Innovation and Interdependence: Evidence from Gene-Editing Technology*

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Abstract

Technological breakthroughs often disrupt patterns of social and economic practice, prompting calls for government oversight. What challenges confront states as they regulate novel technologies? We argue that breakthroughs induce regulatory arbitrage as well as a heretofore unstudied phenomenon: international public backlash spillovers. First, technological advancement generates forum shopping behavior as private actors race to develop the new technology. Researchers and firms may seek to evade national rules by relocating to more permissive jurisdictions. Second, public unease about new technologies creates the potential for backlash in the wake of controversial applications. This backlash can spill across borders: accidents or misuse in one jurisdiction undermine support for research and commercial development elsewhere. Together, these processes link the regulatory fate of states, undermining their ability to regulate in isolation. We test these mechanisms in the domain of gene editing, a field which has been transformed by the introduction of CRISPR technology in 2012. We find support for our argument using novel data on scientific employment patterns and a new survey experiment examining public backlash.

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1 Introduction

Technological breakthroughs are a defining feature of contemporary life. Recent advances in fields like biotechnology, digital finance, and artificial intelligence promise improved welfare through enhanced health, productivity, and economic growth. They also pose significant risks if applied in ways that cause social harm or violate ethical norms. The contemporary 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.

As a result, governments often face pressure to regulate the development and application of breakthrough technologies. They craft rules to guide the path and speed of technological progress, balancing the economic and social potential of technological change against the risk of disruption and harm. Recent efforts to regulate artificial intelligence technology exemplify this process. Countries often make different regulatory choices — imposing more restrictive or permissive rules on the use of a particular technology — as governments align regulations with public preferences and social norms.

In this paper, we explore the constraints that confront governments as they regulate breakthrough technologies. We focus specifically on a set of regulatory dilemmas that arise due to spillovers across national jurisdictions. While national governments are free to craft their own regulations, outcomes in one country depend on the regulatory choices made in other states. This strategic interdependence (Schelling, 1960) reduces states' policy autonomy, complicating efforts to govern novel technologies. While canonical international political economy scholarship focuses on the distributional effects of regulations, particularly with regard to trade policy (Mansfield & Mutz, 2009; Milner, 1988; Peters, 2015; Rho & Tomz, 2017), we show that regulators are sensitive to both international economic pressure and non-material ethical fears of technological use.

We identify two specific mechanisms that link countries' regulatory efforts in the wake of

technological breakthroughs. First, breakthroughs trigger a race to develop and commercialize the new technology, increasing incentives for forum shopping across states. Differences in national regulations create opportunities for regulatory arbitrage whereby private actors relocate scientific and commercial development to more permissive jurisdictions. In some cases, governments will face pressure to weaken standards to lure researchers, firms, and capital from elsewhere. While regulatory arbitrage and competition are well-established features of national governance (Genschel & Plumper, 1997; Mosley, 2000), we argue that technological breakthroughs often exacerbate the problem by increasing the perceived returns of relocation.

The second mechanism is rooted in public attitudes regarding technological breakthroughs. Because new technologies involve risks of harm or misuse, they generate apprehension among citizens and potential consumers (Zhang & Dafoe, 2019). When controversies occur, they may spur public backlash and undermine support for related research and commercial development in the state in which the violation occurs. We argue that backlash can spill 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. We are not aware of existing scholarship that examines international spillovers in public backlash. Nonetheless, we argue that it is an important challenge in the governance of disruptive technologies.

Both mechanisms describe how technological breakthroughs reshape regulatory pressure, operationalized by scientific flows and public opinion, weakening states' ability 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 means that effective national governance cannot insulate a country from poor regulation in another jurisdiction. These dynamics 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 refers to the targeted manipulation of an organism's genetic material. 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 recognition of the technology's revolutionary capacity for "rewriting the code of life," CRISPR architects Emmanuelle Charpentier and Jennifer Doudna received the Nobel Prize in Chemistry in 2020.[2] The development of CRISPR greatly expanded the development and application of gene-editing technology while also triggering concerns about unethical or harmful misuse. We argue that these conditions facilitate the two mechanisms described above.

We probe the mechanisms with two sets of empirical tests. We first analyze a novel dataset on gene scientist employment to examine patterns of regulatory arbitrage. Specifically, we leverage the 2012 introduction of CRISPR as a temporal shock to examine how national regulation shapes the cross-border movement of gene-editing researchers. Our results are consistent with theoretical expectations: we observe a pronounced acceleration of relocation to countries with weaker gene-editing regulations after 2012.

To test for spillovers in public backlash, we implement a survey experiment in which American respondents react to a hypothetical controversy involving the birth of genetically-altered infants, varying the country in which the controversial gene-editing activity occurred. We find that both foreign and domestic gene-editing controversies negatively affect domestic public support for gene-editing research.

Our paper adds to a growing literature on international competition, cooperation, and technological change (Canfil, 2021; Drezner, 2019; Jia *et al.*, 2022; Milner & Solstad, 2020;

[1]The acronym CRISPR stands for "clustered regularly interspaced short palindromic repeats." The term was coined by Ishino *et al.* (1987)

[2]Royal Swedish Academy of Sciences, "Press release: the Nobel Prize in Chemistry 2020," October 2020.

Perlman, 2020). We develop a theory of regulatory dilemmas in technology governance and offer new evidence in a domain, biotechnology, 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 (Ayoub & Payne, 2016; Buchanan & Keohane, 2015), we know less about governance of scientific issues in non-security sectors.[3] Biotechnology, in particular, is likely to increase in salience as governments and citizens grapple with the unprecedented technological progress in this domain. Our paper is an important initial step in examining this field.

More broadly, we identify two theoretical mechanisms — regulatory arbitrage and spillovers in public backlash — that link countries' fates as they govern breakthrough technologies. In doing so, we demonstrate how technological shocks interact with patterns of economic and political exchange to induce spillover effects among countries (Keohane & Nye, 1977). These mechanisms have clear implications for the design of international institutions, which are likely to be charged with managing these spillovers (Koremenos *et al.*, 2001).

The following section reviews international relations research on technological advancement, underscoring the distinction between incremental innovation and technological breakthroughs. Section 3 develops our argument about regulatory dilemmas in the wake of breakthroughs. We provide context on the field of gene editing in Section 4, and then present our empirical results in Section 5. A final section concludes.

2 Technology & International Politics

International relations scholars have identified a range of political outcomes associated with technological advancement.[4] Researchers have long been interested in the effects of tech-

[3]For exceptions, see Oye & Wellhausen (2009) and Perlman (2020).

[4]Follow the conventional definition in economics, we conceptualize technological advancement as a new process or method that increases productivity, enabling actors to produce more output with fewer inputs.

nology on interstate bargaining and conflict. Military technology affects the severity of the security dilemma and the stability of interstate cooperation (Jervis, 1978). Medical innovations such as vaccines and field medicine alter battlefield tactics and combat effectiveness (Fazal, 2014). More broadly, technological innovation and adoption shape the economic and military power of states (Drezner, 2019). This provides strong incentives for governments to invest in technology, especially when they confront external threats (Taylor, 2012) and when the international system is more competitive (Milner & Solstad, 2020).

In addition to shaping state behavior, technological innovation has allowed citizens, firms, and political groups to forge new transnational links. Communications technology facilitates cooperation among advocacy groups (Hall *et al.*, 2020; Keck & Sikkink, 1999) as well as transnational extremist movements (Gohdes, 2018; Mitts, 2021). Improvements in transportation, financial, and digital technologies lowers the costs of transnational exchange, spurring waves of globalization and deepening economic interdependence (Rogowski, 1987; O'Rourke & Williamson, 2001). These advancements increase cross-border flows of information, money, and goods, generating new opportunities for coercion and cooperation among states (Keohane & Nye Jr, 1973; Farrell & Newman, 2019).

These new patterns of international and transnational exchange create regulatory dilemmas for governments. For example, governments face conflicting incentives regarding the desired pace of technological adoption and continued innovation. They frequently want to limit the social and economic disruptions associated with new technologies, but a restrictive regulatory posture risks putting the country at a competitive disadvantage (Milner & Solstad, 2020; Taeihagh *et al.*, 2021). More broadly, governments grapple with the increasing cross-border mobility of information and economic assets that often accompanies technological innovation. This enhanced mobility and the associated threat of exit can constrain governments' ability to craft domestic policy in many domains (Genschel & Schwarz, 2011; Mansfield & Rudra, 2021).

We build on this body of work, examining how technology and the transnational flows it facilitates pose regulatory challenges for states. While existing research has largely focused on long-term technological shifts, we examine the political effects of *technological breakthroughs* – sudden, disruptive innovations that dramatically transform or replace existing processes. Technological breakthroughs are distinct from incremental improvements in that they contain a high degree of new knowledge (Dewar & Dutton, 1986), establish a foundation for future advancements, and accelerate further innovation (Doraszelski, 2004). These breakthroughs often trigger a phase of intense competition to improve, apply, or adapt the relevant technology (Hill & Rothaermel, 2003).

Examples of technological breakthroughs include the discovery of nuclear fission, the invention of the integrated circuit, and the recent development of generative artificial intelligence tools. Each of these technologies represents a large and sudden advancement over existing methods, spurring new opportunities and concerns about potential applications. We argue that breakthroughs merit distinct scholarly attention for two reasons. First, they create an environment of excitement, uncertainty, and anxiety that poses unique regulatory dilemmas for states. Second, the choices made by scientists, firms, and regulators in the aftermath of breakthroughs often serve as critical junctures (Collier & Collier, 2002), guiding the technology's future trajectory.[5] In the next section, we unpack two important theoretical processes that shape regulatory power in this environment.

3 Regulating Technological Breakthroughs

We argue that technological breakthroughs pose a set of unique regulatory challenges for governments. Two key dynamics often arise in the wake of breakthroughs: (1) enhanced opportunities for regulatory arbitrage and (2) spillovers in public backlash. Technological

[5]For example, the Eisenhower administration's decision after the nuclear fission breakthrough to share nuclear energy expertise with other states has shaped the use, spread, and development of nuclear technology.

breakthroughs trigger these processes by pushing technology to a new and uncertain frontier – inciting both a race for further development and substantial public anxiety. While the two dynamics are distinct, they both tend to reduce the policy autonomy of national governments as they formulate a regulatory response to new technologies.

The two processes we identify are far from exhaustive, and different policy domains are likely to have unique features that shape the autonomy and incentives of regulators.[6] Our study is an important initial step in characterizing the distinct economic and political environment of technological breakthroughs. A key implication of our argument is that breakthroughs can link the regulatory fate of states, constraining their ability to govern technology in isolation. We develop the logic of each mechanism below and then describe how they may interact.

3.1 Regulatory Arbitrage

Our first mechanism focuses on how technological breakthroughs redistribute patterns of research and production across borders. Breakthroughs set off a race to develop and commercialize new applications of the technology (Cubero *et al.*, 2021). If national rules differ in the constraints they put on technology, researchers and firms have incentives to relocate to more permissive jurisdictions. This process of regulatory arbitrage means that technological development shifts toward countries with less onerous regulation, potentially increasing the risk of accidents, misuse, or controversial applications.

Three assumptions underpin the argument that technological breakthroughs accelerate regulatory arbitrage. First, the breakthrough must increase the perceived economic or status returns of adopting and further developing the technology. This assumption holds when

[6]Many breakthroughs create or exacerbate global public goods problems that are difficult to resolve via uncoordinated national policy (e.g., the invention and diffusion of the international combustion engine has exacerbated the problem of climate change). The externalities associated with new technologies provide a separate motivation for a coordinated policy response.

technological advancement creates new economic opportunities by lowering production costs and allowing novel markets to emerge (Shea, 1998). After a breakthrough is introduced, researchers, entrepreneurs, and firms race to develop applications to exploit these opportunities. The stakes of this competition are significant. The estimated global market for artificial intelligence, for example, was $184 billion in 2024 and will exceed $826 billion by 2030.[7] The quantum computing and advanced robotics industries are similarly expected to grow drastically over the next decade.[8] Pioneer firms may secure a first-mover advantage that endures even as competitors subsequently enter the market (Lieberman & Montgomery, 1988; Agarwal & Gort, 2001), providing substantial motivation for technological development.

Second, there must be inconsistencies in national regulation such that some jurisdictions are more favorable to rapid technological development. The magnitude of regulatory divergence is likely to differ across issue areas. In the domain of gene editing, inconsistent rules stem from different cultural and religious norms, historical experiences, and state capacity (see Section 4.1). Early-stage governance of artificial intelligence differs between the United States and Europe in terms of the pace, scope, and depth of regulation (Cha, 2024). In general, national regulatory action tends to lag behind technological breakthroughs (Canfil, 2020). This can increase inconsistency in the global regulatory landscape since the use of novel technologies is often governed by a diverse set of legacy rules originally crafted for other issues.

Third, researchers and firms must have sufficient freedom of movement to relocate to more permissive jurisdictions. Their ability to do so is shaped by the physical, legal, and political constraints that shape cross-border mobility. Some technologies require significant physical capital that makes relocation difficult. In other cases – often when technologies have direct

[7] "Market Insights: Artificial Intelligence - Worldwide," *https://www.statista.com/outlook/tmo/artificial-intelligence/worldwide*, Accessed 20 June 2024.

[8] "Quantum Computing Market to Grow Exponentially; Increasing Product Applications to Generate Remunerative Market Opportunities: Fortune Business Insights," *Global News Wire*, 4 March 2022.

military applications – states strategically limit the mobility of technological expertise or material inputs.[9] More routinely, scientists are able to collaborate with colleagues abroad and seek employment in other jurisdictions if they wish. Firms similarly may have latitude to shift activities overseas. Generally, we expect technological breakthroughs to accelerate arbitrage behavior when actors have the ability to relocate across national borders. If constraints on movement are prohibitive, states can adopt restrictive regulatory postures without increasing forum-shopping behavior (Mosley, 2000).

When these three conditions are met, technological breakthroughs tend to relocate research and development to less restrictive regulatory environments – a hypothesis we test in Section 4. These incentives can set the stage for regulatory competition among governments as permissive jurisdictions lure investment and human capital from more restrictive countries.[10] An implication of this process is that, in a counterfactual world with fewer arbitrage opportunities, technological development is likely to receive more oversight but advance more slowly.

3.2 Spillovers in Public Controversies

The second regulatory dilemma arising from technological breakthroughs is based in public attitudes towards new technologies. Public opinion affects the trajectory of the technological development in several ways. Most directly, public attitudes influence regulation, which sets the pace and direction of technological development (Baron & Herzog, 2020). Beliefs about the safety and morality of new technologies shape consumer demand for associated products (Zhang & Dafoe, 2019), which is a key driver of commercial development.

[9]For example, after World War II the United States placed visa restrictions and travel controls on scientists with nuclear weapons expertise.

[10]International relations scholars have found evidence for regulatory arbitrage and competition on issues like tax policy, financial regulation, and environmental standards (Trachtman, 1993; Angelini & Cetorelli, 2003; Konisky, 2007; Genschel & Schwarz, 2011), though countervailing pressures can sometimes generate a "race to the top" (Genschel & Plumper, 1997; Porter, 1996; Prakash & Potoski, 2006).

We argue that public attitudes about new technologies are often fragile. Technological breakthroughs challenge existing systems of practice and introduce uncertainty about the safety and morality of the new technology. Most technologies are susceptible to misuse, unethical applications, or harmful accidents. With no pre-existing reference frame to anchor individuals' views and moderate extreme reactions, high profile events can create profound shifts in public opinion. For example, the infamous nuclear accidents at Chernobyl and Three Mile Island impacted global public support for nuclear energy years after the events (Verplanken, 1989; Lindell & Perry, 1990; Nohrstedt, 2005).

Public anxiety and uncertainty is highest in the period following technological breakthroughs, when the path of future technological development is unclear. This period is particularly susceptible to public backlash when controversies arise. Revelations of unanticipated effects or scandalous applications of the new technology can quickly turn public opinion against it, leading to reductions in public funding and knee-jerk regulatory responses that constrain even responsible scientific activity.

The recent history of gene therapy provides an example of such backlash. In 1999, 18-year old Jesse Gelsinger joined a clinical trial at the University of Pennsylvania for a gene therapy treatment. Unlike the other trial participants, Gelsinger suffered an unexpected and ultimately fatal immune response. The tragic death led to an immediate and precipitous drop in public support and consumer demand for gene therapies. As Nobel Prize-winner and gene-editing pioneer 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).

This example illustrates how an uncertain environment with few consistent cues engenders instability in public attitudes. As a result, novel technologies that rely on public support often progress in fits and starts, with periods of promising technological advancements interrupted by crises of public confidence. The related field of genetically-modified organisms

sees a related dynamic, where media exposure to controversies has been found to meaningfully affect public opinion (Prakash & Kollman, 2003; Drezner, 2008; Vigani *et al.*, 2012). Ciocca *et al.* (2021) similarly note the potential for "hype-induced backsliding" in the field of artificial intelligence.

Notably, public backlash often occurs in, but is not limited to, the jurisdiction in which a controversy occurs. Citizens may respond to accidents or misuse abroad by reducing their support for the technology at home. We argue backlash is usefully conceptualized as a negative spillover that spans national borders. While the choice to reduce regulatory barriers can bring economic rewards, there are also costs associated with lax regulation, including the potential for domestic public backlash. Because backlash spreads across jurisdictions, these costs are not fully internalized by the home country. Controversies may damage support for new technologies even in jurisdictions that are comparatively well-regulated. While regulatory arbitrage has been documented in other contexts, we are not aware of existing scholarship that examines the potential for international spillovers in public backlash. Nonetheless, we expect that it is an important regulatory challenge that emerges whenever a technological breakthrough is associated with safety risks or ethical concerns.

3.3 Mechanism Interaction

Figure 1 visualizes the two theoretical processes outlined above. On the left, the arbitrage mechanism is activated when a technological breakthrough occurs and countries diverge in how they regulate its application and development. This triggers forum-shopping as research activity relocates to weakly regulated jurisdictions. On the right, the public backlash mechanism is activated when a controversy emerges over the use of the technology in a given country. We anticipate this will decrease public support for the technology in other countries. The black arrows in the figure indicate hypothesized causal relationships in each mechanism which we formally test in the empirical section below.

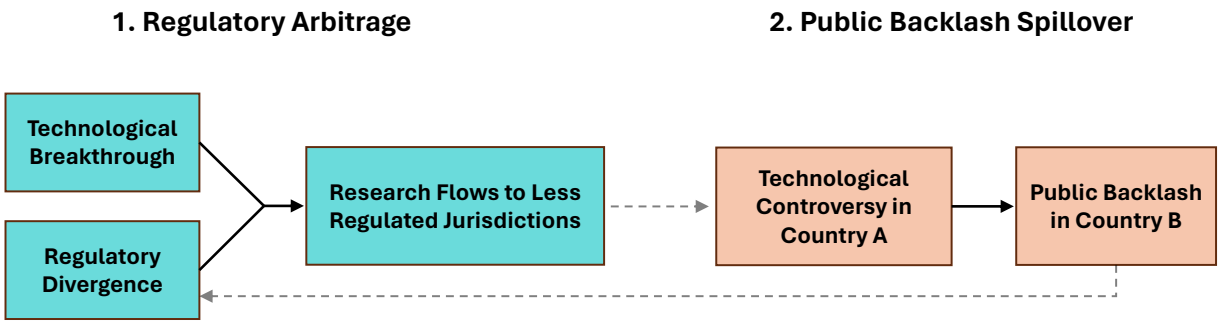

Figure 1: Illustration of the Theoretical Mechanisms and Their Interaction

While each process can occur in isolation, there is reason to believe that they interact. We speculate that there are two principal sources of interaction, which are represented by the dashed arrows in Figure 1. First, the regulatory arbitrage mechanism is likely to increase the likelihood of technological controversies. Strategic forum-shopping by scientists and firms means that more technological development occurs in poorly regulated environments. If actors in these environments are more likely to"push the envelope" in ways that incite scandals and arouse public anxiety, we should expect more frequent technological controversies as a result. Even if states anticipate this undesired outcome, they have strong incentives to maintain weak regulations: doing so allows them to capture the benefits of a permissive regulatory posture (the attraction of profit and scientific capital) while spreading the costs across other parties (the risk of a diffuse backlash that spills across borders).[11] In other words, the potential for public backlash spillovers may serve to reinforce the competitive pressures emerging from the arbitrage mechanism.[12]

A second interaction could occur if the backlash created by technological controversies triggers a regulatory response in other jurisdictions in addition to at home. Once controversies happen, they may effectively reduce regulatory divergence by prompting other countries

[11]This undesired outcome could be resolved if states upheld a common regulatory standard – one reason why many call for an internationally coordinated policy response to technology governance.

[12]Controversies are not limited to low-regulation jurisdictions: actors in highly regulated states may initiate technological scandals that further depress global public confidence in the technology.

to impose more onerous regulatory constraints in response to public concern. An implication of this interaction is that the two mechanisms could jointly produce a long-term equilibrium of regulatory *convergence* across countries. [13]

South Korea's experience in the biotechnology industry at the turn of the 21st century provides a useful illustration of the mechanisms we seek to examine. Spurred by its robust scientific infrastructure and permissive regulatory environment, South Korea became a leader in cloning technology in the late 1990s. High profile experiments in cloning, including the successful cloning of animals and reports of clones of human embryos, aroused public anxiety and led the government to explicitly ban human cloning in 2002.[14] But cloning research on embryonic stem cells continued to be funded and lauded by the government. In late 2005, reports surfaced that the country's most celebrated cloning researcher had fabricated findings and coerced female lab members to donate eggs for his research. The ensuing scandal soured public support for related technologies in Korea and abroad. The Korean government strengthened regulations and increased scrutiny of cloning research (Hong, 2008). In addition to illustrating public opinion dynamics, the episode offers some support for regulatory arbitrage dynamics. Domestic scientists immediately objected to the new regulations, arguing "that only the Republic of Korea was regressing at a time when foreign scientists [had] started research on somatic [..] cells" (Hyeon *et al.*, 2023). In the ensuing years, Korean scientists moved their labs to the US, China, Qatar, and other less-regulated countries in

[13]Evidence for policy convergence since the 2012 introduction on CRISPR is mixed and incomplete. Regulatory changes have proceeded slowly as states assess the extent to which contemporary gene editing is different from classical genetic engineering (Vogel, 2018). Several states, including China and South Korea, took steps to strengthen regulations since the He Jiankui controversy, though some challenge whether these are sufficient (Vogel, 2018; Ghosh, 2023). Even as international guidelines continue to advocate for caution in advancing the technology (UK Royal Society, 2023), both the UK and US approved new gene-editing therapies for sickle cell disease in late 2023.

[14]Claims by the South Korean company Clonaid that it successfully cloned a human baby turned out to be a hoax, though it still played a pivotal role in encouraging the government to strengthen regulations.

order to continue research (Zastrow, 2017).[15] We provide an expanded discussion of the the Korea example in Appendix A.6. The following section turns to the field of gene editing, the basis for our empirical tests.

4 Gene Editing: Technological and Political Landscape

We look for evidence of our two mechanisms in the domain of gene editing, a field that has been transformed by scientific advances over the past decade. The purpose of gene editing is to suppress or alter the biological traits of an organism. The field emerged in the 1970s, when scientists began splicing together naturally-occurring genetic material, and by the early 2000s scientists were leveraging cells' own DNA-repair technology to selectively edit specific genes (Gupta *et al.*, 2014).

The emergence of the CRISPR method in 2012 represents a particularly significant breakthrough in gene-editing technology. The name CRISPR — an acronym for "clustered regularly interspaced short palindromic repeats" — refers to a series of repeating DNA sequences originally found in bacteria. These sequences allowed bacteria to recognize and destroy the DNA of harmful viruses. Scientists repurposed this technique for programmable gene editing (Jinek *et al.*, 2012). The result was a significantly more accurate, efficient, and economical tool for altering DNA.

In the years since its development, CRISPR has become the dominant gene-editing technology (Carroll, 2018).[16] Like other breakthrough technologies, CRISPR dramatically reduces the costs associated with editing genes: by 2019, a gene-editing template that cost $1000 to design using rival technologies could be produced with CRISPR for $65 (Shwartz,

[15] In the words of Hyeon *et al.* (2023): "The Republic of Korea's Bioethics Act was enacted in a way that allowed too much research. As a result, life science researchers have deviated and the level of regulation of the Bioethics Act has increased, hindering research development."

[16] Figure A1 in the appendix shows the frequency of CRISPR patent applications compared to rival methods like TALENs and ZFNs.

2019). CRISPR's low cost and ease of use have contributed to its rapid diffusion to laboratories around the world.[17]

The CRISPR technological breakthrough has stimulated a "biotechnological revolution" in basic research, clinical care, agriculture, and other fields (Knott & Doudna, 2018). New gene therapies are being developed to treat cancer and correct harmful genetic mutations (Khan *et al.*, 2016). Agricultural producers are applying CRISPR to both plants 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 and treatments for COVID-19 (Straiton, 2020).

4.1 Regulation of Gene-Editing Technology

The use of gene-editing technology is governed by a fragmented patchwork of norms, national laws, and international guidelines. When targeted gene editing first became feasible in the 1970s, scientists attempted to construct self-governing arrangements for 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 (Berg & Mertz, 2010).

In recent years, similar efforts have sought to establish new norms for the research community. A 2019 conference of geneticists called for a global five-year ban on editing DNA in human eggs, sperm, or embryos that are brought to term (Lander *et al.*, 2019); how-

[17]In Appendix Figure A2, we display the number of laboratories registered with AddGene, a popular genetic material repository for peer-reviewed genetics research. An employee of this repository estimated that 25% of requests are for CRISPR-related materials (Interview by authors, 11.25.2019). American laboratories are the largest group, followed by China, France, Japan, India, and Germany.

ever, there is dissent about this approach even among the most prominent gene researchers (Cohen, 2019). The lack of consensus creates uncertainty about appropriate applications of gene-editing technology, potentially contributing to misuse. In addition, it is unclear whether voluntary, decentralized rules can succeed in an era when gene-editing technology is more accessible and diffusely distributed than in the 1970s.

As gene-editing technology progressed, national regulations began to supplement scientific norms. Early U.S. guidelines built upon the partial gene-editing moratorium of 1973-4 (Baskin *et al.*, 2016). Other countries followed suit as the technology 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.[18] Some have less formal "guidelines" prohibiting germline editing, while others are more permissive in the constraints they place on the technology (Araki & Ishii, 2014; Ishii, 2017). Figure 2 displays a composite measure of national gene-editing regulations combining information from three recent surveys of regulatory policies.[19] Countries are shaded according to regulatory rigor, with darker shades indicating more restrictive national rules.[20]

Inconsistent rules across countries stem, in part, from different historical experiences and cultural expectations regarding the appropriate use of gene-editing technology. For example, Germany's experience with unethical experiments during the Nazi regime has shaped the state's regulation of human subjects research. South Korea's strict biological research guidelines arose in response to high-profile research ethics controversies (Resnik *et al.*, 2006). The United States maintains comparatively weaker regulations for gene editing, consistent with a

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

[19]Source data are from Araki & Ishii (2014), Isasi *et al.* (2016), and Baylis *et al.* (2020). For details on these measures and the construction of the composite measure, see Section 5.1.

[20]Countries with no identifiable gene-editing regulations are not colored.

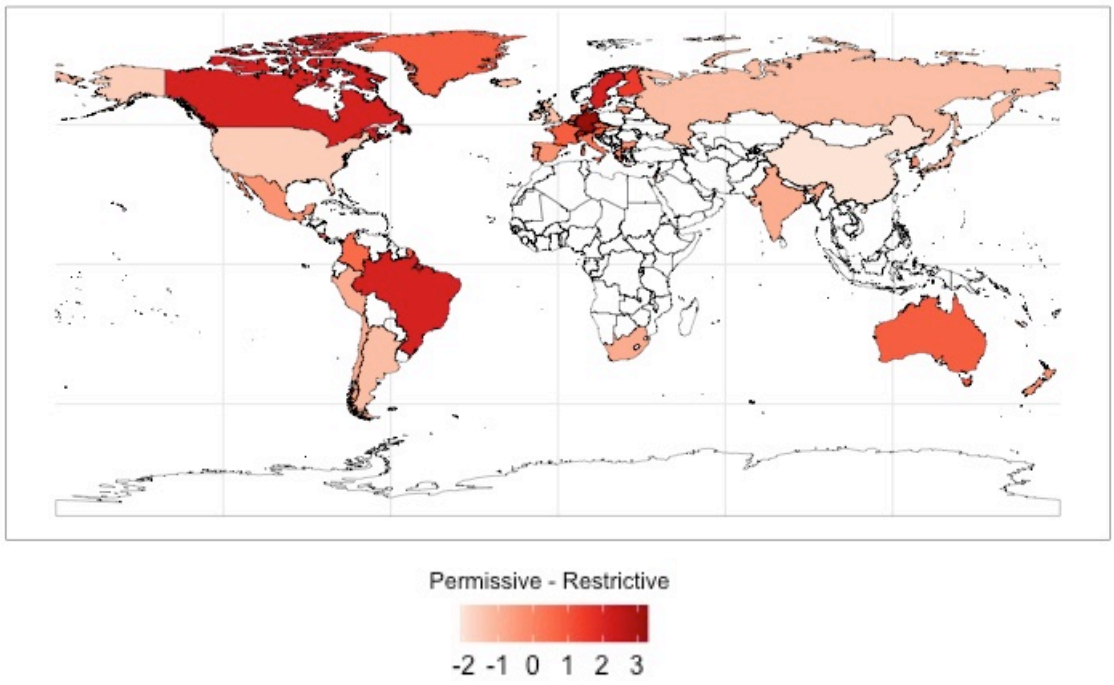

Figure 2: *National Regulation of Gene-editing Technology.* Thirty-nine countries are rated by the permissiveness of national gene-editing technology regulations. Ratings combine data from Isasi *et al.* (2016), Araki & Ishii (2014), and Baylis *et al.* (2020). See Section 5.1 for details on the coding and source data.

policy process that is more receptive to industry influence.[21] Permissive regulations in China are driven in part by pressure to outpace Western countries in technological innovation as well as resistance to international biotechnology standards (Kleiderman & Ogbogu, 2019). In many cases, however, outdated 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 political cleavages common to other issue areas (e.g., geopolitical rivalries or North-South divisions). A set of legacy international agreements, negotiated in the 1990s in reaction to concerns about

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

cloning, provide a precedent for global governance of genetic research.[22] In recent years, however, formal international institutions have been slow to develop rules despite calls for new global standards.[23] The World Health Organization is among the few intergovernmental organizations explicitly addressing the issue, releasing a set of non-binding recommendations in 2021 for appropriate oversight of human genome editing (WHO, 2021).

4.2 Arbitrage and Backlash in Gene-Editing Technology

CRISPR is clear case of a technological breakthrough that reduces the ability of states to independently regulate gene-editing research and applications due to its low cost and high public salience. While there are longstanding concerns about regulatory arbitrage in genetic research,[24] recent innovations have increased both the demand and ability to circumvent regulatory constraints.

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 worth approximately $3.8 billion and is projected to exceed $10 billion in the next five years (Ugalmugle & Swain, 2020). The most direct applications are in the healthcare industry, where firms are developing gene therapies to address a range of disorders and chronic illnesses. Other sectors like agriculture, veterinary medicine, and industrial production processes also increasingly draw on gene-editing technology (Brinegar *et al.*, 2017). Given the array of market applications, the competition for these economic returns is fierce.

Firms have lobbied governments to lower regulations on the technology in order to capture

[22]The 1997 Oviedo Convention prohibits human cloning, genetic screening for non-health purposes, and the misuse of innovations in biomedicine and bans. The 1997 Universal Declaration on the Human Genome and Human Rights and subsequent UNESCO declarations address genetic data and trade in genetic resources.

[23]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.

[24]The potential for regulatory arbitrage was raised in the 1970s as several clinical trials moved to Europe and South America to sidestep burdensome rules in the United States (Baskin *et al.*, 2016).

these economic benefits. European plant breeders have pressed the EU to relax gene-editing restrictions, arguing that existing rules put them at a competitive disadvantage.[25] South Korea recently instituted a review of rules on gene therapy research in order to maintain its competitiveness in medical technology (Ji-young, 2017). In the United States, the government bowed to agricultural producers' demands to weaken restrictions on gene-edited crops and livestock (Cancryn & Crampton, 2021). Other countries have announced similar regulatory reviews or new public initiatives to capitalize on gene-editing technologies.[26]

When regulatory barriers remain, actors have moved research and development to more permissive rules. Baylis (2019) describes several incidents in which US-based scientists relocated embryonic genetic research on embryonic DNA to clinics in Mexico and Ukraine "so as to not violate US federal law" (46).[27] Isaacson (2021) similarly reports that entrepreneurs seeking to develop gene-editing applications in reproductive care openly acknowledge the ability to evade strict regulations.[28]

As with other technologies, however, rapid progress has been accompanied by public anxiety and fears of misuse. Actors in both academia and industry are keenly aware that continued research depends on managing public anxiety about gene editing. Participants at a 2015 conference on gene editing, for example, called for slowing down the more controversial germline gene-editing research "in order to create a safe political space" (Isaacson, 2021, 288). Historically, controversies regarding one application of gene-editing technology have

[25]Max Planck Institute, "Regulating genome edited organisms as GMOs has negative consequences for agriculture, society and economy", `https://www.mpg.de/13748566/position-paper-crispr.pdf`.

[26]Policymakers in New Zealand are reviewing the country's gene-editing regulations (Morton, 2019), and the Russian government recently announced a collaboration with Rosneft to develop gene-editing technology (Morton, 2020).

[27]The Ukraine clinic now boasts patients from Ukraine, the US, Israel, and Spain in further evidence of forum-shopping for gene-editing products (Baylis, 2019, 47).

[28]An entrepreneur responded to questions about FDA regulations of CRISPR for gene-editing babies by saying that "clinics did not have to be in the US. There would likely be other countries where the procedure would be allowed, and people who could afford gene-edited babies would be willing to travel" (Isaacson, 2021, 286).

diminished investor interest more broadly (Gardner, 2020), as reflected in the Jesse Gelsinger tragedy. Advocates for scientific and national regulation of gene editing frequently cite "increasing legitimacy and trust" as a primary goal (Kuzma *et al.*, 2018, 23). Aiyegbusi *et al.* (2020), for example, identify public perceptions of gene therapies as "central to their uptake and use."

Concern about inappropriate genetic modification escalated in 2018, when the Chinese scientist He Jiankui announced the birth of the world's first gene-edited infants. He used CRISPR to genetically alter several embryos in order 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 traits that will pass to subsequent generations.[29] Calls for a global moratorium on some avenues of gene-editing research swiftly followed the revelation of He's experiment (Lander *et al.*, 2019). Recognizing the potential for public backlash, leading scientists were quick to condemn the research. A senior colleague accused He of "jeopardizing the entire field of genetic engineering" (Isaacson, 2021, 306).[30] Chinese scientists working in the field of gene editing expressed concern after the sentencing "that the international condemnation that followed He's explosive announcement in 2018 might have a wider chilling effect on CRISPR work in China" (Cyranoski, 2020).

In summary, the recent history of gene-editing research provides suggestive evidence that technological breakthroughs are associated with both public anxiety and attempts to evade stringent regulations. In the following section, we look for systematic evidence of regulatory arbitrage and public backlash spillovers in this field.

[29]In Appendix Section A.4, we illustrate this public backlash using data from Twitter posts surrounding the He Jiankui controversy. In a sample of over 50,000 tweets, we demonstrate that posts about gene-editing increase in volume, negative sentiment, and moral outrage in multiple countries following the scandal.

[30]After initially heralding the achievement, China sentenced He and two colleagues to three years in prison for "illegal medical practice" (Cyranoski, 2020).

5 Empirical Tests

We present two empirical tests of the mechanisms outlined above. First, we leverage data on scientific employment to examine patterns of regulatory arbitrage. Because we expect the CRISPR revolution to accelerate arbitrage behavior, we use the year in which CRISPR was introduced as a cutpoint in the analysis. We test whether gene-editing researchers are systematically more likely to move to countries with weaker regulations after 2012. We also examine whether countries with permissive regulations benefit from increased scientific collaboration, patent applications, and clinical trial development in this period.

For the second test, we identify the presence of public backlash using an original online survey experiment on American respondents. We randomly assign information about a hypothetical gene-editing controversy and examine its effect on public support for gene-editing research and policy. 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 towards gene-editing use and policy in the United States.

5.1 Regulatory Arbitrage

We argue that, in the wake of technological breakthroughs, actors seek to evade strict regulations by relocating to jurisdictions with weaker rules. To test this claim, we analyze employment patterns of over 100,000 gene researchers. We also look for evidence of forum shopping in the commercial development of gene-editing technology using data on clinical trials and patent applications.

Our independent variable for these tests is the rigor of national regulations governing gene-editing technology. We develop a composite national regulatory score drawn from three distinct sources: Isasi *et al.* (2016) rates the stringency of national regulations related to gene-editing, Araki & Ishii (2014) focuses on heritable gene-editing regulations, and Baylis

et al. (2020) collects data on rules for research using genetically modified embryos.[31]

The three measures are positively correlated but prioritize different applications of gene-editing technology. We combine them into a broad measure of each country's regulatory environment via principal components analysis. This provides a continuous, cross-national measure of gene-editing regulation for 39 countries that engage in gene research and clinical development.[32] Cross-national variation in these regulations is visualized in Figure 2. The regulatory scores are centered at zero and range from -2.1 to 3.3, with higher values indicating more restrictive regulations.

To look for evidence of accelerated arbitrage, we examine whether gene scientists are more likely to relocate to countries with more permissive regulatory standards following the introduction of CRISPR in 2012. Theoretically, institutions located in countries with more permissive regulatory standards will be comparatively more attractive destinations for researchers in the post-CRISPR era. We examine employment patterns of researchers who have published scientific papers in the field of gene editing. We extract all published articles on the topic of "genetic engineering" from 2002-2021 from *PubMed*, a large database of biomedical publications. We match these articles with a separate database, *Web of Science*, to identify the institutional affiliations of the authors in the *PubMed* sample.[33] This process enables us to identify an author's country of employment at the time of an article's publication. The search yields approximately 120,000 papers and over 100,000 unique gene-editing researchers.

Using this record of scholarly publications, we construct a dataset of researcher movement. We structure our data as a series of directed country-dyads. An observation reflects

[31] Appendix A.7 details the construction of the composite measure.

[32] The three data sources vary widely in geographic coverage. Thirty-nine countries are classified by at least two sources. For these countries, we impute the missing scores before estimating the principal components.

[33] We exclude two sets of researchers: 1) those without a listed institutional affiliation, and 2) those with very common names (appear 100 times or more in our sample). We classify each researcher's country of employment using their institutional affiliation.

the number of gene researchers who relocate from country i to country j in year t.[34] In the year 2005, for example, twelve scientists who were most recently employed in Japan published papers while employed in the United Kingdom. Another ten moved in the opposite direction, relocating from the United Kingdom to Japan. We also include observations representing scientists who remain in their "home country": in 2005, 737 researchers most recently employed in the UK remained there and published papers. These counts of gene scientist relocations serve as the dependent variable in the tests below.

Of the 262,377 employment records we observe in our sample, 27% represent relocation across international borders while 73% remain in their country of prior employment. While international relocations occur for many reasons (institutional prestige, more generous funding, familial ties, etc.), we argue that the regulatory environment of each country shapes decisions on the margin, and that the effect of regulatory differences will be larger in the CRISPR era.

To test these patterns systematically, we construct a variable, `Regulatory Difference`, that subtracts the former country regulatory score from the researcher's country of current employment. Positive values mean that the destination country has stricter regulations than the origin country. We interact this variable with an indicator for the time period (2012-present) when the CRISPR breakthrough is hypothesized to accelerate forum-shopping behavior. These models exploit the technological shock of CRISPR to estimate how employment patterns respond to regulation in the wake of technological breakthroughs. We expect the introduction of CRISPR to magnify the effect of regulatory differences. If we are correct, we should observe a negative and statistically significant coefficient for the interaction term; this indicates that researchers are more likely to seek out permissive jurisdictions after the

[34] As the ability of scientists in a given country to publish research may be related to the state of gene-editing technology, we restrict the sample to researchers who published at least one paper before the introduction of CRISPR in 2012. The data therefore reflect employment relocations among gene scientists who were active researchers before the technological shock.

CRISPR breakthrough.

We include a battery of control variables to address confounders related to each country's national economic output, human capital, and commitment to research funding. We include `GDP` to account for each country's overall economic capacity and `GDP per capita` for its level of development. To address the possibility that a country's underlying scientific capacity drives both gene-editing regulations and employment patterns, we use several controls for scientific capital. These include an annual count of patent applications in a country (`Patents`) and a measure of annual `R&D` expenditure for each country.[35] As an additional measure of scientific capacity, we include a count of the number of elite universities in each country (`Universities`), along with the average ranking of national universities according to the Times Higher Education World University Rankings.[36] Separately, we add an indicator for same-country pairings to account for the high propensity of researchers to remain employed in the same country over time. We include dyad fixed effects in some specifications to control for features specific to each country pair.

Table 1 reports the results of several linear models estimating the effect of regulatory difference on scientific relocation, before and after the CRISPR breakthrough. Standard errors are clustered by country dyad. Column 1 presents a baseline model with the `Regulatory Difference` measure, an indicator for 2012-present (`CRISPR`), and the interaction term. The positive and statistically significant coefficient for the `CRISPR` variable indicates a higher propensity for employment relocation after 2012. This suggests that the technological shock generally increased cross-border mobility of researchers. More importantly, the interaction term `Regulatory Difference` $\times$ `CRISPR` is negative and significant, indicating that restrictive jurisdictions become substantially *less* attractive destinations after 2012. This result is consistent with enhanced flows of researchers into more permissive

[35]GDP, patent, and R&D data are from the World Bank's World Development Indicators (WDI).

[36]The Times rankings include the top 1,906 global universities across 108 countries.

	DV: Scientific Relocation		
	(1)	(2)	(3)
Regulatory Difference	−0.010	0.038	0.038
	(0.010)	(0.028)	(0.028)
CRISPR	9.355***	9.423**	1.971**
	(3.409)	(4.370)	(2.597)
Regulatory Difference×CRISPR	−0.025*	−0.034**	−0.034**
	(0.014)	(0.017)	(0.017)
Controls		✓	✓
Dyad FE			✓
Observations	22,730	22,730	22,730

Table 1: *Employment Relocation of Gene Researchers*: Linear model estimates for the volume of gene-editing researchers who relocate to institutions in another country. Columns 2 and 3 control for GDP, GDP per capita, Patent applications, R&D expenditures, and number and mean rank of elite higher education institutions (coefficients not shown; we include these measures for both the origin and the destination country). Standard errors are clustered by country dyad. Statistical significance is denoted by: *p<0.1; **p<0.05; ***p<0.01.

jurisdictions in the wake of the CRISPR breakthrough. Columns 2 and 3 find broadly similar results after adding the full set of covariates as well as dyad fixed effects. Substantively, a one-unit increase in `Regulatory Difference` reduces scientific relocation by approximately 0.03 researchers per year after the CRISPR breakthrough. This modest effect is meaningful once aggregated over the time period. For example, the results suggest that a high-regulation country like Germany has lost approximately 31 gene-editing researchers due to forum shopping from 2012-2019.

A possible challenge to inference is that permissive jurisdictions (e.g., China, Ireland, and the United States) may be attractive destinations for scientists for reasons other than their regulatory environment. While many potential motivations are addressed via control variables, we also conduct a placebo test to examine whether researchers in unrelated fields

relocate to locations with permissive gene-editing regulations in this time period. In Appendix Table A1, we replicate the analysis above using employment patterns of researchers in an unrelated field. We see no significant change in relocation patterns after 2012.

Finally, to gauge whether forum-shopping behavior extends beyond the relocation of gene scientists, we probe a series of other outcomes – scientific coauthorships, gene therapy clinical trials, and gene-editing patent applications – that might be similarly responsive to arbitrage behavior. These tests are structured at the country-year level and include the same control variables listed above. In Column 1 of Table 2, we examine whether gene-editing researchers in highly regulated jurisdictions are incentivized to seek more international coauthors as an alternative means to evade national rules. The positive interaction coefficient suggests that scientists working in strict jurisdictions may have increased international coauthorship after 2012, but the estimated effect is not statistically significant. In Columns 2 and 3, we find evidence that strict regulatory environments tend to experience fewer registered clinical trials and a lower volume of relevant patent applications after the introduction of CRISPR in 2012.

5.2 Public Backlash

We next examine cross-national spillovers arising from public controversies via a survey experiment. The survey examines backlash among the general public in response to a hypothetical, norm-violating application of gene-editing technology. 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 a sample of 1,075 Americans quota-

	Dependent variable:		
	Int'l Coauthors	Clinical Trials	Patents
	(1)	(2)	(3)
Regulation	412.26***	−259.681***	−37781.362***
	(90.319)	(26.414)	(5630.606)
CRISPR	7.782***	2.163***	134.264**
	(1.395)	(0.622)	(53.068)
Regulation×CRISPR	0.856	−1.083*	−180.149***
	(0.728)	(0.575)	(53.900)
Controls	✓	✓	✓
Observations	602	602	550

Table 2: *Effect of National Regulations on Coauthorship, Clinical Trials, Patents.* The table displays coefficient estimates and dyad-clustered standard errors from a linear model. Statistical significance is denoted by: *p<0.1; **p<0.05; ***p<0.01.

sampled to US census margins.[37] 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 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.

[37]See Appendix A.3 for full survey text and Table A2 for sample summary statistics. While the survey was fielded on a sample of 1,200 respondents, we restrict our sample to the 1,075 individuals who passed pre-treatment attention checks. Our survey was conducted on the platform Lucid, and 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.

Respondents randomly assigned to the control condition continue directly to the outcome questions; treated respondents read additional information about a gene-editing controversy. Among treated respondents, we randomize whether the controversy occurs in the US, UK, or China. The treatments are presented as a hypothetical news article set in near future. 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.

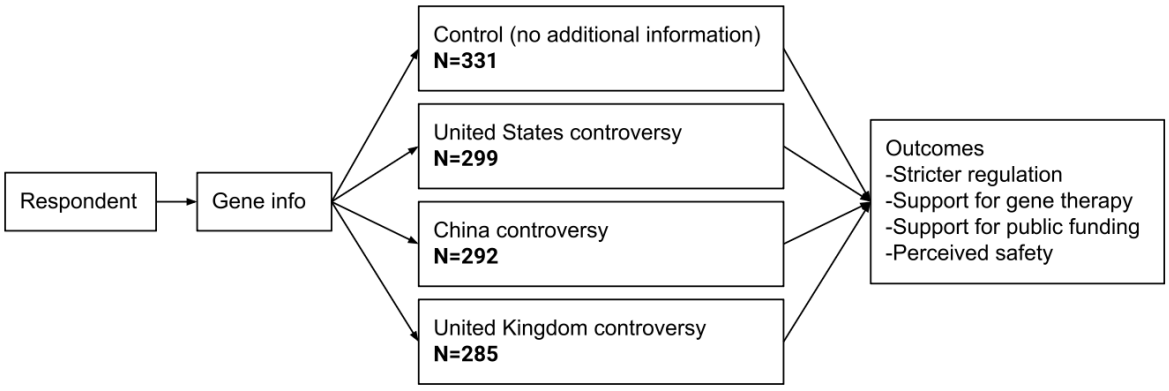

Figure 3: *Survey schematic*

After treatment assignment, respondents rate their agreement with the following four statements on a scale of 0 (no agreement) to 10 (complete agreement).

- 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 public confidence in the safety of gene-editing technology and support for continued development. Respondents' answers constitute our dependent variables in the analyses below. Figure 3 visually depicts the survey structure.

Our theory of public backlash against breakthrough technologies generates several empirical predications. First, we expect that respondents who read about a controversy in their own country will be less supportive of gene-editing research. If such "domestic public backlash" exists, the domestic controversy treatment should increase demand for strict regulation, decrease support for gene therapies, reduce willingness to fund gene-editing research, and depress 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 4. Coefficients represent the treatment effect of exposure to a gene-editing controversy, compared to the control (no controversy) condition.[38] Within each panel, we display the effect of a domestic controversy, a foreign controversy in the United Kingdom, and a foreign controversy in China.

We find evidence of domestic public backlash in three of four outcomes. Relative to a baseline of reading only the introductory text explaining gene-editing technology, 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 ($p = 0.02$) and public funding for gene-editing research ($p < 0.01$). They also have diminished perceptions of the safety and responsibility of scientific research ($p = 0.05$) 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 ($p = 0.61$). 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 A4 for the distribution of responses).

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 ($p < 0.01$). Respondents also reduce confidence in the responsibility of US scientists ($p = 0.02$) and support for gene therapies ($p < 0.01$) in the China condition. The UK controversy does not affect perceptions

[38]See Table A3 in the appendix for point estimates and standard errors. Table A4 reports similar results among respondents who passed an alternative attention check.

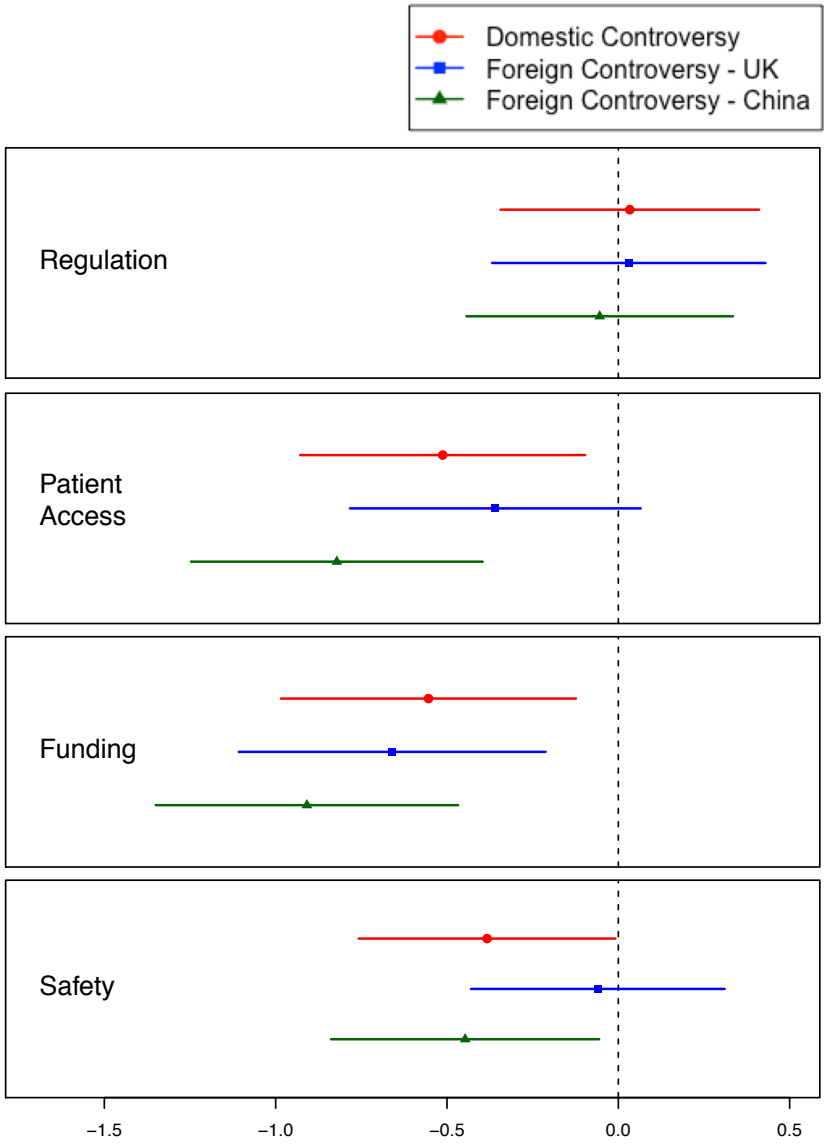

Figure 4: *Public Response to Gene-Editing Controversy.* The figure shows the treatment effect of a hypothetical gene-editing controversy in the US, UK, and China, with 95% confidence intervals. The panels report effects on the four dimensions of public support listed above.

of safety but does decrease support for gene therapies ($p = 0.07$). 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. Controversial research in one national jurisdiction nega-

tively impacts domestic support for gene editing in other countries for a number of public policy outcomes. Notably, we find this effect even though the foreign controversy imposes no direct material consequence on respondents.[39] Instead, citizens appear to draw generalized inferences about the safety and morality of new technologies based on their use abroad.

6 Conclusion

This paper offers new insight into a set of international spillovers associated with governance of technological breakthroughs. Two mechanisms link breakthroughs to regulatory dilemmas: arbitrage and spillovers in public backlash. Regulatory arbitrage is likely to occur when countries maintain disparate rules and technological breakthroughs increase the motivation to move to less strictly regulated jurisdictions. Using novel data on scientific employment, co-authorship, clinical trials, and patents, we test whether regulatory arbitrage occurs in the wake of scientific breakthroughs. We show that, after the discovery of CRISPR, weaker national regulations lure more scientific talent.

Additionally, controversial applications of technology trigger public backlash that can spill across national boundaries. To our knowledge, 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, abandoned commercial applications, and harsh regulatory responses. We demonstrate the mechanism in an original survey experiment on American respondents and confirm its external validity using social media data from a real-life controversy. The consequences of permissive regulation are not limited to a single country: if controversial misuse occurs in one jurisdiction, the resulting backlash spills across

[39]In some cases, technological controversies could directly affect the global commons, prompting more immediate concerns about material welfare (e.g., cross-border environmental impacts of nuclear accidents). Our experimental vignette is unlikely to trigger these concerns.

national boundaries. Our findings support the existence of a public backlash spillover that can undermine confidence in gene-editing technology.

Taken together, our results suggest that technological breakthroughs can create dilemmas for states as they craft national regulations. Breakthroughs accelerate regulatory arbitrage and threaten to destabilize public opinion through technological accidents or misuse in other countries – both of which erode the policy autonomy of states. Together, these mechanisms provide states with compelling incentives to lower regulatory barriers beyond their preferred level, ex ante. 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.[40] If misuse does occur, the resulting public backlash could reduce demand for the technology or lead to knee-jerk regulatory reactions, halting continued progress. While we do not test all of these implications in this paper, they provide promising avenues for future research.

Our empirical tests shed new light on the politics of biotechnology, an understudied but increasingly important domain, but these dynamics are also likely to recur in the governance of breakthrough technologies more generally. Future research expanding empirical tests to other fields is needed to assess the generalizability of our argument. In addition to contemporary technologies like artificial intelligence, historical disruptions such as the nuclear energy and information technology revolutions may have similarly presented regulatory dilemmas via these mechanisms. Different states may also be more or less susceptible to the mechanisms we posit: variation in domestic industries, historical experiences, regime type, and status concerns could affect countries' ability to manage governance in the face of technological breakthroughs.

[40]While we do not directly test the effect of regulation on scientific scandals, we observe a positive correlation between weak regulatory environments and retractions in gene editing studies (see Appendix A.5).

By illuminating how regulation of technology is constrained by spillovers across states, our findings make an implicit case for international policy coordination (Oye *et al.*, 2014). International institutions are designed to manage interdependence and reduce transaction costs (Keohane, 1984; Haggard & Simmons, 1987). The recent guidelines adopted by the World Health Organization (WHO, 2021) are consistent with this function. The recommendations establish a floor of basic ethical and safety protections and encourage harmonization of disparate rules governing the technology. If successful, this would limit the scope for regulatory competition and reduce the risk of scandalous applications.

More broadly, our paper helps outline a new agenda for understanding how technologies affect interstate cooperation and the demand for global governance. Emerging technologies shape a range of transnational spillovers in addition to the two we emphasize here. Genetic manipulation of the natural environment, including vegetation or insect populations, can easily traverse national jurisdictions. Similarly, the use of digital currencies may disrupt international financial systems or exacerbate collective action problems like carbon emissions. Advancements in artificial intelligence and robotics could reshape labor demand in ways that interact with the politics of trade, human rights, or military competition. Future work should test and expand upon these effects of technological innovation.

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1 Appendix

A.1 Tables

	DV: Mental Health Scientist Relocation	
	(1)	(2)
Regulatory Difference	0.048	−42.89
	(0.047)	(33.28)
CRISPR	0.118	14.09
	(0.147)	(9.63)
Regulatory Difference × CRISPR	0.023	−0.006
	(0.078)	(0.0146)
Controls		✓
Dyad FE		✓
Year FE		✓
Observations	20,592	14,435

Table A1: *Placebo Test: Employment Relocation of Mental Health and Eating Disorder Researchers*: Linear model estimates for the volume of mental health and eating disorder researchers who relocate to institutions in another country. Column 2 includes the following controls (not shown): *GDP origin country*, *GDP destination country*, *GDP per capita origin country*, *GDP per capita destination country*, *Patent Applications origin country*, *Patent Applications destination country*, *R& D origin country*, and *R&D destination country*. Standard errors are clustered by country dyad. Statistical significance is denoted by: *p<0.1; **p<0.05; ***p<0.01.

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 A2: *Survey sample statistics*. For each category, we report the proportion of respondents who fit into the category among those that answered the relevant question.

	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 Respondents who pass Manipulation Check*. Results of the survey experiment on the sample of respondents who successfully pass a manipulation 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

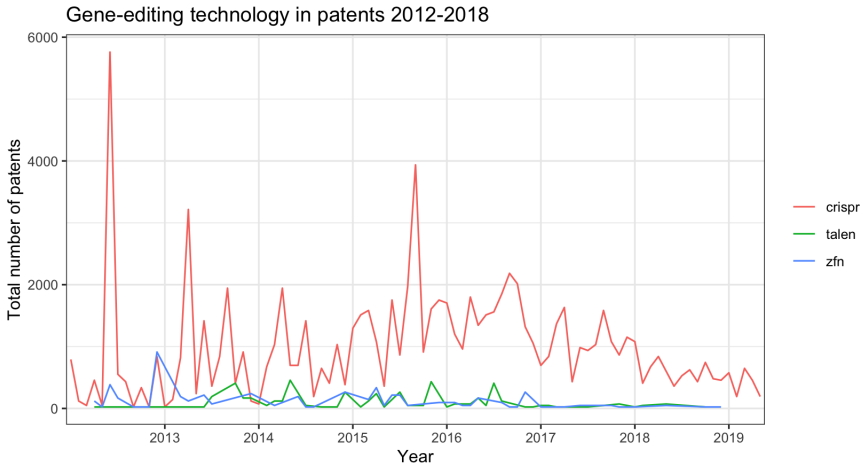

Figure A1: *Gene-editing Patent Applications, 2012-2018*: The figure displays annual patent applications related to CRISPR (red), TALENS (green), and ZFN (blue) technologies. Data from Oribit Intelligence.

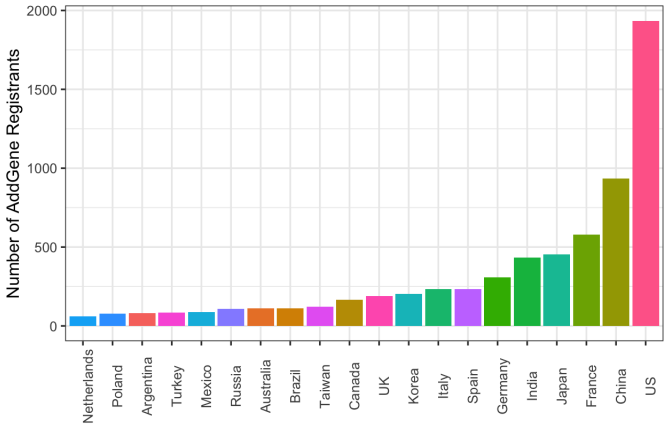

Figure A2: *AddGene Registered Researchers by Country of Origin*: Number of researchers registered on the AddGene website by country of origin. Data collected by authors. AddGene is an organization that stores and disseminates genetic material used in published studies. AddGene has served as a popular repository for CRISPR plasmids since Jinek *et al.* (2012) used it to store materials from their landmark paper. Researchers 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. Although CRISPR-related materials are a minority of AddGene's repository, they are among the most commonly requested plasmids from researchers.

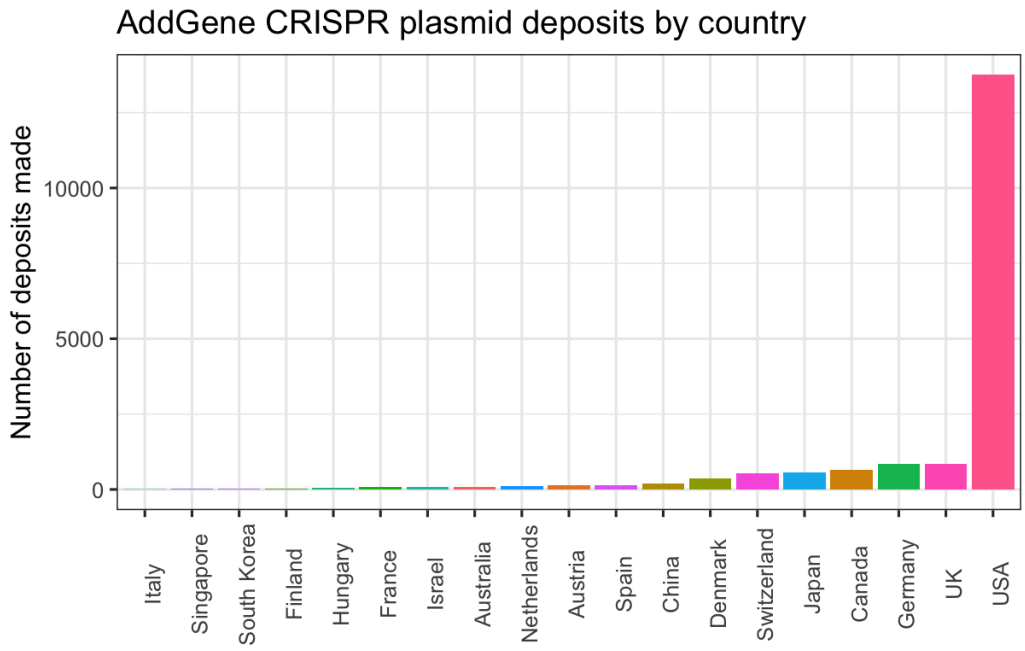

Figure A3: *AddGene depositors by Country of Origin.* Data collected by authors.

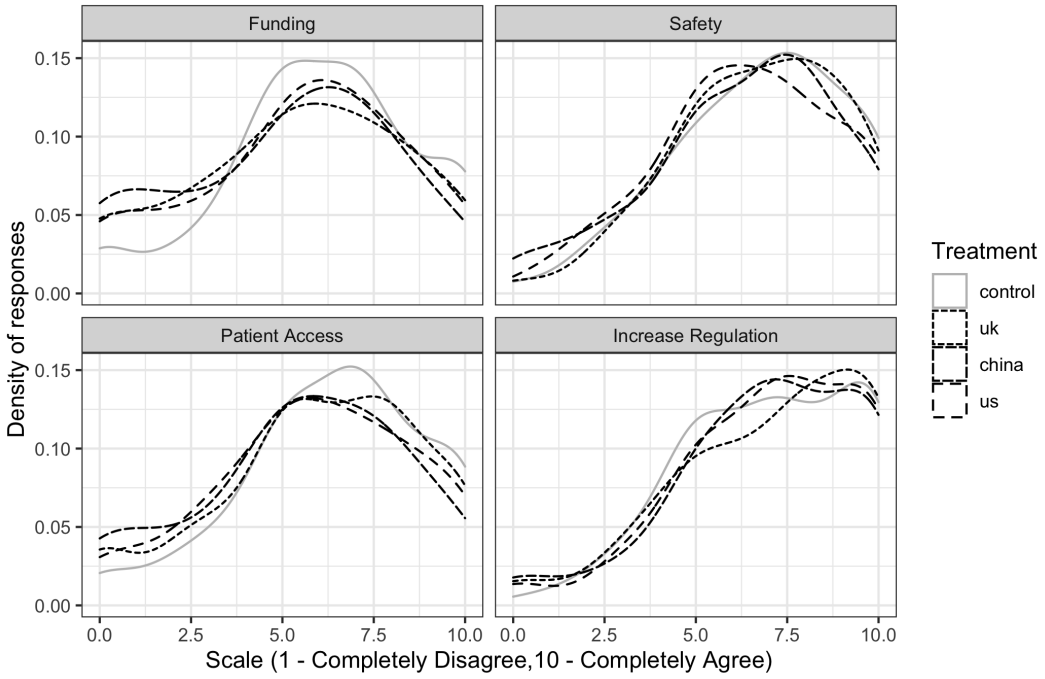

Figure A4: *Distribution of Responses for Outcome Variables.* The figure displays the distribution of responses by treatment condition for each of four outcomes.

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

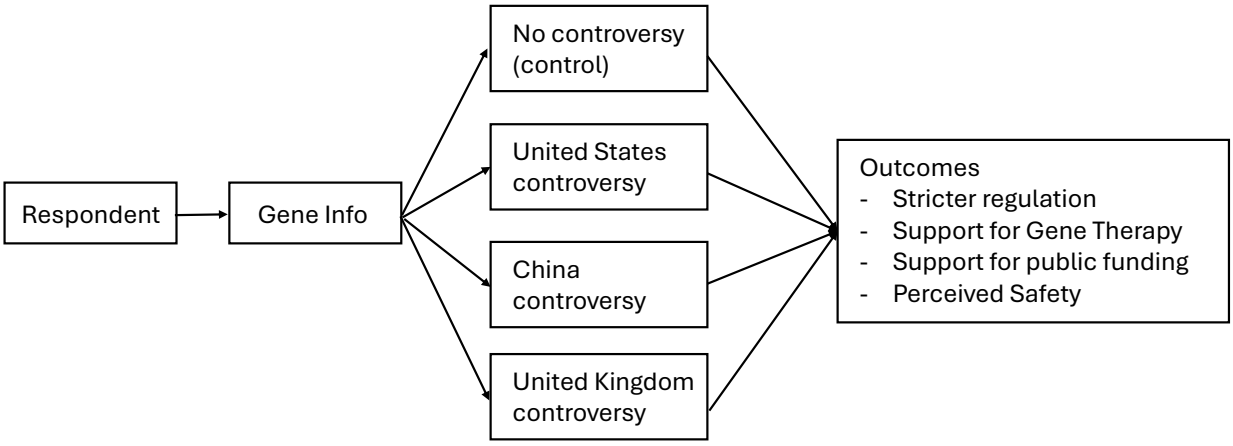

Figure A5: *Survey schematic.*

A.4 Public Backlash: social media data

We follow (Müller *et al.*, 2020) in scraping and analyzing tweets with the keyword CRISPR. Using Twitter's API through Barrie & Ho (2021)'s R package, *academictwitter*, we pulled approximately 50,000 tweets that contain the word "CRISPR" in the 50 days prior to and after the He Jiankui controversy.[1] The bottom panel of Figure A.5.1 shows a histogram of the appearance of CRISPR in tweets over this time period. Using a bag-of-words procedure, we take the average sentiment of each tweet by identifying the proportion of positive words in the tweet. Higher proportions indicate higher levels of positive sentiment. Only English-language tweets are included in the sentiment analysis. Only tweets with at least one word with a positive or negative valence are included in this sample. The top panel of Figure A.5.1 displays change in average sentiment over time.

While sentiment in tweets does capture overall public opinion of Twitter users towards CRISPR technology, new research suggests that certain forms of expression on social media are more likely to drive conversations (Brady *et al.*, 2021). In particular, tweets expressing moral outrage receive higher levels of positive feedback online and are therefore more likely to be seen and to influence online sentiment (Brady *et al.*, 2021). We use Brady *et al.* (2021)'s measure of moral outrage to understand whether controversial events in CRISPR technology influence not only sentiment, but the type of language that drives greater engagement with the overall conversation. We note that moral outrage is a form of negative sentiment. We measure the number of words stems associated with moral outrage in each tweet. The middle panel of Figure A.5.1 displays change in moral outrage over time. Table A.5.1 reports the pre-post change in sentiment and outrage expressed in tweets.

[1] We exclude replies and retweets in our analysis.

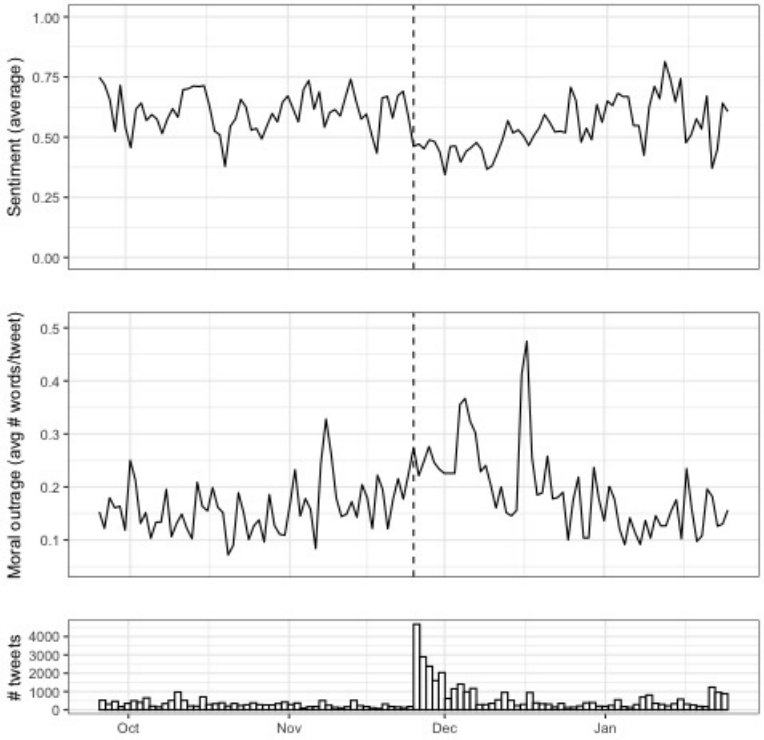

Figure A.4.1: *CRISPR tweet sentiment*: Top panel: sentiment analysis of tweets including the word "CRISPR" from September 2018 - January 2019. Higher values indicate more positive sentiment. Middle panel: moral outrage in same sample of tweets. Higher values indicate more moral outrage. Bottom panel: histogram of number of tweets per day. Dashed black line on November 26, 2018, the day the He Jiankui controversy became public. Data collected by authors.

Subsetting the data to only tweets with identifiable geolocation data for the associated Twitter user, we replicate the main analysis by user country. We limit our analysis to English-language tweets, which likely affects the composition of countries in this sample. Figure A.5.2 displays the results for countries with more than 10,000 unique tweets that mention CRISPR. As Figure A.5.2 shows, the revelation of the gene-editing controversy produced negative sentiment in the days afterwards for every country in the sample. Importantly, the scandal did not occur in any of these countries. (China is not included in the sample as the country blocks access to Twitter for regular users.[2])

[2]`https://help.twitter.com/en/rules-and-policies/state-affiliated-china`

	Dependent variable:	
	Sentiment	Moral Outrage
	(1)	(2)
Post-He Jiankui	-0.110^{***}	0.062^{***}
	(0.006)	(0.004)
Constant	0.609^{***}	0.158^{***}
	(0.005)	(0.003)
Observations	21,856	50,839
R^2	0.013	0.004
Adjusted R^2	0.013	0.004
Note:	*p<0.1; **p<0.05; ***p<0.01	

Table A.4.1: *Change in Tweet Sentiment.* Average tweet sentiment and number of expressions of moral outrage before and after the news of the He Jiankui controversy broke on November 26, 2018. *Sentiment* refers to expressions of positive sentiment and is only measured for tweets with at least one word that expresses positive or negative sentiment; positive values indicate more positive sentiment. *Moral outrage* refers to words that are categorized as expressing moral outrage and indexes the number of words per tweet that reflect this sentiment; positive values indicate increased outrage. Robust standard errors in parentheses. Sample is all English-language tweets mentioning "CRISPR" from September 2018 - January 2019.

In addition to expressing a particular form of negative sentiment, posts that use the language of moral outrage also generate greater engagement in the form of likes and retweets (Brady *et al.*, 2021). Using a dictionary of moral outrage terms (e.g., "abhor", "hate", "shame"), we measure the extent of moral outrage expressed in tweets.The top panel of Table A.4.2 confirms that tweets that contain higher levels of moral outrage are liked and retweeted more often. Tweets with greater positive sentiment are liked more (but not retweeted more). The bottom panel shows that moral outrage tweets are not more liked or retweeted post-scandal. In contrast, negative sentiment tweets are retweeted and liked more often post-scandal. These results 1) confirm that moral outrage tweets have greater engagement in the realm of gene-editing and 2) show that negative sentiment tweets are engaged with at

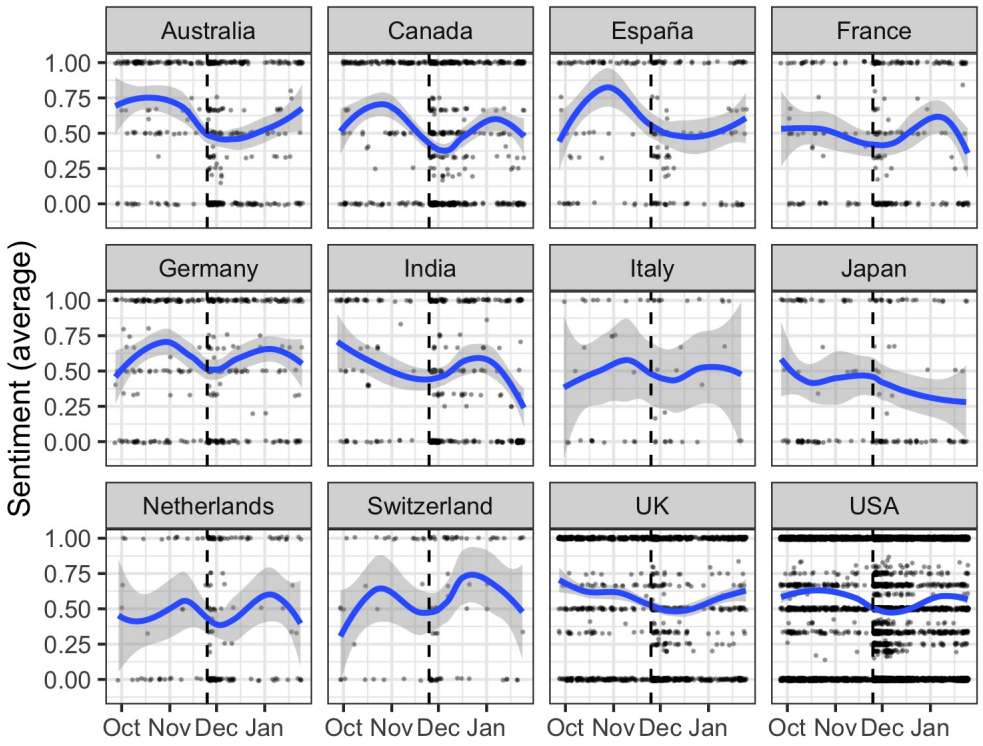

Figure A.4.1:*CRISPR tweets by location*: Sentiment analysis of tweets including the word "CRISPR" from September 2018 to January 2019 by Twitter user location. Only countries with over 10,000 CRISPR-related tweets included. Higher values indicate more positive sentiment. Blue line is a fitted loess model; grey bar indicates 95% confidence interval. Dashed black line on November 26, 2018, the day the He Jiankui controversy became public. Data collected by authors.

higher rates post-scandal. Combined with prior findings about higher numbers of negative sentiment and moral outrage tweets in response to scandal, this suggests even greater levels of public opinion shifts to anti-gene-editing sentiment after scientific scandals. The finding is particularly salient when one considers that public policy attitudes are driven by social cues from peers in addition to elites (Kertzer & Zeitzoff, 2017).

These results confirm the external validity of our experimental findings. The He Jiankui scandal was salient to the public as evidenced by the steep increase in tweets about gene-editing technology after the scandal was made public. These tweets were also more negative and contained higher levels of moral outrage. Finally, geo-located tweets confirm that the

	Dependent variable:			
	Retweets	Likes	Retweets	Likes
	(1)	(2)	(3)	(4)
Moral Outrage	0.715***	1.373***		
	(0.185)	(0.349)		
Sentiment			−0.022	0.877**
			(0.205)	(0.402)
Observations	50,839	50,839	21,856	21,856
	(5)	(6)	(7)	(8)
Moral Outrage	1.066**	2.332**		
	(0.444)	(1.023)		
Sentiment			0.556	2.035**
			(0.385)	(0.944)
Post-He Jiankui	−0.022	−0.421*	0.352	0.058
	(0.107)	(0.236)	(0.364)	(0.746)
Moral Outrage*Post-He Jiankui	−0.455	−1.214		
	(0.487)	(1.075)		
Sentiment*Post-He Jiankui			−0.846*	−1.816*
			(0.452)	(1.023)
Observations	50,839	50,839	21,856	21,856

Table A.4.2: *Tweet Virality.* Correlation between average tweet sentiment and number of expressions of moral outrage with tweet virality (likes and retweets). *Sentiment* refers to expressions of positive sentiment and is only measured for tweets with at least one word that expresses positive or negative sentiment; positive values indicate more positive sentiment. *Moral outrage* refers to words that are categorized as expressing moral outrage and indexes the number of words per tweet that reflect this sentiment; positive values indicate increased outrage. Robust standard errors in parentheses. Sample is all tweets mentioning "CRISPR" from 9-25-2018 to 1-25-2019. Bottom panel displays pre-post results on virality.

scandal, which occurred in China, had effects on international public opinion about gene-editing technology.

A.5 Regulations and Scientific Retractions

We directly test for a correlation between regulatory stringency and scientific scandals through data on scientific retractions in the field of genetic editing. Retractions may occur for many reasons including ethical malfeasance, data manipulation, and data errors. Retractions are characterized as scandals in the scientific community (Azoulay *et al.*, 2017) and have significant negative effects on the field of study in which they occur (Azoulay *et al.*, 2015). Within our sample of gene-editing papers, 674 unique scientists were involved in 121 redacted papers as indicated in the *PubMed* database. We identify a clear negative correlation between the level of regulation in a country and the number of redactions ($\rho = -0.39$, $p = 0.02$) as well as the proportion of retracted papers ($\rho = -0.28$, $p = 0.12$) in a given country. Figure A.5.1 visualizes these relationships.

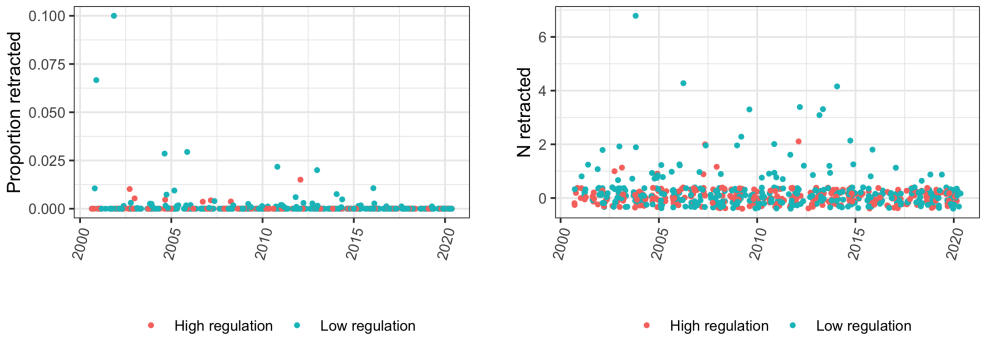

Figure A.5.1: *Regulations and Scientific Retractions.* Left panel depicts proportion of papers published by scientists located in a given country in a given year that were retracted. Right panel depicts raw numbers of retracted papers by country-year.

A.6 Korea Case Study

South Korea was a leader in biotechnology at the turn of the century, but a series of domestic scandals soon led to increased regulation and an exodus of scientific talent. Shortly after the first successful cloning of an animal (Dolly the sheep) in Scotland in 1997, Korean scientists claimed to have created the first clones of human embryos (Rick Weiss, n.d.). The Korean government, along with other nations across the world, began to consider regulating research on cloning human embryos in response (Rick Weiss, n.d.). Before the legislation was enacted, in 2002, a Korean woman was reported implanted with a cloned embryo in a global scandal involving a United States-based cult (Jung, 2010). In the ensuing investigation (in which the scandal was revealed to be a hoax), a spokesperson for CloneAid, the company claiming credit for the cloned embryo, said "the company was not concerned by the investigation, because at present South Korean law does not ban human cloning and the procedure took place abroad" (bbc, 2002a). By the end of the year, the government had passed the Bioethics and Biosafety Act (BioAct) which explicitly banned human cloning (bbc, 2002b).

Research into cloned embryos, however, continued. Celebrated Korean scientist Woo Suk Hwang published groundbreaking research, largely funded by the Korean government, on generating stem cells from cloned human embryos in Science and Cell in 2004 (nat, 2005). In reporting on his research, Hwang directly commented on the threat of regulation from the Korean government. Hwang told the New York Times, "If Korea were to prohibit therapeutic cloning research, we would have to go to other countries where it is permitted – Singapore, mainland China, maybe Great Britain. But my hope is that the Korean government will give us the license to do this kind of research. If they don't, we will move" (Dreifus, 2004). By 2005, reports surfaced that Hwang had coerced female lab members to donate eggs for the research (Zastrow, 2017) . The Korean government quickly modified the BioAct to prohibit domestic egg donation for research purposes (Jung, 2010).

Four years passed before the BioAct-established National Bioethics Commission would

even consider approving research involving human embryonic stem cells (Jung, 2010). Korean scientists continued to make progress on embryonic stem cells but conducted their research abroad due to regulation. Scientists based in Korea developed on the first cloned human embryos in Los Angeles using American egg donors (Zastrow, 2017). Another group of scientists made major breakthroughs in the genetic repair of embryos in Oregon (Ji-young, 2017). One lab regularly works with researchers in Iran, using embryos left over from local fertility clinics (Zastrow, 2017). A South Korean bioengineering company specializing in genetic editing recently set up shop in Qatar (doh, 2020). Researchers lobbied the government to loosen regulations to allow research and development of genetic engineering technologies in Korea heavily (Cyranoski, 2019). In 2019, the BioAct was finally revised to allow gene therapy research to move forward in the country (Jin-woo & Kim, 2019).

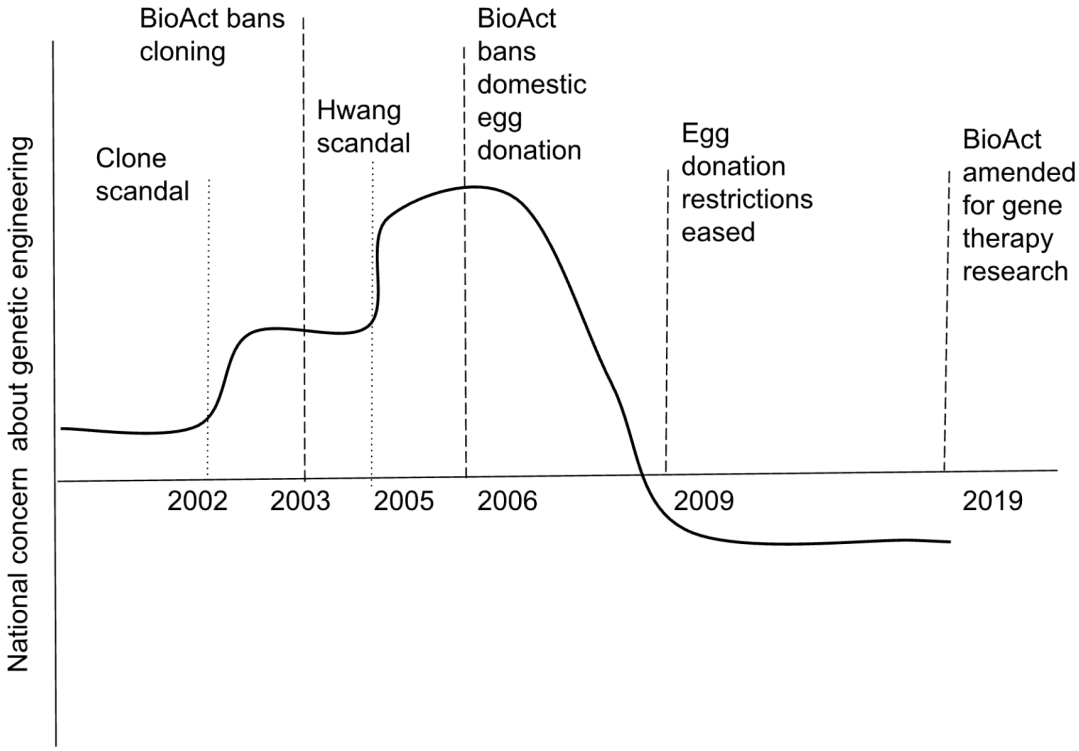

Figure A.6.1: *Illustration of theory*

A.7 Gene-editing Regulation Data

? classify national regulations on a range of gene editing-related issues, including gene therapy, human germline editing, and genetic diagnosis. Countries are rated as "permissive," "intermediate," or "restrictive" on each issue; we transform these into a 1-3 scale of increasing regulatory rigor and average across the fields to generate a single national regulatory score. **?** provide a separate classification of countries based on the regulation of heritable genetic editing. The categories include "ban based on legislation," "ban based on guidelines," "restrictive," and "ambiguous," which we transform into a 1-4 scale. **?** examine national rules regarding the use of genetically modified in vitro embryos in laboratory research. **?** provide a similar measure 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. The authors categorize countries' regulatory approach as *prohibitive*, *prohibitive with exceptions*, *indeterminate*, or *permissive* based on a review of national legislation, guidelines, and codes of conduct which we transform into a 1-4 scale.

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