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Preface

The Fall edition features an article by professors John Keown, DPhil, PhD, DCL, and David Patton, PhD on the law and ethics of lockdowns. Many people worldwide, particularly those with disabilities and the elderly, suffered greatly not only as a result of the Covid-19 pandemic but also as a result of the lockdowns. In this article the authors set out widely-accepted ethical criteria for assessing when coercive public health measures are justified. They then review the empirical evidence, not least concerning the benefits and costs of the lockdowns, and conclude that lockdowns as instituted in the UK (and, presumptively, in many other jurisdictions) appeared to breach those criteria. They suggest that before any future decision is made about imposing a lockdown, scrupulous account be taken of the nature, quality and extent of the evidence concerning: the potential benefits of a lockdown; the potential harms, and the necessity for compulsory rather than voluntary measures.

The second article, by Daniel P. Casey, PhD, et al., investigates factors that may explain levels of stem cell research across different countries. Stem cell trials from *clinicaltrials.gov* were counted and categorized based on the country, the type of stem cell used, and whether that type is ethically controversial. The trial data were compared with characteristics of the countries such as population and GDP. They looked at the general ethical position of the countries by ranking their favorability toward abortion via their legislation. They found GDP, which may be indicative of the interest and means a nation can put toward research, to be the most predictive measure of stem cell use. No correlation was found with national abortion legislation, which is an indicator of ethical positions on life issues in a country. Thus, it would seem that the use of stem cells, namely the significantly greater use of adult stem cells over other more controversial types, is likely to be more influenced by their scientific utility and not by other social or ethical opinions. In addition, ESC and other ethically controversial research does not appear to be necessary for the US to dominate worldwide stem cell research.

In the third article, Jennifer Wright, MD, examines the complex biological and psychological series of events that commence at fertilization and continue through parturition between the preborn human organism and his or her mother. These events extend far beyond the physical connection between an adult patient and contained tissue. This article reviews evidence in support of various aspects of this bond and its implications for care of the maternal patient.

The fourth article, by Byron Calhoun, MD, analyzes the available evidence contributing to the controversy that exists about the effects of medication abortion on the incidence of preterm birth (PTB). Medication abortion of various types continues to be touted as a safe alternative to surgical abortion, and without increased risk for PTB. There is a paucity of evidence regarding medication abortion and PTB, but available papers are reviewed here. There is moderate-quality evidence supporting the contention that medication abortions which require surgical completion increase PTB rates more than surgical abortion alone.

The fifth article is AAPLOG's position paper on "Ethical Research Involving Fetal Human Subjects." This guideline discusses the moral status of the human fetus, the state of ethics for medical research on vulnerable subjects, aspects of medical research using human fetal tissue, and the necessity of including fetuses as a protected class under vulnerable populations in research.

The sixth article is AAPLOG's position paper on "Limiting Conscience Rights in Obstetrics and Gynecology." This paper provides a detailed analysis of the ethical flaws in ACOG Committee Opinion 385, which claimed to speak on behalf of the entire profession of Obstetrics and Gynecology, and proposed that conscience rights of healthcare professionals have limits with regard to certain aspects of patient care. Despite calls for revision from many within the profession, Opinion 385 was reaffirmed in 2016, without revision.

This edition concludes volume 38 of *Issues in Law & Medicine*, the first year that *Issues* is being published solely as an open access, electronic journal, available free of charge at *IssuesinLawandMedicine.com*. The ILM open access website is completely new and the editors hope you enjoy its new look and user friendly format. Thank you for your continued support of *Issues in Law and Medicine*

Barry A. Bostrom, J.D.
Editor-In-Chief

Articles

Law, Ethics and Lockdowns: Impacts on Life, Liberty and the Economy

John Keown, MA, DPhil, PhD, DCL* and
David Paton BSc, MA, PhD**

ABSTRACT: Many people worldwide, particularly those with disabilities and the elderly, suffered greatly not only as a result of the Covid-19 pandemic but also as a result of the lockdowns. In this article we set out widely-accepted ethical criteria for assessing when coercive public health measures are justified. We then review the empirical evidence, not least concerning the benefits and costs of the lockdowns, and conclude that lockdowns as instituted in the UK (and, presumptively, in many other jurisdictions) appeared to breach those criteria. We conclude that any future proposal to lockdown should be subjected to the strictest ethical scrutiny, and that a lockdown should not be contemplated unless it could be convincingly demonstrated that the benefits would substantially outweigh the harms; that it would be proportionate, and that legal coercion would be strictly necessary.

Keywords: Covid-19; lockdowns; ethics; public health; law; economy

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Introduction

A major policy response to the Covid-19 pandemic across the globe was the "lockdown." One definition is: "a temporary condition imposed by governmental authorities (as during the outbreak of an epidemic disease) in which most people are required to refrain from or limit activities outside the home involving public contact (such as dining out or attending large gatherings)."[1]

Although lockdowns admit of varying types and degrees, and may be imposed on a national, regional or local basis, they typically involve the suspension, by law, of basic human rights and freedoms such as freedom of association and the right to work or to run a business. For example, in March 2020 Ferguson et al. recommended a policy of suppressing Covid-19 by way of working from home; social distancing of the entire population; the home isolation of infected people and household quarantine of their family members, and the possible closure of businesses, schools and universities.[2] The imposition of such measures by law comfortably meets the definition of a lockdown.

In this article, we examine the role ethics should play in imposing and evaluating lockdowns for viruses like Covid-19. Typical of the policy approach taken in many western countries were the lockdowns imposed in England in 2020-2021. These involved what Lord Sumption, the former Justice of the UK Supreme Court, described as "the most significant interference with personal freedom in the history of our country."[3] The justification for the lockdowns was to prevent the National Health Service (NHS) being overwhelmed by patients with Covid-19 and to prevent the scores or even hundreds of thousands of deaths that it was feared would otherwise occur, especially among some of the most vulnerable members of the community such as the elderly and people with disabilities.[4] Proponents could also point to the fact that lockdowns were the policy response favoured by governments and their public health

[1] "Lockdown" in the Merriam Webster Dictionary. https://www.merriam-webster.com/dictionary/lockdown.

[2] Neil Ferguson et al., *Impact of Non-Pharmaceutical Interventions (NPIs) to Reduce COVID-19 Mortality and Healthcare Demand*. Imperial College London (2020). https://doi.org/10.25561/77482.

[3] Jonathan Sumption, *This is How Freedom Dies: the Folly of Britain's Coercive Covid Strategy*, The Spectator (28 October 2020).

[4] Ironically, these were among the groups who suffered disproportionately from the lockdowns. See William F. Sullivan et al., *Ethics Framework and Recommendations to Support Capabilities of People with Intellectual and Developmental Disabilities during Pandemics*, 19 Journal Of Policy And Practice In Intellectual Disabilities 1 (2022); Kevin de Sabbata et al., *Covid -19 Policies and their Unequal Impact on the Rights and Dignity of Disabled People*, UK Pandemic Ethics Accelerator (2022). https://ukpandemicethics.org/wpcontent/uploads/2022/07/Disability-project-ethics.pdf

advisors across the globe, starting with China and followed by the UK, the US and Australasia.

Despite the profound and unprecedented interference by lockdowns with people's basic rights and freedoms, and their hugely costly social and economic effects, there has hitherto been relatively little analysis from an ethical perspective of the question whether they were justified. This lack is particularly noticeable in relation to business, though an exception is the work of Jain, Jain and Li[5] who used survey data to examine contrasting attitudes amongst US residents towards measures focusing on reducing infections compared to those focused on protecting the economy. (In particular, we are aware of little research addressing the specific question of what ethical principles should underpin government restrictions on private businesses, despite the dramatic impact of such interventions on business performance; on employment; on employee and employer wellbeing and, due to the associated financial support including furlough payments, on public finances.[6])

In this article, we seek to help fill this gap by addressing the ethical criteria for determining when lockdowns might be justified and applying them to the restrictions imposed in England by the UK Government.[7] England expe-

[5] Shalini S. Jain et al., *Sustaining Livelihoods or Saving Lives? Economic System Justification in the Time of COVID19*, 183 Journal Of Business Ethics 71 (2023). https://doi.org/10.1007/s10551-022-05091-4.

[6] A number of papers have examined how managers should ethically respond to the pandemic in terms of protecting employees and other business practices: see Tim Manuel and Terri L. Herron, *An Ethical Perspective of Business CSR and the COVID-19 Pandemic,* 15(3) Society And Business Review 235 (2020); Herman Aguinis et al., *Understanding Employee Responses to COVID-19: a Behavioral Corporate Social Responsibility Perspective,* 18(4) Management Research 421 (2020); Dejun T. Kong and Liuba Y. Belkin (2021), *You Don't Care for Me, so What's the Point for Me to Care for Your Business? Negative Implications of Felt Neglect by the Employer for Employee Work Meaning and Citizenship Behaviors amid the COVID-19 Pandemic,* 181 Journal Of Business Ethics 645 (2022). https:\\doi.org/10.1007/s10551-021-04950-w. Danny Miller et al., *Are Socially Responsible Firms Associated with Socially Responsible Citizens? A Study of Social Distancing during the Covid-19 Pandemic*, 179 Journal Of Business Ethics 387 (2021). https://doi.org/10.1007/s10551-021-04858-5.

A further stream of literature analyses corporate philanthropic responses to Covid-19. See, for example, Hanwen Chen et al., (2021) *Adversity Tries Friends: a Multilevel Analysis of Corporate Philanthropic Response to the Local Spread of COVID-19 in China,* 177 Journal Of Business Ethics 585 (2021). https//doi.org/10.1007/s10551-021-04745-z, and Iana Shaheen et al., *Resource Scarcity and Humanitarian Social Innovation: Observations from Hunger Relief in the Context of the COVID-19 Pandemic.* 182 Journal Of Business Ethics 597 (2023). https://oi.org/10.1007/s10551-021-05014-9. Finally, Ehsan Poursoleyman et al., *Did Corporate Social Responsibility Vaccinate Corporations Against COVID-19?,* Journal Of Business Ethics (2023) https://doi.org/10.1007/s10551-023-05331-1 consider whether prior investment in corporate social responsibility was able to protect companies against some of the consequences of the pandemic.

[7] Covid policy in the UK was a devolved matter for Wales, Scotland and Northern Ireland, so decisions over lockdowns were the responsibility of their respective administrations. As

rienced a significant level of Covid infections and on a number of occasions during 2020 and 2021 the UK Government implemented a panoply of restrictions including home working, business and school closures, capacity limits and social distancing. As such, England provides a valuable case-study. Given ongoing discussion of possible re-imposition of lockdowns in response to future pandemics, the issues considered here continue to be both globally relevant and timely. We seek to answer two key research questions. First, were lockdown policies adopted by the UK government ethically justified?[8] Second, how might sound ethical analysis improve policy responses in future pandemics?

We will conclude that the English lockdowns failed to meet the standard ethical criteria for coercive public health interventions such as those endorsed by Childress and colleagues and by the Nuffield Council on Bioethics. In particular, we question whether, in the UK at least, any serious inquiry was conducted into whether they would prove effective in achieving their goal (a goal which, moreover, seemed regularly to shift); whether, even if they were to prove effective, any benefits would outweigh the obvious costs, and whether less restrictive measures would have sufficed. We will note that the UK Government not only failed to implement its own ethical framework for responding to pandemic influenza published in 2007 but also deliberately sidelined bodies that existed to provide expert ethical input.

In the next section, we provide a timeline of the restrictions and lockdowns in England. In section 3, we outline the ethical criteria relevant to evaluating lockdowns. In section 4, we examine evidence on the costs and benefits of the lockdowns. Section 5 assesses the extent to which the restrictions met the ethical criteria. Finally, we summarize our conclusions.

The Lockdowns in England: A Timeline

On 23 March 2020 the then Prime Minister, Boris Johnson, issued a "stay at home" order.[9] A gradual easing of restrictions began on 1 June with the phased re-opening of schools and the re-opening of "non-essential" shops on 15 June and parts of the hospitality sector on 4 July. Many businesses (e.g. casinos, nightclubs and live attendance at sporting events) remained shut and further national restrictions were gradually introduced including compulsory face coverings in July, followed by a ban on meetings of more than six people (the "rule of six") and a 10pm curfew on the hospitality sector in September. A

England does not have a devolved Government, policy decisions were the responsibility of the UK Government in Westminster.

[8] The devolved administrations in Scotland, Wales and Northern Ireland imposed lockdowns that were, if anything, more severe in nature and duration than in England.

[9] Despite the fact that the law imposing the lockdown did not come into force until three days later.

three-tier system of restrictions came into effect on 14 October, which involved a range of regional-specific business closures and other restrictions. A second lockdown was imposed on 5 November and was replaced on 2 December with another three-tier regime of restrictions, raised to four tiers for certain areas on 21 December. England entered a third lockdown on 5 January 2021.

A four-step "roadmap" of relaxation started in March with the re-opening of schools; permission for two people to engage in recreation in outdoor public spaces and the expiration of the "stay at home" order. On 12 April non-essential retail businesses and public buildings re-opened. On 17 May indoor venues such as pubs and cinemas re-opened. On 14 June the Prime Minister announced that step four would be delayed to allow acceleration of the vaccination programme. 19 July saw the end of most limits on social contact and the re-opening of the final sectors of the economy such as nightclubs. On 10 December 2021, under the government's "Plan B", face masks were made compulsory once again in most public indoor venues and an NHS "Covid Pass" was required to enter certain places like nightclubs. These restrictions were removed starting in January 2022 and by 24 February virtually all domestic restrictions and limits on businesses had been ended.[10] In many parts of the UK, all restaurants and bars were completely closed for indoor service for 5 months from November 2020 to 2021. Some businesses (e.g. nightclub venues and casinos) were shut continuously for 16 months from March 2020.

The lockdown restrictions were, then, extensive both in nature and duration. Were they ethically justified?

Ethical Criteria for Coercive Public Health Measures

James Childress and colleagues mapped the terrain of public health ethics in 2002.[11] The terrain included a set of general moral considerations. They

[10] Institute for Government, *Timeline of UK Government Coronavirus Lockdowns and Measures, March 2020 to December 2021* (2022). timeline-coronavirus-lockdown-december-2021_0.png (30001505) (instituteforgovernment.org.uk. Although the third lockdown lacked legal force until 6 January, the government nevertheless announced it would come into effect on 5 January. See https://www.gov.uk/government/news/prime-minister-announces-national-lockdown

[11] James F. Childress et al., *Public Health Ethics: Mapping the Terrain*, 30 Journal Of Law, Medicine And Ethics 170 (2002). Another ethical framework was later provided by the Nuffield Council on Bioethics. See: Nuffield Council on Bioethics, *Public Health: Ethical Issues* (2007). https://www.nuffieldbioethics.org/publications/public-health. See also Nuffield Council on Bioethics, *Rapid Policy Briefing. Ethical Considerations in Responding to the COVID-19 Pandemic* (2020) https://www.nuffieldbioethics.org/publications/ethical-considerations-in-responding-to-the-covid-19-pandemic and *Ethical Tools for Decision-makers. Responding to Public Health Threats* (2022). https://www.nuffieldbioethics.org/publications/ethics-tools-for-decision-makers-responding-to-public-health-threats. A third framework is the Siracusa Principles, published by the American Association for the International Commission of Jurists in 1984 to determine when it is justifiable to limit or derogate from the International Covenant on Civil and Political Rights in the case of public emergencies: *Siracusa Principles on the*

listed nine: producing benefits; avoiding, preventing and removing harms; producing the maximal balance of benefits over harms and other costs (often called utility); distributing benefits and burdens fairly (distributive justice) and ensuring public participation, including the participation of affected parties (procedural justice); respecting autonomous choices and actions, including liberty of action; protecting privacy and confidentiality; keeping promises and commitments; disclosing information as well as speaking honestly and truthfully (often grouped under transparency); and building and maintaining trust.

Whichever particular moral theory one adopted, they added, these general moral considerations broadly captured the moral content of public health ethics. Although it was not possible to develop an algorithm to resolve conflicts among the moral considerations, Childress et al proposed a list of five conditions to determine when it was justifiable to promote public health, even when so doing conflicted with other moral commitments such as individual liberty, namely: effectiveness; proportionality; necessity; least infringement and public justification. The conditions were similar to the "strict scrutiny" test applied in US constitutional law: a state must show a "compelling interest" for infringing a fundamental liberty; that its methods are "strictly necessary" to achieve that interest, and that it has adopted the "least restrictive alternative."

The five conditions rightly set a very high bar. First: effectiveness. It was essential to demonstrate effectiveness, that infringing one or more moral considerations would probably protect public health. It was, second, also essential to establish proportionality, that the probable public health benefits outweighed the infringed moral considerations. The positive features had to be weighed against the negative. Third, was the policy necessary to secure the public health goal? The fact that a policy would infringe a general moral consideration pro-

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Limitation and Derogation Provisions in the International Covenant on Civil and Political Rights (1985). Siracusa-principles-ICCPR-legal-submission-1985-eng.pdf (icj.org). The Siracusa Principles were recently supplemented, in light of the human rights violations by the public health response to the pandemic, by the *Human Rights Principles in Public Health Emergencies* (2023): www.ohchr.org/sites/default/files/documents/new-york/events/hr75-future-generations/PGs-on-Human-Rights-and-Public-Health-Emergencies-26-June-2023.pdf.

For other ethical reflections see the following papers on selective lockdowns of the elderly: Julian Savulescu and James Cameron, *Why Lockdown of the Elderly is Not Ageist and Why Levelling Down Equality is Wrong*, 46 Journal Of Medical Ethics 717 (2020); on the alternative of mandatory contact tracing: Lucie White and Philippe van Basshuysen, *How to Overcome Lockdown: Selective Isolation Versus Contact Tracing*, 46 Journal Of Medical Ethics 724 (2020); on the nature of freedom in the trade-off between freedom and health: Alberto Giubilini, *Freedom, Diseases and Public Health Restrictions*, 37 Bioethics 1 (2023); on "dominating risk impositions": Kritika Maheshwari and Sven Nyholm, *Dominating Risk Imposition,s* 26 Journal Of Ethics 613 (2022); and on fairness in restricting liberty in the interests of security: Garrett Cullity, *Liberty, Security and Fairness*, 25 Journal Of Ethics 141 (2021).

vided a strong moral reason to seek an alternative policy. Proponents of coercive over voluntary policies must have an honest belief, for which they could give supportable reasons, that coercion was necessary. Fourth, even when a policy met the above three conditions, public health agents should minimise its deleterious impact. For example, when a policy infringed autonomy, public health agents should seek the least restrictive alternative. The fifth condition, public justification, required public health agents to provide a public explanation of and justification for their infringing policy. Citizens should be treated as equals.

Transparency was essential to creating and maintaining public trust and to establishing accountability. This condition required soliciting input from the public and the government in the formulation of policy and then justifying that policy, and this was especially important when a general moral consideration was infringed, "as with coercive protective measures to prevent epidemics." At a minimum, public accountability involved transparency in openly seeking information from those affected and in honestly disclosing relevant information to the public.

Public health accountability addressed the duty of public health experts to work with the public and scientists to identify, define and understand the threats to public health and the risks and benefits of ways to address them. Sometimes individual interests must yield to collective needs, but the requirement of public accountability ensured that such trade-offs would be made openly and that reasons, grounded in ethics, would be provided to those affected. It was not, moreover, sufficient to show that an individual's actions had some adverse effects on others: it was necessary to show that those adverse effects were significant enough to warrant overriding individual liberty.

Finally, in many situations the most defensible public health approach was one that *expressed* community rather than one that *imposed* it through coercion. Expressing community had, all things being equal, priority over imposing community.[12] We take that to mean that encouraging people to act for the common good was preferable to compelling them to do so.

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[12] Similarly, the ethical framework proposed by the Nuffield Council (*supra* note 11) required restrictive measures such as lockdowns to be effective, proportionate and necessary, and to be justified publicly and transparently. The *Siracusa Principles* (*Id.*) state (para. 51): "The severity, duration, and geographic scope of any derogation measure shall be such only as are strictly necessary to deal with the threat to the life of the nation and are proportionate to its nature and extent." And the recent *Principles and Guidance* (*Id.*) provide (para.16.1) that public health responses that limit human rights must be temporary, for a legitimate and specific public health purpose and have strict regard to the principles of legality, necessity, proportionality and non-discrimination. They add (para. 19.3) that police powers may only be used as a last resort, when strictly necessary and when less restrictive measures would be ineffective.

Relevantly, in 2007 the UK Department of Health published a brief, six-page ethical framework for responding to an influenza pandemic.[13] Its fundamental principle was equal concern and respect: everyone mattered, and everyone mattered equally. The harm that might be suffered by every person mattered, and so minimizing harm was a central concern. The fundamental principle subsumed seven individual principles: respect; minimizing harm; fairness; working together; reciprocity; keeping things in proportion; flexibility, and good decision-making. Good decision-making required openness as to what decisions were being taken and why; inclusiveness; accountability; and reasonableness: decisions should be rational, based on appropriate evidence and the result of an appropriate process.

In our analysis in section 5 of whether the lockdowns were ethically justified we will seek to arrive at a sound prudential judgment informed by the ethical criteria advanced by Childress et al (and the other ethical frameworks we cited.) We shall also mention the guidance on mitigating the risks of pandemic influenza that was published by the World Health Organisation in 2019.[14] We will, first, consider in section 4 a question central to the ethical analysis of lockdowns: what were their benefits and their costs and did the benefits outweigh the costs? This is not to adopt a crudely utilitarian moral calculus. Our ethical assessment is compatible with the broad understanding of benefits and costs inherent in the ethical framework we have outlined, which attaches ethical significance not only to saving lives and preventing ill-health, but to basic human rights and freedoms including the freedom to associate with family and friends and the right to work. Nor do we purport to commensurate radically different types of goods, such as life, work and education, to calculate the "right" answer. This is not, however, to suggest that those adopting a wholly or largely utilitarian approach will disagree with our analysis or conclusions.[15] Nor do we expect that those who adopt a virtue ethics approach will disagree. It might be argued that the restrictions expressed social solidarity, especially with the most vulnerable. However, compliance is scarcely virtuous if it is mandated, and one is hardly promoting solidarity by supporting measures that

[13] Department of Health UK, *Responding to Pandemic Influenza. The Ethical Framework for Policy and Planning* (2007). https://webarchive.nationalarchives.gov.uk/ukgwa/20130104202555/http:/www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_080751

[14] World Health Organization, *Non-Pharmaceutical Public Health Measures for Mitigating the Risk and Impact of Epidemic and Pandemic Influenza* (2019). https://www.who.int/publications/i/item/non-pharmaceutical-public-health-measuresfor-mitigating-the-risk-and-impact-of-epidemic-and-pandemic-influenza

[15] Julian Savulescu et al., *Utilitarianism and the Pandemic* 34 Bioethics 620 (2020).

are either futile or harmful, especially to the most vulnerable. Virtue ethics is not virtue-signalling.

A Review of the Benefits and Costs of Lockdowns

As in most countries, the original basis for instituting lockdowns in the UK was that, otherwise, Covid-19 cases would continue to increase to levels at which health services would be overwhelmed, resulting in hundreds of thousands of deaths. This assessment relied on modelling conducted by Neil Ferguson's team at Imperial College, London.[16]

It is now clear, however, that the *growth* of infections had started to slow some time before the formal lockdown was announced in England on 23 March 2020. The Chief Medical Officer, Chris Whitty, acknowledged this fact in an interview in July of that year.[17] Indeed, using data on Covid-related deaths, Wood has demonstrated that not only was the rate of *growth* of infections decreasing before each of the three English lockdowns (March 2020, November 2020 and January 2021), but also that most likely the actual *rate* of new infections was already decreasing.[18] The implication of this finding is that the modelling predictions that infections would otherwise have risen to unsustainable levels were invalid.[19] In other words, even in the absence of lockdowns, the UK would not have experienced the hundreds of thousands of deaths suggested by Ferguson et al. This conclusion is supported by the experience of Sweden, which never instituted a formal lockdown and had only limited mandatory business closures. Although Sweden differs from the UK in many respects, it experienced a very similar growth of infections in early 2020. Further, in March 2020, modellers predicted that in the absence of lockdown, Sweden would experience a similar per capita death rate from Covid to

[16] *Supra* note 2.

[17] See https://www.thetimes.co.uk/article/chris-whitty-blames-poor-planning-for-lockdown-in-bad-tempered-health-committee-d5kb3fmw2#:~:text=The%20coronavirus%20pandemic%20was%20probably,of%20lack%20of%20testing%20capacity%E2%80%9D. (22 July 2020).

[18] Simon Wood, *Inferring UK COVID-19 Fatal Infection Trajectories from Daily Mortality Data: Were Infections Already in Decline Before the UK Lockdowns?* 78 Biometrics 1127 (2022). For the first lockdown, deaths data provide the main way of inferring earlier infection trends, though Wood's conclusions are supported by data from the NHS Covid-19 Triage system. For later lockdowns, we have more direct evidence from the Office for National Statistics (ONS) estimates of infection prevalence. These corroborate Wood's finding that infections were decreasing before the January 2021 lockdown.

[19] Knowledge that infections were decreasing pre-lockdown was only ascertainable post-hoc. However, based on published hospital deaths data, it was clear from as early as mid-April that the infection peak had been reached. Despite this, the lockdown continued unabated for several months.

that forecast for the UK. For example, Walker et al. suggested[20] that without a lockdown Sweden would experience between 66,400 and 90,200 Covid-related deaths by the end of July 2020.[21] The actual number proved to be 5,721.[22]

Although it is clear now that the huge number of deaths projected by the Imperial College modelling in the absence of suppression strategies was unrealistic, this does not necessarily mean that lockdowns had no impact on mortality. It is still possible, for example, that the UK lockdowns accelerated the decline in infections that would have happened anyway and that, in the short run at least, averted some deaths.

As with any other significant policy intervention, a rational approach involves evaluating both the marginal costs and marginal benefits. A stream of research over the past two years has provided significant evidence on both sides of the equation. Identifying causal policy impacts, however, is not without difficulties. One reason for this is that policy decisions can be endogenous. For example, governments face pressure to put in place business closures and lockdowns when infections and deaths are increasing. As a result, we may observe a spurious correlation between a restriction and an increase in infections. Alternatively, if restrictions are imposed as an infection wave comes to a peak, we may falsely attribute a reduction in infections that would have occurred anyway as being caused by a particular intervention.

Despite the difficulties in disentangling causality, a number of empirical studies have taken account of policy endogeneity in different ways. The best studies examine trends in relevant metrics (cases, hospitalisations or deaths) before and after policy changes (allowing for appropriate time lags) relative to changes in areas in which policies were not implemented. Further, to establish a suitable counter-factual and to avoid spurious correlation, studies need to control for trends in the run up to the policy intervention and must also be careful to ensure to control for other relevant differences between those areas subject and not subject to the policy.

Allen's survey of the empirical studies of the impact of lockdowns on Covid-related outcomes has concluded: "There is almost no consistent evidence that strong levels of lockdown have a beneficial effect, and given the large levels of statistical noise in most studies, a zero (or even negative) effect

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[20] Patrick G.T. Walker et al., *The Global Impact of COVID-19 and Strategies for Mitigation and Suppression*. Imperial College London, (2020). https://doi.org/10.25561/77735.

[21] The mortality estimates for individual countries are contained in an online appendix to the paper here: https://view.officeapps.live.com/op/view.aspx?src=https%3A%2F%2Fwww.imperial.ac.uk%2Fmedia%2Fimperial-college%2Fmedicine%2Fmrc-gida%2FImperial-College-COVID19-Global-unmitigated-mitigated-suppression-scenarios.xlsx&wdOrigin=BROWSELINK

[22] As reported by the Public Health Agency of Sweden: www.folkhalsomyndigheten.se/smittskydd-beredskap/utbrott/aktuella-utbrott/covid-19/statistik-och-analyser/bekraftade-fall-i-sverige/

cannot be ruled out."[23] Allen estimates that a reasonable range for the impact of lockdowns on Covid-related mortality is a reduction of between zero and 20%.[24]

The limited number of systematic reviews on the evidence are consistent with this conclusion. Lezadi et al., [25] Talic et al. [26] and Herby et al.[27] all find some evidence that lockdowns reduced Covid mortality but with generally modest effects. For example the meta-analysis conducted by Herby et al. estimates the impact of lockdowns finding an average effect of around 3%.[28]

Some individual papers have reported somewhat higher estimates of the impact of lockdowns on mortality. For example, Arnon et al.[29] estimated that lockdowns in the US reduced mortality by as much as 25% in the first few months of the pandemic. Notably, the authors concluded that enforced business closures were much less effective than mandates restricting individual movement.

More recently, Mader and Rüttenaur[30] use the Generalised Synthetic Control Method (GSCM) on data from 169 countries to identify causal effects on mortality and Covid infections from a range of non-pharmaceutical interventions (NPIs) including business closures and stay-at-home measures. GSCM involves creating a synthetic set of control countries that are statistically similar (including in terms of pre-intervention trends) to countries subject to the particular intervention. The authors are unable to find a consistent, significant impact on either mortality or infections from any NPI.

Given the statistical uncertainty and difficulties in identifying a true causal effect, we cannot rule out that lockdowns have some marginal impact

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[23] Douglas Allen, *Covid Lockdown Cost/Benefits: a Critical Assessment of the Literature* 29 International Journal Of The Economics Of Business 1 at 15 (2022).

[24] *Id.* Note that his review covers empirical estimates of lockdown impacts based on real data and excludes studies based on models which are constructed on the assumption that lockdowns avert deaths.

[25] Shabnam Lezadi et al., *Effectiveness of Non-Pharmaceutical Public Health Interventions Against COVID-19: A Systematic Review and Meta-Analysis* 16 PLoS ONE: e0260371 (2021).

[26] Stella Talic et al., *Effectiveness of Public Health Measures in Reducing the Incidence of Covid-19, SARS-CoV-2 Transmission, and Covid-19 Mortality: Systematic Review and Meta-Analysis* British Medical Journal 375: e068302 (2021).

[27] Jonas Herby et al., *A Literature Review and Meta-Analysis of the Effects of Lockdowns on Covid-19 Mortality,* 200 Studies In Applied Economics (2022).

[28] *Id.* The 3% figure relates to studies of "shelter-in-place" orders which are close to the lockdown definition used in this paper. See Nicolas Banholzer et al., *Comment on "A Literature Review and Meta-Analysis of the Effects of Lockdowns on COVID-19 Mortality"* SSRN Working Paper (2022) https://papers.ssrn.com/sol3/papers.cfm?abstract_id=4032477 for a critique of attempts to apply the meta-analysis approach to Covid-19 outcomes.

[29] Alexander Arnon et al., *Epidemiological and Economic Effects of Lockdown*, 20 Brookings Papers On Economic Activity (Fall, 2020).

[30] Sebastian Mader and Tobias Rüttenauer, *The Effects of Non-Pharmaceutical Interventions on COVID-19 Mortality: a Generalized Synthetic Control Approach across 169 Countries*, Frontiers Of Public Health (April, 2022) https://doi.org/10.3389/fpubh.2022.820642.

on Covid-related mortality. However, even the upper end of the estimates of benefit appear to be an order of magnitude lower than the *projected* numbers of deaths averted on which lockdown decisions were originally taken. For example, during the first UK lockdown (and allowing for the lag between infections and likely date of death), there were about 30,000 Covid-related deaths. Using Allen's range of between 0 and 20% mortality reduction, that implies that the first UK lockdown may have averted between zero and (at best) around 7,000 Covid-related deaths. This stands in stark contrast to the modelled estimates by Ferguson et al. on which the UK lockdown decision was based, that lockdown would avert several hundred thousand deaths.

Evaluating the costs of lockdowns is also fraught with difficulty. A reduction in business activity which occurs after restrictions are imposed could well be caused by those restrictions, but it might also be the case that the reduction would have happened even in the absence of restrictions due to behavioural responses to trends in infections. Further, although there are economic costs from compulsory business closures, the broader welfare costs of restrictions are much harder to calculate, though clearly very significant.

The published data on government expenditure directly aimed at supporting lockdown restrictions provides some idea of the orders of magnitude involved. The National Audit Office Cost Tracker reports that total UK Government has incurred expenditure totalling £376 billion (around $450 billion) as a result of the pandemic. Much of this expenditure is the result of policy choices. For example, £84 billion has been spent supporting businesses affected by lockdowns and other restrictions[31] and a further £70 billion on the furlough scheme supporting employees temporarily laid off due to restrictions.[32] Total spending in those two areas exceeded the total annual budget for the NHS in 2021 of £136 billion. But these figures are likely to represent only a small part of the full welfare cost of lockdowns and other restrictions experienced by consumers and businesses.

There have been a number of attempts to subject lockdowns to cost-benefit analysis. The four key studies (Allen,[33] Miles et al.,[34] Rowthorn and Maciejowski,[35] and Lally[36]) each adopt contrasting approaches to estimating lockdown

[31] Philip Brien and Matthew Keep, *Public Spending During the Covid-19 Pandemic*, House of Commons Library (September 2023).

[32] Andy Powell et al., *Coronavirus Job Retention Scheme: Statistics*, House of Commons Library (December 2021).

[33] *Supra* note 23.

[34] David Miles et al., *Living with COVID-19: Balancing Costs against Benefits in the Face of the Virus*, 253 National Instiute Economic Review R60-R76 (July, 2020).

[35] Robert Rowthorn and Jan Maciejowski, *A Cost–Benefit Analysis of the COVID-19 Disease*, 36 Oxford Review Of Economic Policy (S1) S38 (2020).

[36] Martin Lally, *A Cost–Benefit Analysis of COVID19 Lockdowns in Australia*, 40 Monash Bioethics Review 62 (2022).

costs and examine data from different countries and time periods. However, all conclude that on any conventional basis for evaluating the benefit of mortality avoided, the costs of lockdowns were far in excess of any possible benefit. For example, Miles et al calculate that even if the first UK lockdown averted as many as 20,000 deaths (a figure far in excess of the upper end of plausible estimates), and using the lowest plausible estimate of lockdown costs, lockdown would have caused a net loss of nearly £200 billion.[37] Similarly, Allen concludes that using the upper bound estimate of a 20% mortality reduction from lockdowns in Canada, the lowest estimate of lockdown costs would exceed the benefits by a factor of 35.[38]

An important further consideration is that the preceding analysis focused only on Covid-19 related mortality. Even if lockdowns averted Covid-19 related mortality, they may also have *caused* other deaths. This might be due to several reasons. Most obviously, strong public health messaging encouraging people to stay at home may have contributed to patients delaying presenting with symptoms and, hence, being referred for investigation. Related to this, lockdowns may also have contributed to delays in diagnosis and treatment following referral. For example, most general practitioners and most NHS hospital outpatient clinics ran services that were significantly reduced and, more often than not, conducted by telephone or over the internet. There are few data on the adverse impact of these changes on the quality of healthcare, though it is well known that cancer survival is negatively affected by delays. One recent systematic review and meta-analysis disclosed that a delay of only one month in cancer treatment can increase the risk of death by around 10%.[39] Lockdowns may also increase deaths from causes such as suicide, alcohol or, in the long run, obesity due to enforced loneliness, isolation or lack of exercise. On the other hand, lockdowns may also have positive impacts on mortality such as fewer road accidents due to reduced commuting.

Given all this, an alternative approach to estimating mortality effects is to focus on the impact of lockdown on excess mortality. This approach also has the benefit of avoiding measurement issues such as misdiagnoses or miscategorization of Covid-related deaths. To the best of our knowledge, just two empirical studies to date have assessed the impact of lockdowns on excess mortality. Williams et al. used UK excess mortality data from the first wave and concluded that "the first national lockdown in England and Wales had a net mortality increasing effect."[40] Agrawal et al. used an event study framework on data from

[37] *Supra* note 34.
[38] *Supra* note 23, at 19.
[39] Timothy P. Hanna et al., *Mortality due to Cancer Treatment Delay: Systematic Review and Meta-analysis*, 371 British Medical Journal m4087 (2020).
[40] Sam Williams et al., *COVID-19 Mortalities in England and Wales and the Peltzman Offsetting Effect*, 53(60) Applied Economics 6995 (2021).

43 countries and all US states. They found that, following the introduction of "shelter-in-place" policies (lockdowns), excess mortality increased on average. Further, they found no evidence that areas implementing lockdowns earlier or longer had lower excess deaths than those implementing later lockdowns.[41] The limited literature warrants caution before coming to firm conclusions. But the current state of evidence indicates that *lockdowns probably had little or no net effect in reducing overall mortality*. On this basis, the cost-benefit calculations discussed above are, to put it mildly, even less favourable to lockdowns.

The finding in the literature to date that lockdowns had only a limited impact even on Covid-related mortality may seem something of a puzzle. Part of the explanation lies in unintended behavioural effects of some aspects of lockdowns and which may have had the perverse effect of increasing infections. For example, the Night Time Industry Association reported that the announcement of a second English lockdown led to a significant rise in illegal music events.[42]

Equally significant is the role of voluntary behaviour change. There is considerable evidence that people change their behaviour and reduce risk in response to rising Covid-19 infections irrespective of formal restrictions. Goolsbee and Syverson found that that legal restrictions explained just 7% of reductions in consumer traffic in the US, with the vast majority of reductions attributable to voluntary behaviour change.[43] Further, voluntary reductions in movement and social mixing will be strongest amongst the most vulnerable, meaning that changes induced by legal restriction change are likely to have only limited impact on hospital admissions and mortality. Herby similarly concluded that behaviour change caused by mandatory measures such as business closures and lockdowns accounts for just 9% of changes to infection growth, with the remaining 91% being due to voluntary behaviour changes.[44]

The role of voluntary behaviour change is important in any ethical assessment of lockdowns. As discussed previously, if similar outcomes can be

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[41] Virat Agrawal et al., *The Impact of COVID-19 Shelter-in-place Policy Responses on Excess Mortality*, Health Economics 32 (11, Nov) 2499-2515 (2023)

[42] https://www.nme.com/news/music/second-lockdown-sparks-unprecedented-increase-in-illegal-raves-across-england-2807238

[43] Austan Goolsbee and Chad Syverson, *Fear, Lockdown, and Diversion: Comparing Drivers of Pandemic Economic Decline 2020*, 193 Journal Of Public Economics 104311 (2021).

[44] Jonas Herby, *A First Literature Review: Lockdowns only had a Small Effect on COVID-19*, SSRN (January 2021). https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3764553.

Kamerlin and Kasson similarly found that voluntary measures achieved significant behaviour alterations (and little discernible increased population covid mortality) in Sweden. Shina C.L. Kamerlin and Peter M. Kasson, *Managing Coronavirus Disease 2019 Spread with Voluntary Public Health Measures: Sweden as a Case Study for Pandemic Control*, 71(12) Clinical Infectious Disease 3174 (December, 2020).

achieved by voluntary means including non-statutory government advice and guidance, the case for lockdowns backed by legal force is much harder to make.

A reasonable challenge to this conclusion is whether the case for lockdowns at the time they were first instituted might have been reasonable given the evidence available at that time. This point was addressed directly in the independent report by Dr. Ashley Croft, commissioned by the Scottish Covid Inquiry.[45] Dr. Croft's assessment of the evidence base for lockdowns in early 2020 was as follows: "there was either insufficient evidence in 2020 to support their use – or alternatively, no evidence; the evidence base has not changed materially in the intervening three years."[46]

An Ethical Evaluation of the Lockdowns

In the light of the ethical framework we sketched in section 3 and the evidence we reviewed in section 4, were lockdowns ethically justified? We must be careful about criticising the lockdown policy with the benefit of hindsight. We must also be careful to make full allowance for the seriousness of the pandemic, the speed with which it developed, and the not unreasonable fear (that could only have been heightened by seriously inadequate pandemic preparation, illustrated by the inadequate supplies of personal protective equipment) that it would, in the absence of radical measures, overwhelm the health service. Nevertheless, it was doubtful even at the time the lockdowns were initially imposed, let alone in the wake of the obvious and enormous harms that they would and did inflict, that they met the ethical criteria we outlined.[47]

It seems clear that the lockdowns fell well short of the "strict scrutiny" standard laid down by Childress et al. The UK government, which seems to have been *far* from alone in this respect, failed to demonstrate (i) that the lockdowns would produce substantial benefits (ii) that those benefits would outweigh their obvious, enormous and long-lasting costs or (iii) that the hoped-for benefits could not have been achieved by voluntary behavioural changes encouraged and informed by public health education as opposed to highly restrictive measures enforced by the criminal law.[48] (And in England,

[45] Ashley Croft, *Report for the Scottish COVID-19 Inquiry* (July, 2023). www.covid19inquiry.scot/sites/default/files/2023-07/Dr-Croft-epidemiology-report.pdf

[46] *Id.* at 74.

[47] As early as 17 March 2020, public health experts such as Ioannidis pointed out the paucity of evidence for interventions such as lockdowns and shutting schools as well as the possibility that such interventions might cause unintended behavioural consequences that could feasibly worsen the situation, John P.A. Ioannidis, *A Fiasco in the Making? As the Coronavirus Pandemic Takes Hold, We are Making Decisions Without Reliable Data*, Stat (2020) www.statnews.com/2020/03/17/a-fiasco-in-the-making-as-the-coronavirus-pandemic-takes-hold-we-are-making-decisions-without-reliable-data/

[48] Steven Kraaijeveld, *COVID-19: Against a Lockdown Approach*, 13(2) Asian Bioethics Review

enforcement by the police was generally rigorous and sometimes draconian.) Remarkably, it remains doubtful whether the UK Government (and possibly any government) conducted a serious cost-benefit analysis before locking down. Moreover, Pykett et al.[49] role) Wilson et al.[50] provide evidence that the government deliberately sidelined bodies that existed to provide expert ethical input.

In August 2022, a revealing interview with the then Chancellor of the Exchequer (or Treasury Secretary) Rishi Sunak MP (who would later become Prime Minister) provided a disturbing insight into the decision-making process.[51] He disclosed that the decision to lockdown was largely a response to the modelling by Neil Ferguson and colleagues at Imperial College, London, discussed above. Ferguson and colleagues did not explore the wider social and economic costs of lockdown, (which they acknowledged would be enormous and which was not part of their model) but neither, admitted Sunak, did the UK Government. Indeed, he claimed he had not even been allowed to talk about the trade-offs within Cabinet and the official line had been not even to acknowledge them.[52]

Sunak further reported that the then Prime Minister had wanted to present the lockdown policy as "following the science" rather than a policy decision, and the lockdown policy was effectively determined by SAGE (the Scientific Advisory Group for Emergencies). Not even members of the Cabinet knew how this committee arrived at its recommendations. Typically, Sunak said, ministers would be shown SAGE analysis pointing to horrific "scenarios" if lockdown was not imposed or extended, but not even he could find out their assumptions and rationales. It was only in December 2021, when he and others had access to alternative modelling from J.P. Morgan, questioning SAGE's prediction that without a fourth lockdown deaths could reach 6,000 per day, that a further lockdown was averted.

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195 (2020).

[49] Jessica Pykett et al., *Ethical Moments and Institutional Expertise in UK Government COVID-19 Pandemic Policy Responses: Where, When and How is Ethical Advice Sought?*,19(2) Evidence & Policy 236 (2023).

[50] James Wilson et al., *Providing Ethics Advice in a Pandemic, in Theory and in Practice: a Taxonomy of Ethics Advice*, Bioethics 1 (2023). https://onlinelibrary.wiley.com/doi/10.1111/bioe.13208

[51] Fraser Nelson, *The Lockdown Files: Rishi Sunak on What We Weren't Told*, The Spectator (27 August 2022).

[52] The recent emergence of ministerial communications on social media (https://www.telegraph.co.uk/news/lockdown-files/) seems to confirm the dysfunctional decision-making process at the heart of government. As does evidence being submitted to the ongoing official inquiry into the pandemic: https://www.telegraph.co.uk/news/2023/10/30/covid-inquiry-uk-news-latest-boris-johnson-dominic-cummings/

Moreover, Sunak added, the public had been subject to systematic efforts to raise the perceived threat level from the virus while being kept in the dark about the likely effects of lockdown. He said: "We helped shape that: with the fear-messaging, empowering the scientists and not talking about the trade-offs."[53] He did not argue that lockdown had been a mistake, but his frank admissions are consistent with the view that the process leading to their imposition failed to meet the ethical criteria for imposing such an extreme and coercive policy.

Lord Sumption observed[54] that the Sunak interview demonstrated three important points: (i) that the scientific advice was more superficial and inconsistent than the government let on (ii) that the government stoked fear, resorting to manipulative advertising and extravagant graphics[55] and (iii) that the government not only ignored the catastrophic collateral damage done by the lockdown but actively discouraged discussion of it.

This revealing window onto the flawed decision-making process within the UK Government may help to explain why most governments failed to follow the guidance on dealing with pandemic influenza that had been published by the WHO only the year before.[56] That guidance was careful to set out the evidence base for the various measures it considered, not least the quarantining of exposed individuals. Significantly, it did not recommend quarantine, even of those who had been exposed to the virus, let alone those who had not, in any circumstances. It read: "Home quarantine of exposed individuals to reduce transmission is not recommended because there is no obvious rationale for this measure, and there would be considerable difficulties in implementing it."[57] Commenting on the ethical aspects of quarantine, the guidance observed that the main ethical concern was freedom of movement, a concern which was greater than in relation to the isolation of infected individuals because evidence on the effectiveness of quarantine varied and because quarantine restricted the movement of asymptomatic and mostly uninfected individuals. Moreover, mandatory quarantine increased such ethical concern considerably. Further, household quarantine could increase the risk of household members becoming infected.[58]

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[53] *Supra* note 51.

[54] Jonathan Sumption, *Little by Little the Truth of Lockdown is Being Admitted: It was a Disaster*, The Times (29 August 2022).

[55] See Laura Dodsworth, A State Of Fear: How The UK Government Weaponised Fear During The Covid-19 Pandemic (London: Pinter and Martin, London, 2021).

[56] *Supra* note 14.

[57] *Id.* at 47.

[58] *Id.* at 46. Although the ethical literature on lockdowns is surprisingly limited, it is noteworthy that our concerns about whether the lockdowns were justified are being echoed in relation to countries including the US and Australia: see Eric Winsberg et al., *How Government Leaders Violated Their Epistemic Duties During the SARS-CoV-2 Crisis*, 30(2) Kennedy Institute Of Eth-

Conclusions

It is possible to imagine extreme scenarios in which a temporary lockdown might in principle be justified on public health grounds. However, because lockdowns involve grave and legally-enforced restrictions of basic rights and liberties, they must be rigorously and transparently justified.

The UK Government failed to demonstrate that the lockdowns were either a necessary or a proportionate response to the virus, evidently omitting even to conduct a cost-benefit analysis. A flawed decision-making process led to a flawed public policy. It claimed that its lockdown policy was "following the science" but some of "the science" was questionable and, in any event, a decision to close down society is a matter of prudential moral judgment, not scientific judgment. A decision to lock society down is no more a matter for scientists than a decision to go to war is a matter for the military. Moreover, although the conduct of each government would have to be considered on its merits, it is fair to stay that the UK Government appears to have been far from alone in breaching the standard ethical criteria for resorting to such an extreme measure.

A key question is why governments resorted to coercive measures when the evidence suggests that voluntary behavioural changes tended to have more significant effects? Even the modelling by Ferguson et al. which was so influential in persuading politicians to impose the lockdown pointed out: "it is highly likely that there would be significant spontaneous changes in population behaviour even in the absence of government-mandated interventions."[59] While it is proper for Government to "follow the science" (after subjecting it to proper scrutiny[60])it is even more important for it to "follow the ethics." In the case of the UK at least, the government failed even to follow its own ethical policy for responding to pandemics, formulated back in 2007, or to seek ethical input from expert bodies which were well-placed to provide it.

The policy approach taken by the UK (and it would appear many other governments) seems to have focussed too narrowly on the suppression of the virus. Although this approach was motivated by a good end (seeking to protect life and health), the means it involved infringed a range of other important human goods including family, friendship, faith, education, and work. Life is

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ics Journal 215 (2020); Eric Winsbserg et al., *This Paper Attacks a Strawman but the Strawman Wins: A reply to van Basshuysen and White*, 31(4) Kennedy Institute Of Ethics Journal 429 (2021); Katharina Ó Cathaoir, Human Rights in Times of Pandemics: Necessity and Proportionality *in* Morten Kjaerum et al. (eds), COVID-19 And Human Rights (London: Routledge, 2021); Euzebiusz Jamrozik, *Public Health Ethics: Critiques of the "New Normal"*, 40 Monash Bioethics Review 1 (2022), and Samuel Director and Christopher Freiman *Civil Liberties in a Lockdown: The Case of COVID-19*, Journal Of Medicine And Philosophy 1 (2023). doi/10.1093/jmp/jhad037/7259830

[59] *Supra* note 2, at 3.

[60] Griffin Trotter, *COVID-19 and the Authority of Science*, 35 HEC Forum 111 (2023).

not a supreme moral good. To seek to prolong it by closing schools and colleges and depriving children (who were at particularly low risk from the virus) of the good of knowledge and education; by denying people freedom to exercise religion by closing places of worship; by denying friends and family the opportunity to share precious (including final) moments together; by depriving employers and employees of the good of work and in many cases their very livelihoods, and by undermining the economy, both local and global, is tantamount to "vitalism", a tunnel-visioned focus on prolonging life at all costs. Even adopting a blinkered focus on the preservation of life, there appears to have been inadequate consideration given to the very low risk the virus presented to the vast majority of people[61] and to the number of lives that would be lost through lockdown policies themselves.

Lockdowns also aggravated social inequalities by imposing measures that hit the poor and disadvantaged hardest, such as people with disabilities,[62] the elderly and manual workers who could not work remotely. Further, the UK Government clearly failed in its duty to be open and transparent with the public about the questionable evidential basis on which they were resorting to restrictions and about the enormous and ongoing costs lockdowns and business closures would involve to society.[63]

Assessing lockdowns against the five criteria comprising the "strict scrutiny" framework advocated by Childress et al., a good case can be made that the UK Government failed to meet any, apart perhaps from considering, however inadequately, the number of lives it thought lockdowns would save or prolong.

The contrast with Sweden is instructive. Its Corona Commission, which was set up in June 2020 and reported in February 2022,[64] concluded that while the Swedish response to the virus was in some respects flawed, its policy of

[61] Estimates of the infection fatality rate (IFR) continue to vary, but it is generally agreed that the IFR was extremely low for younger groups and those not suffering from other health issues. For example, the analysis in the *Lancet* by the Covid-19 Forecasting Team indicates a pre-vaccine IFR of 0.0023% for 7-year olds, rising to 1% for 60-year olds. Covid-19 Forecasting Team, *Variation in the COVID-19 Infection–Fatality Ratio by Age, Time, and Geography During the Pre-Vaccine Era: a Systematic Analysis*, 399 The Lancet 1469 (2022). Pezzullo et al. estimate an overall IFR of 0.035% for people under 60. Angelo M. Pezzullo et al., *Age-Stratified Infection Fatality Rate of COVID-19 in the Non-Elderly Informed from Pre-Vaccination National Seroprevalence Studies*, 216 Environmental Research 114655 (2023).

[62] See the sources cited *supra* note 4.

[63] Stephen Thomson and Eric C. Ip, *COVID-19 Emergency Measures and the Impending Authoritarian Pandemic*, 7 Journal Of The Law And Biosciences 1 (2020).

[64] Corona Commission, *Final Report: Summary in English* (2022) https://coronakommissionen.com/wp-content/uploads/2022/02/summary_20220225.pdf. By contrast, the terms of reference of the British inquiry were not even published until June 2022; it did not begin hearing evidence until June 2023 and it may cost upwards of £200 million. https://www.instituteforgovernment.org.uk/explainer/covid-19-inquiry. The link to the inquiry's website is: https://covid19.public-inquiry.uk/

not locking down and of relying instead on advice, recommendations and voluntary compliance was "fundamentally correct." The Commission added that lockdowns are not necessary to deal with a new, serious epidemic. They infringed people's freedom in a way that was defensible only in the face of very extreme threats; there were serious questions about their long-term sustainability, and many countries that had imposed them had significantly worse outcomes than Sweden.[65]

In this paper, we have restricted our analysis to lockdowns. However, the principles we outline here could easily be applied to other Covid-19 policies such as mask and vaccine mandates. For example, Girma and Paton[66] have found that vaccine mandates for care home workers in England had no observable impact on mortality amongst elderly residents but led to a significant and potentially damaging reduction in staffing. Had such policies been subject to a more rigorous ethical analysis when being proposed, it is likely that at least some of the adverse consequences of the restrictive Covid-19 policy might have been avoided.

Looking to the future, we believe the experience of the past few years vividly demonstrates the importance of putting a clear, coherent and transparent set of ethical values and principles at the heart of the decision-making process.[67] The very heavy ethical burden of justifying such extreme policies as lockdowns lies firmly on those who would seek to impose them. Indeed, in the light of the experience of, and the evidence generated by, the Covid pandemic, we find it difficult to envisage any circumstances in which a lockdown of society in response to a future public health crisis would meet the ethical criteria we have set out.

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[65] *Supra* note 64, at 3:9.

[66] Sourafel Girma and David Paton, *Covid-19 Vaccines as a Condition of Employment: Impact on Uptake, Staffing and Mortality in Elderly Care Homes*, Management Science (2023) doi.org/10.1287/mnsc.2023.4832

[67] Degeling et al. have questioned the value of ethical frameworks in responding to pandemics. Chris Degeling et al., Why Ethical Frameworks Fail to Deliver in a Pandemic: Are Proposed Alternatives an Improvement? 37 Bioethics 806 (2023). In our view, the key problem with the response to the Covid-19 pandemic was not that the ethical frameworks were not useful but that they were ignored. Indeed, while we acknowledge the importance of prudential judgment in responding to the particular circumstances that emerge, we cannot see how governments can feasibly respond in an ethical manner to a pandemic in the absence of reasonably clear prior guidance as to what would, and would not, qualify as ethical courses of action. We may add that, to help inform government decision-making, we see merit in the proposal of a "red team" of experts to evaluate input, scientific and ethical, that governments receive from their own advisors: see Carl Heneghan, We Need a Covid Inquiry – But This Isn't It, The Spectator (4 November 2023).

How Controversy and Socioeconomic Factors Influence Stem Cell Research

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Abstract: Adult stem cells dominate worldwide stem cell clinical trials. We investigated factors that may explain levels of stem cell research across different countries. Stem cell trials from clinicaltrials.gov were counted and categorized based on the country, the type of stem cell used, and whether that type is ethically controversial. The trial data were compared with characteristics of the countries such as population and GDP. We looked at the general ethical position of the countries by ranking their favorability toward abortion via their legislation. We found GDP, which may be indicative of the interest and means a nation can put toward research, to be the most predictive measure of stem cell use. No correlation was found with national abortion legislation, which is an indicator of ethical positions on life issues in a country. Thus, it would seem that the use of stem cells, namely the significantly greater use of adult stem cells over other more controversial types, is likely to be more influenced by their scientific utility and not by other social or ethical opinions. In addition, ESC and other ethically controversial research does not appear to be necessary for the US to dominate worldwide stem cell research.

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Introduction

Stem cells have the ability to self-renew and differentiate.[1] Self-renewal means that a cell has the capacity to make copies of itself. Differentiation means that the cells can turn into other types of cells. Major categories of stem cells include adult stem cells (ASCs),[2] cancer stem cells (CSCs),[3] embryonic stem cells (ESCs),[4] perinatal stem cells (PSCs),[5] fetal stem cells (FSCs),[6] and induced pluripotent stem cells (iPSCs).[7] ESCs, PSCs, and iPSCs have a differentiation ability called pluripotency which means that a single cell of this type can become any cell type in the adult human body.[8] ASCs and FSCs are usually multipotent which means that a single source of these cells can only differentiate into a few different cell types.[9]

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[1] Gilbert, SF. 2014. *Developmental Biology*. Sunderland, MA: Sinauer Associates, Inc, 320; Alberts, B, A Johnson, J Lewis, M Raff, K Roberts, and P Walter. 2002. *Molecular Biology of the Cell*. 4: 401. New York: Garland Science; Wolpert, Lewis, Cheryll Tickle, T Jessell, P Lawrence, E Meyerowitz, E Robertson, and J Smith. 2011. *Principles of Development*. Oxford: Oxford University Press, 600; Schoenwolf, GC, SB Bleyl, PR Brauer, and PH Francis-West. 2009. *Larsen's Human Embryology*. Philadelphia: Elsevier, 162; Wilt, FH, and SC Hake. 2004. *Principles of Developmental Biology* New York: W.W. Norton & Company, 18; National Institute of Health. 2001. "The Adult Stem Cell." Stem Cell Information. 2001; Carlson, BM. 2009. *Human Embryology and Developmental Biology*. Philadelphia: Mosby, 54.

[2] Dulak, Józef, Krzysztof Szade, Agata Szade, Witold Nowak, and Alicja Józkowicz. 2015. "Adult Stem Cells: Hopes and Hypes of Regenerative Medicine." *Acta Biochimica Polonica* 62 (3): 329–37. https://doi.org/10.18388/abp.2015_1023.

[3] Wang, Tao, Sarah Shigdar, Michael P. Gantier, Yingchun Hou, Li Wang, Yong Li, Hadi Al Shamaileh, et al. 2015. "Cancer Stem Cell Targeted Therapy: Progress amid Controversies." *Oncotarget* 6 (42):

[4] Damdimopoulou, Pauliina, Sergey Rodin, Sonya Stenfelt, Liselotte Antonsson, Karl Tryggvason, and Outi Hovatta. 2016. "Human Embryonic Stem Cells." *Best Practice and Research: Clinical Obstetrics and Gynaecology* 31: 2–12. https://doi.org/10.1016/j.bpobgyn.2015.08.010.

[5] Antoniadou, Eleni, and Anna L. David. 2016. "Placental Stem Cells." *Best Practice and Research: Clinical Obstetrics and Gynaecology* 31: 13–29. https://doi.org/10.1016/j.bpobgyn.2015.08.014; Can, Alp, and Sercin Karahuseyinoglu. 2007. "Concise Review: Human Umbilical Cord Stroma with Regard to the Source of Fetus-Derived Stem Cells." *Stem Cells* 25 (11): 2886–95. https://doi.org/10.1634/stemcells.2007-0417; Couto, Pedro S, Alexey Bersenev, and Frances Verter. 2017. "The First Decade of Advanced Cell Therapy Clinical Trials Using Perinatal Cells (2005 – 2015)." *Regenerative Medicine* 12 (8): 953–68;

[6] Soubelli, Valentina, Pascale V. Guillot, and Paolo De Coppi. 2016. "Induced Pluripotent Stem (IPS) Cells from Human Fetal Stem Cells." *Best Practice & Research Clinical Obstetrics & Gynaecology* 31 (June): 112–20. https://doi.org/10.1016/j.bpobgyn.2015.08.007; Götherström, Cecilia. 2016. "Human Foetal Mesenchymal Stem Cells." *Best Practice and Research: Clinical Obstetrics and Gynaecology* 31: 82–87. https://doi.org/10.1016/j.bpobgyn.2015.11.010.

[7] Hirschi, KK, S Li, and K Roy. 2013. "Induced Pluripotent Stem Cells for Regenerative Medicine" 6 (8): 277–94. https://doi.org/10.1021/nn300902w.Release.

[8] Redfield, EE. et al. 2021. "Types of Stem Cells Used in US-Based Clinical Trials Between 1999 and 2014." Catholic Social Science Review. 26:175.

[9] Redfield. 2021. 174.

ESC and FSC research are ethically and politically controversial because they involve the destruction of human organisms at an embryonic or fetal stage of development.[10] Despite predictions of ESC research's promise in prestigious journals[11] and support from research institutes and nonprofit organizations, ESCs have had little success in producing clinical trials or treatments.[12] Instead, clinical trials are dominated by ASCs[13] and the only stem cell treatments that have received FDA approval are with adult stem cells.[14] Some argue that the lack of ESC and FSC success is due to the ethical controversy of human ESCs and FSCs.[15] Perhaps political concerns related to their ethically controversial nature have hindered treatments and clinical trials. In contrast, treatments and clinical trials with less controversial stem cells such as ASCs might be inflated due to their less controversial nature. On the other hand, ESCs and FSCs may be used in few clinical trials and treatments because they are just less useful scientifically.

The purpose of this study is to analyze factors that may influence the types of stem cells used in clinical trials worldwide. We investigated various social and economic factors across countries to see whether they could be used to predict the number or distribution of stem cell clinical trials. Factors analyzed

[10] While FSCs are normally controversial, they could be obtained after a miscarriage which would not be controversial. However, the authors are not aware of any published examples of FSCs derived in this way. In addition, the non-controversial stem cell types could be derived in controversial ways. For example, iPSCs could be derived from tissue obtained after an abortion. ASCs, iPSCs, and PSCs are categorized as widely accepted here because they are commonly derived in an ethical way and are not controversial when derived ethically.

[11] The journal *Stem Cells* published an article in 2010 on their position statement on hESC research. In this statement, *Stem Cells* commended FDA's approval of use of hESCs in clinical trials for spinal cord injury treatment. Regarding the development of iPSCs in clinical trials, *Stem Cells* stated that iPSCs should be "compared with the gold standard of hESC at every step of experimentation." Stojkovic M, Pittenger MF, Nolta JA, Lako M, Lappin TR, Murphy MJ Jr. Stem Cells' position statement on hESC research. Stem Cells. 2010 Sep;28(9):1A. doi: 10.1002/stem.517. PMID: 20809560. https://doi.org/10.1002/stem.517; In *Nature*, Dr. Dieter Egli, acclaimed professor of Colombia University, predicted that embryonic stem cell research would "lead to unprecedented discoveries that will transform life." Cyranoski, David. 2018. "How human embryonic stem cells sparked a revolution." *Nature* (555):428-430. https://www.nature.com/articles/d41586-018-03268-4

[12] Redfield. 2021. 161-191.

[13] Redfield. 2021. 169-191.

[14] Prentice, D & Tarne, G. (2007) Treating Diseases with Adult Stem Cells. *Science Magazine*, 1-16. https://www.science.org/doi/10.1126/science.315.5810.328b

[15] Baumgartner, Fritz. 2019. "Human Embryonic Stem Cell Research, Abortion, and Publication Bias in the New England Journal of Medicine." *The Linacre Quarterly*. 86 (1):103-114 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6537346/; Boonstra, Heather D. 2016. "Fetal Tissue Research: A Weapon and a Casualty in the War Against Abortion." Guttmacher Institute. https://www.guttmacher.org/gpr/2016/fetal-tissue-research-weapon-and-casualty-war-against-abortion

were a country's gross domestic product (GDP), GDP per capita, population, and abortion legislation. A correlation between a country's stem cell clinical trials and its abortion legislation may suggest that the stem cell research in a country is being affected by ethical perspectives since abortion and embryonic stem cell research are undeniably linked.[16] If a correlation between a country's stem cell clinical trials and other factors such as GDP, GDP per capita, and/or population is found, it would suggest that ethical biases/perspectives are not the major influence in stem cell research and thus stem cell research choices would be more likely to be due to scientific utility. While previous studies have examined the treatments and uses of stem cells in clinical trials,[17] we are not aware of any studies that examine clinical trials across countries and the potential influences on the types of stem cell clinical trials conducted.

Methods

Clinical trials involving stem cells were categorized based on the country where the stem cell research was conducted and the type of stem cell used. Countries were categorized by GDP, population, and favorability to abortion.

Data Collection

Studies involving the use of stem cells between 1999 and 2014 that were registered on 'https://clinicaltrials.gov' were found, according to previous methods.[18] Briefly, we searched the term(s) "stem cell," "umbilical cord blood," "Wharton's jelly," "perinatal," "perinatal cell," and "perinatal stem cell." We also searched the term "stem cell" in the World Health Organization database and

[16] Jensen, David A. 2008. "Abortion, embryonic stem cell research, and waste." *Theor Med Bioeth.* 29(1):27-41

[17] Desai, Amar, Yan Yan, and Stanton L Gerson. 2018. "Concise Reviews: Cancer Stem Cell Targeted Therapies: Toward Clinical Success." *Stem Cells Translational Medicine* 34: 1–7. https://doi.org/10.1002/sctm.18-0123;

Hovatta, Outi, Sergey Rodin, Liselotte Antonsson, and Karl Tryggvason. 2014. "Concise Review: Animal Substance-Free Human Embryonic Stem Cells Aiming at Clinical Applications." *Stem Cells Translational Medicine* 3 (11): 1269–74;

Jackson, Wesley M, Leon J Nesti, and Rocky S Tuan. 2012. "Concise Review: Clinical Translation of Wound Healing Therapies Based on Mesenchymal Stem Cells." *Stem Cells Translational Medicine* 1 (1): 44–50;

Ilic, Dusko, Liani Devito, Cristian Miere, and Stefano Codognotto. 2015. "Human Embryonic and Induced Pluripotent Stem Cells in Clinical Trials." *British Medical Bulletin* 116: 19–27. https://doi.org/10.1093/bmb/ldv045;

Couto, Pedro S, Alexey Bersenev, and Frances Verter. 2017. "The First Decade of Advanced Cell Therapy Clinical Trials Using Perinatal Cells (2005 – 2015)." *Regenerative Medicine* 12 (8): 953–68;

Trounson, Alan, and Courtney Mcdonald. 2015. "Review Stem Cell Therapies in Clinical Trials : Progress and Challenges." *Stem Cell* 17 (1): 11–22. https://doi.org/10.1016/j.stem.2015.06.007; Li, Matthew D, Harold Atkins, and Tania Bubela. 2014. "The Global Landscape of Stem Cell Clinical Trials" 9 (1): 27–39 https://pubmed.ncbi.nlm.nih.gov/24236476/;

[18] Redfield. 2021. 169-191.

found that all of the 969 clinical trials that resulted were either already in our data (963) or did not meet our criteria (6).

The stem cells used in the trials were classified as one of six types. Stem cells taken from the inner cell mass of a blastocyst, which is an organism at an embryonic level of development, were classified as ESCs.[19] Cells derived from harvested fetal tissue such as aborted fetuses were FSCs.[20] Cells that were reprogrammed to become pluripotent, immortal cells were iPSCs.[21] Cells acquired from an individual after birth were ASCs.[22] Cells taken from extrafetal membranes such as the placenta, umbilical cord, and amniotic sac at the time of birth were PSCs.[23] Cells derived from cancerous tissue were CSCs.[24]

```
import openpyxl
import requests
from bs4 import BeautifulSoup
print("Make sure that the excel file you are using is put in the same folder location as this program\n")
print("I also suggest using a copy of whatever file you are using since this program will write over any
existing cell data if you choose a column with data already in it\n\n")
print("It should take the program about 0.6 seconds per study to retrieve the country information\n\n\n")
excelSheet = input("Excel file name:      ") + ".xlsx"
print("\n\n")
countryColumn = input("Enter the letter of the Column that you would like the country put in:      ")
print("\n\n")
column = countryColumn.upper()
wb = openpyxl.load_workbook(excelSheet)
sheet = wb['Sheet1']
count = 0
for row in sheet:
    count +=1
    cell = str('A' + str(count))
    cellValue = sheet[cell].value
    print(count)
    country = ""
    if count >1:
        URL = "https://clinicaltrials.gov/ct2/show/" + cellValue + "?term=" + cellValue + "&draw=2&rank=1"
        page = requests.get(URL).text
        soup = BeautifulSoup(page, 'lxml')
        this=soup.findAll('td', class_='ct-header3')
        text = str(this)
        list1 = text.split("</td>")
        countryList=[]
        for item in list1:
            if "padding-top:2ex" in item:
                newList = item.split(">")
                location = newList[1]
                newerList = location.split(",")
                country = newerList[0]
            if country not in countryList:
                countryList.append(country)
        countryListAsString =""
        thisCount = 0
        for country in countryList:
            if thisCount >0:
                countryListAsString += ", "
            countryListAsString += country
            thisCount += 1
        cell = str(column + str(count))
        sheet[cell] = countryListAsString
wb.save(excelSheet)
print("\n\n          ALL DATA HAS BEEN SAVED TO FILE\n\n\n\n")
input("          CLOSE PROGRAM")
```

Figure 1. Program written in python to determine location of clinical trials.

[19] Damdimopoulou. 2016.
[20] Soubelli. 2016. 112-20.
[21] Hirschi. 2013. 277-94. Soubelli. 2016. 112-20
[22] Dulak. 2015. 329-37.
[23] Soubelli. 2016. 112-20.
[24] Wang. 2015.

The country in which each trial was carried out was determined from the registry with a program written in python (Fig. 1). If multiple countries were listed for a trial, it was counted as a separate trial for each country involved, thus the total number of trial counts seen in Table 2 (5574), is higher than the actual number of registered trials (4287) used in our analysis. If a clinical trial employed stem cells that matched with multiple categories, it was recorded as falling under all applicable categories. Trials listed separately for Czechia and the Czech Republic were merged under Czech Republic. The countries Algeria, Lebanon, South Africa, Cayman Islands, Hong Kong, Taiwan, and Puerto Rico were removed from the data set. Those countries either did not have proper trial listings, did not have abortion information, or had jurisdictional and sovereignty questions. In total, 63 countries were included in our analysis after these exclusions (Table 1).

Table 1. Countries used in analysis, organized by continent. 63 total countries were included in the analysis.

North America	Colombia	Austria	Greece	Belarus	**Asia**	Malaysia
United States	Peru	Switzerland	Portugal	Lithuania	China	Saudi Arabia
Canada	**Europe**	Sweden	Ireland	Luxembourg	Korea	Indonesia
Mexico	Germany	Denmark	Slovakia	Serbia	Israel	Jordan
Jamaica	France	Poland	Croatia	Iceland	India	Philippines
South America	Italy	Czech Republic	Slovenia	Latvia	Iran	Vietnam
Brazil	Spain	Russian Federation	Bulgaria	Uruguay	Singapore	**Oceania**
Argentina	United Kingdom	Norway	Romania	**Africa**	Turkey	Australia
Panama	Belgium	Finland	Estonia	Egypt	Japan	New Zealand
Chile	Netherlands	Hungary	Ukraine	Tunisia	Thailand	

Studies that did not involve the usage of stem cells or progenitor cells were also excluded from this study. For example, clinical trials that involved the usage of cells from the stems of plants (i.e. "plant-stem cells") were excluded. When a clinical trial indicated the involvement of "stem cells", it was classified according to the subtype of stem cells used which are adult, embryonic, fetal, perinatal, induced pluripotent, and cancer stem cells. Clinical trials that did not mention "stem cells", but did mention "progenitor cells", were merged with the appropriate stem cell category. A trial was included if it involved the administration of stem cells, improved the usage of stem cells, or derived stem cells for a potential treatment, even if they were not the main intervention. A trial was not included if it did not administer, isolate, or examine stem cells even if it potentially altered a patient's stem cells (see NCT01167166 for example) or only examined patients who had previously received stem cells. If stem cells were mentioned in a trial, but there was no indication of the type of stem

cell used, it was classified as using stem cells, but no particular subtype was assigned.

Table 2. Counts of trials by stem cell type used for countries with five most total trials in analysis and counts of trials for all countries used in analysis.

	Adult	Embryonic	Extraembryonic	Embryo Proper	Induced Pluripotent	Cancer	Total
United States	2354	4	173	1	18	45	2604
Germany	275	0	5	0	0	4	284
France	227	1	10	0	3	3	244
China	171	0	54	0	0	7	232
Italy	191	2	11	0	0	3	207
Total Trial Counts for 64 Countries	5062	12	360	2	27	111	5574

A system to rank the favorability of countries to abortion was developed. The legal status of abortion in different countries was determined using data from the Population Division of the United Nations Department of Economic and Social affairs for the year 2013[25] (unpopulation.org). We chose 2013 as the year to represent abortion policy as this was the most recent year that had data available within the timeframe of our dataset (1999-2013) and the majority of the clinical trials occurred in the latter half of the timeframe.

We determined the number of countries with each abortion law and ranked the laws from the least common to most common. A weighted rating was created for each law and we normalized the ratings so that they would add up to 100. If a law allowing abortion was found in many countries, such as allowing abortion for the life of the mother, it was given a lower rating. In one country abortion was not allowed for any reason and this rating was set at zero. If a law allowing abortion was found in fewer countries, such as allowing abortion on demand, it was given a higher rating. Initial ratings were calculated by the following equation:

$$\frac{\text{total countries} - \text{no. of countries allowing abortion for that reason}}{\text{total no. of countries}} \times 100$$

After the initial ratings were determined, final ratings were calculated by normalizing the initial ratings so that they added up to a maximum rating of 100.

[25] United Nations. 2013. "World Abortion Policies 2013." Department of Economic and Social Affairs Population Division. https://www.un.org/en/development/desa/population/publications/pdf/policy/WorldAbortionPolicies2013/WorldAbortionPolicies2013_WallChart.pdf

Table 3. Number of countries where abortion is allowed for a particular reason along with associated abortion favorability ratings.

Legal grounds on which abortion is permitted United Nations - Department of Economic and Social Affairs - Population Division (2013)								
Abortion Allowed for	**None**	**Life of Mother**	**For Woman's Physical Health**	**For Woman's Mental Health**	**Rape/ Incest**	**Fetal Impairment**	**Economic or Social**	**On Demand**
Countries	1	62	55	53	51	48	41	36
Initial Rating	0	1.56	12.70	19.64	24.53	31.37	45.83	64.29
Normalized Rating	0	0.78	6.35	9.83	12.27	15.69	22.93	32.16

Population and GDP data from 2013 for each country was taken from the World Bank Group[26] and used to calculate GDP per capita for each country. ASCs, PSCs, iPSCs, and CSCs were characterized as "widely accepted" while ESCs and FSCs were characterized as "controversial." We used data from 2013 in order to match the timeframe of our clinical trial dataset.

Statistical Analysis

The dependent variable in our analysis was the number of stem cell clinical trials and the independent variables were the following: GDP, GDP per capita, abortion rank, and population. Both linear and multiple regression analyses were run to examine the correlations between these variables. A standardized residuals outlier test was run on the linear regressions in Microsoft Excel, with outliers removed if $r_i > 3$. Each linear regression is analyzed for outliers independent of the other regressions. For the multiple regressions, variables with significant p-values ($p < 0.05$) were identified and a second regression analysis was conducted only for those variables (GDP and population). Multiple regression equations were created from the coefficients of the intercept, GDP, and Population.

A χ^2 test of association was used to determine whether abortion legislation, GDP, GDP per capita, and/or population were associated with the number of stem cell clinical trials. For this test, GDP was grouped into tiers according to methods used by Pew Research.[27] The first tier goes up to two-thirds the median GDP, the middle tier being two-thirds to two times the median, and the upper tier being two times the median and above. The countries were grouped

[26] data.worldbank.org

[27] Bennet, Jesse; Fry, Richard; Kochhar, Rakesh. 2020. Are You in the American Middle Class? *Pew Research Center*. https://www.pewresearch.org/fact-tank/2020/07/23/are-you-in-the-american-middle-class/

by population in a similar manner and the three tiers run against the sums of trials of each type of stem cell. Lastly, countries were grouped by GDP per capita into the three tiers and the χ^2 test was run with the counts of each type of stem cell trial for each tier. Significance was assessed at $p < 0.05$.

Results

The highest correlation with abortion rank is seen where abortion rank explains 8.48% of CSC trials (Fig. 2D). Abortion rank explains 2.22% of ASC trials (2B), 1.80% of PSC trials (2C), 0.30% of iPSC trials (2E), and 0.42% of ESC trials (2F).

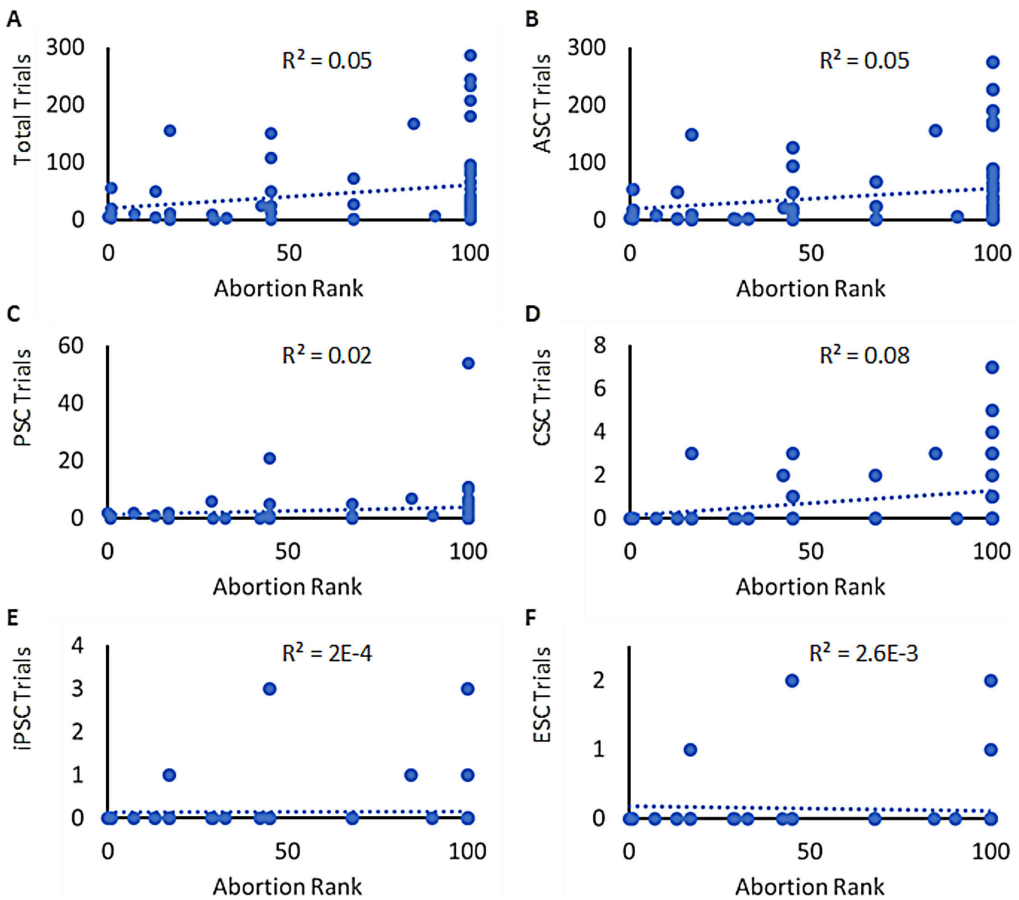

Figure 2. Stem Cell Clinical Trials vs Abortion Rank. A) Total stem cells B) Adult stem cells (ASC) C) Perinatal (PSC) D) Cancer (CSC) E) Induced pluripotent (iPSC) F) Embryonic (ESC). Each coordinate represents a particular country. Fetal stem cells are not included because no clinical trials remain when outliers are removed from that graph using the standardized residuals test.

There is a relatively low correlation between GDP per capita and number of stem cell clinical trials across countries. GDP per capita has the highest correlation with CSC trials at 19% (3D). GDP per capita explains 9.3% of ASC trials (3B), 2.0% of iPSC cell trials (3E), 1.0% of ESC trials (3F), and 0.050% of the PSC trials (3C).

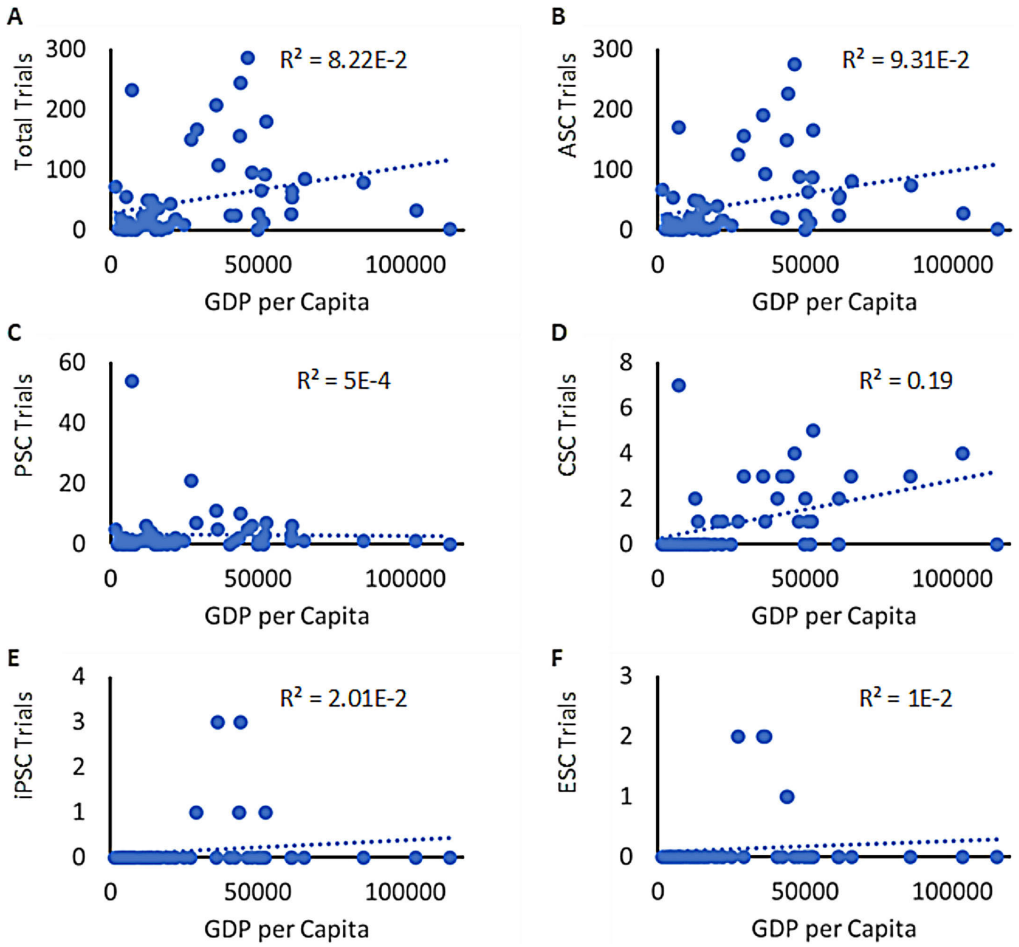

Figure 3. Stem Cell Clinical Trials vs GDP per Capita. A) Total stem cells B) Adult stem cells (ASC) C) Perinatal (PSC) D) Cancer (CSC) E) Induced pluripotent (iPSC) F) Embryonic (ESC). Each coordinate represents a particular country. Fetal stem cells are not included because there are no clinical trials when outliers are removed from that graph using the standardized residuals test.

There is a relatively high correlation between GDP and the number of stem cell clinical trials. The highest correlation is seen with GDP explaining 82.2% of ESC (Fig. 4F). GDP also explains a large percentage of PSC trials at

70.7% (4C), 67.5% of ASC trials (4B), and 64.2%, of FSC trials (4G). GDP explains a much lower percentage of CSC trials at 28.4% (4D) and only 6.38% of iPSC trials (4E).

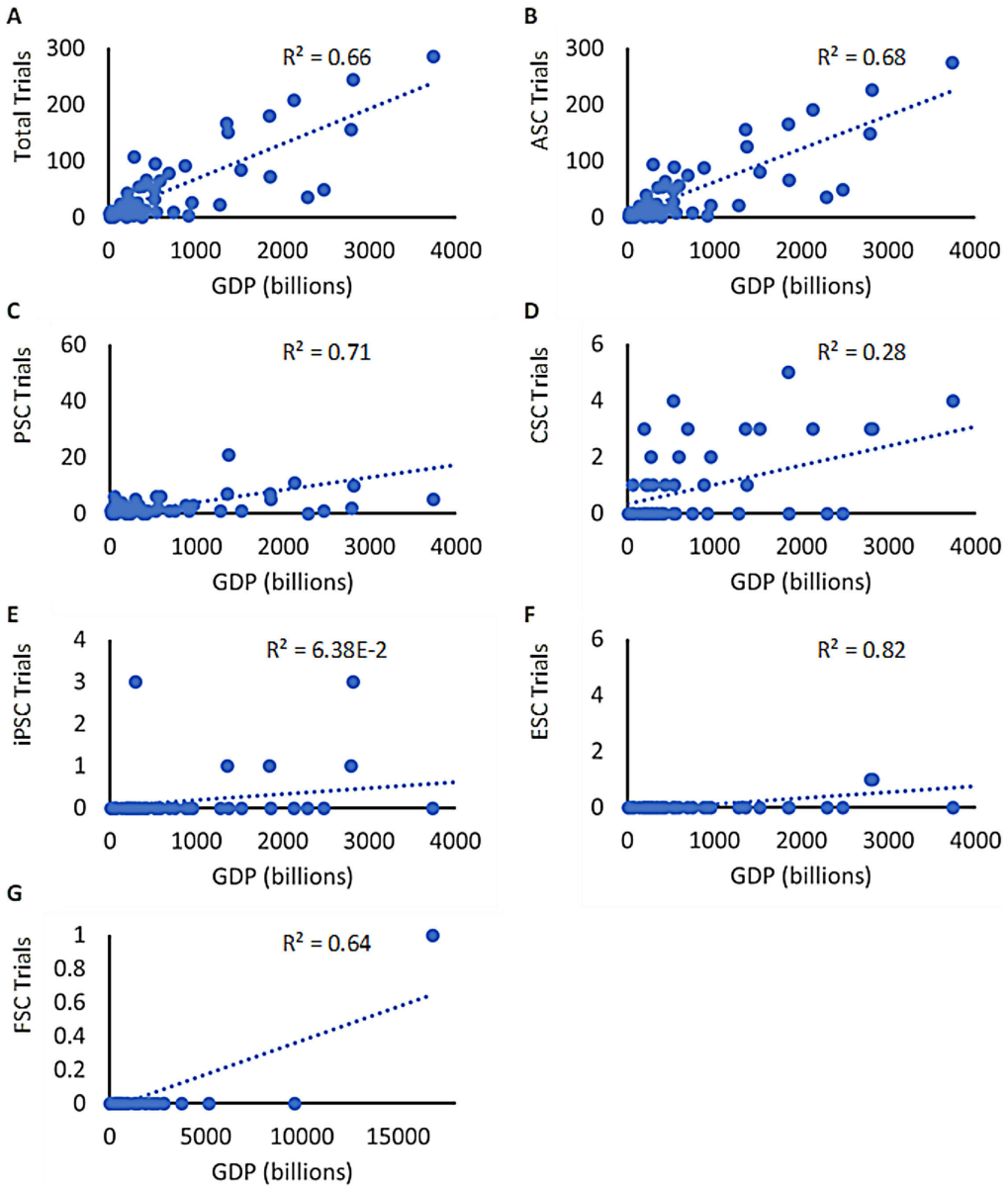

Figure 4. Stem Cell Clinical Trials vs GDP. A) Total stem cell trials B) Adult stem cells (ASC) C) Perinatal (PSC) D) Cancer (CSC) E) Induced Pluripotent (iPSC) F) Embryonic (ESC) G) Fetal (FSC). Each coordinate represents a particular country.

Population predicted less than 15% of clinical trials in four of the five stem cell types. PSCs stand out with the highest correlation at 47.5% (Fig. 5C). CSCs and ASCs have similar correlations, as population explains 10.1% of CSC trials (5D) and 5.75% of ASC trials (5B). ESC and iPSC clinical trials have very low correlations with population at 0.170% (5F) and 0.19% (5E) respectively.

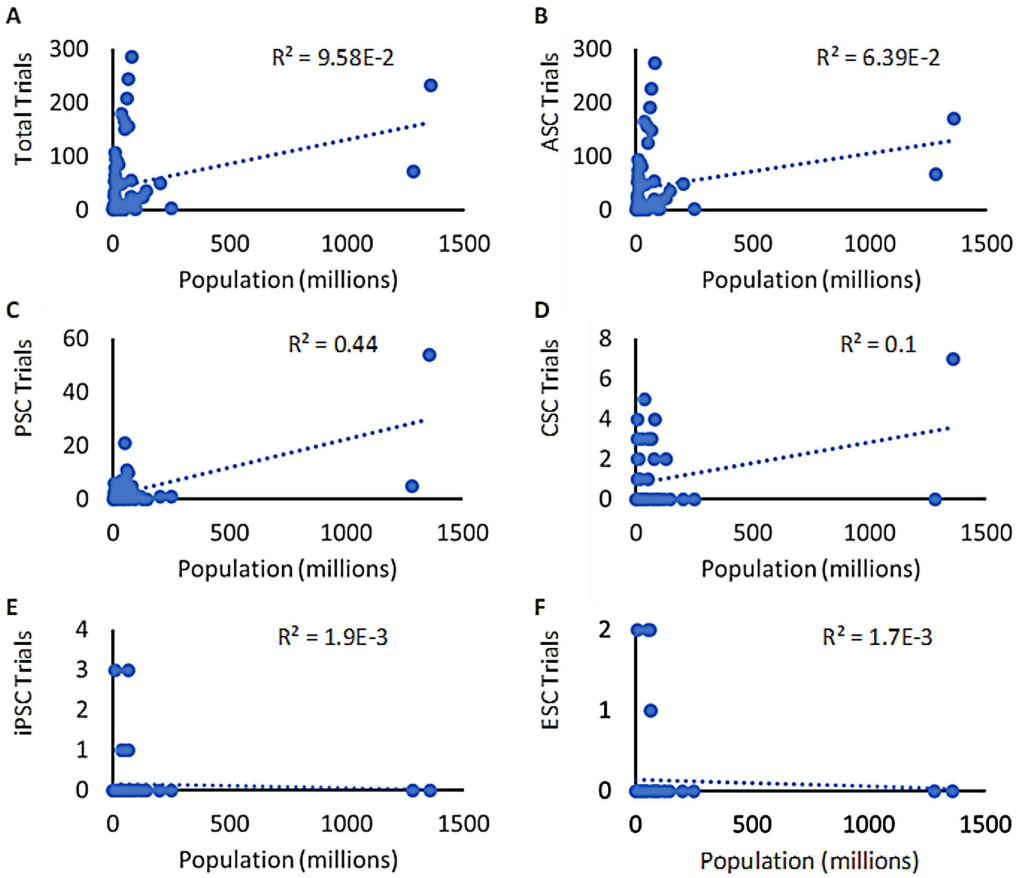

Figure 5. Stem Cell Clinical Trials vs Population. A) Total stem cell trials B) Adult stem cells (ASC) C) Perinatal (PSC) D) Cancer (CSC) E) Induced Pluripotent (iPSC) F) Embryonic (ESC). Each coordinate represents a particular country. Fetal stem cells are not included because no clinical trials remained when outliers are removed from that graph using the standardized residuals test.

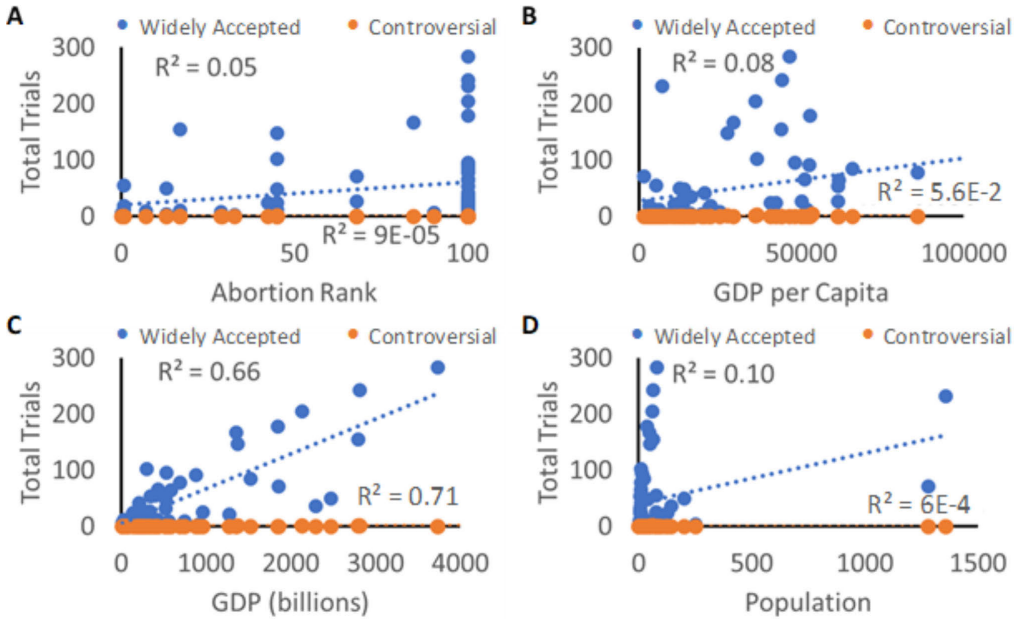

Figure 6. Clinical Trials Grouped as "Widely Accepted" or "Controversial" compared to predictive factors. A) Abortion Rank B) GDP per Capita C) GDP D) population.

Trials of widely accepted stem cells (ASCs, CSCs, PSCs, and iPSCs) and controversial stem cells (ESCs and FSCs), follow similar patterns of correlation with the three independent variables. Both show low correlations with GDP per capita, predicting only 8.28% of widely accepted trials and 5.6% of controversial trials (Fig. 6B). Population also had little predictivity, with 9.69% for widely accepted trials and 0.06% for controversial trials (6D). Likewise, Abortion rank shows low correlation at 5% for widely accepted and 9E-3% for controversial (6A). GDP, however, continues to exhibit high correlation with 66.38% for widely accepted and 70.49% for controversial (6C).

The multiple regression test is used to determine which variables have statistical significance when tested as a group. GDP and population are the only dependent variables that result in a significant p-value when in regressions with clinical stem cell trials.

For each multiple regression equation for the different stem cell trials, the GDP coefficients all have positive values (Table 5). This indicates the direct relationship between GDP and stem cell trials. The population coefficients all have negative values in the multiple regression equations, indicating the inverse relationship between population and stem cell trials (Table 5). ASC clinical trials display coefficients with the highest absolute values, meaning that GDP and population have the strongest effect on ASC clinical trials (Table 5).

Table 4. Multiple regression p-values of stem cell trial types with GDP and population across countries. The variables abortion rank and GDP per capita were not included in the final multiple regression model because they did not have a significant p-value when in initial multiple regression analysis and were thus excluded from the final models.

p-values	GDP	Population
Adult	5.91E-24	1.1E-06
Perinatal	5.56E-24	9.9E-03
Cancer	5.57E-25	1.1E-06
Induced Pluripotent	2.6E-19	4.1E-06
Embryonic	1.23E-10	1.8E-03
Fetal	4.49E-07	2.4E-02
Total Trials	3.47E-24	1.7E-06
Controversial	3.43E-24	1.8E-06
Widely Accepted	9.13E-11	1.7E-3

Table 5. Multiple regression equations of stem cell trial types with GDP and population across countries. y = number of stem cell trials.

Stem Cell Trial Type	Multiple regression equations
Adult	y = -20.99 + 0.12*GDP - 0.43*Pop
Perinatal	y = -3.01 + 8.92E-03*GDP - 1.54E-2*Pop
Cancer	y = -0.63 + 2.83E-03*GDP - 9.50E-03*Pop
Induced Pluripotent	y = -0.28 + 9.16E-04*GDP - 3.79E-03*Pop
Embryonic	y = 0.02.75E-2 + 2.18E-04*GDP - 9.82E-04*Pop
Fetal	y = -4.61E-03 + 4.80E-05*GDP - 2.11E-04*Pop
Total Trials	y = -24.88 + 0.14 * GDP + -0.46*Pop
Controversial	y = 0.02.29E-2 + 2.6E-04*GDP - 1.19E-03*Pop
Widely Accepted	y = -24.90 + 0.13*GDP - 0.46*Pop

FSC clinical trials had coefficients with the smallest magnitude, meaning that GDP and population have the weakest effect on clinical trials with FSCs. (Table 5).

All regressions with abortion rank as the dependent variable had correlations below 5%. GDP per capita explains 4.79% of abortion rank (Fig. 7C), GDP explains 1.59% of abortion rank (Fig. 7A), and population explains nearly 0% of abortion rank (R^2 = 3E-05, Fig. 7B).

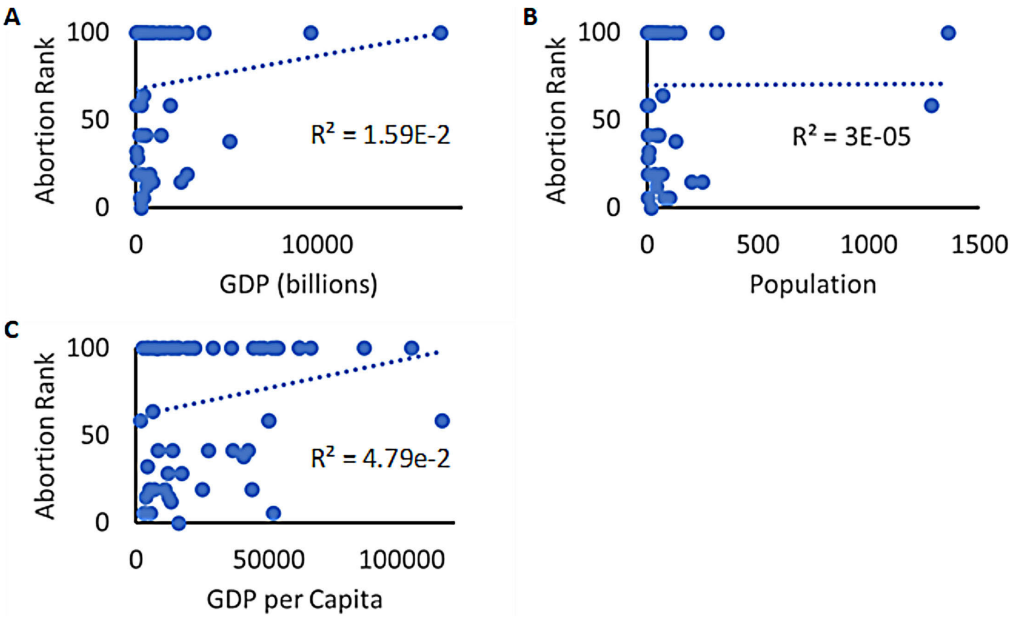

Figure 7. Collinearity between abortion rank and other factors. A) GDP, B) population, or C) GDP per capita.

Abortion rank does not exhibit a significant relationship with any of the other predictive factors, including GDP which is the best predictor of stem cell use. In all of the regressions, the United States was an outlier most frequently (80% of all singular and multiple regressions) due to the country's stem clinical trials exceeding all other countries by a significant amount. While the United States was the most common outlier, other notable outlier countries were Israel (20%), China (15%), and Japan (10%). No other countries were an outlier in more than one regression.

Table 6. χ^2 test of association. The trial type refers to the type of stem cell clinical trials conducted (i.e. ASC, CSC, ESC, FSC, iPSC, or PSC). The trial controversy variable contains two levels: widely accepted stem cell types (includes ASC, CSC, iPSC, and PSC clinical trials added together) and controversial stem cell types (includes ESCs and FSCs).

	A) Trial Type vs GDP	B) Trial Type vs GDP per Capita of Country	C) Trial Type vs Population of Country	D) Trial Type vs Abortion Policy	E) Trial Controversy vs Abortion Policy
p-value	0.23	2.78E-11	0.24	1.00	0.93

χ^2 tests of association revealed that the type of clinical trials a country undertakes are not significantly affected by GDP, population, or abortion policy (Table 6). GDP per capita did show a significant association with the types of stem cell clinical trials ($p = 2.78E\text{-}11$). Individual values from χ^2 calculations indicate this significance is due to PSC use (Table 7). If PSCs in the first tier of GDP per capita are excluded, there is no significant association between GDP per capita and stem cell type. The χ^2 test showed no association between the types of stem cell clinical trials and abortion policies. Similarly, abortion policies did not affect whether a country conducted clinical trials that are ethically controversial or widely accepted trials. If US data is excluded, there is no change in statistical significance.

Table 7. χ^2 results for each category in trial types vs GDP per capita. The calculated χ^2 value for PSC trials of the 1st GDP per capita division is significantly higher than all others. The first tier contains countries in the lowest third of GDP per capita. The third tier contains countries in the highest third of GDP per capita.

GDP per capita tiers	ASC	ESC	PSC	FSC	iPSC	CSC
1st	2.901	0.96	53.93	0.16	2.15	0.38
2nd	02.98E-3	0.76	0.48	0.12	1.63	0.44
3rd	0.254	0.27	5.85	4.57E-2	0.62	0.13

Discussion

In this study we grouped worldwide stem cell clinical trial data according to the country and type of stem cell used. Socioeconomic factors of the countries were compared with the clinical trial data to understand how these factors influence the use of stem cells in clinical trials. Most countries in our study had relatively permissive abortion laws (Table 3). For example, 36 of the 63 countries allowed abortion for all the circumstances laid out by the United Nations as of 2013. Only eight countries allow abortion in fewer than three of the

circumstances we evaluated, and Chile is the only country to not permit abortion under any circumstance. It is notable that the range of abortion favorability of the analyzed countries is relatively small compared to the numbers of stem cell clinical trials conducted. The abortion rank range for most countries is 17 to 100 (half of them being 100); while clinical trial counts, not including the United States (2620) ranges from 1 to 286 with more even distribution. With abortion favorability as an indicator of the ethical positions of the country, it seems that most countries have similar abortion ethics even though they have very different levels of stem cell research.

Abortion favorability and population were poor predictors of clinical trial numbers and the types of stem cells chosen for research (Figs. 2 & 5 and Table 6D & 6C).). These results suggest that neither population, nor ethical controversy over abortion affect stem cell research choices. PSCs are an exception as they have a relatively high correlation with population (R^2=0.44). One potential explanation for the relatively high correlation between perinatal stem cells and population is that since perinatal stem cells are typically acquired from extraembryonic tissues after birth, countries with more births (higher population) would produce more stem cells for this research. However, the correlation seems to be largely due to just one data point (China) that when removed completely changes the trendline and drops the R^2 to 1.2E-2. Therefore, the high correlation is more likely to be an artifact and does not appear to be reflective of trends across all countries.

GDP per capita was also generally a poor predictor of clinical trial numbers (Fig. 3) indicating that relative prosperity of a country's people (GDP per capita) does not influence the amount of stem cell clinical research. However, the χ^2 test indicates that GDP per capita does influence which types of clinical trials are chosen with countries with a low GDP per capita disproportionately choosing perinatal stem cell research (Table 6B). However, this χ^2 result is an artifact caused by China. Despite the second highest GDP, China's immense population yields a very low GDP per capita; but the number of clinical trials performed by China do not fit with the other countries in the lowest GDP per capita bracket. If China is excluded from the χ^2 test, GDP per capita does not influence which types of clinical trials are chosen.

GDP was the best predictor of clinical trial numbers with most regressions having an R^2 over 0.6 (Fig. 4). While higher GDP generally promotes greater numbers of stem cell clinical trials, the χ^2 analysis indicates that GDP does not affect which stem cell types are chosen for clinical trials (Table 6A). Even though ESC clinical trials were most correlated with GDP, according to the multiple regression equations the GDP coefficient (slope) was much higher with ASCs (0.12) than with ESCs (2e-4). This demonstrates that for a given increase in GDP, more ASC clinical trials will be generated than ESC clinical trials. These results show that for a given amount of money, countries across

the world invest more in ASC research than ESC research, suggesting a worldwide recognition of the greater usefulness of ASCs compared to ESCs and all other stem cell types.

Both the controversial and widely accepted stem cells had relatively high correlations with GDP (R^2=0.66, R^2=0.71, Fig 6.). Groupings based on controversy showed no notable association with abortion favorability (Fig. 6A) suggesting that preexisting ethical views do not encourage or discourage particular types of stem cell research. The significant predictivity of GDP suggests again that choices are driven by economics and not by ethics or controversy.

The United States by far surpasses all other countries in the number of stem cell clinical trials. A few other countries such as Israel (20%), China (15%), and Japan (10%) were found as outliers semi-regularly but the United States was removed from nearly all comparisons (80%) because it produces such a disproportionate share of stem cell clinical trials. These results suggest that concerns that 'the United States will fall behind in stem cell research if ESC research is not supported', are unfounded.[28] The dominance of the United States in stem cell research is mostly driven by ASCs and research with ESCs contributes very little to clinical trials in the US or any other nation.

While the ratio of controversial to widely accepted stem cell trials changes slightly (0.25% to 0.30%) when the United States is removed, the number of adult stem cell trials (2708) still significantly outnumbers all other types with perinatal being the next highest (187). Given that the United States so greatly surpasses other countries in trial counts as well as GDP, a more detailed analysis of the United States, perhaps comparing the same factors for individual states may provide a better picture of factors that influence stem cell research and whether interstate trends match trends seen throughout the world.

Conclusion

Similar to other studies,[29] this study used data that is a few years older than the publication date due to the time it takes to compile and analyze the data. While we rated abortion favorability in a country based on the reasons that abortion was legally acceptable, abortion favorability could also be estimated in other ways such as gestational age limits or public polling. Another limit of our study is that we used one year to represent abortion policy (2013) while our

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clinical trial data spans a number of years (1999-2014). However, there are few differences in abortion legislation over the timeframe of the study and most of the clinical trials occur in later years of the study. Therefore, using one year to represent abortion legislation is not likely to significantly change results or conclusions. Future studies that explore other ways to estimate abortion attitudes could help to confirm our findings.

A likely explanation of our results is that ASCs are indeed more scientifically meritorious and so the more prosperous countries will be apt to conduct greater amounts of trials involving those types. Our results indicate that the significant discrepancy in the use of ASCs versus all other types is not a result of any controversy or biases but is likely to be representative of what is most useful. Advantages of ASCs include multipotency, lack of tumor formation, being well tolerated by the recipient's immune system, lack of ethical controversy and popular support.[30] Multipotency potentially decreases differentiation toward undesired cell types. The popular support and lack of controversy allows potential treatments to be acceptable to the maximum number of potential patients and thus may be a more profitable investment for a company. These key advantages are likely to be the reason why ASCs dominate clinical trials. In addition, because there are many different types of multipotent ASCs it is possible to potentially get any cell type needed by choosing the correct ASC for the particular application even without pluripotency. PSCs probably have the second highest number of clinical trials because they are the only stem cell type besides ASCs that don't form tumors, and are well tolerated by the recipient's immune system.[31] However, their pluripotency may be a disadvantage compared to ASCs, as PSCs[32] ESCs, iPSCs, and FSCs probably have fewer clinical trials because ESCs and iPSCs have the disadvantage of teratoma formation, ESCs and FSCs are generally rejected by the patient's immune system, and all three of these stem cells types have the disadvantage of tumor formation.[33]

In addition, ESC and other ethically controversial research does not appear to be necessary for the US to dominate worldwide stem cell research. Future studies that explore other ways to gauge scientific utility or abortion attitudes could help to confirm that the dominance of noncontroversial stem cells in clinical trials are due to their greater scientific merit.

[30] Redfield. 2021. 174.
[31] Ibid, 175.
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[33] Ibid.

Maternal-Fetal Bonding

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ABSTRACT: A complex biological and psychological series of events commence at fertilization and continue through parturition between the preborn human organism and his or her mother, which extends far beyond the physical connection between an adult patient and contained tissue. This guideline reviews evidence in support of various aspects of this bond and its implications for care of the maternal patient.

***Key Words*: pregnancy, attachment, bonding, interventions**

Background

During pregnancy, an intense bond develops between mother and child. This bond is crucial for both the emotional and physical well-being of the child. The normal development of this bond progresses from knowing the child exclusively through the lens of the maternal body to later learning and appreciating who the child is as an individual.[1] In early pregnancy, the only signs of the developing pregnancy are through the mother's body. The mother develops physically visible signs such as swollen breasts and a discoloration of the cervix that make visible the developing life that is not yet large enough to be seen on his/her own. As pregnancy progresses, the child becomes more recognizable through detection of the heartbeat, distinct fetal movements, and ultrasound images. The mother is thus able to bond to a specific human being who is distinct from herself. Mother and child are then separated at time of delivery when the cord is cut. The bond that had been forming persists and allows the mother to now care for her infant outside of the womb.

The forming of this bond between the mother and child involves interactions at both the physiological and psychological levels. The physiologic

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interplay between mother and child via hormones and signals created and transferred through the placenta have been detailed in obstetric textbooks.[2] An example of this is estrogen metabolism in which the fetal adrenal glands produce the initial precursor which is modified by the placenta and then secreted in different forms into both the maternal and fetal systems. Similarly, signals from the placenta alter maternal metabolic homeostasis to allow the mothers metabolism to preferentially transfer to the fetus the nutrients he/she needs.

Beyond hormones, there is a permanent physiologic bond created between the mother and the child through microchimerism, that is "the long term presence within an individual of a low level of cells derived from a different individual."[3] During pregnancy, fetal cells enter the mother and become established. These fetal cells can persist for decades following pregnancy.[4,5] There is evidence that these fetal cells can even integrate into and influence the maternal brain.[6,7] Similarly, maternal cells can enter the fetus. This has been demonstrated by detecting HLA-disparate maternal cells in immunocompetent offspring well into adult life.[8] This exchange of cells occurs very early in pregnancy and is actually increased in instances of induced abortion.[9,10]

As the physical signs of pregnancy become translated into the mother's psychological experience, it leads to development of a psychological bond.[11] This transition into the role of mother also leads to change in self-concept.[12] There is an ongoing development of maternal-fetal bonding that tends to strengthen and mature throughout the pregnancy.[13-16] In early pregnancy, the mother is not able to know specific characteristics of her child and can only imagine who her child is. She must then transition from these prenatal representations of a "fantasized child" to postnatal representations of her "actual child."[17] The mother must come to know the child in the womb both through his/her connection to the mother and as a separate being with different characteristics, physical needs and emotions.[18]

When assessing strategies to increase maternal-fetal bonding, it is important to be able to assess the degree to which bonding is occurring. Historically, maternal-fetal attachment has been defined as "the extent to which women engage in behaviors that represent an affiliation and interaction with their unborn child."[19] In much of the literature there is an emphasis on improving maternal-fetal attachment. There is now an increasing focus on maternal-fetal "bonding" versus "attachment." While these constructs are similar, the term bonding emphasizes the role of the mother in assuming her role of caring for the child. Attachment has historically been focused more on the child's reliance on the parent to meet his/her needs. Thus, the literature is shifting toward a greater use of the term "bonding" while older instruments to assess these constructs have used the term "attachment."

Specifically, there are three widely used surveys to assess the bond between mother and unborn child. In 1981, Cranley published the Maternal-Fetal

Attachment Scale.[19] This questionnaire focuses primarily on self-evaluation of maternal behaviors in five subscales: differentiation of self from fetus, interaction with fetus, attributing characteristics and intentions to the fetus, giving of self, and role taking. Future researchers chose to focus on more emotional assessments of bonding versus behavioral. Muller published the Prenatal Attachment Inventory which is a 29-item instrument that uses a Likert scale to assess the degree of affectionate relationship for the fetus with statements such as "I feel love for the baby."[20] The Maternal Antenatal Attachment Scale developed by Condon is a 19-item questionnaire also focused on emotional attachment.[21] In contrast to the scale published by Cranley, Condon's scale is more specifically focused on attachment to the fetus as a person versus being focused on the actions assumed within the motherhood role.

These scales have been used to correlate the degree of maternal-fetal bonding with important prenatal and postnatal outcomes. There is a positive association between maternal-fetal attachment scale scores and health practices such as smoking cessation during pregnancy.[22-24] Multiple studies have demonstrated the link between antenatal bonding and postnatal bonding.[25-28] This in turn correlates with better attunement to infant states and more accurate interpretation of infant cues[29] and can predict better social affective developmental outcomes of the infant.[30] For the mother, the quality of maternal–fetal bonding independently predicts postpartum depressive and anxiety symptoms.[31]

Clinical Q&A

Q. What Factors are Associated with Improved Maternal-fetal Bonding?

The quality of maternal-fetal bonding is strongly associated with the quality of the mother's other significant relationships. In one study, the most important determinant of maternal-fetal attachment identified was perceived social support.[32] In another, the quality of the maternal-fetal relationship was best predicted by the romantic caregiving responsiveness to her partner and the woman's own psychological health.[33]

Q. What Factors Increase Risk for Poor Maternal-fetal Bonding?

The capacity of a mother to successfully bond with her preborn child can be influenced by a history of interpersonal trauma or unhealthy relationships in her own life.[34-36] These traumas can lead to early maladaptive schemas and insecure attachment styles within the mother that impair the mother's ability to bond with her child.[37-39] Depression, anxiety, and poor social support are all associated with poor maternal-fetal attachment.[32,40-43]

In addition, teenagers are at a particularly high risk for impaired bonding. Teenagers tend to develop attachments more slowly than adults do. In one cohort, the risk of persistent poor bonding remains elevated in teenagers with low first trimester attachment scores and history of pregnancy termination.[44]

Q. What Interventions have been shown to Increase Maternal-fetal Bonding?

For women at risk of poor maternal-fetal bonding, there are many suggestions for strengthening this relationship. Given the variable reasons mothers may have poor bonding, there is unlikely to be a standardized approach. Instead, interventions should be tailored to the underlying risks for poor bonding.[45]

Multiple studies have assessed the role of educational interventions with high success rates. Topics have included physiology of pregnancy and childbirth, awareness of the feelings and perceptions of the embryo, the concept of attachment, attachment behavior, control of anxiety and negative thoughts, patterns of proper sleep, exercise and nutrition during pregnancy, and relaxation training.[46-49] These educational programs have been linked to improvement in infant mental health variables from birth all the way to the first year.[46,50]

Simple interventions to increase awareness of fetal characteristics at prenatal visits may also impact bonding. When midwives explain the fetal position by taking the hand of each participant and touching the head or the buttocks of the fetus, it has been correlated with increased maternal awareness of fetal position and improved maternal-fetal attachment.[51] A randomized controlled trial showed that women who were taught to do fetal kick counts at 28-32 weeks gestation had significantly higher maternal-fetal attachment scores after 1 month of counting.[52] A more recent trial found conflicting results about the impact of fetal movement counting, which was likely due to baseline characteristics of the populations studied.[53]

Ultrasound is likely to be more beneficial in the early stages of maternal-fetal bonding before a clear mental construct of the fetus as a person is developed. In the mid-trimester, a 3D ultrasound appears to be more impactful for helping to develop this construct than a 2D ultrasound and positively impacts bonding.[54] The impact of the ultrasound seems to be mediated by the clarity of the images.[55] By the time a woman reaches the third trimester, ultrasound appears to be beneficial only for select mothers, such as those with high levels of depressive symptoms at baseline.[56]

Finally, interventions that improve maternal health and wellbeing can strengthen the mother's ability to bond with her fetus. A randomized controlled trial demonstrated that listening to music during pregnancy is

linked to lower psychosocial stress and increased maternal-fetal bonding.[57] Another program focused on teaching women to sing lullabies also found it was a positive experience that allowed the mothers to express complex emotions they were experiencing.[58] A composite intervention that included dancing and singing sessions resulted in higher prenatal attachment scores than controls who did not have prenatal courses.[48] Deliberate involvement in a Qi exercise group resulted in higher post-test maternal-fetal interaction scores.[59] A pilot study showed a 2-week program of prompting mindfulness behaviors via a text messaging system enhanced maternal-fetal bonding.[60]

Q. What is the Impact of Prenatal Genetic Testing on Maternal-fetal Bonding?

There are concerns that there are social pressures to conform with prenatal testing which may unintentionally burden expectant mothers.[61] After completing an exploratory analysis, sociologist Rothman concluded that if the decision to continue pregnancy rests on the results of prenatal testing, it creates a state of "tentative pregnancy." That is, the state of total attachment normally demonstrated early in pregnancy is delayed. Instead of the child being seen as good by nature of his or her existence, the child must be deemed "worthy" of surviving depending on the test results. The mother delays attachment early in pregnancy and then must try to catch-up after she decides to continue pregnancy.[1]

Further studies have provided evidence that the decision to have prenatal screening and/or testing delays, if not permanently impairs, maternal-fetal bonding.[62] In a qualitative study of first trimester screening in Denmark, most patients did look forward to having an ultrasound but said they would terminate if abnormal.[63] Having a quad screen can delay the developmental trajectory of prenatal attachment even if low risk results are obtained.[64] In a separate observational study, mothers who were highly informed about genetic testing were again found to have delayed attachment to their fetuses but were able to catch up after results were received.[65] Expert testimony to the Senate Subcommittee on Science, Technology, and Space of the Committee on Commerce, Science, and Transportation summarized these studies and clinical experience with the concern that the anxiety and lack of joy with prenatal diagnoses attaches a stigma to the child and causes "irreparable damage. . . to the family bond."[66] Though data are limited, it is likely that all women who wrestle with the decision of if they should continue a pregnancy are at risk for similar challenges to impaired early bonding.

Q. What is the Impact of Previous Pregnancy Loss on Maternal-fetal Bonding?

There is mixed data concerning the impact of previous pregnancy loss on maternal-fetal bonding. A longitudinal study demonstrated that a history of miscarriage decreased maternal-fetal attachment in the first trimester, but those differences resolved by the third trimester.[67] Among Iranian women, those who had a history of pregnancy loss scored lower on behaviors related to differentiation of self from fetus (items like "I can imagine myself taking care of the baby" and "I picture myself feeding the baby") but they scored the same on interactions with the fetus, attribution of characteristics to the fetus, giving of self, and role-taking.[68] However, in another cross-sectional study, researchers were unable to identify significant Prenatal Attachment Inventory score differences between parents with and without a previous pregnancy loss.[69]

Summary of Recommendations and Conclusion

The following recommendations are based on good and consistent scientific evidence (Level A):

1) Quality of maternal-fetal bonding is linked to postnatal attachment and indicators of infant psychological wellbeing.
2) Mothers with insecure attachments and interpersonal trauma are at increased risk for poor maternal-fetal bonding.
3) Educational interventions can improve maternal-fetal bonding in at-risk mothers.

The following recommendations are based on limited and inconsistent scientific evidence (Level B):

1) In at-risk women, ultrasound may have a role in improving maternal-fetal bonding.
2) Prenatal diagnostic testing and the resultant "tentative pregnancy" can negatively impact maternal-fetal bonding.

The following recommendations are based primarily on consensus and expert opinion (Level C):

1) An emphasis should be placed on maternal-fetal "bonding" versus "attachment" because this better reflects the directional relationship of the mother caring for the child and learning to meet his or her needs.

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Medication Abortion and Preterm Birth

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ABSTRACTS: Considerable controversy exists about the effects of medication abortion on the incidence of preterm birth (PTB). Medication abortion of various types continues to be touted as a safe alternative to surgical abortion, and without increased risk for PTB. There is a paucity of evidence regarding medication abortion and PTB, but available papers are reviewed here. There is moderate-quality evidence that medication abortions which require surgical completion increase PTB rates more than surgical abortion alone.

Background

Preterm Birth

Preterm birth (PTB), defined as delivery before 37 weeks of gestation, leads to 3 million annual deaths worldwide, and combined with low birth weight, PTB is estimated to cost over 100 million disability adjusted life-years.[1] The incidences of PTB range from 6-8% in Europe, Australia, and Canada[2,3] to 9-12% in Asia and Africa.[4,5] The rate of PTB in the U.S. was 10.2% in 2019.[6] In the U.S., the rate of delivering a low birth weight (LBW) infant, defined as less than 2500 grams, is 8.3%, with most LBW infants born before 35 weeks.[7] Preterm births before 32 weeks continues to represent 1.4% of singleton births in the U.S.[1]

The increased risk for PTB after surgical abortion is likely due to physical trauma associated from dilation and removal of intrauterine contents

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during pregnancy.[8] The association of PRB with medication abortion has been less actively studied, although medication abortion has been offered as a less traumatic alternative. Medication abortion now represents 53% of all abortions in the United States.[9]

Medication Abortion and PTB

The putative mechanisms by which mifepristone may increase the risk for PTB is not clear but may include decreasing maternal immune defenses (since mifepristone has glucocorticoid effects and is associated with maternal sepsis),[22] or adverse remodeling associated with cervical ripening.[23]

Mifepristone is a powerful progesterone receptor blocker. Its mechanism is thought to be through effects on the decidua of the endometrium, but it also blocks progesterone receptors throughout the entire body, including the cervix. Animal studies have also revealed effects regarding inflammatory cytokines, and that the "long-term impact of such chemically induced cervical changes is unclear."[24]

Animal studies in mice revealed that the sudden loss of progesterone function involved premature activation of the term ripening in the mouse along with partial activation of resident neutrophils and macrophages similar to the post-partum repair phase of cervical remodeling. Further, mifepristone up-regulates genes Chi313 Ptgs1, and Cox 1.[25]

The long-term effects of biochemical changes in the cervix due to mifepristone, along with genetic upregulation of a number of genes, is unclear. If mifepristone administration causes remodeling, short- or long-term cervical instability may increase the risk for future PTB.

There are few studies assessing the rate of PTB after medication abortion. The largest study included 419,879 nulliparous women in Finland with singleton deliveries between 1996 and 2013.[10] The authors compared women with prior medication abortion, surgical abortion, and no prior abortion. 365,356 women (87%) had no prior abortion, 13,450 (3.2%) had a prior medication abortion, 38,659 (9.2%) had a prior surgical abortion, and 2,414 (0.6%) had prior medical *and* surgical abortions. Authors calculated adjusted odds ratios (aOR) accounting for maternal age, marital status, city dwelling, tobacco use, and year of childbirth.

In this study, preterm birth was more prevalent in women with prior surgical abortion or surgical plus medication abortion, but not in women who had medication abortions alone. Confounders in this study included smoking, a known risk factor for PTB, which was more common among those who had a prior abortion, and birth year of the child after the abortion, which is consistent with trends in improved neonatal care. Prior to 2010, there were also more surgical abortions. This difference in timing means that surgical abortions

happened more often before significant improvements in neonatal care. This could confound outcomes such as neonatal death after preterm birth. This study found the well-known association between surgical abortion and PTB, and re-demonstrated that later gestational age at surgical abortion is associated with more preterm birth, although this effect was not identified for medication abortion. Medication abortion was associated with *lower* odds of PTB before 37 weeks (aOR 0.83, 95% CI 0.74-0.89). The adjusted odds ratio of PTB before 32 weeks and before 28 weeks were not significantly different from the population without prior abortion (aOR 0.83, 95% CI 0.64-1.08 and aOR 0.94, 95% CI 0.68-1.30).

The next largest study was done by Planned Parenthood in China, and included 4,925 women without prior abortion, 4,931 with prior medication abortion, and 4,800 with prior surgical abortion.[11] The rate of PTB before 37 weeks in this study was 3.7% with no self-disclosed abortion history, 2.9% after medication abortion, and 3.0% after surgical abortion.

The rate of PTB after medication abortion before 7 weeks was not significantly different from the rate in women who reported no prior abortion (OR 0.78, 95% CI 0.60-1.01), nor was this different from PTB rates in women who had medication abortion between 7 and 16 weeks (OR 0.77, 95% CI 0.53-1.10).

There was also no difference in PTB rates after medication abortion with curettage, compared to women with no prior abortion (OR 0.94, 95% CI 0.65-1.34), and there was *less* PTB after medication abortion without curettage compared to women with no prior abortions (OR 0.87, 95% CI 0.55-0.93). This study also reported that medication abortions were not associated with higher PTB rates compared to surgical abortion, regardless of whether they were completed with curettage (0.87, 95% CI 0.66-1.14) or not (1.15, 95% CI 0.79-1.67).

These findings cannot be interpreted as equivalent to preterm birth rates in the U.S., however, because all deliveries in this study prior to 28 weeks were termed spontaneous abortions, and no neonates born before 28 weeks were resuscitated. This may falsely depress reported PTB rates since it does not include any births between 20 and 28 weeks, which are counted as preterm births in U.S.

As mentioned above, the study relied on women to self-report their previous abortions status, which could lead to reporting bias given the rigorously-enforced one child policy still in place in the early 2000s. Without confirmation of self-reported abortion in medical records, it is possible that women in the control group of "no prior abortion" had in fact undergone an abortion by some means, and preferred not to report it.

Finally, the rate of curettage after medication abortion in this population (25.3% by patient report) exceeds the rate of surgical completion of medication abortion in the U.S. (usually below 6% before 70 days), which may relate to

the late gestational age up to 16 weeks of medication abortion in this study.[12] This high rate of curettage muddies the distinctions between medication and surgical abortion groups, and the multiple challenges with external validity make this study difficult to generalize to a U.S. population.

Subsequently, another study out of China, by Liao *et al* evaluated the effects of repeated first trimester medication abortions with mifepristone on preterm birth in subsequent pregnancies in a cohort of 19,527 women from seven hospitals between 2006 and 2009.[13] The study was interview-based with delivery outcomes available in 18,323 women (94%). 7558 reported a prior abortion, of whom 7478 had complete follow-up (99%). Of 10,681 who denied a prior abortion, 10,546 had complete follow-up (99%).

Nulliparous women with abortions were divided into three groups by the type of abortion (medication, surgical, or medication requiring surgical completion), and compared to controls without prior abortion history for rate of PTB. Of the women with a prior abortion, 24% had one medication abortion, 7.4% had more than one medication abortion, and 16% had medication abortions completed surgically. The rate of curettage after medication abortion was 20.3% in this study, similarly elevated far beyond U.S. rates. In this population, a history of one or multiple successful first trimester medication abortions was *not* associated with a higher risk of PTB in singleton subsequent pregnancies.

Medication abortions completed surgically was associated with *increased* odds of subsequent PTB before 37 weeks (OR 2.18, 95% CI 1.51-4.42), which correlates to a relative risk (RR) of 1.9. If this relative risk was applicable to the U.S. population, then medication abortion completed surgically would increase a woman's baseline risk of PTB from 10.2% to 19.8%.

Medication abortion completed surgically was also associated with increased odds of delivery before 32 weeks (OR 3.61, 95% CI 1.43-4.93), corresponding to a relative risk of 2.9 and an increase in the baseline risk of PTB from 10.1% to 29.1%.

Focusing on medication abortions before 7 weeks completed surgically, there was still increased odds of PTB (OR 1.69, 95% CI 1.02-3.16), which corresponds to a RR of 1.6 and an increase in PTB risk from 10.2% to 16.1% if applicable to a U.S. population.

Like the previously mentioned study by Chen *et al*, this study was interview-based, not linked with medical records, meaning that reporting and recall bias may affect the data quality. Family size practices in China during this study were similar to that during the previous study. Of the two studies with very different findings, it is not clear which is superior or which can be applied to the U.S.

Medication Abortion and LBW

Zafran *et al* analyzed an Israeli database to examine PTB rates in women with prior medication abortion, prior surgical abortion, and no prior abortion.

There was *no increased* risk of PTB and LBW in patients with medication abortion compared to patients without abortions (OR 2.4, 95% CI 0.4-12.6).[14] This study involved 70 women with medication abortion and 210 controls. According to their calculations, they had sufficient power to be able to discern a 10% difference between their baseline of 5% PTB and medication abortion. This 10% difference, which is larger than the baseline prevalence of the outcome, indicates that the sample size in this retrospective study is too small to detect small or moderate (but real) differences in PTB rates that would impact clinical practice or policy.

Männistö *et al* compared PTB rates after medication abortions to those after surgical abortions in Finnish women, and found no difference in risk of PTB (OR 0.87, 95% CI 0.68-1.13), or LBW (OR 0.90, 95% CI 0.68-1.19).[15] Since surgical abortion is a well-known risk factor for PTB, this may not be reassuring. The same authors later compared the rates of PTB after first- and second-trimester medication abortions; rates were similar (aOR 0.97, 95% CI 0.57–1.66).[16]

Virk *et al* 2007 used Danish data to compare rates of PTB and LBW after medication abortion compared to surgical abortion.[17] The rate of PTB after medication abortion was 5.45%, and after surgical abortion, 6.7%. These were not significantly different (RR 0.88, 95% CI 0.66-1.18). There was also no difference in LBW (RR 0.82, 95% CI, 0.61-1.11), which suggests that medication abortion may be associated with an increase in PTB like the increase related to surgical abortion.

Conclusions

There is contradictory evidence on the effect of medication abortion and risk of subsequent PTB. Available papers suggest that the rate of PTB after medication abortion is lower than that is. The heterogeneity of data may be due to varying rates or techniques for curettage. Sharp curettage, compared with vacuum aspiration causes more pain[18] and is associated with more complications in some studies.[19,20] Second trimester surgical abortions, which are less common than first trimester surgical abortions, can lead to even further trauma related to fetal dismemberment and maternal internal laceration.[21]

In addition to these unmeasured differences in the background of studies comparing medication abortion and surgical abortion, unexpected effects in the data suggest that confounders are not completely controlled for. For example, curettage after failed medication abortion causing less PTB than no curettage at all in China suggests that control groups with no prior abortion may include women with undisclosed curettage procedures in the past. These factors prompt caution when interpreting the limited data available.

Summary of Recommendations and Conclusion

The following recommendations are based on limited and inconsistent scientific evidence (Level B):

1) Women with a history of medication abortion may be at increased risk of preterm birthif surgical completion was required.

The following recommendations are based primarily on consensus and expert opinion (Level C):

2) Further systematic study of preterm birth rates in populations who have a history of medication abortion is needed.

3) Studies may be limited if medication abortions are reported as spontaneous miscarriages, if they are dependent on voluntary patient disclosure about medical and surgical abortions, or if curettage is subsequently performed.

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Ethical Research Involving Fetal Human Subjects

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ABSTRACT: Fetal tissue research refers to research using several types of tissue, including but not limited to samples obtained from aborted fetuses, cell lines derived from aborted fetuses, and in rarer cases, living previable neonates who have survived an abortion attempt. The ethical questions surrounding each type of tissue procurement are not identical, but do share similarities.

This guideline on fetal tissue research discusses the moral status of the human fetus, the state of ethics for medical research on vulnerable subjects, aspects of medical research using human fetal tissue, and the necessity of including fetuses as a protected class under vulnerable populations in research. The debates connected to embryo stem cell research and other research related to embryos are beyond the scope of this document.

Background

The embryonic period and the fetal developmental period are divided by the eighth week after fertilization (ten gestational weeks). The first eight weeks after conception are focused on the basic differentiation of organ systems whereas the fetal period of about thirty weeks is focused on organ development to adapt to extrauterine life. Human fetal tissue research is regarded by some of the scientific community as cornerstone to medical advances, due to the unique properties of fetal tissue, such as the capacity to give rise to human cell lines. Similar to all research on human subjects, fetal tissue research involves important ethical principles and a knowledge of the historical development of ethical safeguards. Research in human subjects has produced substantial clinical and social benefits

throughout history, especially after its expansion in the late 19th century. The aspirations of ethical research are noble, as described by the French physiologist Claude Bernard: "The principle of medical and surgical morality consists in never performing on a man an experiment that might be harmful to him to any extent, even though the result might be highly advantageous to science."[1] Unfortunately, this primary goal of medical research has failed to consistently adhere to this original aspiration.[2]

The history of medical research involving human subjects involves ample instances of ethically questionable or blatantly unethical research, most notably during and after the Second World War. Ethical guidelines were then established to ensure human subjects are selected and treated according to ethical and moral standards that would guarantee their safety and well-being. The Code of Nuremberg[3] and the Declaration of Helsinki[4] are the two oldest documents securing patients' medical research rights. The first document established the basic ethical principles that should be followed to promote and ensure respect for all human subjects and protect their health and rights. While the second is an authoritative guideline that stated that no national, ethical, legal or regulatory requirement should be allowed to reduce or eliminate any of the protections for human subjects outlined earlier in the Declaration.[5]

The challenge for human subject researchers is to continue to conduct their work while remaining faithful to foundational principles of ethics, justice, and human rights. Despite the substantial progress in safeguards and protections, one group of human subjects has been left on the fringes: humans in their first stages of development.

The Moral Status of the Fetus

Discussions on medical research on fetal tissue must first determine whether a human fetus has moral status as a human organism, thereby requiring similar ethical obligations as toward any other human subject. "Moral status" ascribes equal obligations and rights based on membership in a protected group. Such status can be applied not only to living beings but also to cadavers and cemeteries which reveal the moral standing due to law, ethics, and duties

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of respect.[6] Moral status in the case of human fetuses continues to be debated with regard to research and abortion and the history and some principles are outlined below.

Michael Tooley and Mary Anne Warren proposed a view of reality called *body-self dualism* in the 1980s. This argument proposes that biology alone does not confer moral status to a human being and personhood is acquired with consciousness, concluding that human fetuses should not be considered a person and therefore do not have moral status and the right to life.[7,8] This argument was buttressed by Alberto Giubilini and Francesca Minerva, who also deny moral status to newborns because they lack the properties that justify an individual's right to life.[9] These arguments are based on arbitrary limits that define personhood, including the physical development of a heartbeat, developmental milestones like the ability to feel pain, or the development of consciousness, such that being deprived of life would represent a loss to oneself. This utilitarian argument has permeated legislation regarding abortion and the legal framework of the last 50 years.

The dualistic and utilitarian view of fetuses as non-persons without a moral claim to life is countered by an argument based on embryology. This view claims that human fetuses are simply human beings at different degrees of maturation in their species-specific developmental trajectory.[10] Robert George and Christopher Tollefsen support this position that all persons are *human animals*, therefore from the moment of sperm-egg fusion within fertilization, a new human being begins existing with personhood and all the rights and dignity associated with it.[11] The same moral status would be conferred to all members of the human species in any stage of development because they share the same nature. *Nature* for George and Tollefsen resembled a traditional Aristotelian understanding: nature is an intrinsic, species-specific *cause* for an organism's behavior including its development, capabilities, and higher order mental capacities, like consciousness, rationality and goal-seeking. Thus, even though human fetuses do not share the same capabilities or higher behaviors as adult humans due to their developmental stage, they share the same nature and essential orientation as members of the same species, whereas other ani-

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mal fetuses do not have the same developmental trajectory, despite being at the same developmental stage.

The embryological basis supporting moral status for embryos is as follows: at fertilization, when a sperm cell unites with an ovum, the two gametes cease to be, and a zygote is formed in its original one-celled stage. The zygote begins to grow by differentiated cell division into an embryo, including all its genetic and epigenetic constitution.[12] From the zygote stage onwards, this new human organism proceeds in a continuum of regular, predictable, and coordinated bodily development, progressing invariably towards the mature stage of human development, if not deprived of suitable external circumstances. Even in the beginning of an embryo's life, what exists is not a mere bundle of homogeneous cells;, rather, gene expression already differs at the two-cell stage, even more so at the four-cell stage and so on.[13,14] Unlike gametes, which die if they do not fuse, every stage of embryonic and fetal differentiation is oriented toward holistic growth and development of these predetermined human capacities. Thus, each human embryo and fetus is a living human organism, doing exactly what he or she is meant to do at his or her particular stage of life. In fact, the same can be said of infant development, child and adolescent development, even adult development. There is no point in time at which a human being is any more or less of a human being based on developmental milestones.

While embryology cannot answer philosophical or ethical questions, it does support the moral status of human beings in earliest stages of development and inform the ethical debate of research in fetal tissue. If a human embryo or fetus is categorically a human being, it raises the question of whether it is just to kill or perform medical experimentation on such human subjects, when there is no proportionate medical benefit to the subject.

The State of Ethics for Medical Research

The history of bioethics in general, and American bioethics specifically, is marked by a succession of political and legal reactions to the reported abuse and exploitation of the weakest and most vulnerable members of the human population, beginning with the practice of research in human subjects.

In studying the gross abuses committed during the Second World War and exposed during the Nuremberg Trial, Henry Beecher, a Harvard professor

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of Anesthesiology and clinical researcher, was the pioneer in identifying the lack of protection for human subjects in the United States. His findings, published in the landmark article "Ethics and Clinical Research,"[15] demonstrated that "unethical or questionably ethical procedures are not uncommon." He cited twenty-two published research papers in which human subjects received no therapeutic benefits. Most studies did not mention consent, most subjects were not aware they were being studied and many were members of vulnerable populations (e.g., soldiers, indigent patients, prisoners, institutionalized children with severe intellectual disabilities, the elderly, and the terminally ill). Even though his assessment concluded with a positive assurance about the state of the medical field in America and his proposals for change were modest, the article shocked the medical community and the public.

As a result of Beecher's study, accompanied soon after by the Tuskegee syphilis study scandal and the public outrage it caused, American research for human subjects entered a new era, characterized by ample intervention of Congress and the Federal government. Federal law[16] defines human subjects research as a systematic investigation designed to develop or contribute to generalized knowledge. By its own logic, the primary goal is not to care for or cure said subjects but to acquire understanding from observation or intervention. This framework challenges researchers to reconcile the need for medical advances with the foundational principles of medical ethics and human rights.

The four ethical principles originally laid out by Thomas Beauchamp and James Childress are beneficence, nonmaleficence, autonomy, and justice.[17] The principle of beneficence is the obligation to treat human subjects ethically by respecting their autonomous decisions and protecting them from harm. Medical research should ultimately be oriented towards the good of patients. In distinction to nonmaleficence, this principle is one of positive requirements, meaning that the research team has an active duty to benefit subjects when possible. In contrast, nonmaleficence rests in the Hippocratic maxim to do no harm, and it manifests itself in risk assessment and careful oversight in the context of research studies.

The principle of respect for persons, also described as autonomy, derives from the understanding that all persons have intrinsic and unconditional worth and, therefore, should have the power to make rational decisions and moral choices, namely, self-determination. Certain persons have built-in or

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[15] Beecher HK. Ethics and Clinical Research. *N Engl J Med*. 1966;274(24):1354-1360. doi:10.1056/nejm196606162742405

[16] 45 CFR 46. HHS.gov. https://www.hhs.gov/ohrp/regulations-and-policy/regulations/45-cfr-46/index.html. Accessed August 7, 2022.

[17] Varkey B. Principles of Clinical Ethics and Their Application to Practice. *Med Princ Pract*. 2021;30(1):17-28. doi:10.1159/000509119

external factors that diminish their capacity to exert their autonomy, and are entitled to additional protections as they are vulnerable to abuse. One example is incomplete development of judgment such as in childhood or severe intellectual disability. Another is that of power disparities such as exist for incarcerated persons. These groups are entitled to additional protection.[18] Some authors even argue that these protections need to be so extensive as to exclude them as human research subjects, especially in cases when the benefit to the individual is assumed to be minimal or null.

The last ethical principle presented by Beauchamp and Childress is justice. There are several categories of justice, but the most relevant type used in human subject research and clinical ethics is distributive justice, which refers to the fair, equitable, and appropriate distribution of health care resources.[19] The Belmont Report, an US Department of Health and Human Services (HHS) guideline for ethical research, does not expand in detail on the principles of justice, but does make general claims about just and unjust practices. It states that imposing burdens exclusively on a specific population is unjust, using the Tuskegee study as an example since the subjects—underprivileged black men—had life-saving treatment withheld in order not to interrupt the observational study, even long after such treatments became generally available. The principle of justice is at the heart of the debate on research ethics in human subjects and is specifically relevant in the use of fetal tissue.

Medical Research Using Fetal Tissue

Fetal tissue obtained from aborted fetuses has been used in medical research for many decades. In the last sixty years, there has been an effort to apply a utilitarian and pragmatic approach to its use and transform it into "the right tools for the job," as described by sociologist Anselm Strauss.[20] Human fetal tissue research proponents claim its use has led to significant advances in science and medicine. Even if true, as discussed previously in Beecher's paper, medical progress does not excuse abuses of human subjects and researchers must uphold ethical standards, least history repeat itself.

In the early 1970s, there were several research reports on just-aborted but still-living previable infants.[21] Once these facts were made known to the public, scientists justified these practices by appealing to the valuable knowledge that might yield in service of maternal-fetal health and by stating that just-aborted

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[18] The Belmont Report. HHS.gov. https://www.hhs.gov/ohrp/regulations-and-policy/belmont-report/read-the-belmont-report/index.html. Accessed August 7, 2022.

[19] Blustein J. The History and Moral Foundations of Human-Subject Research. 2007;86(2):82-85. doi:10.1097/phm.0b013e31802f00cd

[20] Strauss A. Work and the Division of Labor. *The Sociological Quarterly*. 1985;26(1):1-19. doi:10.1111/j.1533-8525.1985.tb00212.x

[21] Snead OC. *What It Means to Be Human*. Harvard University Press; 2020:23-27.

infants were too biologically immature to survive outside of the womb (the gestational ages in these experiments were between 20-23 weeks[22,23]). The findings from these studies were brought to a Congressional hearing, and in 1973, the National Research Act imposed a moratorium on federally funded research on living human fetuses, before or after induced abortion, unless such research is done to support that individual fetus' survival.

The initial aim of a committee tasked with studying these events was to obtain information about the means, ends, benefits, and harms of fetal tissue research and to explore how it related to the topic of abortion. Protections for the preborn were not extended further because the Supreme Court decision on *Roe v. Wade was* released just eighteen months prior. This decision disrupted the legal and policy landscape by introducing a constitutional right to abortion and a new jurisprudential framework for its regulation, thereby altering the laws of all fifty states.[24] Nonetheless, the Supreme Court's decision on abortion did not eliminate ethical issues related to fetal tissue research, but only covered them with a "veil of silence" due to a lack of legal protection for fetuses before and after abortion.[25]

There are several additional considerations regarding fetal tissue research: Fetal tissue economy, legal protection guidelines, and consent. The NIH has governing policies on the acquisition and use of human fetal tissue for research purposes,[26] and these guidelines aim to avoid abuse and ethical improprieties. Nonetheless, there are very little data available regarding the processes of selection, acquisition, or distribution of fetal tissue for research in America. The lack of transparency in this field is a frequent cause of public concern and distrust, as corroborated by Catherine Waldby and Robert Mitchell in their book *Tissue Economies*. According to these authors, fetal cell tissue research transforms an unwanted pregnancy into a "valued resource" by using the female reproductive labor as tools for research that will bring no benefit to pregnant women or the fetus.[27] The transactional approach to using female bodies to extract research material is cited as a grave ethical and moral concern

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[22] Ramsey P. *The Ethics of Fetal Research*. New Haven: Yale University Press; 1975:71.

[23] Adam PAJ, Raina N, Rahiala E-L, Kekomaki M. Oxidation of glucose and D-B-OH-Butyrate by the early human fetal brain. 2008;64(1):17-24. doi:10.1111/j.1651-2227.1975.tb04375.x

[24] Chamberlain G. An artificial placenta. *American Journal of Obstetrics and Gynecology* . 1968;100(5):615-626. doi:10.1016/s0002-9378(15)33387-1

[25] Snead OC. *What It Means to Be Human*.; 2020:33-35.

[26] Policies on The Acquisition And Use Of Human Fetal Tissue (HFT) For Research Purposes In The Intramural Research Program At NIH | NIH Office Of Intramural Research. https://oir.nih.gov/sourcebook/ethical-conduct/special-research-considerations/policies-procedures-use-human-fetal-tissue-hft-research-purposes-intramural/policies. Accessed August 7, 2022.

[27] Waldby C. *Tissue Economies*. Durham: Duke University Press Books; 2006:1-31.

to the authors and demands oversight to protect the pregnant woman and her fetus from predatory situations and abuse.

Julie Kent, a UK sociologist, cites the importance of transparency in an article focusing on the fetal tissue economy.[28] The tissue acquisition process deserves to be better understood and considered in discussions about how fetal tissue research transforms the connections between life and death. Similar to what is observed in the US, the author concludes there is very little oversight of this type of research and that the path from the collection site to the laboratory is unclear.[28] The collection and transparent distribution of such data are imperative for ethical discussions regarding fetal tissue.[28]

Regarding protections for research on human subjects, the National Institutes of Health (NIH) provides regulations and guidelines that include a subsection on pregnant women, human fetuses, and neonates.[29] Nonetheless, the guideline promotes the "research imperative," allowing experimentation on fetuses and non-viable neonates if "the purpose of the research is the development of important biomedical knowledge that cannot be obtained by other means."[29] However, the NIH guidelines fail to define what constitutes important biomedical knowledge. Since fetuses currently have no legal rights under American law, these NIH protections are insufficient and would be deemed unethical if applied to any other vulnerable population. It has been a long-standing ethical value in the research that "utter helplessness demands utter protection," but the NIH guideline fails to provide this kind of protection to fetal life.[29]

Another critical concern is the NIH guideline fails to define the standards for fetal viability for research purposes. Fetal viability is usually defined as the point when a human fetus can survive outside the mother's body. Due to development in medical technology, this threshold has been reduced substantially in the last few decades (for example, it was 28 weeks by the time *Roe v Wade* was decided, and the consensus is now around 23-24 weeks; some centers of medical excellence have successfully discharged infants born at 22 weeks). This definition is problematic, especially in using fetuses acquired after abortion for research purposes since most fetuses are viable in all stages of pregnancy unless removed from their natural environment. For this reason, some have proposed a gestational age of viability for research purposes, limiting the use of fetuses 4-6 weeks before medical viability due to possible dating errors.[30] Even

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[28] Kent J. The fetal tissue economy: From the abortion clinic to the stem cell laboratory. *Social Science & Medicine*. 2008;67(11):1747-1756. doi:10.1016/j.socscimed.2008.09.027

[29] Subpart B - Additional Protections for Pregnant Women, Human. HHS.gov. https://www.hhs.gov/ohrp/regulations-and-policy/regulations/45-cfr-46/common-rule-subpart-b/index.html. Accessed August 7, 2022.

[30] Ramsey P. *The Ethics of Fetal Research*. New Haven: Yale University Press; 1975:75-78.

this mild limitation to using fetuses and previable neonates for research has been denied on claims that any protection would limit abortion rights.

Conclusion

Human fetuses are a group of human subjects that remain without full ethical and legal protections. Until the existing laws guiding fetal tissue research are amended, human subject research as a whole is inadequate and harms vulnerable subjects. Public trust in research is highly dependent on ethical and legal protections and on the perception of autonomy, beneficence, nonmaleficence, and justice. Extending protections to human fetuses strengthens the rights of human subjects and the ethical foundation and validity of the critical research.

Q. Are Women Allowed to Consent to Research on Fetal Tissue on Behalf of the Fetus if They are Obtained Through Induced Abortion? Is this Similar to Use of Embryos Obtained During In Vitro Fertilization?

Voluntary informed consent is the cornerstone of ethical research. The question of voluntary informed consent in human fetal tissue research is must reach certain standards, namely, the research subject must have the legal capacity to consent and should be able to exercise free power of choice without the intervention of any element of force, fraud, deceit, duress, overreaching, or other ulterior forms of constraint or coercion.[31] It is also essential to provide the research subject with sufficient knowledge and comprehension of the elements involved in the research to enable the person to make an informed decision.[32] In the case of fetal tissue research, research requirements are lowered since the requirement for consent is limited compared to what is required in fetal research outside of the context of induced abortion.[33]

First, little information is given to women seeking abortion on what fetal research entails. In one study analyzing women's views on fetal tissue research in the US, all information provided to the research subjects is quoted as follows "Sometimes scientists conduct research using the tissue remains of the pregnancy to study different diseases. Scientists call it fetal tissue research.

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[31] Blustein J. The History and Moral Foundations of Human-Subject Research. 2007;86(2):82-85. doi:10.1097/phm.0b013e31802f00cd

[32] Trials of War Criminals Before The Nuernberg Military Tribunals Under Control Council Law No. 10 (Volume 2) - Digital Collections - National Library Of Medicine. http://resource.nlm.nih.gov/01130400RX2. Accessed August 7, 2022.

[33] 42 U.S. C. § 289g-1 & 289g-2; 42 CFR § 46.201. https://www.govinfo.gov/content/pkg/USCODE-2020-title42/pdf/USCODE-2020-title42-chap6A-subchapIII-partH-sec289g-1.pdf. Accessed August 7, 2022.

Research is allowed if the woman provides consent."[34] This researcher concluded that women's perspectives on fetal tissue research were nuanced and can be viewed as a choice that is both respectful to the fetus and meaningful to the woman whose pregnancy has ended. Still, the question remains, how much is understood about the realities of fetal research?

Another qualitative focus-group,[35] study solicited the opinion of women on the use of fetal tissue for research. Women initially expressed enthusiasm for donating aborted fetuses for experimentation, which was understood as a good thing, but as participants gained information and thought more carefully about the implications of such a decision, the support radically diminished. The lack of knowledge about how aborted fetuses are handled in the laboratory was one of the main issues for changing opinions, as it invoked in participants a perceived *duty of care* that women feel towards their offspring. Regarding fetal stem cell research, participants described troubling feelings associated with renewal, regeneration, and immortality of the tissue, which was understood as somehow reinstating and even developing the fetus' physical existence and social biography, the very thing abortion is meant to eliminate. The author concluded that participants had co-produced a tendency to refuse to donate aborted fetuses by the end of the focus groups, once more knowledge on the topic had been acquired.

This study exemplifies the concerns that generalized consent is not fully informed, truly voluntary consent. Proper consent would require more specific discussion between the woman and the health care team about fetal tissue storage, research aims, and methods of research. Such disclosure would potentially change the woman's mind in consenting to research but would at least meet minimum requirements for disclosure.[36]

Another essential point is the suitability of a woman to consent to the use of fetal tissue obtained after induced abortion. Fetuses, infants, and children are a protected class in human research because they cannot provide informed consent due to developmental immaturity. It is understood that medical research should only be allowed in this population if the experiment brings direct benefit and minimal risk of harm. Parents are required to consent because they are viewed as proxies acting in the child's best interest, but this is not the case in the context of abortion. In this situation, it would be most appropriate to use the standard applied to children with no guardians available to participate

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[34] Spach NC, Jaffe EF, Sullivan KA, et al. Pregnant Individuals' Views on Fetal Tissue Research in the United States. 2021;138(5):755-761. doi:10.1097/aog.0000000000004576

[35] Pfeffer N. What British women say matters to them about donating an aborted fetus to stem cell research: A focus group study. *Social Science & Medicine*. 2008;66(12):2544-2554. doi:10.1016/j.socscimed.2008.01.050

[36] Ramsey P. *The Ethics of Fetal Research*. New Haven: Yale University Press; 1975:89-99.

in consent and thus categorically exclude fetuses obtained from elective abortions from participation in experimental research.

Clinical testing after miscarriage or stillbirth is not part of this ethical challenge, so long as the tissue is treated with respect. Further ethical work is necessary to determine whether donation of fetal remains after spontaneous pregnancy loss should aid scientific research, much like parents' decision to donate the body of a recently deceased child to science or medical education. In this situation, the moral repugnance associated with performing research after an iatrogenic death is absent.

Q. What Changes Should be Put in Place to Protect Fetal Research Subjects?

Ethics in research using fetal tissue does not compare equitably with human tissue research, which has a well-established history of safeguards that are absent for embryos and fetuses. For this reason, changes are necessary not only in fetal research but in the legal, ethical, and social climates within which such research occurs. Firstly, there is a need for change in our culture to value life and the overturn of *Roe v Wade* by the *Dobbs v Jackson* decision in June of 2022 allows society us to address legal and ethical spheres to include fetuses, a much-needed action that has been halted for 50 years.

The first step to ascribing equality and fundamental human rights to fetuses is to acknowledge their moral status and to grant them the same legal and ethical protections given to all other members of our species when subjected to research. In doing so, fetal tissue research is, in fact, medical research involving a human subject that is vulnerable and not yet developmentally capable of agency or choice. Human subjects deemed vulnerable should receive specifically considered protections, and to require this level of protection to human fetuses is to apply the ethical principle of justice. A just society requires standards to be applied in a consistent matter, so any protections granted by national and international guidelines for medical research involving human subjects should be extended to fetuses and fetal tissue.

According to the Declaration of Helsinki, corroborated by the Belmont Report, "medical research involving human subjects may only be conducted if the importance of the objective outweighs the risks and burdens to the research subject," and that "medical research with a vulnerable group is only justified if this group should stand to benefit from the knowledge, practices or interventions that result from the research." As it currently stands, fetal tissue research fails to comply with both standards since fetuses are used in a utilitarian fashion as tools to produce medical progress in general, without any benefit to them or maternal-fetal specific conditions. This is ethically reprehensible and demands to be corrected immediately.

One argument from proponents of fetus tissue research is that it should be viewed as a donation of biological tissue. There are two main reasons why this premise is invalid. First, the fetus is not a part of the mother's body but a whole new individual with moral status, worthy of rights and respect. For this reason, it is unjust to treat a fetus simply as organs or body parts. Secondly, there is the question of appropriate informed consent and a suitable surrogate or proxy for this consent . Fetuses, especially in the context of abortion, are the most vulnerable class in human research because they cannot give informed consent due to developmental immaturity and they lack of proxies that are acting in their best interest. In this situation, the standard applied to children with no guardians is appropriate, requiring categorical exclusion of fetuses from induced abortions from participation in experimental research. If this is not done, the industry complies with a utilitarian perspective of life and death that is detrimental to a culture that values equality and justice.

Finally, guidelines for research on human subjects are well-established in treatment of the dying and the condemned. These disenfranchised groups deserve and are granted respect, and it is a breach of research ethics to misuse, coerce, or abuse them. Even in extreme cases, such as prisoners on death row, our society has long established it is unethical and, in most cases, illegal to subject them to research or organ donation. The punishment of death, a controversial topic in jurisprudence, is still seen as a solemn event that ought to preclude inhumane treatment or abuse of both the person and the subsequent corpse. In places where abortion remains legal, fetal tissue should be viewed with the same respect as condemned prisoners: their remains should be humanely treated and disposed with human dignity

Summary of Recommendations and Conclusion

The Following Recommendations are Based on Good and Consistent Scientific Evidence (Level A):

1) Informed consent specific to fetal tissue research should be broadly available to women after spontaneous abortion. It should briefly describe the existing types of fetal tissue, the manner of use of fetal tissue, and the possible implications the research might produce.

The following recommendations are based on limited and inconsistent scientific evidence (Level B):

1) Fetuses should be held by the same standards applied to other human research subjects and protected as a vulnerable class according to national and international guidelines.
2) Fetal tissue research should be permissible only in fetuses derived from spontaneous abortion or previable preterm labor.

The Following Recommendations are Based Primarily on Consensus and Expert Opinion (Level C):

1) Fetal tissue research in fetuses resulting from induced abortion should be proscribed, and fetal organs and remains should be disposed of in a dignified manner.

Limiting Conscience Rights in Obstetrics and Gynecology

American Association of Pro-Life Obstetricians and Gynecologists*

ABSTRACT: The American College of Obstetricians and Gynecologists (ACOG) released a Committee Opinion in November 2007 titled "The Limits of Conscientious Refusal in Reproductive Medicine." This document, claiming to speak on behalf of the entire profession of Obstetrics and Gynecology, proposed that conscience rights of healthcare professionals have limits with regard to certain aspects of patient care. Despite calls for revision from many within the profession, this document was reaffirmed in 2016, unchanged. This document provides a detailed analysis of the ethical flaws in ACOG Committee Opinion 385.

Key Words: ACOG, conscience, opinion, objection

Background

Flawed Assumptions

Committee Opinion 385 of the American College of Obstetricians and Gynecologists (ACOG) outlines the concept of conscience and that it may sometimes conflict with patients' desires regarding particular medical interventions. It then goes on to list four criteria to determine appropriate limits to conscience and concludes with several recommendations: potential for imposition, effect on patient health, scientific integrity, and potential for discrimination.

This detailed opinion on the right of conscience contains several flawed assumptions. First, the document assumes that patient autonomy

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is the final arbiter of treatment decisions. However, physician beneficence has traditionally been accepted as the first and final arbiter of treatment decisions. Physicians are trained to pursue only what is good for their patients, and this orientation towards the patient's best interest was essential to maintain trust in the healing profession and provide the best care. However, this led to paternalism, wherein the physician unilaterally made medical decisions without accounting for patients' perspectives about treatment.

In Western medicine, this imbalance began to change in the 1960's and 1970's such that patient autonomy, i.e., the right to self-determination, was appropriately accorded much greater weight. Patient autonomy gradually came to be seen as highest on the hierarchy of ethical principles, even outweighing the physician's concept of beneficence in many instances. But patient autonomy is not absolute. Patients cannot demand treatment interventions that are contrary to evidence-based medicine or standards of care. They cannot insist on unnecessary or harmful diagnostics or interventions. Conversely, there are times when the physician's exercise of beneficent care is supported and even lauded, e.g., treatment and prevention of suicide.

This flawed assumption that patient autonomy supersedes physician conscience is exemplified when ACOG states "although respect for conscience is important, conscientious refusals should be limited" based on four criteria, which are overly broad and biased. While physician autonomy is also not absolute, this tipping of the balance so strongly in favor of the patient based on assertions is ethically troubling.

A second flawed assumption Opinion 385 makes is that negative patient autonomy (the right to refuse) and positive patient autonomy (the right to demand) are morally equivalent.

Negative patient autonomy is nearly inviolable; it is rarely justified to impose unwanted treatment on a patient who has capacity and makes an informed decision. However, positive patient autonomy carries much less moral obligation. Patient demands are routinely denied by conscientious physicians for such things as unnecessary surgery, unwarranted antibiotics, inappropriate medical tests, etc., even in those situations where the requested treatment is within the bounds of accepted practice or in instances when other physicians might accede to the request for patient satisfaction or monetary gain.

Such physician refusals are generally based on patient beneficence, that such interventions are not in the patient's best interest. For decades, a physician has also been permitted to decline a patient's request based on his or her conscience. To not do so implies that the patient's right to access to specific treatment options outweighs the physician's right to avoid moral complicity in an action that he or she believes to be immoral.

This ACOG opinion supports this incorrect implication, as noted by its repeated referral to physicians as "providers." There is a major conceptual dif-

ference between a professional who professes allegiance to standards (those shared by the profession, as well as personal ethical standards) and a "provider," a technician who merely provides whatever is requested of him or her.

A third flawed assumption that Opinion 385 makes is that matters of conscience for the professional are matters of personal opinion. The (limited) concept of conscience as "self-knowledge" is expressed by ACOG when they define it as the "private, constant, ethically attuned part of the human character." This is a truncated and incomplete view of conscience. A person's conscience is inseparable from his or her worldview or religious beliefs.

> In the history of ethics, the conscience has been looked upon as the will of a divine power expressing itself in man's judgments, an innate sense of right and wrong resulting from man's unity with the universe, an inherited intuitive sense evolved in the long history of the human race, and a set of values derived from the experience of the individual.[1]

> Recognizing this divine origin of an individual's conscience, a conscience clause is defined as "a clause in a general law exempting persons whose religious scruples forbid compliance therewith...[2]

ACOG reiterates its incomplete view of conscience when they claim "...not to act in accordance with one's conscience is to betray oneself." This is a small, private view of conscience. ACOG admits to no betrayal outside the self, such as to the community or to a higher power that sets such standards. In reality, to betray one's conscience is to have effects on the community: examples of failures in research conduct or in abuses of vulnerable patients in gynecology are examples of individual moral failures propagating harms to the community.

A fourth flawed assumption made by Opinion 385 is that *prima facie* values can and should be overridden in the interest of other moral obligations that outweigh them. ACOG admits that respect for conscience is a value, but they go on to say it is only a prima facie value. This is not so much a flawed assumption as one that is distorted. A *prima facie* value is one that is accepted on its own merit, without need for proof, though it may be contested and shown to be invalid in a particular circumstance. By emphasizing the possibility of override, and claiming conscience is only a prima facie value, they imply that this is of little consequence.

Criteria to Determine Appropriate Conscience Limits

In its section on "Potential for Imposition," the Opinion conflates refusal to provide a requested service by the professional with imposition of the professional's beliefs. It is instead an instance of negative professional autono-

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[1] Conscience. In Gale Group (Ed.), The Columbia Electronic Encyclopedia (2000 ed.).

[2] Conscience clause (n.d.). In Webster's Revised Unabridged (11th ed).

my. The professional's refusal does not preclude the patient from seeking or obtaining the requested service elsewhere. Geographic or sociologic constraints are separate and distinct.

The section on "Effect on Patient Health" could make a strong case for bodily harm to the patient (pain, disability or death), but ACOG expands the definition of "health" to include "a patient's conception of well-being."[3] Thus, the document asserts incorrectly that the patient's wishes, whatever they may be, trump professional autonomy.

In addition, they define the physician's fiduciary duties to include an obligation "to protect patients' health." Again, they could make this point vis-à-vis an obligation to protect from bodily harm, but they distort it by implying the patient's autonomy takes precedent over the physician's conscience. The example they use here is a conscientious refusal to do a tubal sterilization at the time of Cesarean section, claiming that the "attendant and additional risks" of a second surgical procedure should override the physician's conscience.

ACOG also minimizes the physician's obligation to promote fetal well-being. Though initially couched in terms of "protecting the safety of women," the implication is that this protection includes the "patient's conception of well-being" invoked earlier. But protecting women to the point of entertaining abortion due to the patient's personal concept of well-being is to violate the obstetrician's obligation to promote fetal well-being. The obstetrician has two patients—the woman and the preborn human person, the fetus. ACOG correctly prioritizes protecting the health of the woman, as this is the primary modality of caring for the fetal patient. Without caring for the mother, we cannot care for the fetus—but some acts on the mother (acts done in the name of her concept of well-being) do not advance her health and can even attack the fetus. The physician of conscience abides by the principle to "first, do no harm," and not cause pain, disability, or death to either patient, while still maintaining the duty to care for the woman as one of two patients.

In its section on "Scientific Integrity," ACOG correctly speaks against support for conscientious refusal based on invalid consequential reasoning. Some claims of conscientious objection are not genuine: a physician with a conscientious objection to personal involvement in an act might try to hide behind a potential adverse outcome as an excuse for his or her concern. He or she should speak openly about their objection being based on their moral convictions, not a potential adverse outcome. But in the same paragraph, ACOG incorrectly concludes from this that there is no room for discussing evidence of adverse

[3] American College of Obstetricians and Gynecologists. ACOG Committee Opinion No. 385 November 2007: the limits of conscientious refusal in reproductive medicine. Obstet Gynecol. 2007 Nov;110(5):1203-8. doi: 10.1097/01.AOG.0000291561.48203.27. PMID: 17978145.

effects and the uncertainty about such evidence. Claims of concern about adverse effects of certain morally-fraught acts still deserve conversation, even if they cannot completely justify a conscience refusal.

In its section on "Potential for Discrimination," the document begins with a valid argument that patients should be treated alike and without discrimination. Thus, a physician who has a conscientious objection to doing a certain procedure is not justified in refusing the procedure for one patient while providing it for another equivalent patient. However, the example they use is fallacious: refusing to provide contraceptive assistance to an affluent patient who may be able to procure it elsewhere may be justified, they say, while doing so for a poor young mother without transportation is not because it is unjust. But this is not justified, a provider should not discriminate based on socioeconomic status, but should act according to a consistent moral standard that does not discriminate between patients but opposes procedures based on moral principles.

The Opinion goes on to claim as "oppressive" the denial of reproductive services for a homosexual couple while providing the same for a married heterosexual couple. The AMA clearly states in its Principles of Medical Ethics that "A physician shall...except in emergencies, be free to choose whom to serve..." Assisted Reproductive Technology is not an emergency service.

Critiques of Recommendations

The Opinion closes with recommendations including that "[a]ny conscientious refusal that conflicts with a patient's well-being should be accommodated only if the primary duty to the patient can be fulfilled."

Reproductive services, as distinct from care of complications after a service, are rarely matters of life and death. The assertion that a physician's "obligation" to provide elective reproductive services outweighs the physician's autonomous conscience is contrary to medicolegal tradition, including Supreme Court case law in the U.S.

The Opinion then ignores the issue of moral complicity by recommending that "physicians and other health care professionals have the duty to refer patients...to other providers if they do not feel that they can in good conscience provide the standard reproductive services that their patients request." Some physicians may be willing to follow this, but others believe their involvement in the referral process involves moral wrongdoing, for without their involvement, the morally troublesome procedure would not have happened.[4] This makes the referral *itself* morally objectionable, an option not ever entertained in the Opinion.

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[4] Orr RD. The role of moral complicity in issues of conscience. American Journal of Bioethics, November 2007, in press.

Finally, the Opinion asserts an obligation for providers with conscientious objections to remain nearby providers with no objections in order to assure patients have options: "Providers with moral or religious objections should either practice in proximity to individuals who do not share their views or ensure that referral processes are in place so that patients have access to the service that the physician does not wish to provide." This recommendation ignores the context that patients in "resource-poor areas" may be without access to many services (neurology, dermatology, dental surgery), and no other professional society insists that all health care services must be available to everyone at all times. Certainly, a physician in such an area should be willing to provide emergency services in which he or she is adequately trained. However, there is no compunction to provide elective reproductive procedures.

There is equally no societal obligation to ensure convenient access to all elective health care services for everyone, even though the Opinion recommends that lawmakers advance policies that compromise conscience protection with access to procedures like induced abortion.

Clinical Questions and Answers

Q. Are there reasonable aspects to Committee Opinion 385?

Opinion 385 notes that "health care providers must impart accurate and unbiased information so that patients can make informed decisions about their health care. They must disclose scientifically accurate and professionally accepted characterizations of reproductive health services."

This is a reasonable recommendation. A duty to present accurate information does not, however, prevent him or her from expressing his or her moral beliefs on the matter, so long as patients are treated with respect.

The Opinion goes on to explain that "where conscience implores physicians to deviate from standard practices, including abortion, sterilization, and provision of contraceptives, they must provide potential patients with accurate and prior notice of their personal moral commitments. In the process of providing prior notice, physicians should not use their professional authority to argue or advocate these positions."

This is not an unreasonable recommendation in situations of individual practitioners in an elective healthcare setting. In rare circumstances, it could become problematic or unworkable in situations of cross coverage and in emergency settings. However, most services under consideration in the Opinion are not typical emergency services, such as delivery, miscarriage care, or care for complications from reproductive procedures; instead, services such as assisted reproductive techniques and abortion are outpatient and elective.

In the same vein, the Opinion concludes that "in an emergency in which referral is not possible...providers have an obligation to provide medically indicated and requested care regardless of the provider's personal moral objections."

This recommendation is valid, though direct feticide is never medically indicated. The pro-life provider can provide emergent delivery or treatment of ectopic pregnancy in these situations, and this is not ethically equivalent to direct feticide or dismemberment.

Q. What was the response to Opinion 385 among pro-life physicians?

Since its original publication in 2007, the Opinion has generated significant pushback among organizations such as the U.S. Congress, the office of the secretary for Health and Human Services, the American Association of Pro-life Obstetricians and Gynecologists, the Christian Medical and Dental Association, and the Catholic Medical Association.[5] Although a revision of the Opinion was promised in 2008, the Opinion was reaffirmed in 2016 without changes.

[5] Committee Opinion 11: Non-Representation of Pro-Life OB/GYNs in the American College of Obstetricians and Gynecologists. Issues Law Med. 2022 Fall;37(2):221-230. PMID: 36629768

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