

Medical Research Today : The Geography of Vulnerable Populations



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Global Race for Excellence in Research

The Countries Leading The World In Scientific Publications

Number of science & engineering articles published in peer-reviewed journals in 2018

Country	Total	Global share
China	528,263	20.67%
United States	422,808	16.54%
India	135,788	5.31%
Germany	104,396	4.08%
Japan	98,793	3.87%
United Kingdom	97,681	3.82%
Russia	81,579	3.19%
Italy	71,240	2.79%

The Countries With The Most STEM Graduates

Recent graduates in Science, Technology, Engineering & Mathematics (2016)

China	4.7m
India	2.6m
United States	568,000
Russia	561,000
Iran	335,000
Indonesia	206,000
Japan	195,000

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- India and China (both LMIC) have produced highest STEM graduates.
- Nature and other Journals Waiver of Open Access Fees for LMIC
- Pressure to Publish and Conduct Large Scale Research
- LMIC Huge Population, Technical Workforce, Cheaper Medications, Less Regulatory Control

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Scientific Workforce, Global Ambitions and Research Advancement



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Population Vulnerability

Macklin R. (2003). Bioethics, vulnerability, and protection. *Bioethics*, 17(5-6), 472-486.

Schroeder, D., et al (2019). Exploitation Risks in Collaborative International Research. In: *Equitable Research Partnerships. Springer Briefs in Research and Innovation Governance*. Springer, Cham.

Ruth Macklin- "vulnerable people can be exploited even if they are not harmed, and harmed even if they are not exploited"

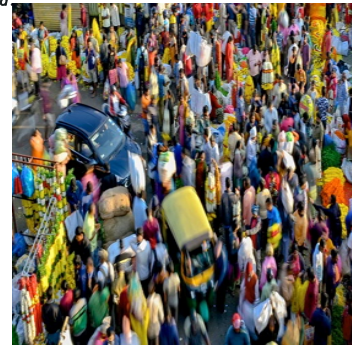
Vulnerability is understood to be a Universal Ontological Condition of Human Existence

Incapable of Protecting their Own Interests, Greatest Risk, Poor Physical, Socioeconomic Status

Most Disadvantaged sub-segment of the Population, Need Maximum Protection in Research

Due to their Circumstances, Vulnerable Communities Inclined to Participate in Studies

Extreme Poverty, History of Colonialism, Lack of Transparency and Accountability



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Ethical Dumping – Exploitation/Misconduct in Collaborative Global Research

- Extreme Power Differentials between Researchers in HICs and Stakeholders in LMICs
- Exploitation -Coercive/ Moral Failing , Instrumentalizes People , Disadvantages the Vulnerable
- Moral Decision – Exploiter(Intended/Unintended), Ignorance Not a Justification for Exploitation
- Vulnerable Population Coerced to Accept (No alternatives- ART Pregnant Women/Placebo)



Schroeder, D., et al (2019). Exploitation Risks in Collaborative International Research. In: Equitable Research Partnerships. SpringerBriefs in Research and Innovation Governance. Springer, Cham.

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Bioethics, Vulnerability and Declaration of Helsinki

Core of Bioethical Inquiry, Early Bioethical Literature Lacked the Concept of Vulnerability.

DOH Landmark Mandated-Protection of the Individual -Vulnerable to Harm through Research

Individuals, Groups or Entire Country can be Vulnerable, Giant Pharma/Industrialized Researchers

Lack of Oversight of Research Ethics Compliance, Lack of Resources. Infrastructure- Compliance

Unethical Practices Considered Acceptable (in certain institutions and situations)






Rogers, W., Mackenzie, C., & Dodds, S. (2012). Why bioethics needs a concept of vulnerability. International Journal of Feminist Approaches to Bioethics, 5(2), 11–28.


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Chronicles of Ethical Violations in Vulnerable Populations (since DOH 2103 update)

A Spill Over Virus Study in Bat Hunting Tribe (Bomrr Tribe) in Nagaland India 2019

-  Bat Hunting/ Eating for Centuries without Overt Viral Diseases, Filovirus Antibodies
-  International Collaborators Involved – NUS Duke University Singapore, NCBS India, Wuhan Institute of Virology – *Plos Neglected Tropical Diseases*
-  All Clearances were Obtained, Protected Tribe – Blood Withdrawal without Informed Consent

Dovih, P., et al (2019). Filovirus-reactive antibodies in humans and bats in Northeast India imply zoonotic spillover. *PLoS neglected tropical diseases*, 13(10), e0007733.



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Chronicles of Ethical Violations in Vulnerable Populations (since DOH 2103 update)

Ethical violations during a clinical trial of a covid-19 vaccine by India's Bharat Biotech and ICMR




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7 Participants in Peoples Hospital Bhopal were not informed if they were given the Vaccine or the Placebo

The Trial Objectives were not Disclosed, Reimbursement and Medical Management of Adverse Reactions were not Mentioned.

Death of 1 trial Participant, Silence of All Agencies Involved

The Forum for Medical Ethics *"The testimonies demonstrate inducement which represents a breach of the tenet of voluntary participation without inducement or coercion. Many participants were misled to enroll in the trial, their vulnerabilities preyed upon."*



BMJ | C. India: Doctors call for investigation into allegations of ethical abuse in covid-19 vaccine trial BMJ 2021; 372 :n131


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Chronicles of Ethical Violations in Vulnerable Populations (since DOH 2103 update)

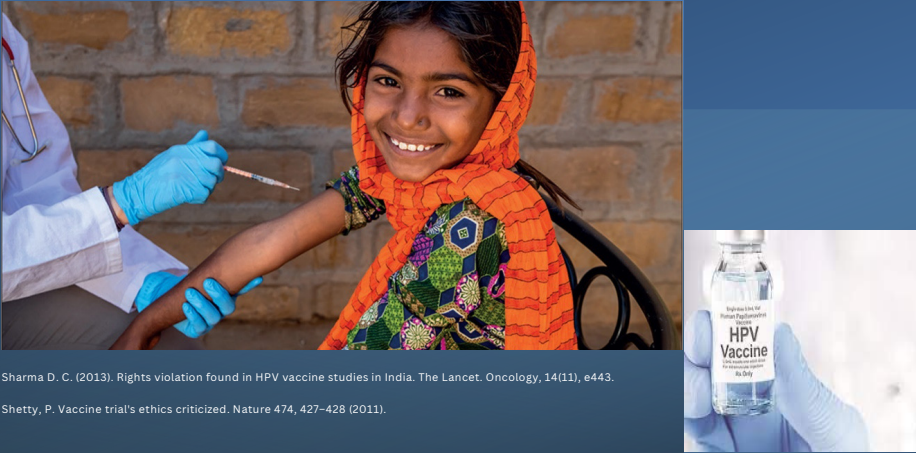
Sharma D. C. (2013). Rights violation found in HPV vaccine studies in India. *The Lancet- Oncology*, 14(11), e443.

Shetty. P. Vaccine trial's ethics criticized. *Nature* 474, 427-428 (2011).

- ICMR and PATH / GATES Foundation HPV Vaccine "Demonstration Project" India – 2009-2011.
- Gardasil, MSD, the Indian subsidiary of Merck and Co. Inc. 14000 children in Rural Andhra , 16000 girls in Gujarath- 7 deaths
- 30 million girls in 40 nations by 2020 (Africa, South America, Vietnam -Poorest Vulnerable Countries)
- HPV Vaccine administered before Marketing Approval, Lack of Consent and Clarity . Terminology (Demonstration Project Instead of Clinical Trials)



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Sharma D. C. (2013). Rights violation found in HPV vaccine studies in India. *The Lancet. Oncology*, 14(11), e443.

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Chronicles of Ethical Violations in Vulnerable Populations (since DOH 2103 update)

Seeding Trial (Marketing Project) Compensation for Faulty Hip Replacements - ASR (Articular Surface Replacement) Johnson and Johnson 2004-2010



CAN A METALLIC INSERTION KILL?


IMPLANT CONTROVERSY

- In August 2010, safety concerns surfaced in ASR hip systems
- Manufactured and observed to have a defect that led to erosion over time
- Release of broken bone fragments, surgery site, loosening of implant, accumulation of metal particles in body, and high levels of metal concentrations in blood among other complications
- A 2011 study stated that hip replacement may be associated with increased risk of melanoma and prostate cancer and with increase of multiple myeloma and leukemia among other things (see lower slide)

J&J'S VERSION

- Johnson & Johnson has not found any patient who has had total hip complications associated with its ASR
- Unlike surgery to total hip
- ASR continues to be used and for people who are not of full weight
- ASR is not a total hip replacement
- All patients should follow up with their surgeons to hip implant evaluation even if they do not experience hip symptoms
- There is no proven connection between hip implants and melanoma or leukemia
- Hip implants are not ASR

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4700 Patients Underwent Hip Replacement, 1080 Traceable, Revision Surgery (15000 units India)

Problem with the Quantum of Compensation in 2017 (2.5 billion USD for 8000 US Patients)

No Faulty Findings in Trial - Journal Article and its Rebuttal

Kindsfater, Kirk & Lesko, Jim. (2017). Survivorship of a modular acetabular cup system: medium- to long-term follow-up. *Arthroplasty*.

Egilman, D. S., Steffen, J. E., Fassler, E. A., & Reardon, K. J. (2018). Letter to the editor on "Survivorship of a modular acetabular cup system: medium- to long-term follow-up". *Arthroplasty today*, 4(3), 392–393.

Steffen, J. E., Fassler, E. A., Reardon, K. J., & Egilman, D. S. (2018). Grave fraudulence in medical device research: a narrative review of the PIN seeding study for the Pinnacle hip system. *Accountability in research*, 25(1), 37–66.

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HIV Cure Research and Quality of Informed Consent

Henderson G. E. (2015). The ethics of HIV "cure" research: what can we learn from consent forms?. *AIDS research and human retroviruses*, 31(1), 56–63.

- Cure trials – Minimizing or Eradication Virus in Circulation and Reservoirs
- Balanced Ethical Oversight- Cautious Use of the Word "Cure"
- HIV Remission Vs Eradication- Over Amplification of Benefits of Intervention
- Conflicting Messaging - Lexicon- Functional Cure, Permanent Cure
- Surrogate End Points- Modify CCR5 Protein, Viral Load Changes




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HIV Cure Research and Global Implementation

Dubé, K., Kanazawa, J et al (2021). Ethics of HIV cure research: an unfinished agenda. BMC medical ethics, 22(1), 83

- HIV Cure Research- Uncertain Outcomes Boston Patient HST, Mississippi Child ART
- Lack of Biomarkers to Accurately Predict Rebound
- Countries with Larger Pool of PLWH (Thailand, India, Africa)
- Indian Institute of Science Education and Research Bhopal circRNA (ciTRAN)
- Analytical treatment interruption (ATI), Infection Transmission to Partners
- Separate Section of Scientific Uncertainty of Intervention (Informed Consent)



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ECHO Consortium Trial and Ethical Violations in Africa (since DOH 2103 update)

Generating new knowledge “this goal can never take precedence over the rights and interests of individual research subjects’ (World Medical Association, 1964)

- Incentives, Coercive Language, Concealing the real nature Trial during Recruitment
- ECHO Consortium Trial (WHO, Gates Foundation) DMPA, LNG, IUD (2015)
- HIV acquisition by Three Methods (Labelling RCT- Clinical versus Controlled)
- Lack of Literacy to Understand IC (regional language), Increase HIV with DMPA(Equipoise)
- Violation of Central Tenet of DOH, Disregard for Women/Girls LICs.



Image IPPF

Sathyamala C. (2022). In the name of science: Ethical violations in the ECHO randomised trial. Global public health, 17(12), 4014–4029

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HIV/AIDS Research : Sub-Saharan Africa

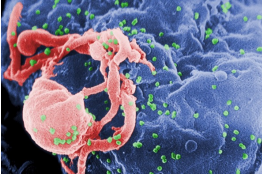
Over Researched Community and Vulnerable to Ethical Violations, Research Fatigue

Many Academics Studying the Same Problem, Proxy Ethical Standards and Safeguards

Sub-Saharan Africa in particular bears 50% of the global burden of the HIV Pandemic

Potential Barrier to Community Participation in Research

Koen, J., Wassenaar, D., & Mamotte, N. (2017). The 'over-researched community': An ethics analysis of stakeholder views at two South African HIV prevention research sites. *Social science & medicine* (1982), 194, 1-9.



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Future Directives : HIV Research in Vulnerable Populations in Resource Limited Settings

- Ethical Issues in Vulnerable Population Centers around Informed Consent, Despite the Heterogeneity of Studies and Settings.
- Fundamental Pre-requisite- Adequate and Comprehensive Informed Consent Tailored to the Population
- Involvement of Cultural Representatives and Community Leaders
- Complex Issues Include- Diminished Autonomy, Language Barriers, Monetary Inducement and Lack of Transparency.
- Promotion of Higher Ethical Standards for Future Research, an Informed Consent that is Truly and Culturally Relevant.

Mystakidou, K., Panagiotou, I., Katsiragakis, S., Tsilika, E., & Parpa, E. (2009). Ethical and practical challenges in implementing informed consent in HIV/AIDS clinical trials in developing or resource-limited countries. *SAHARA J : journal of Social Aspects of HIV/AIDS Research Alliance*, 6(2), 46-57.

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