Barred from better medicine?
Reexamining regulatory barriers to the inclusion of prisoners in research

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ABSTRACT

In 2015, President Obama announced plans for the Precision Medicine Initiative® (PMI), an ambitious longitudinal project aimed at revolutionizing medicine. Integral to this Initiative is the recruitment of over one million Americans into a volunteer research cohort, the All of Us® Research Program. The announcement has generated much excitement but absent is a discussion of how the All of Us® Research Program—to be implemented within the context of social realities of mass incarcerations and racial disparities in criminal justice and healthcare—might exacerbate health disparities. We examine how attainment of Initiative’s stated goals of reflecting the diversity of the American population and including all who are interested in participating might be impeded by regulatory and administrative barriers to the involvement of participants who become incarcerated during

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longitudinal studies. Changes have been proposed to the federal policy for human subjects research protections, but current regulations and administrative policies—developed under a protectionist paradigm in response to scandalous research practices with confined populations—dramatically limit research involving prisoners. Our review provides rationale for the development of Initiative policies that anticipate recruitment and retention obstacles that might frustrate inclusivity and exacerbate health disparities. Furthermore, we question the effective ban on biomedical and behavioral research involving prisoners and advocate for regulatory reforms that restore participatory research rights of prisoners. Disparities in health and justice are intertwined, and without regulatory reforms to facilitate participatory research rights of prisoners and careful planning of viable and responsible recruitment, engagement, and retention strategies, Initiative could miss discovery opportunities, exacerbate health disparities, and increase levels of distrust in science.

KEYWORDS: ELSI, human subjects, PMI, prisoners, research oversight, vulnerable populations

The National Institutes of Health (NIH) has launched the Precision Medicine Initiative® (PMI), an ambitious 10-year longitudinal project planning to involve the collection and study of biospecimens, electronic health records, surveys, and extensive lifestyle and behavioral data via mobile apps and sensors and a target cohort of one million individuals that is reflective of the nation’s diversity.1 The PMI website boasts, ‘Anyone in the United States will be able to voluntarily enroll’, and NIH Director Dr. Francis Collins has indicated the PMI wants to include participants ‘from all walks of life’.2,3 The PMI Working Group underscored the importance of an inclusive cohort in its final report; noted exclusions of any kind—even exclusion of groups considered to be vulnerable populations—would undermine the project’s scientific integrity and potential to improve healthcare for all; and made two specific recommendations relevant to the present discussion, as shown in Table 1.4 The NIH has acknowledged that creating such an inclusive cohort will be challenging and necessitate modernization of current regulatory frameworks in order to accommodate and provide appropriate oversight for participatory research.5,6,7,8 Nevertheless, there has been little public

1 Precision Medicine Initiative Working Group Report to the Advisory Committee to the Director, NIH, The Precision Medicine Initiative Cohort Program-building a Research Foundation for 21st Century Medicine 79 (2015).
2 National Institute of Health, Participation: A Role for Everyone, NIH 2016, https://www.nih.gov/precision-medicine-initiative-cohort-program/participation (accessed Dec. 21, 2016).
3 NIH Press release, NIH Awards $55 Million to Build Million-Person Precision Medicine Study, NIH 2016, https://www.nih.gov/news-events/news-releases/nih-awards-55-million-build-million-person-precision-medicine-study (accessed Dec. 21, 2016).
4 Precision Medicine Initiative Working Group Report, supra note 1, at 78.
5 Francis S. Collins & Harold Varmus, A New Initiative on Precision Medicine, 372 NEW ENGL. J. MED. 793–95 (2015). doi:10.1056/NEJMp1500523.
6 For example, Rosamond Rhodes, Rethinking Research Ethics, 5 AM. J. BIOETHICS 7–28 (2005). DOI: 10.1080/15265160590900678.
7 For example, G. Owen Schaefer, Ezekiel J. Emanuel & Alan Wertheimer, The Obligation to Participate in Biomedical Research, 302 JAMA 67–72 (2009). DOI: 10.1001/jama.2009.931.
8 For example, Paul Wicks, Video Q&A: Patients Leading the Direction of Clinical Research–An Interview with Paul Wicks, 12 BMC MED. 118 (2014). DOI: 10.1186/s12916-014-0118-1.
Table 1. Relevant Recommendations from the PMI Working Group. (emphasis added)

Recommendation 7.2: NIH should carefully examine issues related to inclusion of three special populations: children, decisionally impaired individuals, and PMI cohort participants who become incarcerated after enrollment. NIH should develop specific approaches to address the needs of these individuals so that they may be included and retained in the cohort.

Recommendation 7.3: The PMI-CP should anticipate the need for special provisions to allow for continued engagement and follow up with participants who have undergone life events or other changes that alter their participation status or capacity.

discussion about the challenges to inclusivity or potential ways in which those challenges can be overcome, which is concerning given recruitment for the PMI All of UsSM Research Program9 is imminent. Here, we examine one specific challenge for the PMI: the inclusion of individuals who are or become incarcerated during the Initiative. We use this study as an example to demonstrate the importance of comprehensive regulatory reforms for research that enable the participation of prisoners.

THE SOCIAL CONTEXT IN WHICH PMI WILL BE IMPLEMENTED
The PMI will not be implemented in an ideal world (where all individuals have equal access to healthcare and equal opportunity to participate in biomedical research and to share in its benefits) but within the context of societal realities of mass incarcerations and a criminal justice system that disproportionately affects minorities. The USA has one of the largest prison populations and highest incarceration rates in the world. According to the Bureau of Justice Statistics, there are approximately 6.85 million adults (1 in 36, or 2.8% of the US population) under correctional supervision, with 1.5 million held in state and federal correctional facilities, 744 thousand held in local jails, and 4.7 million on probation or parole. The incarceration rate in 2014 was 900 per 100,000 US adults.10,11,12 The lifetime likelihood of imprisonment of US residents born in 2001 for men was 1 in 9 and women was 1 in 56.13 Incarceration rates vary greatly by racial and ethnic background (as shown in Table 2), and these disparities in incarceration rates vary among states. In Pennsylvania, eg African Americans make up 10.6% of the population but 48.7% of the prison population, and the racial disparity in the incarceration rate shows nearly nine African Americans to one European American.14,15

9 NIH Press Release, PMI Cohort Program Announces New Name: the All of UsSM Research Program, NIH Oct. 12, 2016, https://www.nih.gov/precision-medicine-initiative-cohort-program/PMI-cohort-program-announces-new-name-all-us-research-program (accessed Dec. 21, 2016).
10 Danielle Kaeble et al., Correctional Populations in the United States, 2014, D.O.J. NCJ 249513 (2015).
11 E. Ann Carson, Prisoners in 2014, D.O.J. NCJ 248955, 15 tbl. 10 (2015).
12 The Sentencing Project, Criminal Justice Facts (2014), http://www.sentencingproject.org/criminal-justice-facts/ (accessed Dec. 21, 2016).
13 Id.
14 A. Nellis, The Color of Justice: Racial and Ethnic Disparity in State Prisons, 16 tbl. A (2016) http://www.sentencingproject.org/wp-content/uploads/2016/06/The-Color-of-Justice-Racial-and-Ethnic-Disparity-in-State-Prisons.pdf (accessed Dec. 21, 2016).
15 The Sentencing Project, supra note 12.
Table 2. U.S. Prisoner Statistics at a Glance.

**Incarceration Rate\(^d\)**

| Category                  | Rate     |
|---------------------------|----------|
| Total (of all ages)       | 690 per 100,000 |
| Adults (18 years and older)| 900 per 100,000 |

**Imprisonment Rate\(^b,c\)**

| Category                  | Rate     |
|---------------------------|----------|
| Total (of all ages)       | 470 per 100,000 |
| Adults (18 years and older)| 610 per 100,000 |

**Total U.S. Prison Population\(^d\)**

| Category                  | Number   |
|---------------------------|----------|
| Incarcerated              | 2,224,400 State/Federal 1,561,500 |
|                           |          Local 744,600 |
| Community Supervision     | 4,708,100 Probation 3,864,100 |
|                           |          Parole 856,900 |

**Lifetime Likelihoods of Incarceration\(^e\)**

| Gender     | Average | White | Hispanic | Black |
|------------|---------|-------|----------|-------|
| Male       | 1 in 9  | 1 in 17 | 1 in 6   | 1 in 3 |
| Female     | 1 in 56 | 1 in 111 | 1 in 45  | 1 in 18 |

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\(^a\)Kaeble et al., *supra* note 10, tbl. 2.

\(^b\)Id. tbl. 3.

\(^c\)The incarceration rate is the estimated number of inmates held in state, federal, or local facilities per 100,000 U.S. residents, whereas the imprisonment rate is the estimated number of inmates in state or federal facilities that have been sentenced to more than one year per 100,000 U.S. residents.

\(^d\)Kaeble et al., *supra* note 10.

\(^e\)The Sentencing Project, *supra* note 12.

Both the absolute numbers of individuals in this vulnerable population (ie prisoners) whom the PMI has expressed an interest in including and these disparities in incarceration rates are relevant to the PMI’s viable retention strategies. Incarceration rates that disproportionately affect racial and ethnic minorities, who are already underrepresented in biomedical research, are a serious concern for longitudinal, participatory studies.\(^\text{16}\) In addition to over-sampling strategies for recruitment of under-represented minorities into *All of Us*, PMI must prepare for the collateral damage that mass incarcerations and racial disparities in criminal justice cause—eg biased interruptions and drop-outs of not only the individual who becomes incarcerated but also family members and friends whose interest and available time to commit to the study might wane. High incarceration rates suggest programmatic challenges for the PMI, including the need to track participants to identify when they become prisoners in any jurisdiction and managing the potential disruptions (eg involuntary suspension of participation or disengagement).

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\(^\text{16}\) See eg, Emily A. Wang & Christopher Wildeman, *Studying Health Disparities by Including Incarcerated and Formerly Incarcerated Individuals*, 305 JAMA 1708 (2011) (explaining the likely impact of incarceration on the Coronary Artery Risk Development in Young Adults or CARDIA study).
Moreover, inclusion of prisoners is particularly important for the study of conditions and diseases that disproportionately affect prisoners at higher rates than the general non-prisoner population. Prisoners are reported to suffer higher rates of infectious disease, chronic conditions, and mental health conditions (including, for example, hepatitis C, HIV/AIDS, tuberculosis, oral health problems, mental health problems, substance use disorders, diabetes, heart disease, and cancer). Yet there are few national health data sets that include any information relevant for examining associations between incarceration and health. The World Health Organization has acknowledged, ‘public health can no longer afford to ignore prison health’, and others have started to consider prisoner health as ‘integral’ to the public health system. As Wakai et al. (2009) have noted, it is impossible ‘to provide effective evidence-based care for inmates’ unless research is conducted to understand ‘their particular circumstances, health histories, and environmental exposures’. Nevertheless, there are scarce data involving prisoners or their perspectives on research.

A BRIEF HISTORY OF RESEARCH INVOLVING PRISONERS

The history of prisoners’ involvement in biomedical research that led to proscriptive regulations in 1978 to protect prisoners from exploitation (but were, we believe, an over-correction and have functioned as an effective ban on prisoner participation in research) has been well documented elsewhere. It does, however, warrant a special note that research involving prisoners during its peak in the 1960s and 1970s is appropriately described as research conducted on prisoners as subjects (as opposed to a more equitable process of research conducted with prisoner-participants as partners).

16 For example, Karishma A. Chari et al., National Survey of Prison Health Care: Selected Findings, 96 NATL. HEALTH STAT. REP. 1 (2016).
17 For example, Sara Wakai et al., Conducting Research in Corrections: Challenges and Solutions, 27 BEHAV. SCI. L. 743 (2009).
18 Cyrus Ahalt et al., Confined to Ignorance: The Absence of Prisoner Information from Nationally Representative Health Data Sets, 27 J. GEN. INT. MED. 160 (2012). DOI: 10.1007/s11606-011-1858-7.
19 Id.
20 Health in Prisons, A WHO GUIDE TO THE ESSENTIALS IN PRISON HEALTH (Lars Moller et al. eds., 2007), at viii.
21 Jörg Pont, Ethics in Research Involving Prisoners, 4 INT’L J. PRISONER HEALTH 184, 191 (2008). DOI: 10.1080/17449200802473107.
22 Wakai et al., supra note 18, at 744.
23 But see Paul P. Christopher et al., An Exploratory Study of Therapeutic Misconception Among Incarcerated Clinical Trial Participants, 7 AJOB EMPIRICAL BIOETHICS 1 (2016) and Paul P. Christopher et al., Exploitation of Prisoners in Clinical Research: Perceptions of Study Participants, 38 IRB: ETHICS & HUM. RES. 1 (2016).
24 For example, Ruth Faden, ed. Prisoners: Captive research population, in The Human Radiation Experiments: Final Report Of The President’s Advisory Committee, 263, 263–283 (Advisory Committee on Human Radiation Experiments, 1996); V. H. Bonham & Jonathan D. Moreno, Research With Captive Populations in The Oxford Textbook Of Clinical Research Ethics, 461, 461–74 (Ezekiel J. Emanuel et al. eds., 2008); K. C. Kalmbach & Phillip M. Lyons, Ethical and Legal Standards for Research in Prisons, 21 BEHAV. SCI. L. 559 (2003) DOI: 10.1002/bdl.533; Sharona Hoffman, Beneficial and Unusual Punishment: An Argument in Support of Prisoner Participation in Clinical Trials, 33 I.N. L. REV. 475 (1999); ALLEN M. HORNBLLUM, ACRES OF SKIN: HUMAN EXPERIMENTS IN HOLMESBURG PRISON (1998); Osagie K. Obasogie, Prisoners as Human Subjects: A Closer Look at the Institute of Medicine’s Recommendations to Loosen Current Restrictions on Using Prisoners in Scientific Research, 6 STAN. J.C.R. & C.L. 41 (2010), http://repository.uchastings.edu/faculty_scholarship/1359 (accessed Dec. 21, 2016).
including experiments for understanding cholera, pellagra, malaria, gonorrhea, herpes, influenza, cosmetic safety, testicular radiation, and chemical warfare agents. Stated bluntly, the research involved experimentation that non-prisoners would refuse. For example, by 1972 more than 90% of investigational drug toxicity testing was conducted on prisoners. Confinement and pressures of prison cultures (including power dynamics, susceptibility to monetary inducements, and boredom) seemingly provided an ‘unlimited supply of available, trackable, and willing subjects’. Prisons became known as a special environment in which voluntary informed consent is inherently problematic because the possibility of coercion is high and in which the dangers of exploitation are escalated compared to those risks in society.

**CURRENT BARRIERS TO RESEARCH INVOLVING PRISONERS**

Federal regulations for research are set generally in subpart A of 45 C.F.R. part 46 (otherwise known as the ‘Common Rule’). These regulations set forth the federal policy to ensure that federally funded research involving humans is conducted ethically and does not unjustifiably or unreasonably place humans in danger. The Common Rule requires research protocols to be reviewed by institutional review boards (IRBs) to evaluate the benefits and risks before the research begins, provide oversight during the study, and ensure research is conducted pursuant to voluntary, informed consent by each participant. Research involving prisoners, classified as a ‘vulnerable population’, must also comply with specific regulations of subpart C of 45 C.F.R. part 46. For regulatory purposes, ‘prisoner’ is defined as ‘any individual involuntarily confined or detained in a penal institution’ and includes those detained after sentencing as well as those awaiting arraignment, trial, or sentencing. Regulatory exemptions are not available for research involving prisoners. Moreover, the extra regulations of subpart C apply not only when prisoners are the focus of the study’s recruitment but also when participants incidentally become prisoners during the study.

In addition to subpart C’s provisions regarding composition of the IRBs and additional findings required before IRBs approve research, subpart C, 45 C.F.R. §46.306(a), permits only that research fitting one of four categories: (1) studies of the criminal behavior and incarceration (such as causes, effects, and processes); (2) studies of prisons as institutions; (3) studies of conditions affecting prisoners as a class, subject to conditions; and (4) studies of practices that benefit and likely improve the individual’s health or well-being, subject to conditions. Unless one of the aforementioned categories is applicable, ‘biomedical or behavioral research...shall not involve prisoners as subjects’. Subpart C also requires that researchers obtain certification for their projects by the

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26 For example, Osagie K. Obasogie, *Prisoners as Human Subjects: A Closer Look at the Institute of Medicine’s Recommendations to Loosen Current Restrictions on Using Prisoners in Scientific Research*, 6 STAN. J.C.R. & C.L. 41 (2010), http://repository.uchastings.edu/faculty_scholarship/1359 (accessed Dec. 21, 2016); Barron H. Lerner, *Subjects or Objects? Prisoners and Human Experimentation*, 356 NEW ENGL. J. OF MED. 1806 (2007). DOI: 10.1056/NEJMp068280.
27 Faden, supra note 25.
28 Nancy N. Dubler, *The Burden of Research in Prisons*, 4 IRB 9 (1982), at 10.
29 Office of Human Research Protections, 46 C.F.R. §46.303(c) (2009).
30 For example, Office of Human Research Protections, *Guidance on the Involvement of Prisoners in Research*, U.S. DEPT. OF H.H.S. (2003), http://www.hhs.gov/ohrp/regulations-and-policy/guidance/prisoner-research-ohrp-guidance-2003/ (accessed Dec. 21, 2016).
Secretary of the Department of Health and Human Services (DHHS), typically done through the Office of Human Research Protections (OHRP).\textsuperscript{31} If a participant becomes incarcerated during a study not originally approved as research involving prisoners, the individual’s participation is to be immediately suspended; no interactions, interventions, or exchanges of identifiable private information are to occur; researchers are to notify the IRB; and the IRB must re-review the protocol to ensure the requirements of subpart C are met before participation may resume.\textsuperscript{32} A waiver to the subpart C provisions is available for epidemiological research that has the sole purpose either to describe a disease’s prevalence or incidence or to study potential risk factors for a disease but only if the research involves no more than minimal risk, involves only an inconvenience to the prisoners, and is not particularly focused on prisoners.\textsuperscript{33}

There are also administrative barriers to research involving prisoners. Prisoners are not under uniform supervision but are held in federal, state, local, and sometimes private facilities, and proposed research must also comply with policies of the appropriate authority. The Federal Bureau of Prisons (BOP) Program Statement 1070.07 is clear: ‘The project must not involve medical experimentation, cosmetic research, or pharmaceutical testing’.\textsuperscript{34} As an example of state policy, the PA Department of Corrections policy similarly states, ‘The use or employment of an inmate as a subject in any medical, pharmaceutical, or cosmetic experiments or testing is prohibited’, and the authority allows only research that increases knowledge of correction practices, management, or facilities.\textsuperscript{35} Two of the largest private companies in the US prison system, Corrections Corporation of America and GEO Group, have no publicly available online policy statements regarding research.

\textbf{REFORMS SUGGESTED, PRISONERS IGNORED}

In the 1970s when the regulations to curtail biomedical research involving prisoners were being contemplated, some prisoners complained of being excluded from research opportunities.\textsuperscript{36} Calls to reconsider the bans on research involving prisoners intensified in the 1980s in connection specifically with the HIV/AIDS epidemic and the need for clinical trials.\textsuperscript{37} For example, Dubler and Sidel (1989) concluded that despite the challenges to obtaining ‘voluntary and uncoerced choice classically envisioned by the

\textsuperscript{31} Id.

\textsuperscript{32} Office of Human Research Protections, Prisoner Research FAQs, U.S. Dept. of H.H.S. 2016, https://www.hhs.gov/ohrp/regulations-and-policy/guidance/faq/prisoner-research/index.html (accessed Dec. 21, 2016).

\textsuperscript{33} Proposed Waiver of the Applicability of Certain Provisions of Department of Health and Human Services Regulations for the Protection of Human Subjects for Department of Health and Human Services Epidemiologic Research Involving Prisoners as Subjects, 67 Fed. Reg. 62432 (proposed Oct. 7, 2002); Waiver of the Applicability of Certain Provisions of Department of Health and Human Services Regulations for Protection of Human Research Subjects for Department of Health and Human Services Conducted or Supported Epidemiologic Research Involving Prisoners as Subjects, 68 Fed. Reg. 36930 (June 20, 2003).

\textsuperscript{34} Program Statement: Research, 1070.07, B.O.P. Pp. 4 (1999), https://www.bop.gov/policy/progstat/1070_007.pdf (accessed Dec. 21, 2016).

\textsuperscript{35} Research Activities Policy, Policy No. 2.1.2, P.A. Dept. of Corrections (2007), http://www.cor.pa.gov/About%20Us/Documents/DOC%20Policies/02.01.02%Research%20Activities.pdf (accessed Dec. 21, 2016).

\textsuperscript{36} Roy Branson, \textit{Prison Research: National Commission Says ‘No, Unless...’}, 7 HASTINGS CTR. REP. 15 (1977) (citing Report and recommendations: research involving prisoners, National Commission, Oct. 1, 1976, at §).

\textsuperscript{37} Nancy N. Dubler & Victor W. Sidel, \textit{On Research on HIV Infection and AIDS in Correctional Institutions}, 67 MILBANK Q. 171 (1989) and Theodore M. Hammett & Nancy N. Dubler, \textit{Clinical and Epidemiologic Research
regulations’ in a prison setting, prisoners should be allowed to participate in clinical trials lacking placebo arms for any illness in which there is not yet standard, accepted treatment.  

In 2007, the Institute of Medicine (IOM) issued an extensive report, ‘Ethical Considerations for Research Involving Prisoners’, in which it examined past and present research involving prisoners and applicable regulations. The IOM made five major recommendations:

1. that the definition of prisoner be expanded to include incarcerations as well as other situations when liberty is constrained by correctional authorities, such as probation or parole;
2. that the rules apply uniformly regardless of funding source or type of correctional facility and the creation of a national public database of research involving prisoners;
3. that the category-based approach be replaced by a risk-based approach, in which direct benefits for each prisoner-participant outweigh the risks;
4. that the ethical framework be updated to promote ‘collaborative responsibility’; and
5. enhance the systematic oversight for research involving prisoners, including more proactive monitoring by IRBs.

The IOM recognized that a realignment of the research regulatory framework is necessary to ensure that prisoners share in access to research, have a partnership role in that research, and are adequately protected by uniform rules. Nonetheless, the IOM reiterated that biomedical research must remain restricted when involving prisoners, recommending that it be permissible only when (1) the proposed research on a new prevention or treatment option has some evidence of safety and efficacy or (2) the ratio of prisoners to non-prisoners involved does not exceed 50%.

Not until 2011 was the first major action taken to reform research regulations when the DHHS published an advanced notice of proposed rulemaking (ANPRM). The ANPRM focused recalibrating oversight within a revised, risk-based framework. Despite the IOM’s thorough analysis and recommendations, the ANPRM did not propose any revisions specific to subpart C, acknowledge the IOM’s report, or otherwise discuss research involving prisoners. Rather, the ANPRM was explicitly focused narrowly on the Common Rule itself and drafters noted that the proposed changes could affect the subparts in ways that would require their subsequent harmonization.
Table 3. NPRM Questions Regarding Research Protections for Prisoners.

| Question Number | Question for Public Comment |
|-----------------|-----------------------------|
| Question No. 25 | ‘Should research involving prisoners be allowed to use any or all of the exclusions found at §101(b)(2) and (3), as currently proposed?’ |
| Question No. 57 | ‘Public comment is sought on whether research involving prisoners should be permitted to apply any or all of the exemption categories found at proposed §104, either if the research consists mostly of non-prisoners and only incidentally includes some number of prisoners, as proposed in the NPRM, or if the research intends to involve prisoners as research subjects’. |
| Question No. 58 | ‘Would it be preferable for language at §104(b)(2) to resemble the 2002 epidemiologic waiver criteria and state that the exemptions apply except for research where prisoners are a particular focus of the research?’ |

years later, when DHHS issued a Notice of Public Rulemaking (NPRM) in 2015, it again expressly declined the opportunity to reform subpart C. Nevertheless, three of the 88 questions posed for public comment (Questions 25, 57, and 58 shown in Table 3) inquired whether the proposed exclusions (at proposed §101(b)(2) and (3)) and exemptions (at proposed §104) should apply if not to all research involving prisoners then at least to those research projects in which the targeted population is predominantly non-prisoners. While the stated intent of this potential change is to relax constraints on prisoners’ involvement in non-research activities or ‘low risk’ research activities, the actual language of the proposed regulatory text is contradictory and convoluted. Moreover, if research is planned with an equitable design (ie if researchers and participants are both anticipated to have access to individual data and results from the study) as PMI has been publicized, exemptions proposed at §104(f) are not available.

The ANPRM and NPRM both sparked extensive public commenting, with more than 1050 public comments on the ANPRM and more than 2100 comments on the NPRM; however, a review and content analysis of these comments, as highlighted in Tables 4 and 5, revealed scant coverage of how research involving prisoners might be affected. In 2002 when the epidemiological research waiver was first proposed, that action drew little attention or opposition (ie only 14 comments were submitted, 12 of which were supportive of the policy change). The NPRM has been severely criticized, calling into question the legitimacy of any regulations that might, on its basis, be issued without opportunity for the public to review a full detailed proposal and contribute to its refinement. A focused critique by Guerrnie, McGuire, and Majumder demonstrates how the NPRM ‘will potentially impede’ not only the PMI but also other efforts

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42 Federal Policy for the Protection of Human Subjects, 80 Fed. Reg. 53954 (proposed Sept. 8, 2015).
Table 4. Summary of Comments to the ANPRM and NRPM.

| Comments mentioning 'Prisoner' or 'Inmate' | ANPRM | NRPM |
|------------------------------------------|-------|------|
| N = 46                                   | N = 73|

| Source of Comments                  | ANPRM | NRPM |
|-------------------------------------|-------|------|
| Academia                            | N = 36| N = 41|
| Government                          | N = 2 | N = 3 |
| Industry                            | N = 4 | N = 1 |
| Public                              | N = 3 | N = 9 |
| Unknown                             | N = 1 | N = 19|

| Framing of Comments                  | ANPRM | NRPM |
|-------------------------------------|-------|------|
| Participatory Framework             | N = 1 | N = 3 |
| Protectionist Framework             | N = 21| N = 35|
| Neither                             | N = 24| N = 35|

| Position Advocated                  | ANPRM | NRPM |
|-------------------------------------|-------|------|
| Revisions to Subpart C governing involving prisoners in research | N = 5 | N = 5 |
| Fewer restrictions on prisoner involvement in research              | N = 6 | N = 20|
| More restrictions on prisoner involvement in research                | N = 4 | N = 3 |

to build a medical information commons.\textsuperscript{43} In June 2016, the National Academies of Science, Engineering, and Medicine emphatically rejected the proposed reforms, called for the NPRM’s withdrawal, and advocated for a comprehensive, robust review of the regulations to be performed by a new national commission dedicated to the task.\textsuperscript{44} If a piecemeal approach to regulatory reform moves forward and focuses only on the Common Rule, the research and healthcare gap between prisoners and non-prisoners will only widen.

**RESEARCH PARTICIPATION DENIED: ‘IT’S FOR THEIR OWN PROTECTION’**

As Carol Levine described in 1988, ‘the basic approach to the ethical conduct of research...was born in scandal and reared in protectionism’.\textsuperscript{45} The restrictive federal

\textsuperscript{43} Christi J. Guerrini, Amy L. McGuire & Mary A. Majumder, *Clearing Complexity from the Common Rule NPRM*, 3 J. L. BIOSCI. 257 (2016). DOI: 10.1093/jlb/lsw026.

\textsuperscript{44} Committee on Federal Research Regulations and Reporting Requirements: A New Framework for Research Universities in the 21st Century; Committee on Science, Technology, and Law; Board on Higher Education and Workforce; Policy and Global Affairs, National Academies of Sciences, Engineering, and Medicine, *Optimizing the Nation’s Investment in Academic Research: A New Regulatory Framework for the 21st Century* 170 (2016). DOI: 10.17226/21824.

\textsuperscript{45} Carol Levine, *Has AIDS Changed the Ethics of Human Subject Research?* 16 J. L. MED. ETHICS 167–173 (1988). DOI: 10.1111/j.1748-720X.1988.tb01942.x
Table 5. Excerpts from Comments to the ANPRM and NPRM.

| Comment to ANPRM | Sreekant Murthy | “The fundamental objectives of FDA and the Common Rule are to ensure and enhance that clinical trials are conducted uniformly, appropriately and ethically…OHRP and FDA should synchronize to create comparable provisions for vulnerable populations such as children, prisoners and pregnant women so they too could benefit from participating in trials’. |
| Comment to NPRM | University of Texas System (submitted by Patricia Hurn) | ‘Allowance for exclusion of some studies involving prisoners may actually facilitate research that could be beneficial to them’. |
| Comment to NPRM | American Psychiatric Association (submitted by Nevena Minor) | “The PR [Proposed Rule] lists categories of research subjects “vulnerable to coercion or undue influence, such as children, prisoners, pregnant women, physically or mentally disabled persons, or economically or educationally disadvantaged persons.” APA however disagrees that someone, by virtue of falling into certain of these categories, is inherently vulnerable to coercion or undue influence. While some research involving these populations may require special considerations, we fear that the PR’s blanket pronouncements may exclude individuals with such characteristics from participating in research, in violation of the Belmont Principle of respect for persons and their right to choose. This could also have the perverse effect of hindering in the long-term the development of treatments and cures for various diseases benefitting those individuals these restrictions purport to protect…” |
| Comment to NPRM | WIRB-Copernicus Group (submitted by David Borasky) | ‘Prisoners are currently over-protected to the point of justice inequities in research. Research involving prisoners should be allowed under these exclusions [found at §101(b)(2) and (3) as proposed in NPRM]’ |

Policy on research involving prisoners is rooted in a now 40-year-old report from the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, the architects of the protectionist philosophy that undergirds federal research regulations. That philosophy has been challenged in deference to an arguably...
more equitable one—participation. Responsible research involving prisoners continues to require diligence and oversight to ensure voluntariness and overcome the potential for consent to be an act of acquiescence or compliance with a perceived requirement or preference by prison officials who control the prisoners’ liberties and privileges, compromised by an individual’s inability to understand the scope of the research and risks, and tainted by research incentives that seem minor to non-confined populations but amount undue influences within the prison setting (eg such as an opportunity to escape boredom or crowded spaces or access to snacks). While policies to shield prisoners from exploitation remain important, it is time to recognize existing regulations have become handcuffs restricting prisoners’ ability to participate. Existing bioethics literature lacks careful evaluation of prisoners’ participation in research from a participatory perspective, although there have been a few advocates calling for a relaxation of prisoner research restrictions. Recent research efforts, including PMI, mark a noticeable shift in the scientific enterprise that values individuals as meaningful research partners (ie not passive subjects or mere data sources but active collaborators in the design, conduct, and publication of research). Regulatory reforms must be reconsidered such that these developing norms can be adequately taken into account. Researchers must be encouraged to think critically and inclusively in research design so that individuals from vulnerable populations are not unnecessarily excluded simply because of their vulnerable status, which could only widen the divide between those privileged to enjoy the benefits of science.

Participating in science and enjoying benefits from the advancement of science are human rights. Some have even described participation in research as a duty. At a minimum, contributions to science are a form of community service that should be acknowledged and facilitated. Restoring participatory research rights for prisoners could enable the development of innovative accelerated rehabilitative disposition programs that inspire STEM careers. Furthermore, it could enable prisoners, despite physical separation from society, to have positive, shared experiences with family and friends who participate in research together and additionally function as one way to mend, preserve, or strengthen their connections with society. Finally, we caution that as precision medicine and integration of research in healthcare become standard practice, continued ‘protection’ of prisoners from research activities might constitute a deliberate indifference to their human and constitutionally protected right to adequate healthcare, a point which we elaborate below. Innovative, responsible approaches to destigmatize research involving prisoners and enable participatory research for conditions and health outcomes of particular relevance for that vulnerable population should be encouraged with appropriate support and oversight.

47 See Supplemental Materials.
48 Pont, supra note 22, 184; see also Lynn Pasquerella, Confining Choices: Should Inmates’ Participation in Research be Limited? 23 THEO. MED. BIOETHICS 519 (2002); Lawrence O. Gostin, Biomedical Research Involving Prisoners: Ethical Values and Legal Regulation, 297 JAMA 737 (2007), DOI: 10.1001/jama.297.7.737; Lerner, supra note 26. But see Obsogie, supra note 26. http://repository.uchastings.edu/faculty_scholarship/1359 (accessed Dec. 21, 2016) and Vivian Lee, Prisoner Participation in Clinical Research Trials: A Fundamental Right Under the Eighth Amendment?, 33 J. LEG. MED. 541 (2012). DOI: 10.1080/01947648.2012.739063.
49 Universal Declaration of Human Rights, G. A. Res. 217A (III), UN Doc. A/810 at 71, Article 27(1) (1948).
50 Schaefer et al., supra note 7.
IMPROVING PRISON HEALTHCARE THROUGH THE INTEGRATION OF RESEARCH

It is perhaps ironic that prisoners comprise the one segment of American society that has been recognized as having a constitutional right to adequate healthcare but are simultaneously excluded from the activities intended to improve healthcare outcomes. Healthcare in the correctional setting must align with ‘contemporary standards of decency’ to avoid ‘unnecessary suffering’. Accordingly, prisoner medicine must meet baseline requirements set by the US Constitution, federal laws, and standard of care, although practically that bar is set very low. In some circumstances, inadequate medical services in prisons can violate the prohibition against cruel and unusual punishment. The test as to whether prison officials can be held accountable for providing inadequate medical services has been a subjective one of ‘deliberate indifference’, ie whether there was knowledge and a disregard of a serious medical need.

Courts have not always viewed this prisoner right to healthcare through this lens of cruel and unusual punishment, however. As other scholars have observed, prior to the Estelle v Gamble decision by the Supreme Court, at least one court understood the obligation to provide healthcare to prisoners as arising precisely from the decision

51 For example Spicer v. Williamson, 191 N.C. 487, 132 S.E. 291 (1926).
52 For further discussion of the nuances of the research-care constructed dichotomy, see Tom L. Beauchamp & Yashar Saghai, The Historical Foundations of the Research-Practice Distinction in Bioethics, 33 THEOR. MED. BIOETHICS 45–56 (2012) and Nancy E. Kass et al., The Research-Treatment Distinction: A Problematic Approach for Determining Which Activities Should Have Ethical Oversight, 43 HASTINGS CENT. REP. S4–15. (2013). DOI: 10.1002/hast.133.
53 Estelle v. Gamble, 429 U.S. 97, 104, 97 S. Ct. 285, 291 (1976), rehearing denied 429 U.S. 1066, 97 S. Ct. 798 (1977).
54 A review of the caselaw reveals that it is quite difficult to establish a case of inadequate healthcare provided to a prisoner. Establishing a claim requires a prisoner to demonstrate more than negligence, more than typical medical malpractice in a non-prison setting, and even more than gross negligence.
55 Gamble, supra note 53 at 104, 97 S. Ct. at 291. There is also extensive scholarship on the topic of ‘deliberate indifference’, including eg JOHN W. PALMER, CONSTITUTIONAL RIGHTS OF PRISONERS 226–35 (5th ed., 1997); Brittany Bondurant, The Privatization of Prisons and Prisoner Healthcare: Addressing the Extent of Prisoners’ Right to Healthcare, 39 N. ENGL. J. CRIM. CIV. CONF. 407 (2013); Carrie S. Frank, Must Inmates Be Provided Free Organ Transplants: Revisiting the Deliberate Indifference Standard, 15 GEO. MASON U. C.R. L.J. 341, 355 (2004); Michael C. Friedman, Cruel and Unusual Punishment in the Provision of Prison Medical Care: Challenging the Deliberate Indifference Standard, 45 VAND. L. REV. 921 (1992); Rose Carmen Goldberg, The Antidotes to the Double Standard: Protecting the Healthcare Rights of Mentally Ill Inmates by Blurring the Line Between Estelle and Youngberg, 16 YALE J. HEALTH POL’Y, L. & ETHICS 111 (2016); Kari Larsen, Deliberately Indifferent: Government Response to HIV in U.S. Prisons, 24 J. CONTEMP. HEALTH L. & POL’Y 251 (2008); Lori A. Marschke, Proving Deliberate Indifference: Next to Impossible for Mentally Ill Inmates, 39 VAL. U. L. REV. 487 (2004); Marc J. Posner, The Estelle Medical Professional Judgment Standard: The Right to those in State Custody to Receive High Cost Medical Treatments, 18 AM. J. LAW MED. 347 (1992); Christopher Quinn, The Right to Refuse Medical Treatment or to Direct the Course of Treatment: Where Should Inmate Autonomy Begin and End? 35 N. ENGL. J. CRIM. CIV. CONF. 453 (2009); Ira P. Robbins, Managed Health Care in Prisons as Cruel and Unusual Punishment, 90 J. CRIM. L. & CRIMINOLOGY 195 (1999); Richard Siever, HMOs Behind Bars: Constitutional Implications of Managed Healthcare in the Prison System, 58 VAND. L. REV. 487 (2004); Jason L. Stern, Prison (In)Justice: An Examination of the Deliberate Indifference Standard in 42 U.S.C. § 1983 Jail-Suicide Claims, 10 SETON HALL CIR. REV. 173 (2013); Joel H. Thompson, Today’s Deliberate Indifference: Providing Attention Without Providing Treatment to Prisoners with Serious Medical Needs, 45 HARV. C.R.-C.L. L. REV. 635 (2010).
56 Farver v. Brennan, 511 U.S. 825, 827 (1994).
57 Kenneth Kipnis, Social Justice and Correctional Health Services, in MEDICINE AND SOCIAL JUSTICE: ESSAYS IN THE DISTRIBUTION OF HEALTHCARE 373, 373–86 (Rosamond Rhodes et al. eds., 2nd ed., 2012).
to remove the individuals from the societal context in which those individuals are in a position to help themselves. From this perspective, incarceration is a juridic disability to which the government has a responsibility to address. This view is accentuated as prisoner healthcare programs, if federally operated or assisted, are also subject to Title II of the Americans with Disabilities Act (ADA) and Section 504 of the Rehabilitation Act of 1973.

A recent legal development adds another layer of complexity and further support for the argument that modernizing the federal policy for research participant protections should not overlook prisoner participatory rights. An overarching goal of the Patient Protection and Affordable Care Act (or ACA) is to eliminate health disparities, and Section 1557 of ACA prohibits discrimination in health programs and activities on the basis of protected class status (which includes disability as well as race, color, national origin, sex, age, and English proficiency). The Final Rule on Section 1557, which took effect on July 18, 2016, is intended to apply to biomedical research and provides a private right of action for all protected classes for disparate treatment as well as disparate impacts. Some, including Elger and Spaulding (2010), have argued that prisoners should enjoy the same access to biomedical research opportunities as non-prisoners.

International human rights law also lends support to the notion that prisoners not be unnecessarily restricted from precision medicine. The United Nations in its resolution on the treatment of prisoners stated clearly, ‘Prisoners shall have access to the health services available in the country without discrimination on the grounds of their legal situation’. As precision medicine becomes available in the USA, the reasonable interpretation is that this resolution would also indicate that precision medicine should not be denied to prisoners by simple virtue of their prison status.

This (viewed in light of the racial disparities in our criminal justice system, bolstered by an understanding of incarceration as a juridic disability, and recognition of the limits on prison regulations infringing on constitutional rights) opens the door to both criticism and liability for the exclusion of prisoners from biomedical research.

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58 For example, Williamson, supra note 51.
59 Kipnis, supra note 57.
60 See e.g., P.A. Dep’t of Corr. v. Yeskey, 524 U.S. 206, 210 (1999) and Kiman v. N.H. Dep’t of Corr., 451 F.3d 274, 287 (1st Cir. 2006).
61 42 U.S.C. §12101–12213.
62 29 U.S.C. §701–797.
63 pub. L. No. 111-148, 124 Stat. 119 (2010).
64 Janell Ross, Affordable Care Act May Help Close Gap on Health Disparities, THE ATLANTIC, Apr. 9, 2014. http://www.theatlantic.com/politics/archive/2014/04/affordable-care-act-may-help-close-gap-on-health-disparities/430800/ (accessed Dec. 21, 2016).
65 81 Fed. Reg. 31376, 31385 (2016).
66 Bernice S. Elger & Anne Spaulding, Research on Prisoners - A Comparison Between the IOM Committee Recommendations (2006) and European Regulations, 24 BIOETHICS 1 (2010). DOI: 10.1111/j.1467-8519.2009.01776.x.
67 G.A. Res. 45/111, Annex, U.N. Doc. A/RES/45/111/Annex (Dec. 14, 1990).
68 When prison regulations infringe upon constitutional rights (such as retained freedoms of speech and expression, medical care, and equal treatment under the law), the regulations are invalid unless reasonably related to legitimate penological interests. Turner v. Safley, 482 U.S. 78, 89 (1987). See also Timothy Zick, Prisoners’ Rights, FACULTY PUBLICATIONS PAPER 1151 (1991). http://scholarship.law.wm.edu/facpubs/1151 (accessed Dec. 21, 2016).
opportunities and specifically precision medicine solely on the basis of their prisoner status. The scales of justice, respect for persons and autonomy, and beneficence weigh in favor of allowing prisoners, if they so choose, to engage as scientific partners without regard to their prisoner status. The policy position that imprisonment precludes an individual’s exercise of research participatory rights or necessitates a suspension or forfeiture of the individual’s rights to participate in research requires, in the current era of participatory research, re-examination and justification rather than blind acceptance. We cannot allow the mere possibility of exploitation be indisputable grounds for exclusion of the individuals from research. A proper recalibration of regulatory oversight to risks and benefits would involve a reconsideration of the inclusion of prisoners in biomedical research (at least wherein the recruitment strategy is not focused solely on the participation of prisoners).

**RECOMMENDATIONS FOR PMI**

The NIH’s goal to make PMI inclusive of prisoners is commendable but presents significant pragmatic, multifaceted challenges. Cohort retention strategies must consider ways to identify the causes for fluctuating levels of involvement levels for particular PMI research activities and anticipate snowball effects (in order to develop approaches to promote positive effects and mitigate negative ones). Additionally, structural pressures based in funding milestones (eg quotas for ‘full participants’ that PMI enrollment centers must meet) could inadvertently lead to segments of the population being passed over by enrollment centers in order to concentrate on other segments not at as susceptible to attrition due to incarcerations. If regulatory reforms restore prisoner participatory research rights, the PMI has tremendous opportunity to illuminate a trove of scientific questions (eg how do the confined spaces, the built environments, affect microbiomes?) that could improve the health of prisoners and non-prisoners alike.

**CONCLUDING COMMENTS**

The purpose of this article was not to close the discussion of ethical, legal, and social issues regarding the inclusion of prisoners in biomedical research generally. Rather, it was precisely to convey the urgency with which a renewed and deep discussion is needed. Disparities in criminal justice and health are inextricably linked, and we have an affirmative duty69 to eliminate racial discrimination in all its forms, including disparate impacts, from both. Forty years ago the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research 70 was concerned “that prisoners not be unjustly excluded from participation in research”; 71 yet the Commission focused on paternalistic protections from research rather than push for a more just and fair distribution of access to research and benefits and burdens of research. It was true then and remains true today that whether or not prisoners are included in biomedical research

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69 For example, International Convention for the Elimination of All Forms of Racial Discrimination. U.S., Sept. 28, 1966, ratified Oct. 21, 1994, 660 U.N.T.S. 195; G.A. Res. 2106 (XX), Annex, 20 U.N. GAOR Supp. (No. 14) at 47, U.N. Doc. A/6014 (1966).

70 Established by the National Research Act, Pub. L. No. 93-348, 88 Stat. 342 (1974).

71 Branson, supra note 36, at 18 (citing Report and recommendations: research involving prisoners, National Commission, Oct. 1, 1976, at 5).
has symbolic significance for society.\textsuperscript{72} In today’s context of participant-centered research and healthcare, we ought to take another look so that we may learn from the past and shape the future. PMI’s success will undoubtedly be affected by our willingness to do so.

**SUPPLEMENTARY DATA**

Supplementary data are available at *JLBIOS* online.

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\textsuperscript{72} Larry I. Palmer, *Should Prisoners be Permitted to Serve as Subjects of Research?* FACULTY PUBLICATION PAPER No. 521 (1976), at 7, http://scholarship.law.wm.edu/facpubs/521 (accessed Dec. 21, 2016).