21 |
| \$50-75,000 | 0.14 |
| $> \$75{,}000$ | 0.10 |
| Region | |
| Northeast | 0.21 |
| Midwest | 0.20 |
| South | 0.38 |
| West | 0.22 |

Table A1: *Survey sample statistics.* For each category, we report the proportion of respondents who fit into the category among those that answered the relevant question.

| | control (N=331) | | uk (N=285) | | china (N=292) | | us (N=299) | |
|---|---|---|---|---|---|---|---|---|
| | Mean | Std. Dev. | Mean | Std. Dev. | Mean | Std. Dev. | Mean | Std. Dev. |
| Income (1-24) | 9.3 | 7.4 | 8.9 | 7.3 | 9.3 | 7.4 | 9.0 | 7.2 |
| Education (1-8) | 4.5 | 2.0 | 4.4 | 2.0 | 4.3 | 1.9 | 4.5 | 2.0 |
| Female | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 |
| Age | 43.5 | 17.0 | 44.4 | 16.2 | 46.1 | 17.3 | 45.0 | 17.1 |
| Party (1-10) | 4.7 | 3.5 | 5.4 | 3.5 | 5.3 | 3.6 | 5.1 | 3.6 |
| Political Attention (1-5) | 3.6 | 1.2 | 3.5 | 1.2 | 3.5 | 1.2 | 3.6 | 1.2 |

Table A2: Balance Table of Covariates in Survey Experiment

| | *Dependent variable:* | | | |
|---|---|---|---|---|
| | Regulations | Access | Funding | Safety |
| | (1) | (2) | (3) | (4) |
| US Controversy | 0.030 | $-0.515^{**}$ | $-0.551^{**}$ | $-0.380^{**}$ |
| | (0.193) | (0.213) | (0.220) | (0.192) |
| UK Controversy | 0.037 | $-0.365^{*}$ | $-0.641^{***}$ | $-0.055$ |
| | (0.203) | (0.216) | (0.228) | (0.188) |
| China Controversy | -0.048 | $-0.820^{***}$ | $-0.910^{***}$ | $-0.450^{**}$ |
| | ( 0.198) | (0.217) | (0.225) | (0.200) |
| Observations | 1,197 | 1,193 | 1,198 | 1,199 |
| Adjusted $R^2$ | $-0.002$ | 0.010 | 0.012 | 0.004 |

Table A3: *Survey Results*. Estimated treatment effects and robust standard errors for the survey experiment. Effects are relative to the control condition (no additional informattiton). Statistical significance is denoted by: $^{*}$p<0.1; $^{**}$p<0.05; $^{***}$p<0.01.

| | *Dependent variable:* | | | |
|---|---|---|---|---|
| | Regulations | Access | Funding | Safety |
| | (1) | (2) | (3) | (4) |
| US Controversy | −0.109 | −0.644*** | −0.572** | −0.416** |
| | (0.197) | (0.223) | (0.231) | (0.199) |
| UK Controversy | −0.531** | −0.742*** | −1.165*** | 0.080 |
| | (0.237) | (0.269) | (0.286) | (0.219) |
| China Controversy | −0.104 | −1.170*** | −1.347*** | −0.447** |
| | (0.223) | (0.240) | (0.254) | (0.224) |
| Observations | 955 | 952 | 954 | 955 |
| Adjusted $R^2$ | 0.002 | 0.023 | 0.032 | 0.006 |

Table A4: *Survey Experiment Results on Attentive Sample.* Results of the survey experiment on the sample of respondents who successfully pass an attention check. We check for attention by asking treated individuals in which country gene-editing occurred. Statistical significance is denoted by: *p<0.1; **p<0.05; ***p<0.01

## A.2: Figures

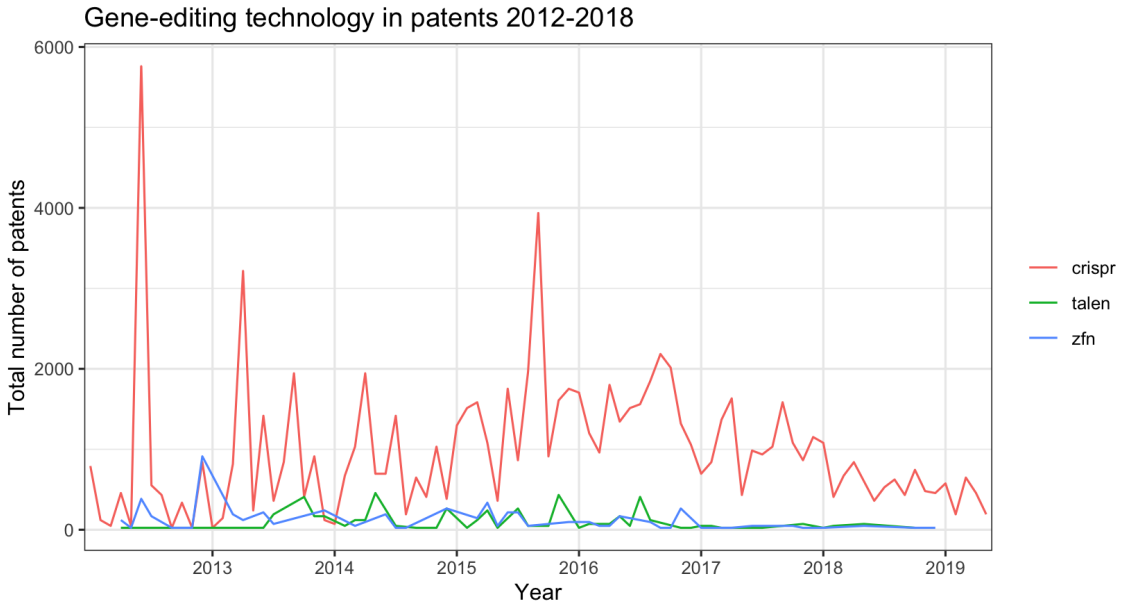


Figure A1: *Gene-editing Patent Applications, 2012-2018*: The figure displays annual patent applications related to CRISPR (red), TALENS (green), and ZFN (blue) technologies. Data from Oribit Intelligence.

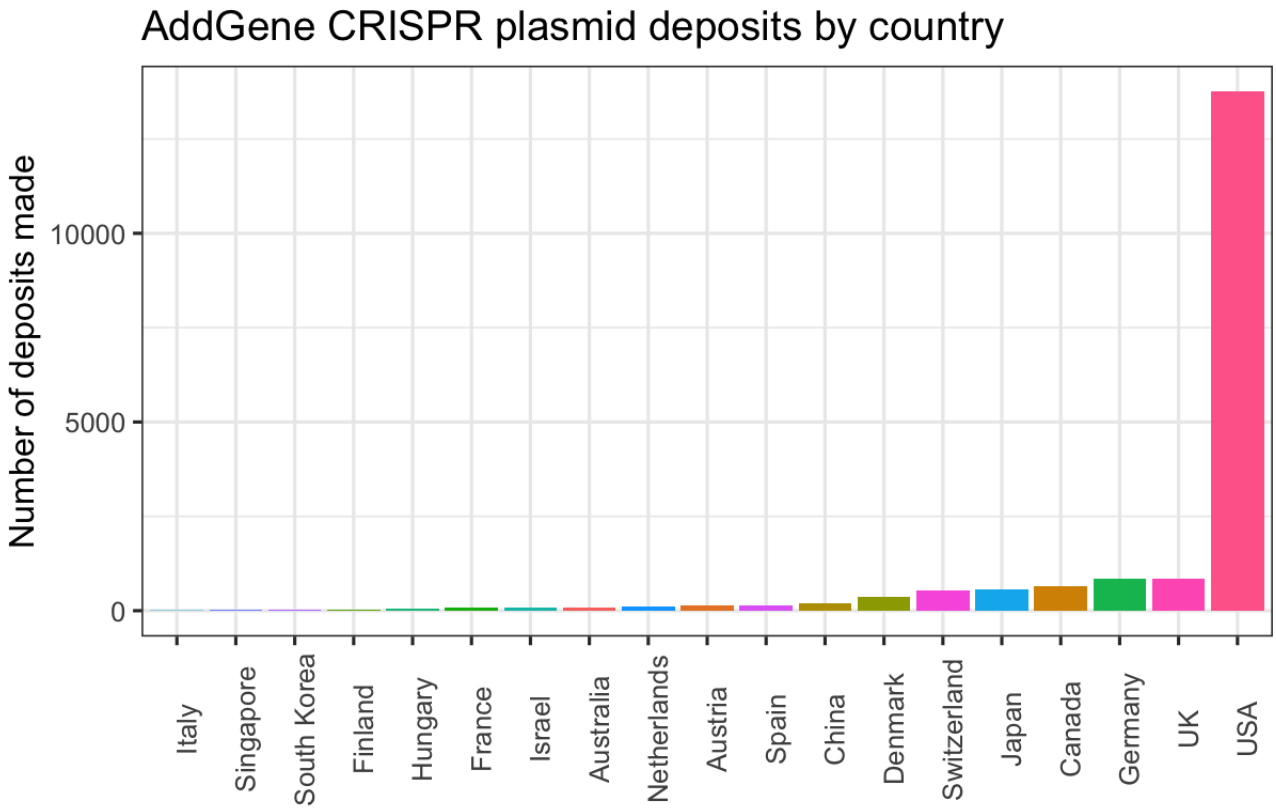


Figure A2: *AddGene depositors by country*

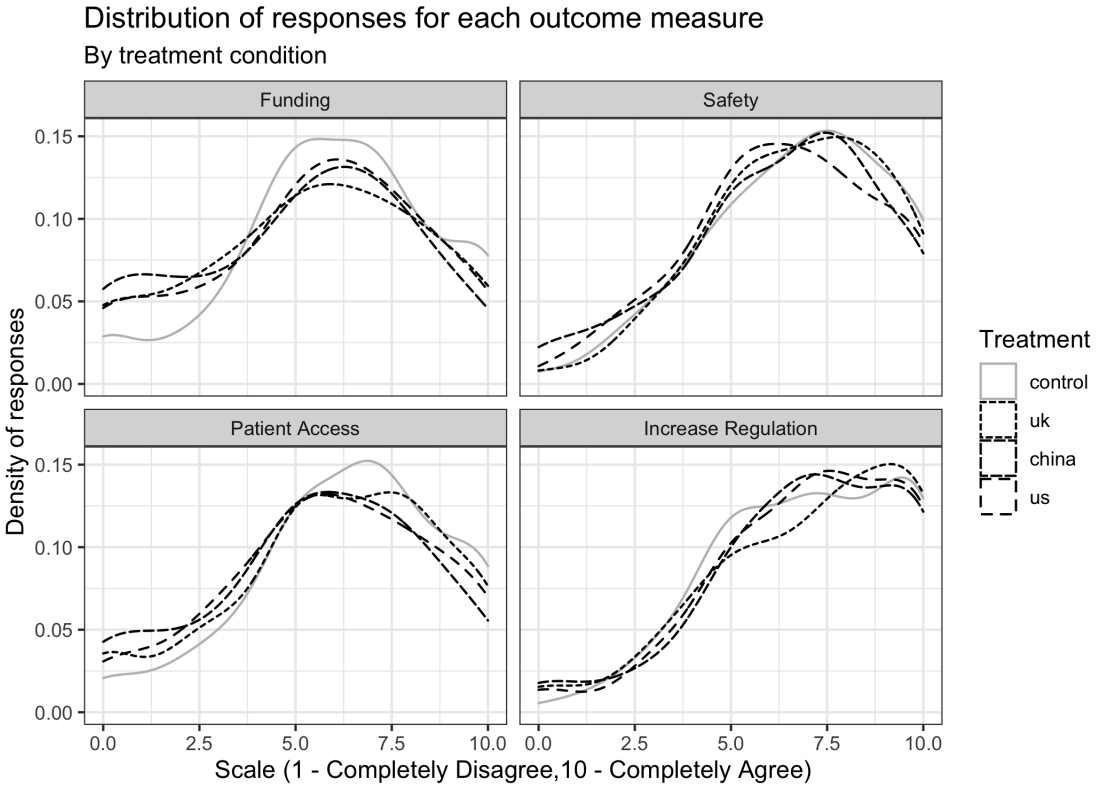


Figure A3: *Distribution of Responses for Outcome Variables.* The figure displays the distribution of responses by treatment condition for each of four outcomes.

## A.3: Survey Experiment Consent and Text

In line with the APSA Principles and Guidance for Human Subjects Research, the author who provided the funding for this experiment submitted the survey protocol to the relevant Institutional Review Board (IRB) Human Subjects Committee prior to launching the survey experiment. The IRB reviewed this survey experiment and granted an exemption under federal regulation 45 CFR 46.104 (2)(ii) (IRB Protocol ID 2000027424). The survey does not contain deceptive material, intervene in political processes, or collect sensitive and/or personally identifiable information.

Respondents were recruited through Lucid, an automated marketplace that connects researchers with online research participants. The authors compensated Lucid $1 per completed interview. Lucid contracts with suppliers who provide financial incentives to survey respondents in the form of cash, gift cards, or loyalty reward points. All respondents are voluntary participants based in the United States. For further details, see `https://luc.id/wp-content/uploads/2019/10/Lucid-IRB-Methodology.pdf`.

Before beginning, potential respondents are informed that the study is voluntary and assured that their responses will be kept confidential. We then ask for their informed consent:

> You are invited to participate in a research study that will take approximately 15 minutes to complete. You will be asked to answer some questions about yourself and your preferences.
>
> There are no known or anticipated risks to you for participating.
>
> Participation in this study is completely voluntary. You are free to decline to participate, to end participation at any time for any reason, or to refuse to answer any individual question without penalty or loss of compensation. The researcher will not know your name, and no identifying information will be connected to your survey answers in any way. The survey is therefore anonymous.

> If at any time you have questions or concerns about the survey or your rights or welfare as a research subject, contact [Author name] at [Author email].
>
> If you would like to talk with someone other than the researchers to discuss problems or concerns, to discuss situations in the event that a member of the research team is not available, or to discuss your rights as a research participant, you may contact the [Author's university] Human Subjects Committee, [phone number], [email]. Additional information is available at [Link to statement of research participant's rights at Author's university].
>
> If you would like to participate, simply click the 'I agree to participate' box below, then click the >> button to start the survey.

After a set of demographic questions, all respondents are provided the following information:

> Now you will read some information related to recent advances in biotechnology.
>
> All organisms, from bacteria to lizards to humans, have molecules called DNA, or deoxyribonucleic acid. These DNA molecules contain the genetic code for each organism. DNA provides the instructions that determine an organism's physical characteristics and control how it develops, functions, and reproduces.
>
> In recent years, scientists have developed new gene-editing technologies that can permanently alter an organism's DNA. These technologies allow scientists to make targeted changes to DNA molecules in plants and animals, modifying their biological traits. For example, scientists have edited the genes of wheat plants to make them easier to grow.

Respondents are then randomly assigned to one of four conditions:

1. Control - no additional information
2. Domestic Controversy

3. Foreign Controversy (UK)
4. Foreign Controversy (China)

Those assigned to conditions 2-4 additionally read a hypothetical news article regarding a gene-editing controversy. We show the text for the Foreign Controversy (UK) here.

> Below you will read a hypothetical news article about the use of gene-editing technology. The article describes events that could take place in the future. After you have read about the situation, we will ask for your opinions.
>
> **Birth of Genetically Altered Babies in the UK Provokes Outcry**
>
> January 25, 2021
>
> [LONDON]– A British research team announced that they have used a new gene-editing technology to alter the DNA of a group of infants. In an unprecedented intervention, scientists on the research team deleted a set of genes believed to be linked to breast and prostate cancer. The deleted genes are not considered essential to basic biological functions in humans, but the long-term effects of their removal are unclear. The research team plans to periodically examine the infants throughout their lives to assess any side effects of the genetic alteration.
>
> The disclosure this week of the research — carried out in the UK — has sparked urgent debate about the ethics of genetic alteration. The infants' birth represents a significant and controversial leap in the use of gene-editing technology. The British study has also increased concerns about a future in which parents produce "designer babies" with selectively improved traits, such as height or intelligence.

Finally, we ask respondents to rate their agreement with four statements on a scale from zero to ten.

Please indicate your level of agreement with the following statements, with "0" representing complete disagreement and "10" representing complete agreement.

- Research involving gene editing should be more strictly regulated in the US
- US patients should have access to medical treatments that involve gene editing
- The US government should provide funding for gene editing research
- Most US scientists conduct their research in a safe and responsible manner