National Institutes of Health
Office of Science Policy

Science Policy and Personalized Medicine

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Office of Science Policy
National Institutes of Health

PMC Policy Meeting
April 16, 2019

Overview

- Science Policy at the NIH

- Intersection of Science Policy and Personalized Medicine
  - Data sharing
  - Privacy
  - Applicability
  - New paradigms in clinical research

Science Policy at the NIH

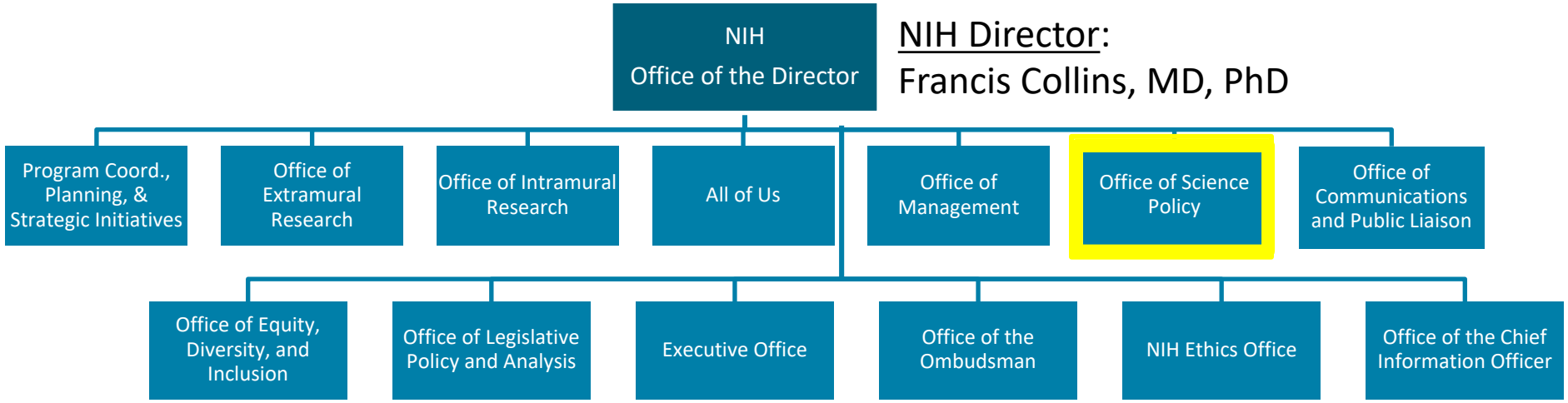
NIH Organization

Science Policy at the NIH

- The Office of the Director (OD) is the central NIH office for its 27 Institutes and Centers
- The NIH Office of the Director is responsible for setting policy for NIH and for planning, managing, and coordinating the programs and activities of all the NIH components

NIH Office of the Director (OD)

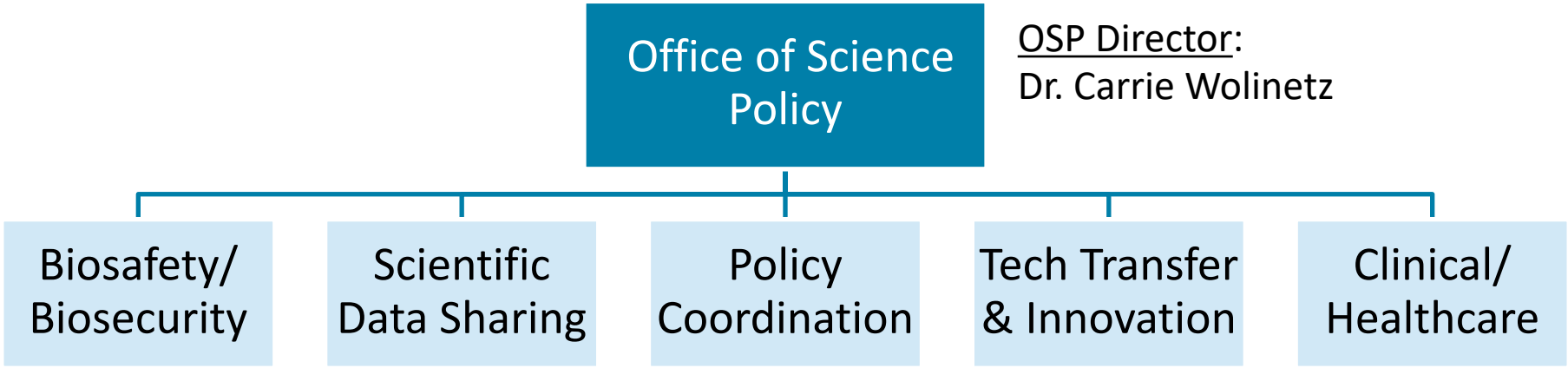
Science Policy at the NIH



- The NIH Office of Science Policy (OSP) is within the NIH Office of the Director and is one of 10^{+} principal offices
- OSP's mission is to promote biomedical research progress through development of sound and comprehensive policies for the conduct and oversite of biomedical research

NIH Office of Science Policy (OSP)

Science Policy at the NIH

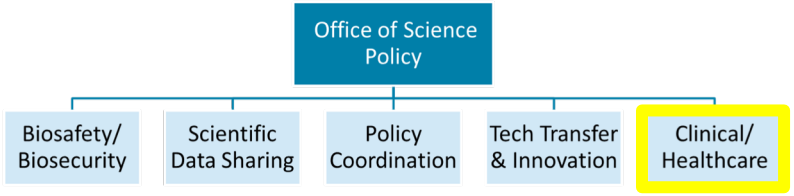


Policy Divisions:

- Biosafety, Biosecurity, & Emerging Biotechnology
- Scientific Data Sharing
- Science Policy Coordination, Collaboration & Reporting
- Technology Transfer & Innovation
- Clinical & Healthcare Research

OSP Clinical & Healthcare Research

Science Policy at the NIH



Clinical Research Policy

Healthcare Research Policy

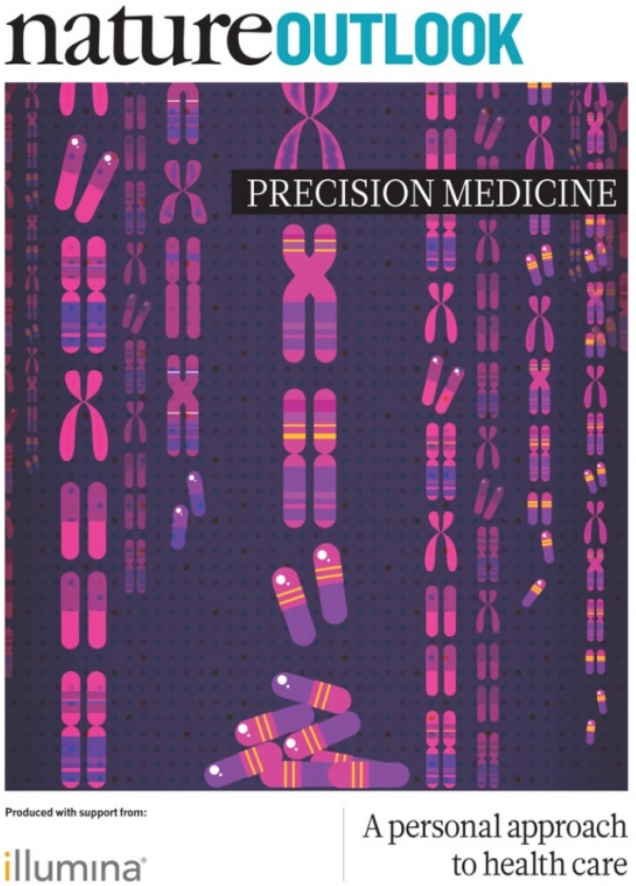
Clinical Trials Policy

- Promotes policies that safeguard the interests and well-being of research participants
- Assesses issues related to research involving human subjects, biospecimens, participant data, and bioethics
- Facilitates policies for translating clinical research discoveries into healthcare and public health settings

Intersections for NIH Policy and Personalized Medicine

What is Precision Medicine Today?

- An approach to disease treatment and prevention that takes into account individual variability in lifestyle, environment, and genes
- A radical shift in how each of us can receive the best care possible based on our unique makeup
- Based on an old concept, but needing new insights, technologies, and science in order to advance



Tailoring Health Care

- The right treatment
- The right patient
- The right time

Why now? - Timing is Everything

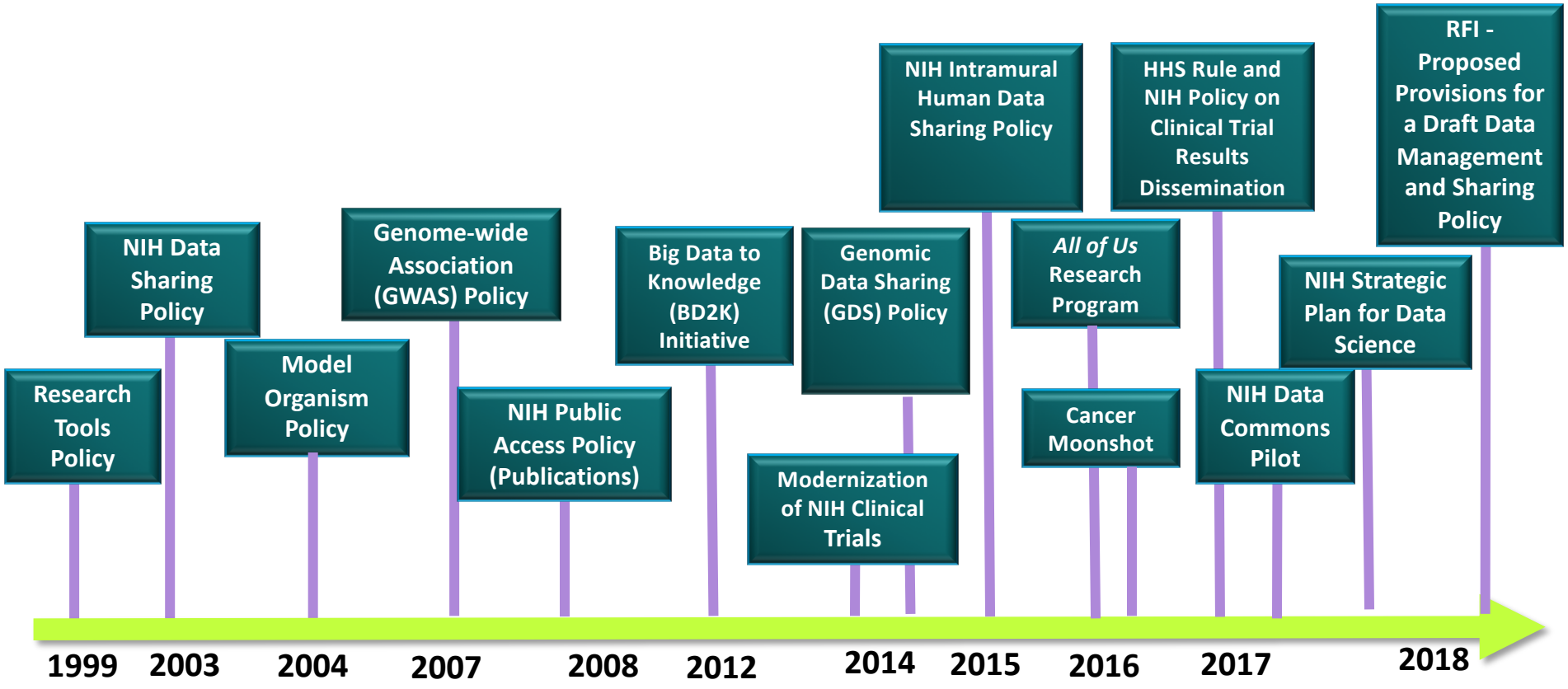
- Advances in our understanding of disease
  - Large-scale genome-based research cohorts established across the world
  - Availability of new data – microbiome, diagnostics, and sensor data
- Facilitated by large scale collection and sharing of data that can be used to identify new pathways/targets
- Personalized medicine approaches are becoming standard of care in some instances
  - Collecting and using an individual's unique characteristics to tailor treatment
- Participants are now partners in clinical care and research

Data Sharing

Advancing Biomedical Research and Precision Medicine Through Data Sharing

- **Preserves scientific record**
  - Sharing encourages better data management
  - Not all results are published
- **Facilitates research integrity**
  - Validation of experiments/results
  - Ethical obligation to human subjects
  - Transparency for greater trust
- **Advances science and application**
  - "Standing on the shoulders of giants"
  - Accelerate translation of results into practice
  - Suggest new hypotheses
  - Innovation of statistical methods, resources, and tools
- **Increases efficiency**
  - Large volumes of data generated more than enough for one team to analyze
- **Fosters rigor and reproducibility**
  - Enables data generated from one study to be used to explore additional research questions
  - Less money spent on duplicating (and revalidating) existing data, more budget dollars for funding advanced research
- **Facilitates portfolio planning**
- **Achieves synergies when combining data**
  - Increases statistical power and value

NIH – A History of Data Sharing



NOT-OD-19-014 DRAFT Policy Provisions for NIH Data Management and Sharing Policy

- **Oct 10: Comment on proposed provisions and required elements for data management and sharing plans** (60+ day period)
  - Foundation for a future NIH policy for data management and sharing
  - Sought comments on
    - Definition of "scientific data"
    - Data Management and Sharing Plan requirements
    - Optimal timing to consider in implementing various parts of a new policy
  - Policy Provisions - Proposed requirements:
    - Submission of a data management and sharing plan
    - Sharing scientific data resulting from NIH-funded or supported research
- **189 submissions; national and international stakeholders**

Privacy

Privacy Considerations?

Reidentification

RESEARCH

GENETIC PRIVACY

Identity inference of genomic data using long-range familial searches

Yaniv Erlich[1,2,3,4]*, Tal Shor[1], Itsik Pe'er[2,3], Shai Carmi[5]

Consumer genomics databases have reached the scale of millions of individuals. Recently, law enforcement authorities have exploited some of these databases to identify suspects via distant familial relatives. Using genomic data of 1.28 million individuals tested with consumer genomics, we investigated the power of this technique. We project that about 60% of the searches for individuals of European descent will result in a third-cousin or closer match, which theoretically allows their identification using demographic identifiers. Moreover, the technique could implicate nearly any U.S. individual of European descent in the near future. We demonstrate that the technique can also identify research participants of a public sequencing project. On the basis of these results, we propose a potential mitigation strategy and policy implications for human subject research.

Consumer genomics has gained popularity (*1*). As of April 2018, more than 15 million people have undergone direct-to-consumer (DTC) autosomal genetic tests, with about

perpetrator from a crime scene sample and uploaded the profile to GEDmatch, a database that contains ~1 million DNA profiles. The GEDmatch search identified a third-degree cousin (*12*). Ex-

BuzzFeed News

We Tried To Find 10 BuzzFeed Employees Just Like Cops Did For The Golden State K...

SCIENCE

We Tried To Find 10 BuzzFeed Employees Just Like Cops Did For The Golden State Killer

The Golden State Killer case has triggered a boom in "genetic genealogy" for solving crimes. But how hard is it to find people by sleuthing in their family trees?

Peter Aldhous
BuzzFeed News Reporter

Posted on April 9, 2019, at 9:16 a.m. ET

Tweet Share Copy

A year ago, when cops captured Joseph James DeAngelo, the suspected Golden State Killer, the world woke up to the power of genetic genealogy. DeAngelo was identified because DNA he left at the scene of a 1980 double murder partially matched the profiles that a few of his distant relatives had uploaded to a public website to research their family history. Based on those matches, a team of detectives drew up family trees that eventually led them to DeAngelo, suspected of at least 13 murders and more than 50 rapes.

In the year since, more than 50 other criminal cases have been cracked using similar methods, launching a new forensic science industry. One estimate has suggested that more than half of the US population could be found in this way — although genealogists have warned that, in practice, complications like adoptions or misunderstandings over who is the biological father of a child can throw an investigator off track.

How hard is it to crack cases in this way? And what issues does it raise, as police recruit genealogists to help them solve crimes by sifting through the perpetrators' extended family trees?

In the end, I identified 6 out of our 10 volunteers. Four of those cases I solved by tracking them down through their relatives' family trees, much as the cops did with DeAngelo. In a twist I didn't anticipate, I found two more not through their relatives, but simply because their ancestry indicated that their family came from a specific country — raising uncomfortable questions about genetic racial profiling.

Certificates of Confidentiality

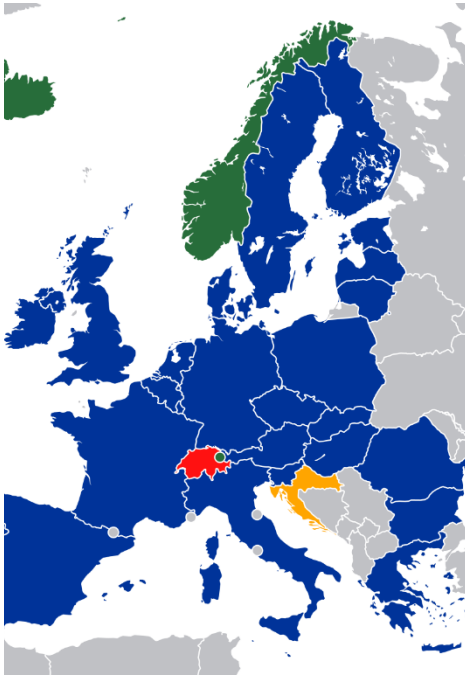
- Established in 1970, authorized persons engaged in research to withhold names or other identifiers of research participants in criminal, civil, administrative, legislative, and other proceedings
- 21st Century Cures strengthened Certificates to prohibit voluntary disclosure by persons engaged in research in which identifiable, sensitive information is collected unless disclosure is within a statutory exception
  - All copies of identifiable, sensitive information are protected in perpetuity as long as they were collected under the protection of a Certificate

NIH Policy on Certificates of Confidentiality

- Applicable NIH-funded research is deemed to be automatically issued a Certificate without an application
- NIH will continue to consider applications for Certificates for non-federally funded research within agency's mission until further notice
- Institutions are responsible for determining whether a research project is within the scope of the Policy
- NIH Policy became effective October 1, 2017

E.U. General Data Protection Regulation (GDPR)

- Legally binding, comprehensive regulation enacted May 25, 2018
- Regulates processing and transfer of personal data relating to individuals in the European Economic Area (EEA)
  - 28 EU member states plus Iceland, Liechtenstein and Norway
- Broadly defines personal data covered by GDPR
  - any information that relates to an identified or identifiable living individual
  - different pieces of information that when collected together can lead to the identification of a particular person
  - deidentified data is subject to GDPR
- High cost for non-compliance and breaches



GDPR designed to counteract widespread and/or unregulated acquisition and use of personal data…not to impede biomedical research

Impact on Biomedical Research

- While not intended to target biomedical research, GDPR does regulate the use, processing, and transfer of personal data collected in the EEA for clinical and observational research
- Data transfers from EEA to US therefore require a legal pathway, but such pathways…
  - do not yet exist (adequacy determination, code of conduct)
  - conflict with US law (standard contractual clauses)
  - have yet to be explored (explicit consent, public interest, development of new standard clauses)
- In uncertain implementation context, risk-averse GDPR interpretations have delayed and halted EEA-US research collaboration

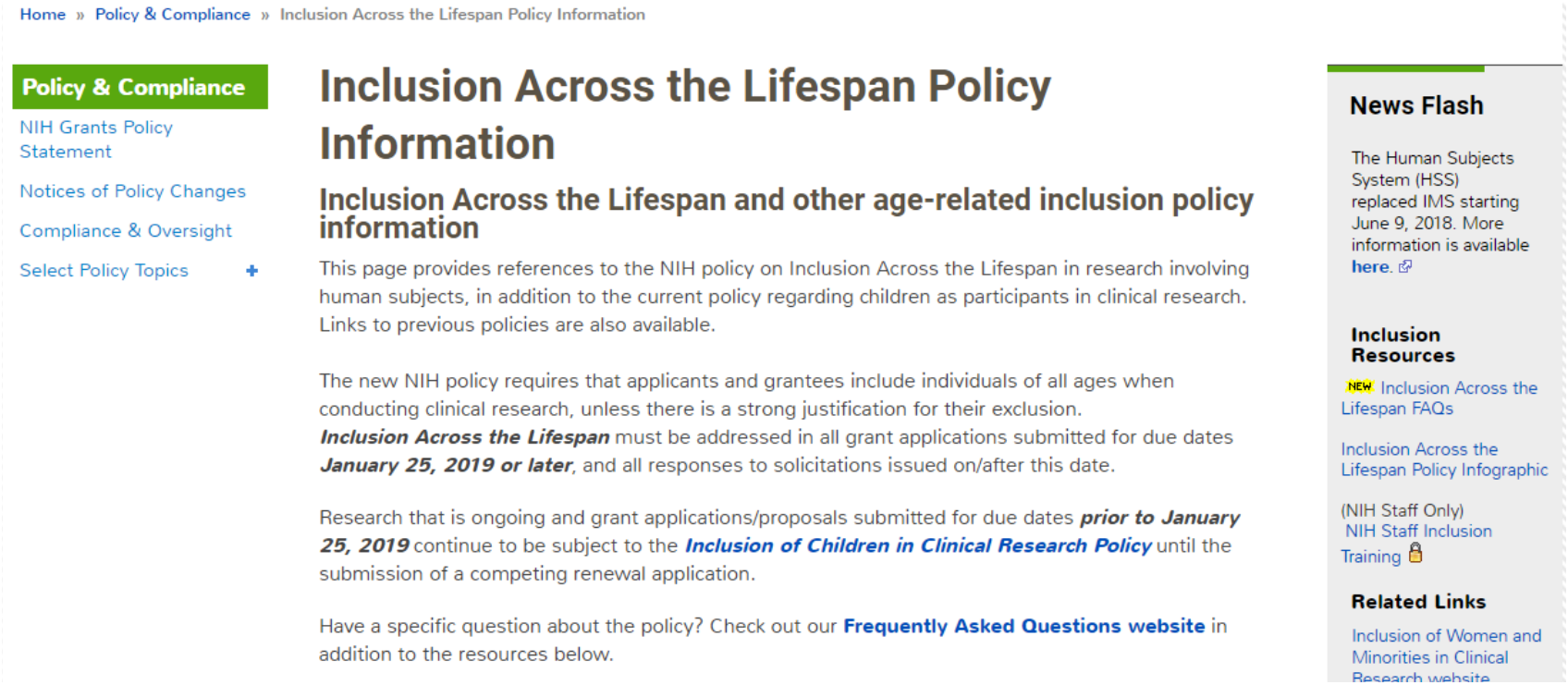
Path Forward

- Collaboration and cooperation are needed to identify implementable solutions consistent with EU and US laws and standards
- Benefits to finding “solutions” are high for biomedical research
  - harmonized consent and data sharing will enable pooled analyses to power innovative trials and advance science
- GDPR is not the only regulation that will challenge data sharing
  - South Africa Protection of Personal Information Act (POPIA)
  - Brazil General Data Protection Law (effective 2020)
  - US-wide and California-specific

Applicability

Applicability of Personalized Medicine Advances

Inclusion



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Policy & Compliance

NIH Grants Policy Statement

Notices of Policy Changes

Compliance & Oversight

Select Policy Topics +

Inclusion Across the Lifespan Policy Information

Inclusion Across the Lifespan and other age-related inclusion policy information

This page provides references to the NIH policy on Inclusion Across the Lifespan in research involving human subjects, in addition to the current policy regarding children as participants in clinical research. Links to previous policies are also available.

The new NIH policy requires that applicants and grantees include individuals of all ages when conducting clinical research, unless there is a strong justification for their exclusion.
Inclusion Across the Lifespan must be addressed in all grant applications submitted for due dates ***January 25, 2019 or later***, and all responses to solicitations issued on/after this date.

Research that is ongoing and grant applications/proposals submitted for due dates ***prior to January 25, 2019*** continue to be subject to the ***Inclusion of Children in Clinical Research Policy*** until the submission of a competing renewal application.

Have a specific question about the policy? Check out our **Frequently Asked Questions website** in addition to the resources below.

News Flash

The Human Subjects System (HSS) replaced IMS starting June 9, 2018. More information is available **here**.

Inclusion Resources

NEW Inclusion Across the Lifespan FAQs

Inclusion Across the Lifespan Policy Infographic

(NIH Staff Only)
NIH Staff Inclusion Training

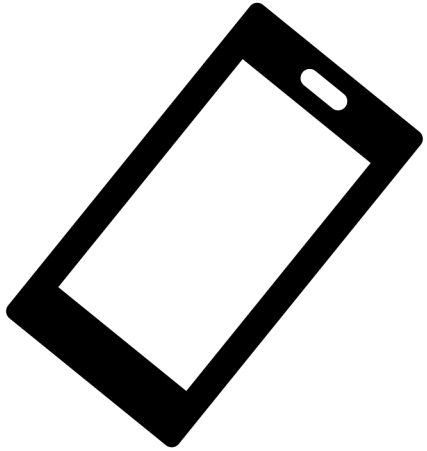
Related Links

Inclusion of Women and Minorities in Clinical Research website

New Paradigms in Clinical Research: Digital Health

Digital Revolution in Research

- Mobile devices are transforming clinical practice
- Over 46,000 mHealth apps in the Apple App store in Q4 2018*
- Remote monitoring wearables expected to increase by >400% by 2021
- Commonplace use in research and healthcare leading to rapid growth in clinical applications



* https://www.statista.com/statistics/779910/health-apps-available-ios-worldwide/

Digital Health and Personalized Medicine

- DH enhances precision medicine approaches for disease treatment by capturing individual variability in physiology, behavior, setting, and environment through mobile/wearable sensors and geospatial data collection
- DH Potential: temporally dense data collection, enhanced diagnosis and monitoring, real-time tracking to prevent and manage disease, lower healthcare costs, and increased accessibility

Digital Health and NIH

- NIH supports research using digital health technologies:
  - Physical activity, medication adherence, diabetes management, rapid screening for TB, rapid diagnosis of nutrient deficiency, neurological assessment, smartphone confocal microscope
  - Supports platforms to enable flexible, scalable, and secure digital health research and data collection

Challenges

- Privacy and confidentiality concerns with constant data collection
- Quality/interoperability/comparability of results is variable or unknown; proprietary algorithms not transparent to patients and clinicians

New Paradigms in Clinical Research: All of Us Research Program

Participants as Partners

- Equal partners in research
  - Involved in determining what research is conducted, what data is collected, the analyses that are performed, and how data is returned
- Long-term engagement

Research Participants Want Information Back

Public opinion survey

2,601 responses were analyzed.

79% supported the program

54% said they would definitely or probably participate if asked

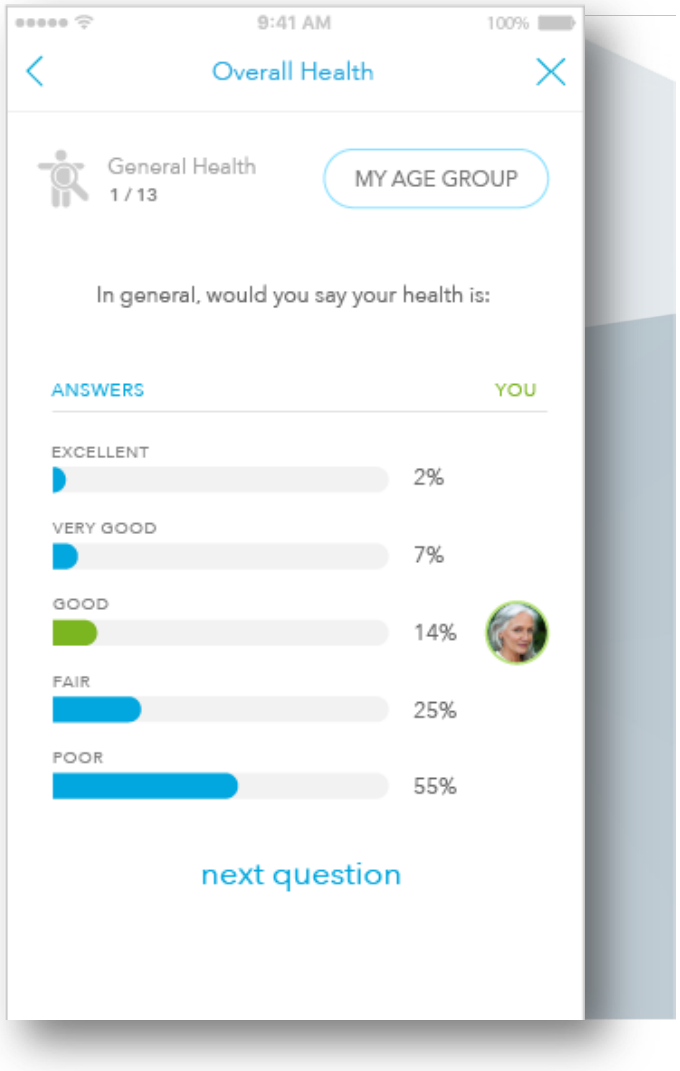
- Little variability among demographic groups
- Most important incentive for participation: **learning about one's health information**

Kaufman DJ, Baker R, Milner LC, Devaney S, Hudson KL (2016):
A Survey of U.S. Adults' Opinions about Conduct of a Nationwide Precision Medicine Initiative Cohort Study of Genes and Environment.
PLOS ONE 11(8): e0160461. doi:10.1371/journal.pone.0160461

Return of Information

Participants may receive:

- Individual health information
- Survey data (comparative)
- EHR data, claims data
- Research results
- Ongoing study updates
- Aggregated results
- Scientific findings
- Opportunities to be contacted for other research opportunities



Genomics plans

- Genotyping & WGS for all 1M participants
- Genetic Counseling Resource
- Pilot of return of results with 40k diverse participants
- **What to return?**
  - Begin with medically actionable genomic results return
    - **Facilitated return:** Medically actionable monogenic variants (AoU Medically Actionable Panel (AoUMAP)) via the Genetic Counseling Resource
    - **Access**: Uninformative AoUMAP results
    - **Access**: Typical and atypical pharmacogenomic CPIC A variants

Medically Actionable Variants (use ACMG guidance for secondary findings)

Type	Genes
Tumor Predisposition Breast/ovarian, Li-Fraumeni, Peutz-Jeghers, Lynch, Polyposis, Von Hippel-Lindau, MEN1/2, Medullary thyroid cancer, PTEN hamartoma syndrome, Retinoblastoma, Paraganglioma/pheochromocytoma, Tuberous sclerosis complex, WT1-related Wilms' tumor, NF2	BRCA1/2, TP53, STK11, MLH1, MSH2, MSH6, PMS2, APC, MUTYH, BMPR1A, SMAD4, VHL, MEN1 RET, PTEN, RB1, SDHD, SDHAF2, SDHC, SDHB, TSC1, TSC2, WT1, NF2
Connective Tissue Dysplasia Ehlers-Danlos vascular type, Marfan, Loeys-Dietz, Familial aortic aneurysms and dissections	COL3A1, FBN1, TGFBR1, TGFBR2, SMAD3, ACTA2, MYH11
Cardiac Hypertrophic cardiomyopathy, dilated cardiomyopathy, Arrhythmia	MYBPC3, MYH7, TNNT2, TNNI3, TPM1, MYL3, ACTC1, PRKAG2, GLA, MYL2, LMNA, RYR2, PKP2, DSP, DSC2, TMEM43, DSG2, KCNQ1, KCNH2, SCN5A
Metabolic Hypercholesterolemia, Wilson disease, Ornithine transcarbamylase deficiency	LDLR, APOB, PCSK9, ATP7B, OTC
Pharmacogenetic Malignant Hyperthermia	RYR1, CACNA1S

59 Genes, 1000s of Variants, 27 Conditions

Pharmacogenomics return: CPIC-A Genes

CPIC LEVEL	CLINICAL CONTEXT	LEVEL OF EVIDENCE	STRENGTH OF RECOMMENDATION
A	Genetic information should be used to change prescribing of affected drug	Preponderance of evidence is high or moderate in favor of changing prescribing	At least one moderate or strong action (change in prescribing) recommended.

Quick glance at where the program is now

TO DATE…

212,000 Participants have begun the enrollment process

>129,000 Participants have completed the full protocol

>75% are under-represented in biomedical research

300+ sites now enrolling

Biobank > 1.3M tubes

Developed data warehouse to collect, clean, curate, de-identify the data

COMING SOON:

Research Portal to be open with initial public dataset

Genomics and return of results pilot

Questions?

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