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Ethical arguments regarding the return of research results

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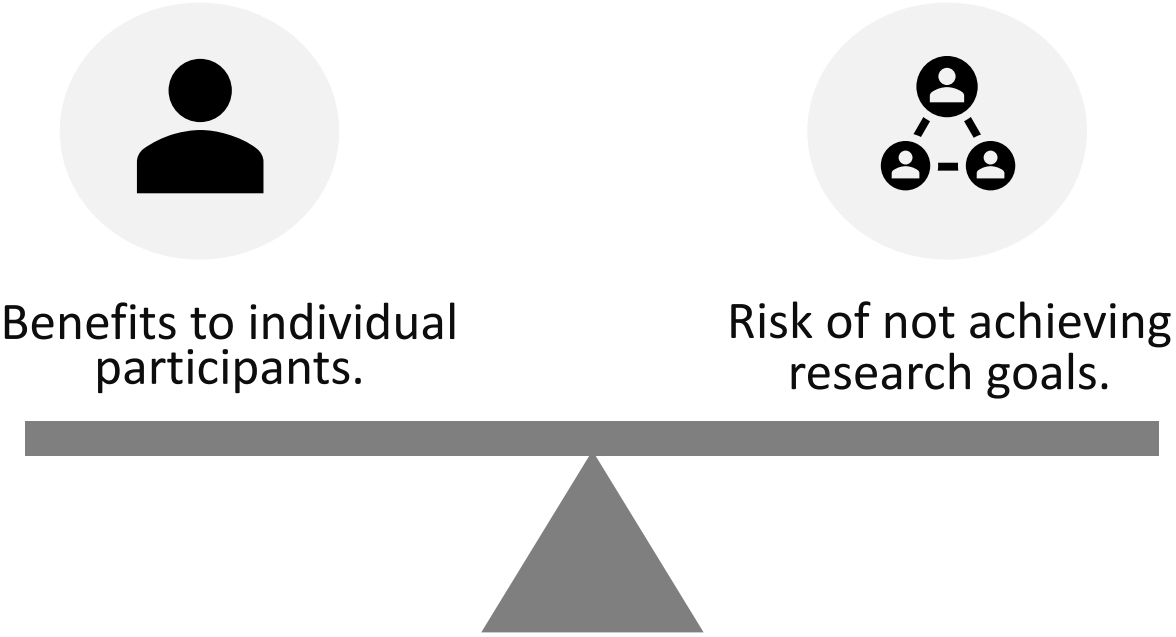
Returning results: What's the debate?



- Goal of research enterprise is to produce new knowledge for the collective good
- Higher resource costs to return results (distract from research goals)

A shift in the ethical principles

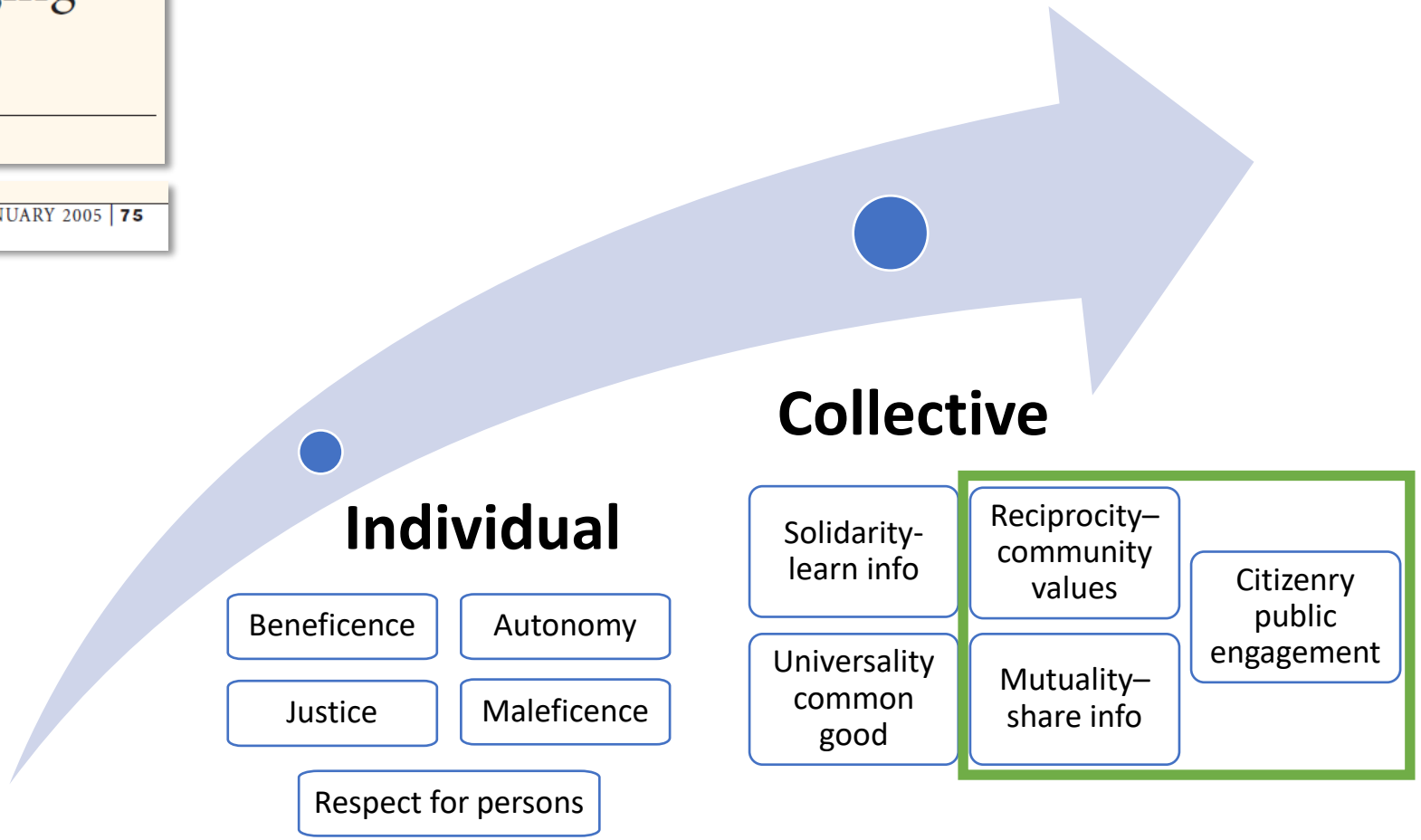

SCIENCE AND SOCIETY

Human genetic research: emerging trends in ethics

Bartha Maria Knoppers and Ruth Chadwick

NATURE REVIEWS | GENETICS

VOLUME 6 | JANUARY 2005 | 75



An evolution in policy

Pre-2006

Many IRBs require consent form to state that participants **will not be given their individual results.**

2006

NHLBI **recommends return of individual results** associated with significant disease risk, important health or reproductive implications, and proven therapies or preventive interventions.

2008-2012

NHLBI recommendations updated; other NIH-supported research groups publish consensus recommendations which **support returning individual research results.**

2013

ACMG **recommends return of medically actionable secondary findings** in context of clinical exome/genome sequencing.

2013

Presidential Commission on Bioethics publishes report on ethical management of secondary/incidental findings, including in research contexts.

2014

Consensus statement from CSER/eMERGE recommend researchers offer results that are **valid, medically important, and actionable** if found during course of analysis.

2018

National Academies of Science, Engineering and Medicine recommends researchers **should return results** of high potential value to participants where feasible, if generated from labs with appropriate quality management systems.

2020

ASHG statement **recommends recontacting** research participants with updated results and supports initial return of results.

2021

GA4GH statement **supports return of actionable research results.**

Bookman et al (2006) *Am J Hum Genet*; Fabsitz et al (2010) *Circ Cardiovasc Genet*; Wolf et al. (2008) *J Law Med Ethics*; Wolf et al (2012) *Genet Med*; Presidential Commission for the Study of Bioethical Issues (2013); Green et al (2013) *Genet Med*; Jarvik et al (2014) *Am J Hum Genet*; Bombard et al (2020) *Am J Hum Genet*; GA4GH POL 007 v1.0: June 24 2021; Lewis et al (2021) *Genome Med*; Thorogood et al (2019) *Eur J Hum Genet*

Current policy


Lewis et al. Genome Medicine (2021) 13:115
https://doi.org/10.1186/s13073-021-00928-5
Genome Medicine
COMMENT
Open Access

An international policy on returning genomic research results

Anna C. F. Lewis[1,2,3*], Bartha Maria Knoppers[4] and Robert C. Green[2,3,5,6]

Abstract

The Global Alliance for Genomics and Health has approved a policy for the return of clinically actionable genomic research results, the first such policy approved by an international body. The policy acknowledges the potential medical benefits to millions of individuals who are participating in genomics research. It ties the pace of implementation to each country's clinical standards, including for the return of secondary findings, and urges funders to set aside resources to support responsible return.


ASHG POSITION STATEMENT

The Responsibility to Recontact Research Participants after Reinterpretation of Genetic and Genomic Research Results

Yvonne Bombard,[1,2,3,*] Kyle B. Brothers,[1,4] Sara Fitzgerald-Butt,[5,6] Nanibaa' A. Garrison,[1,7,8] Leila Jamal,[1,5,9] Cynthia A. James,[5,10] Gail P. Jarvik,[11,12] Jennifer B. McCormick,[1,13] Tanya N. Nelson,[14,15,16,17,18] Kelly E. Ormond,[1,19] Heidi L. Rehm,[20,21,22] Julie Richer,[14,23,24] Emmanuelle Souzeau,[25,26] Jason L. Vassy,[20,27,28] Jennifer K. Wagner,[1,29] and Howard P. Levy[1,30,31]

Initial return of results

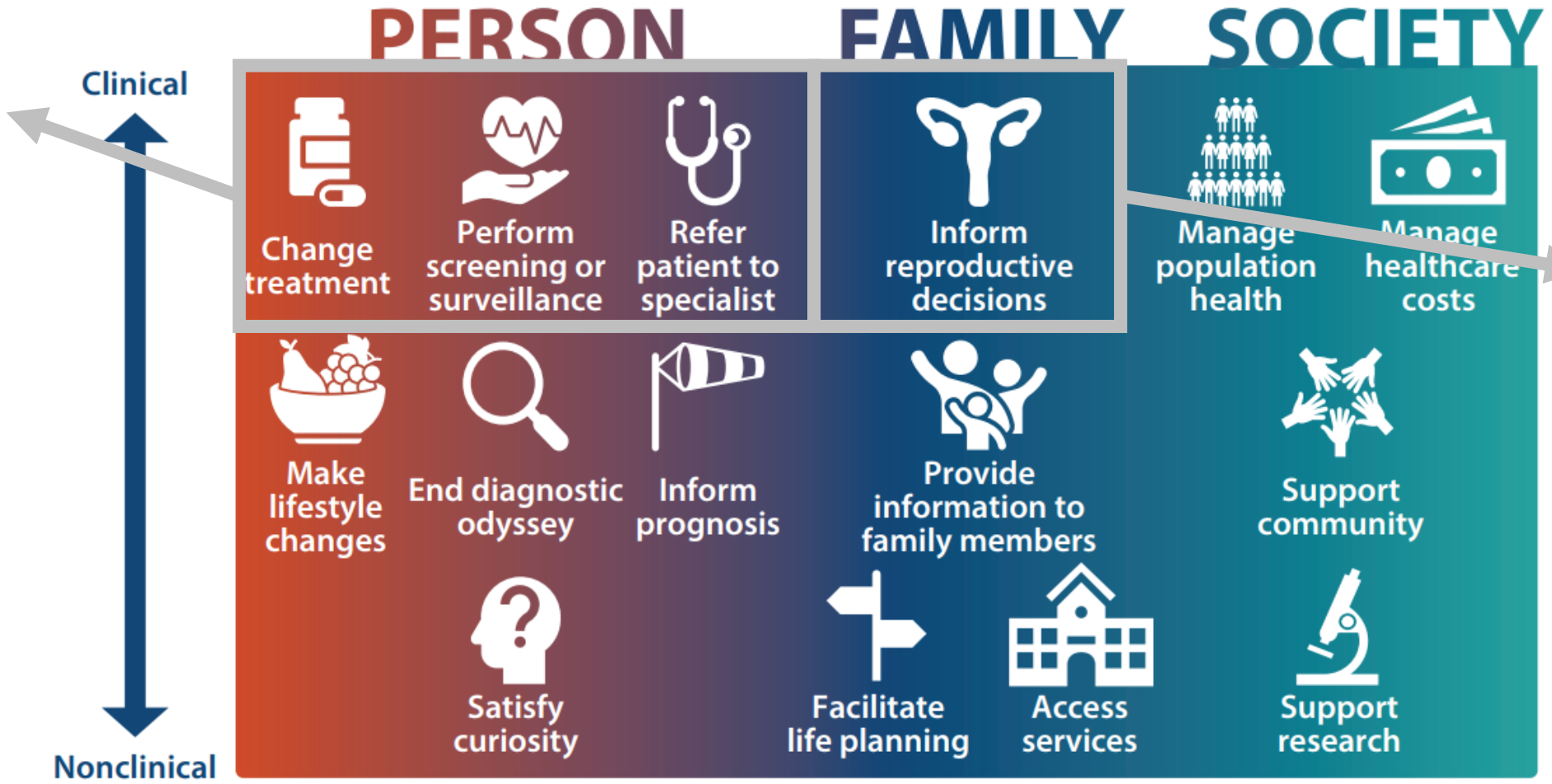
- Statements from NAS and GA4GH support return of individual research results.
- Policies highlight importance of a clear protocol for return of results, informed consent, incorporation of participant preferences, validation of research results, and access to appropriate expertise and resources for return of results.

Recontact with updates over time

- ASHG strongly recommends recontacting participants to offer updated results related to the phenotype under study/results expected to affect medical management, if participant has consented to return of results, can be identified, and study has active funding.
- No responsibility to scan for changes in variant interpretation.

The spectrum of actionability

Pathogenic *FBN1* variant for Marfan syndrome



Carrier status for autosomal recessive phenylketonuria

Figure 1

The spectrum of actionability, which includes benefits for the person, the family, and society.

Goddard et al (2022) *Annu Rev Genom Hum Genet*

Widening the lens of actionability: A matter of perspective

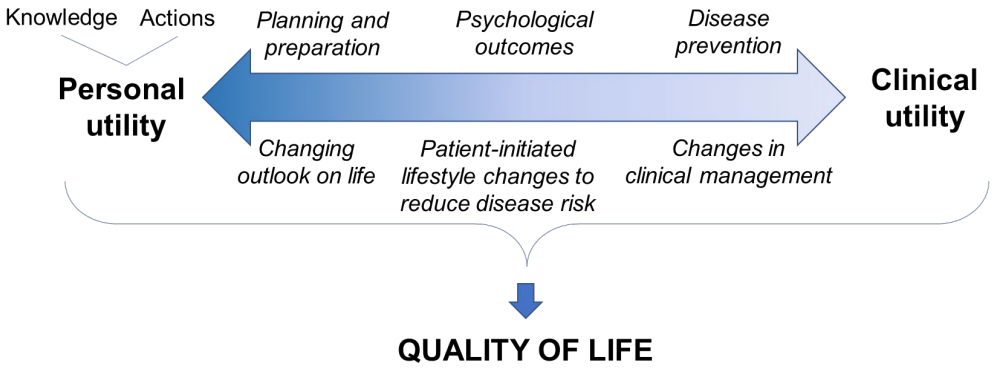
Scientist/Analyst

Clinician

Patient/Participant

ClinGen Semiquantitative Framework
Severity of disease
Likelihood of disease
Efficacy of intervention
Nature of intervention
Level of evidence

Immediate actionability	Clinical actions Reproductive planning Lifestyle changes Patient counseling
Future actionability	Pharmacogenomics Information management e.g., EHR documentation



Berg et al (2016) *Genet Med;* Webber et al (2018) *Hum Mut;* Hunter et al (2016) *Genet Med*

Sebastian et al (2021) *Eur J Hum Genet*; Mackley et al (2017) *Genet Med;* Lerner et al (2017) *Genet Med*; Delanne et al (2019) *Eur J Med Genet*

Mighton et al (2020) *Eur J Hum Genet*

Operationalizing Actionability

WHYY PBS npr

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WHY HEALTH EQUITY MATTERS

Early genetic testing can lead to better health outcomes. So why are patients of color not tested at the same rates?

By Sojourner Ahébée · November 25, 2021

Home // Racial Equity and Health Policy // **Racial Disparities in Cancer Outcomes, Screening, and Treatment**

Racial Disparities in Cancer Outcomes, Screening, and Treatment

Michelle Tong , Latoya Hill , and Samantha Artiga

Published: Feb 03, 2022

EurekAlert! | AAAS

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NEWS RELEASE 27-APR-2022

Study shows importance of ensuring participant and provider follow-up after a genetic screening result

New research from the Healthy Nevada Project® finds that a confirmed diagnosis does not always result in changes to patient care

Peer-Reviewed Publication

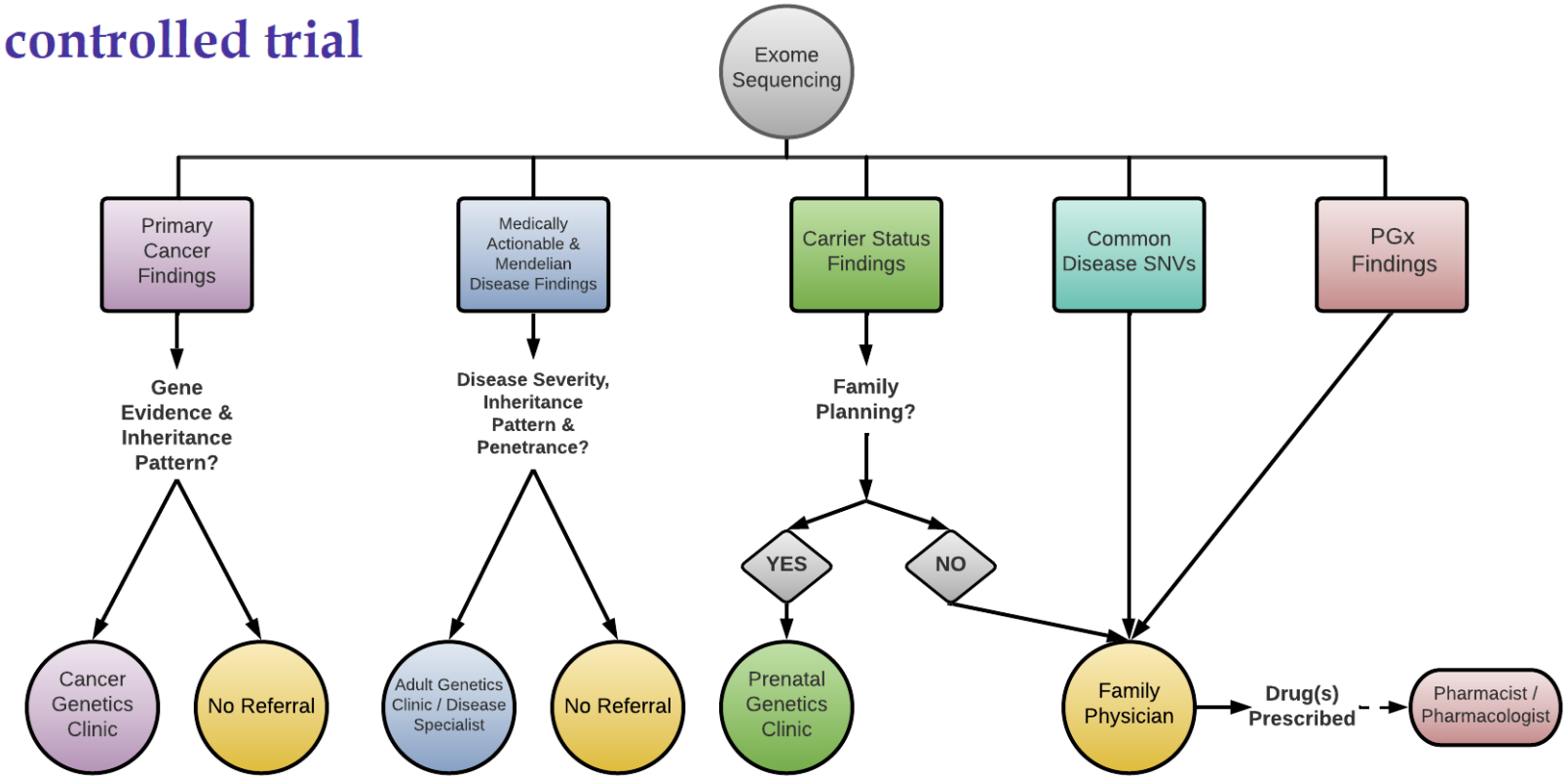
DESERT RESEARCH INSTITUTE

Reno, Nev. (April 27, 2022) – Presenting individuals with potentially life-altering health information doesn't mean the individuals – or their healthcare providers – will act on it. Follow-up education and conversations about actionable care plans with patients and their doctors are key next steps, according to new research from the Healthy Nevada Project.

Enabling Actionability

BMJ Open Health outcomes, utility and costs of returning incidental results from genomic sequencing in a Canadian cancer population: protocol for a mixed-methods randomised controlled trial

Kodida* Reble* et al *Under review*



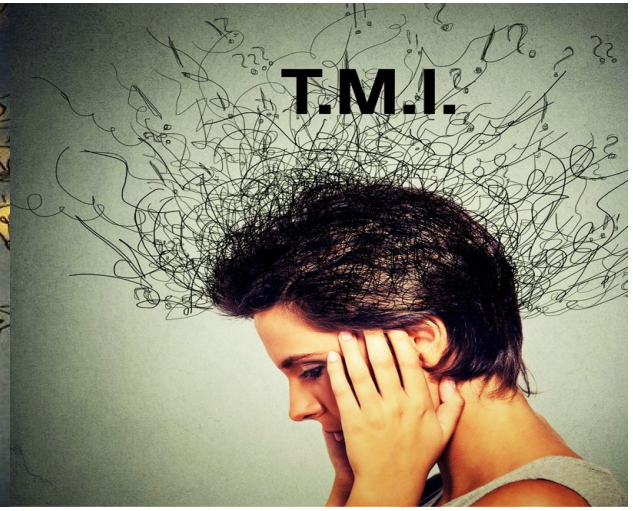
Informed consent or cognitive overload?

WIRED

MEGAN MOLTENI SCIENCE OCT 10, 2018 7:00 AM

So Much Genetic Testing. So Few People to Explain It to You

Personal genomics is booming, but there's a nationwide shortage of genetic counselors who can make sense of that DNA data.



Digital Tools: Quality & Efficiency

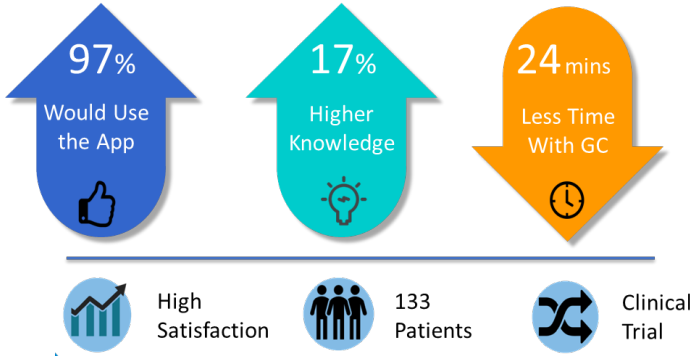
A systematic review found most digital genomic tools have a favourable effect on patient outcomes & efficiencies.

	Knowledge / Understanding	Decision making	Patient engagement	Psychosocial well-being	Behavior & management changes	Family communication
# of studies that measured the outcome	58	33	42	35	24	19
Favorable	55	28	40	23	18	17
No effect	3	5	2	11	6	2
Unfavorable	0	0	0	1	0	0

Lee, Shickh et al (2022) *J Med Genet*

Genomics Adviser

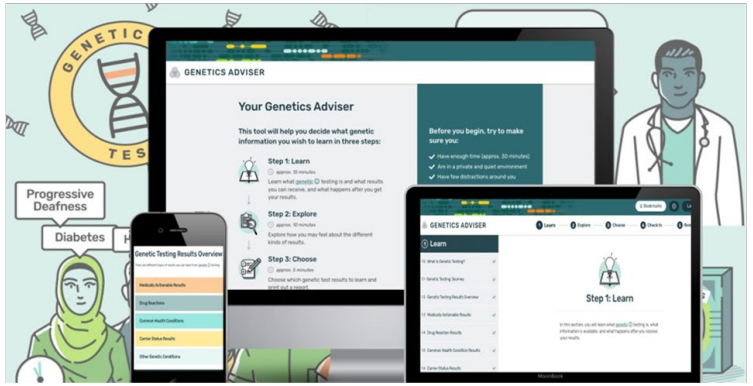
Decision aid for secondary findings



Bombard et al (2020) Genet Med

Genetics Adviser:

RoR for Any Tests, Results & Populations



Digital tools for RoR

www.nature.com/gim

Genetics inMedicine

Check for updates

ARTICLE

The role of digital tools in the delivery of genomic medicine: enhancing patient-centered care

Salma Shickh[1,2,31], Sara A. Rafferty[3,4,31], Marc Clausen[2], Rita Kodida[2], Chloe Mighton[1,2], Seema Panchal[5], Justin Lorentz[6], Thomas Ward[5], Nicholas Watkins[5], Christine Elser[7,8], Andrea Eisen[6], June C. Carroll[5,9], Emily Glogowski[10], Kasmintan A. Schrader[11,12], Jordan Lerner-Ellis[13,14,15], Raymond H. Kim[3,7,8], David Chitayat[3,4,5], Cheryl Shuman[3,4], Yvonne Bombard[1,2✉], Incidental Genomics Study Team*

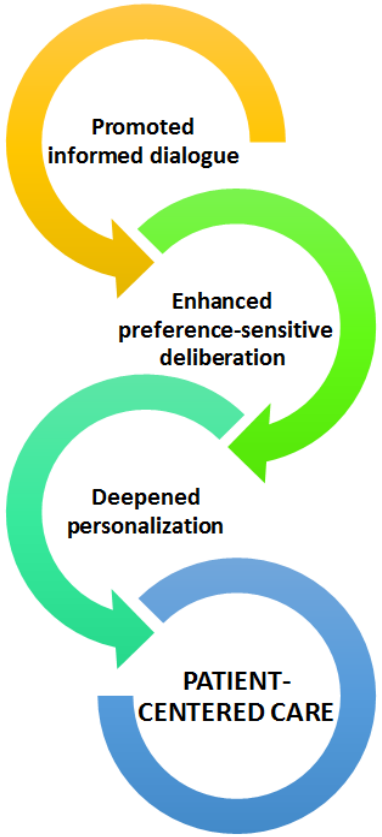
Genetics in Medicine (2021) 23:1086–1094; https://doi.org/10.1038/s41436-021-01112-1

NATURE REVIEWS | GENETICS

How digital tools can advance quality and equity in genomic medicine

Yvonne Bombard[1,2✉] *and Robin Z. Hayeems*[2,3]

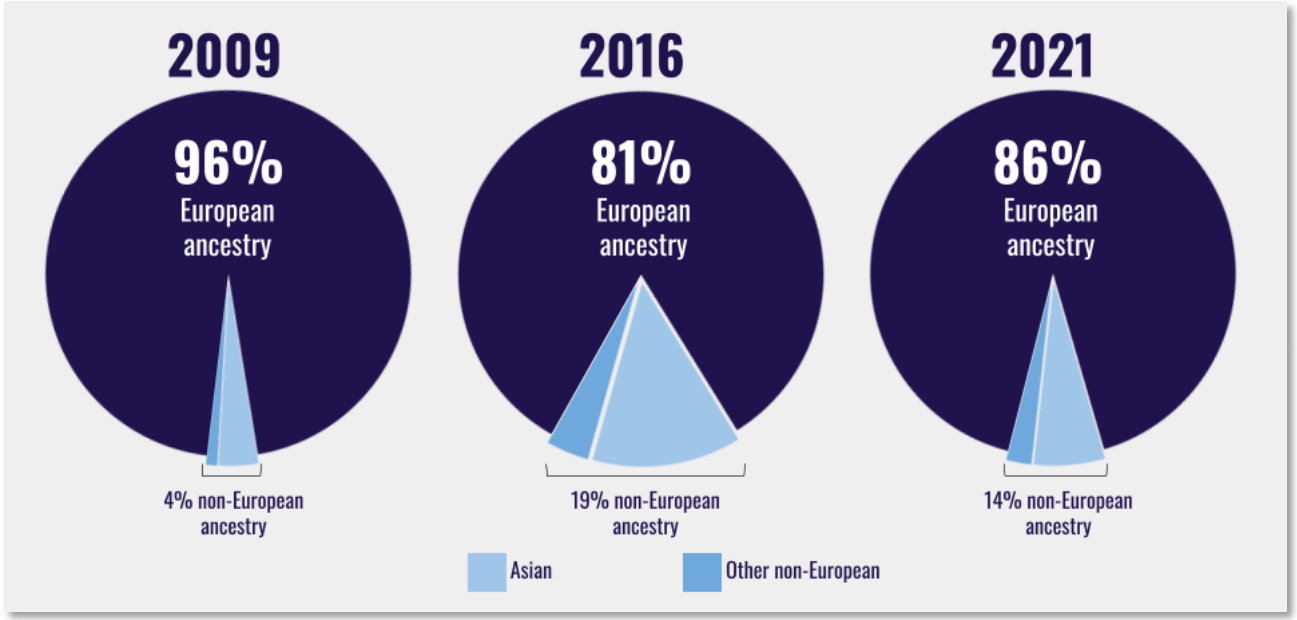
Now more than ever, digital applications are essential to accessing genetics services and optimizing their delivery. At this watershed moment, digital solutions must be balanced with the merits of human interaction, without compromising quality or exacerbating existing genomic and technological disparities.



- Promoted engagement during the course of the session
- Facilitated deliberation around the participants' preferences and perceived harms and benefits
- Enabled personal reflection on a wide set of experiences and circumstances

Salma Shickh et al (2021) Genet Med

Equity Considerations



Adapted from Popejoy & Fullerton (2016) Nature and Fatumo et al. (2022) Nature

The NEW ENGLAND JOURNAL of MEDICINE

SPECIAL ARTICLE

Genetic Misdiagnoses and the Potential for Health Disparities

Arjun K. Manrai, Ph.D., Birgit H. Funke, Ph.D., Heidi L. Rehm, Ph.D., Morten S. Olesen, Ph.D., Bradley A. Maron, M.D., Peter Szolovits, Ph.D., David M. Margulies, M.D., Joseph Loscalzo, M.D., Ph.D., and Isaac S. Kohane, M.D., Ph.D.

Summary

There is increasing impetus to return actionable genomic results from research.

“Actionability” is operationalized & conceptualized differently by different stakeholders.

Clinical follow-up for participants with actionable results is a key issue.

Digital tools could support consent, return of results, and recontact with updates.

Equity must be prioritized so that existing disparities are not exacerbated.

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