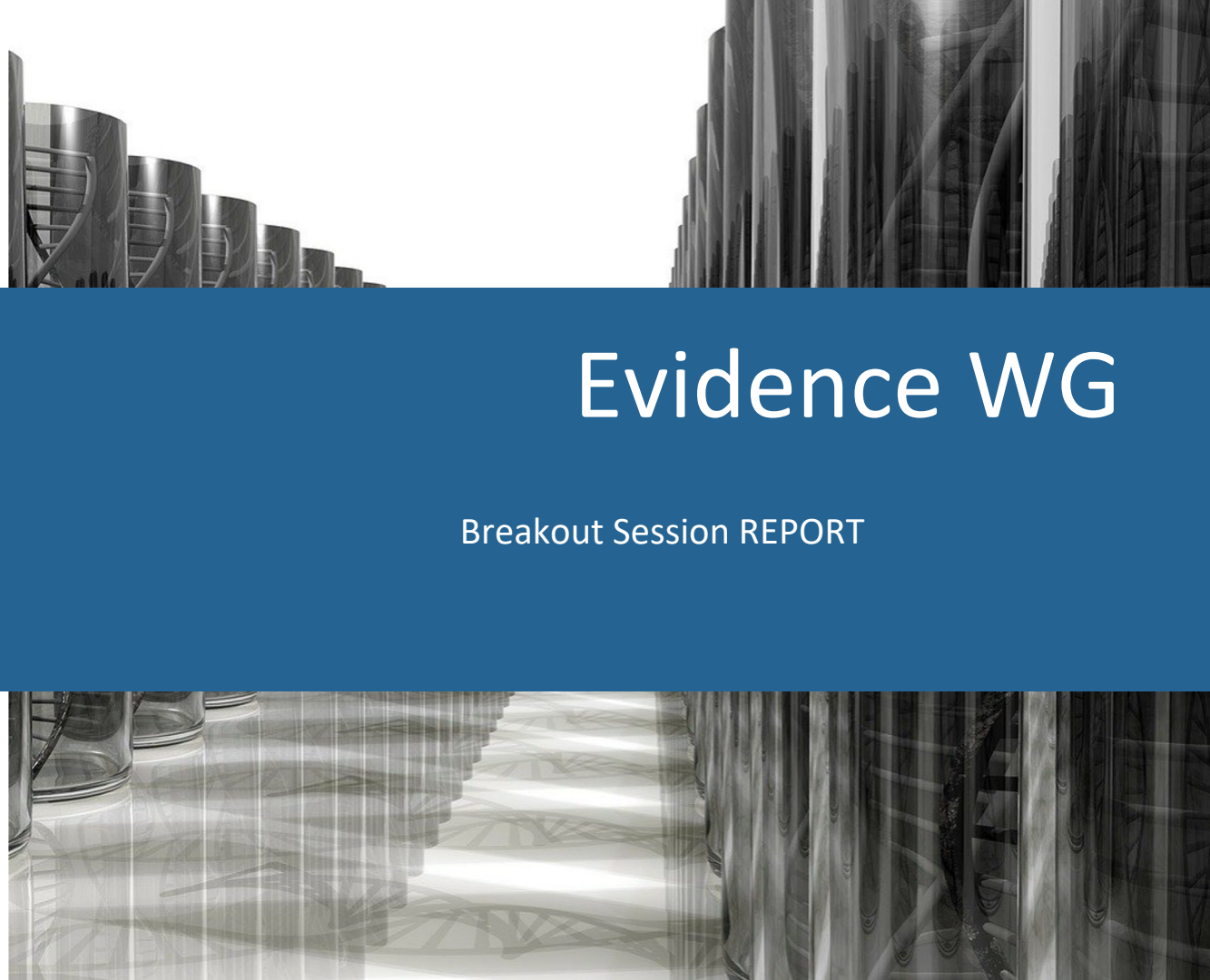
8 May 2020

Virtual
Santiago

Evidence WG

Breakout Session REPORT



Global Genomic
Medicine Collaborative

Aim

Assess, and regularly update, current evidence of clinical utility of genomic medicine for polygenic disorders (= with no major gene, e.g., coronary artery disease)

Target examples, when published :

- **PRS of CAD allows better prevention in tested, normal subjects**
- **PRS of CAD allows better therapy in patients with myocardial infarct**

List of Diseases within scope of Evidence WG

- Coronary artery disease
- Hypertension
- Inflammatory Bowel disease
- Multiple sclerosis
- Psoriasis
- Systemic Lupus Erythematosous
- Manic depression
- Schizophrenia
- Depression (common)
- Sepsis
- Alzheimer
- Amyotrophic lateral sclerosis
- Obesity
- Diabetes type II (not MODY)
- Diabetes type I
- Chronic Kidney Disease
- Breast cancer (not BRCA1 / BRCA2)
- Colon cancer (not HNPCC, not FAP)
- Prostate cancer

Parallel Tasks

1. Expert review: search Pubmed+ manual curation

> Identify studies demonstrating clinical utility of GM in polygenic or nearly demonstrate => use as seed studies in (2)

2. Develop search engine for scanning evidence of GM in polygenic dis.

Use list of disease and seed studies

Grant Wood (Information Technol & Flagship) liaised to GA4GH colleagues (Bevan Koopman, David Hansen; CSIRO, Brisabe, Au):

Parallel Tasks (2)

1. Snapshot of current evidence, polygenic risk scores. **TO DO**
    - Expert adjustment of query terms string.
    - Query literature (PubMed) for evidence of clinical utility (Strong/moderate/loose)
    - Manually curate items, in duplicate
2. Regular Updates of current evidence: **TO DO**
    - Finalize list of diseases of interest
    - Automated tool, via Grant, with CSIRO colleagues (Brisabane, Au)

Time Frame

1. Snapshot of current evidence, polygenic risk scores. — 2020, fall
    - Expert adjustment of query term.
    - Query literature (PubMed) for evidence of clinical utility (Strong/mid/loose)
    - Manually curate items, in duplicate
2. Regular Updates of current evidence: — 2022
    - Finalize list of diseases of interest
    - Automated tool, via Grant, with CSIRO colleagues (Brisabane, Au)

Outline

- Missions of the Evidence WG
- Work Setting
- Scope of DNA variants we target
- Tasks

MISSIONS of the Evidence WG

monitor evidence of clinical utility of genomic medicine (polygenic)

assess current evidence

update regularily

promote awareness about the current evidence available to support genomic medicine. Including low- and middle-income countries

Genomic Medicine = using DNA data to improve health

PREVENTION, in healthy persons : mitigate risk using DNA data

PRECISION, in affected patients : adjust therapy using DNA data

SCOPE of DNA variants for genomic medicine

Somatic DNA variants , in Cancer

Inherited (germ-line) DNA variants, in genetic disorders

Monofactorial

Chromosomal: Down S,…

Mendelian: Sickle Cell, Cystic fibrosis
BRCA1/2, MODY,
PharmacoGx

1 major gene

Multifactorial: polygenic predisposition : Coronary Artery Disease,
IBD, MS, depression, obesity, diabetes…

0 major gene

= our scope

TASKS of the Evidence WG, Santiago 6 May 2020

1. **List diseases** with significant polygenic susceptibility, for which we want to seek evidence of clinical utility of GM (e.g., Coronary Artery Disease) . Review criteria.
2. Identify studies with evidence, or near-evidence = **SEED STUDIES** > feed-in semi-automated search method > measure and monitor (and publish)
3. Compile evidence in Mendelian / Near Mendelian (e.g., BRCA; Rare disorders) (expert review)

List diseases with significant polygenic susceptibility

- Coronary artery disease
- Hypertension
- Inflammatory Bowel disease
- Multiple sclerosis
- Psoriasis
- Manic depression
- Schizophrenia
- Depression (common)
- Sepsis
- Alzheimer
- Amyotrophic lateral sclerosis
- Obesity
- Diabetes type II (not MODY)
- Diabetes type I
- Breast cancer (not BRCA1 / BRCA2)

CRITERIA

INCLUSION

- Studies which show that patients' genomic data can be used to modify and improve health outcomes, be it by process (e.g. diet adherence, increased screening, treatment, process outcome, intermediate outcome, and health outcome)
- Can include behavioural studies
- Not necessarily randomized studies

EXCLUSION

- Studies not using genomic data (i.e. other -omics; gene expression, etc)
- Cancer studies (Studies of the somatic genome (tumour profiling))
- Pharmacogenomic studies
- Highly penetrant monofactorial disease-related studies (Mendelian, including monogenic CNVs)
- Microbial/metagenomics-related studies
- Expression profiling studies
- Association studies or observational studies, including genome-wide association studies (GWAS)
- Studies without a measure of health outcome, process outcome, and intermediate outcome
- Pure methodology/technical studies (e.g. design of a protocol for obtaining genomic DNA from saliva)

Pubmed query 06 May 2020

	# papers
(((((Genomic Medicine) AND Clinical Outcome) NOT Pharmacogen*) NOT Tumour) NOT Somatic) NOT Review	825
Polygenic risk score	1025
(((((polygenic risk) AND Clinical Outcome) NOT Pharmacogen*) NOT Tumour) NOT Somatic) NOT Review	56

Patient health outcome

Hypothesis:
testing cardiovascular risk alleles will improve patient outcome

Measuring outcome is not trivial

- Process outcome
- Intermediate outcome
- Clinical outcome
- Cost outcome

- ➢ diet
- ➢ plasma cholesterol
- ➢ myocardial infarction
- ➢ money saved or not

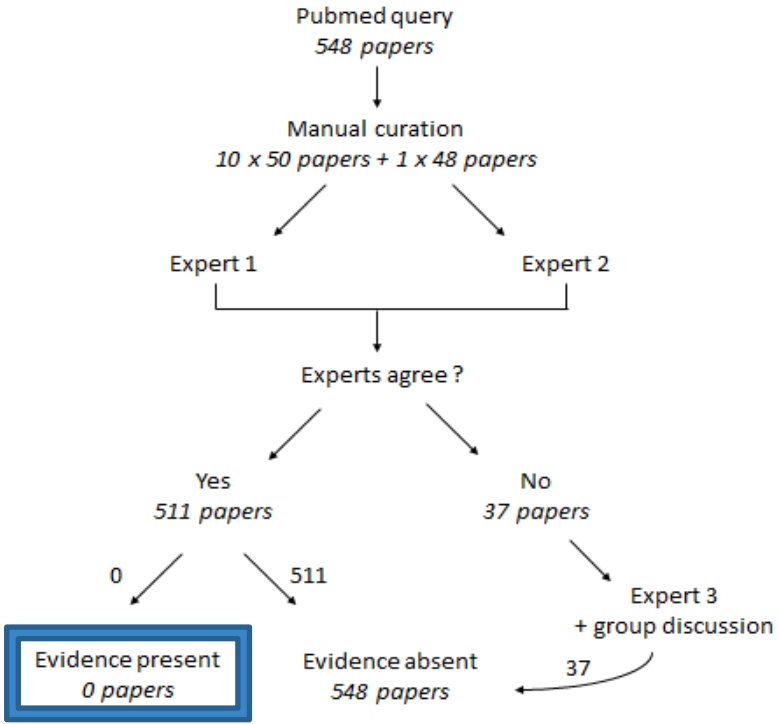
PubMed query + manual curation

(((((Genomic Medicine) AND Clinical Outcome) NOT Pharmacogen*) NOT Tumour) NOT Somatic) NOT Review

548Papers retrieved
Each assessed by 2 members of the WG for fitting

Short paper, likely to be highly cited

Genetics in Medicine : rejected
Public Health Genomics : submitted



Next steps

- Re-do : measure available evidence iteratively
- Evidence for cost-effectiveness:
  Collect, and liaise with other WG > lay public, decision makers
- Flag research related to Genomic Medicine in clinical research registries
  - ❑ clinicaltrials.gov
  - ❑ https://www.clinicaltrialsregister.eu

=> genomic medicine implementation registry

Section Title

Section Title

- Use if you want to include a description or outline for the section

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Ex. What is the current weather in your location?

a. Raining
b. Overcast
c. Sunny
d. Snowing
e. ….


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