‘Our’ Biobank, ‘Your’ Results: The Why, What, When and How of Returning Results to Biobank Participants

‘Big Genetics’ Sessions

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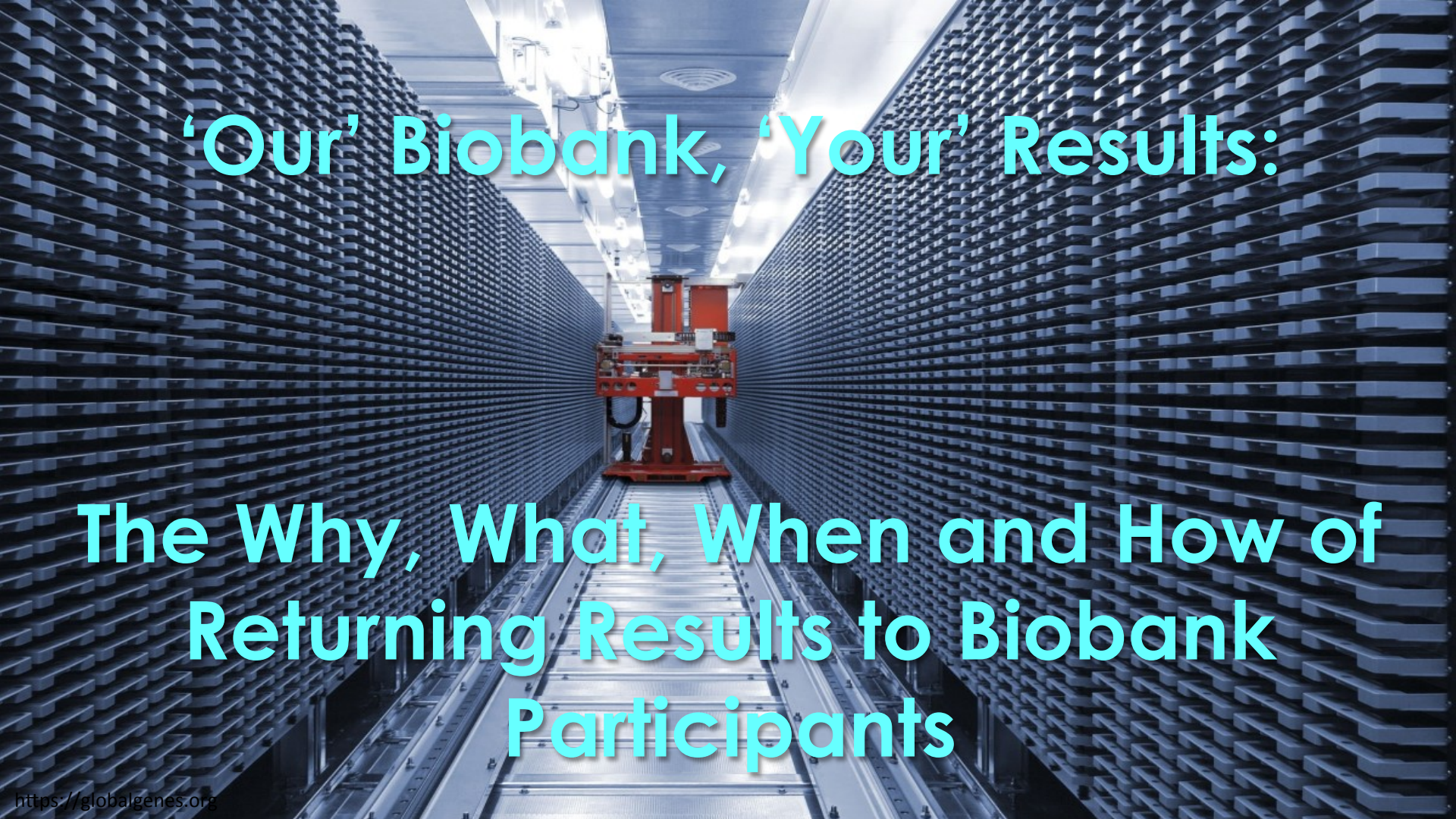

‘Our’ Biobank, ‘Your’ Results:

The Why, What, When and How of Returning Results to Biobank Participants

Disclosure Slide: Matthew Taylor (2018)

I have financial ties that may (or may not) relate to the content of this presentation that are disclosed to the University of Colorado:

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- *American Board of Medical Genetics and Genomics*
- *American college of graduate medical education (ACGME)*
- *Arca Biopharma Inc.*
- *Array Biopharma*
- *Biomarin Pharmaceuticals, Inc.*
- *CU Medicine*
- *GeneDx*
- *Genzyme, a Sanofi Company*
- *Guidepoint Global*
- *Hershey Decker Drake*
- *Inspired Opinions(Schelsinger)*
- *Rocket Pharma*
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Session Objectives

- Describe the structure and goals of Research Biobanks
- Contrast the categories of genetic testing results generated by Biobanks
- Evaluate the strategies and challenges of returning genetic testing results to Biobank participants.

Describe the structure and goals of Research Biobanks

https://ukbiocentre.com/

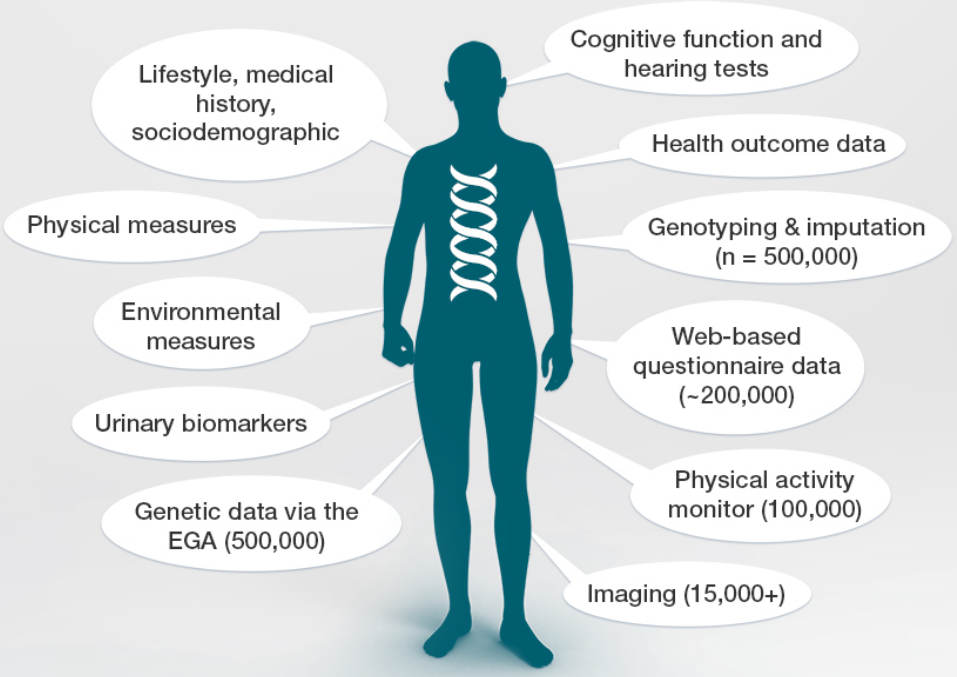
biobank uk

Improving the health of future generations

B3 Africa

BRIDGING BIOBANKING AND BIOMEDICAL RESEARCH ACROSS EUROPE AND AFRICA

Data on UK Biobank participants



"Traditional" Genetic Research

- ~Single Disease(s)
- Subjects know (trust) Investigator(s)
- Standard informed consent
- Study design known
- Return of results historically not anticipated
- Sample-Silo model

Biobanks are "Different"

- Stored indefinitely
- Used for unspecified research, unforeseen at time of consent.
- System-wide access vs. identifiable researchers that participants know and trust.

Courtesy-Marilyn Coors


Some Ethical Considerations
Risks / Benefits of Biobanks
Privacy
Broad Consent
Return of Individual Results
Incidental Findings
Ownership / Commercialization
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https://www.genomicspolicy.org

Biobanks: Risks / Reward

RISKS

- Security Breach
- Genetic Discrimination
- Genotype/Phenotype
- Future Uses Unknown
- Family Information
- Change Mind in Future
- Criminal Justice uses
- Benefits take time, if ever

BENEFITS

- Better, singular, security
- Advance understanding of many diseases
- Future uses flexible
- Increased size = increased discovery power
- Cross-validation
- Longevity of research

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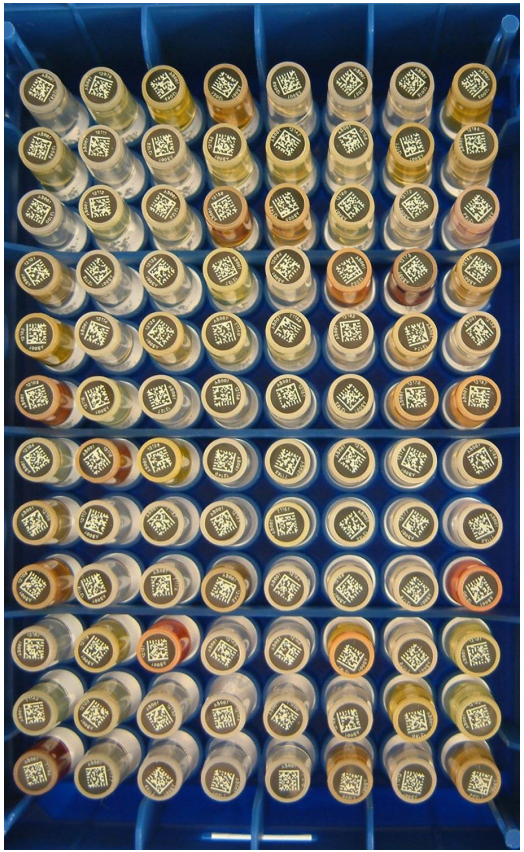
Other, Pragmatic, Benefits of Biobanks

- 'Institutional' Biobank has broader benefit
  - open to ~all researchers
  - each sample has many purposes
  - greater R.O.I./sample
  - Cross validation possible
- Accrual precedes hypothesis
  - Disease-agnostic / Hypothesis-neutral
  - Speed of discovery accelerated
  - Can establish genotype cohorts in real time
- Potential to re-contact participants
- Education / Genomic Visibility



https://ki.se/en/research/

Generic Biobank Workflow

Standard Consent vs Broad Consent

- Disclosure regarding **specific research** study.
  - Describe risks and benefits
- Donors can withdraw samples
- Approved research
- Comprehensive understanding is the goal
  - Traditional, often face-to-face
- Investigator is your provider
- ***Consent***

- Allows use of samples in **unforeseen future** studies
  - Alludes to risks/benefits
- Donors can withdraw samples.
- Approved research.
- Comprehensive information about research is not possible.
  - "Short" Permission Forms.
- Investigator is your health system
- ***Permission***

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Contrast the categories of genetic testing results generated by Biobanks

https://www.mercatornet.com

‘Genetic Testing’ In Biobanks

Platforms

Catch & Hold	SNP Array	Sequencing
• No pre-planned sequencing • Investigator fueled	• MEGA (or other) • Less data / less $	• WES or WGS • More data / more $

‘Genetic Testing’ In Biobanks

Return of Results

Research Only	Research Mostly	Research & Clinical
• Discovery Only • No RoR	• Desire to give back • Research RoR	• CLIA infrastructure • Planned Clinical RoR

‘Genetic Testing’ In Biobanks

Possible ways to Return Results

Face-to-Face	Tele-Genetics	Video-Assisted	Direct Reporting
• Geneticist & Counselor • Other (trained) provider	• Geneticist & Counselor • Other (trained) provider	• Portions of RoR are delivered by video	• To Provider • To Patient • +/- Access to expert

Evaluate the strategies and challenges of returning genetic testing results to Biobank participants.

http://www.momandfitness.com/

Colorado Center for Personalized Medicine

- Biobank
  - Primary Consent → Sample Collection → MEGA SNP Array → Then what?
- Subset of MEGA data→ 'Reportable' to ~~participants~~ patients
  ① Pharmacogenetics (individual patients)
  ② Genetic disease carrier status (relatives/offspring)
  ③ Ancestry (patient/family)
  ④ Genetic Disease Risk (individual patients ~1%)

Pilot Return of Results: Genetic Disease Risk

- Q1 2018:
  - Initial MEGA results → no results process
- Pilot RoR Proposed to
  - Return initial results (n ~10)
  - Understand challenges & resources needed
  - Inform future RoR processes

Pilot Process

- Pilot Team:
  - Genetic counselors x 4, Molecular Laboratory Director, Genetics Ethicist, Medical Geneticist
- Process: (Division of labor and consensus based)
  - Face-to-face and e-discussions using shared documents
  - Identified key steps in process
  - Developed workflow, documents, assessment plan
  - Iteratively refined process

Pre-contact:

- Confirm primary consent, date signed, and Molecular lab is ‘ready’ to report
- Genetic counselor ‘assigned’ as point-person for each participant; ~ no chart review
- Established physical space, date/time for participant visits

Pre-cont

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Telephone Contact:

- Contact participants (2 GCs); cover key talking points; generic voicemail
- Check for clarity/questions; schedule visit; mail/ email secondary consent
- EPIC documentation & Internal assessment

Pre-contact:

- Confirm primary consent, date signed

Telephone Contact:

- Contact participants (2 GCs); cover key
- ail
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- sent

Face-to-Face Visit

- Introductions, contracting, basic genetics, participant questions
- Secondary consent → lab order
- Results reporting to patient, discussion, questions, next steps
- EPIC documentation / letter / assessment

Pre-contact:

- Confirm primary consent, date signed
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Telephone Contact:

- Contact participants (2 GCs): cover key

Face-to

- Intro
- gene
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- EPIC
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Post Visit:

- Internal Process Review and refinement (ongoing)
- Post-Visit phone call assessment questions
- Continue to assess / refine process

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Face-to-Face Visit

- Introductions, contracting, basic genetics, participant questions
- Secondary consent → lab order
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Pilot RoR Progress-Summary Data

- July – August 2018
- 12 Participants contacted
  - 9 Responders
  - 9 Visits
    - all chose to receive results
  - 3 Non-responders
    - Letters will be sent out

	Time (hrs)	Team
Pre-Contact	0.5 – 1.25	GC & MD
Contact	0.25 – 0.5	GC
Visit	1.25 – 1.75	GC (2) & MD
Post Visit	0.25 – 0.5	MD & SC
Lab Result	3.0 – 4.0	Lab Dir

	Men	Women
Gender	4	5
Ages	40-80	30-80
Mutations	BRCA1, ACTA1	BRCA1, TNNI3, MYBPC3, MYH7, RYR1

RoR-Individual Data

Pt	Age	M/F	Medical History	Fam Hx	Prior Gen	Gene	Condition	Notes
1	45	M	Migraines	Early BrCa	No			
2	35	F	Hepatitis, Liver xplant	Multiple OvCa	No			
3	65	M	HTN, asthma	NA	No			
4	55	F	CAD, HTN, chronic pain	BrCa	No			
5	85	F	Recurrent BrCa	Cancers	No			
6	25	F	Pituitary adenoma	HTN	No			
7	55	F	DM, HepC, Muscle pain	Asthma	No			
8	55	M	P. vera	None	No			
9	75	M	DJD, HTN	None	No			

*Likely Pathogenic

RoR-Individual Data

Pt	Age	M/F	Medical History	Fam Hx	Prior Gen	Gene	Condition	Notes
1	45	M	Migraines	Early BrCa	No	BRCA1	Breast-Ovarian Ca	
2	35	F	Hepatitis, Liver xplant	Multiple OvCa	No	BRCA1	Breast-Ovarian Ca	
3	65	M	HTN, asthma	NA	No	BRCA1	Breast-Ovarian Ca	
4	55	F	CAD, HTN, chronic pain	BrCa	No	TTNI3	Hypertrophic CM	
5	85	F	Recurrent BrCa	Cancers	No	MYBPC3	Hypertrophic CM	
6	25	F	Pituitary adenoma	HTN	No	MYH7	Hypertrophic CM	
7	55	F	DM, HepC, Muscle pain	Asthma	No	RYR1	Central Core/ Mal. HT	
8	55	M	P. vera	None	No	BRCA1	Breast-Ovarian Ca	
9	75	M	DJD, HTN	None	No	ACTA1*	Hypertrophic / Dilated CM	

*Likely Pathogenic

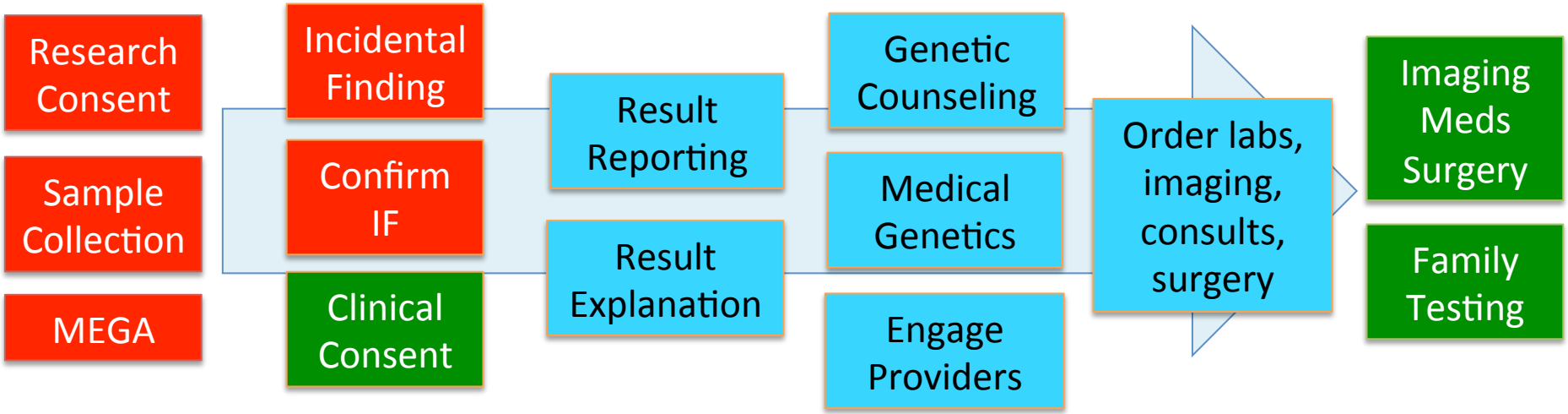
RoR-Individual Data

Pt	Age	M/F	Medical History	Fam Hx	Prior Gen	Gene	Condition	Notes
1	45	M	Migraines	Early BrCa	No	BRCA1	Breast-Ovarian Ca	M-BrCa(40s), MGP (cancer)
2	35	F	Hepatitis, Liver xplant	Multiple OvCa	No	BRCA1	Breast-Ovarian Ca	Relatives with OvCa; Rec. CancerGen (**Brother**)
3	65	M	HTN, asthma	NA	No	BRCA1	Breast-Ovarian Ca	Father had Neck 'mass'
4	55	F	CAD, HTN, chronic pain	BrCa	No	TTNI3	Hypertrophic CM	**Sister** (with BrCa) came to visit; Echo review = HCM
5	85	F	Recurrent BrCa	Cancers	No	MYBPC3	Hypertrophic CM	Recurrent BrCa; (**Daughter**)
6	25	F	Pituitary adenoma	HTN	No	MYH7	Hypertrophic CM	
7	55	F	DM, HepC, Muscle pain	Asthma	No	RYR1	Central Core/ Mal. HT	Life long muscle problems; anesthesia problems
8	55	M	P. vera	None	No	BRCA1	Breast-Ovarian Ca	
9	75	M	DJD, HTN	None	No	ACTA1*	Hypertrophic / Dilated CM	Physician; no cardiac problems (**Son**)

**Likely Pathogenic*

Next Steps / Ongoing Discussions

- Tracking follow-up / letters to non-responders
- Evaluation / Assessment (ongoing)
  - internal observations & Participant feedback
- Scaled up numbers → scaled down per-patient-resources




Reflection