ge²p² global foundation
governance, ethics, evidence, policy, practice

Genomic Medicine :: Governance, Ethics, Policy, Practice – A Monthly Digest

July 2023 Number 06

Genomic medicine – spanning pre-clinical basic science through clinical development and translation to daily patient interventions – continues to evolve at an extraordinary pace. Advances in the scientific and technical dimensions of genomic medicine are extensively communicated through the peer-reviewed journal literature and supporting grey literature.

Complementing this technical literature is a growing body of research, analysis and commentary addressing the governance, ethics, regulation, and policy dimensions of genomic medicine. Much of this content is communicated through academic journals and grey literature. This digest intends to capture and curate the most substantive examples of this non-technical content.

Further, we intend this digest to provide a useful summary of key strategic and programmatic announcements from across the genomic medicine ecology as issued by multilateral agencies, INGOs, governments/regulatory bodies, academic and research institutions, consortiums and collaborations, foundations, investors, and commercial organizations.

Given the complexity and velocity of the field, we recognize that this digest will be indicative, not exhaustive. We invite suggestions and ideas on how it can evolve to be more useful.

The digest is a program of the GE2P2 Global Foundation which is solely responsible for its content. Questions and comments should be directed to the Editor or Associate Editor:

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With this edition we substantially increase our coverage of the genomic medicine landscape and organize content as below:

Milestones, Strategic Announcements, Research, Actions

In this section, we will present what we assess to be significant developments in the genomic medicine field and provide helpful, additional context via an Editor's Note where indicated. Please help us strengthen this section by alerting us to developments we may not have included.

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Editor's Note

The published proceedings of the Summit below represents an important milestone in completing the cycle of three international meetings held over eight years around governance of human genome editing and associated issues [Washington, 2015; Hong Kong, 2018, London, 2023]. Complementing the published proceedings is the video content capturing the London summit keynotes, speakers and panels available on The Royal Society site: https://royalsociety.org/science-events-and-lectures/2023/03/2023-human-genome-editing-summit/

Third International Summit on Human Genome Editing - Expanding Capabilities, Participation, and Access: Proceedings of a Workshop—in Brief

(2023 :: 15 pages
Contributor(s): National Academies of Sciences, Engineering, and Medicine; Policy and Global Affairs; Steve Olson, Rapporteur
PDF: https://nap.nationalacademies.org/download/27066
Overview
On March 6-8, 2023, at the Francis Crick Institute in London, the UK Royal Society and Academy of Medical Sciences, the U.S. National Academy of Sciences and National Academy of Medicine, and UNESCO-The World Academy of Sciences held the Third International Summit on Human Genome Editing. A follow-up to earlier international summits held in Washington, DC, in 2015 and in Hong Kong in 2018, the third summit examined scientific advances that have occurred since the previous summits and the need for global dialogue and collaboration on the safe and ethical application of human genome editing. The first two days of the summit focused largely on somatic human genome editing, where the cells being altered are non-reproductive cells - as a result genetic changes cannot be passed on to future generations. The third day of the summit broadened the discussion to include heritable human genome editing, in which genetic changes could be passed on to descendants. This publication highlights the presentations and discussions of the event [as well as the statement issued by the organizers just after the Summit].

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Editor's Note

Among key issues engaged during the London Summit above was access, equity and affordability of gene therapies, especially in low resource settings. We feature the IGI analysis below which was underway during the Summit and published earlier in July. We assess that it presents compelling starting points to address equity, access and affordability by considering fundamental structural changes in the ecosystem supporting current gene therapy development.

Making Genetic Therapies Affordable and Accessible

Innovative Genomics Institute July 2023 :: 75 pages
PDF: https://innovativegenomics.org/atf-report/
Overview

While genetic therapies hold the promise of targeted treatments that address the underlying causes of diseases, their staggering cost may keep them out of reach for those who need them most.

At the Innovative Genomics Institute, our mission is to develop genetic therapies that are affordable and accessible to all.

Starting in Winter 2021, IGI's Public Impact team, led by Melinda Kliegman, assembled a task force of 30 experts charged with first exploring key drivers of high prices and proposing alternative approaches to developing and deploying a genetic therapy that could reach more patients.

Key Findings

Pricing: We put forward a dynamic cost-plus model for pricing new genetic therapies that could lead to a sticker price that is 10x less than genetic therapies on the market.

Organization and Funding Models: Besides for-profit corporations (C-corps), non-profit medical research organizations and public benefit corporations (B-corps) offer alternative organizational structures that could, in theory, reduce the sticker price. For these to be successful lower-cost capital (requiring a lower rate of returns) is needed to control costs.

Intellectual property: Academic technology transfer offices (TTOs) can play a significant role in improving affordability and access via licenses provisions and requiring access plans.

Manufacturing: Manufacturing a genetic therapy to stringent regulatory standards is a key driver of cost. We discuss various innovations, point-of-care manufacturing and regulatory streamlining that could lower prices while maintaining safety and efficacy.

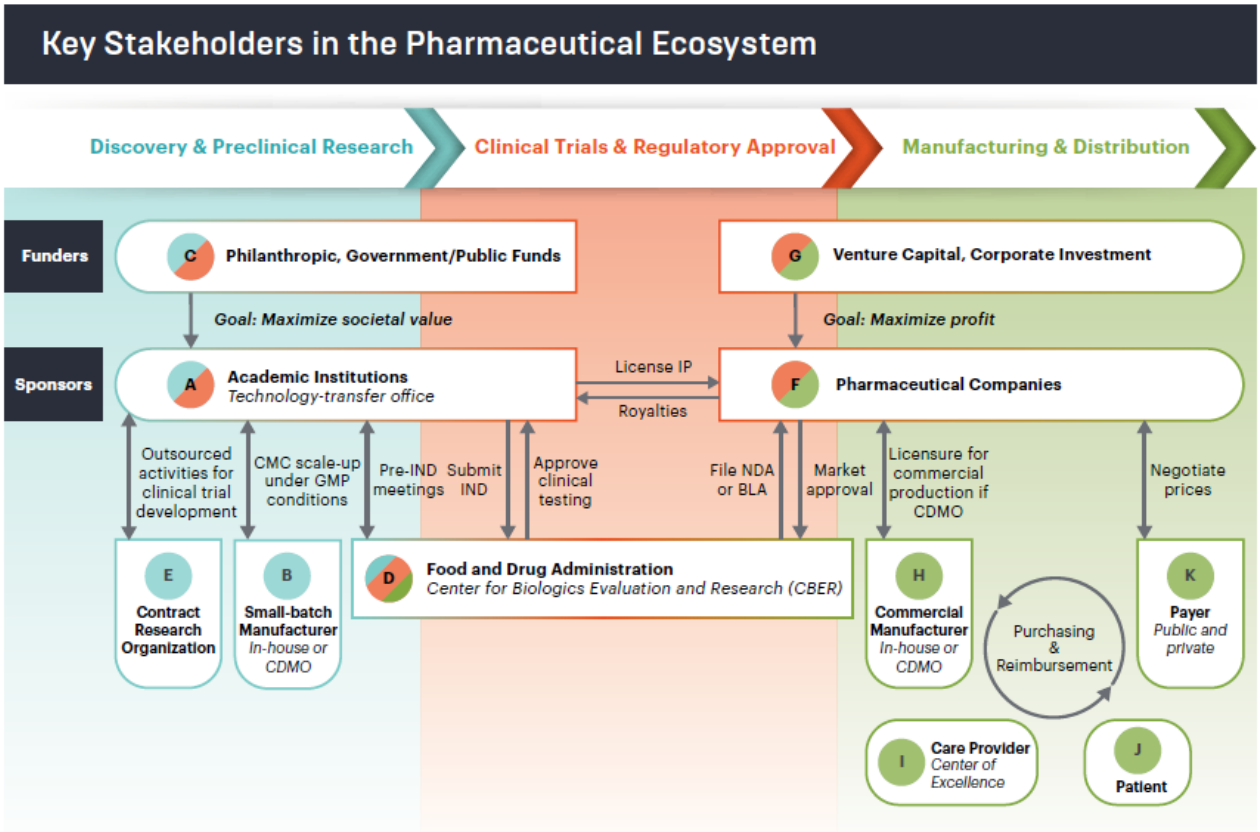

Figure 2: The Key Stakeholders and Interactions Involved in Bringing a Genetic Therapy from Conception to Patients

EXECUTIVE SUMMARY *[Excerpt; Editor's text bolding]*

…**This report is the conclusion of a year-long deliberation by 30 individuals with expertise spanning from preclinical development of genetic therapies to healthcare economics, intellectual property rights, and biomanufacturing, with the goal of identifying concrete steps to make genetic therapies**

affordable and accessible. Genetic therapies hold the potential of transformational health outcomes, yet at prices surpassing $3M, affordability and access are of significant concern to patients and payers alike. We evaluated alternative approaches to developing and deploying a genetic therapy that would reach more patients. We discussed how a non-traditional entity would be organized and financed and how it might price a genetic therapy. We also scoped manufacturing efficiencies and identified strategies for intellectual property (IP) and pricing.

The three decade history of cell and gene therapy shows that academic institutions are the primary originators of novel therapeutic strategies and typically accept government and philanthropic grants to conduct research, generating significant intellectual property. In turn this IP is licensed to for-profit organizations who further develop the product. This model belies a contradiction for academic institutions; while most have a public benefit mission, which supports making final products generated with university IP affordable and accessible, they generate valuable income from licensing intellectual property and are reasonably concerned about requirements that would deter licensees. **We believe that changes to intellectual property licensing practices are one of the easiest/ first changes that academic institutions can take to promote access**. We propose that academic institutions should impose reasonable requirements in licenses that ensure access to life-saving therapies. Some recommendations include explicitly supporting academic technology transfer offices (TTOs) in activities to improve affordability and access, consideration of non-exclusive licenses particularly in low- and middle-income countries, and the development of access plans that identify how the product will reach patients without private insurance or facing other barriers to access.

With regard to organizational models that can operate in parallel to publicly traded, for-profit companies, **Task Force members first evaluated existing, non-traditional, pharmaceutical entities. They determined a mixed organizational model comprising an academic institution, a nonprofit medical research organization (MRO), and a public benefit corporation (PBC) could be an ideal structure.** The MRO would accept funding from grants and private philanthropy to conduct research, it could concentrate intellectual property, conduct clinical trials, and generate further income by selling priority review vouchers from FDA approvals. Subsequently, the MRO could license core technology to a PBC, which could price a drug based on the cost of goods and labor to manufacture, plus some surplus to ensure sustainability. For example, a PBC could manage manufacturing, distribution, and negotiations with payers. The PBC would also be charged with fundraising and expanding sources of revenue by working with socially-oriented VC firms and seeking early investment from payers or offering services.

Lastly, we would like to acknowledge that manufacturing a genetic therapy to stringent regulatory standards is a key driver of cost. While entities currently developing therapies need to comply with existing regulations, the FDA has shown an impetus to update regulatory requirements to make products more accessible. In particular, we expect that increased regulatory support for point-of-care manufacturing models would drive down prices and allow greater geographic access while not reducing the safety or efficacy of the treatments. We provide examples where other governments, who have supported point-of-care manufacturing models, have increased affordability.

In the year since we initiated this report several companies have decided to either delay or discontinue further development of genetic therapies in their pipeline, some for explicit business reasons. From our analysis, it seems that in addition to challenging manufacturing and delivery mechanisms, **the need to generate enough capital to recoup investments is confounding**. We present concrete actions that academic institutions and downstream stakeholders can take to address these issues, allowing more therapies to enter the market and thereby improve access through competition.

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Editor's Note
This month marks two years since the WHO Expert Advisory Committee on Developing Global Standards for Governance and Oversight of Human Genome Editing issued three reports including recommendations [available here: https://www.who.int/publications/i/item/9789240030381]. There are open questions about what has happened of substance since. We include the WHO call-for-experts below [just expired] primarily to reflect further on the functions/remit of the technical advisory group in formation.

WHO - Call for Experts: Technical Advisory Group on Genomics

DEADLINE: 16 July 2023

This call builds on WHO's enduring efforts in the field of Genomics and follows the publication of the Report "Accelerating access to genomics for global health: promotion, implementation, collaboration, and ethical, legal and social issues" by the WHO Science Council in 2022.

The WHO is now seeking to establish a Technical Advisory Group on Genomics to Support and provide technical guidance on activities implemented by the WHO Secretariat to accelerate access to genomics technologies for global health, with a particular focus on human genomics.

WHO welcomes expressions of interest from professionals with expertise in a diverse set of fields related to genomics (and in particular human genomics), the application of genomics technologies for cancer, congenital disorders, rare diseases, R&D in the field of genome-based knowledge, and implementation of genomics technologies. Attention will also be given to ensure inclusion of relevant expertise in ethics, law and relevant social sciences domains.

Functions of the Technical Advisory Group on Genomics

In its capacity as an advisory group to the WHO, the Technical Advisory Group will have the following functions:

- Support and provide technical guidance on activities implemented by the WHO Secretariat to accelerate access to genomics technologies for global health, with a particular focus on human genomics;
- Review and recommend priority activities for consideration by WHO in order to accelerate access to genomics technologies for global health, including promotion and advocacy in addition to technical activities;
- Contribute to, and advise the WHO Secretariat's on efforts in convening discussions by scientists, policymakers, patient advocates, clinicians, lawyers, ethicists, and others to develop genomics-related guidance and reports;
- Support WHO to bringing attention to regional and sub-regional opportunities and experiences in genomics;
- Contribute to assessing, and report annually to the WHO Secretariat, on progress in accelerating access to genomics for global health;
- Undertake other duties and functions consistent with these Terms of Reference, when requested by the WHO Secretariat.

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Editor's Note
One of the key disease areas addressed in the London Summit referenced above was sickle cell disease [SCD], where important advanced continue in the cell-gene space with obvious and fundamental challenges in terms of equity and access. We note with concern the Lancet Commission's positioning of these advanced interventions as requiring 15+ years before reaching global impact [see 2040 horizon text].

The Lancet Haematology
Comment|Online First

The Lancet Haematology Commission on sickle cell disease: key recommendations

The sickle cell disease Commissioners
Published: July 11, 2023 DOI: https://doi.org/10.1016/S2352-3026(23)00154-0
[Excerpts]
…Cellular therapies

Haematopoietic stem-cell transplantation with a matched sibling donor has been established as an effective cure for sickle cell disease. However, although there have been major advances in technique and thousands of procedures performed, fewer than 1% of people with sickle cell disease have been cured in this way. The use of this treatment is rare because it is expensive, requires sophisticated medical facilities, and suitable donors are not available for most individuals. Haematopoietic stem-cell transplantation is associated with clinically significant morbidity and mortality and has therefore been largely reserved for the most severely affected patients. Technological advances are starting to solve some of these problems by expanding the potential numbers of donors and reducing toxicity, with the potential to cure far more individuals with sickle cell disease in the relatively near future, assuming resources can be put in place in all countries to make this possible.

In parallel, ex-vivo gene therapy is emerging as an alternative option, and although this is currently a hugely expensive experimental treatment, it might be available commercially soon. Less toxic conditioning and in-vivo gene therapy have the potential to provide affordable and more widely accessible treatments in the future.

The Commission recommends accelerated development of these stem cell therapies, with a view to providing safe and accessible cures globally by 2040, and that future trials should develop approaches specifically for use in LMICs.…

Conclusions

Better public health and research programmes for sickle cell disease are needed in all countries, although the greatest need is in LMICs, where most individuals with the condition live and where the majority of people with sickle cell disease still die in childhood. Most of the recommendations in this Commission require immediate actions on the part of governments to provide basic levels of care for people with sickle cell disease, including screening programmes and genetic counselling; the provision of specialist clinical services and adequately trained staff; and access to essential medicines, including protection against infection and hydroxyurea. The cost of newborn screening and these basic medicines is beyond the reach of most individuals living in sub-Saharan Africa and India and needs to be directly funded by governments. With adequate engagement of governments, the changes identified in this Commission are achievable and will improve the quality and quantity of life for people with sickle cell disease throughout the world.

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Institution/Organization Announcements *[list in early formation]*

We recognize this this listing is incomplete, unbalanced and skewed to the Global North…please help us make it more complete, more inclusive, and more useful by recommending additional organizations/institutions/ programs to monitor.

Academy of Medical Sciences [UK] [accessed 20 July 2023]
https://acmedsci.ac.uk/
News
Five priorities to make biomedical science green
Monday 5 June 2023

Africa CDC - Institute of Pathogen Genomics [IPG] [accessed 20 July 2023]
https://africacdc.org/institutes/ipg/
Africa PGI is an initiative of the Africa CDC Institute for Pathogen Genomics, a continent-wide leadership initiative established in 2019 to support public health pathogen genomics and bioinformatics across Africa.
News & Announcements
The Africa CDC hands over sequencing equipment to the Republic of Cameroon
4 July 2023
"…will enable the Republic of Cameroon as part of joint efforts to strengthen pathogen genomic surveillance…"

African Society of Human Genetics [accessed 20 July 2023]
https://www.afshg.org/
Press Releases
[No new digest content identified]

Paul G. Allen Frontiers Group [to 21 Jul 2023]
https://alleninstitute.org/news-press/
News
[No new digest content identified]

ARM [Alliance for Regenerative Medicine] [to 21 Jul 2023]
https://alliancerm.org/press-releases/
Selected Press Releases
[No new digest content identified]

BMGF - Gates Foundation [to 21 Jul 2023]
https://www.gatesfoundation.org/ideas/media-center
Press Releases and Statements
[No new digest content identified]

Bill & Melinda Gates Medical Research Institute [to 21 Jul 2023]
https://www.gatesmri.org/news
The Bill & Melinda Gates Medical Research Institute is a non-profit biotech organization. Our mission is to develop products to fight malaria, tuberculosis, and diarrheal diseases—three major causes of mortality, poverty, and inequality in developing countries. The world has unprecedented scientific tools at its disposal; now is the time to use them to save the lives of the world's poorest people
News: Articles and Publications
[No new digest content identified]

American College of Medical Genetics [accessed 20 July 2023]
https://www.acmg.net/
The ACMG is the only nationally recognized interdisciplinary professional membership organization that represents the interests of the entire medical genetics team including clinical geneticists, clinical laboratory geneticists, and genetic counselors.

News & Releases

ACMG SF v3.2 list for reporting of secondary findings in clinical exome and genome sequencing: A policy statement of the American College of Medical Genetics and Genomics (ACMG)

June 22, 2023

…"We continue to balance the goals of providing secondary findings to patients while striving for a minimum list of the most actionable, and impactful, secondary findings," said lead author and co-chair of the ACMG SFWG, David T. Miller, MD, PhD, FACMG.

American Board of Medical Genetics and Genomics (ABMGG) [accessed 20 July 2023]

http://www.abmgg.org/pages/resources_appeal.shtml

The mission of the ABMGG is to serve the public and medical profession by establishing professional certification standards and promoting lifelong learning as well as excellence in medical genetics and genomics.

[No new digest content identified]

American Society of Human Genetics (ASHG) [accessed 20 July 2023]

http://www.ashg.org/

We work to advance human genetics and genomics in science, health, and society through excellence in research, education, and advocacy.

Press Releases

ASHG Awarded Five-Year, $7.1-Million Contract for Genomics and Public Service Fellowship Program

June 20, 2023

American Society for Gene and Cell Therapy [ASGCT] [accessed 20 July 2023]

https://asgct.org/

News/Publications

ASGCT's 2023 Q2 Landscape Analysis Field Report

July 13, 2023

The second quarterly report of 2023 from ASGCT and Citeline is available now! The Gene, Cell, & RNA Therapy Landscape report is the only field-wide report covering the therapeutics pipeline, clinical targets, developer progress, and more.

Highlights from this issue include:

:: Approval of six therapies, including two gene therapies that are the first to be approved for their respective indications

:: More gene therapies moving into Phase II trials in the past quarter than have in more than a year

:: A six percent increase in dealmaking over the previous quarter and a quarterly high in the last year

ARRIGE [accessed 20 July 2023]

https://www.arrige.org/

News

ARRIGE Scientific Committee Statement about EC proposal on New Genomic Techniques regulation in plants

15 July 2023

Broad Institute of MIT and Harvard [accessed 20 July 2023]
A collaborative research institute focused on genomics and personalized medicine, undertaking various projects in genomic medicine.
https://www.broadinstitute.org/
Latest News
News 07.19.2023
Researchers reprogram gene therapy viral vectors to bind specific protein targets

CDC – Office of Genomics and Precision Public Health
https://www.cdc.gov/genomics/default.htm
Population-based Genomic Screening Programs: The Need for Optimal Implementation to Ensure Health Equity
Population genomic screening of adults has emerged as a strategy to promote prevention of common diseases such as cancer and heart disease among persons with genetic conditions. This type of screening has the potential to identify millions of currently undetected people in the United States who are at risk of preventable diseases for which evidence-based
Posted on June 20, 2023 by Nandana D. Rao, W. David Dotson, Muin J. Khoury, Office of Genomics and Precision Public Health, National Center on Birth Defects and Developmental Disabilities, Centers for Disease Control and Prevention, Atlanta, Georgia

Center for Genetics and Society [USA] [accessed 20 July 2023]
www.geneticsandsociety.org
… a non-profit public affairs and policy advocacy organization working to encourage responsible uses and effective societal governance of human genetic and reproductive biotechnologies.
Press
[No new digest content identified]

Center for the Ethics of Indigenous Genomic Research [CEIGR] – University of Oklahoma [accessed 20 July 2023]
https://www.ou.edu/cas/anthropology/ceigr
[No new digest content identified on website]

Published in Variant Bio
CEIGR Training Provides Key Insights Into the Social and Ethical Implications of Genomic Research
Sarah LeBaron von Baeyer, PhD
18 July 2023

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Francis Crick Institute [accessed 20 July 2023]
https://www.crick.ac.uk/news-and-reports
News
New genome editing film highlights the 'Lost Voices' of people living with genetic conditions
Type: News 13 July 2023

Publication of our annual animal research numbers
Type: News 13 July 2023

New study to develop genetic therapies for muscular dystrophy
Type: News 11 July 2023

Ethics & Genetics [accessed 20 July 2023]
http://www.ethicsandgenetics.org/
We are an independent, non-partisan, not-for-profit civil society organisation, campaigning for public awareness and democratic participation in the governance of genetic technology.
[No new digest content identified]

FDA Cellular & Gene Therapy Guidances
https://www.fda.gov/vaccines-blood-biologics/biologics-guidances/cellular-gene-therapy-guidances
Manufacturing Changes and Comparability for Human Cellular and Gene Therapy Products; Draft Guidance for Industry – Call for Comment
FDA - Issued by: Center for Biologics Evaluation and Research 07/13/2023
Docket Number: FDA-2023-D-2436
Draft Guidance PDF: https://www.fda.gov/media/170198/download
Deadline: comments on the draft guidance by September 12, 2023
The management of manufacturing changes presents many challenges for human cellular therapy or gene therapy (CGT) products due to the complexity of these products. We, FDA, are providing you, sponsors of Investigational New Drug Applications (INDs) and applicants of Biologics License Applications (BLAs) for CGT products, with recommendations regarding product comparability and the management of manufacturing changes for investigational and licensed CGT products. The purpose of this guidance is to provide FDA's current thinking on 1) management and reporting of manufacturing changes for CGT products based on a lifecycle approach, and 2) comparability studies to assess the effect of manufacturing changes on product quality.

Genetic Alliance [accessed 20 July 2023]
http://www.geneticalliance.org/
News/Press Releases
[No new digest content identified]

Genomic Medicine Alliance [accessed 20 July 2023]
https://www.genomicmedicinealliance.org
…a global academic research network which aims to build and strengthen collaborative ties between academics, researchers, regulators and also members from the general public interested in genomic and personalized medicine.
[No new digest content identified]

The Genomic Medicine Foundation [accessed 20 July 2023]
https://www.genomicmedicine.org
The Genomic Medicine Foundation is a non-profit organization providing up to date and evidence-based information on genetics/genomics relevant to clinical medicine and healthcare.
News, Events
The IX International Cardiovascular Genomic Medicine Conference
October 23 - October 24

Surgeon's Quarter Mission Hall Edinburgh, 1 Roxburgh Place
Edinburgh, Scotland EH8 9SU

Global Genomic Medicine Consortium [G2MC} [accessed 20 July 2023]
https://g2mc.org/
G2MC is an international community formed to advance the implementation of genomic medicine and improve health for all.
G2MC News
G2MC Quarterly Newsletter – June 2023
Read about G2MC's latest news, updates, events and more in the June 2023 newsletter.
2023-06-28

Genomic Medicine Clinics for Rare Genetic Disorders: Potential for Expansion and Collaboration
The Genomic Medicine Clinics for Rare Genetic Disorders pilot project completed its initial goal of implementing exome sequencing for the diagnosis of rare uncharacterized and undiagnosed diseases in six clinical sites located in low- and middle-income countries.
2023-06-28

Global Citizens' Assembly on Genome Editing (GCA) [accessed 20 July 2023]
https://www.globalca.org/
Latest News
[No new digest content identified]

Genomics England [accessed 20 July 2023]
https://www.genomicsengland.co.uk/
We partner with the NHS to provide whole genome sequencing diagnostics. We also equip researchers to find the causes of disease and develop new treatments – with patients and participants at the heart of it all.
Latest
21 Jun 2023
Genomics England seeks new members for its ethics and access committees

Genetics Society of America (GSA) [accessed 20 July 2023]
http://genetics-gsa.org/
Using the tools of genetics and genomics, nearly 6,000 GSA members from more than 50 countries around the world investigate a wide variety of biological questions and applications.
News
[No new digest content identified]

HHMI - Howard Hughes Medical Institute [to 21 Jul 2023]
https://www.hhmi.org/news
Press Room
[No new digest content identified]

H3Africa [accessed 20 July 2023]
https://h3africa.org/
News
[No new digest content identified]

Innovative Genomics Institute
https://innovativegenomics.org/about-us/
The IGI is composed of diverse researchers at the University of California, Berkeley, the University of California, San Francisco, and the University of California, Davis. Together, our scientists have powerful combined expertise. They conduct world-class research, driven by the real possibility of using genome engineering to treat human diseases, end hunger, and respond to climate change.
News
Making Genetic Therapies Affordable and Accessible: IGI's New Recommendations
July 6, 2023 Press Releases
By Hope Henderson
In 2022, IGI's Public Impact Team launched a year-long Affordability Task Force (ATF) project aimed at solving one of the trickiest challenges for genomic medicines: price.,,, "Our focus is on accessibility for low-income individuals living in the United States, and also on accessibility for individuals in low and middle-income countries. This is particularly crucial for sickle cell disease, which is one of our flagship projects," says Kliegman. To learn more about the ATF and read the complete ATF Report with recommendations for how to bring down prices for genomic therapies, click here.

INSERM [to 21 Jul 2023]
https://www.inserm.fr/en/home/
Press Releases
[No new digest content identified]

NIH [to 21 Jul 2023]
http://www.nih.gov/
News Releases
[No new digest content identified]

NIH National Human Genome Research Institute (NHGRI) [accessed 20 July 2023]
https://www.genome.gov/
News
NHGRI's Intramural Research Program enters new phase
July 06, 2023
…NHGRI is also excited to have recently awarded the American Society of Human Genetics (ASHG) over $7 million to support the new Genomics and Public Service Fellowship Program. The program will expand on the existing joint fellowships between the two organizations and will help early-stage professionals interested in policy, communications, education, and program management gain hands-on skills and experience in genomics.

NIH – All of Us Research Program [accessed 20 July 2023]
https://allofus.nih.gov/news-events/announcements

An historic effort to collect and study data from one million or more people living in the United States. The goal of the program is better health for all of us. Our mission is to accelerate health research and medical breakthroughs, enabling individualized prevention, treatment, and care for all of us. This mission is carried out through three connected focus areas that are supported and made possible by a team that maintains a culture built around the program's core values.

Announcements

Applied Genomics and Biological Technologies (AGBT) Precision Health Meeting Workshop: Leveraging the All of Us Researcher Workbench to Advance Precision Health

In this workshop at the AGBT Precision Health Meeting, attendees will learn about the extensive data available on the All of Us Researcher Workbench. They will also complete an example genomic analysis. The workshop will be held on September 7 from 2:45 – 4:15 p.m.

Review the AGBT Precision Health Meeting Agenda

Type: Event

Institut Pasteur [to 21 Jul 2023]

https://www.pasteur.fr/en/press-area

Press Documents

[No new digest content identified]

Nuffield Council on Bioethics [to 21 Jul 2023]

https://www.nuffieldbioethics.org/news

News

[No new digest content identified]

Penn Center for Global Genomics & Health Equity [University of Pennsylvania] [accessed 20 July 2023]

https://globalgenomics.med.upenn.edu/index.php

Latest News

[No new digest content identified]

The Royal Society [accessed 20 July 2023]

https://royalsociety.org/

What's New

[No new digest content identified]

UNESCO–The World Academy of Sciences [accessed 20 July 2023]

https://twas.org/

News

[No new digest content identified]

Wellcome Sanger Institute [accessed 20 July 2023]

https://www.sanger.ac.uk/

A leading genomics research institute in the United Kingdom, known for its work in sequencing genomes and understanding the role of genetics in health and disease.

News

18 Jul 2023

New cholera substrains in Bangladesh uncovered by genomic surveillance confirm the importance of vaccination

A new study has analysed and tracked the spread of this bacterial disease within a vulnerable community, highlighting the importance of ...

17 Jul 2023

Prime Editing

Prime editing is the latest technique that enables scientists to alter the DNA of a living cell. It builds on CRISPR-Cas9 technology, and offers the potential to edit human cells to treat genetic diseases.

WHO - Human genome editing [accessed 20 July 2023]
https://www.who.int/teams/health-ethics-governance/emerging-technologies/human-genome-editing
News; Publications
[No new digest content identified]

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Academic Journal Watch

With this edition we establish a baseline of journals we will monitor on an ongoing basis, complemented by key articles from other peer-reviewed journals identified through google scholar and other search methods. If you would like to suggest a journal to be monitored for this section, please contacts the editors as above.

The American Journal of Bioethics
23:7, 1-4, 20 June 2023
Guest Editorials
Innovating for a Just and Equitable Future in Genomic and Precision Medicine Research
Deanne Dunbar Dolan, Mildred K. Cho & Sandra Soo-Jin Lee

This special issue of the American Journal of Bioethics comprises ELSI research focused on equity and inclusion of diverse public in genomic and precision medicine research. Articles in this issue represent work presented at the **5th ELSI Congress**: Innovating for a Just and Equitable Future held June 1-3, 2022, a biennial conference supported by the National Human Genome Research Institute (NHGRI) at the National Institutes of Health (NIH) and organized by the ELSI Congress 2022 Organizing Committee.

Introduction

From its inception, genomics has been a speculative endeavor, fixated on a far-off horizon that would deliver on the promise of targeted diagnostics and individualized therapeutics (Fortun 2008). More recently, the data-driven approach of precision medicine research furthers this trajectory by investigating individual differences in genes, environment, and lifestyle (Jooma et al. 2019). The substantial investment in genomic and precision medicine has begun to yield clinically useful interventions, yet questions about benefit and access create uncertainty about our ability to achieve equity goals. If the prediction by the National Human Genome Research Institute that "individuals from ancestrally diverse backgrounds will benefit equitably from advances in human genomics" by 2030 is to be taken seriously, ethical, legal, and social implications (ELSI) research must engage with the meaning of equity and questions about whether and how genomic and precision medicine can achieve these goals in a geopolitical landscape characterized by extreme economic inequality and structural racism (Chancel and Piketty 2021; Green et al. 2020, 690;Yearby, Clark, and Figueroa 2022).

Transparency about scientific practice and the extensive data collection and triangulation necessary for genomic and precision medicine will be critical to the production of trustworthy science (Lee et al. 2019). Sampling bias resulting in research datasets comprised mostly of samples from individuals of European ancestry (Popejoy and Fullerton 2016; 'Tsosie et al. 2021) means that peoples underrepresented in genomic research studies are more likely to receive non-informative or inaccurate genetic test results in the clinic (Burke 2021; Chapman-Davis et al. 2021; Landry and Rehm 2018; Manrai et al. 2016). Unequal access to genetic testing and interventions due to affordability, genetic literacy, and trust in the healthcare system have already undermined implementation of genomic applications (Khoury et al. 2022). Disparities and delays in access to genetic services for low income and minority patients in the U.S. are well documented (Chapman-Davis et al. 2021; Fraiman and Woicik 2021; Gene Hallford et al. 2020; Hoskins et al. 2018; Omorodion et al. 2022; Shields, Burke, and Levy 2008; Wojcik et al. 2023). These barriers are likely to determine which Americans will be able to access and benefit from the substantial public investment in genomic and precision medicine and may undermine public trust in science (Lee 2021; Lee et al. 2019; Reardon et al. 2023).

Fully realizing the promise of equity will require investment in the study of sociopolitical, economic, legal, regulatory, and environmental factors that parallels the public investment in genomics (Lee 2021). Leveraging multidisciplinary expertise and ELSI scholarship to address key questions should be paramount, including scholars and scholarship that can elucidate the roles of the built environment and health systems in facilitating or impeding equitable access, approaches for identifying and prioritizing the interests of communities, the creation of transparent public-private partnerships, and design of effective engagement to define the public good for genomic and precision medicine. This means centering the experiences of marginalized populations to create policies and practices that empower communities underrepresented in biomedical research to negotiate the terms of their research participation, ownership of their data, and the meaning of equitable benefit (Fox 2020; T'sosie et al. 2021).

American Journal of Human Genetics
Volume 110, Issue 7, 6 July 2023, Pages 1021-1033
Review
Studying the impact of translational genomic research: Lessons from eMERGE
Ellen Wright Clayton, Maureen E. Smith, Katherine C. Anderson, Wendy K. Chung, John J. Connolly, Stephanie M. Fullerton, Michelle L. McGowan, Josh F. Peterson, Cynthia A. Prows, Maya Sabatello, Ingrid A. Holm
Summary
Two major goals of the Electronic Medical Record and Genomics (eMERGE) Network are to learn how best to return research results to patient/participants and the clinicians who care for them and also to assess the impact of placing these results in clinical care. Yet since its inception, the Network has confronted a host of challenges in achieving these goals, many of which had ethical, legal, or social implications (ELSIs) that required consideration. Here, we share impediments we encountered in recruiting participants, returning results, and assessing their impact, all of which affected our ability to achieve the goals of eMERGE, as well as the steps we took to attempt to address these obstacles. We divide the domains in which we experienced challenges into four broad categories: (1) study design, including recruitment of more diverse groups; (2) consent; (3) returning results to participants and their health care providers (HCPs); and (4) assessment of follow-up care of participants and measuring the impact of research on participants and their families. Since most phases of eMERGE have included children as well as adults, we also address the particular ELSI posed by including pediatric populations in this research. We make specific suggestions for improving translational genomic research to ensure that future projects can effectively return results and assess their impact on patient/participants and providers if the goals of genomic-informed medicine are to be achieved.

Annals of Internal Medicine
2023; 176:779-787. June 2023
Original Research
Distributional Cost-Effectiveness of Equity-Enhancing Gene Therapy in Sickle Cell Disease in the United States
George Goshua, Cecelia Calhoun, Satoko Ito, Lyndon P. James, Andrea Luviano, Lakshmanan Krishnamurti, and Ankur Pandya
Abstract
Background
Gene therapy is a potential cure for sickle cell disease (SCD). Conventional cost-effectiveness analysis (CEA) does not capture the effects of treatments on disparities in SCD, but distributional CEA (DCEA) uses equity weights to incorporate these considerations.
Objective
To compare gene therapy versus standard of care (SOC) in patients with SCD by using conventional CEA and DCEA. *Design*: Markov model. *Data Sources:* Claims data and other published sources. *Target Population:* Birth cohort of patients with SCD. *Time Horizon*: Lifetime. *Perspective*: U.S. health system. *Intervention*: Gene therapy at age 12 years versus SOC. *Outcome Measures*: Incremental cost-effectiveness ratio (ICER) (in dollars per quality-adjusted life-years [QALYs] gained) and threshold inequality aversion parameter (equity weight). *Results of Base-Case Analysis*: Gene therapy versus SOC for females yielded 25.5 versus 15.7 (males: 24.4 vs. 15.5) discounted lifetime QALYs at costs of $2.8 million and $1.0 million (males: $2.8 million and $1.2 million), respectively, with an ICER of $176 000 per QALY (full SCD population). The inequality aversion parameter would need to be 0.90 for the full SCD population for gene therapy to be preferred per DCEA standards.
Results of Sensitivity Analysis
SOC was favored in 100.0% (females) and 87.1% (males) of 10 000 probabilistic iterations at a willingness-to-pay threshold of $100 000 per QALY. Gene therapy would need to cost less than $1.79 million to meet conventional CEA standards.
Limitation
Benchmark equity weights (as opposed to SCD-specific weights) were used to interpret DCEA results.
Conclusion
Gene therapy is cost-ineffective per conventional CEA standards but can be an equitable therapeutic strategy for persons living with SCD in the United States per DCEA standards.
Primary Funding Source
Yale Bernard G. Forget Scholars Program and Bunker Endowment.

BMJ Global Health
2023;8: e011884, 05 July 2023
Public health use of HIV phylogenetic data in sub-Saharan Africa: ethical issues
Analysis
Euzebiusz Jamrozik, Nchangwi Syntia Munung, Lucie Abeler-Dorner, Michael Parker
Abstract
Phylogenetic analyses of HIV are an increasingly accurate method of clarifying population-level patterns of transmission and linking individuals or groups with transmission events. Viral genetic data may be used by public health agencies to guide policy interventions focused on clusters of transmission or segments of the population in which transmission is concentrated. Analyses of HIV phylogenetics in high-income countries have often found that clusters of transmission play a significant role in HIV epidemics. In sub-Saharan Africa, HIV phylogenetic analyses to date suggest that clusters of transmission play a relatively minor role in local epidemics. Such analyses could nevertheless be used to guide priority setting and HIV public health programme design in Africa for sub-populations in which transmission events are more concentrated.

Phylogenetic analysis raises ethical issues, in part due to the range of potential benefits and potential harms (i.e., risks). Potential benefits include (1) improving knowledge of transmission patterns, (2) informing the design of focused public health interventions for subpopulations in which transmission is concentrated, (3) identifying and responding to clusters of transmission, (4) reducing stigma (in some cases) and (5) informing estimates of the (cost-)effectiveness of HIV treatment programmes. Potential harms include (1) privacy infringements, (2) increasing stigma (in some cases), (3) reducing trust in public health programmes, and (4) increased prosecution of legal cases where HIV transmission, homosexuality or sex work is criminalised. This paper provides analysis of relevant issues with a focus on sub-Saharan Africa in order to inform consultations regarding ethical best practice for HIV phylogenetics.

BMC Health Services Research

Volume 23, Article number: 484 (2023). 13 May 2023

Research

How are health technology assessment bodies responding to the assessment challenges posed by cell and gene therapy?

Michael Drummond, Oriana Ciani, Giulia Fornaro, Claudio Jommi, Eva Susanne Dietrich, Jaime Espin, Jean Mossman & Gerard de Pouvourville

Open access

Abstract

Background

The aims of this research were to provide a better understanding of the specific evidence needs for assessment of clinical and cost-effectiveness of cell and gene therapies, and to explore the extent that the relevant categories of evidence are considered in health technology assessment (HTA) processes.

Methods

A targeted literature review was conducted to identify the specific categories of evidence relevant to the assessment of these therapies. Forty-six HTA reports for 9 products in 10 cell and gene therapy indications across 8 jurisdictions were analysed to determine the extent to which various items of evidence were considered.

Results

The items to which the HTA bodies reacted positively were: treatment was for a rare disease or serious condition, lack of alternative therapies, evidence indicating substantial health gains, and when alternative payment models could be agreed. The items to which they reacted negatively were: use of unvalidated surrogate endpoints, single arm trials without an adequately matched alternative therapy, inadequate reporting of adverse consequences and risks, short length of follow-up in clinical trials, extrapolating to long-term outcomes, and uncertainty around the economic estimates.

Conclusions

The consideration by HTA bodies of evidence relating to the particular features of cell and gene therapies is variable. Several suggestions are made for addressing the assessment challenges posed by these therapies. Jurisdictions conducting HTAs of these therapies can consider whether these suggestions could be incorporated within their existing approach through strengthening deliberative decision-making or performing additional analyses.

BMC Medical Ethics

http://www.biomedcentral.com/bmcmedethics/content

(Accessed 21 Jul 2023)

[No new digest content identified]

BMC Medicine

http://www.biomedcentral.com/bmcmed/content
(Accessed 21 Jul 2023)
[No new digest content identified]

Cell Genomics
Jul 12, 2023 Volume 3 Issue 7
https://www.cell.com/cell-genomics/current
Previews
The human pangenome reference anticipates equitable and fundamental genomic insights
Kelly A. Frazer, Nicholas J. Schork
For the past few years, researchers in the Human Pangenome Reference Consortium (HPRC) have been working to catalog almost all human genomic diversity. Frazer and Schork preview an article recently published in Nature, "A draft human pangenome reference,"1 which represents the initial release of 47 fully phased diploid assemblies of genomes of individuals with diverse ancestries.

OpenPBTA: The Open Pediatric Brain Tumor Atlas
Joshua A. Shapiro, et al., Children's Brain Tumor Network, Pacific Pediatric Neuro-Oncology Consortium
The OpenPBTA is a global, collaborative open-science initiative that brought together researchers and clinicians to genomically characterize 1,074 pediatric brain tumors and 22 patient-derived cell lines. Shapiro et al. create over 40 open-source, scalable modules to perform cancer genomics analyses and provide a richly annotated somatic dataset across 58 brain tumor histologies. The OpenPBTA framework can be used as a model for large-scale data integration to inform basic research, therapeutic target identification, and clinical translation.

Clinical Therapeutics
June 2023 Volume 45 Issue 6 p483-616
http://www.clinicaltherapeutics.com/current
[Reviewed earlier]

Clinical Trials
Volume 20 Issue 3, June 2023
https://journals.sagepub.com/toc/ctja/20/3
[New issue; No digest content identified]

Current Genetic Medicine Reports
Volume 10, issue 3, September 2022
https://link.springer.com/journal/40142/volumes-and-issues/10-3
[Reviewed earlier]

Current Medical Research and Opinion
Volume 39, Issue 7 2023
https://www.tandfonline.com/toc/icmo20/current
[New issue; No digest content identified]

Current Protocols in Human Genetics
Volume 108, Issue 1 December 2020

https://currentprotocols.onlinelibrary.wiley.com/toc/19348258/current
[Reviewed earlier]

Epidemics
Volume 43, June 2023, 100690; 06 June 2023
Article
Optimal capacity sharing for global genomic surveillance
Zsombor Z. Méder, Robert Somogyi
Open access
Abstract
Recent technological advances and substantial cost reductions have made the genomic surveillance of pathogens during pandemics feasible. Our paper focuses on full genome sequencing as a tool that can serve two goals: the estimation of variant prevalences, and the identification of new variants. Assuming that capacity constraints limit the number of samples that can be sequenced, we solve for the optimal distribution of these capacities among countries. Our results show that if the principal goal of sequencing is prevalence estimation, then the optimal capacity distribution is less than proportional to the weights (e.g., sizes) of countries. If, however, the main aim of sequencing is the detection of new variants, capacities should be allocated to countries or regions that have the most infections. Applying our results to the sequencing of SARS-CoV-2 in 2021, we provide a comparison between the observed and a suggested optimal capacity distribution worldwide and in the EU. We believe that following such quantifiable guidance will increase the efficiency of genomic surveillance for pandemics.

Genetics in Medicine
Volume 25, Issue 6, June 2023, 100832; 27 April 2023
Article
Individualized interventions for rare genetic conditions and the research-treatment spectrum: Stakeholder perspectives
Sandra Soo-Jin Lee, Mikaella Caruncho, Wendy K. Chung, Josephine Johnston, Kathryn Tabb, Paul S. Appelbaum
Abstract
Purpose
Advances in the study of ultra-rare genetic conditions are leading to the development of targeted interventions developed for single or very small numbers of patients. Owing to the experimental but also highly individualized nature of these interventions, they are difficult to classify cleanly as either research or clinical care. Our goal was to understand how parents, institutional review board members, and clinical geneticists familiar with individualized genetic interventions conceptualize these activities and their implications for the relationship between research and clinical care.
Methods
We conducted qualitative, semi-structured interviews with 28 parents, institutional review board members, and clinical geneticists and derived themes from those interviews through content analysis.
Results
Individuals described individualized interventions as blurring the lines between research and clinical care and focused on hopes for therapeutic benefit and expectations for generalizability of knowledge and benefit to future patients.
Conclusion
Individualized interventions aimed at one or few patients reveal the limitations of a binary framing of research and clinical care. As a hybrid set of activities, individualized interventions suggest the need for flexibility and new frameworks that acknowledge these activities across the spectrum of research and clinical care.

Genome Medicine
https://genomemedicine.biomedcentral.com/articles
[Accessed 21 Jul 2023]
[No new digest content identified]

JAMA
July 11, 2023, Vol 330, No. 2, Pages 101-198
https://jamanetwork.com/journals/jama/currentissue
Original Investigation
Rapid Whole-Genomic Sequencing and a Targeted Neonatal Gene Panel in Infants With a Suspected Genetic Disorder
Jill L. Maron, MD, MPH; Stephen Kingsmore, MD; Bruce D. Gelb, MD; et al.
has audio
JAMA. 2023;330(2):161-169. doi:10.1001/jama.2023.9350
This prospective multicenter study of 400 hospitalized infants with a suspected genetic disorder evaluated rates of molecular diagnostic yield, time to return of results, and clinical utility by comparing between genomic sequencing and targeted neonatal gene-sequencing testing.

JAMA Health Forum
July 2023, Vol 4, No. 7
https://jamanetwork.com/journals/jama-health-forum/issue
JAMA Forum
What Artificial Intelligence Means for Health Care
David M. Cutler, PhD
open access
JAMA Health Forum. 2023;4(7):e232652. doi:10.1001/jamahealthforum.2023.2652
This JAMA Forum discusses 5 observations about the possible effects of artificial intelligence on medicine.

Journal of Medical Ethics
02 June 2023
Ethical preparedness and developments in genomic healthcare
Extended essay
Bobbie Farsides, Anneke M Lucassen
Open access
Abstract
Considerations of the notion of preparedness have come to the fore in the recent pandemic, highlighting a need to be better prepared to deal with sudden, unexpected and unwanted events. However, the concept of preparedness is also important in relation to planned for and desired interventions resulting from healthcare innovations. We describe ethical preparedness as a necessary component for the successful delivery of novel healthcare innovations, and use recent advances in genomic healthcare as an example. We suggest that practitioners and organisations charged with delivering innovative and ambitious healthcare programmes can only succeed if they are able to exhibit the attribute of ethical preparedness.

The Journal of Pediatrics
Volume 261, October 2023, 113537, 02 June 2023

Reflections on Ethics and Advocacy in Child Health

Genomics Research with Undiagnosed Children: Ethical Challenges at the Boundaries of Research and Clinical Care

Meghan C. Halley, Jennifer L. Young, Charis Tang, Kevin T. Mintz, Sawyer Lucas-Griffin, Audrey Stephannie Maghiro, Euan A. Ashley, Holly K. Tabor, The Undiagnosed Diseases Network

Abstract

Objective

To explore the perspectives of parents of undiagnosed children enrolled in genomic diagnosis research regarding their motivations for enrolling their children, their understanding of the potential burdens and benefits, and the extent to which their experiences ultimately aligned with or diverged from their original expectations.

Study design

In-depth interviews were conducted with parents, audio-recorded and transcribed. A structured codebook was applied to each transcript, after which iterative memoing was used to identify themes.

Results

Fifty-four parents participated, including 17 (31.5%) whose child received a diagnosis through research. Themes describing parents' expectations and experiences of genomic diagnosis research included (1) the extent to which parents' motivations for participation focused on their hope that it would directly benefit their child, (2) the ways in which parents' frustrations regarding the research process confused the dual clinical and research goals of their participation, and (3) the limited clinical benefits parents ultimately experienced for their children.

Conclusions

Our results suggest that parents of undiagnosed children seeking enrollment in genomic diagnosis research are at risk of a form of therapeutic misconception—in this case, diagnostic misconception. These findings indicate the need to examine the processes and procedures associated with this research to communicate appropriately and balance the potential burdens and benefits of study participation.

The Journal of Philosophy of Disability

04 July 2024

Article

Gene Editing Technologies, Utopianism, and Disability Politics

Amber Knight

Abstract

Scholars have long speculated about what a future affected by gene editing technologies might hold. This article enters current debates over the future of gene editing and the place of disability within it. Specifically, I evaluate contemporary utopian thinking about gene editing found in two different schools of thought: transhumanism and critical disability studies, ultimately judging the latter to be richer and more politically promising than the former. If we take it as our goal to protect and promote future people's autonomy interests, I argue that current political efforts should be directed toward modifying ableist environments rather than employing genetic technologies to avoid disability or enhance capacity. The article concludes by drawing from disability justice scholarship to make the case that the "right to an open future" should be understood as the "right to an accessible future," one wherein society is "open" to people with diverse genetic traits and capacities.

The Lancet

Jul 15, 2023 Volume 402 Number 10397 p159-264, e4

https://www.thelancet.com/journals/lancet/issue/current

Comment

Achieving justice in implementation: the Lancet Commission on Evidence-Based Implementation in Global Health
Herbert B Peterson, Queen Dube, Joy E Lawn, Joumana Haidar, Jessamy Bagenal, Richard Horton
on behalf of the Lancet Commission on Evidence-Based Implementation in Global Health

The Lancet Child & Adolescent Health
Jun 2023 Volume 7 Number 6 p367-440, e12
https://www.thelancet.com/journals/lanchi/issue/current
[Reviewed earlier]

Medicine, Health Care and Philosophy
06 June 2023
Scientific Contribution
The fertility of moral ambiguity in precision medicine
Jeanette Bresson Ladegaard Knox & Mette Nordahl Svendsen
Open access
Abstract
Although precision medicine cuts across a large spectrum of professions, interdisciplinary and cross-sectorial moral deliberation has yet to be widely enacted, let alone formalized in this field. In a recent research project on precision medicine, we designed a dialogical forum (i.e. 'the Ethics Laboratory') giving interdisciplinary and cross-sectorial stakeholders an opportunity to discuss their moral conundrums in concert. We organized and carried out four Ethics Laboratories. In this article, we use Simone de Beauvoir's concept of *moral ambiguity* as a lens to frame the participants' experience with fluid moral boundaries. By framing our approach through this concept we are able to elucidate irremediable moral issues that are collectively underexplored in the practice of precision medicine. Moral ambiguity accentuates an open and free space where different types of perspectives converge and can inform each other. Based on our study, we identified two dilemmas, or thematic interfaces, in the interdisciplinary moral deliberations which unfolded in the Ethics Laboratories: (1) the dilemma between the individual and the collective good; and (2) the dilemma between care and choice. Through our investigation of these dilemmas, we show how Beauvoir's concept of moral ambiguity not only serves as a fertile catalyst for greater moral awareness but, furthermore, how the concept can become an indispensable part of the practices of and the discourse about precision medicine.

Nature
Volume 619 Issue 7969, 13 July 2023
https://www.nature.com/nature/volumes/619/issues/7969
[Reviewed earlier]

Nature Biotechnology
Volume 41 Issue 6, June 2023
https://www.nature.com/nbt/volumes/41/issues/6
[Reviewed earlier]

Nature Genetics
Volume 55 Issue 6, June 2023
https://www.nature.com/ng/volumes/55/issues/6
[Reviewed earlier]

New England Journal of Medicine
July 13, 2023 Vol. 389 No. 2
https://www.nejm.org/toc/nejm/medical-journal
[New issue; No digest content identified]

Pediatrics
Volume 152, Issue 1 July 2023
https://publications.aap.org/pediatrics/issue/152/1
[Reviewed earlier]

PharmacoEconomics
Volume 41, issue 7, July 2023
https://link.springer.com/journal/40273/volumes-and-issues/41-7
[Reviewed earlier]

PLoS Genetics
https://journals.plos.org/plosgenetics/
(Accessed 21 Jul 2023)
[No new digest content identified]

Public Health Genomics
2023, Vol. 26, No. 1
https://karger.com/phg/issue/26/1
Review Article
Integrating Genomics into the Care of People with Palliative Needs: A Global Scoping Review of Policy Recommendations
Stephanie White

Molecular Therapy
Volume 31, Issue 7, P1859, 05 July 2023
ASGCT 2023—Gene therapy is becoming medicine-
Editorial
Roland W. Herzog, Courtney Bricker-Anthony
Abstract
The 26th annual meeting of the American Society of Gene Therapy (ASGCT) took place in Los Angeles in May 2023. This year's meeting celebrated the precision that gene therapy has achieved, ranging from gene editing to specific targeting of cancer cells by receptor-engineered lymphocytes. Gene editing in particular took center stage this year during the Presidential Symposium. Jennifer Doudna explained the principle of gene editing using the CRISPR system and its applications in treatment of human diseases, while David Liu enlightened us on the ever-increasing precision of these evolving technologies and expansion of the toolkit to base and prime editors that do not require making DNA breaks. The strong interest in this area was also well reflected by the abstracts presented at the meeting. Gene editing and correction were among the top-performing abstract categories, accounting for 14% of all abstract submissions and 16% of all oral abstract presentations. Moreover, gene editing and correction are expanding into the clinic, as demonstrated by

Haydar Frangoul, who focused on the highly promising outcomes of a clinical trial on gene editing for the treatment of transfusion-dependent β-thalassemia and severe sickle cell disease. Furthermore, J. Keith Joung received the society's Outstanding Achievement Award for his contributions to the development of nucleases for gene editing applications.

Nature Reviews Genetics
(2023), 29 June 2023
Review Article
Genomic newborn screening for rare diseases
Zornitza Stark & Richard H. Scott
Abstract
Rare diseases are a leading cause of infant mortality and lifelong disability. To improve outcomes, timely diagnosis and effective treatments are needed. Genomic sequencing has transformed the traditional diagnostic process, providing rapid, accurate and cost-effective genetic diagnoses to many. Incorporating genomic sequencing into newborn screening programmes at the population scale holds the promise of substantially expanding the early detection of treatable rare diseases, with stored genomic data potentially benefitting health over a lifetime and supporting further research. As several large-scale newborn genomic screening projects launch internationally, we review the challenges and opportunities presented, particularly the need to generate evidence of benefit and to address the ethical, legal and psychosocial issues that genomic newborn screening raises.

Science
Volume 381| Issue 6654| 14 Jul 2023
https://www.science.org/toc/science/current
Special issue: A machine-intelligent world
[No new digest content identified]

Science Translational Medicine
Volume 15| Issue 704| 12 Jul 2023
https://www.science.org/toc/stm/current
[No new digest content identified]

Social Studies of Science
0(0), 20 June 2023
Research Article
After biosovereignty: The material transfer agreement as technology of relations
Sonja van Wichelen
Abstract
Increasingly, countries in the Global South—notably South Africa, Brazil, and Indonesia—are introducing material transfer agreements (MTAs) into their domestic laws for the exchange of scientific material. The MTA is a contract securing the legal transfer of tangible research material between organizations such as laboratories, pharmaceutical companies, or universities. Critical commentators argue that these agreements in the Global North have come to fulfill an important role in the expansion of dominant intellectual property regimes. Taking Indonesia as a case, this article examines how MTAs are enacted and implemented differently in the context of research involving the Global South. Against the conventionally understood forms of contract that commodify and commercialize materials and knowledge, the MTA in the South can be understood as a legal technology appropriated to translate a formerly relational economy of the scientific gift

to a market system of science. As a way of gaining leverage in the uneven space of the global bioeconomy, the MTA functions as a technology for 'reverse appropriation', a reworking of its usage and meaning as a way of countering some of the global power inequalities experienced by Global South countries. The operation of this reverse appropriation, however, is hybrid, and reveals a complex reconfiguration of scientific exchange amidst a growing push for 'open science'.

Pre-Print Servers

Gates Open Research
https://gatesopenresearch.org/browse/articles
[Accessed 21 Jul 2023]
Selected Research
[No new digest content identified]

medRxiv
https://www.medrxiv.org/content/about-medrxiv
[Accessed 21 Jul 2023]
[Filter: All articles]
Selected Research
On the limitations of large language models in clinical diagnosis
Justin Reese, Daniel Danis, J Harry Caufield, Elena Casiraghi, Giorgio Valentini, Christopher J Mungall, Peter N Robinson
medRxiv 2023.07.13.23292613; doi: https://doi.org/10.1101/2023.07.13.23292613
Abstract
Background:
The potential of large language models (LLM) such as GPT to support complex tasks such as differential diagnosis has been a subject of debate, with some ascribing near sentient abilities to the models and others claiming that LLMs merely perform "autocomplete on steroids". A recent study reported that the Generative Pretrained Transformer 4 (GPT-4) model performed well in complex differential diagnostic reasoning. The authors assessed the performance of GPT-4 in identifying the correct diagnosis in a series of case records from the New England Journal of Medicine. The authors constructed prompts based on the clinical presentation section of the case reports, and compared the results of GPT-4 to the actual diagnosis. GPT-4 returned the correct diagnosis as a part of its response in 64% of cases, with the correct diagnosis being at rank 1 in 39% of cases. However, such concise but comprehensive narratives of the clinical course are not typically available in electronic health records (EHRs). Further, if they were available, EHR records contain identifying information whose transmission is prohibited by Health Insurance Portability and Accountability Act (HIPAA) regulations. Methods:
To assess the expected performance of GPT on comparable datasets that can be generated by text mining and by design cannot contain identifiable information, we parsed the texts of the case reports and extracted Human Phenotype Ontology (HPO) terms, from which prompts for GPT were constructed that contain largely the same clinical abnormalities but lack the surrounding narrative.
Results:
While the performance of GPT-4 on the original narrative-based text was good, with the final diagnosis being included in its differential in 29/75 cases (38.7%; rank 1 in 17.3% of cases; mean rank of 3.4), the performance of GPT-4 on the feature-based approach that includes the major clinical abnormalities without additional narrative tests substantially worse, with GPT-4 including the final diagnosis in its differential in 8/75 cases (10.7%; rank 1 in 4.0% of cases; mean rank of 3.9).
Interpretation:

We consider the feature-based queries to be a more appropriate test of the performance of GPT-4 in diagnostic tasks, since it is unlikely that the narrative approach can be used in actual clinical practice. Future research and algorithmic development is needed to determine the optimal approach to leveraging LLMs for clinical diagnosis.

Wellcome Open Research
2023, 7:302. 12 May 2023
Open Letter
REVISED - Towards an appropriate African framework for public engagement with human genome editing: a call to synergistic action
Gerald Michael Ssebunnya
Abstract
The CRISPR-Cas9 system has revolutionised the biotechnology of human genome editing. Human germline gene editing promises exponential benefits to many in Africa and elsewhere, especially those affected by the highly prevalent monogenic disorders - for which, thanks to CRISPR, a relatively safe heritable radical therapy is a real possibility. Africa evidently presents a unique opportunity for empirical research in human germline gene editing because of its high prevalence of monogenic disorders. Critically, however, germline gene editing has raised serious ethical concerns especially because of the significant risks of inadvertent and intentional misuse of its transgenerational heritability. Calls for due prudence have become even more pronounced in the wake of the 2018 case of He Jiankui's 'CRISPR'd babies'. Meanwhile, Africa is seriously lagging in articulating its position on human genome editing. Conspicuously, there has been little to no attempt at comprehensively engaging the African public in discussions on the promises and concerns about human genome editing. Thus, the echoing key question remains as to how Africa should prudently embrace and govern this revolutionary biotechnology. In this article, therefore, I lay the groundwork for the possible development of an appropriate African framework for public engagement with human genome editing and call upon all stakeholders to urgent synergistic action. I particularly highlight the World Health Organisation's possible leadership role in promptly establishing the requisite expert working group for this urgent need.

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Editor's Note
*We include below a number of chapter abstracts from the new book :***Handbook of Bioethical Decisions"**
and will consider inclusion of book chapters [and whole books} as an extension of our literature coverage.

Handbook of Bioethical Decisions

Springer, Cham. 15 June 2023
Selected Chapters

Bioethical Decision-Making About Somatic Cell Genome Editing: Sickle-Cell Disease as a Case Study
Chapter
Christopher Rudge & Dianne Nicol
Handbook of Bioethical Decisions. Volume I. pp 49–77, Collaborative Bioethics, vol 2. Springer, Cham. 15 June 2023
Abstract
Somatic cell genome editing (SCGE) now allows exquisitely precise and targeted non-heritable changes to be made to human DNA. While SCGE has many possible applications, clinical trials indicate its great potential to provide new forms of medical treatment, as well as cures, for a range of prevalent monogenic diseases, including several disorders of the blood (hemoglobinopathies). This chapter provides an overview of the

nature of somatic cells, a discussion of their connection with genetic disease, and a summary of the bioethical issues that attend various therapeutic uses of the system. The chapter takes sickle-cell disease as a case study, identifying the advantages that SCGE promises over the current best treatment, as well as the issues that will likely compel patients, clinicians and others to engage in difficult bioethical decision-making. Lastly, the chapter takes up four bioethical principles—nonmaleficence, beneficence, autonomy and justice—to analyze some of the most pressing bioethical issues associated with SCGE, as well as recent recommendations for governing the technology published by the World Health Organization.

Learning from Icarus: The Impact of CRISPR on Gene Editing Ethics

Chapter

Brendan Parent

Handbook of Bioethical Decisions. Volume I. pp 9–27, Collaborative Bioethics, vol 2. Springer, Cham. 15 June 2023

Abstract

After centuries of crude genetic engineering through crossbreeding, the ability to directly intervene in life's fundamental blueprint led to breakthroughs including longer lasting produce, cheaper insulin without using animal organs, and research animal models demonstrating disease progressions. But this was slow, resource-intensive work. After four decades of moderate technique advancements, CRISPR-Cas9 burst on the scene and blew the doors off previous gene editing (GE) mechanisms. Suddenly, long-standing philosophical thought experiments about whether we should put wings on donkeys and design virtuoso violinists became more concrete possibilities. Most say the ease, speed, and great potential of CRISPR do not fundamentally change the gene editing ethics questions, they just make it more urgent to answer them. But CRISPR traits do change the ethics. They play to our hopes, make us take risks, and might threaten our commitment to solidarity. This chapter explores long-standing GE ethics considerations including utilitarian calculations, "Playing God," transparency and democracy, informed consent, treating disease versus accepting difference, and most importantly fairness and equity. Each ethics issue will be demonstrated through current and near-future gene editing applications, and will focus on how these interplays are impacted by the unique attributes of CRISPR based tools.

Research with Human Biological Samples: Systematization of the Phases and Affected Rights

Chapter

Pilar Nicolás Jiménez

Handbook of Bioethical Decisions. Volume I. Decisions at the bench, pp 279-294; Springer.

Abstract

The legal nature of human biological samples is complex, which implies that their collection, storage, use and transfer for research purposes affect different rights of the subjects. In particular, this study will address the implications for the right to physical integrity, the right of disposal of body parts and the right to the protection of personal data. On the other hand, the concurrence of other interests and rights justifies the design of governance systems that also guarantee the availability of samples to facilitate research, as well as scientific collaboration. Many countries have adopted specific regulations on the use of biological samples for research purposes, but there are no binding international regulations on the subject.
However, certain commonly accepted principles can be identified in this area.

Biobanking in Global Health & Research

Chapter

J. W. Ashcroft & C. C. Macpherson

Handbook of Bioethical Decisions. Volume I. pp 325–343, Collaborative Bioethics, vol 2. Springer, Cham. 15 June 2023

Abstract

Biobanking of patient-derived materials is routine in health care, research, and public health emergencies. Ethical guidelines for biobanking address concerns including some about genetic materials, informed

consent, confidentiality, regulatory environments, and standards of governance. This chapter identifies some limitations of existing guidelines that were apparent to one author during an Ebola outbreak, and specifies five ethical concerns about biobanking that warrant additional attention: misconceptions about biobanking, unknown consequences for donors, socioeconomic inequities that compound vulnerabilities, lasting and proportional benefits in North-South research, and contextual challenges to disclosure and understanding. These affect patients, donors, health systems, research, and policy, and are amplified during public health emergencies.

Ethical and Legal Considerations in Genomic Data Sharing: Evolution of the Discourse and the Road Ahead

Chapter

Adrian Thorogood & Davit Chokoshvili

Handbook of Bioethical Decisions. Volume I. pp 345–369, Collaborative Bioethics, vol 2. Springer, Cham. 15 June 2023

Abstract

The importance of genomic data sharing has long been recognized across a range of contexts, from community resource projects to biomedical research seeking insights into diseases, to the provision of personalized healthcare. However, so far, the opportunities of genomic data sharing at scale have not been fully realized. This chapter explores some of the main ethical and legal issues posed by genomic data sharing among institutions and across jurisdictions. The most vexing issues stem from concerns over data privacy and security, consent, and protection of data subjects' fundamental rights. Additional challenges relate to meeting legal consent and transparency requirements in some jurisdictions (including the European Union) where the recipients and uses of data cannot be fully specified in advance. Ethical and legal data governance frameworks play an important role in addressing these concerns and enabling responsible data sharing. Divergence between regulatory frameworks, privacy protection, consent models, and governance frameworks across contexts and countries remain a barrier to scale data sharing across networks, but can be addressed through a combination of institutional coordination and creative infrastructure design.

Rare Disease Research

Chapter

Francesc Palau & Carmen Ayuso

. Volume I. pp 123–143, Collaborative Bioethics, vol 2. Springer, Cham. 15 June 2023

Abstract

We address ethical issues in the field of rare diseases (RDs) focusing on four aspects that are relevant for research and translation into clinical practice. First, the reuse of personal, health and genomic data, for research purposes, beyond the main purpose for which they were collected. Later, three aspects related to fundamental parts of clinical medicine such as diagnosis, treatment and prevention in relation to RDs. In this context, we address ethical aspects of research and its practical application that have to do with the diagnostic effort in patients with undiagnosed diseases. A third topic is research programs in rare disease therapy and their translation into the treatment of patients. Finally, some points are discussed regarding the incorporation of genomic analysis in newborn screening, having the analysis of genetic variants as a complementary biomarker to biochemical tests that allows expanding the number of RDs in which to act preventively.

Precision Medicine

Chapter

Fruzsina Molnár-Gábor

Handbook of Bioethical Decisions. Volume I. pp 415–439, Collaborative Bioethics, vol 2. Springer, Cham. 15 June 2023

Abstract

Precision medicine combines genetic, environmental and lifestyle variability to inform disease diagnosis, treatment and prevention, allowing exact medical interventions both on individual and population levels.

Data-driven precision medicine measures constitute an informational intervention that is dynamic in time, space and in terms of actors and groups involved, as well as regarding the relevance of results and the causality of decisions. Correspondingly, normative guidance for decision making is characterised by strong proceduralisation. When justifying data processing, the changing role of patients in relation to data processing needs to be respected. It not only influences the design of informed consent, but significantly impacts data security in response to identified risks. Further issues in precision medicine include dealing with anonymisation as well as the return of research results. New tools such as machine learning and its application through neurotechnologies pose challenges to patients' autonomy, benefit production, sharing, justice and equity. In response to the need for dynamic guidance to engage with these particular challenges, procedural measures and tools framing conduct of precision medicine have emerged, including codes of conduct, closer ethics committee scrutiny and data stewardship models. These tools enable ethics-by-design and contribute to coordination between ethical and legal rules.

Ethical Issues in Genetically Modified Foods: From Transgenesis to CRISPR-Cas9 Genome Editing Technology

Chapter

Erick Valdés & Juan Alberto Lecaros

Handbook of Bioethical Decisions. Volume I. pp 723–736, Collaborative Bioethics, vol 2. Springer, Cham. 15 June 2023

Abstract

Traditional ethical quandaries related to GM foods have been addressed profusely throughout the years. Still, some concerns remain regarding potential impacts on human health, natural environment and society. Moreover, the emergence of new genome editing technologies, such as CRISPR-Cas9, has implied relevant breakthroughs for plant and animal breeding. However, this enormous milestone in biotechnology has also raised new and unprecedented quandaries involving ethical, regulatory, policy and global governance dimensions. In this chapter, we analyze some of the ethical concerns that the production of GM foods involves, by addressing and discussing "traditional" issues as well as those emerging from new genome editing techniques.

Ethical Issues Concerning Genetically Modified Animals for the Study of Human Diseases

Chapter

Eduardo Rodríguez Yunta

Handbook of Bioethical Decisions. Volume I. pp 513–525, Collaborative Bioethics, vol 2. Springer, Cham. 15 June 2023

Abstract

The development of genetically modified model organisms for the study of human diseases may be beneficial in the research of causes and possible treatments, but there are serious concerns about animal welfare and safety issues that must be addressed. Guidelines and regulations for the use and care of genetically modified organisms are needed to improve their welfare. The appropriateness of genetically modified organisms suitable for modeling human disease should be evaluated, as well as an analysis of benefits versus harms. In establishing biotechnology using animal models for the study of human disease is important to listen to the public concerns of civilians so that research is subjected to public scrutiny.

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