Introduction to Genetics, Ethics, & Society

BIOS 232

Course overview

1. Connect the historical context of genetics research to its modern-day practice
2. Evaluate the social and ethical implications of genetics research
3. Analyze how societal norms and structures, along with personal identities, biases, and responsibility, impact the conduct of scientific research

Week 1: Principles of Bioethics	Science and Society	History of Heredity
Week 2: **Human Genetic Data**	Race, Ancestry, Genetics, and Identity	
Week 3: Reproductive Genetics	Criminal Justice	Reflections and Actions

Session 3: Introduction to Human Genetic Data

Learning goals

- Identify limitations and concerns around the collection, use, and analysis of human genetic data
- Develop an understanding of the current landscape of genomic data stewardship
- Identify key stakeholders and conflicts of stakeholdership in the collection, use, and analysis of human genetic data

Taught by Pagé Goddard, Meena Chakraborty, & Alanna Pyke

Overview

- 5 min Warm-up
- 6 min Lecture: Intro to genetic data
- 30 min Activity: Stewardship & data policies

break

- 12 min Video + Lecture: Stakeholdership
- 15 min Activity: Perspectives Exercise
- 15 min Lecture: Community-engaged science
- 20 min Activity: Design your ideal study
- Questions & thoughts & next up

Agreed Upon Group Norms

-Be respectful of conflicting opinions

-Commit to learning and growing

-Compassionate listening

-No talking over anyone

-Make space, take space

Warm up

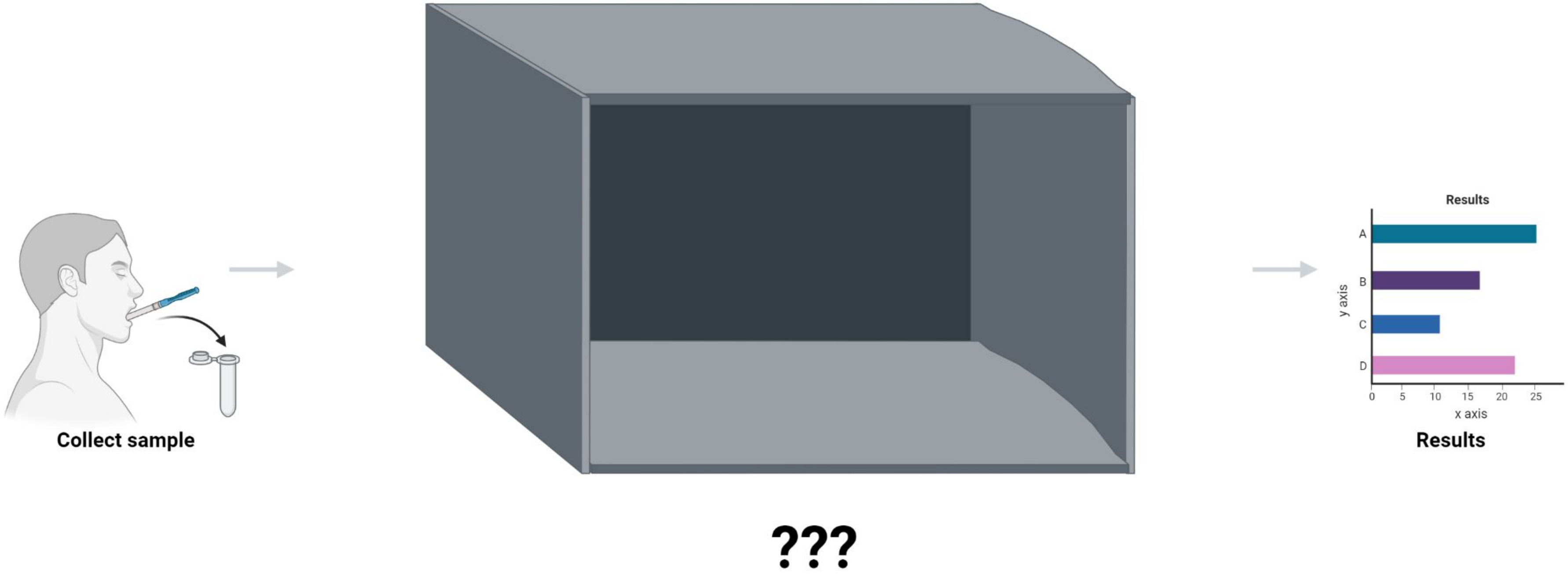
What questions / concerns do you, your family, or your friends have about genetic data?

Genetic Data: Impressions & Concerns

privacy

Intro to Genetic Data

What is genetic material? What does it mean to “donate your DNA” to something?



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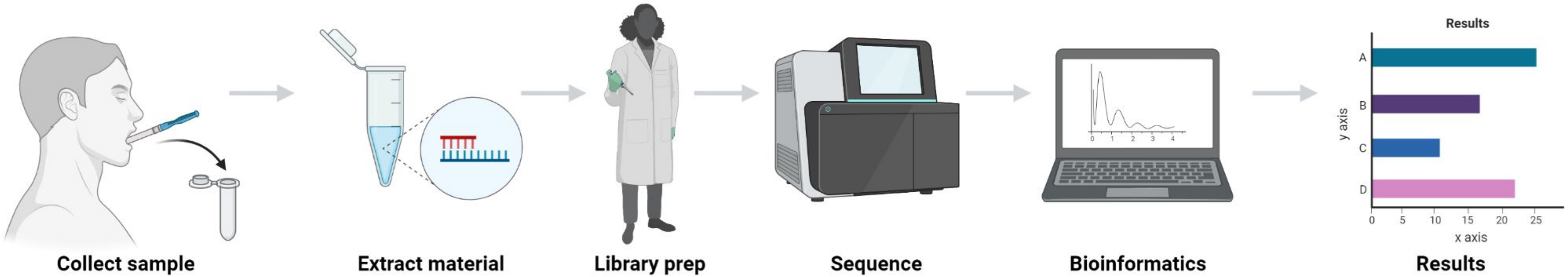
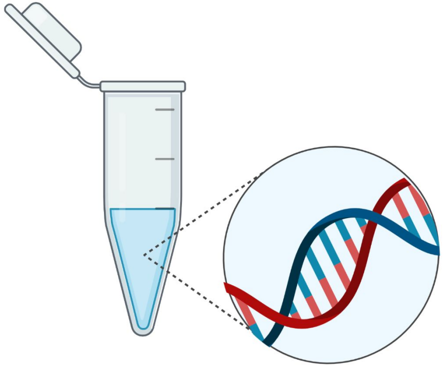


What types of data can be generated?



DNA

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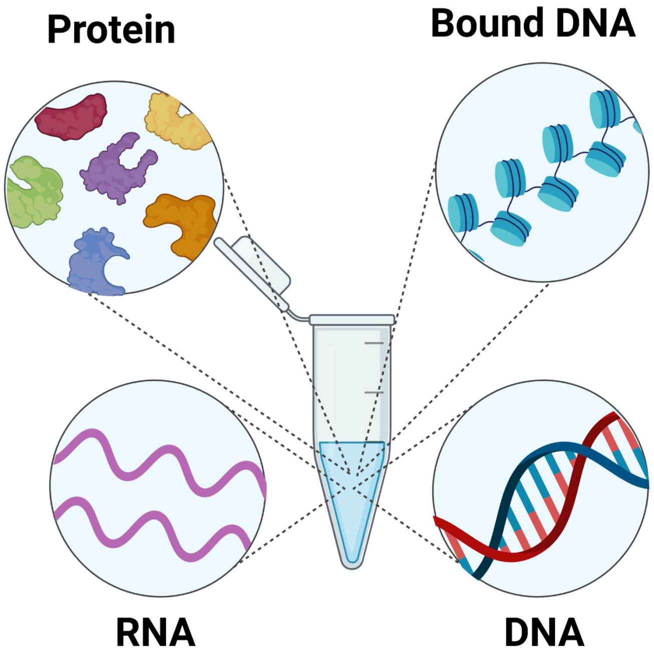

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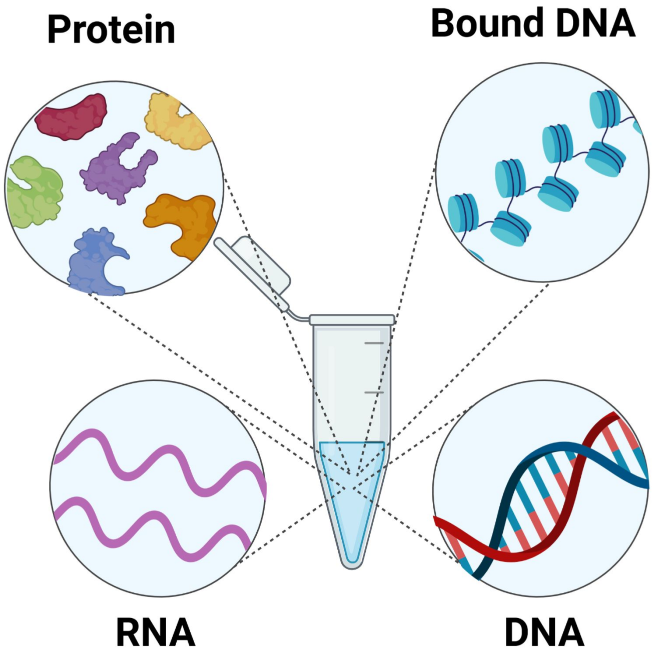

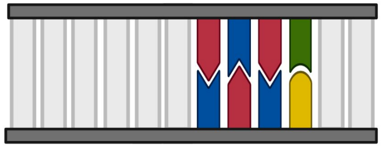

Targeted Sequencing

- Information about specific region
- Hypothesis driven & clinical testing

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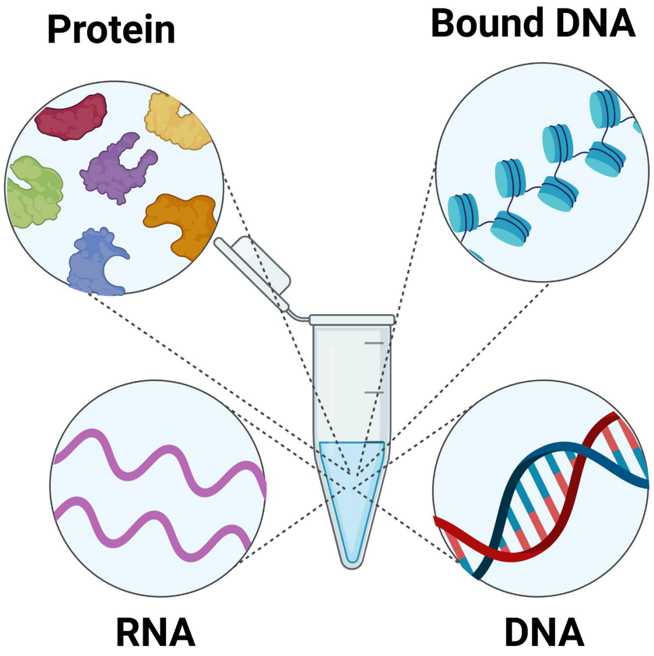

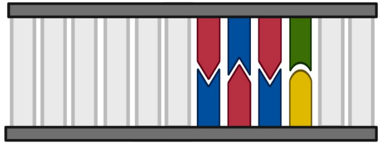

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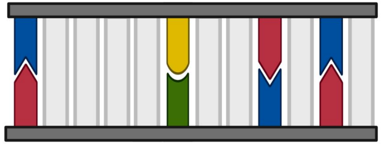

Genotyping Arrays
- genome-wide
- ~1% bases
- Population genetics and genetic epidemiology

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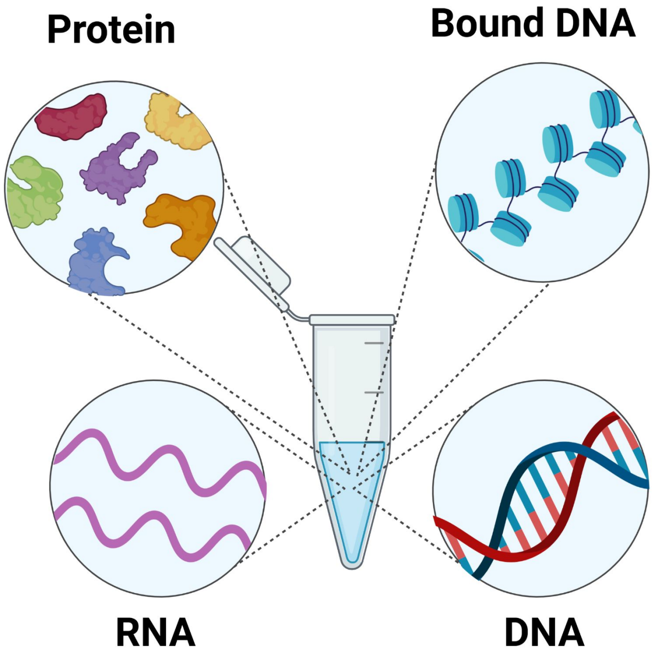

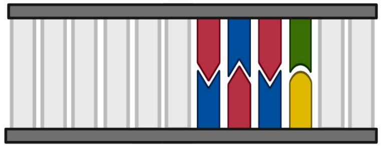

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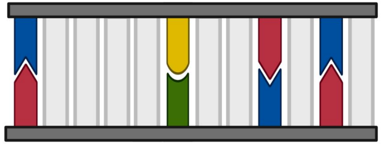

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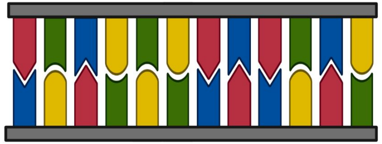

Whole Ome Sequencing
- genome-wide
- as many bases as possible
- Rare and *de novo* variant detection

How can this data be used?

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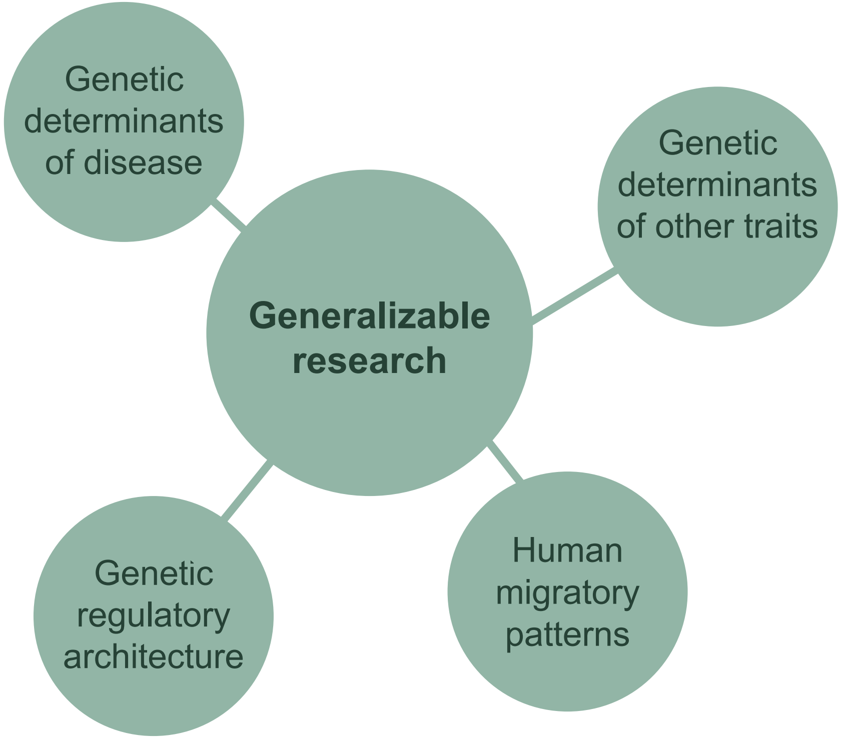

Generalizable research

Genetic determinants of disease

Genetic determinants of other traits

Genetic regulatory architecture

Human migratory patterns

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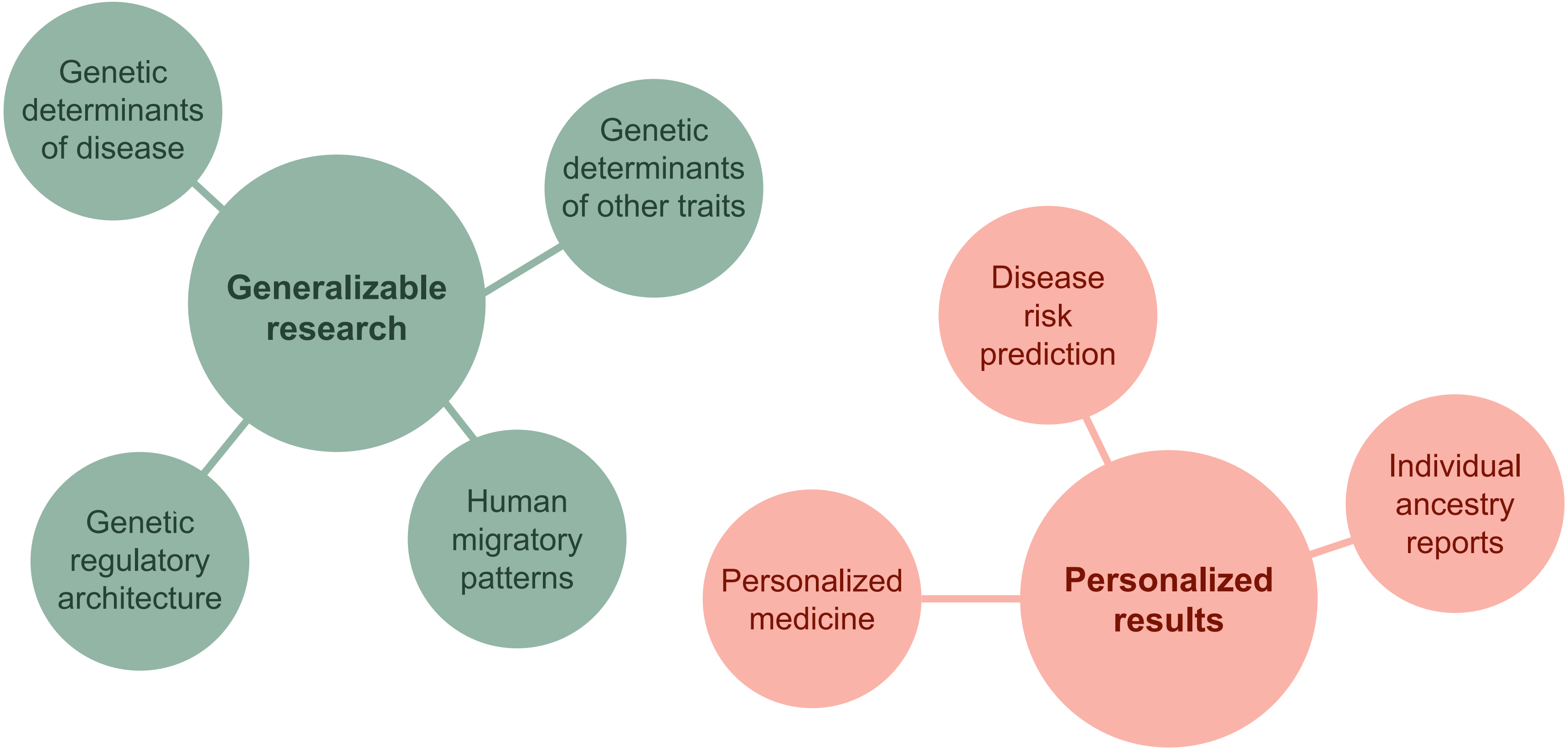
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Personalized results

Disease risk prediction

Individual ancestry reports

Personalized medicine

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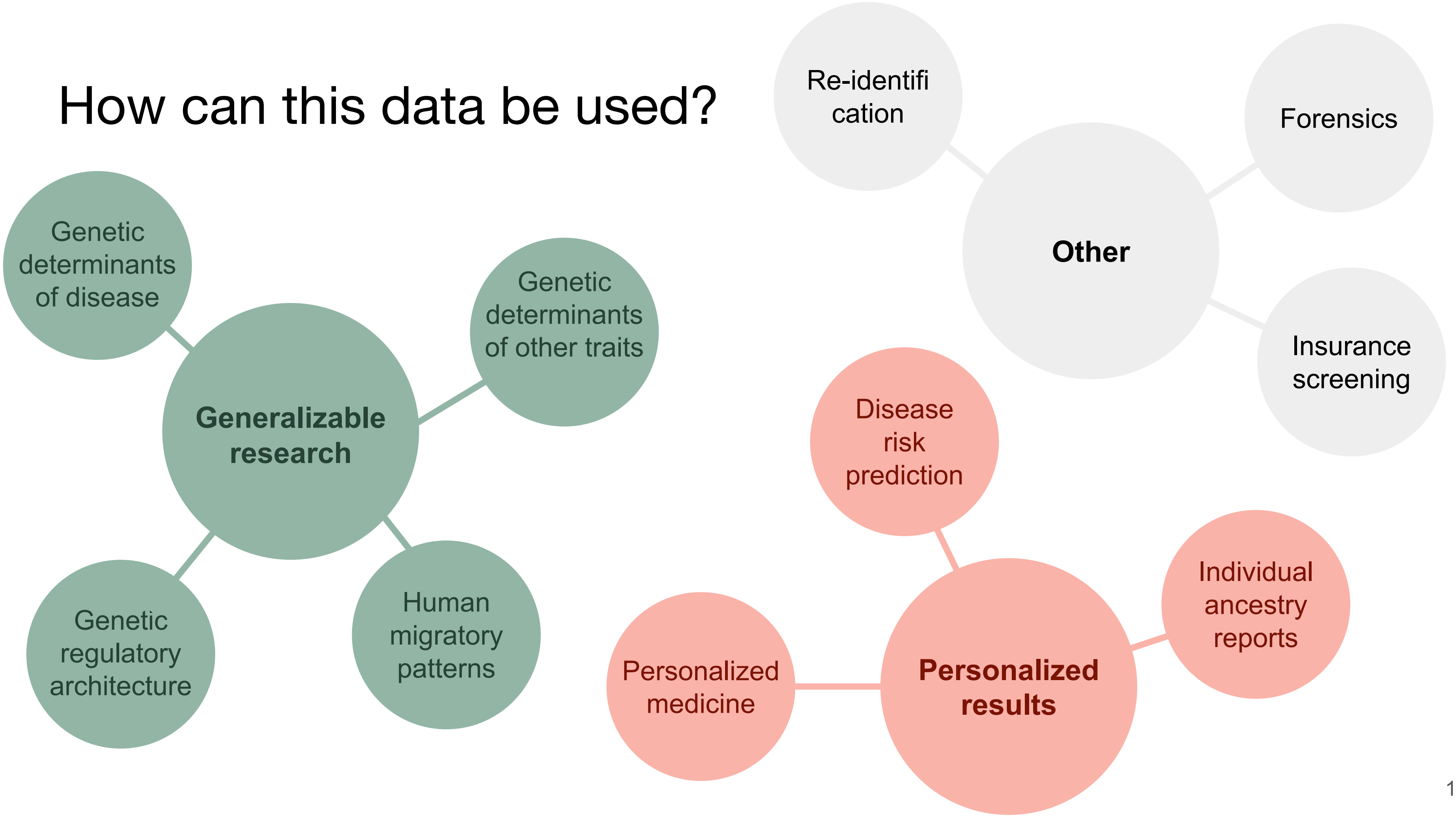

Generalizable research

- Genetic determinants of disease
- Genetic determinants of other traits
- Genetic regulatory architecture
- Human migratory patterns

Personalized results

- Disease risk prediction
- Individual ancestry reports
- Personalized medicine

Other

- Re-identifi cation
- Forensics
- Insurance screening

How **can’t** this data be used?

Genetic Information Nondiscrimination Act of 2008 (GINA)

- prohibits **health insurance discrimination** based on genetic information
  (exceptions: life insurance, long-term care insurance, disability insurance)
- prohibits **employers from requiring/requesting genetic information or testing** of employees
  (exceptions: U.S. military, employers with fewer than 15 employees)

https://www.genome.gov/about-genomics/policy-issues/Genetic-Discrimination

Types of Data Access

Private

- data is not shared outside the initial team

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Restricted

- requires permission from a data manager
- often phenotype & genotype data access is separate

European Genome-phenome Archive (EGA)

NCBI database of Genotypes and Phenotypes (dbGaP)

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NCBI database of Genotypes and Phenotypes (dbGaP)

Unrestricted

- only hoop is finding the correct download link
- de-identified with no phenotype data

1000 Genomes

The Genome Aggregation Database (gnomAD)

Pros and Cons to Data Sharing

Pros

Cons

Pros and Cons to Data Sharing

Replication & **reproducible research**

Promotes research in **diverse datasets**

Larger, **higher quality** studies

Equitable access to data

Larger, **higher quality** studies

Pros

Risk of **privacy attacks**

Lack of participant **autonomy over future studies**

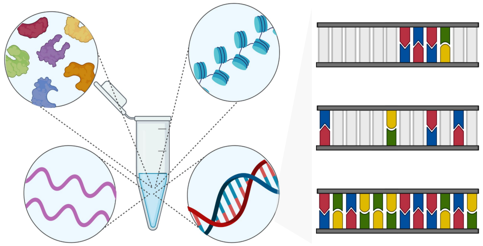
Increased risk of **data selling**

Research **benefits less likely to reach participants**

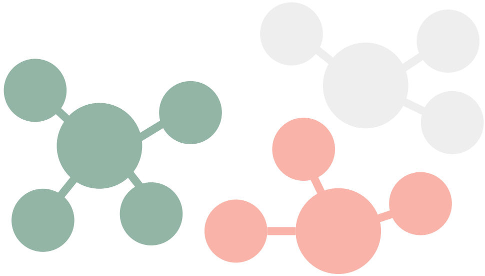
Increased risk of **bad-actors**

Cons

Takeaways



- A single sample can yield many types of data
- Not every study or service sequences everything



- Genetic data can be both broadly and personally impactful if handled well
- Genetic data carries inherent risks for individuals and groups

- Data sharing facilitates reproducible science, improved studies, and innovation
- Data sharing may also put participant privacy and autonomy at risk

Data Policy & Stewardship

Data policy and stewardship

- Collection of data necessitates **data policy**, which outlines:
    - Who **owns** the data
    - Where the data will be **stored**
    - Who the data can be **shared with**
    - What can be **done** with the data (e.g., what **questions** can be asked)
    - Etc.

Data policy and **stewardship**

- **Data stewardship** - actively managing data and ensuring adherence to data policy
- Often, data policy needs to be outlined in a **protocol** that needs to be approved by an **Institutional Review Board**
- Consumers / research participants should be told about data policy **during the consent process**

Entities that deal with human genetic data: four examples

Consumer-facing companies

23&Me: “DNA genetic testing for health, ancestry, and more”

Ancestry: “Family tree, genealogy and family history records”

Research-focused entities

H3Africa: “Human heredity and health in Africa… aims to… study of **genomics and environmental determinants of common diseases** with the goal of improving the health of **African populations**”

UK Biobank: “large-scale biomedical database… **genetic and health information** from half a million **UK** participants… [enables] vital research into the most **common and life-threatening diseases**”

Each entity has participant-facing **policy documents** that explain how data will be managed

Activity: Understanding data policies & data stewardship

Split into 4 groups, assign 1 person to share with big group

15 mins

Each group will be given **four policy documents** (one from each entity) and will try to **find the answer to the question they are assigned** (e.g., what type of data will be collected?)

15 mins

Group share-out

- How do the answers to your question **differ across policies**?
- **Which entities** did particularly a particularly **good/poor job** of answering this question?

Questions to read for

Group 1: what type of data will be collected & generated?

Group 2: what types of analyses / questions will be asked with the data?

Group 3: who (else) has access to the data?

Group 4: how does a participant withdraw permission?

Stakeholdership

Stakeholdership

- A **stakeholder** is one who is *involved with* or *affected by* a course of action
- To define a stakeholder, we must ask:
  - What is the **course of action**?
  - How is this stakeholder **involved or affected** by the action?
  - What is **at stake** for them?

Challenges of assessing stakeholdership in study design

1. Determine **who the stakeholders are**, and their primary motivations
2. **Solicit input** from stakeholders in ways that are equitable and accessible
3. Prioritize and **balance conflicting perspectives**
4. Appropriate, thoughtful, tailored **communication** with each group

Stakeholdership example: Duty to Warn

Haley is a healthy 31-yo with **three sisters** whose **mother had passed away mid-40s from breast cancer** complications. After testing, Haley learns **she has BRCA1 risk-allele** and tells her doctor that she wants to pursue a mastectomy because otherwise it will just feel like a ticking timebomb.

In this discussion, her doctor says, “The next step is to put you in touch with a good breast surgeon. Before we do that, though, **let’s talk about how you want to share this information with your siblings.**”

The blood drained from Ms. Holmes’ face. She pushed her chair away from Dr. Wagner.

“**There’s no way I’d tell my sisters about this**, even if we were close,” she said. “Which we’re not. To be honest, it’s none of your business who I tell and who I don’t. If I had known you were going to pull this on me, I would have gone to another doctor.”

Laberge and Burke. Duty to Warn At-Risk Family Members of Genetic Disease. AMA Journal of Ethics. 2009

Stakeholdership example: Duty to Warn

TLDR: Healthy 31-yo woman with a family history of breast cancer learns she has a major risk allele and adamantly decides against warning her sisters about her own genetic risk.

Course of action:

Stakeholders & stakes:

Laberge and Burke. Duty to Warn At-Risk Family Members of Genetic Disease. AMA Journal of Ethics. 2009

Stakeholdership example: Duty to Warn

TLDR: Healthy 31-yo woman with a family history of breast cancer learns she has a major risk allele and adamantly decides against warning her sisters about her own genetic risk.

Course of action: Informing the third party of their familial risk for genetic disease.

Stakeholders & stakes:

- The patient - privacy and autonomy to decide who she informs
- The physician - protect patient privacy, protect others from known risks, protect self from legal backlash
- The siblings - potentially at risk themselves and could take precautions if warned

Laberge and Burke. Duty to Warn At-Risk Family Members of Genetic Disease. AMA Journal of Ethics. 2009

The Havasupai Tribe: Stewardship & Stakeholdership

https://www.nytimes.com/video/us/1247467672743/blood-journey.html

Activity: Practice identifying stakeholders

Split into **4 groups**

7 mins
In your group reflect on the Havasupai Tribe story from the **perspective of different stakeholders**. The purpose here is not to judge, but reflect and assess.

Guiding questions:

- What is the course of action you are considering?
- Who were the stakeholders and what was at stake for them?
- Where did conflicts arise?
- What are some potential impacts of the outcome?
- Who else might be a stakeholder?

The Havasupai Tribe: Stewardship & Stakeholdership

Context

- Havasupai people observed **high rates of diabetes** within their community
- Contacted **trusted researcher** to investigate
- Researcher brought in geneticist **collaborator** to pursue specific hypothesis

Conflict

- Tribal members were **consented** to genetic study under broad terms and **not made aware of the implications** of broad consent
- **Additional research** was performed and published in **conflict with participant cultural values**

Impact

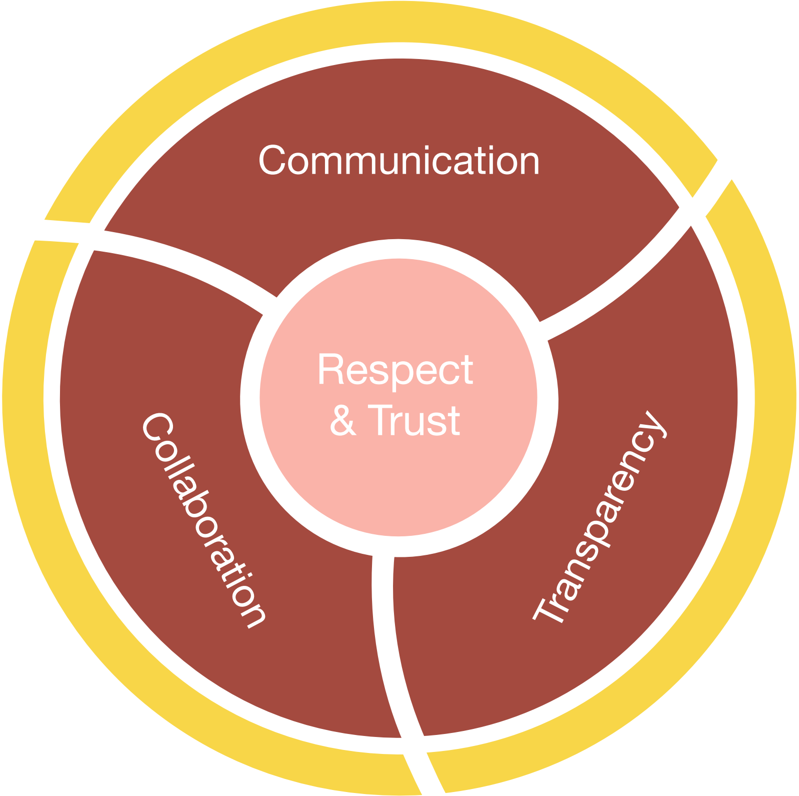
- Havasupai Tribe **successfully sued** on the basis of negligence and lack of informed consent
- **Clear reprimand** of researchers overreaching use of community data
- Precedent set for **questioning old IRBs**

Community-based Participatory Research

The Agency for Healthcare Research and Quality (AHRQ) defines community-based participatory research (CBPR) as a “collaborative research approach that is designed to ensure and establish structures for participation by communities affected by the issue being studied, representatives of organizations, and researchers in all aspects of the research process to improve health and well-being through taking action, including social change” [1]. CBPR, as AHRQ describes it, further entails **shared decision-making power** and **mutual ownership between the community and the researchers**. Over time, researchers have come to recognize that, with community commitment, they could work effectively to assist in identifying and resolving health care disparities [2].

https://journalofethics.ama-assn.org/article/genetic-research-among-havasupai-cautionary-tale/2011-02

Principles of community-based research



Communication

Respect
& Trust

Collaboration

Transparency

Successful community-based research: St. Regis Mohawk Tribe

Context

The reservation is downstream from a superfund site

- General Motors' industrial waste was dumped in the rivers
- PCBs, a carcinogen, was released into environment

Conflict

Polluted waters were affecting the health of community members

- Subsistence living
- Fish intake was leading to dangerous levels of PCB in people
- Affecting breast milk!

Impact

Community-led and initiated study

- Mohawk mothers were participants
- Results published in newspaper and radio
- Research trusted by community members

Activity: Use the principles of community-based participatory research & design a study on cardiac disease

You will be presented with a community-based research scenario and assigned a stakeholder role. Split into **groups based on your assigned roles.**

10 mins

- Take a minute **on your own** to read and reflect on your assigned role & perspectives
- **In your groups,** try to reach a consensus about the study design, data management, and informed consent policies.

20 mins

- **Group discussion**

Activity: Use the principles of community-based participatory research & design a study on cardiac disease

Community background

- **Tight-knit** and strong cultural roots
- **Medically underserved** and most members are **not scientifically trained**
- Have been noticing a **cardiac illness** in community members

Disease background

- tends to affect community members **around birth**
- **pulse and breathing** are affected
- when older, these members **cannot exercise regularly**

Researcher background

- **local** research institution specializing in cardiovascular genetics
- has **never collaborated** with this community before
- trying to write **publications** to get more funding through grants

Activity: Use the principles of community-based participatory research & design a study on cardiac disease

- Community members (non-participants)
- Participant community members
- Community leadership (Tribal government, religious leader, community spokesperson, etc)
- Community members that are also researchers
- Lead researchers
- Research team members (trainees, techs, staff, etc)
- Collaborators
- Research institution administrators
- Funding agencies

Activity: Use the principles of community-based participatory research & design a study on cardiac disease

- **Study design**
  - What research questions do we investigate?
  - What data do we collect & generate?

- **Data management**
  - Who owns & manages the data?
  - What restrictions do we put in place on the data?

- **Study consent**
  - What should be included in the consent form?
  - How will data anonymized, esp if sampling from a small group like a Tribal nation?
  - What information will be returned to the community?
    How will interventions be put in place?
  - Can participants opt to withdraw from the study? How?

Final Thoughts

Data processing and stewardship

- Entities storing genetic data should be good ***data stewards with clear policy***
- Different ***stakeholders*** (researchers, participants, corporations) have different interests in genetic data, which should be balanced when designing a research study

Community-based participatory research

- Communities should be equal partners through each portion of the study
- Mutual respect and trust, communication, transparency, and collaboration should be at the heart of research collaborations

Session 4: Race, Ancestry, Identity, and Genetics

Learning goals

- Examine how and why genetic ancestry and race are used in current genetic studies
- Evaluate inconsistencies and uncertainties in how race, ethnicity, and ancestry are defined and used in genetics over time and between cultures
- Assess the risks and benefits of using genetic ancestry and race in current genetic studies and identify how to mitigate risks
- Evaluate the relationship between identity and genetic ancestry.

Please complete pre-class assignment in Canvas:
2 short readings and a Qualtrics survey!

Taught by Daphne Martschenko,
Alanna Pyke, & Daniel Cotter