FROM ETHICS AND GOVERNANCE COUNCIL TO ETHICS ADVISORY COMMITTEE UK BIOBANK

ANTICIPATING AND RESPONDING TO ETHICAL ISSUES

Anneke Lucassen 19-6-19

FROM EGC TO EAC

EGC established by WT and MRC, when UK Biobank began the recruitment of its participants in 2006.

Acted as an independent guardian of the UK Biobank Ethics and Governance Framework (EGF); monitored and reported publicly on the conformity of the UK Biobank project with that framework

Advised on the interests of research participants and the general public in relation to UK Biobank.

In 2018 EGC recommended that its oversight role would be more effectively discharged by better integration within UK Biobank as an advisory committee of the UK Biobank Board.

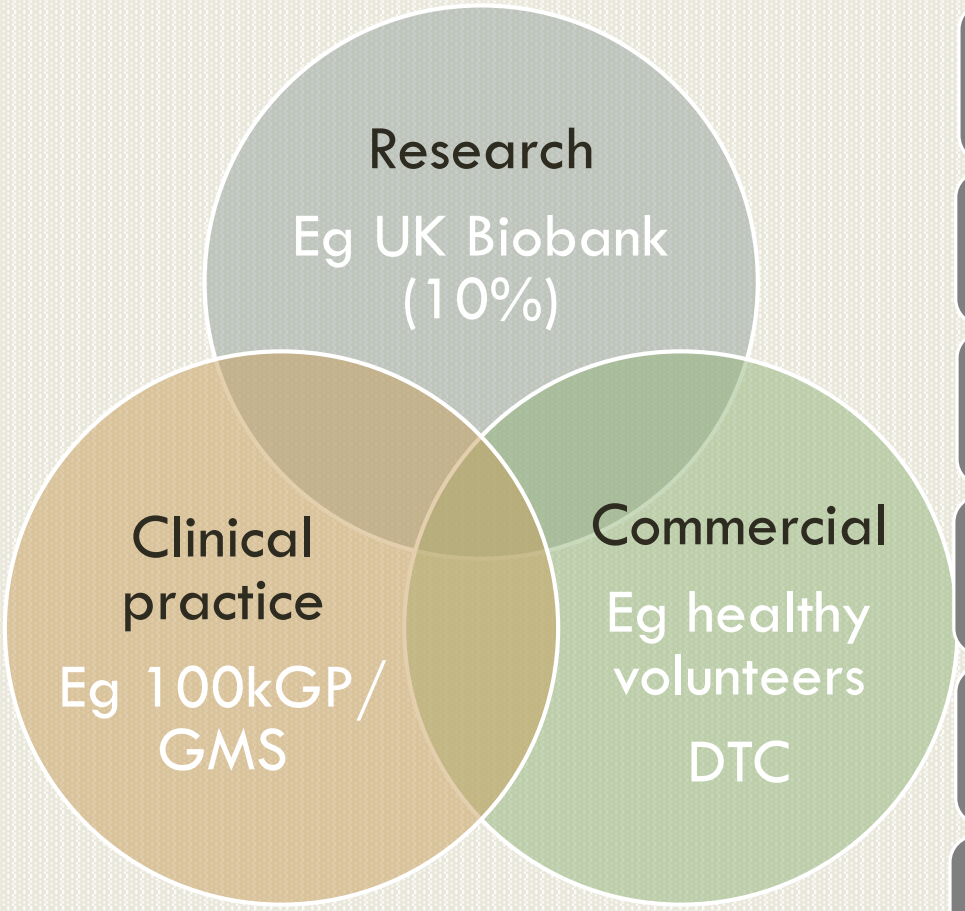
EAC REMIT

To provide advice to the UK Biobank Board on ethical issues that arise during the maintenance, development and use of the UK Biobank resource, including:

1. identifying, defining and examining relevant ethical issues, delivering key research in these areas;
2. providing advice, guidance and recommendations on relevant ethical issues;
3. reviewing and advising on policies which have an ethical dimension that is relevant to UK Biobank.

Expertise: clinical, bioethics, law, philosophy, epidemiology, molecular science, broadcasting,

VISION OF 5 MILLION GENOMES



- Activities will overlap
- Ongoing debate on types of consent for each
- Ongoing debate on types of feedback for each
- Diagnosis and prediction often conflated
- Genomics continues to attract a very deterministic discourse
- UKB data already provides cautionary tales

UKB FINDINGS HELPFUL AT INTERFACE
COMPOSITE EXAMPLE:

- Jane, aged 50, given direct to consumer ancestry test as present
- She sent her raw data for secondary analysis for medical results
- BRCA1 mutation found. She has no known family history of breast or ovarian cancer
- Would like risk reducing mastectomy and oophorectomy
- NHS Sanger sequencing shows NO BRCA1 mutation.
- SNP arrays very bad at 'calling' rare high risk variants.
- 85-95% of **rare variants** called by this DTC test are wrong

FEEDBACK OF RESULTS FROM WGS

1. Analytical validity- SNPs bad at calling rare variants
2. Clinical validity- penetrance of pathogenic mutations in healthy populations

iants in a Population Setting, The American Journal of Human Genetics (2019), https://doi.org/10.1016/j.ajhg.2018.12.015

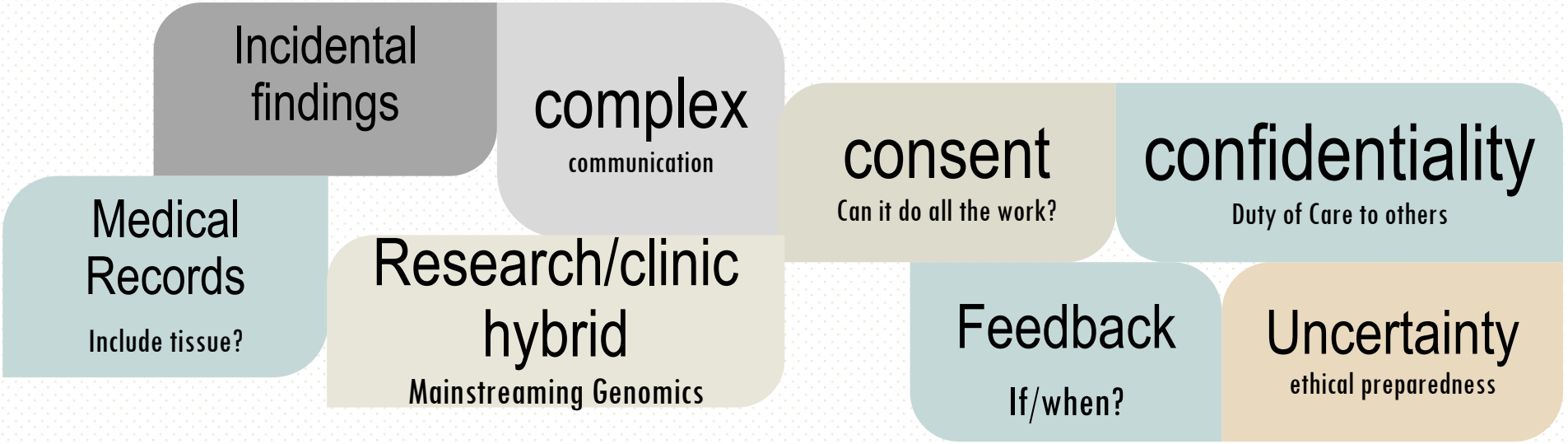
ARTICLE

Assessing the Pathogenicity, Penetrance, and Expressivity of Putative Disease-Causing Variants in a Population Setting

Caroline F. Wright,[1,*] Ben West,[1] Marcus Tuke,[1] Samuel E. Jones,[1] Kashyap Patel,[1] Thomas W. Laver,[1] Robin N. Beaumont,[1] Jessica Tyrrell,[1] Andrew R. Wood,[1] Timothy M. Frayling,[1] Andrew T. Hattersley,[1] and Michael N. Weedon[1,*]

More than 100,000 genetic variants are classified as disease causing in public databases. However, the true penetrance of many of these rare alleles is uncertain and might be over-estimated by clinical ascertainment. Here, we use data from 379,768 UK Biobank (UKB) participants of European ancestry to assess the pathogenicity and penetrance of putatively clinically important rare variants. Although rare variants are harder to genotype accurately than common variants, we were able to classify as high quality 1,244 of 4,585 (27%) putatively clinically relevant rare (MAF < 1%) variants genotyped on the UKB microarray. We defined as "clinically relevant" variants that were

AN AGILE, RESPONSIVE, ETHICS ADVISORY SERVICE FOR UKB RELEVANT FOR CURRENT AND FUTURE ACTIVITY



RELEVANT TO OTHER COHORTS AND OTHER ACTIVITIES

Press release: "the people that most often mentioned religious language like "God" or "pray" in their [Facebook] posts were 15 times more likely to have diabetes than those who used these terms the least."
pennmedicine.org/news/news-rele...