Welcoming Prometheus: Experimental Support for Deregulating Gene Doping

Sarah Polcz[*] & Anna Lewis[**]

The regulation of genetic modification is generating urgent international debate. Athletic competition provides an optimal laboratory for testing policy frameworks: a non-contrived, controlled environment, allowing for isolation of variables of interest. Genetic modification for enhancement (gene doping) is banned by the World Anti-Doping Agency (WADA), and enforced at considerable cost, on the basis that biological innateness is essential to what is valuable in sports. Because athletes will likely be early adopters of genetic modification, this ban is set to disproportionately affect other domains.

We present a normative analysis of current regulation and the first experimental study (n=1000) on American attitudes towards gene doping. Through a series of ten scenarios, we find respondents: support allowing athletes modified to have an advantage competing alongside those born with it (79%); support allowing modified athletes to compete alongside unmodified athletes (54%); endorse creating a separate competitive category (34%). Only 12% support a ban.

[*] John M. Olin Fellow and Gregory Terrill Cox Fellow in Law and Economics, Stanford Law School.
[**] MPhysPhil, PhD in Systems Biology from the Department of Statistics, Oxford.

INTRODUCTION

Eero Mäntyranta was a champion Finnish cross-country skier competing in the 1960s, winning three Olympic golds, two world championships, and setting records as one of the greatest Olympians ever to compete in his sport. He was found to have an abnormally high red blood cell count, which allowed his blood to carry more oxygen, in turn giving him a competitive edge. This led to accusations of cheating, and a cloud of suspicion hung over his victories.[1] His name was cleared two decades later when it was revealed that he naturally had 50% more red blood cells than average due to a rare genetic variant.[2] Two other members of his family who also carried the genetic variant went on to be champion skiers.[3]

If it were possible to give other adult athletes Mäntyranta's genetic variant, should such a procedure be banned? We are not referring here to genetic modification to create so-called designer babies (a *germline* application).[4] Instead, we focus on the ability to modify our genetics as adults (*somatic* applications). While at one point this seemed as if it would be confined to the realm of science fiction, it has recently and rapidly begun to look plausible through a new wave of techniques, CRISPR-Cas9 in particular. The American College of Medical Genetics made an official statement in January 2017 in which they advised the "potential for rapid advance of this approach, and the pressure to apply it clinically, should not

[1] *See generally* David Epstein, *Magic Blood and Carbon-Fiber Legs at the Brave New Olympics*, SCIENTIFIC AMERICAN (Aug. 5, 2016), https://www.scientificamerican.com/article/magic-blood-and-carbon-fiber-legs-at-the-brave-new-olympics/.
[2] *See* Albert de la Chapelle et al., *Truncated erythropoietin receptor causes dominantly inherited benign human erythrocytosis*, 90 PROC. NAT'L ACAD. SCI. 4995 (1993), *available at* http://www.pnas.org/content/90/10/4495.full.pdf (identifying the variant segregating in his extended family).
[3] Epstein, *supra* note 1.
[4] Designer babies are an example of "germline modification," which involves changes that can go on to be inherited. In the genetic modification of adults that we refer to in this article, "somatic modification," the genetic changes are just to the individual in question and are not inherited.

be underestimated."[5] However, the World Anti-Doping Agency (WADA) banned this pre-emptively in 2003 in its inaugural Code of Prohibited Substances (the Code).[6] At the time, genetic modification was an immature technology not yet adequately developed for successful use in humans. Even so, WADA took action on the basis that it would be "contrary to the spirit of sport even if it is not harmful."[7] They branded it "gene doping", thus associating it with language that conjures the image of furtive injections in shadowy locker rooms.[8]

We make the case, using our data, that increasing awareness of the role of genetics in athletic prowess pulls back the curtain on the mystique of natural talent: there is nothing fair about the genetics we happen to be born with. The results of the experimental studies presented here suggest that, if it were not unreasonably harmful, the majority of Americans would not be opposed to genetic modification for performance enhancement in sports. This is in contrast to WADA's position. It is also in contrast to public disapproval of performance enhancing drugs.[9] To date, public attitudes have not been explicitly weighted in WADA's calculus for

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[5] Editorial, *Genome editing in clinical genetics: points to consider—a statement of the American College of Medical Genetics and Genomics*, GENETICS IN MED. (Jan. 26, 2017), http://www.nature.com/gim/journal/vaop/ncurrent/full/gim2016195a.html.

[6] WORLD ANTI-DOPING AGENCY, WORLD ANTI-DOPING CODE (2003), *available at* https://www.wada-ama.org/sites/default/files/resources/files/wada_code_2003_en.pdf, [hereinafter 2003 WADA Code]

[7] 2003 WADA Code art. 4.3.2. Comment. "[T]he use of genetic transfer technology to dramatically enhance sport performance should be prohibited as contrary to the spirit of sport even if it is not harmful." Id.

[8] Consider remarks made in 2015 by then WADA director general David Howman on challenges to the integrity of sport:

> [W]hen the curtain is drawn, what is revealed is a social problem of steroids in schools and amongst our security forces; the presence of the criminal underworld in trafficking prohibited substances; an unregulated supply of non-sanitized drugs through the internet and from profit-making opportunists (including many in local gyms); amateur athletes doping in recreational sports events; young people taking steroids in a bid to look good; and, an overall challenge to the values of sport and its integrity through allied activities such as spot- or match-fixing, bribery and corruption. None of these matters really fall under WADA's express mandate of elite sport, but evidence of all have come to our attention.

Speech by WADA Director General, David Howman, Challenges to the Integrity of Sport, Melbourne, WORLD ANTI-DOPING AGENCY (Oct. 15, 2015), https://www.wada-ama.org/en/media/news/2015-10/speech-by-wada-director-general-david-howman-challenges-to-the-integrity-of-sport.

[9] *AP/AOL Poll: More Than Half Of Baseball Fans Say The Sport Hasn't Done Enough To Curb Use Of Steroids*, IPSOS (Apr. 24, 2006), http://www.ipsos-na.com/news-polls/pressrelease.aspx?id=3059 (showing 84% of respondents cared); *Baseball And Steroids*, CBS NEWS / N.Y. TIMES (Mar. 30, 2008, 6:00 PM),

determining whether substances should or should not be prohibited. WADA has advanced several candidate principles as grounds for prohibiting enhancing methods. We agree with Richard Posner's argument in *In Defense of Prometheus: Some Ethical, Economic, and Regulatory Issues of Sports Doping*, that the only compelling such rationale is the market.[10] Whereas Posner states that fans value sports for their display of relevant natural hierarchies, we depart from Posner by experimentally isolating what factors people care about, and in so doing challenge the centrality of naturalness in what draws us to sports.

Our experimental findings have broad relevance to genetic modification for performance enhancement, despite the athletic focus of the scenarios. Not only is sports an application area of interest in its own right, it is also more broadly relevant: it acts as "a catalyst for [such] discussions, and a social microcosm, a kind of laboratory, where the impact of biotechnology is publically visible and practically displayed."[11] As we have argued elsewhere, athletes are likely to be early adopters of genetic modification technology for several reasons.[12] First, the overlap between genes of interest for diseases that will be early targets for gene therapy and genes of interest for performance enhancement means that the technology may be available early. Second, athletes have shown themselves to be risk takers when it comes to gaining a competitive edge. WADA agree, stating in their St. Petersburg Declaration that

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http://www.cbsnews.com/htdocs/pdf/March31-a-baseball.pdf (showing 82% of respondents who were at least somewhat interested in baseball cared); GfK Roper Public Affairs & Media, *The AP-GfK Poll*, GREENBOOK (Feb. 17, 2009), https://www.greenbook.org/Content/GfK/AP-GfK_Poll_Baseball_Topline.pdf (showing 79% of respondents cared); *Washington Post Poll*, WASHINGTON POST (Jan 6. 2016), http://www.washingtonpost.com/wp-srv/politics/polls/postpoll_20130106.html (showing 53% of respondents cared).

[10] Richard Posner, *In Defense of Prometheus: Some Ethical, Economic, and Regulatory Issues of Sports Doping*, 57 DUKE LAW J. 1725 (2008).

[11] W. Miller Brown, *The Case for Perfection*, 36 J. PHIL. SPORT 127 (2009), *available at* http://www.tandfonline.com/doi/abs/10.1080/00948705.2009.9714752.

[12] Sarah Polcz & Anna Lewis, *CRISPR-Cas9 and the non-germline non-controversy*, 3 J. LAW BIOSCI. 413 (2016).

> [T]he financial and personal rewards for enhanced performance in sport indicate that sport will be one of the areas in which gene-based enhancement is first likely to arise. The world of sport therefore serves as a very effective setting in which to examine broad societal issues of enhancement and the unclear boundary between treatment and enhancement.[13]

The structure of this paper is as follows. Relevant background is given in Part I: Section A covers the legal context; Section B reviews relevant research on doping attitudes; Section C summarizes known links between sports performance and genetics; Section D discusses potential genetic engineering approaches and their possible detection; Section E summarizes our motivations for this study and gives an overview of our experiments. Part II outlines our methodology, including the scenarios posed to research participants in the control and experimental conditions. We give our results and some discussion in Part III. We conclude in Part IV by considering the policy implications of our findings first for sports, and then more broadly.

I. BACKGROUND

A. WADA, the Prohibited List, and Gene Doping

(1) The Creation of WADA and the Reach of the Code

Doping has always been part of sports: the International Olympic Committee (IOC) published its first list of banned substances in 1967, but the permitted or tolerated use of performance

[13] *WADA St. Petersburg Declaration,* WORLD ANTI-DOPING AGENCY (June 11, 2008), https://www.wada-ama.org/sites/default/files/resources/files/WADA_StPetersburg_Declaration_2008.pdf.

enhancing substances (PEDs) goes back at least as far as the Ancient Greeks.[14] But in recent decades, PEDs have become much more effective, and sports of all stripes have been mired in doping scandals.[15] A 2015 study published in *Sports Medicine* estimated that as many as 39 percent of elite international athletes used PEDs.[16]

WADA was set up in 1999, and today its Code has a broad reach. While WADA's prohibition against gene doping is not a sports-industry-wide ban, the consequences for US athletes are far-reaching. In 2014, inter-organizational harmonization led the NCAA, which covers nearly half-a-million student athletes, to amend its bylaws to prohibit gene doping.[17] Consequently, as a result of the collegiate to professional athlete pipeline,[18] many professional athletes will be subject to WADA's gene doping prohibition early in their careers (Gene doping is not prohibited by Major League Baseball, the National Football League, the National Basketball League, or the National Hockey League.[19]) An additional signatory is the International Military

[14] *See* D. R. Mottram, *Banned drugs in sport. Does the International Olympic Committee (IOC) list need updating?*, 27 SPORTS MED. 1 (1999), *available at* https://www.ncbi.nlm.nih.gov/pubmed/10028129; BARRIE HOULIHAN, DYING TO WIN: DOPING IN SPORT AND THE DEVELOPMENT OF ANTI-DOPING POLICY 33 (2002).

[15] *See e.g.*, REED ALBERGOTTI & VANESSA O'CONNELL, WHEELMEN (2013) (examining the doping of cyclist Lance Armstrong); MARK FAINARU-WADA & LANCE WILLIAMS, GAME OF SHADOWS (2006) (discussing the 2002 BALCO scandal); RICHARD H. MCLAREN, The Independent Person 2nd Report (2016), *available at* https://www.wada-ama.org/sites/default/files/resources/files/mclaren_report_part_ii_2.pdf (investigating the Russian doping scandals that led to bans for the Rio Olympics).

[16] Olivier de Hon et al., *Prevalence of Doping Use in Elite Sports: A Review of Numbers and Methods*, 45 SPORTS MED. 57 (2015).

[17] *2016-2017 Banned Drugs*, NAT'L COLLEGIATE ATHLETIC ASS'N, https://www.ncaa.org/sites/default/files/2016_17_%20Banned_%20Drugs_%20Educational_%20Document_20160531.pdf (last visited Jan. 17, 2017). See also *Division I Proposal - 2014-9*, NAT'L COLLEGIATE ATHLETIC ASS'N, https://web3.ncaa.org/lsdbi/search/proposalView?id=3150 (last visited Jan. 17, 2017) ("[A] student-athlete under a drug testing suspension from a national or international sports governing body that has adopted the WADA code shall not participate in NCAA intercollegiate competition for the duration of the suspension. Such suspensions are only applicable to drugs and procedures that are also banned by the NCAA.").

[18] In 2016, 251 of 253 National Football League draft picks were former NCAA players. *Estimated probability of competing in professional athletics*, NAT'L COLLEGIATE ATHLETIC ASS'N (Mar. 10, 2017), http://www.ncaa.org/about/resources/research/estimated-probability-competing-professional-athletics. Upwards of 80% of National Basketball Association players are former NCAA players. *Where the NBA Players Come From*, COLLEGIATE BASKETBALL NEWS, http://rpiratings.com/NBA.php (last visited June 1, 2017). Former NCAA hockey players comprise 30% of the National Hockey League, a number which is rising. *See* Mike G. Morreale, *College hockey's impact on NHL continues to grow*, NAT'L HOCKEY LEAGUE (June 25, 2015), https://www.nhl.com/news/college-hockeys-impact-on-nhl-continues-to-grow/c-772290.

[19] Each sports league's anti-doping rules are subject to negotiation as part of the players' collective bargaining agreements. The National Labor Relations Act stipulates that employee drug testing is a mandatory bargaining

Sports Council, which has over 130 member states and is the second largest multi-discipline sports organization after the IOC. This means that all military personnel competing as part of US Armed Forces Sport are subject to the Code.[20] (The United States Armed Forces are not morally opposed to genetic enhancement; they have shown interest in its military applications.[21])

(2) How the Gene Doping Ban Came to Be

In 2003, in its first iteration of the Code, WADA banned gene modification on the basis that it was "contrary to the spirit of sport even if it is not harmful".[22] How did this come to be? The first discussion of the possible impact of genetic modification on sports focused on its potential health risks. It was presented in a 2001 article in *Molecular Therapy,* which raised concerns about the premature use of gene therapies for athletic enhancement and the potential risks to athletes that might result.[23] The paper was prompted by the success of animal trials of gene therapy for genetic variants known to bolster human athletic performance. When the gene doping ban was at the proposal stage, it was discussed at WADA-convened workshops with no

subject. *See generally* Robert D. Manfred Jr., *Federal Labor Law Obstacles to Achieving a Completely Independent Drug Program in Major League Baseball*, 19 MARQ. SPORTS L. REV. 1 (2008).

[20] Armed Forces Sports, *Anti-Doping*, U.S. DEP'T DEF., http://armedforcessports.defense.gov/Portals/19/Documents/2015%20SOP/Appendix%20L%20Antidoping%20brief.pdf (last visited January 22, 2017).

[21] The Defense Advanced Research Projects Agency (DARPA) has previously put forward proposals for the genetic modification of humans, and there is ongoing speculation that they are actively working toward the creation of "super humans" using genetic modification techniques. *See e.g.*, Damien Gayle, *Army of the future: Soldiers will be able to run at Olympic speed and won't need food or sleep with gene technology*, DAILY MAIL (Aug. 13, 2012 2:56 PM), http://www.dailymail.co.uk/sciencetech/article-2187276/U-S-Army-Soldiers-able-run-Olympic-speed-wont-need-food-sleep-gene-technology.html. DARPA launched solicitation for the project "Advanced Tools for Mammalian Genome Engineering" in 2013. The project's proposal page states that "successful development of technologies for rapid introduction of large DNA vectors into human cell lines will enable the ability to engineer much more complex functionalities into human cell lines than are currently possible." DARPA, *Advanced Tools for Mammalian Genome Engineering*, SBIRSOURCE https://sbirsource.com/sbir/topics/88854 (last visited May 23, 2017). DARPA has actively invested in CRISPR technology. *See e.g., Broad Institute-MIT Partnership Nabs $32M DARPA Contract*, GENOMEWEB (Sep. 25, 2015), https://www.genomeweb.com/business-news/broad-institute-mit-partnership-nabs-32m-darpa-contract (announcing a $32M investment in a CRISPR company in 2015).

[22] 2003 WADA Code, *supra* note 6, at art. 4.3.2.

[23] Theodore Friedmann & Johann Olav Koss, *Gene Transfer and Athletics— An Impending Problem*, 3 MOL. THER. 819 (2001).

public consultation in any of the IOC member states, and without public debate.[24] And while the justification for the ban centered on potential health risks as providing sufficient need for action, the key participants took for granted that even harmless genetic enhancement would be morally reprehensible. The addition of gene modification to the initial edition of the Code was spearheaded by leading gene therapy scientist Theodore Friedmann, the author of the 2001 *Molecular Therapy* article. He also coined the term "Gene Doping".[25] Joe Fore observes that it "seems clear that the very act of labeling this type of genetic modification as "doping" was a significant act, clearly connoting an official negative attitude toward the practice."[26]

(3) The Spirit of Sport and the "Immunity" of the Prohibited List

The Code states a method may be banned if it meets any two of three criteria: health risks, enhancing effects, or conflicts with the spirit of sport.[27] WADA releases yearly updates to the list of prohibited methods (the List), without disclosing for a given inclusion which two criteria it considers to be met, or providing supporting evidence or arguments which would shed light on how the concept of spirit of sport is operationalized.[28] The Code states that the inclusion of methods on the List cannot be legally challenged on the grounds that WADA erred in applying their own criteria.[29] Few challenges by athletes to anti-doping penalties brought to the Court of

[24] See *WADA Gene Doping Symposium Reaches Conclusions and Recommendations*, WORLD ANTI-DOPING AGENCY (Dec. 5, 2005), https://www.wada-ama.org/en/media/news/2005-12/wada-gene-doping-symposium-reaches-conclusions-and-recommendations.
[25] Angela J. Schneider, *The Concept of Doping*, in ROUTLEDGE HANDBOOK OF DRUGS AND SPORT 9, 10 (Verner Møller, Ivan Waddington & John M. Hoberman, eds., 2015) ("[T]here is far less awareness of gene-doping, which has been on WADA's list since its inception (primarily due to the persistent work of genetic researcher Theodore Friedmann).").
[26] Joe Fore, *Moving Beyond Gene Doping: Preparing for Genetic Modification in Sport*, 15 VA. J. L. & TECH. 76, 85 (2010). *See also* Kristin Jo Custer, Note, *From Mice to Men: Genetic Doping in International Sports*, 30 HASTINGS INT'L & COMP. L. REV. 181 (2006) ("WADA has shown a negative perspective toward the practice."). *See generally* Bernat López, *Creating fear: The social construction of human Growth Hormone as a dangerous doping drug*, 48 INT'L REV. SOC. SPORT. 220 (2012), *available at* http://journals.sagepub.com/doi/abs/10.1177/1012690211432209 (discussing the social construction of growth hormone as a doping substance).
[27] 2003 WADA Code, *supra* note 6, at art. 4.3.1.
[28] MARJOLAINE VIRET, EVIDENCE IN ANTI-DOPING AT THE INTERSECTION OF SCIENCE & LAW 440 (2015).
[29] 2003 WADA Code, *supra* note 6, at art. 4.3.3.

Arbitration for Sport[30] have argued the banned substance at issue should not have been prohibited, and in those few cases the immunity of the List has been upheld.[31] Consequently, the Court of Arbitration for Sport has not considered how the spirit of sport criterion fulfills its line drawing function between acceptable and unacceptable methods.[32] A door has been opened to such consideration, however, in a leading case from the European Court of Justice. *Meca-Medina v. Commission* (2006) suggests courts could determine whether the prohibition of a method is excessive beyond what can be justified to achieve the proper conduct of competitive sport.[33] Importantly, such a determination would turn upon the conditions for dividing methods which constitute doping from those which do not.[34] WADA has reason to elaborate the meaning

[30] Pursuant to Article 61 of the Olympic Charter, the Court of Arbitration for Sport settles all disputes related to the Olympic Games, and other competitions when specified by contract. Though appeals are generally unsuccessful, Court of Arbitration for Sport decisions can be appealed to the Federal Supreme Court of Switzerland. FC Shakhtar Donetsk v. da Silva (*Matuzalem*) CAS 2008/A/1519 (Ct. Arb. Sport 2009) is the only CAS decision to date which has been overruled on the merits rather than on procedural grounds. The jurisdiction of the European Court of Justice in Meca-Medina v. Commission, Case C-519/04, [2006] E.C.R. I-6991, was a challenge to the Code based on EU competition law.

[31] *See e.g.*, Fina v. Mellouli, CAS 2007/A/1252 ¶¶ 14-19 (Ct. Arb. Sport 2007). Court of Arbitration for Sport litigator Marjolaine Viret observes, "the immunity of the Prohibited List has not been seriously challenged before CAS panels so far. . .the lack of transparency on the inclusion and revision process to the Prohibited List *de facto* impedes any legal challenge directed against [it]." Viret, *supra* note 29, at 444. See also *Union Cycliste Internationale v. Georges,* TAS 2013/A/3320 ¶ 107 (Ct. Arb. Sport 2014) ("Once the determination regarding the status of a Prohibited Substance or Method has been made by WADA, no Athlete may challenge the inclusion of a substance of method on the Prohibited List based on the argument that these criteria were not really fulfilled. . .").

[32] Decisions from other adjudicative forums in which doping violations have been litigated offer little guidance on the spirit of sport or related concepts to which to turn. As discussed in *supra* note 19 doping prohibitions are subject to collective bargaining rather than institutionally imposed in U.S. professional sports. NCAA doping violations are appealed through the Drug-Testing Subcommittee in an unreported private internal arbitration process. *See* Josephine R. Potuto & Matthew J. Mitten, *Comparing NCAA and Olympic Athlete Eligibility Dispute Resolution Systems in Light of Procedural Fairness and Substantive Justice*, 7 HARV. J. SPORTS ENTERTAIN. LAW 44 (2016). Moreover the NCAA effectively precludes judicial review through its Restitution Rule. *See* Stephen F. Ross, Richard T. Karcher & S. Baker Kensinger, *Judicial Review of NCAA Eligibility Decisions: Evaluation of the Restitution Rule and a Call for Arbitration*, 40 J. COLL. UNIV. LAW 79 (2014). Among the cases which stand as exceptions none address the inclusion of substances on the banned list. Case law from both Canada and Germany implicitly appeals to the intuition that doping rules are normatively justified in excluding substances that would interfere with sports as a test of biological potential, but with inadequate theoretical elaboration. *See e.g.*, Johnson v. Athletics Can., [1997] O.J. 3201, para.29 (arguing it is "necessary to protect the right of the athlete, including Mr Johnson, to fair competition, to know that the race involves only his own skill, his own strength, his own spirit and not his own pharmacologist"); Krabbe v. Int'l Amateur Athletic Fed'n, Oberlandesgericht München [OLG M] [Munich Region Court of Appeal] Mar. 28, 1996, Zeitschrift für Sport und Recht [SpuRt] 133, 134, 1996 (Ger.) (asserting that doping regulations further "the establishment of equal starting and competing conditions.").

[33] *Meca-Medina*, [2006] E.C.R. I-6991, ¶ 45.

[34] *Id.* at ¶ 47.

of the spirit of sport, not only to anticipate a challenge to the List but to bolster the credibility of its processes among stakeholders.

(4) WADA's Pursuit of the Spirit of Sport

Unofficially, WADA has suggested the dividing line is public sentiment. In 2012, David Howman, then-director general of WADA, was paraphrased in an interview as taking the position that the spirit of sport should be determined: "…by the fans… WADA seeks to create and enforce a set of rules that reflect global norms… Most people, as WADA's global surveys have shown, believe that doping is unethical and unsportsmanlike, and this popular belief is what drives policy".[35]

We can assume by "people…believe doping is unethical" Howman means people believe athletes should not use methods of performance enhancement of which they disapprove.[36] Howman refers to global studies carried out by WADA; yet the literature to date does not address methods of enhancement beyond anabolic steroids, growth hormone, EPO and amphetamines.[37] But it does not follow from public opposition to, for instance, anabolic

[35] Joshua Rothman, *Just what's wrong with doping?*, BOSTON GLOBE (July 15, 2012), https://www.bostonglobe.com/ideas/2012/07/14/what-really-wrong-with-sports-doping/qO1GZhk7ay36zoh8GMM18N/story.html.

[36] A literal reading would only support the trivial claim that the public believes athletes should not break doping rules, as distinguished from public opinion as to the methods which should be prohibited and thus constitute doping.

[37] *See e.g.*, Gunnar Breivik et al., *Attitudes towards use of performance-enhancing substances and body modification techniques. A comparison between elite athletes and the general population*, 12 SPORT SOC. 737 (2009); Terry Engelberg et al., *Public perception of sport anti-doping policy in Australia*, 19 DRUGS: EDUCATION, PREVENTION & POL'Y 84 (2012); Brad Partridge et al., *A Comparison of Attitudes Toward Cognitive Enhancement and Legalized Doping in Sport in a Community Sample of Australian Adults*, 3 AJOB PRIMARY RES. 81 (2012); Brad Partridge et al., *"If you're healthy you don't need drugs": Public attitudes towards "brain doping" in the classroom and "legalised doping" in sport*, 3 PERFORMANCE ENHANCEMENT & HEALTH 20 (2014); John Singhammer, *Age and Gender Specific Variations in Attitudes to Performance Enhancing Drugs and Methods. A Cross-Sectional Study*, 21 SPORT SCI. REV. 29 (2012); John Singhammer, *Attitudes Toward Anabolic-Androgenic Steroids Among Non-competing Athletes in Various Types of Sports – A Cross-sectional Study –*, 22 SPORT SCI. REV. 109 (2013); Harry Arne Solberg et al., *Doping in elite sport - do the fans care? Public opinion on the consequences of doping scandals*, 11 INT'L J. SPORTS MARKETING & SPONSORSHIP 2 (2010); Hanspeter Stamm et al., *The public perception of doping in sport in Switzerland, 1995 – 2004*, 26 J. SPORTS SCI. 235–242 (2008).

steroids, that the public is opposed to all enhancement methods; clearly this is not the case. There is no public furor over enhancing surgeries, none of which are banned. Any implication by Howman that the public believes all methods on the List should be prohibited is undermined by a lack of commonplace familiarity with many of the listed methods. Yet WADA's moral authority and credibility in the eyes of stakeholders and the general public are impaired by its failure to provide a coherent rationale for prohibition decisions. More than mere convention, therefore, should support WADA's process of labeling some methods in conflict with the spirit of sport, and therefore doping, while other methods remain acceptable.

WADA has attempted to provide theoretical clarification of the spirit of sport. This proved challenging. In the Code, the Fundamental Rationale characterizes the spirit of sport thus:

> It is the essence of Olympism, the pursuit of human excellence through the dedicated perfection of each person's natural talents. It is how we play true. The spirit of sport is the celebration of the human spirit, body and mind, and is reflected in values we find in and through sport, including:
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> • Ethics, fair play and honesty
> • Health
> • Excellence in performance
> • Character and education
> • Fun and joy
> • Teamwork
> • Dedication and commitment
> • Respect for rules and laws
> • Respect for self and other Participants
> • Courage
> • Community and solidarity

None of the values listed above can obviously serve as a basis for separating "good" substances from "bad" ones. In the context of gene doping, WADA contends that permitting athletes to acquire genetic advantages is unfair. Yet some athletes have always possessed genetic advantages over others, and this is not generally held to undermine the fairness of sports.

Attempts to emphasize 'naturalness' also run into issues. In a 2006 position paper, attempting to justify why athletes are allowed to alter their "natural" state in some ways but not others, WADA's Ethical Issues Review Panel argued only "virtuous" substances and methods of enhancement are allowed.[38] "Virtuous" enhancements in the athletic context, the Panel asserted, require the athlete to "actively engage and interact as part of the process in order to enhance performance". On the other hand, unvirtuous enhancements, which should be prohibited, operate "on the athlete" who is "merely a passive recipient of its benefits." Yet this claim cannot be reconciled with WADA's prohibition practices. There are a range of passive performance enhancing surgical procedures, such as Tommy John surgery, and no surgical enhancements are banned.[39] Moreover, if WADA were to revise the list to reflect the active/passive distinction, this dividing line between virtuous and unvirtuous enhancements would still fail as a rule because it is too broad; even widely accepted methods of enhancing natural talent such as massage would be excluded because they achieve their effects through processes in which athletes are passive recipients.[40] The notion of "natural" with which the IOC and WADA are concerned is not a biological state, but a shifting social construct. Nowhere is this more on display than in recent cases in which some female athletes were required to

[38] *See* Coleman, *infra* note 36, at 1755 n.62.
[39] *See* R. M. Rodenberg & H. L. Hampton, *Surgical doping: a policy loophole?*, 5 INT'L J. SPORT POL'Y & POL. 145 (2013).
[40] DORIANE LAMBELET COLEMAN ET AL., CTR. FOR SPORTS L. & POL'Y, POSITION PAPER: WHETHER ARTIFICIALLY INDUCED HYPOXIC CONDITIONS VIOLATE "THE SPIRIT OF SPORT" (2006), *available at* https://www.law.duke.edu/features/pdf/hypoxiaresponse.pdf.

suppress their natural hormone levels pharmacologically to be allowed to compete in the Olympics.[41]

(5) A New Set of Guiding Values

In 2016 the Ethics Panel adopted a set of guiding values.[42] In setting out these guiding values, WADA subtly distances itself from earlier appeals to what is "natural" and "virtuous" as boundaries of moral significance. Whereas in the Fundamental Rationale, the essence of Olympism is characterized as excellence through the perfection of each person's *natural* talents, in the guiding values it now reads "each person's talents".[43] There is no mention of the *virtuous* enhancement of talents.[44] WADA may be conceding that virtuousness and naturalness have not been theoretically refined in a way that coherently supports the diversity of prohibited methods and distinguishes them from those which are allowed.

In a further welcome development, WADA implies an intention to break from its past of closed-door prohibition decisions by establishing transparency as a guiding value.[45] The rationale for prohibitions is to be made public and moreover, should be based on "the best available scientific evidence".[46] The guiding values do not carve out an exemption from scientific

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[41] *Naturally Occurring High Testosterone Shouldn't Keep Female Athletes out of Competition*, SCIENTIFIC AMERICAN (Aug. 1, 2016), https://www.scientificamerican.com/article/naturally-occurring-high-testosterone-shouldn-t-keep-female-athletes-out-of-competition/. See also *IOC Regulations on Female Hyperandrogenism*, INT'L OLYMPIC COMM. (June 22, 2012), https://stillmed.olympic.org/Documents/Commissions_PDFfiles/Medical_commission/2012-06-22-IOC-Regulations-on-Female-Hyperandrogenism-eng.pdf.

[42] *WADA Ethics Panel: Guiding Values in Sport and Anti-Doping*, WORLD ANTI-DOPING AGENCY, https://www.wada-ama.org/sites/default/files/resources/files/wada_ethics_panel_guiding_values_in_sport_and_anti-doping_june_2016.pdf (last visited May 23, 2017). The first version of the List that could be impacted by these new guiding values will be issued in 2018.

[43] *Id.*

[44] *Id.*

[45] *Id.* ("Transparency: In order to promote open dialogue, public trust and integrity, the rationale and process for any decision, as well as ensuing policy recommendations should be as transparent as practicable.").

[46] *Id.* It will be interesting to see whether they remove cannabis from the List. Cannabis use is low-risk and non-enhancing based on the best available evidence. Commentators have speculated WADA continues to prohibit

support for spirit of sport considerations. It is open to WADA to re-center the spirit of sport around concerns amenable to measurement.

(6) The Market and the Spirit of Sport

One approach would be to deemphasize the values in the Code's Fundamental Rationale. Those values are more characteristic of recreational than elite sports. The spirit of sport could be reframed to reflect features of high-level sports including competition and the spectator enthusiasm it inspires. Richard Posner has argued that the question of sports doping should be approached as a matter of audience preferences.[47] If athletes were allowed to dope and as a result audiences lost interest in elite sports, our society stands to lose little more than spectator enjoyment.[48] He rejects the theoretical project of defining the spirit of sport in grander terms. For Posner, doping prohibitions may be justified and necessary to assure an economically efficient sports market. Other commentators have arrived at the same position[49], which is also supported by pre-WADA rulings in Germany and England.[50]

Posner claims that what sports fans primarily care about is the exhibition of relevant "hierarchies of 'natural' talent"[51]. Although his account is attractive, the centrality of naturalness to that enjoyment is called into question by the pleasure humans derive from the rites associated with many non-biological hierarchies (e.g. monarchy).[52] It is not obvious the

cannabis due to fears that corporate sponsors of IOC-related events would respond negatively to the political signal such a move could be perceived to send. *See* VIRET, *supra* note 29, at 453-455.

[47] Posner, *supra* note 9.

[48] *Id.* at 1739.

[49] *See* Antonio Rigozzi et al., *Doping and Fundamental Rights of Athletes*, 3(3) SWEET & MAXWELL INT'L SPORTS L. REV. 39, 43 (2003).

[50] *See* Krabbe, SpuRt 1996 at 134 (linking doping to damage to the public image of sports); Gasser v. Stinson, (June 15, 1988) Unreported, Queen's Bench Division (Scott J.).

[51] Posner, *supra* note 9, at 1731.

[52] For a review of social science findings on preferences for and the prevalence of hierarchy, see Deborah H. Gruenfeld & Larissa Z. Tiedens, *Organizational Preferences and Their Consequences*, in HANDBOOK OF SOCIAL PSYCHOLOGY 1262 (Susan T. Fiske, Daniel T. Gilbert & Gardner Lindzey eds., 2010).

public will disapprove of competitions including genetically modified athletes, particularly considering the alterations from "at-birth" noted earlier in this article, including surgery, over which there is no uproar. Genetic modification technology is very new and has not acquired the social stigma which is arguably a key distinguishing feature between enhancing interventions deemed "natural" and "unnatural".

Ultimately Posner's claim about what sports fans value is an empirical one and he leaves room for sports fans to prefer something else – for instance super enhanced athletes.[53]

(7) The Costs of Viewing Gene Doping as an Imminent Threat

WADA thinks the prospect of gene doping is imminent. Since 2001 it has spent more than $70 million on research, of which a "significant portion" has been dedicated to gene doping detection research, with the justification that "the size of the effort is appropriate for the size of the threat to sport."[54] Conceding that at the initial time of the ban gene therapy technology had not yet developed sufficiently to be used for "gene doping", WADA justifies this spending by stating that it is "better to be proactive than reactive."[55]

If the public do not agree that genetic modification is against the spirit of sport the money spent on detection methods lacks an appropriate mandate. The ACMG encourages "broad public debate", and desires to draw attention to the application of the technology to non-disease

[53] Posner, *supra* note 9, at 1739.
[54] *Research*, WORLD ANTI-DOPING AGENCY, https://www.wada-ama.org/en/research (last visited Jan 15, 2017); World Anti-Doping Agency, *Gene Doping: An Overview and Update*, 2 PLAY TRUE 12 (2007), *available at* https://www.wada-ama.org/sites/default/files/resources/files/PlayTrue_2007_2_Science_Honing_In_On_Doping_EN.pdf.
[55] World Anti-Doping Agency, *Championing the Science: A Conversation with Arne Ljungqvist*, 2 PLAY TRUE 3 (2007), *available at* https://www.wada-ama.org/sites/default/files/resources/files/PlayTrue_2007_2_Science_Honing_In_On_Doping_EN.pdf.

traits.[56] We set out to test whether WADA's stance on the ethical impermissibility of genetic modification for enhancement is shared by the lay public.

B. Public Opinion on Fairness in Sports

To the best of our knowledge, there have been no public opinion surveys on gene doping published. There are two studies surveying athletes: an unpublished study of 115 US student athletes from 2005 found that 60% thought gene doping was ethically equivalent to steroid use;[57] a survey of 81 Dutch athletes and 52 Kinesiology professors found a high level of support that gene doping formed a serious threat to fair play.[58]

A review paper of 2015 covering public opinion surveys of human enhancement concluded that this is an understudied area.[59] On the topic of genetic modification for human enhancement, none of the papers that met their (broad) inclusion criteria were done in the United States. Two public opinion surveys in Japan found 23% and 29% supportive of genetic modification for human enhancement.[60] A survey of 1229 human genetics experts in the US found that ~25% considered genetic modification for human enhancement at least somewhat acceptable.[61]

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[56] Editorial, *supra* note 5.
[57] *Results from Oregon College Athlete Gene Doping Survey*, GENEFORUM (2005), http://www.geneforum.org/node/489.
[58] Kris Dierickx et al., *The Ethics of Gene Doping: A Survey of Elite Athletes and Academic Professionals*, 3 J. CLINICAL RES. & BIOETHICS 136 (2012), *available at* https://www.omicsonline.org/the-ethics-of-gene-doping-a-survey-of-elite-athletes-and-academic-professionals-2155-9627.1000136.php?aid=8190.
[59] Anne M. Dijkstra & Mirjam Schuijff, *Public opinions about human enhancement can enhance the expert-only debate: A review study*, 25 PUB. UNDERSTANDING SCI. 588 (2015), *available at* http://pus.sagepub.com/content/early/2015/01/19/0963662514566748.
[60] Mary Ann Chen Ng et al., *Attitudes of the Public and Scientists to Biotechnology in Japan at the start of 2000*, 10 EUBIOS J. ASIAN & INT'L BIOETHICS 106 (2000), *available at* http://www.eubios.info/BIOJ2000.htm; Darryl Macer et al., *Changing hopes and concerns about gene therapy in Japan*, 13 J. COM BIOTECH. 209 (2007), *available at* http://commercialbiotechnology.com/index.php/jcb/article/view/206.
[61] Isaac Rabino, *Gene Therapy: Ethical Issues*, 24 THEORETICAL MED. & BIOETHICS 31 (2003), *available at* http://link.springer.com/article/10.1023/A:1022967623162.

There have been no scholarly US public opinion surveys on doping (of any kind) in sports, though there have been several opinion polls that have been conducted in the US. Many of the polls are focused on the perceived scale of the problem.[62] On the issue of how much the public care about doping in baseball, 84% cared in 2006, 82% in 2008, 79% in 2009, and 53% in 2013.[63] A 2005 poll revealed that more than 60% of the public thought that the Major League Baseball (MLB) was not doing enough to combat doping, in 2014, another poll found that number had dropped to 20%.[64] Over that time period the MLB's penalties for doping abuse increased.[65] Some subsequent polls suggested changing attitudes to steroid use in baseball, noting that fans may have become more lenient about whether records should stand if the player was taking steroids at the time.[66] In sum, there is limited data on public opinion of doping in sports, and some data that suggest opinions could be changing.

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[62] *See e.g.*, *National: Mixed Opinion on Baseball Steroid Scandal*, MONMOUTH U. POLL (Aug. 6, 2013), https://www.monmouth.edu/WorkArea/DownloadAsset.aspx?id=40802204287 (over 80% Americans aware of drug use in baseball); *Omnibus Poll*, YOUGOV (June 6, 2013), http://cdn.yougov.com/cumulus_uploads/document/dtc54anvpu/tabs_doping_0605062013.pdf (55% of Americans thought baseball had a major problem with drug use, compared to 51% for cycling); *Olympics Study*, IPSOS PUB. AFF. (Aug. 11, 2008) http://surveys.ap.org/data/Ipsos/national/2008-08-12%20AP%20Olympics%20Topline.pdf (86% of respondents thought drug use "a problem" in the Olympics); Sports & Drugs Poll, YouGov (Nov. 11, 2015), https://d25d2506sfb94s.cloudfront.net/cumulus_uploads/document/c0d22z830j/tabs_OP_Sports_and_Drugs_20151111.pdf, (showing that 51% supported a ban of Russian athletes due to doping).

[63] *AP/AOL Poll: More Than Half Of Baseball Fans Say The Sport Hasn't Done Enough To Curb Use Of Steroids*, IPSOS (Apr. 24, 2006), http://www.ipsos-na.com/news-polls/pressrelease.aspx?id=3059 (showing 84% of respondents cared); *Baseball And Steroids*, CBS NEWS / N.Y. TIMES (Mar. 30, 2008, 6:00 PM), http://www.cbsnews.com/htdocs/pdf/March31-a-baseball.pdf (showing 82% of respondents who were at least somewhat interested in baseball cared); GfK Roper Public Affairs & Media, *The AP-GfK Poll*, GREENBOOK (Feb. 17, 2009), https://www.greenbook.org/Content/GfK/AP-GfK_Poll_Baseball_Topline.pdf (showing 79% of respondents cared); *Washington Post Poll*, WASH. POST (Jan 6. 2016), http://www.washingtonpost.com/wp-srv/politics/polls/postpoll_20130106.html (showing 53% of respondents cared).

[64] *Broad Concern About Steroids Fuels Support for Punitive Rules*, ABC NEWS / ESPN (Mar. 16, 2005, 3:00 PM), http://abcnews.go.com/images/Politics/976a1BaseballSteroids.pdf; *PED Suspensions Warranted, Say Nearly Seven in Ten*, MARIST INST. PUB. OPINION (May 14, 2014), http://maristpoll.marist.edu/wp-content/misc/usapolls/us140407/Baseball/Complete%20May%202014%20USA%20Marist%20Poll%20Release%20and%20Tables.pdf.

[65] Michael S. Schmidt, *Baseball and Union Agree to In-Season Blood Testing for H.G.H.*, THE NEW YORK TIMES, January 10, 2013, https://www.nytimes.com/2013/01/11/sports/baseball/baseball-and-union-agree-to-in-season-blood-testing-for-hgh.html (last visited May 29, 2017).

[66] *Alex Rodriguez and Steroid Use in Baseball*, CBS NEWS / N.Y. TIMES (Feb. 24, 2009, 6:30 PM), http://www.cbsnews.com/htdocs/pdf/Feb09b-BASEBALL.pdf.

There have been public opinion surveys performed outside the US, with the majority showing strong disapproval for doping.[67] A Belgian survey of doping in cycling found that cycling fans are more lenient in their attitudes than non-fans.[68] Another Belgian study found that student opinion may be shifting from zero-tolerance to a more lenient approach.[69] There is conflicting evidence over whether athletes are more or less opposed to doping than the general public.[70]

How much does doping affect fans attitude to sports? In an opinion poll conducted in 2016, 61% of US respondents stated that doping by some athletes decreased the attention they paid to the Olympics by "a lot" (41%) or "some" (20%).[71] A scholarly article that investigated the impact of doping in Major League Baseball found little evidence that doping reduces fan interest, the main economic rationale for anti-doping policies.[72]

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[67] For a survey of Norwegian sports fans showing no tolerance for doping, see Harry A. Solberg et al., *Doping in elite sport - do the fans care? Public opinion on the consequences of doping scandals*, 11(3) INT'L J. SPORTS MARKETING & SPONSORSHIP 2 (2010), *available at* http://www.emeraldinsight.com/doi/pdfplus/10.1108/IJSMS-11-03-2010-B002. *See also* Stephen Moston et al., *Perceived incidence of drug use in Australian sport: a survey of public opinion*, 15 SPORT IN SOC'Y 64 (2011), *available at* http://www.tandfonline.com/doi/abs/10.1080/03031853.2011.625277 (finding low support for doping amongst the Australian public); Hanspeter Stamm et al., *Attitudes towards doping - A comparison of elite athletes, performance oriented leisure athletes and the general population*, 11 EUR J. SPORT & SOC'Y 171 (2014), *available at* http://www.tandfonline.com/doi/abs/10.1080/16138171.2014.11687939 (showing lack of support for doping among Swiss respondents); Hanspeter Stamm et al., *The public perception of doping in sport in Switzerland, 1995 - 2004*, 26 J. SPORTS SCI. 235 (2008), *available at* http://www.tandfonline.com/doi/abs/10.1080/02640410701552914 (recording similar findings for an earlier period).

[68] Daam Van Reeth & Wim Lagae, *Public opinion on doping in cycling: differences among population groups* (HUBrussel Research Paper 2013/14, 2013), https://lirias.kuleuven.be/bitstream/123456789/435755/1/13HRP14.pdf.

[69] Hans Vangrunderbeek & Jan Tolleneer, *Student attitudes towards doping in sport: Shifting from repression to tolerance?*, 46 INT'L REV. SOCIOL. SPORT 346 (2010), *available at* http://journals.sagepub.com/doi/pdf/10.1177/1012690210380579.

[70] *Compare* Elisabeth J. Vargo et al., *Perceptions of assisted cognitive and sport performance enhancement among university students in England*, 3 PERFORMANCE ENHANCEMENT & HEALTH 66 (2014), *available at* http://www.sciencedirect.com/science/article/pii/S2211266915000031 (showing athletes less opposed than the general public), *with* Stamm, *Attitudes towards doping*, *supra* note 70 (showing athletes more opposed).

[71] BBC World Serv., *Doping a Problem but Olympic Success Remains a Driver of National Pride: Global Poll*, GLOBESCAN (Jul. 26, 2016, 11:01 PM), http://globescan.com/images/images/pressreleases/bbc2016-olympics/BBC_Olympics_Pride_Poll_Press_Release_July_25.pdf.

[72] Jeffrey Cisyk & Pascal Courty, *Do Fans Care About Compliance to Doping Regulations in Sports? The Impact of PED Suspension in Baseball*, 18 J. SPORTS ECON. 323 (2015), *available at* http://journals.sagepub.com/doi/pdf/10.1177/1527002515587441.

C. Links Between Genetics and Sports Performance

In this section, we examine how the genetics of athletes is known to affect performance, and hence what types of genetic modification might be considered desirable by athletes.

While there have been no large scale studies regarding the heritability of sports performance, there have been some that confirm the high heritability of sports participation.[73] Moreover, the fact that athletes tend to have specific physiological attributes, and that athletes are often from the same families, suggests that genetics plays a strong role.[74] Already genetic variation in dozens of genes - over 120 individual genetic markers - has been linked to sports performance.[75] Table 1 lists some representative examples which demonstrate that one's genetics influences a range of relevant traits including endurance ability, muscle performance, how the body regenerates after injury, how energy metabolism is regulated, how blood flow if controlled, how pain is perceived, how the body responds to stress, and when sexual development takes place. The underlying genetics is not straightforward, with both common

[73] A study of over 37,000 pairs of twins from seven countries found heritability of exercise participation to be 48-71%. Janine H. Stubbe et al., *Genetic Influences on Exercise Participation in 37.051 Twin Pairs from Seven Countries*, PLOS ONE 1 (Dec. 20, 2006), *available at* http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0000022. An earlier study found that genetic factors account for ~29–62% of the variance in daily exercise behavior and 35–83% of the variance in sports participation. Gaston Beunen & Martine Thomis, *Genetic determinants of sports participation and daily physical activity*, 23 INT'L J. OBESITY S55 (1999), *available at* https://www.researchgate.net/profile/Martine_Thomis/publication/12931043_Genetic_determinants_of_sports_participation_and_daily_physical_activity/links/54aa64300cf200447b258b60.pdf.

[74] Van Jensen & Alex Miller, *Why Basketball Runs in the Family*, WALL ST. J., June 13, 2016, http://www.wsj.com/articles/nba-basketball-runs-in-the-family-1464130236 (reporting that 49% of NBA players are related to an elite athlete).

[75] *See e.g.*, Giuseppi Lippi et al., *Genetics and sports*, 93 BRIT. MED. BULL. 27 (2010), *available at* https://academic.oup.com/bmb/article/93/1/27/306419/Genetics-and-sports; Daniel G. MacArthur & Kathryn N. North, *Genes and human elite athletic performance*, 116 HUM. GENETICS 331 (2005), *available at* http://link.springer.com/article/10.1007%2Fs00439-005-1261-8; Jim L. Rupert, *The search for genotypes that underlie human performance phenotypes*, 136 COMP. BIOCHEM. & PHYSIOL. PART A: MOLECULAR & INTEGRATIVE PHYSIOL. 191 (2003), *available at* http://www.sciencedirect.com/science/article/pii/S1095643302003495. The 120 figure appears in Ildus I. Ahmetov & Olga N. Fedotovskaya, *Current Progress in Sports Genomics*, 70 ADVANCES IN CLINICAL CHEMISTRY 247 (2015), *available at* https://www.researchgate.net/profile/Ildus_Ahmetov/publication/274735844_Current_Progress_in_Sports_Genomics/links/55294fcb0cf29b22c9bf1ee2.pdf.

and rare variants contributing.[76] However, our understanding of the genetics underlying phenotypic traits is rapidly evolving and expanding as new genetic sequencing technologies make large scale studies feasible. In January 2017 the leading genetic sequencing company, Illumina, announced that it would soon be possible to sequence an entire human genome for $100.[77]

A number of genetic testing companies offer advice based on these findings, offering information on genetic predisposition for sports injuries, and identifying individuals with desirable genetics.[78] In 2014, Uzbekistan announced that it would use genetic testing to select individuals as young as 10 for its Olympic training team.[79] In 2015, there were at least 39 companies offering genetic tests directly to consumers, though there is no or little evidence that they actually help prevent injury or select star athletes.[80] Such testing raises multiple ethical concerns, including over eugenics and the treatment of minors.[81]

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[76] For a review of how genetic linkages are ascertained, and some of the complexities involved, see João Guilherme et al., *Genetics and sport performance: current challenges and directions to the future*, 28 REVISTA BRASILEIRA DE EDUCAÇÃO FÍSICA E ESPORTE 177 (2014), *available at* http://www.scielo.br/scielo.php?script=sci_arttext&pid=S1807-55092014000100177.

[77] Meghana Keshavan, *Illumina says it can deliver a $100 genome — soon*, STAT (January 9, 2017), https://www.statnews.com/2017/01/09/illumina-ushering-in-the-100-genome/.

[78] For a review of the availability of tests that help reduce injury, see Gabrielle T. Goodlin et al., *The Dawning Age of Genetic Testing for Sports Injuries*, 25 CLINICAL J. SPORTS MED. 1 (2015), *available at* https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4278350/. For reviews of tests that help identify talented individuals, see Ahmetov, *supra* note 78, Guilherme, *supra* note 79, Marios Kambouris et al., *Predictive Genomics DNA Profiling for Athletic Performance*, 6 RECENT PAT. DNA GENE SEQ. 229 (2012), *available at* https://www.ncbi.nlm.nih.gov/pubmed/22827597, and Stephen M. Roth, *Critical Overview of Applications of Genetic Testing in Sport Talent Identification*, 6 RECENT PAT. DNA GENE SEQ. 247 (2012).

[79] Ron Synovitz & Zamira Eshanova, *Uzbekistan Is Using Genetic Testing to Find Future Olympians*, THE ATLANTIC (Feb. 6, 2014), http://www.theatlantic.com/international/archive/2014/02/uzbekistan-is-using-genetic-testing-to-find-future-olympians/283001.

[80] M. Alison Brooks & Beth A. Tarini, *Genetic Testing and Youth Sports*, 305 JAMA 1033 (2011), *available at* http://jamanetwork.com/journals/jama/fullarticle/645993. A group of world experts issued a consensus statement asserting that "[t]he general consensus among sport and exercise genetics researchers is that genetic tests have no role to play in talent identification or the individualised prescription of training to maximise performance." Nick Webborn et al., *Direct-to-consumer genetic testing for predicting sports performance and talent identification: Consensus statement*, 49 BRIT. J. SPORTS MED. 1486 (2015), *available at* http://bjsm.bmj.com/content/49/23/1486.

[81] Guilherme, *supra* note 79.

D. Gene Therapy for Sports Enhancement

Gene therapy can be broadly defined as using genes to attempt to cure genetic disease. There are several genetic engineering approaches, including replacing a non-functional gene with a healthy copy, inactivating a gene that is not functioning properly, and introducing a new gene.[82] Clinical research started in the 1980s, and by August 2016, there had been over 2400 gene therapy clinical trials.[83] It was not until 2003 that the first gene therapy was approved, in China.[84]

Many of the genetic targets for gene therapy align with potential targets for genetic modification for sports performance enhancement, as highlighted in Table 1.[85] For example, the gene therapy Neovasculgen, used to treat peripheral artery disease, became the second gene therapy drug to be approved in 2011.[86] It delivers the gene VEGF, a candidate for gene doping (it is involved in the generation of new blood vessels, see Table 1). Another potential target for gene doping, inhibition of Myostatin (MSTN, see Table 1), is also a gene therapy target for diseases that cause muscular atrophy. Bioviva, a biotechnology company, is developing a gene therapy involving Myostatin inhibition, and reports successful results on its first test subject, their CEO.[87]

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[82] U.S. Nat'l Libr. Med., *What is gene therapy?*, NAT'L INST. HEALTH, https://ghr.nlm.nih.gov/primer/therapy/genetherapy (last visited Jan. 17, 2017).
[83] J. Gene Med., *Gene Therapy Clinical Trials Worldwide*, ABEDIA (Aug. 2016), http://www.abedia.com/wiley/phases.php.
[84] Sue Pearson et al., *China approves first gene therapy*, 22 NATURE BIOTECH. 3 (2004), *available at* https://www.ncbi.nlm.nih.gov/pubmed/14704685.
[85] *See* David Gould, *Gene doping: gene delivery for olympic victory*, 76 BRIT. J. CLINICAL PHARMACOLOGY 292 (2013), *available at* https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3731603/.
For a list of potential gene modifications in sports, see Ewa Brzeziańska et al., *Gene Doping in Sport – Perspectives and Risks*, 31 BIOLOGY OF SPORT 251 (2014), *available at* https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4203840/.
[86] *Neovasculgen*, HUM. STEM CELL INST., http://eng.hsci.ru/products/neovasculgen (last visited Jan. 17, 2017) (announcing approval in Russia).
[87] *Dual Gene Therapy Has Beneficial Effects On Blood Biomarkers And Muscle Composition*, BIOVIVA (2016), http://bioviva-science.com/blog/dual-gene-therapy-has-beneficial-effects-on-blood-biomarkers-and-muscle-composition.

In recent years, the genetic engineering field has been revolutionized by a new technology called CRISPR-Cas9.[88] First demonstrated as a genome-editing technology in human cells in 2013, the technology enables precise genetic modification at more or less arbitrary points of DNA using a "molecular scissors" approach. CRISPR-Cas9 is widely regarded as revolutionary in part because it is much cheaper, more accurate and more technologically straightforward than earlier technologies.[89]

Successful use of CRISPR has been widely demonstrated in animals, for example the creation of beagles with no Myostatin.[90] Muscular Dystrophy is an early target of CRISPR gene therapy, with success already reported in healing Muscular Dystrophy in mice.[91] Variants in the relevant gene, DMD, have been associated with athlete status.[92] The first clinical trial involving CRISPR started in China in October 2016, and the first trial in the US is due to start in the Spring of 2017.[93]

Genetic modification using CRISPR-Cas9 or a related technology would fall under the "gene doping" ban. How could it be detected? The IOC's medical and scientific director, Richard Budgett, announced that athlete samples collected during the 2016 Rio Olympics will be tested

[88] Its first reported use in human cells appears in Le Cong et al., *Multiplex Genome Engineering Using CRISPR/Cas Systems*, 339 SCIENCE 819 (2013), *available at* https://www.ncbi.nlm.nih.gov/pubmed/23287718.
[89] *See* Antonio Regalado, *Engineering the Perfect Baby*, 118 MIT TECH. REV., May-June 2015, at 26.
[90] Antonio Regalado, *First Gene-Edited Dogs Reported in China*, MIT TECH. REV. (Oct. 19, 2015), https://www.technologyreview.com/s/542616/first-gene-edited-dogs-reported-in-china/.
[91] Jocelyn Kaiser, *CRISPR helps heal mice with muscular dystrophy*, SCIENCE (Dec. 31, 2015, 2:00 PM), http://www.sciencemag.org/news/2015/12/crispr-helps-heal-mice-muscular-dystrophy.
[92] Ahmetov, *supra* note 78.
[93] David Cyranoski, *CRISPR gene-editing tested in a person for the first time*, NATURE (Nov. 15, 2016), http://www.nature.com/news/crispr-gene-editing-tested-in-a-person-for-the-first-time-1.20988; Sara Reardon, *First CRISPR clinical trial gets green light from US panel*, NATURE (June 22, 2016), http://www.nature.com/news/first-crispr-clinical-trial-gets-green-light-from-us-panel-1.20137.

for EPO gene doping subsequent to the games.[94] The test will look for minor differences between the structure of the introduced gene and the naturally occurring one; similar strategies have been proposed elsewhere.[95] It is unclear how reliable this testing will be, and whether it will require muscle biopsies. It should be noted that WADA have been under criticism for not allowing their tests to be statistically validated and on at least one occasion one of their tests was found invalid by the Court of Arbitration for Sports.[96] WADA funds research to develop gene doping detection.[97]

A review of approaches to gene doping detection is given in E. Brzeziańska et al.[98] Other strategies involve comparing the gene expression of an athlete to a control group of people.[99] This strategy suffers from the fact that there is a spread of naturally occurring levels of gene products. For example, testosterone abuse is typically assessed via the testosterone/epitestosterone (T/E) ratio, but the "natural" level for this ratio is known to be

[94] Sarah Everts, *Athletes at Rio Olympics face advanced antidoping technology*, CHEMICAL & ENGINEERING NEWS, Aug. 8, 2016, at 25, *available at* http://cen.acs.org/articles/94/i32/Athletes-Rio-Olympics-face-advanced.html.

[95] A. Baoutina et al., *"Implementation of method for erythropoietin gene doping detection in WADA accredited laboratories"*, WORLD ANTI-DOPING AGENCY, https://www.wada-ama.org/sites/default/files/resources/files/final_report_13c36ab_dr._baoutina.pdf (last visited Jan. 17, 2017); Liping Chung et al., *Novel Biomarkers of Human Growth Hormone Action from Serum Proteomic Profiling Using Protein Chip Mass Spectrometry*, 91 J. CLINICAL ENDOCRINOLOGY & METABOLISM 671 (2006), *available at* https://academic.oup.com/jcem/article-lookup/doi/10.1210/jc.2005-1137; Françoise Lasne et al., *"Genetic Doping" with erythropoietin cDNA in primate muscle is detectable*, 10 MOLECULAR THERAPY 409 (2004), *available at* https://www.ncbi.nlm.nih.gov/pubmed/15336641/.

[96] Veerpalu v. Int'l Ski Fed'n, CAS 2011/A/2566 (Ct. Arb. Sport 2013), *available at* http://www.tas-cas.org/fileadmin/user_upload/Bulletin_2013_2_complete.pdf.
See also Donald A. Berry, *The science of doping*, 454 NATURE 692 (2008), *available at* http://www.nature.com/nature/journal/v454/n7205/full/454692a.html ("The processes used to charge athletes with cheating are often based on flawed statistics and flawed logic."); Arne Ljungqvist et al., *Doping: world agency sets standards to promote fair play*, 455 NATURE 1176 (2008), *available at* http://www.nature.com/nature/journal/v455/n7217/full/4551176a.html (offering WADA's response); Editorial, *A level playing field?*, 454 NATURE 667 (2008), *available at* http://www.nature.com/nature/journal/v454/n7205/full/454667a.html ("Drug testing in sport aims to promote fair play, but the science behind the tests needs to be more open.").

[97] *USADA Funded Research*, U.S. ANTI-DOPING AGENCY, http://www.usada.org/science/research/usada-funded-research/ (last visited January 17, 2017).

[98] Brzeziańska, *supra* note 88.

[99] *See e.g.*, Evanthia Diamanti-Kandarakis et al., *Erythropoietin abuse and erythropoietin gene doping: detection strategies in the genomic era*, 35 SPORTS MED. 831 (2005), *available at* https://www.ncbi.nlm.nih.gov/pubmed/16180943/.

genetically determined. Specifically, a genetic variant that is found in 9% of Swedish males but 67% of Korean males is associated with considerably lower natural testosterone levels.[100] It is likely that the threshold value for testing positive for testosterone abuse will be based on genotype in the future.[101]

As our knowledge of how our genetics shapes our characteristics evolves, thanks to ever cheaper DNA sequencing approaches and the large studies this enables, we gain more insight into which genetic variation gives a performance edge. In tandem with this, our ability to modify an individual's genetics is being very actively pursued in the field of gene therapy for disease. The knowledge and technology for genetic modification for performance enhancement in sports is finally looking less like science fiction.

E. Overview of this Study

Recent technological advances make the prospect of genetic modification for performance enhancement in sports much more realistic (see Sections C and D). WADA has stated that such enhancement is contrary to the spirit of sport. In Section A we argued that the spirit of sport should reflect the public's views. There has been a surprising paucity of work that aims to assess public opinion on doping in general, and none that assesses what has become known as "gene doping" (Section B).

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[100] Jenny Jakobsson et al., *Large Differences in Testosterone Excretion in Korean and Swedish Men Are Strongly Associated with a UDP-Glucuronosyl Transferase 2B17 Polymorphism*, 91 J. CLINICAL ENDOCRINOLOGY & METABOLISM 687 (2006), *available at* https://academic.oup.com/jcem/article-lookup/doi/10.1210/jc.2005-1643; *Impact of UGT2B17 gene deletion on the steroid profile of an athlete*, 3 PHYSIOLOGICAL REP. 1 (2015), *available at* https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4760435/.

[101] For suggestions on how to make testing thresholds dependent on genetics, see Larry D. Bowers, *Testosterone Doping: Dealing with Genetic Differences in Metabolism and Excretion*, 93 J. CLINICAL ENDOCRINOLOGY & METABOLISM 2469 (2008), *available at* https://academic.oup.com/jcem/article-lookup/doi/10.1210/jc.2008-0977, and Jenny Jakobsson Schulze et al., *Substantial advantage of a combined Bayesian and genotyping approach in testosterone doping tests*, 74 STEROIDS 365 (2009), *available at* https://www.ncbi.nlm.nih.gov/pubmed/19056415.

We set out to investigate the following areas, which we cover in our Results and Discussion. Does it matter how you came by a genetic advantage, by birth or via a procedure? (Section A) Should those who have elected for genetic modification be able to race against those who have not? Should there be separate categories? (Section B). The role of language in explaining the level of support for genetic modification (Section E). Concerns about equity of access to the technology (Section F). Comparison of genetic modifications that affect cognitive, as opposed to physical, attributes (Section G). Support for the genetic modification of minors (Section H). How attitudes vary across demographics (Section I). Sections B, C and K contain more general discussion.

II. METHODOLOGY

We ran ten scenarios. Our base case scenario was answered by 400 US based individuals, with representation across age (18-55), gender, and education level. We performed strata based sampling using ten strata. The size of each stratum was determined based on US 2010 Census data. We used the following strata, separately for men and women: 18-23 year olds, 24-34 year olds with college level education, 24-34 year olds without college level education, 35-55 year olds with college level education, 35-55 year olds without college level education.

The study was run on the Prolific survey platform.[102] Use of this platform gave us access to several dozen demographic data points on each participant, including age, gender, educational level and political affiliation. Participants were financially rewarded for their time through this platform at a rate of $0.50.

[102] Prolific is an Oxford University Innovation company. PROLIFIC, https://www.prolific.ac (last visited Jan. 22, 2017). Participants are prescreened according to researcher specified criteria.

Our remaining nine scenarios were presented across three groups of three scenarios to each of 200 people (n = 600 in total). The quota was the same as for the base case, except the older age bracket extended to age 40 instead of 55.[103] Participants were financially rewarded for their time at a rate of $0.80.

The Base Case scenario was the following:

> Scientists have discovered Gene Z relates to success in long distance competitive running. Gene Z enables more oxygen to be carried in the blood. Gene Z is not enough on its own; hard work, training, and diet are important contributing factors to winning.
>
> It is well known that scientists can now give Gene Z to people who are not born with it, at low cost. Some people will experience side effects, including higher likelihood of injury.
>
> Many race winners in the past 50 years have had Gene Z. A person without Gene Z would be less likely to win, even with hard work, training, and the right diet.

In choosing our base case example of a genetic variant affecting blood oxygen, we aimed to disentangle the question of attitudes to genetic modification for performance enhancement from attitudes towards genetic changes that alter appearance.

[103] When we compared our base case scenario to the other scenarios we subsampled the base case respondents to match the same age range.

In the other scenarios, each participant responded to two variants of the base case scenario, as well as one scenario involving minors. The six variants of the base case were:

a) Naturally Gifted: in this scenario, no mention was made of the possibility of changing whether or not someone had Gene Z.
b) Biomolecule, natural differences: instead of Gene Z, the scenario referred to *Biomolecule V*, and mentions that *Different individuals' bodies naturally produce differing amounts of biomolecule V*.[104]
c) Biomolecule, no mention of natural differences: as for Scenario (b), but no mention of naturally occurring differences
d) Drug: as for Scenario (c), but referring to *Drug V* rather than *Biomolecule V*
e) Cost: identical to the base case, except the scenario read *at a cost of $100,000* rather than *at low cost*
f) Mental: identical to the base case, except instead of *Gene Z enables more oxygen to be carried in the blood*, the scenario read *Gene Z helps athletes feel a sense of reward after training and therefore helps them stick to a more intense training regime.*

The main scenario involving minors read:

> Jamie is 11 years old and wants to be a long-distance runner. Jamie was not born with Gene Z. Those who have Gene Z before they go through puberty will develop more efficient muscles and go on to have an advantage in long distance running over those who did not have Gene Z during puberty. (If

[104] A biomolecule is a molecule that is present in living organisms.

Gene Z is introduced after puberty it gives no advantage). Both Jamie and Jamie's parents would like for Jamie to be given Gene Z before puberty.

It is well known that scientists can now give Gene Z to people who are not born with it (including minors), at low cost. Some people will experience side effects, including higher likelihood of injury.

The three versions were

i) Development window: as above

ii) No development window: as above, but without any mention that the change needs to happen before puberty

iii) Scholarship: as (ii), but with the following addition, *Many students who have won athletic scholarships to college in the past 50 years have had Gene K. A student long distance runner without Gene K would be less likely to win an athletic scholarship to college, even with hard work, training, and the right diet.*

Our surveys asked participants to react to statements concerning the scenarios on a 7 point Likert scale (Strongly Disagree, Disagree, Somewhat Disagree, Neither Agree nor Disagree, Somewhat Agree, Agree, Strongly Agree).

In addition to reactions to scenarios, in our base case we also asked a randomly chosen half of the participants for their reaction to the statement *Athletes should be allowed to dope* and the other half for their reaction to *Athletes should be allowed to take performance enhancing drugs*. We also asked whether our participants watched more than one hour of sports per week, and whether they considered themselves religious.

To estimate the precision of our estimates from this survey we used the bootstrap procedure, which is a resampling approach.[105] This is as recommended by the American Association of Public Opinion Research.[106] Hypothesis testing was also performed using bootstrapping.[107]

Our data is publicly available.[108]

III. RESULTS AND DISCUSSION

A. Does it Matter How You Came by a Genetic Advantage?

We asked for reaction to the following statement concerning our base case scenario (see Methodology for scenario):

> *Statement 1: People who have chosen to acquire Gene Z should be permitted to race with people who were born with Gene Z.*

[105] James G. MacKinnon, *Bootstrap Hypothesis Testing*, in HANDBOOK OF COMPUTATIONAL ECONOMETRICS 183-213 (David A. Belsley & Erricos John Kontoghiorghes eds., 2009). We generated 100,000 independent "resamples" by randomly selecting 400 respondents with replacement from the original survey data set. Resamples were formed using the same 10 strata as our survey, such that we matched the same number of respondents from each stratum in each subsample. For our 100,000 resamples, we computed the statistic of interest (in this case the proportion of respondents who agreed or were indifferent to the question), and used the variability in these estimates as the basis of the confidence intervals reported. The confidence interval assumes that our estimates are approximately unbiased.

[106] *AAPOR Guidance on Reporting Precision for Nonprobability Samples*, AM. ASS'N PUB. OPINION RES. (Apr. 22, 2016), http://www.aapor.org/getattachment/Education-Resources/For-Researchers/AAPOR_Guidance_Nonprob_Precision_042216.pdf.

[107] For two cases we wished to compare (e.g. women's responses versus men's, or answers to one question versus answers to a variant question), the null hypothesis is that the responses come from the same distribution. Let the size of the first sample be N and the second M. We created 100,000 samples of the combination of the two cases, and calculated the difference between the proportion of agreed and indifferent of the first N of each subsample and the proportion of agreed and indifferent in the final M of each subsample. We then compared the observed difference in proportion of agreed and indifferent to the list of 100,000 bootstrapped differences, and report as the p-value the fraction of times the bootstrapped difference had a greater magnitude than the observed difference.

[108] The data is available at https://github.com/sarahpolcz/Welcoming_Prometheus.

This statement was designed to probe whether people were concerned with how someone came to have a *particular* genetic advantage -- via the natural lottery of birth, or via a procedure. Our hypothesis was that because this scenario makes salient the unlevel playing field in terms of "natural" talent, respondents might not object to this type of procedure. In other words, the setup was never fair to begin with: some people through no merits of their own are dealt a more favorable hand and this procedure enables fairness to be achieved. We found that 79% of people (N=400) agree or are indifferent to Statement 1, upholding our hypothesis, and suggesting that how someone came to have a genetic advantage (through birth or by acquiring it later than life) does not matter to the majority of the public.

Depending on their response to Statement 1, participants were asked to state why they answered the way they did via stating their support for a series of propositions (a different series for those in agreement and those in disagreement). Of those who disagreed, 54% (9% overall) are opposed to genetic modification of any type. This leaves just 12% of people who would accept with genetic modification under some circumstances, but just not in this sports example. See Figure 1.

Of those who agreed, the statement with most support was *You either have a gene or you don't, doesn't matter how you got it* (79%). There was also broad support for the two other statements presented, *Sports would be a fairer test if the biological playing field were more level* (67%), and *It would be hard to test whether someone was born with a gene or had it added later, so it would be pointless to try and prevent this happening* (68%).

In comparison to the only other public opinion surveys of genetic modification for performance enhancement that we are aware of, those conducted in Japan between 1991 and 2000, our

results show a much higher level of acceptance.[109] One difference is that those surveys asked for reaction to very general statements, in contrast to our specific scenarios.[110] Another is that they were conducted over 15 years ago, and in a different country.

We should stress with reference to our scenario that the genetics underlying sports performance are complicated.[111] Although the genetic example is modelled on a real case, the picture is rarely so clear cut. And, as stressed in our scenario, no genetic advantage would ever be sufficient for a winning edge, with hard work and training still being necessary.

B. Should Genetic Modification for Gaining a Performance Edge be Banned?

Our second statement was designed to directly test public reaction to what WADA terms "gene doping", i.e. if this were available as a performance-enhancing option, with some not choosing the advantage.

> *Statement 2: People who have chosen to acquire Gene Z should be permitted to race with people who have chosen not to acquire Gene Z*

Given the lack of any prior research on public opinion of genetic modification for performance enhancement in sports, rather than have a Hypothesis, we were interested to see what people's reactions were. 54% of people (N=400) agreed with or were indifferent to Statement 2. Those

[109] In response to the question "How do you feel about scientists changing the genetic makeup of human cells to: Improve the physical characteristics that children would inherit," 28% agreed in 1993; to "[i]mprove the intelligence level that children would inherit" 26% agreed; and to "[m]ake people more ethical" 24% agreed. Macer, *supra* note 63. In 2000, the figures were 29%, 27% and 24% respectively. Chen Ng, *supra* note 63.
[110] Reactions to more concrete scenarios tend to be more predictive of actual opinions. *See* Andy Peytchev, *Global versus Specific Questions for the Consumer Expenditure Survey*, BUREAU LAB. STAT., https://www.bls.gov/cex/methwrkshp_pap_peytchev.pdf (last visited Jan. 18, 2017).
[111] Guilherme, *supra* note 79.

who disagreed were asked why, via their reaction to the statements *People who have acquired Gene Z should not be permitted to race at all* and *There should be a separate category for those who do not have Gene Z*. Of the 46% of respondents who disagreed with Statement 2, 39% agreed that they should not be permitted to race at all and 74% thought there should be a separate category. In Figure 2, we include those who agreed to both statements in support for a separate category. 12% of people thought they should not be allowed to race at all. Compare this to the 9% of people who were opposed to genetic modification of any type - the difference because of cheating is very slight. The primary judgment is against genetic modification, not against cheating.

Statements 1 and 2 draw attention to different aspects of gene doping. Statement 1 draws attention to the unlevel biological playing field, whereas Statement 2 gives the exact analogy to doping. Those who disagreed with Statement 2 but not Statement 1 appear inconsistent, but the high level of support for separate categories helps explain what is going on: both seek to group genetically similar individuals together, whatever the source of their genetic profile.

The high degree of support for a separate competition category for those without the particular genetic advantage lead us to design a Scenario, (a), which was identical to the base case except lacking mention of the possibility of a procedure to gain the genetic advantage.

In reaction to the slightly modified Statement 2 (*People who were born with Gene Z should be permitted to race with people who were not born with Gene Z*), 14% of our respondents disagreed, thus suggesting that a minority of people are opposed to the status quo. 43% of people agreed or were indifferent to *People who were born without Gene Z should have a race category that people who were born with Gene Z cannot compete in* (See Figure 3).

C. Discussion on Access to Genetic Advantage

Our results in Sections A and B bring to light different perspectives on the theme of access to genetic advantage. We discuss three of these perspectives below.

(1) Promoting natural talent is not necessarily fair

As discussed in Section A of the Introduction, WADA's judgments of what counts as cheating rely on moral intuitions of fairness, and on the idea of promoting natural talent. Our results demonstrate that these two constructs are dissociable. Insofar as our respondents equate promoting natural talents with what is fair, they are conceiving natural talents as character-based traits or intangibles. It does not seem that natural physical endowments are associated with the spirit of sport, which would have predicted a different response pattern, namely that genetic endowments would be viewed as natural gifts worthy of competitive protection.

One way to conceive of fairness is equality of opportunity. Our scenario presents one way in which equality of opportunity can actually be enhanced - by mitigating the consequences of a chance of birth.

(2) The Incentive for Genetic Modification

As the pool of potential Olympians grows, the winners are increasingly genetic outliers. Stephen Hsu argues that the "whole enterprise of competitive athletics has been, in effect, a search algorithm for genetic outliers," and that moreover, we are finding that genetics has more

of an impact than performance enhancing drugs: Usain Bolt easily beat the records of previous champions, including those elite athletes who had also been taking anabolic steroids.[112]

WADA aims to protect an athlete's ability to compete in doping-free sports. If anyone were permitted to dope, then others would be forced to also do so in order to stay competitive. With other techniques, it is the taking of substances by others that provides incentive to dope. When we consider genetic outliers, incentives to dope arise from their mere presence. If the aim is to protect athletes' rights to a doping free sport, then in a world of low barriers to genetic modification, it could be consistent for WADA to ban genetic outliers because they create an environment in which "clean" athletes will be pressured to resort to gene doping to remain competitive.

(3) Consistency with an Alternative Vision of the Spirit of Sport

WADA's concept of the spirit of sport represents what some have termed an essentialist view of natural talent. In this view, natural talent equates to biological potential.[113] Our evolving understanding that luck in the genetic natural lottery shapes our abilities challenges this view. So does the prospect of our genetics being mutable through genetic modification. These developments may sever the alignment between the spirit of sport and natural talent, in favor of rewarding excellence produced through judgment and choice.[114] Our results are consistent

[112] Stephen Hsu, *We Are Nowhere Close to the Limits of Athletic Performance*, NAUTILUS (Aug. 11, 2016), http://nautil.us/issue/39/sport/we-are-nowhere-close-to-the-limits-of-athletic-performance ("Bolt's times weren't just faster than anyone else in the world. They were considerably faster even than those of a world-class runner from the previous generation that was using performance-enhancing drugs.").

[113] For an argument that current anti-doping policy rests on dubious claims as to what is natural or normal, see Bengt Kayser et al., *Current anti-doping policy: a critical appraisal*, 8 BMC MED. ETHICS 2 (2007). *See also* Savulescu et al., *Why we should allow performance enhancing drugs in sport*, 38 BRIT. J. SPORTS MED. 666 (2004) (arguing that this view of sports as finding the person with the most biological potential was "the old naturalistic Athenian vision of sport: find the strongest, fastest, or most skilled man.").

[114] Savulescu, *supra* note 116, at 666 ("Humans are not horses or dogs. We make choices and exercise our own judgment. We choose what kind of training to use and how to run our race. We can display courage, determination, and wisdom. We are not flogged by a jockey on our back but drive ourselves. It is this judgment that competitors exercise when they choose diet, training, and whether to take drugs. We can choose what kind

with this approach: genetic modification would be part of exercising choice. In this view, the role of non-choice factors, such as possessing unearned genetic variants advantageous for performance, should be minimized.

D. Discussion on the Support for Separate Categories

There are separate categories in several sports, even at the Olympic level, where one is aiming to locate the absolute best of the best. Most notably there are separate categories for men and women, some with different sub-events and rules.[115] Other categories include weight, for martial arts and for rowing.

The case of female hyperandrogenism is an example of the IOC's willingness to use underlying biology to define categories. Before the London 2012 Olympics the IOC declared that it would be testing testosterone levels to determine who was permitted to compete in the female category.[116] This approach was abandoned for the Rio Olympics in 2016 following a 2014 ruling by the Court of Arbitration for Sport, partly because of the underlying biological

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of competitor to be, not just through training, but through biological manipulation. Human sport is different from animal sport because it is creative.").

[115] For example, the events that female and male gymnasts compete in are different. *Gymnastics Artistic*, INT'L OLYMPIC COMM., https://www.olympic.org/gymnastics-artistic (last visited Jan. 22, 2017). There are also differences in required elements for figure skating. *Judging System: Technical Panel Handbook: Single Skating*, INT'L SKATING UNION (July 24, 2016), *available at* http://www.usfigureskating.org/content/2016-17%20TPHB%20Singles.pdf.

[116] *IOC Regulations on Female Hyperandrogenism*, INT'L PARALYMPIC COMM. (June 22, 2012), https://stillmed.olympic.org/Documents/Commissions_PDFfiles/Medical_commission/2012-06-22-IOC-Regulations-on-Female-Hyperandrogenism-eng.pdf.

complexity.[117] The International Association of Athletics Federations has indicated it will challenge this ruling.[118]

The 14% who disagree that those with the genetic advantage should race in the same category (Results Section B) are not unlike those who oppose women with female hyperandrogenism competing alongside other women. Caster Semenya has dominated the women's sprinting scene on the occasions that she has been allowed to compete without taking hormone suppressants. A female sprinter who has raced alongside Caster, Paula Wright, has said: "I don't like the idea of anyone being excluded… but we have to keep our sport fair, which means deciding where the genetic and performance advantage is too much."[119] Lynsey Sharp, who came 6th to Caster's 1st in the Rio 800m said "Everyone can see it's two separate races" while Polish Joanna Jozwik, who finished 5th, said "I'm glad I'm the first European, the second white".[120]

With some degree of success, biological categories are created to reflect the diversity and spectrum of athletes' physical endowments for the Paralympics. Akin to the genetic case, no

[117] Talha Khan Burki, *Hyperandrogenism rule no longer in play at Rio Olympics*, 4 LANCET DIABETES ENDOCRINOL. 820 (2016). Part of the overturn rested on the overlap between the distributions of testosterone levels in men and women. The case involved additional biological complexity, as high levels of testosterone were acknowledged to only confer an advantage in the presence of working androgen receptors, which many of the athletes in question did not have. Chand v. Athletics Fed. of India, CAS 2014/A/3759 p547 (Ct. Arb. Sport 2015), http://www.tas-cas.org/fileadmin/user_upload/AWARD_3759__FINAL___REDACTED_FOR_PUBLICATION_.pdf.

[118] *Sebastian Coe indicates IAAF will challenge female testosterone ruling*, GUARDIAN (Aug. 11, 2016, 8:30 AM), https://www.theguardian.com/sport/2016/aug/11/caster-semenya-sebastian-coe-iaaf-cas-testosterone-olympics.

[119] Tim Layden, *Is it fair for Caster Semenya to compete against women at the Rio Olympics?*, SPORTS ILLUSTRATED (Aug. 11, 2016), http://www.si.com/olympics/2016/08/11/caster-semenya-2016-rio-olympics-track-and-field.

[120] Tom Morgan, *Caster Semenya wins 800m: beaten GB finalist Lynsey Sharp criticises rule changes over 'obvious' hyperandrogenous women*, THE TELEGRAPH (Aug. 21, 2016, 3:14 PM), http://www.telegraph.co.uk/news/2016/08/21/lynsey-sharp-criticises-obvious-hypoadrogenous-women-having-bein/; Mark Critchley, *Rio 2016: Fifth-placed Joanna Jozwik 'feels like silver medallist' after 800m defeat to Caster Semenya*, INDEPENDENT (Aug. 22, 2016), http://www.independent.co.uk/sport/olympics/rio-2016-joanna-jozwik-caster-semenya-800m-hyperandrogenism-a7203731.html.

crisp categorical distinctions exist, nevertheless, meaningful distinctions are possible which are generally supported by athletes and fans. Factors such as muscle tone, short stature, balance, limb length are all used.[121]

Given the complexities of genetic contributions to performance, defining separate categories seems impractical. However, this may change in the future.

E. Why the High Level of Support for Performance Enhancement via Genetic Modification?

In reaction to the statement *Athletes should be allowed to dope*, 17% of our participants agreed or were indifferent.

Why might one think that genetic modification as a form of performance enhancement would be more acceptable than doping? We set out to test two different hypotheses. First, that the genetic modification scenario would be more supported because it makes salient the fact that there is no level playing field to begin with. And second, that branding something as "doping" or even as a "drug" would prime people with negative associations.

To test the first hypothesis, we designed Scenarios (b) and (c) (see Methods), and asked for reactions to Statement 2. Both scenarios refer to "Biomolecule V" instead of "Gene Z", and Scenario (b) differs from (c) only by the inclusion of one sentence: *Different individuals' bodies*

[121] *Layman's Guide to Paralympic Classification*, INT'L PARALYMPIC COMM., https://www.paralympic.org/sites/default/files/document/120716152047682_ClassificationGuide_2.pdf (last visited Jan. 18, 2017); *Raza Point score table for IPC Athletics*, INT'L PARALYMPIC COMM. (Jan. 20, 2011), https://www.paralympic.org/sites/default/files/document/120719101234998_2011_01_20_Raza_Point_score_table_for_IPC_Athletics_2011_-_Explanation.pdf.

naturally produce differing amounts of biomolecule V. We found less support for Scenario (c) ($p = 0.05$, Figure 4), thus supporting our hypothesis that making salient the natural lottery may play a role in support of performance enhancement via genetic modification.

To test the second hypothesis, we designed Scenario (d), which differs from (c) only in referring to *Drug V* rather than *Biomolecule V*. We found much less support for *Drug V* than *Biomolecule V* ($p < 10^{-5}$) for Statement 2. There was however significantly more support for *Drug V* than for the statement *Athletes should be allowed to dope* ($p < 10^{-5}$), again highlighting the importance of framing language. See Figure 4.

As discussed, there are no moral lines when it comes to performance enhancement. Instead, rules are defined, and those that make the rules make the case that the rules are good ones, usually by claiming to capture what is fair and within the spirit of sport. Those that make the rules thus have a lot of power, as what they ban is associated with the unethical. Our data strongly supports the importance of language, and highlights the significance of WADA's pre-emptive move to ban any form of genetic engineering. WADA's actions determine the language that is used, i.e. "gene doping". If the public are not primed to think of genetic modification as doping, our data shows support for its use.

F. How Much of a Concern is Equity of Access?

Equity of access is often given as a reason to oppose performance enhancement in sports. We were thus interested in how changing the cost described in our scenario would affect public opinion. Our base case mentions that the procedure can be performed at low cost. We designed Scenario (e) to be identical to our base case with the exception that the procedure was available

at a cost of $100,000. We found no statistically significant difference in the level of support for this scenario compared to our base scenario on either Statement 1 or Statement 2.

This result seems surprising. There are at least three different factors that we think may contribute. The first is that equity of access to sporting success is a complete mirage anyway: success is bought by the quality of the coaching, the precision of the diet, the quality of facilities, the access to a broader team of support staff, all of which cost money. Second, that this form of equity of access competes with the unequal opportunity with regard to the genetics you are born with. And third that Americans are used to living in a society where people can spend their money as they choose; for example, in a pay-to-access healthcare system for both necessary and elective procedures high cost is normalized. Americans in general do not have a problem with people paying to improve themselves and their opportunities.

G. How Does Support Differ for a Cognitive as Supposed to a Physical Modification?

Our base case scenario states that *Gene Z enables more oxygen to be carried in the blood.* We were interested in how the level of support would differ for a different genetic advantage, this one affecting cognitive properties: *Gene Z helps athletes feel a sense of reward after training and therefore helps them stick to a more intense training regime* (Scenario (f)). Our intuitions were conflicting on this comparison. On the one hand, the cognitive change is less directly related to what the competition (long distance running) is testing, and might thus have more support. On the other hand, the cognitive modification might have less support because people thought it would be directly altering something more essential to the true self of the person.

We found more support for the cognitive modification for both Statement 1 ($p = 0.04$) and Statement 2 ($p = 0.01$), thus highlighting that which genetic modification is at stake can affect public opinion.

The public will likely have different attitudes towards different genetic modifications because the social consequences and meanings of different traits are varied. We think the differences in attitudes to different types of genetic modification represents a rich vein of possible future research.

H. How Much Support for the Genetic Modification of Minors for Sporting Performance?

Some genetic modifications could only have an impact if made before or during a developmental window. For example, genetic variation linked to being taller would not produce extra height if introduced after someone had finished growing. Because of the possibility of desirable genetic modification that would need to be performed on minors, we wanted to test public opinion of genetic modification for sports performance on minors. See Methods for the scenario, which states that both 11-year-old Jamie and their parents are keen on the modification, and that the modification must be made *before they go through puberty*. We asked for the degree of support for the following statement: *Jamie should be permitted to acquire Gene Z.*

We found that 75% of our respondents agreed or were indifferent to this statement. 53% of those who disagreed (13% overall) see issues with genetic modification of minors, see Figure 6.

We also ran a version of the scenario (Scenario (ii)) making no mention of the development window, and found no statistically significant difference in level of support.

Finally, we ran a version of the scenario which, like Scenario (ii), made no mention of the developmental window, but with the following additional information:

> Many students who have won athletic scholarships to college in the past 50 years have had Gene K. A student long distance runner without Gene K would be less likely to win an athletic scholarship to college, even with hard work, training, and the right diet.

Again, we found no statistically significant difference in level of support for this scenario.

Previous work has highlighted that many of the early applications of genetic modification may be for minors, because of the existence of a developmental window for modifications to take effect.[122] Attitudes toward modification of minors are also of interest because the pipeline for competitive athletics in modern US society often begins during childhood, thus potentially incentivizing modification at this advantageous time.

One might have anticipated low support for the genetic modification for minors, owing to issues of informed consent, but this is not what we observe.

[122] Sarah Polcz & Anna Lewis, *CRISPR-Cas9 and the non-germline non-controversy*, 3 J. LAW BIOSCI. 413 (2016).

I. Differences Between our Different Demographic Strata

We find no difference in our sample size of 400 in the opinions between men and women for our base case scenario to either Statement 1 or 2. Those without college level education tend to be more supportive, though this effect was only statistically significant at the 0.05 level for Statement 1. Those who are younger were more supportive for both Statement 1 and Statement 2. We found no statistically significant difference between Republicans and Democrats, or between those who self-reported as religious and those who did not. We did find that those who reported watching an hour or more sports per week were less supportive than those who did not for Statement 1 (74% compared to 84%, p=0.006), though not for Statement 2.

In general, younger people and men tend to view biotechnology more favorably.[123] That younger people are more supportive of genetic modification for performance enhancement in sports is thus not surprising. That we find no difference in the attitudes of men and women is more surprising. There is some evidence that mothers are keener to have their children genetically tested for common diseases than fathers, so it is possible that there is something about genetics that is causing women to be more supportive in this instance.[124] That those who watch more sports were less supportive of Statement 1 adds a data point to the conflicting evidence for whether sports fans care more or less about doping than the general public (see Introduction). We have no hypothesis to extend as to why those with less education tended to

[123] George Gaskell et al., *Europeans and Biotechnology in 2002*, EUR. COMMISSION (Mar. 21, 2003), *available at* http://ec.europa.eu/public_opinion/archives/ebs/ebs_177_en.pdf.

[124] There have been a series of Eurobarometer surveys on biotechnology and the life sciences, consistently finding more support by younger people across a broad range of biotechnologies. Kenneth P. Tercyak et al., *Parents' Attitudes Toward Pediatric Genetic Testing for Common Disease Risk*, 127 PEDIATRICS e1288 (2011), *available at* https://www.researchgate.net/publication/51059997_Parents'_Attitudes_Toward_Pediatric_Genetic_Testing_for_Common_Disease_Risk.

be more supportive, but we do think this highlights the importance of moving beyond expert opinion in setting policy in this domain.

J. Relation to Other Genetic Technological Developments

We propose that our surprising-to-some results of general support for permitting gene modified athletes to compete may be understood in the context of related genetic technological developments that are gaining social acceptance. Awareness of, and comfort with, these developments is percolating into popular consciousness. In this section, we discuss some recent technological developments that we contend raise immediate difficulties for the ban.

Genetic modification is presumably banned because it interferes with the natural lottery of birth that sets your genetics. But since 2003 there have been several advances aside from the possibility of genetic modification of adults that impact the natural lottery.

First, parents using donated sperm or eggs are now able to genetically screen the donor, improving the probability that resulting children will be selected for traits such as athleticism.[125]

Second, it is now a routine part of an IVF cycle to genetically screen embryos pre-implantation.[126] While this is currently only standardly performed for trisomies such as Down

[125] For example, the Seattle Sperm Bank allows customers to select donors based on athleticism and lists evidence of athletic achievement such as "Division I" athlete and "professional soccer player." *Top Athletes*, SEATTLE SPERM BANK, https://www.seattlespermbank.com/athletes/ (last visited Jan. 18, 2017). GenePeeks allows for predicting "Virtual Progeny," with those selecting a sperm or egg donor a target market. GENEPEEKS, https://www.genepeeks.com (last visited Jan. 22, 2017).

[126] Robert Klitzman et al., *Preimplantation Genetic Diagnosis (PGD) on In-Vitro Fertilization (IVF) Websites: Presentations of Risks, Benefits and Other Information*, 92 FERTILITY & STERILITY 1276 (2009), *available at* https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2950118/ (revealing that by 2008 70% of IVF clinics were advertising Preimplantation Genetic Diagnosis).

Syndrome, the technology is already mature enough to screen for any genetic variant known to be associated with a particular trait.[127] In *The End of Sex*, Hank Greely argues that in 20 years, people in developed countries will regularly use genetic testing in combination with embryo selection in order to maximize the chances their child will have the traits they desire.[128] As the process of egg freezing continues to drop in price and grow in popularity, women will typically be able to provide enough eggs for the creation of dozens of embryos from which to make a trait-informed selection.[129]

Third, embryos may be edited for desired traits. Embryo modification is an example of a *germline* application. In contrast to the modification of adults, the subject of this article, germline modification involves introducing changes that could be inherited by future generations. In 2015 the first successful editing of a human embryo was announced by a team of Chinese researchers.[130] Although germline editing is at the center of an ongoing ethical controversy, it seems inevitable that the risk of germline editing protocols will be lowered and this practice will make its way into first therapeutic, and then enhancement clinical applications in human reproduction.[131] When this occurs, IVF labs will be able to leverage contemporary genetic knowledge to make edits in fertilized embryos that are optimized for performance.

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[127] Brock A. Peters et al., *Detection and phasing of single base de novo mutations in biopsies from human in vitro fertilized embryos by advanced whole-genome sequencing*, 25 GENOME RES. 426 (2015), *available at* http://genome.cshlp.org/content/25/3/426.full?sid=d792542d-2090-4f59-a75a-ffedfb6cae7a.

[128] HENRY T. GREELEY, THE END OF SEX AND THE FUTURE OF HUMAN REPRODUCTION (2016).

[129] A summary of some recent experimental advances is given in J. Bénard et al., *[Fertility preservation in women of the childbearing age: Indications and strategies]*., 45 J. GYNECOL. OBSTET. BIOL. REPROD. (PARIS) 424 (2016). *See also* Robert W. Rebar, *Advances in Infertility Treatment: Oocyte Cryopreservation and Comprehensive Chromosome Screening*, NEJM JOURNAL WATCH (Apr. 4, 2016), http://www.jwatch.org/na40320/2016/04/04/advances-infertility-treatment-oocyte-cryopreservation-and.

[130] Puping Liang et al., *CRISPR/Cas9-mediated gene editing in human tripronuclear zygotes*, 6 PROTEIN & CELL 363 (2015). In 2016, Chinese researchers announced editing the genome of a human embryo for a second time, to make it resistant to HIV infection. Xiangjin Kang et al., *Introducing precise genetic modifications into human 3PN embryos by CRISPR/Cas-mediated genome editing*, 33 J. ASSIST. REPROD. GENET. 581 (2016).

[131] *See e.g.*, George Church, *Perspective: Encourage the innovators*, 528 NATURE S7 (2015); Edward Lanphier et al., *Don't edit the human germ line*, 519 NATURE 410 (2015).

The current Code would not apply to a person produced through donor selection or embryo selection for traits giving a performance edge in sports. And yet they are the result of a process of intentional, unnatural, genetic selection, and the outcome is similar to genetic enhancement as an adult. It seems probable that at least some countries will incentivize their citizens to use genetic screening of embryos and donor selection with a view to producing future Olympians.[132] Would an athlete who was edited as an embryo be subject to the Code? This would require drawing a line of continuous legal identity from the grown athlete to an ex utero embryo, which is a stage at which personhood is not legally recognized.[133] What if a future athlete were genetically modified as an infant? Notwithstanding updates to the Code, such a person would be excluded from competing for life. To date, life bans have only been handed down to athletes who knowingly and repeatedly competed using prohibited enhancing substances.[134]

These technological developments will change the genetic makeup of athletes on the Olympic field, maybe as early as four Olympics from now for embryo screening.[135] But which of these technologies should be considered to leave natural talents intact? Our results suggest the public think WADA's placement of the natural/unnatural line is not fair. As these related technologies develop, this natural/unnatural distinction will be further challenged, and it will be even harder to justify a ban on somatic genetic modification.

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[132] For an argument on the importance of Chinese eugenic ambitions, see Geoffrey Miller, *2013: What *Should* We Be Worried About?*, EDGE, https://www.edge.org/response-detail/23838 (last visited Jan. 18, 2017).
[133] Louisiana has granted juridical personhood to ex utero embryos. La. R.S. 9:123-124 (2012). Nevertheless, the constitutionality of this provision is open to debate. *See* Diane K. Yang, Note, *What's Mine is Mine, But What's Yours Should Also Be Mine: An Analysis of State Statutes that Mandate the Implantation of Frozen Preembryos*, 10 J. L. & POL'Y 587, 595-596 (2001).
[134] Hasani Gittens, *Banned for Life!: 12 Others Who Have Been Ousted from Their Sport*, NBC NEWS (Apr. 30, 2014, 5:33 AM), http://www.nbcnews.com/storyline/nba-race-furor/banned-life-12-others-who-have-been-ousted-their-sport-n93111.
[135] If these procedures begin to meaningfully select for athletic performance within the next four years, then children born via these technologies will be old enough to compete in the games by 2032.

IV. CONCLUSION

Despite the professed aim of reflecting global ethical norms, WADA banned gene doping on the basis of moral intuition, with no regard for the public's view. Indeed, there has been no prior examination of public opinions on gene doping. The time is ripe to remedy this given (that) recent technological developments (that) have changed the landscape. CRISPR-Cas9 has removed genetic modification from the realm of science fiction. This and related advances, such as our ability to select which embryos to implant based on genetics, have blurred the line as to the meaning of natural talent.

We designed a series of experiments to probe public attitudes and were careful to isolate the impact of several variables: whether the genetic advantage was acquired (via modification) or inherited; equity of access; terminology; type of effect (physical versus mental); whether the modification happened to a minor. We carried out these experiments via recruiting 1000 US based individuals, with representation across age (18-55), gender, and education level.

We found that the majority of people (79% agreed or indifferent) thought that those who acquired a genetic advantage via a procedure should be able to compete with those who were born with the same genetic advantage. We found that 54% of people agreed or were indifferent to allowing those who had chosen to acquire a genetic advantage to compete. The majority of those who disagreed were supportive of separate categories for competition based on underlying genetics. There are several other directions that empirical work could take in this area. For example, our study only considered genetic variation that is naturally occurring within human populations. How would attitudes change if the genetic variation instead came, for example, from animals?

We also found strong evidence that the language used to describe performance enhancement affects public opinion. WADA's ban of 2003, which should have been shaped by the public, may instead have influenced public opinion through the stigmatization associated with the "gene doping" label.

We have argued that the public's opinion matters. Our results suggest that at least in the United States, their opinion does not align with WADA's on the boundaries of the spirit of sport. We thus think it vital to have public consultation. Public engagement is particularly important given that opinion can be expected to evolve in reaction to recent technological developments. As sports is a global enterprise, public opinion beyond the US should also be ascertained, and may well prove different.[136]

The case of genetic modification presents an opportunity for WADA to clarify aspects of their decision-making process more generally. Perhaps genetic modification warrants the establishment of its own category alongside Substances or Methods, given that as a technology it may change our shared understanding of natural talent. At the moment, it is no more than a somewhat awkward line item in a laundry list of prohibitions. Moreover, whereas all other items on the prohibited list have temporary effects, resulting in temporary bans, genetic modification can be permanent.

Finally, genetic modification has the potential to significantly impact various domains: the job market, the marriage market, combat, disability and criminal justice, among others. Thinking

[136] A study found that 40% of Russians and 7% of Britons approve of genetic modification ("changing genes") to enhance "special skills." Lev Gudkov et al., *Human Genetic Improvement: a comparison of Russian and British public perceptions.*, 134 BULL. MED. ETHICS 20 (1998). By way of comparison, 55% of Russians and 29% of Britons approve of vitamin supplements for the same purpose. *Id.* For reasons to believe the Chinese may think very differently to Americans, see Miller, *supra* note 135.

about ramifications for sports is important for two reasons. First, it is an accessible way to create a framework both for assessing impact and for rolling out policy in the aforementioned areas. Athletic competitions are closed system with defined rules, clear outcomes, and artificial scarcity. The sporting environment has the benefit of being controlled enough to probe variables of interest, without being contrived. And second, sports will be an arena where we see early adoption of genetic modification for performance enhancement. WADA's negative attitude may have a chilling and disproportionate effect on more general attitudes and could inhibit adoption in other contexts where clearer benefits exist. We are faced with decisions on how to balance the potential gains of this new technology against threats (perceived or otherwise) of such an unprecedented advance. Experimental assessment of public attitudes to genetic modification in sports represents a unique opportunity to gather data, assess feedback, adjust course, and inform broader policy.

FIGURES AND TABLES

Table 1: Genes related to performance enhancement in sports, and their strong overlap with targets for gene therapy

Genetic variation in several genes is relevant to gaining a performance edge in sports. There is a high overlap between these genes and those that are targets for gene therapy.

Gene	**Role of Gene**	**Example genetic variation**	**Work related to gene therapy**
EPOR	Determines red blood cell count	Variant that enables blood to carry >50% more oxygen[137]	Animal studies motivated by treatment for anemia associated with chronic renal failure and thalassemia[138]
COL5A1	Part of collagen, the main component of connective tissue	Variant associated with likelihood of Achilles tendon injuries[139]	

[137] Chapelle, *supra* note 2.
[138] S. Zhou et al., *Adeno-associated virus-mediated delivery of erythropoietin leads to sustained elevation of hematocrit in nonhuman primates*, 5 GENE THERAPY 665 (1998), *available at* https://www.ncbi.nlm.nih.gov/pubmed/9797871; B. Gavish et al., *Adiabatic compressibility of globular proteins*, 80 PROC. NAT'L ACAD. SCI. 750 (1983), *available at* https://www.ncbi.nlm.nih.gov/pmc/articles/PMC393457/.
[139] G. G. Mokone et al., *The COL5A1 gene and Achilles tendon pathology*, 16 SCAND. J. MED. & SCI. SPORTS 19 (2006), *available at* https://www.ncbi.nlm.nih.gov/pubmed/16430677.

SLC6A4	Control of serotonin levels	Variant that produces more serotonin more common in athletes than non-athletes[140]	
VEGF	Involved in growing new blood vessels	Variant that gives higher oxygen uptake before and after aerobic training[141]	Human trials for treatment of chronic critical leg ischemia[142]
IGF	Involved in muscle repair and growth	Genetic variation associated with more of this gene product is more common in power athletes[143]	Animal studies to demonstrate utility for those recovering from injury and for the elderly[144]
PPAR	A regulator of metabolism	Genetic variant associated with endurance performance[145]	Animal studies for treatment of atherosclerosis[146]

[140] E.V. Trushkin et al., *Association of SLC6A4 Gene 5-HTTLPR Polymorphism with Parameters of Simple and Complex Reaction Times and Critical Flicker Frequency Threshold in Athletes during Exhaustive Exercise*, 150 BULL. EXP. BIOLOGY & MED. 471 (2011), *available at* https://www.ncbi.nlm.nih.gov/pubmed/22268046.
[141] Steven J. Prior et al., *DNA sequence variation in the promoter region of the VEGF gene impacts VEGF gene expression and maximal oxygen consumption*, 290 AM. J. PHYSIOL. HEART & CIRC. PHYSIOL. H1848 (2006), *available at* http://ajpheart.physiology.org/content/290/5/H1848.full.pdf+html.
[142] Kou-Gi Shyu et al., *Intramuscular vascular endothelial growth factor gene therapy in patients with chronic critical leg ischemia*, 114 AM. J. MED. 85, *available at* https://www.ncbi.nlm.nih.gov/pubmed/12586226/.
[143] Sigal Ben-Zaken et al., *Can IGF-I polymorphism affect power and endurance athletic performance?*, 23 GROWTH HORMONE & IGF RES. 175 (2013), *available at* https://www.ncbi.nlm.nih.gov/pubmed/23850449.
[144] Sukho Lee et al., *Viral expression of insulin-like growth factor-I enhances muscle hypertrophy in resistance-trained rats*, 96 J. APPLIED PHYSIOL. 1097, *available at* https://www.ncbi.nlm.nih.gov/pubmed/14766764/.
[145] I.I. Ahmetov et al., *Association of a PPARD polymorphism with human physical performance*, 41 MOLECULAR BIOLOGY 776 (2007), *available at* http://link.springer.com/article/10.1134/S002689330705010X; Vihang A. Narkar et al., *AMPK and PPARδ agonists are exercise mimetics*, 134 CELL 405 (2008), *available at* https://www.ncbi.nlm.nih.gov/pubmed/18674809/.
[146] G. Li et al., *Hematopoietic knockdown of PPARδ reduces atherosclerosis in LDLR−/− mice*, 23 GENE THERAPY 78 (2016), *available at* http://www.nature.com/gt/journal/v23/n1/abs/gt201578a.html.

BDNF	Involved in neural development	Variants that affect psychological response to stress and motivation to exercise[147]	Animal studies motivated by improving progression of Huntington's disease[148]
MSTN	Myostatin; inhibits muscle differentiation and growth	Variants that reduce levels of myostatin lead to muscle growth[149]	Animal studies and human trials for those with muscle diseases and as a protection against muscle loss with age [150]
ACTN3	Component of the contractile apparatus in fast skeletal muscle fibers	Elite sprinters are more like to carry a certain variant[151]	

[147] Muaz Belviranli et al., *The relationship between brain-derived neurotrophic factor, irisin and cognitive skills of endurance athletes*, 44 PHYSICIAN & SPORTS MED. 290 (2016), *available at* http://www.tandfonline.com/doi/full/10.1080/00913847.2016.1196125; A. Pokrwka et al., *Genes in Sport and Doping*, 30 BIOLOGY SPORT 155 (2013), *available at* https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3944571/.
[148] B. Connor et al., *AAV1/2-mediated BDNF gene therapy in a transgenic rat model of Huntington's disease*, 23 GENE THERAPY 283 (2016), *available at* http://www.nature.com/gt/journal/v23/n3/full/gt2015113a.html; H. Fukui et al., *BDNF gene therapy induces auditory nerve survival and fiber sprouting in deaf Pou4f3 mutant mice*, SCI. REP. 2 (Nov. 12, 2016), http://www.nature.com/articles/srep00838.
[149] Markus Schuelke et al., *Myostatin Mutation Associated with Gross Muscle Hypertrophy in a Child*, 350 NEW ENG. J. MED. 2682 (2004), *available at* https://www.ncbi.nlm.nih.gov/pubmed/15215484.
[150] *Dual Gene Therapy Has Beneficial Effects On Blood Biomarkers And Muscle Composition*, BIOVIVA (2016), http://bioviva-science.com/blog/dual-gene-therapy-has-beneficial-effects-on-blood-biomarkers-and-muscle-composition; Janaiah Kota et al., *Follistatin Gene Delivery Enhances Muscle Growth and Strength in Nonhuman Primates*, 1 SCI. TRANSLAT'L MED. 6ra15 (2009), *available at* https://www.ncbi.nlm.nih.gov/pubmed/20368179/ (examining Follistatin in the same pathway).
[151] Nan Yang et al., *ACTN3 Genotype Is Associated with Human Elite Athletic Performance*, 73 AM. J. HUMAN GENETICS 627 (2003), *available at* https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1180686/.

HBB	Haemoglobin; enables blood to carry oxygen	Variants that affect cardiorespiratory adaptation[152]	Animal studies and human trials for treatment of Beta Thalassemia[153]

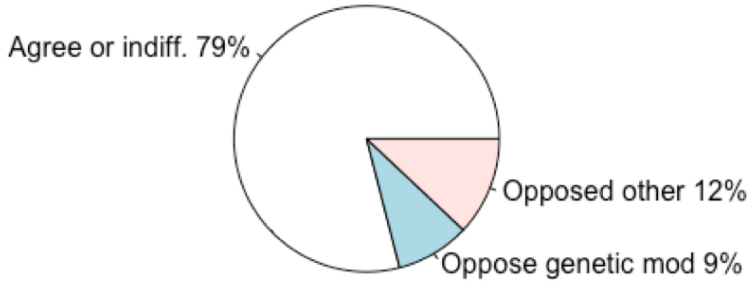

Figure 1: People who have chosen to acquire Gene Z should be permitted to race with people who were born with Gene Z

In response to Statement 1 "People who have chosen to acquire Gene Z should be permitted to race with people who were born with Gene Z" *(see scenario in Methodology), 79% Agreed or were indifferent. Of those who disagreed, 9% overall agreed that* "Humans shouldn't interfere with genetics under any circumstances". *N=400.*

[152] Z. He et al., *Polymorphisms in the HBB gene relate to individual cardiorespiratory adaptation in response to endurance training*, 40 BRIT. J. SPORTS MED. 998 (2006)*, available at* https://www.ncbi.nlm.nih.gov/pubmed/16990440.
[153] Zhanhui Ou et al., *The Combination of CRISPR/Cas9 and iPSC Technologies in the Gene Therapy of Human β-thalassemia in Mice*, SCI. REP. 6 (Sep. 1, 2016), http://www.nature.com/articles/srep32463; *Genome Editing for Hemophilia: A Next Step in Genetic Therapy*, CHILD. HOSP. PHILA. (Apr. 4, 2014), http://www.chop.edu/pages/genome-editing-hemophilia-next-step-genetic-therapy.

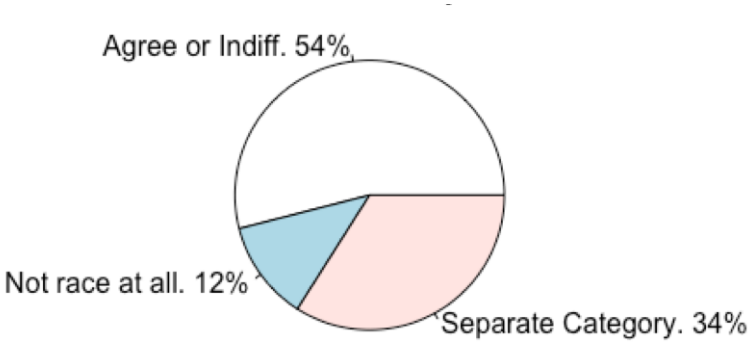

Figure 2: People who have chosen to acquire Gene Z should be permitted to race with people who have chosen not to acquire Gene Z

In response to Statement 2 "People who have chosen to acquire Gene Z should be permitted to race with people who have chosen not to acquire Gene Z" *(see scenario in Methodology), 54% Agreed or were indifferent. Of those who disagreed, 34% overall agreed that* "There should be a separate category for those who do not have Gene Z". *N=400.*

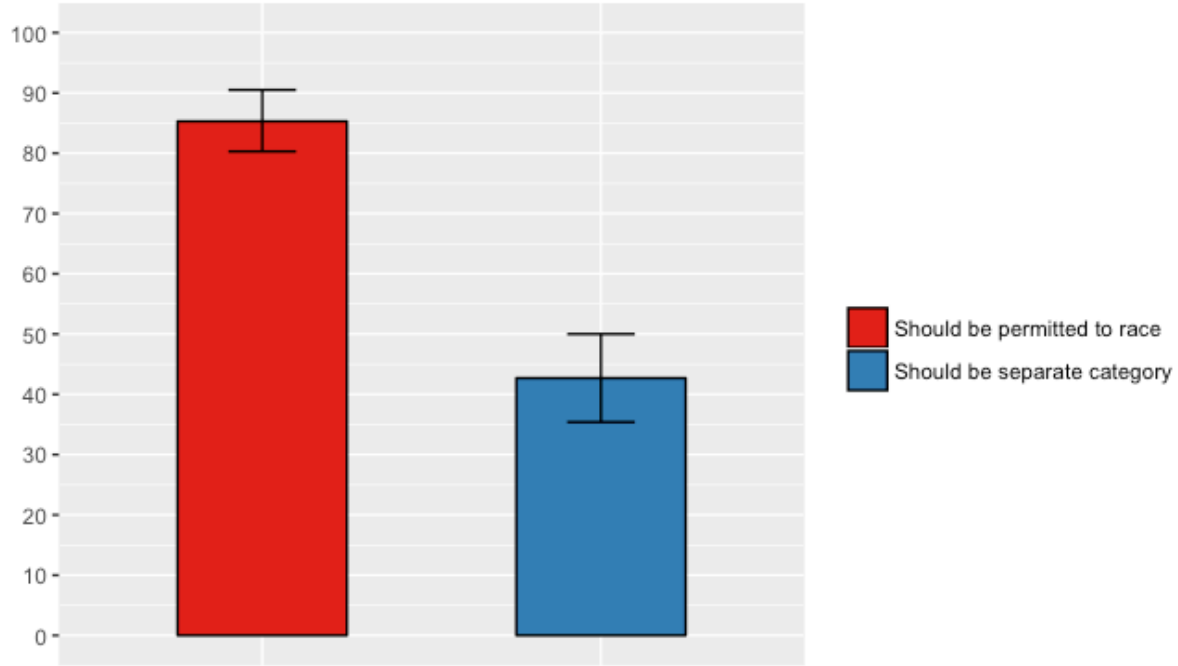

Figure 3: Attitudes to those born with Gene Z

In response to a modified version of Statement 2 "People who were born with Gene Z should be permitted to race with people who were not born with Gene Z" *given Scenario (a) (see Methodology), 86% Agreed or were indifferent. In response to a modified version of Statement 2* "People who were born without Gene Z should have a race category that people who were born with Gene Z cannot compete in" *for the same scenario, 43% Agreed or were indifferent. N=200.*

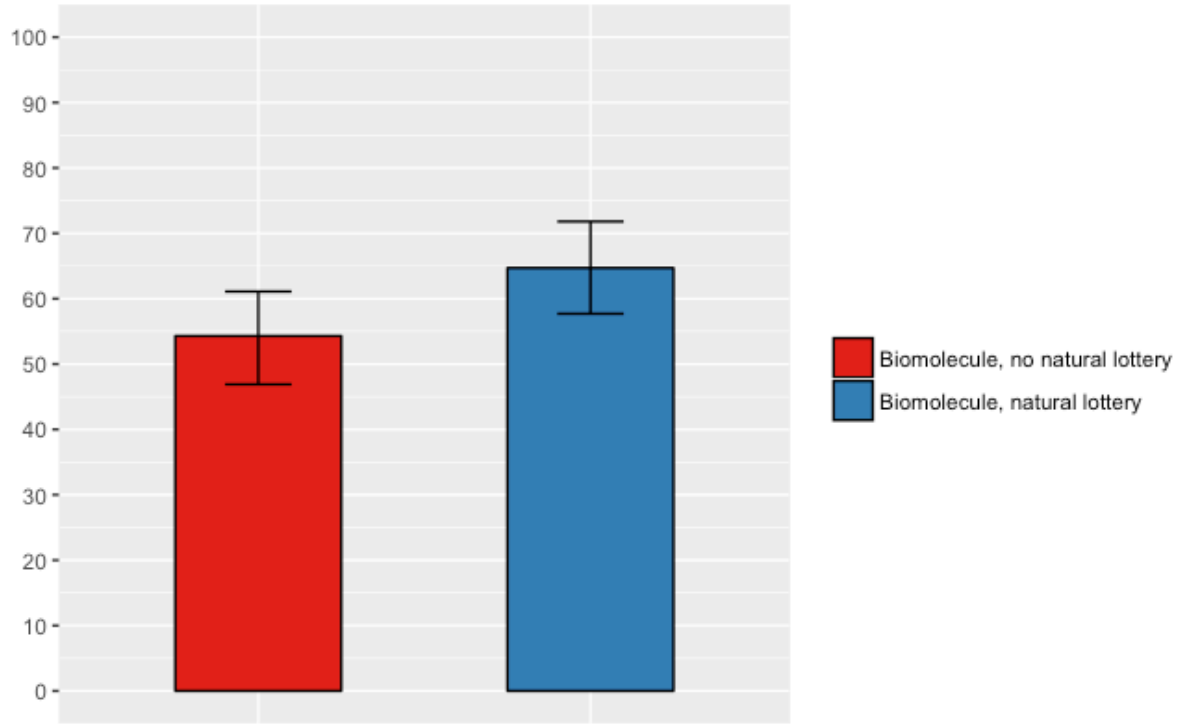

Figure 4: People who receive more Biomolecule V should be permitted to race with people who have chosen not to receive more Biomolecule V

*In response to a modified Statement 2 "*People who receive more Biomolecule V should be permitted to race with people who have chosen not to receive more Biomolecule V"*following Scenarios (b) and (c) (see scenarios in Methodology), where (b) contained the additional information "*Different individuals' bodies naturally produce differing amounts of biomolecule V". *63% Agreed or were indifferent to (b), and 56% to (c). (N=200, given to separate groups of people).*

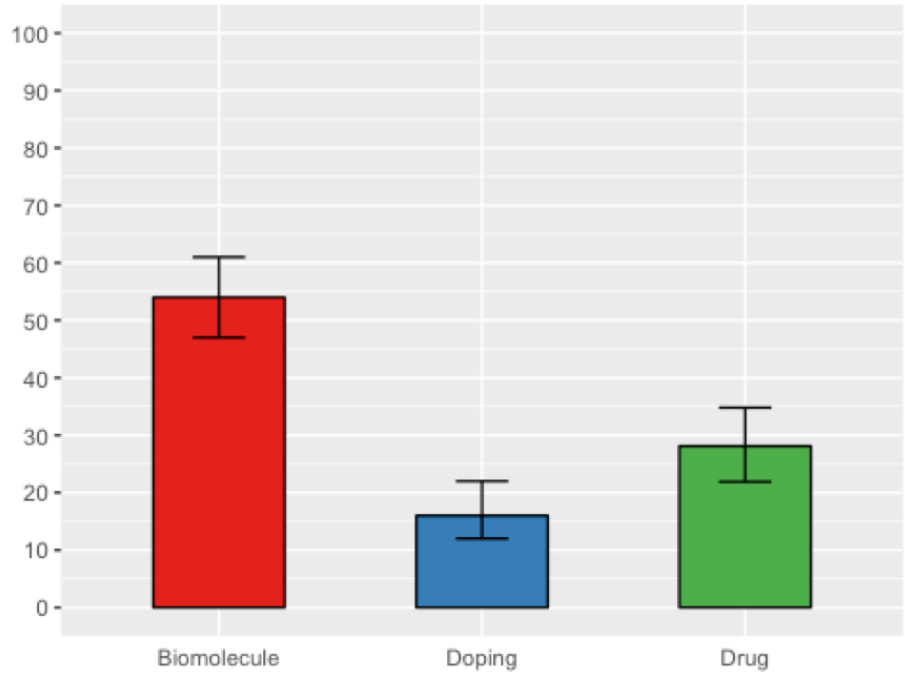

Figure 5: Effect of language in attitudes to performance enhancing drugs in sport

In response to a modified Statement 2 People who receive more Biomolecule V should be permitted to race with people who have chosen not to receive more Biomolecule V *to Scenario (c) (see Methodology), 56% Agreed or were indifferent. (N=200). In response to an identical set-up, but using the term "drug" rather than "biomolecule" (Scenario (d)), 29% Agreed or were indifferent. (N=200, separate people). In response to the statement "Athletes should be allowed to dope", 17% Agreed or were indifferent (N=200).*

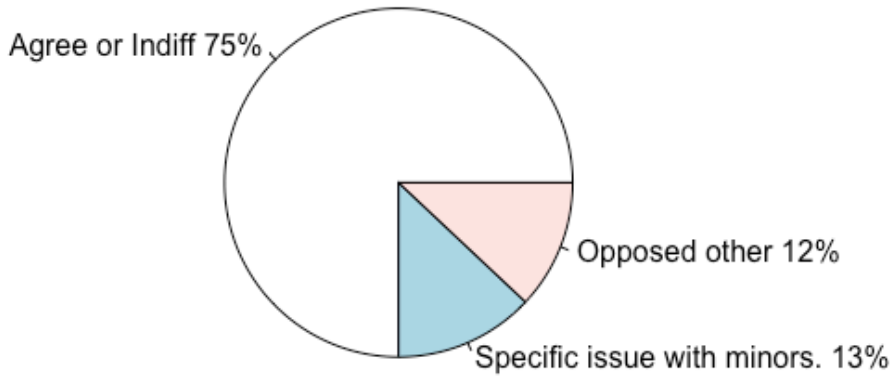

Figure 6: Support for genetic modification of minors

In response to the Statement Jamie should be permitted to acquire Gene Z *(see Minors scenario in Methodology), 75% Agreed or were indifferent. Of those who disagreed, 13% overall agreed that* It is acceptable for adults to be genetically modified but it is not acceptable for children to be genetically modified. *N=200.*