Day 1
November 3, 2021

IHCC Q4 Members Virtual Workshop

International 100K+ Cohort Consortium

Welcome and Introduction

Peter Goodhand

CEO, Global Alliance for Genomics and Health (GA4GH)
Co-Chair, International HundredK+ Cohorts Consortium
Canada

Geoff Ginsburg, MD, PhD

Director, Duke University
Center for Applied Genomics
Co-Chair, International HundredK+ Cohorts Consortium
USA

Nov 3, 2021

IHCC November Workshop: “IHCC Link”

Geoff Ginsburg
Peter Goodhand
Co-Chairs

Happy Birthday IHCC

Relevant History

- 2015: NIH compiled information on large cohort programs (≥100K participants)
- 2017: HIROs agreed to bring cohorts together, to encourage data sharing, improve efficiencies, & maximize investments
- March 2018: First Cohorts Summit at Duke University
- Summer 2018: Formation of IHCC
- April 2019: Second Cohorts Summit in Iceland
- May 2020 & 2021: Third and Fourth (Virtual) Summits

G2MC

Global Genomic Medicine Collaborative

Global Alliance for Genomics & Health

Collaborate. Innovate. Accelerate.

GA4GH

Goals for IHCC Link

- Review and discuss the IHCC 5-year strategy including each Working Group's specific Action-Plans for implementation
- Progress of the IHCC pilot projects: Discuss future plans and potential for new collaborations
- Update: Data Science for Health Discovery and Innovation in Africa
- Discuss current data collection methods for both Environmental/Climate and Race/Ethnicity/Ancestry information
- Develop new knowledge of funding agency opportunities including resources and methods for submitting successful grant applications

Achievements 2021

- Completion of 5-year strategic plan
- Submission of NIH U24 for 5 years of funding
- Planning for Wellcome Trust submission (January 2022)
- Chan-Zuckerberg Initiative funding
- Seven cross-cohort projects underway
- International Cohorts Atlas expansion
- Evergreen policy agenda

Pilot Projects

Project	PI	Institution	Funders	# cohorts	# LMIC cohorts
Polygenic risk scores (PRS)	Hakon Hákonarson (USA)	Children's Hospital of Philadelphia (CHOP)	NIH & WT	6	2
Exploring the role of genetically determined BMI in infancy, childhood, and early adulthood on colorectal cancer development in later life	David J. Hughes (Ireland)	University College Dublin, International Agency for Research on Cancer (IARC), University of Texas	NIH & WT	4	1
High-Throughput Metabolomic Biomarker Measures in Diverse Ancestries	Hakon Hákonarson (USA)	Children's Hospital of Philadelphia (CHOP)	NIH & WT	4	3
Opioid cohort consortium (OPICO) to investigate the effects of regular opioid use on mortality and on cancer development	Paul Brennan (France)	International Agency for Research on Cancer (IARC)	NIH & WT	10	4
Global Mental Health Impact of the COVID-19 Pandemic	Jordan Smoller (USA) Sarah Bauermeister (UK) & Andre Brunoni (Brazil)	Massachusetts General Hospital, Oxford University, University of Sao Paulo Medical School	NIH & WT	12	3
Novel coronavirus host susceptibility study in South Africa (COVIGen-SA)	Michele Ramsay (S. Africa)	Wits Health Consortium	NIH & WT	3	3
Strengthening biospecimen collection for Global Longitudinal Population Studies in the COVID-19 era	John Chambers (Singapore)	Nanyang Technological University	Chan Zuckerberg Initiative (CZI)	4	3
Davos Alzheimer's Collaborative (DAC) - Pilot PRS	Hakon Hákonarson (USA)	Children's Hospital of Philadelphia (CHOP)	DAC	7	4

New Steering Committee Members

Nicky Mulder, Ph.D.
Principal investigator of H3ABioNet (H3Africa), S. Africa

Catterina Ferreccio M.D., M.P.H.
Director of the MAUCO Cohort, Chile

Kobus Herbst, M.Sc.
Director of the SAPRIN Cohort, S. Africa

New Steering Committee Members

Michèle Ramsay, Ph.D.
Project Leader of the AWI-Gen Consortium Study (H3Africa), S. Africa

Reza Malekzadeh, M.D.
Director of the Persian Cohort and the Golestan Cohort, Iran

Rahman Jamal, M.D., Ph.D.
Project Leader of the Malaysian Cohort, Malaysia

New Steering Committee Members

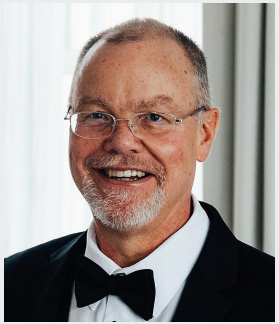
Nicki Tiffin, Ph.D., M.P.H.
***Co-Lead*: Policy and Systems Working Group**
Associate Professor at Centre for Infectious Disease Research in Africa (CIDRI), University of Cape Town, S. Africa

Paballo Chauke, M.Sc.
***Co-Lead*: Training and Workforce Working Group**
Bioinformatics Training and Outreach Coordinator for H3ABIONET, S. Africa

Albert Tenesa, Ph.D.
***Co-Lead*: Training and Workforce Working Group**
Co-Principal Investigator of the Coronagene cohort, UK

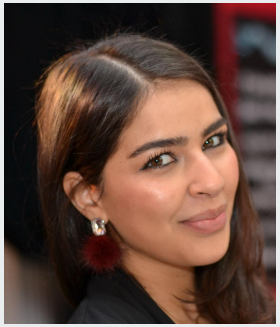
Our Amazing Secretariat

Scott



Ludy

Farah



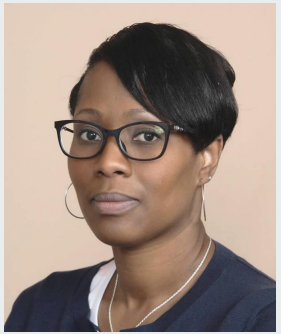
Meredith

John

Carles

Chris

Ida



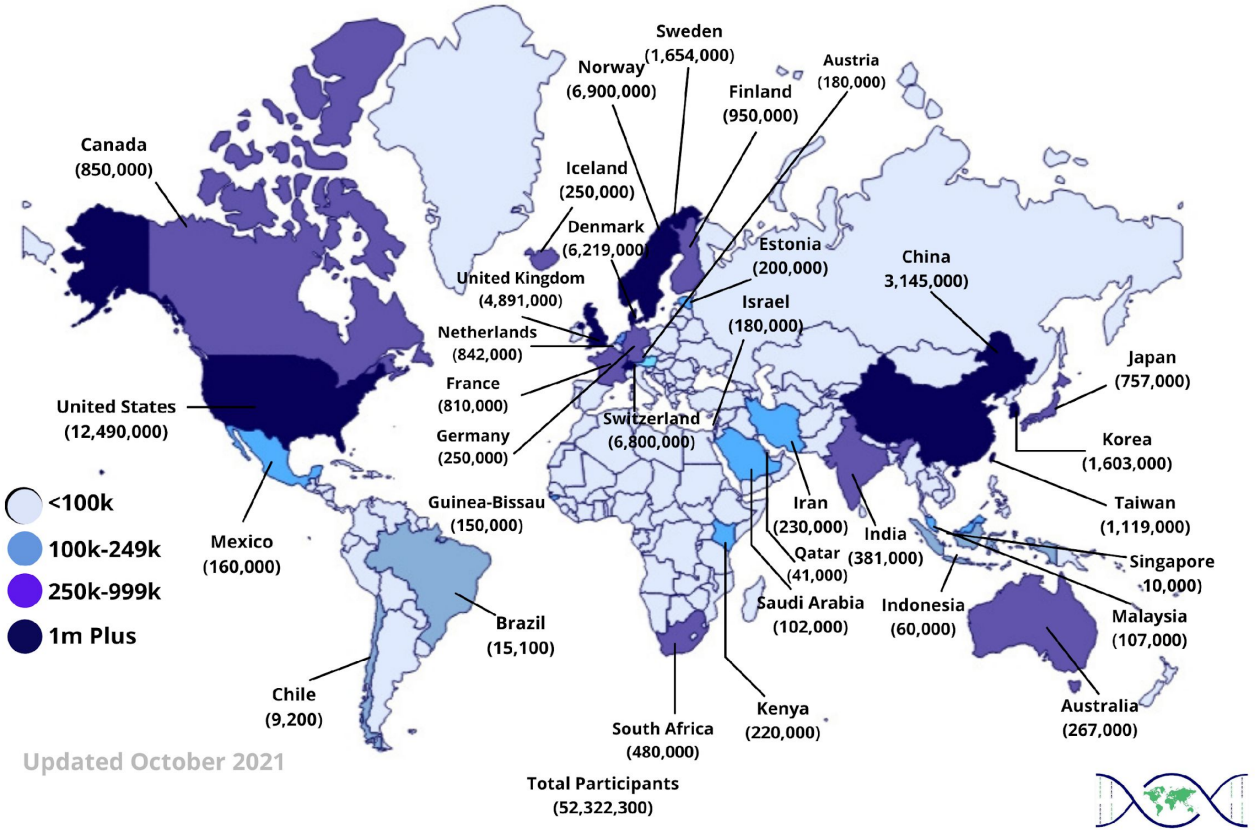
Ytina

Brittany

Chip

Teji

IHCC Member Cohorts Across The Globe



110 Cohorts, 48 Countries, >50,000,000 Participants

IHCC Funding Organizations

Implementing the IHCC Strategic Plan

VISION
A global community of cohorts working together to advance science and improve health for all.

MISSION
To forge cohort connections that revolutionize population health science by providing sustainable data infrastructure, cultivating a collaborative research environment, and promoting policies and best practices that foster connectivity, interoperability, and reciprocity.

Our Values and Guiding Principles (IIDEA)

- We are **INTENTIONAL**
- We have **INTEGRITY**
- We embrace **DIVERSITY**
- We strive for **EQUITY**
- We act with **AUDACITY**

Strategic Directions

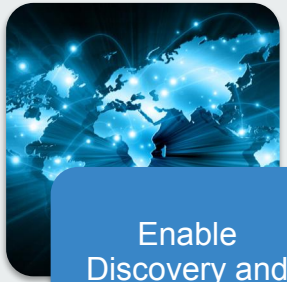
In the next 3 to 5 years, we will focus our efforts to...

1. Demonstrate that IHCC Generates Impactful Science
2. Enable Discovery and Connectivity of Cohorts for Collaboration
3. Make it Possible for All Cohorts to Contribute to IHCC Scientific Challenges
4. Build a Strong Governance and Operational Foundation

IHCC Strategic Directions

Demonstrate that IHCC Generates Impactful Science

- Scientific Strategy & Cohort Enhancement WG
- Scientific Project Subcommittee



Enable Discovery and Connectivity of Cohorts for Collaboration

- Data Standards & Infrastructure WG

Make it Possible for ALL Cohorts to Contribute to IHCC Science Challenges

- Policy & Systems WG
- Training & Workforce WG

Build Strong Governance and Operational Foundation

- Staffing and Operations Subcommittee
- Inclusivity and Reciprocity Subcommittee
- Marketing and Communications Subcommittee
- Summit Subcommittee

Working Group (WG) Action Plans

- Today, the WG leaders will present their proposed action plans for implementation during the next 1-3 years
- This meeting with then breakout into 4 separate sessions (one per WG) to discuss specific action plans, define responsibilities, timing of execution and next steps for the next 12 months
- Each WG will report the results of their breakout session discussions to the broader workshop audience

Please join and engage! We need you!

Subcommittees Remits

Scientific Project Subcommittee → Reviews and approves IHCC scientific projects, including those involving partnerships with external organizations or Industry Members, and provides feedback regarding process, goals, and timeline.

Summit Subcommittee → Plans, reviews, supports preparation and evaluates Summits

Staffing and Operations Subcommittee → Ensure right-sized staff and resources to get the work done

Inclusivity and Reciprocity Subcommittee → Review and improve IHCC's internal policies and practices to ensure equity, inclusion, and reciprocity

Marketing and Communications Subcommittee → Develop and reinforce brand and identity; member onboarding and communication

Relevant Secretariat Staff
+
2 SC members

Please join and engage! We need you!

Execute the Communication plan

- Develop short and long-term plans for communicating the essence of the IHCC Strategic Plan
- Integrate vision, mission and values in our communications (social media, website, newsletters, emails)
- Review our branding to be aligned to the Strategic plan: developing a new logo, email signature graphic, updated presentation slides, resources and guidance to adhere to the Strategic Plan

Be on the lookout!

IHCC Strategic Plan (SP) Implementation Roadmap

Achieving the IHCC Strategic Plan

We are thankful to all those who participated and provided valuable input into the development of the IHCC Strategic Plan.

The IHCC is continuing to grow and reach new milestones and frontiers.

Through the guiding principles and strategic directions set forth in the strategic plan, we will achieve our vision as a global community of cohorts working together to advance science and improve health for all.

Day 1 Outline

- IHCC Funded Project Presentations
  - Live panel discussion
- 15 minute break
- Working Group High Level Overviews
- Working Group Strategic Planning Implementation Breakouts
- 15 minute break
- Working Group Report Back and Day 1 Summary

IHCC Funded Project Presentations

Nicky Mulder, PhD

Professor
University of Cape Town

Principal Investigator
H3ABioNet

South Africa

Session Overview

Session Topics:

- Exploring the role of genetically determined BMI in infancy, childhood and early adulthood on colorectal cancer development in later life
- High-Throughput Metabolomic Biomarker Measures in Diverse Ancestries
- OPICO to Investigate the Effects of Regular Opioid Use on Mortality and on Cancer Development
- COVID and Mental Health
- Novel Coronavirus Host Genomic Study - South Africa COVIGen-SA
- COVID Biospecimen Collection Asia
- Davos Alzheimer's Collaborative (DAC) — Foundational Phase
- Polygenic Risk Scores (PRS) Projects for IHCC and DAC

Session Speakers:

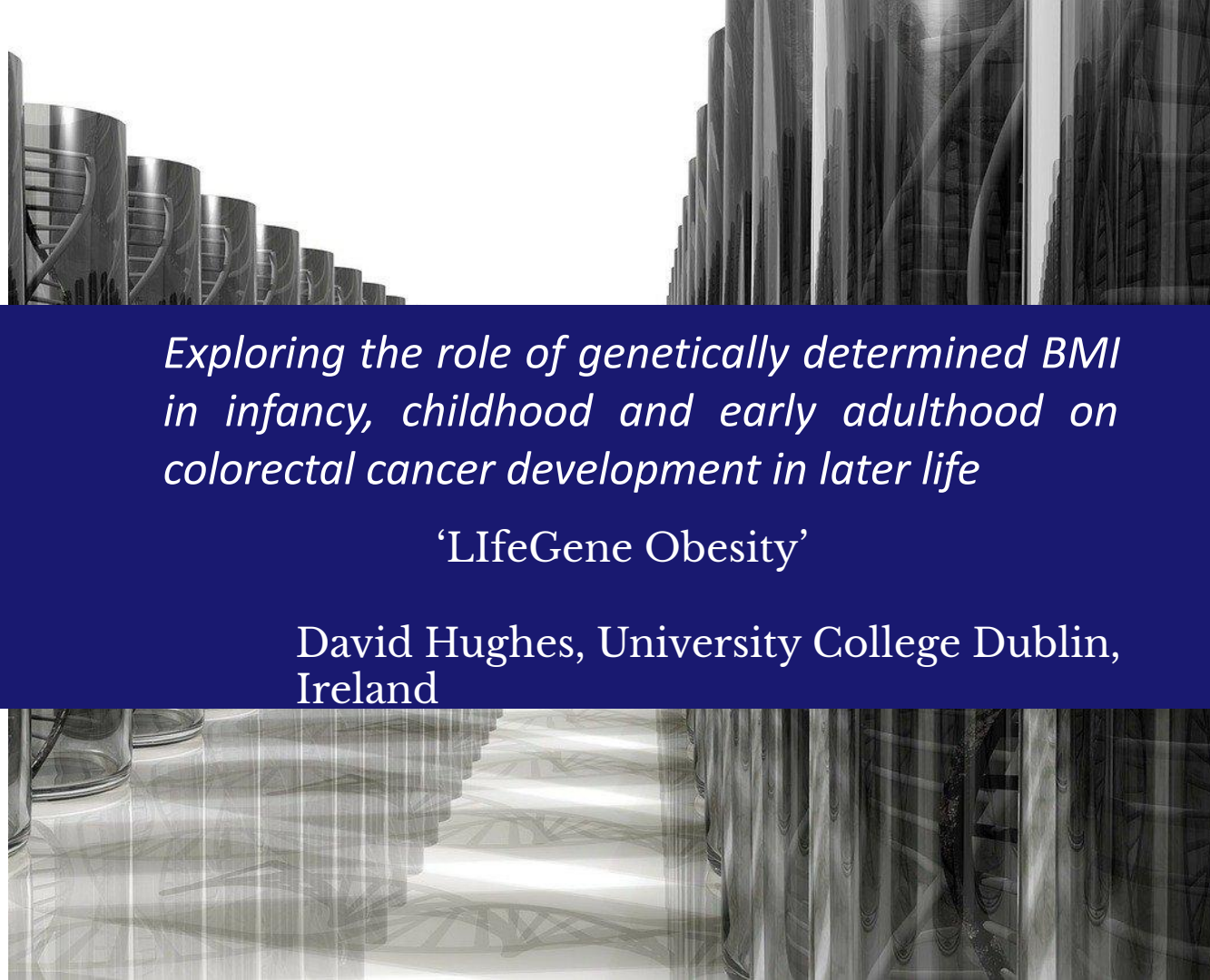
- David Hughes, BSc, PhD, PGDE
- John Connolly, PhD
- Mahdi Sheiki, MD, PhD
- Sarah Bauermeister, MSc, PhD
- Michèle Ramsay, PhD
- Ananya Gupta, PhD
- Rhoda Au, PhD
- Patrick Sleiman, PhD

David Hughes BSc, PhD, PGDE

Assistant Professor
Cancer Epidemiology,
University College Dublin

Ireland

November 3rd & 4th, 2021

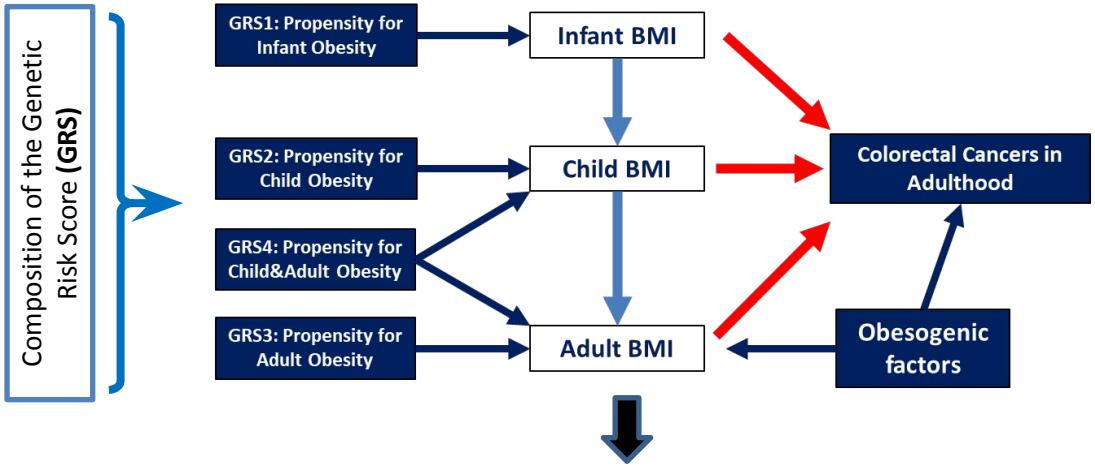


Exploring the role of genetically determined BMI in infancy, childhood and early adulthood on colorectal cancer development in later life

'LIfeGene Obesity'

David Hughes, University College Dublin, Ireland

Project Analytical Strategy



- The GRS will be calculated from the sum of risk alleles corresponding to obesity phenotypes - weighted by the effect size estimate of the corresponding GWAS on the phenotype
- Cause specific risks for the GRS-cancer associations will be estimated using logistic regression models or Cox proportional hazard, as appropriate

Obesity Variables for Stratified Analyses / Adjustment:

- Early life obesity assessed by birth weight (UKBB only)
- Adult obesity assessed by: (1) WHO BMI categories, (2) duration of obesity during adult life, (3) Cross categorization of weight/waist-circumference (UKBB, GECCO, EPIC)

Dietary, Lifestyle Variables Stratified Analyses / Adjustment (UKBB, GECCO, EPIC):

- Healthy Lifestyle (HLI) and Mediterranean Diet (MDS) Scores
- Physical activity, alcohol intake, alcohol drinking pattern, smoking patterns
- By Sex (men/women), by age group at study enrolment and at diagnosis (<40, 40 to <60, ≥60 years old)

Polygenic Risk Score

a weighted sum of the number of risk alleles

$$\mathrm{PRS} = \beta_1 \mathrm{SNP}_1 + \ldots + \beta_m \mathrm{SNP}_m$$

- β, the effect size estimated by different approaches
- m, the number of SNPs included in the polygenic risk score

Additional exploratory analyses:

- By levels of pre-diagnostic circulating CRP, C-peptide, and by calculated metabolic syndrome (MetS) score (EPIC, UKBB where possible)

Project Timelines (1st May 2021- 31st October 2022)

Time	Month 1-6	Month 7-12	Month 13-18
Objectives			
1. Construct different life stage Genetic Risk Scores to associate with colorectal cancer development [all cohorts]:			
Approval from UKBB, EPIC, and GECCO datasets for extraction of existing relevant data *(for objectives 1, 2)*	✓		
Additional: MR analysis of early and later life adiposity on CRC risk	✓*		
Construction of life-course 'obesity predisposition' SNP-based Genetic Risk Scores (GRS 1 to 4 from infant to adulthood obesity)	✓		
Assessment of GRS values for BMI and CRC development risk (all cohorts)			
2. Determine whether the assessed CRC risks are modified by body size at different life stages, exposure to obesogenic factors in adult life, or by sex [all cohorts] *(exploratory analyses)*			
3. Assess association of the GRSs with BMI-trajectories and age categories of CRC onset			
4. Assess association between the GRSs and important mechanisms of obesity-mediated CRC development, i.e., metabolic dysfunction and inflammation, using existing biomarker measures [EPIC & UKBB] (*exploratory analyses*)			
Review and update of work plans / Project meetings	✓		
Write up & Publish a high-impact manuscript & other dissemination activities	✓*		

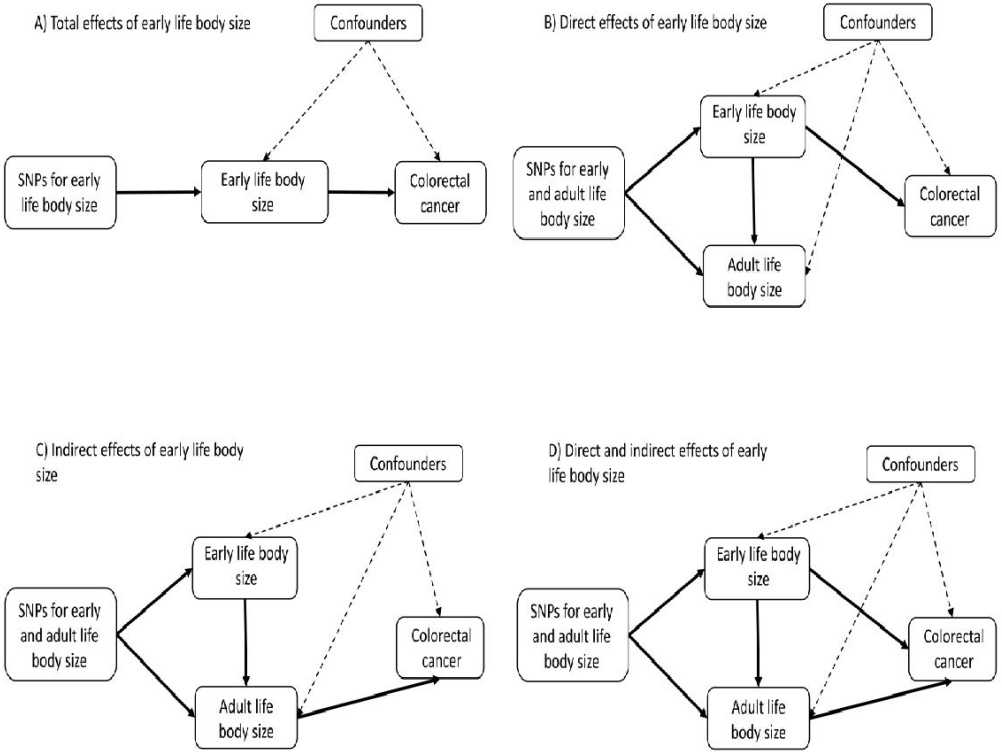
Separating the Effects of early and later life adiposity on CRC risk: A Mendelian randomization (MR) study*

MR analysis of possible causal relationships between body size at 10 years old and adulthood with CRC risk

Combination of GWAS body size data from UK Biobank (n = 453,169)

Plus, CRC data from meta-analysis of 3 genetic consortia, CORECT, CCFR, & GECCO, of up to 125,478 participants (58,131 cases and 67,347 controls)

MR instruments for early life body size (305 SNPs) and adult body size (557 SNPs) explained an estimated 4.5% and 6.4% of variability in early life and adult body size traits, respectively



*Currently under review in *Cancer Research*: ***Childhood adiposity putatively influences colorectal cancer risk due to a long-term effect of remaining overweight throughout the life course*** (Papadimitriou et al 2021).

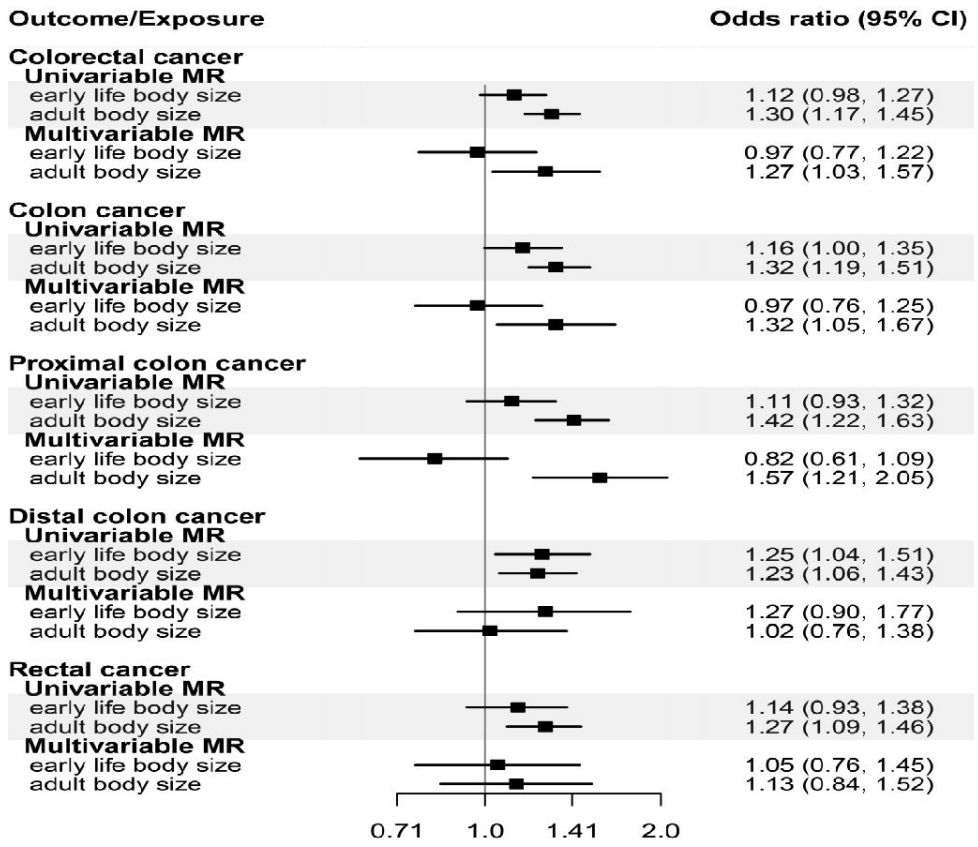
Summary Results

Some positive genetically predicted effects prior to adjustments (univariable MR) between early body size and CRC risk, strongest for colon cancer and distal cancers

After accounting for adult body size, the direct effect estimates - towards the null for CRC and colon cancer while similar magnitude, but more imprecise estimate, was observed for distal colon cancer

Adult body size was estimated to increase colorectal, colon, and proximal colon cancer risk

Overall: Effect of early life body size are more likely linked to the retaining of that weight during adulthood, which in turn increases CRC risk



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Acknowledgements

IARC-EPIC, LYON, FRANCE

Mazda Jenab

Neil Murphy

Heinz Freisling

Nikolaos Papadimitriou




& all EPIC-associated colleagues

& all subjects participating in the EPIC study

UKBB, GECCO, CORECT, & CCFR cohorts

Rory Collins (UKBB); Ulrike Peters (GECCO)

& all associated colleagues

& all subjects participating in these studies

MD ANDERSON,HOUSTON, TX, USA

Veronika Fedirko


https://www.ukbiobank.ac.uk/researchers/

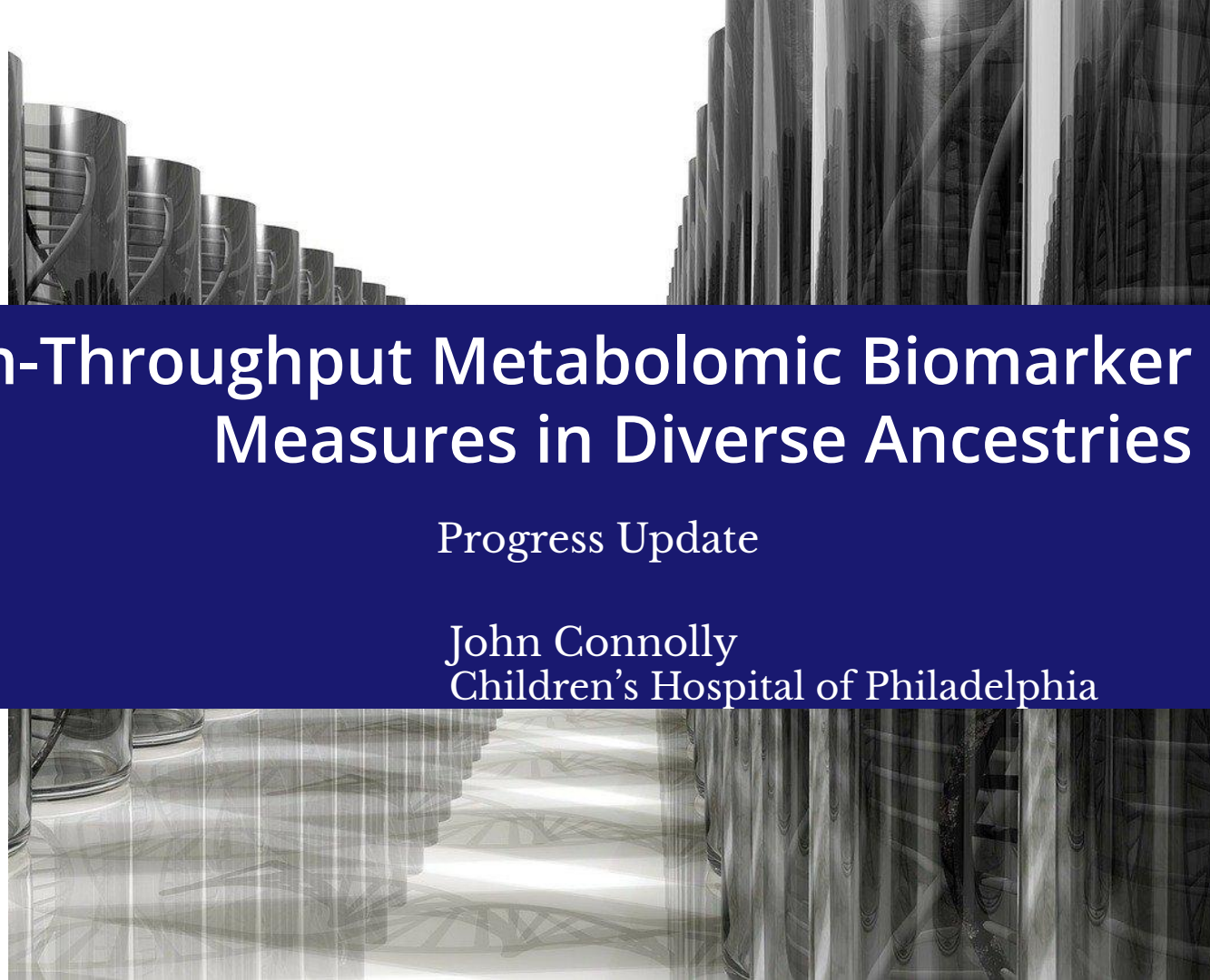
John Connolly, PhD

Neuropsychologist
Children's Hospital of Philadelphia Center for Applied Genomics

Scientific Strategy and Cohort Enhancements Workgroup Coordinator
International HundredK+ Cohorts Consortium

USA

3rd Nov 2021



High-Throughput Metabolomic Biomarker Measures in Diverse Ancestries

Progress Update

John Connolly
Children's Hospital of Philadelphia

Outline

- Project Overview
- Preliminary Data & Lessons Learned
- Timeline & Next Steps

High-Throughput Metabolomic Biomarker Measures in Diverse Ancestries

Principal Investigators

- Adam Butterworth, University of Cambridge & **South Asian Cohorts**
- Andre Brunoni, Universidade de São Paulo & **ELSA-Brasil**
- Arash Etemadi, National Cancer Institute, NIH & **Golestan Cohort Study**
- Hakon Hakonarson, **Children's Hospital of Philadelphia**

Team Members

- John Connolly, Patrick Sleiman (CHOP)
- Praveen Surendran (South Asian Cohorts)
- Alexandre Pereira (ELSA)

Background

- Chronic diseases impose a high burden on the health system.
- Health outcomes can be significantly improved through early diagnosis and intervention.
- Early diagnosis often unavailable particularly for individuals in low and middle income countries and minority populations in high income countries.
- Metabolic profiling represents a highly-scalable model for risk prediction and prevention.
    - Because of its relatively low cost, it offers a route to individualized medicine for these populations.

Aims

- Generate Metabolic Profiles on 5,000 Individuals with Genetic and/or Health Outcome Data.
- Analyses of associations with phenotypes of interest
- Analyses of association between metabolic metabolite levels (such as lipid profiles) and genetic data

Participating Cohorts

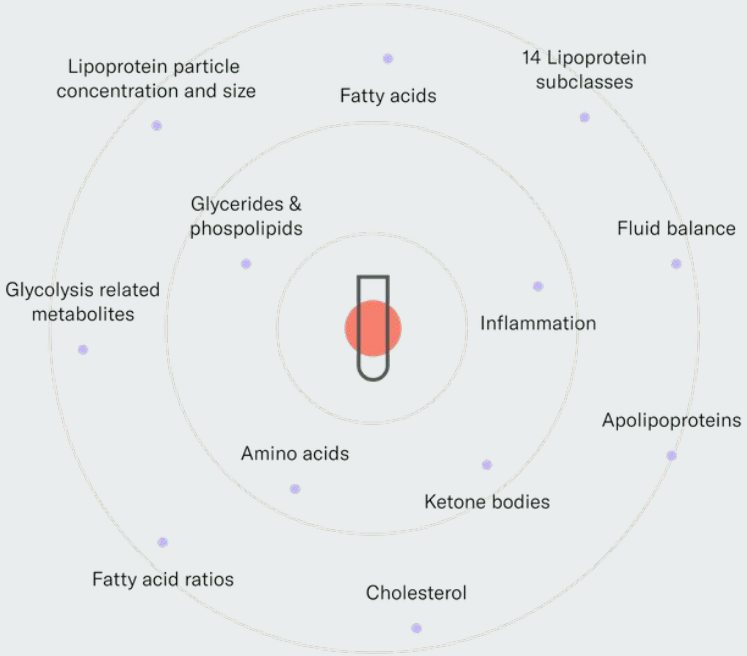
Cohort Name	Study samples	Principal Investigator/Lead(s)
South Asian Cohorts (BELIEVE)	1,500 samples of South Asian ancestry from Dhaka, Bangladesh	Adam Butterworth
ELSA-Brasil	1,000 samples from Brazilian civil servants	Andre Brunoni
Golestan Cohort Study	1,000 samples from Northeast Iranian general population	Arash Etemadi
Children's Hospital of Philadelphia (CHOP)	1,500 samples of African American children	Hakon Hakonarson

Target Phenotypes

Cohort Name	Study samples	Phenotypes
South Asian Cohorts (BELIEVE)	1,500 samples of South Asian ancestry from Dhaka, Bangladesh	Diabetes
ELSA-Brasil	1,000 samples from Brazilian civil servants	Broad-based
Golestan Cohort Study	1,000 samples from Northeast Iranian general population	Ischemic heart disease
Children's Hospital of Philadelphia (CHOP)	1,500 samples of African American children	22q11.2 deletion Autoimmune and autoinflammatory

Nightingale Platform

- NMR-based (Nuclear Magnetic Resonance spectroscopy) platform
- 228 biomarkers
- 100µl of plasma or serum



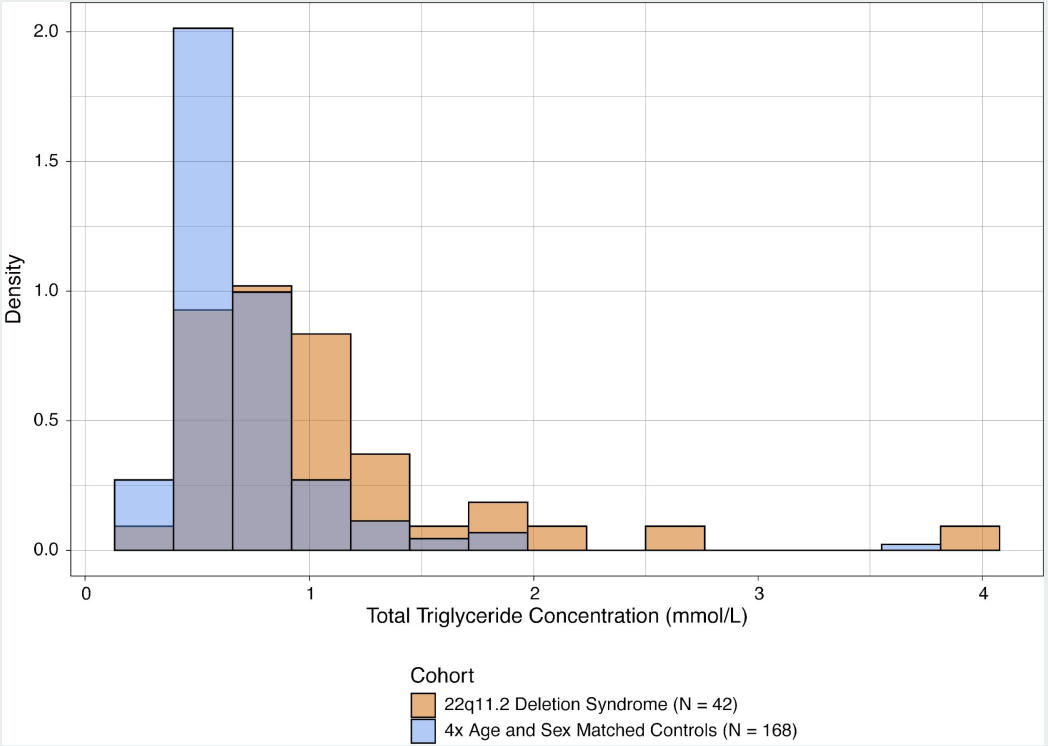
Progress & Timeline Overview

Preliminary Data

- Significant signals for
  - Obesity
  - Asthma
  - Sickle cell disease
  - Type 1 diabetes
  - 22q11.2 deletion syndrome
- Hypothesis driven in analytical approach

Preliminary Data

Metabolomics Recovers Known Elevations in Triglyceride Concentrations Among Individuals with 22q11.2 Deletion Syndrome



Lessons Learned

- Collective bargaining works
- Nightingale platform is efficient with little requirement in terms of overheads
- IHCC publication policy works
- Template for expansion

Next Steps

- Publication
  - IHCC Guidance and policy
- Data-Sharing
  - IHCC Data Atlas
  - Metabolights - EMBL-EBI
- Study Expansion
  - Several cohort members with existing data
  - Prospectively expand to more sites

Thank You

Funding & Support

Wellcome Trust
National Institutes of Health
IHCC

Principal Investigators

Adam Butterworth: **South Asian Cohorts**
Andre Brunoni: **ELSA-Brasil**
Arash Etemadi: **Golestan Cohort Study**
Hakon Hakonarson, **Children's Hospital of Philadelphia**

Study Team

Ian Campbell (CHOP)
Patrick Sleiman (CHOP)
Praveen Surendran (South Asian Cohorts)
Alexandre Pereira (ELSA)
Huiqi Qu (CHOP)

Mahdi Sheikh, MD, PhD

Medical Doctor and Cancer Epidemiologist

Genomic Epidemiology Branch of the International Agency for Research on Cancer (IARC - WHO)

France

03 November 2021

Opioid Cohort Consortium (OPICO) to investigate the effects of regular opioid use on mortality and on cancer development

Mahdi Sheikh, MD, PhD
International Agency for Research on Cancer (IARC - WHO)

Outline

- Overview of the project and its aims
- Engaging LMIC cohorts
- Challenges and solutions
- What went well (wins)
- Plans for publications
- Call for participation

Global crisis of opioid use

- Thousands of deaths and billions in economic losses each year
- Long-term health consequences remain unknown

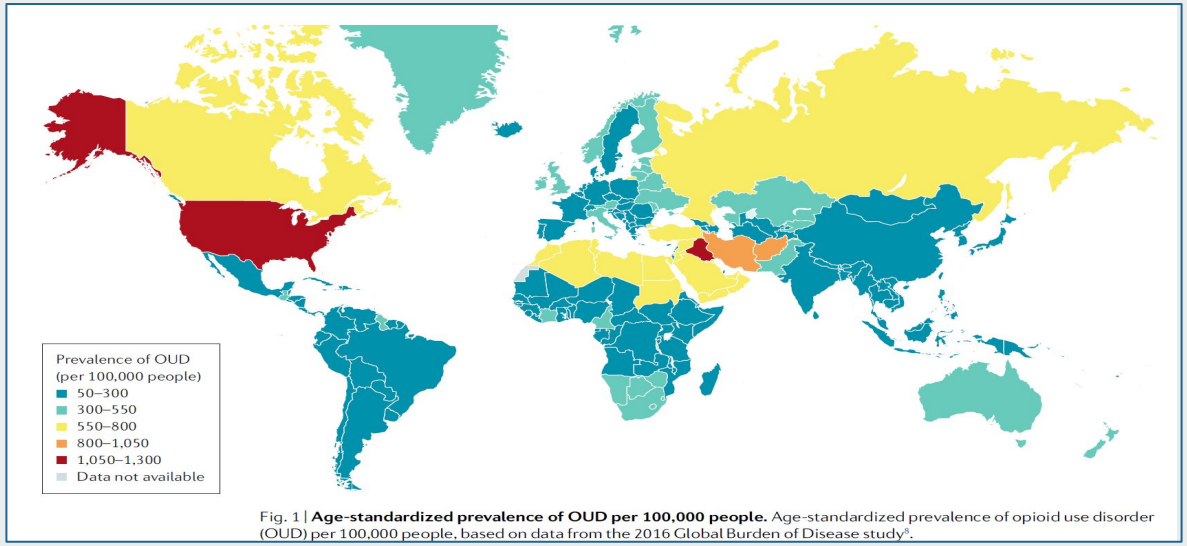


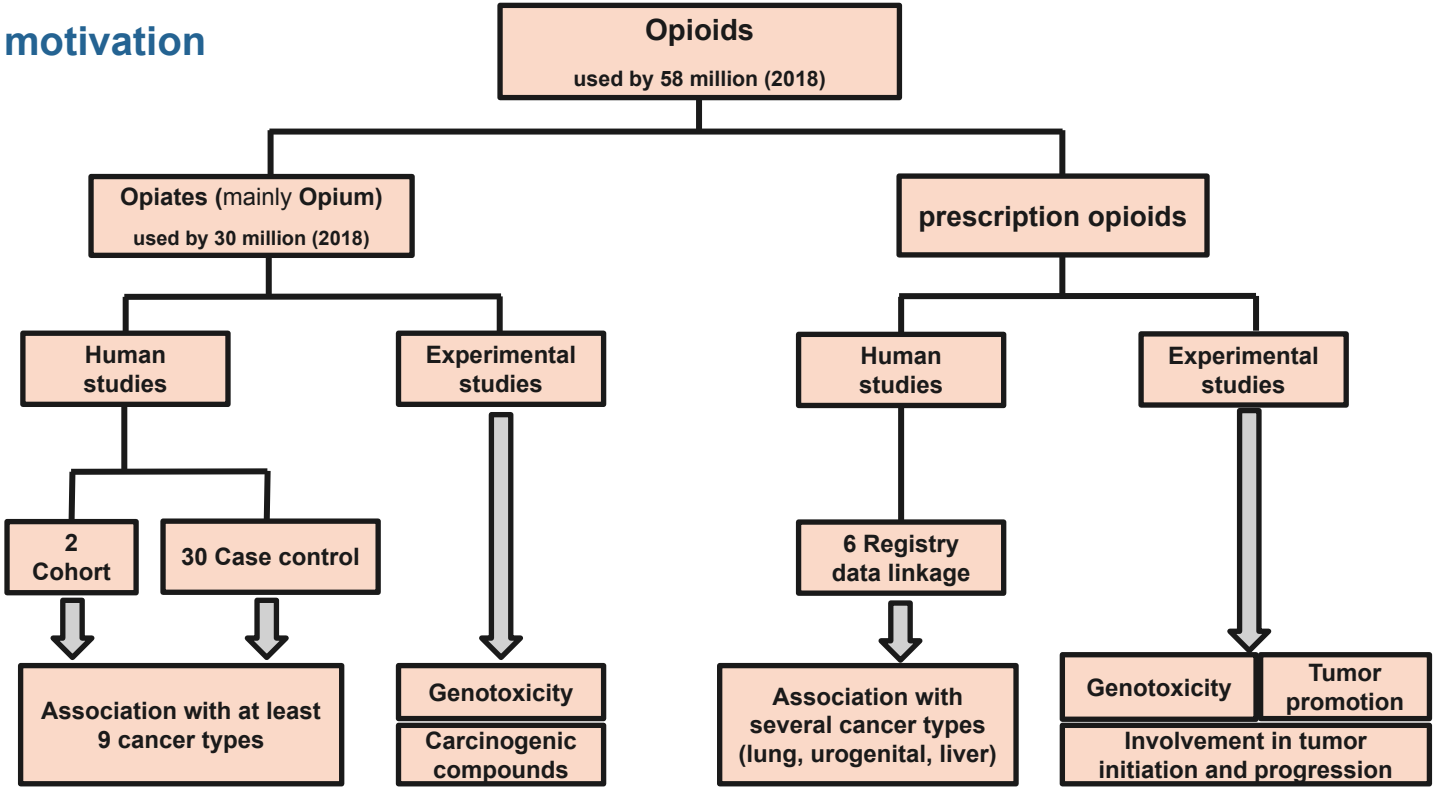
Fig. 1 | **Age-standardized prevalence of OUD per 100,000 people.** Age-standardized prevalence of opioid use disorder (OUD) per 100,000 people, based on data from the 2016 Global Burden of Disease study[6].

Opioids Definition

- **Natural opioids (opiates):** opium and its natural derivatives
- **Semi-synthetic opioids:** synthesized in labs from natural opioids
- **Synthetic opioids:** synthesized in labs using the same chemical structures of natural opioids to mimic their effects

Natural prescription opioids
Morphine, Codeine, Thebaine, Powdered Opium, Opium syrup
Semi-synthetic prescription opioids
Benzhydrocodone, Desomorphine, Diamorphine, Dihydromorphine, Dihydrocodeine, Etorphine, Ethylmorphine, Hydrocodone, Hydromorphone, Nalbuphine, Nalorphine, Nicomorphine, Oxycodone, Oxymorphone,
Synthetic prescription opioids
Alfentanil, Alphaprodine, Alphacetylmethadol, Bezitramide, Buprenorphine, Butorphanol, Carfentanil, Dezocine, Dextromoramide, Dextropropoxyphene, Dihydroetorphine, Diphenoxylate, Dipipanone, DPDPE, Eluxadoline, Fentanyl, Ketobemidone, Levacetylmethadol, Levorphanol, Lofentanil, Meptazinol, Methadone, Methadyl acetate, Normethadone, Noscapine, Oliceridine, Papaveretum, Pentazocine, Pethidine (Meperidine), Piritramide, Phenazocine, Phenoperidine, Remifentanil, Sufentanil, Tapentadol, Thebaine, Tilidine, Tramadol

Scientific motivation



Opium consumption classified by IARC Monographs into Group1 / Carcinogen to humans

Many limitations in the current evidence on opioid effects

Confounding effects and biases from linkage studies

No opioid use data in most cohorts

Limited number of opioid users in cohorts with opioid use data

Comprehensive consortium-based approach is needed

Overview of the Opioid Cohort Consortium (OPICO)

Grant support

- International Hundred K+ Cohort Consortium / Global Genomic Medicine Collaborative

Overarching aim

- To build a **strong international resource** for multidisciplinary scientific studies on the use of opioids and their long-term effects

Main exposure

- Use of prescription opioids from medication questionnaire
- Use of prescription opioids from linkage to national medication dispensing records

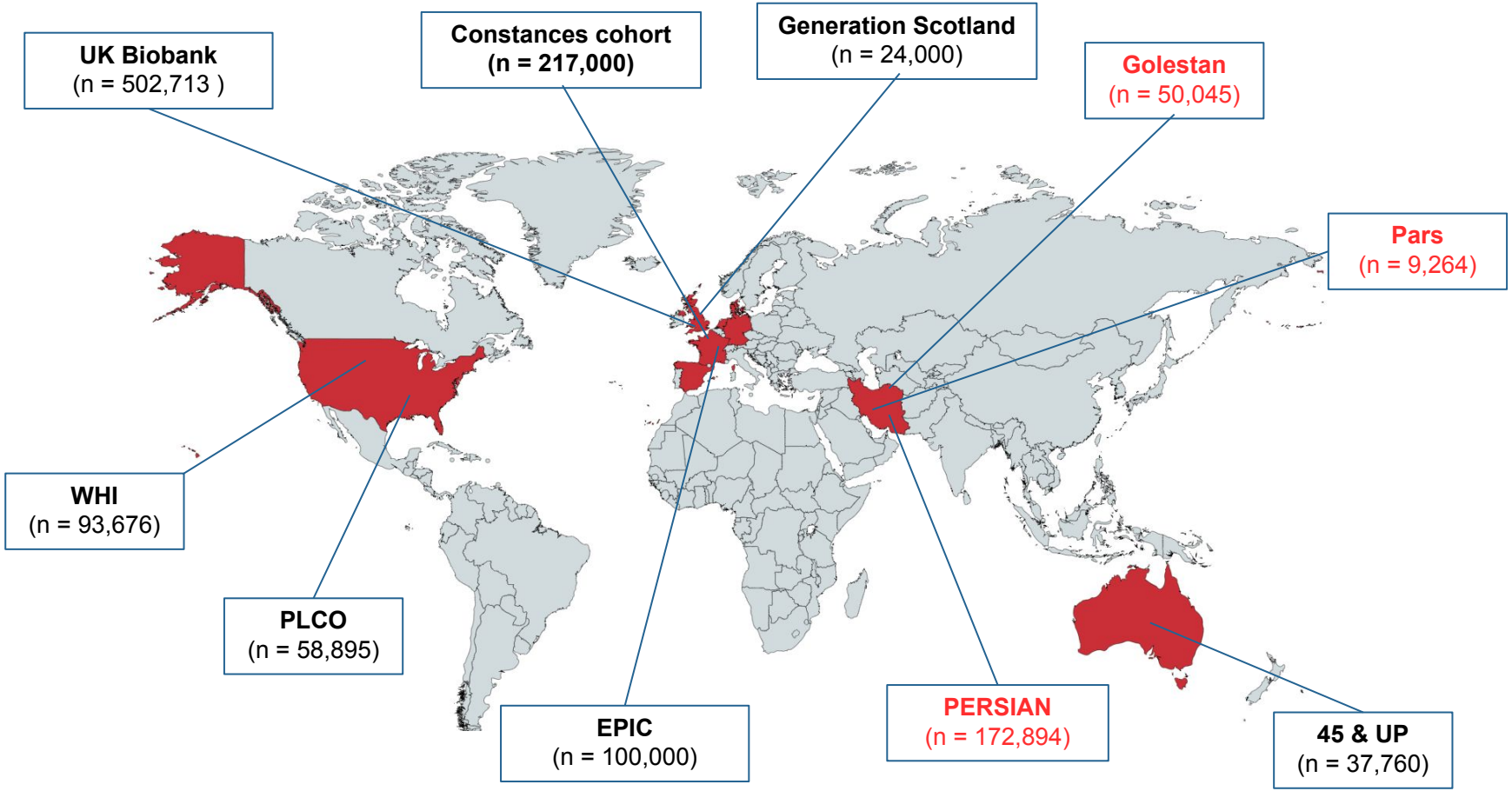
Main outcomes

- **Cancer analysis:** diagnosis of any cancer type / digestive cancers / respiratory cancers / urinary tract cancers / brain cancer
- **Mortality analysis :** death from any cause / death from circulatory diseases / respiratory diseases / digestive diseases / cancer

Aims & Approach

- Organize data on opioid use from prospective cohorts
- Compile data on opioid use in cohorts through linkage to national records
- Assess the type, distribution, and extent of opioid use across diverse populations
- Determine the association of opioid use with cancer incidence and mortality

OPICO cohorts (n=1,266,247 participants)



Cohorts with medication data participating in OPICO

Number of total participants and the subcategory of opioid users in the OPICO				
Cohort Study	**Participants (N)**	**Total opioid users N (%)**	**Medication data**	**Linkage source**
Golestan cohort	50,045	8,519 (17.0%)	Questionnaire	N/A
PERSIAN cohort	172,894	21,557 (12.4%)	Questionnaire	N/A
45 and up cohort	37,760	8,603 (22.7%)	Linkage	PBS (Australia)
UK Biobank cohort	502,713	25,864 (5.1%)	Questionnaire	N/A
Scottish Family Health Study	24,000	2,082 (8.6%)	Linkage	SPI (Scotland)
Pars cohort	9,264	818 (8.8%)	Questionnaire	N/A
PLCO Cancer Screening Trial	58,895	25,187 (42.7%)	Linkage	Medicare (USA)
Women Health Initiative (WHI)	93,676	8,430 (8.9%, estimated)	Questionnaire	N/A
EPIC (French)	100,000	4,000 (4%, estimated)	Linkage	Insurance Plan
CONSTANCES	217,000	8,680 (4%, estimated)	Linkage	CNDS (France)
Total	**1,266,247**	**113,740 (8.9%)**		

Challenges and solutions (1)

Challenge:

Defining opioid exposure and coding opioids medications

- Different names (brad & generic names)
- Different countries
- Different data sources (questionnaires & national records)
- Different coding systems

Solution:

- Working closely with local expert pharmacoepidemiologists in each country
- Using the WHO classification system (The Anatomical Therapeutic Chemical (ATC) Classification System)
- Using available online mapping resources (online WHO tool, user-defined R packages, available publications and codes from previous researches)

Challenges and solutions (2)

Challenge:

Harmonizing opioid exposure data

- Different sources: questionnaire data (lifelong medication use data) vs. Registry based data (data over a limited period)
- Different types: different type and routes of opioids

Solution:

- Defining a timeline of 12 months before recruitment as the time of exposure to opioids
- Assessing the effects of long-term use vs. short-term use
- Assessing the effects of suing strong vs. weak opioids
- Harmonizing different opioids based on the Oral Morphine Equivalent unit (OME)
- Assessing the cumulative used opioids

Challenges and solutions (3)

Challenge:

- Some included cohorts cannot send their linked data to IARC due to their national regulations for data protection and security

Solution:

- Using an additional distributed analysis model
- Analyze the data from these cohorts using the corresponding secure platform
- Perform meta-analyses using the aggregated outputs from these cohorts

Wins: feasibility of compiling opioid use data in cohorts with linkage

Collaboration with:

- Cancer Council NSW, Australia (Prof. Canfell, Dr. Weber, Dr. Sarich)
- University of NSW Sydney (Prof. Pearson)

Australian 45 and Up Study

- Recruited 267,153 adults (2006 – 2009) / General population of NSW

Linked to the Pharmaceutical Benefits Scheme (PBS)

- Australia's national drug subsidy program

Lessons learned from the feasibility study:

Identification of the:

- **policy of medication dispensing / subsidy program**
- **pricing of opioids at the time of cohort recruitment**

Reasons:

- To minimize the possible misclassifications
- To identify the inclusion and exclusion criteria

Example from the Feasibility Study:

Australia → co-payment program for prescriptions

- different thresholds for 'concessional beneficiaries' vs. 'general beneficiaries'

In 2008 (45 and up recruitment period):

- Co-payment for 'concessional beneficiaries' = $5.00
- Co-payment for 'general beneficiaries' = $31.30.
- Many opioid medications in Australia are priced $20 - $25
- These medications were not recorded in the linked national data source (PBS database) when dispensed to general beneficiaries.

- Only 37,760 participants who were concessional beneficiaries at recruitment were included

- We compiled opioid use for all included participants, of whom 8,603 (22.8%) were users of opioids

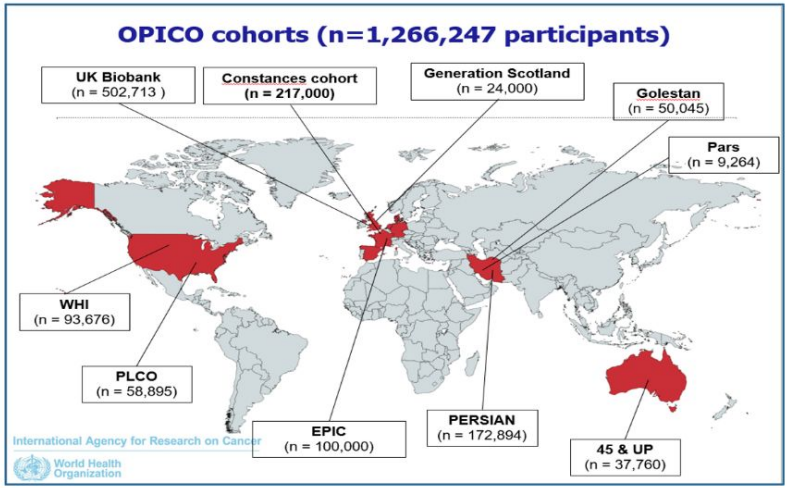
Plans for publications

- Consortium Profile
- Methodology paper on the methods of compiling opioid use data in prospective cohorts using linkage to national medication dispensing records

Required data from cohorts to participate in OPICO

- ❑ **Use of opioids**
  - questionnaires
  - data linkage to national records
- ❑ **Outcomes at follow-up**
  - vital status
  - cause of death
  - diagnosis of cancer
  - type of cancer
- ❑ **Dates or equivalent follow-up times**
- ❑ **Demographics**
  - age
  - sex
  - ethnicity
  - socioeconomic indicator
- ❑ **Smoking cigarettes**
- ❑ **Alcohol intake**
- ❑ **Chronic health conditions**
  - Diabetes
  - Hypertension
  - inflammatory conditions

Contribution to the OPICO



IARC / Genomic Epidemiology Branch

Dr. Mahdi Sheikh **Dr. Hilary Robbins** **Dr. Paul Brennan**



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Acknowledgement

International agency for Research on Cancer (France)
- Paul Brennan
- Hilary Robbins
- Pietro Ferrari

Tehran University of Medical Sciences (Iran)
- Reza Malekzadeh
- Hossein Poustchi

Morgan State University (USA)
- Farin Kamangar

National Cancer Institute (USA)
- Neal Freedman

Cancer Council Australia (Australia)
- Karen Canfell
- Marianne Weber
- Peter Sarich

The University of NSW Sydney (Australia)
- Sallie-Ann Pearson
- Louisa Degenhardt

University of Edinburgh (Scotland)
- Archie Campbell

Australian National University (Australia)
- Emily Banks

Fred Hutchinson Cancer Research Center (USA)
- Lesley Tinker

INSERM (France)
- Marcel Goldberg
- Sofiane Kab

Wake Forest University (USA)
- Chris Gillette
- Mara Vitolins

Sax Institute (Australia)
- Kerrin Bleicher

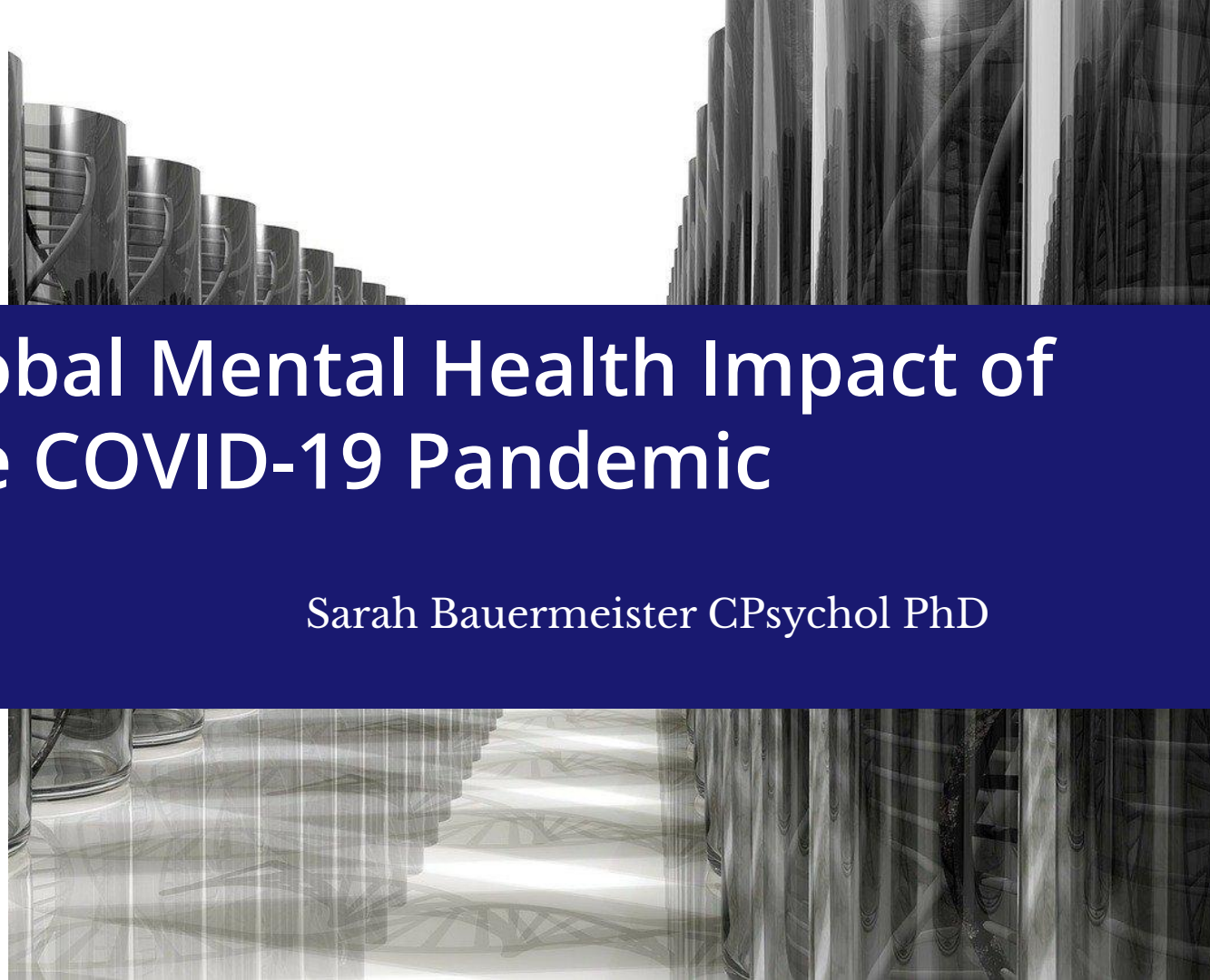
Sarah Bauermeister, CPsychol, PhD

University of Oxford
Senior Scientist & Data Manager

Cohort Representative
Dementias Platform UK (DPUK)

UK

03rd November 2021



Global Mental Health Impact of the COVID-19 Pandemic

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Sarah Bauermeister CPsychol PhD
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Dementias Platform UK
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IPq HCFMUSP
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USP

MGH 1811 MASSACHUSETTS GENERAL HOSPITAL

HARVARD MEDICAL SCHOOL

Project Overview

- The COVID-19 pandemic has brought an unprecedented set of challenges impacting the mental health of populations around the world.
- The IHCC COVID-19 Mental Health & Behavioral Impact Scientific Working Group is leveraging the unique platform of the IHCC consortium to address pressing questions related to COVID-19 and mental health.
- Harnessing the power of 19 (others pending) cohorts (n= 1.4 m) this three site project aims to:
    - Catalogue and categorise all cohorts according to purpose
    - Harmonise a set of domains and variables for cross-cohort investigations
    - Conduct cross-site and cross-cohort analyses to address core scientific questions

Data Corpus

Cohort	Country	Baseline size
All of Us	USA	426,000
Brazilian High Risk Cohort Study	Brazil	
ELSA Brazil	Brazil	2,007
ELSA UK	UK	12,099
FinnGen	Finland	320,000
Generation Scotland	Scotland	20,128
PsycheMERGE	USA	
MGB Biobank	USA	130,000
SAPRIN	South Africa	50,000
UKB	UK	502,491
University College of London (federated collaboration)	UK	25,538
HRS	USA	20,000
KLOSCAD (Korean Longitudinal Study on Cognitive Aging and Dementia)	South Korea	6,818
Einstein Aging Study	USA	2,200
HELIAD, and 2 other studies from Greece	Greece	1,943
São Paulo Ageing & Health Study	Brazil	2,072
Monongahela-Youghiogheny Healthy Aging Team (MYHAT)	Australia	1,982
Invece.Ab	Italy	1,321
Irish Longitudinal Study of Ageing (TILDA)	Ireland	6,000
Total		**1,530,599**

Trajectories of common mental disorders before and during the Covid-19 pandemic (ELSA-Brazil)
D Fatori & A Brunoni et al., São Paulo (submission underway)

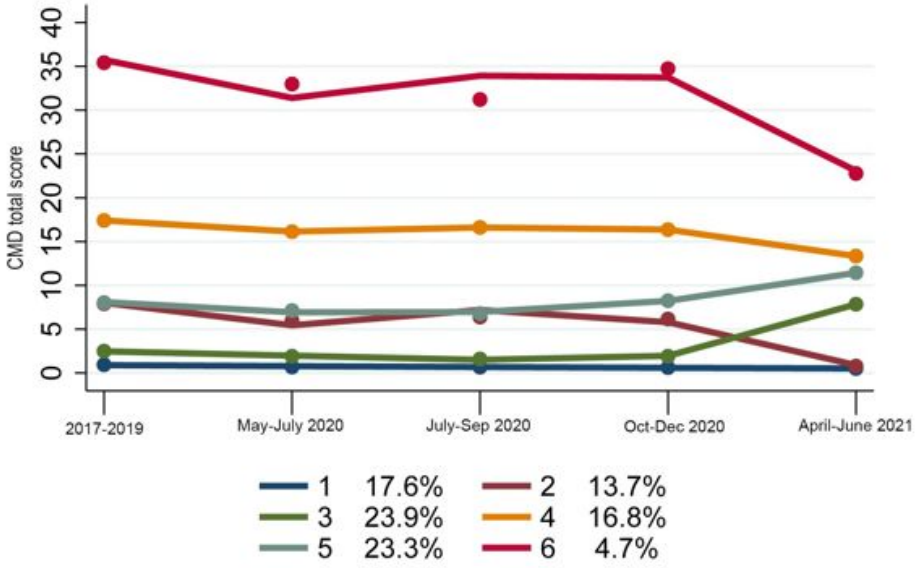
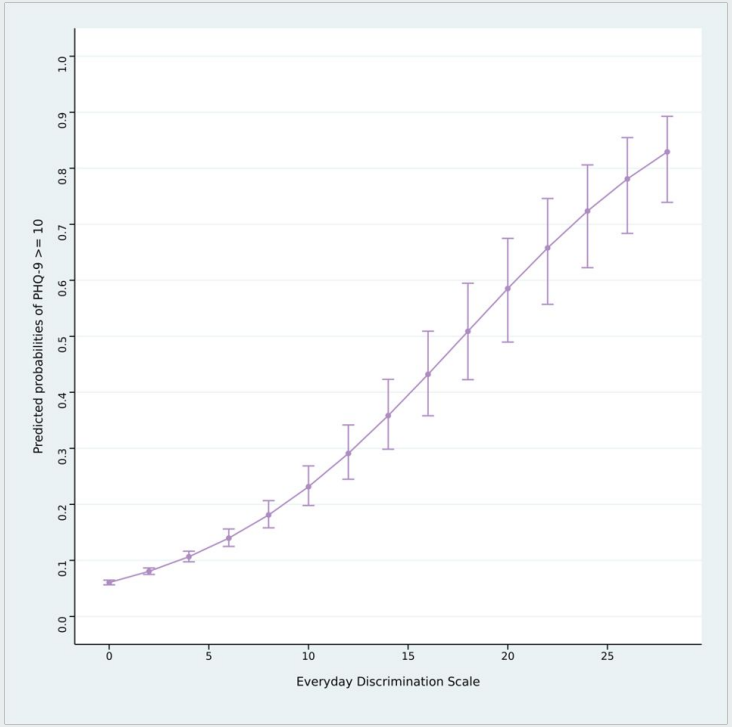


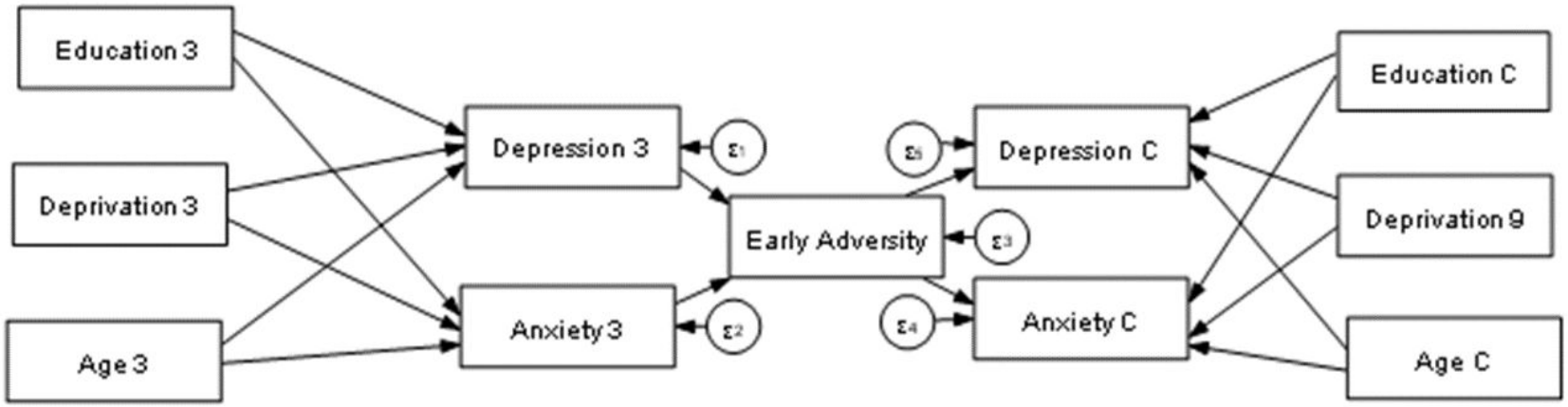
Figure 1. Trajectories of common mental disorders before and during the COVID-19 pandemic (N=2,705).

Effect of perceived discrimination due to race and ancestry on depressive symptoms during the COVID-19 pandemic: a repeated-measures study in the All of Us Research Program

Y Lee & J Smoller et al., Harvard (to be submitted)



Biopsychosocial risk factors for pre- and pandemic psychiatric disorders in ELSA UK, ELSA Brazil, TILDA & HRS
S Bauermeister et al., Oxford (in progress)



Harmonisation of data domains and variables for investigating the global mental health impact of Covid-19

J Bauermeister et al. (in progress)

- 1 Age (banded)
- 2 Gender (0,1)
- 3 Ethnicity (coded)
- 4 Education (coded levels)
- 5 Living alone (0,1)
- 6 Living with children (0,1)
- 7 Living area (coded type)
- 8 Annual household income (<,> 30k)
- 9 Diagnosed mental health conditions (0,1)
- 10 Diagnosed physical health conditions (0,1)
- 11 Self report memory complaints
- 12 Depression (PHQ-9)
- 13 Anxiety (GAD-7)
- 14 DASS (stress)
- 15 Life satisfaction (ONS wellbeing)
- 16 Loneliness (UCLA-3)
- 17 Exercise (self report, banded)
- 18 Face to face contact (self report, banded)
- 19 Any covid data (0,1)
- 20 Cognition memory (score)
- 21 Global cognition (MMSE/MoCA)
- 22 Discrimination
- 23 Economic activity (coded levels)
- 24 Country
- 25 Smoking (banded)
- 26 Alcohol consumption (banded)
- 27 Substance use (0,1)
- 28 Family disease history
- 29 Disabilities
- 30 Digital behaviour
- 31 Any diagnosed psychosis
- 32 Personality
- 33 Socioeconomic status
- 34 Health in general

Presentations

1. Abstract submitted: ADAA (Anxiety & Depression Conference) Denver USA March 2022: ‘Mental health consequences of perceived discrimination during the Covid-19 pandemic’.(Lee et al.)

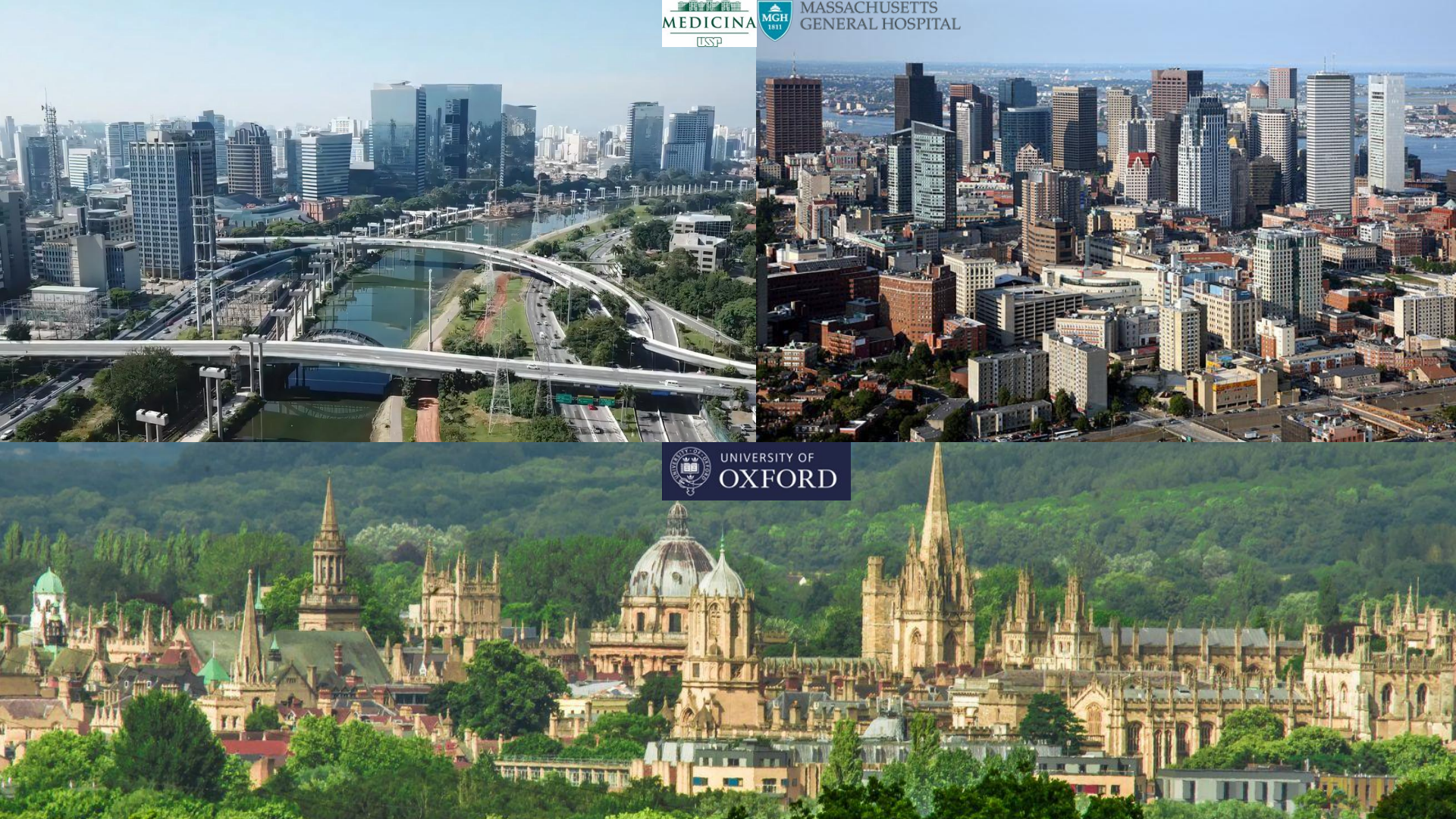
2. Presentation (oral) Centre for Ageing Research (C4AR) Lancaster UK (online) October 2021: ‘Biopsychosocial risk factors for pre- and pandemic psychiatric disorders in ELSA UK ’ (S Bauermeister)

3. Presentation (oral) Dementias Platform UK and the Korea Brain Research Institute (online) seminar October 2021: ‘‘Biopsychosocial risk factors for pre- and pandemic psychiatric disorders in ELSA UK’ (S Bauermeister)

Conclusion

The project continues to attract global interest:

- Collaboration has been initiated with University College London Covid-19 Social Study and the ELSA UK cohort (resilience and discrimination)
- A proposal has been submitted to collaborate with a Covid-19 specific platform investigating: 'Effect of life course stressors and cognitive status on mental health outcomes during the Covid-19 pandemic' (5 cohorts)
- Collaboration initiated with ELSA UK, ELSA Brazil, TILDA, HRS to investigate cross-cultural effects of discrimination on mental health during Covid-19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UNIVERSITY OF
OXFORD

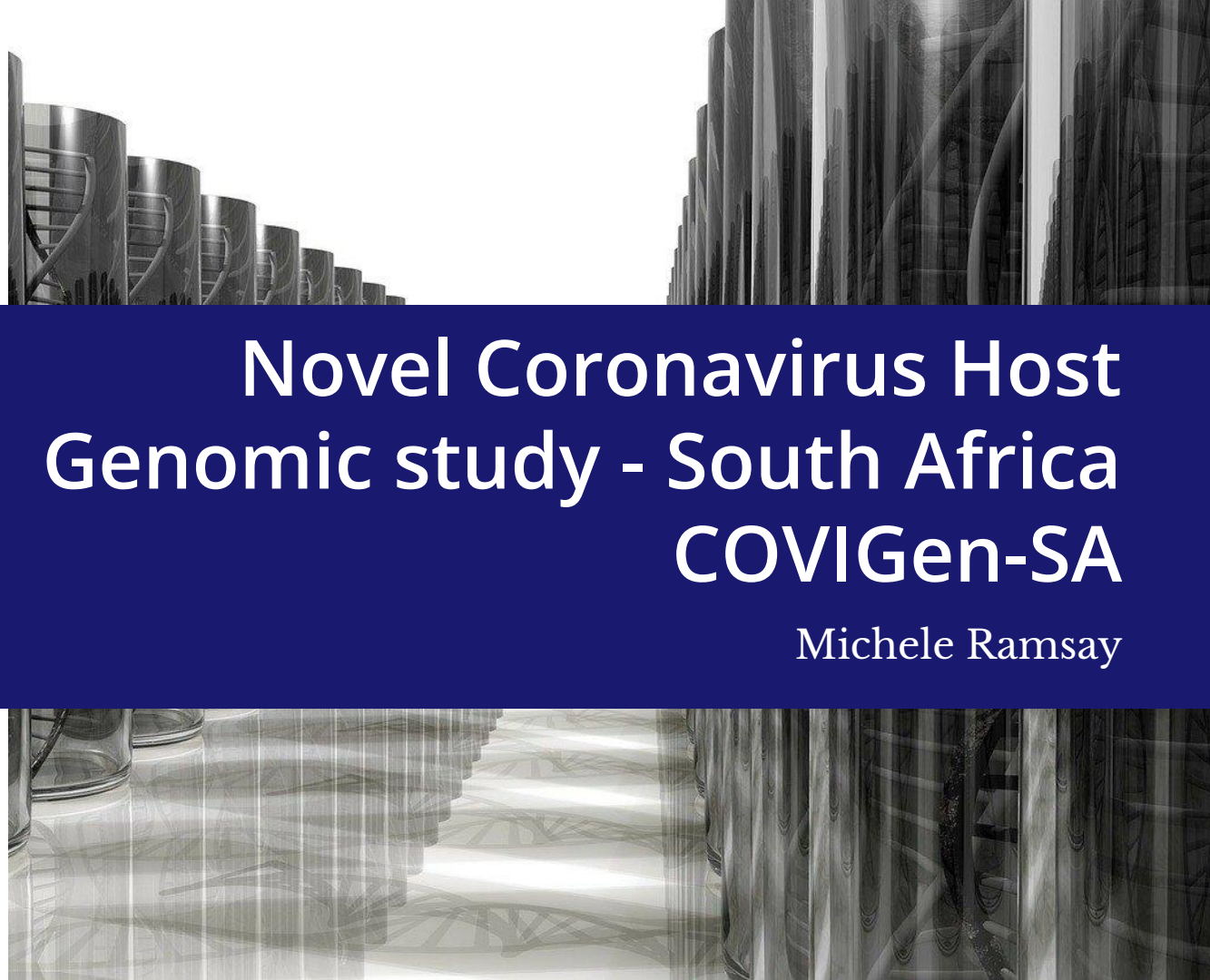
Michèle Ramsay, PhD

Professor in Human Genetics
University of the Witwatersrand

Director
SBIMB

South Africa

November 2021



Novel Coronavirus Host Genomic study - South Africa COVIGen-SA

Michele Ramsay

International 100K Cohort Consortium

Outline

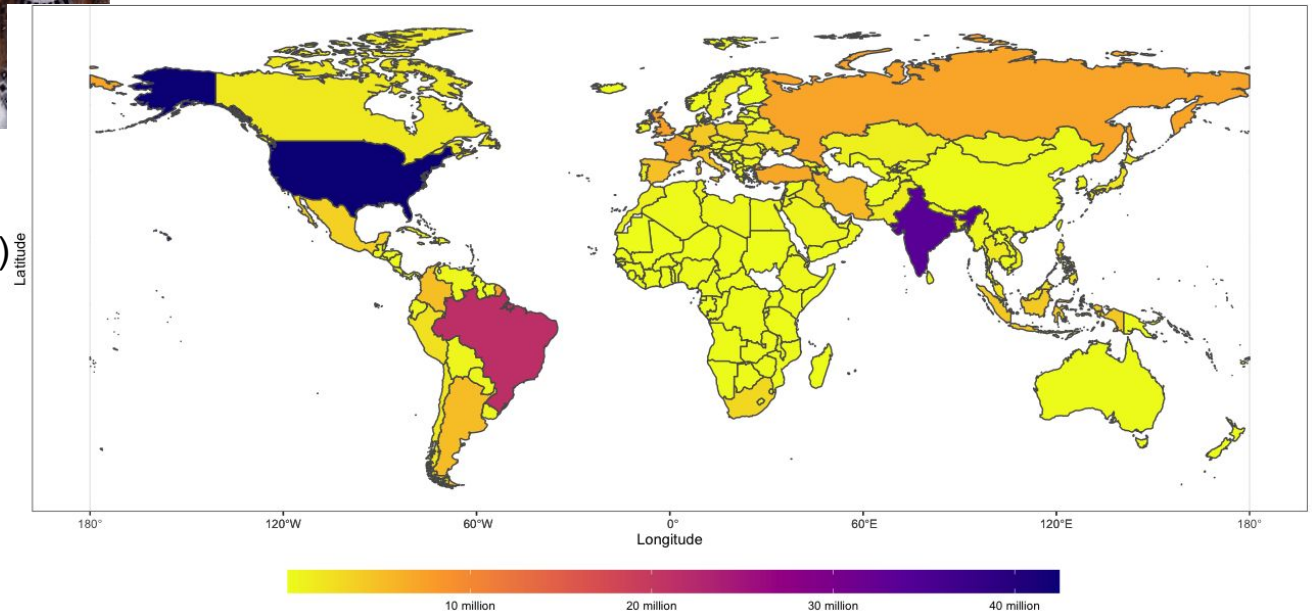
- COVID-19 globally and in Africa
- COVIGen-SA update
- Challenges & Next steps

WITS UNIVERSITY

COVIGEN-SA

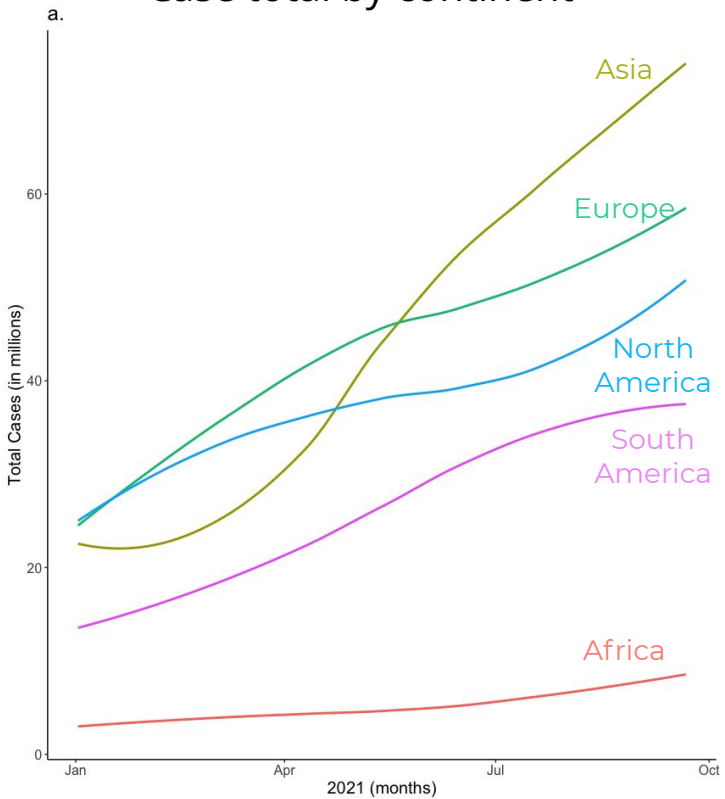
Coronavirus Host Genomics Study – South Africa

Total cases per country (as of 21 September 2021)

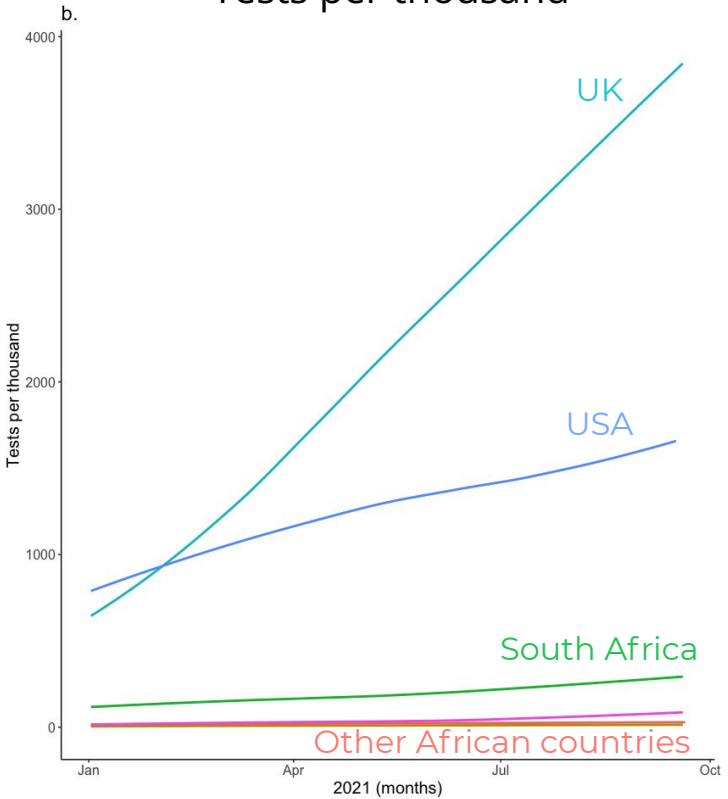


South Africa (28 October 2021)
2,921,114 cases
89,104 deaths

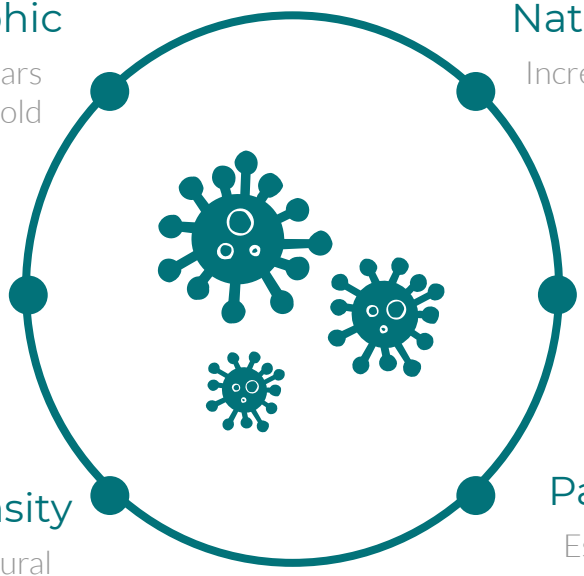
Case total by continent



Tests per thousand



Africa’s low burden



Young demographic

Median age < 20 years old

Natural Selection

Increased frequency of protective alleles

Warmer climate

Unfavorable conditions for viral spread

Trained immunity

From other vaccines like BCG

Lower urban density

Numerous rural communities

Past experience

Established infection control measures

COVIGen - SA

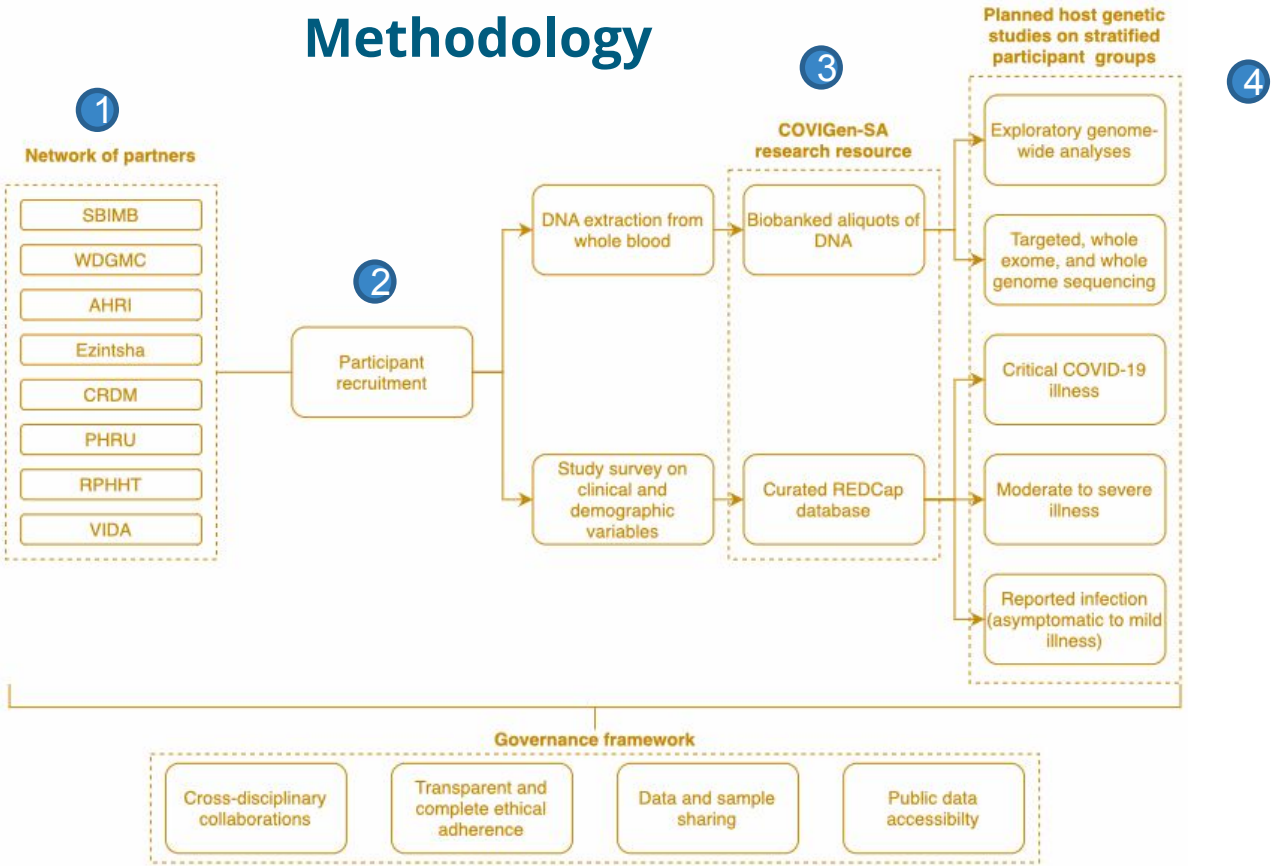
Aim

A platform for COVID-19 research that accounts for individual variability in the genetics and health backgrounds of Black South Africans, in line with a precision medicine approach.

Objectives

1. Establish a research resource of harmonised clinical and genetic data for a large sample of SARS-CoV-2 positive Black South Africans
2. Conduct a multi-approach investigation into host genetic factors affecting COVID-19 susceptibility and severity

Methodology



Corona Virus Host Genomics Study - South Africa (COVIGen-SA)

Ethics: M200642
Biobank: M200469, BEC20200401

Partners

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University of the Witwatersrand

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Principal Investigator

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Postdoctoral Fellow

Heather Seymour
PhD candidate

Wits Donald Gordon Medical Centre
University of the Witwatersrand

Dr June Fabian
Principal Investigator

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Medical Bioethicist

Sr. Heather Maher
Research Nurse

Ezintsha
Wits Reproductive Health & HIV unit
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Head of Clinical Research

Nkuli Mashabane
Research Operations Strategy

Vaccines and Infectious Diseases Analytics (VIDA) research unit
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Dr Kobus Herbst
Chief Information Officer

Dr Emily Wong
Infectious Disease Scientist

Centre for HIV and Sexually Transmitted Infections
National Institute for Communicable Disease

Prof Caroline Tiemessen
Centre Head

Studies

ADORE

A single-arm, phase 3, pilot study investigating the efficacy of Doravirine in adults living with HIV experiencing virological failure on first-line Efavirenz-based antiretroviral therapy with non-nucleoside reverse transcriptase inhibitor resistance

Ethics: 191109B

ADVANCE

A randomised, phase 3, non-inferiority study of DTG + TAF + FTC compared with DTG + TDF + FTC and EFV + TDF + FTC in patients infected with HIV-1 starting first-line antiretroviral therapy

Ethics: 160606B

COVER

A multi-center, randomised, open label study of Nitazoxanide (NTZ), or Sofosbuvir and Daclatasvir (SOF/DCV), compared to no pharmacological intervention for the prevention of COVID-19 disease in healthcare workers at high risk of exposure to SARS-CoV-2

Ethics: 200613B

DORA

A single arm, phase 3 study, exploring the safety of Doravirine-based first-line antiretroviral therapy for women of reproductive potential living with HIV - a pilot switch study strategy in South Africa

Ethics: 191108

DUACT

A randomised, double-blind, study comparing the efficacy, safety and tolerability of oral administration of Ribavirin (RBV) and Nitazoxanide (NTZ) versus placebo in SARS-CoV-2 virus infected patients

Ethics: 200903B

Pregnant women
Ethics: 200405

Healthcare Workers
Ethics: 200405

Hospital Surveillance
Ethics: 200405

National syndromic surveillance for pneumonia in South Africa

A national surveillance programme aimed at estimating and monitoring syndromic pneumonia and associated pathogen, including SARS-CoV-2

Ethics:

PHIRST-C

A Prospective Household observational study of Influenza, Respiratory Syncytial virus and other respiratory pathogens community burden and Transmission dynamics in South Africa - Coronavirus

Ethics: 150808

Pot Prev

The Potentially Preventable Burden of Community-acquired Pneumonia in South African adults, in the era of widespread Paediatric PCV13 Immunisation and Antiretroviral Therapy Rollout

Ethics: 171009

SAPRIN

South African Population Research Infrastructure Network

Ethics: 171009

Vukukazi

A population multi-omits cohort

Ethics: BE560/17

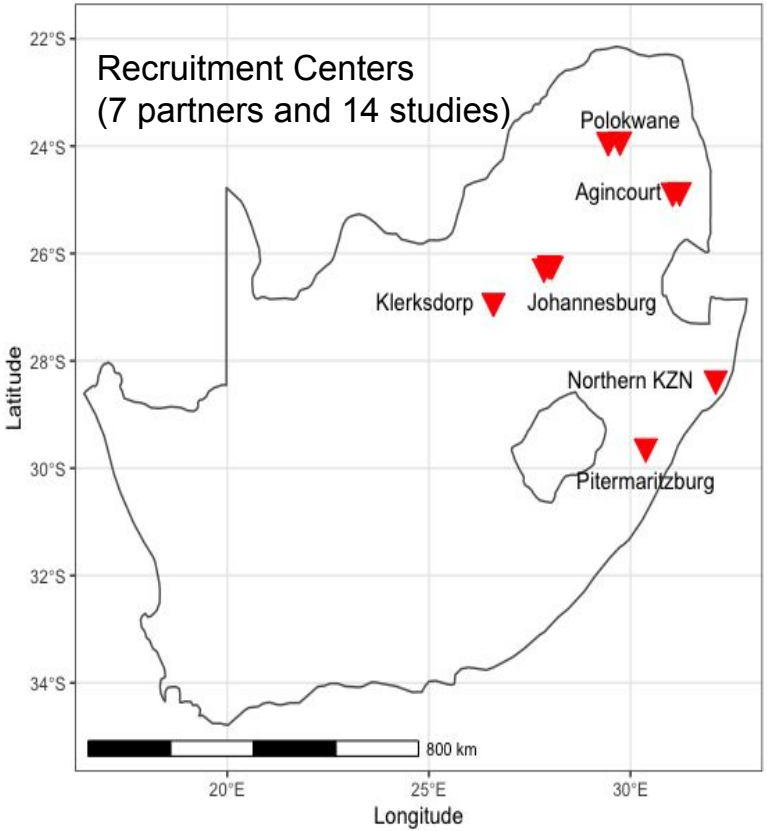
COVID-19 Hospital study

Ethics:

Principal Investigators

COVIGen - SA

- Total records: **1707**
- SARS-CoV-2 positive: **1080** (63%)
- Severe COVID-19: **221** (20%)
  (supplemental oxygen, ICU admission and/or ventilation)
- Asymptomatic or mild symptoms: **859**
- Genotyped: **576**
- Additional funded genotyping: **576**

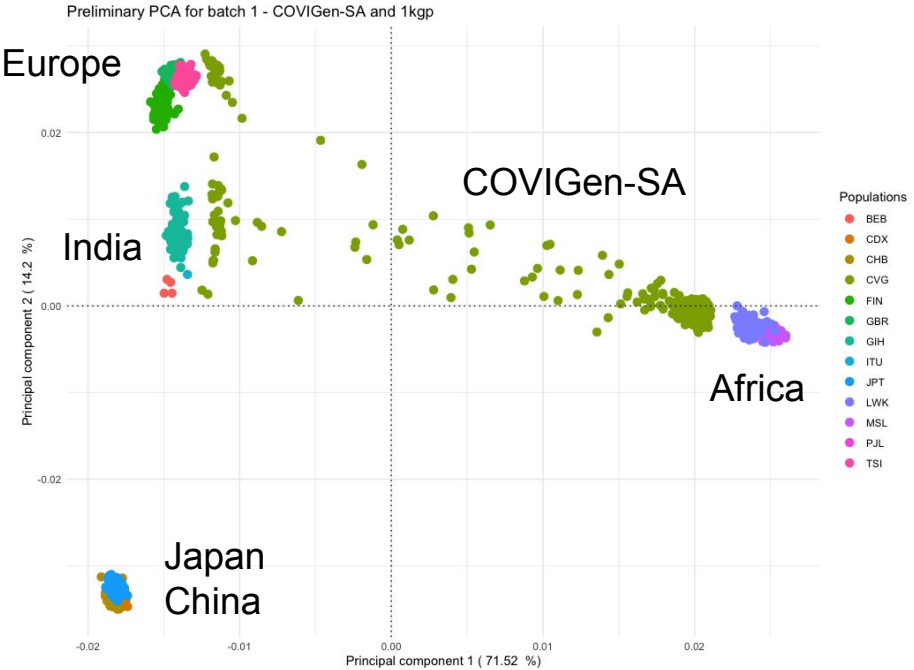


Genotyping: Principal Component Analysis

572 individuals

1 517 137 SNPs following QC cutoffs:

- Missingness per SNP: 0.1
- Missingness per individual: 0.1
- Minor allele frequency: 0.05
- Hardy-Weinberg threshold: 0.0000001
- Autosomal markers only



Plot based on 22 226 SNPs

Challenges and Next Steps

- Integrating phenotype data
- Increasing number of severe COVID-19 cases
- Resources for further genotyping

- Focus on partnerships and recruitment
- Publish cohort paper
- Analyze preliminary data
- Partner with other host genomics studies

International HundredK+ Cohorts Consortium (IHCC)
Linking cohorts, understanding biology, improving health

Alive
AFRICAN LEADERSHIP IN VACCINOLOGY EXPERTISE

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Ananya Gupta, PhD

Researcher
NIHR Global Health Research Unit and Network on Diabetes and Cardiovascular Disease in South Asia

UK

COVID-19 in South Asian communities

Ananya Gupta

LKC School of Medicine, Singapore
Imperial College London, UK

Imperial College London

LEE KONG CHIAN SCHOOL OF MEDICINE

NANYANG TECHNOLOGICAL UNIVERSITY SINGAPORE

Imperial College London

Non-communicable disease in South Asian populations

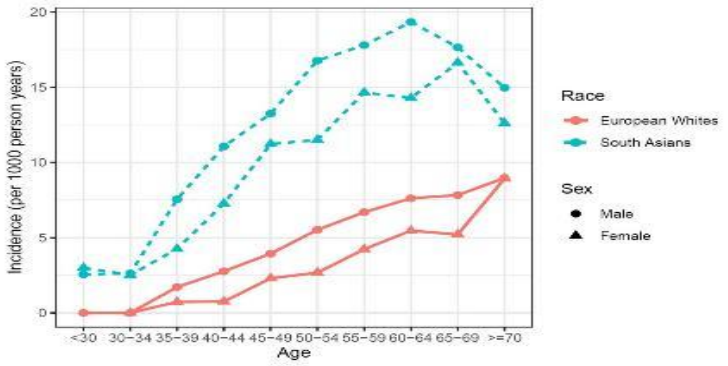
Group Aims

Aetiology: What are the behavioural, environmental and molecular factors that drive chronic disease in Asian populations?

Translation: How can we deliver 'Personal' and 'Population' based approaches for health promotion in Asian settings?

T2D incidence: South Asians vs Europeans

A.



B.

Model	RR (95%CI) of T2D in South Asians vs Europeans	P=
Age , sex	2.62 (2.33 to 2.96)	6.1E-56
+ BMI, WHR	2.66 (2.34 to 3.01)	4.6E-53
+ Glycaemic traits	2.23 (1.93 to 2.58)	6.6E-28
+ Physical activity	2.19 (1.90 to 2.57)	2.4E-26
+ Amino acids	2.21 (1.90 to 2.57)	8.4E-25
+ Genetic risk score	2.11 (1.80 to 2.47)	9.9E-21

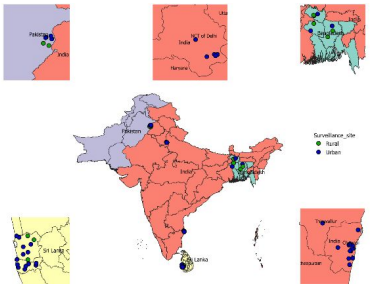
Global Health Research Unit Surveillance study

150,000 South Asians with rich phenotypes and samples

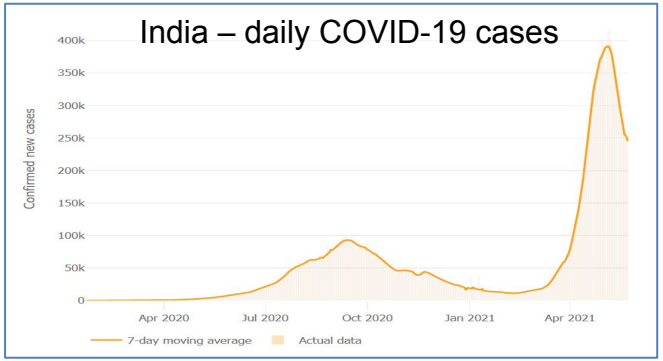
Global Health Research Unit
on Diabetes and Cardiovascular Disease in South Asians

FUNDED BY
NIHR | National Institute for Health Research

wellcome

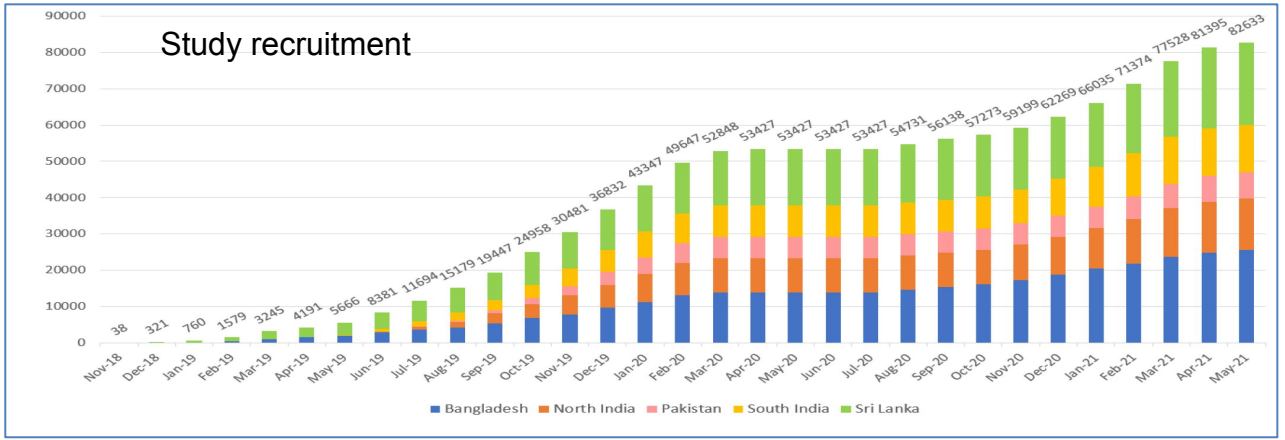


COVID-19
and study activity



Lockdown 1

Wave 2



Pre-COVID

Phase 1

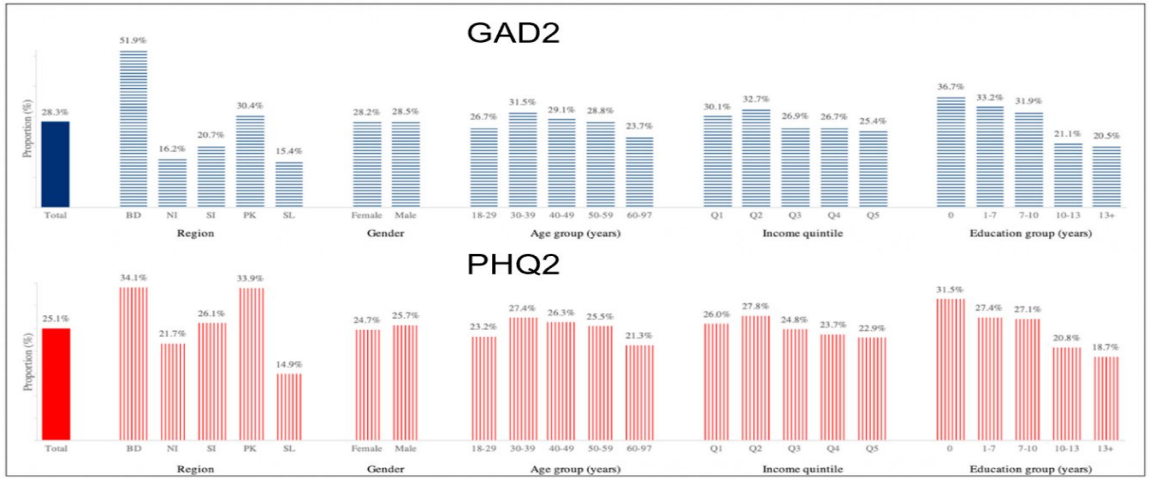
Phase 2

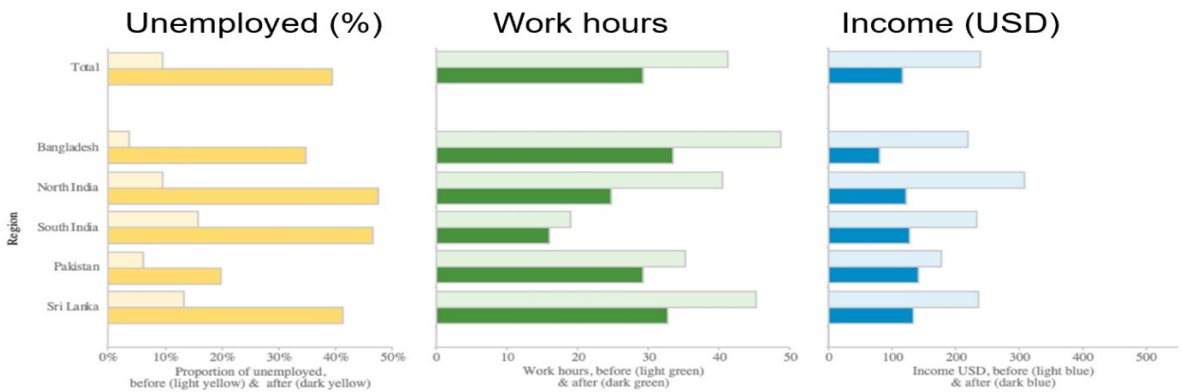
Phase 1

June 2020

28,909 participants re-interviewed

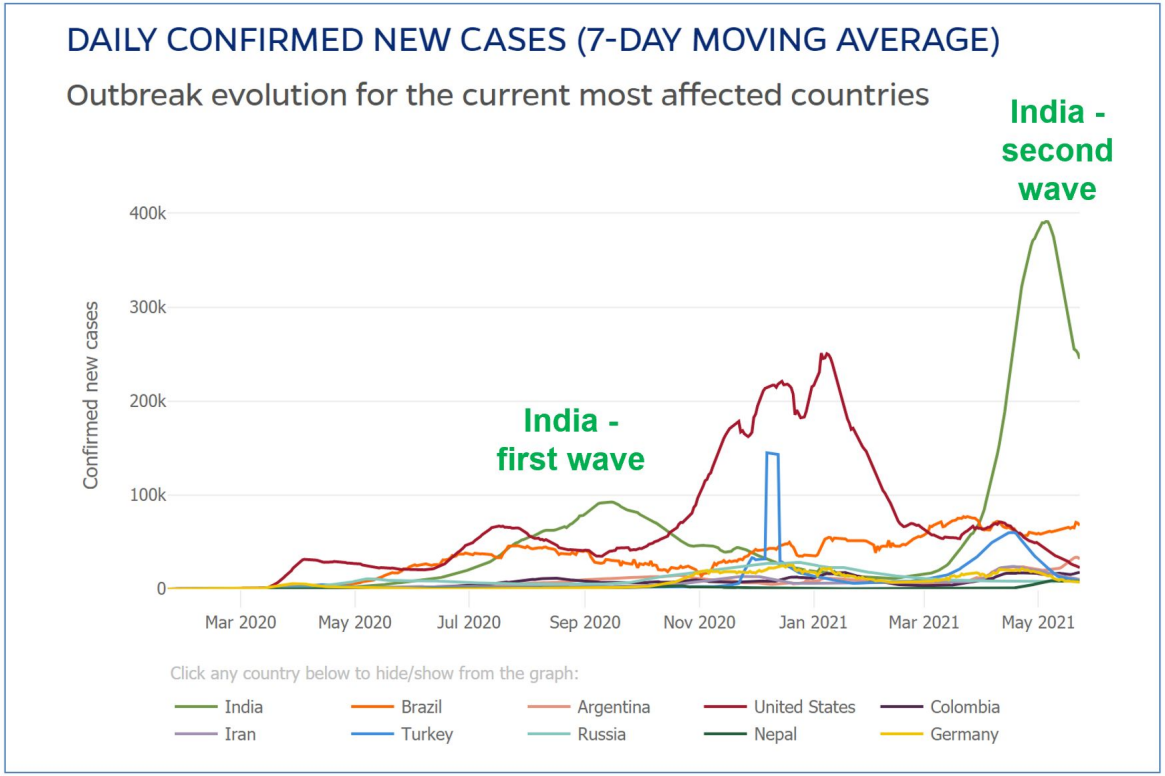
1% reported symptoms suggestive of COVID-19





Kusuma et al. SSM. 2021

Impact of COVID-19 in South Asians



UK Biobank: South Asians are at increased risk of COVID-19

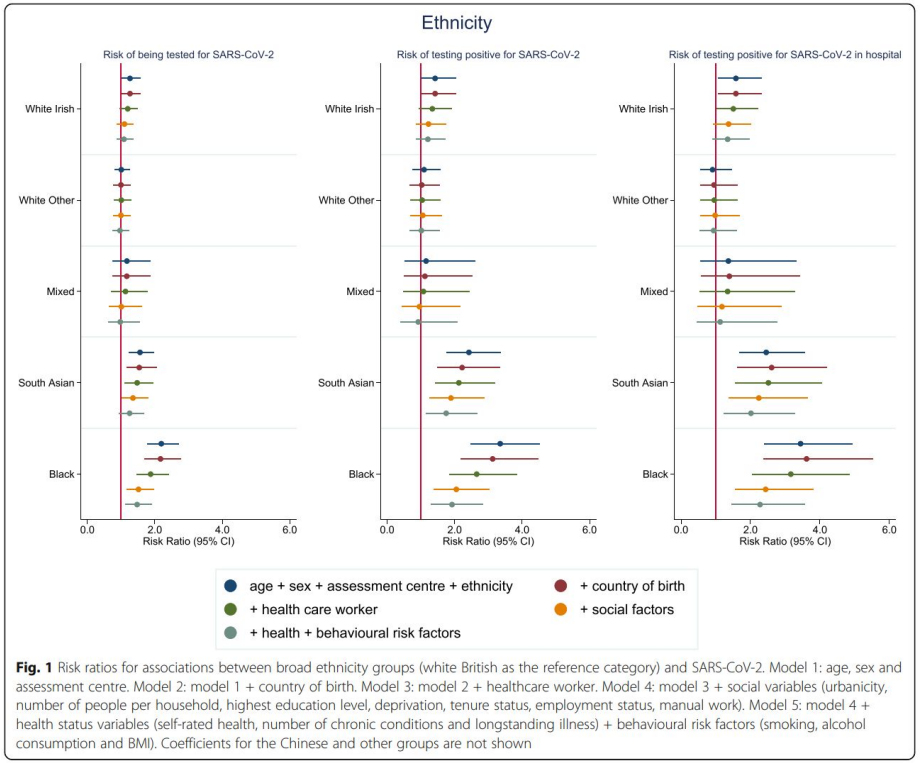


Fig. 1 Risk ratios for associations between broad ethnicity groups (white British as the reference category) and SARS-CoV-2. Model 1: age, sex and assessment centre. Model 2: model 1 + country of birth. Model 3: model 2 + healthcare worker. Model 4: model 3 + social variables (urbanicity, number of people per household, highest education level, deprivation, tenure status, employment status, manual work). Model 5: model 4 + health status variables (self-rated health, number of chronic conditions and longstanding illness) + behavioural risk factors (smoking, alcohol consumption and BMI). Coefficients for the Chinese and other groups are not shown

Article

Factors associated with COVID-19-related death using OpenSAFELY

https://doi.org/10.1038/s41586-020-2521-4
Received: 15 May 2020
Accepted: 1 July 2020
Published online: 8 July 2020
Check for updates

Elizabeth J. Williamson[1,6], Alex J. Walker[2,6], Krishnan Bhaskaran[1,6], Seb Bacon[2,6], Chris Bates[3,6], Caroline E. Morton[2], Helen J. Curtis[2], Amir Mehrkar[2], David Evans[2], Peter Inglesby[2], Jonathan Cockburn[3], Helen I. McDonald[1,4], Brian MacKenna[2], Laurie Tomlinson[1], Ian J. Douglas[1], Christopher T. Rentsch[1], Rohini Mathur[1], Angel Y. S. Wong[1], Richard Grieve[1], David Harrison[5], Harriet Forbes[1], Anna Schultze[1], Richard Croker[2], John Parry[3], Frank Hester[3], Sam Harper[3], Rafael Perera[2], Stephen J. W. Evans[1], Liam Smeeth[1,4,7] & Ben Goldacre[2,7]✉

COVID-19 mortality amongst >23M people using UK electronic medical records

	Age/sex adjusted	'Fully adjusted'
White	1.00 (ref)	1.00 (ref)
Mixed	1.62 (1.26–2.08)	1.43 (1.11–1.84)
South Asian	1.69 (1.54–1.84)	1.45 (1.32–1.58)
Black	1.88 (1.65–2.14)	1.48 (1.29–1.69)
Other	1.37 (1.13–1.65)	1.33 (1.10–1.61)

Potential limitations

- UK Biobank: 7,323 South Asians
- OpenSAFELY:
  - No biological samples
  - Incomplete baseline data
- Limited data for South Asia

Phase 2

Aims

- Determine the incidence of COVID-19 and its major complications in South Asian populations from India and the UK.
- Identify the primary risk factors predicting adverse COVID-19 outcomes in South Asians.
- Investigate whether known / novel risk factors account for differences in COVID-19 outcomes between South Asians and Europeans

Outcome variables

Primary COVID-19 endpoints:

i. Total: all with confirmed SARS-CoV2 infection

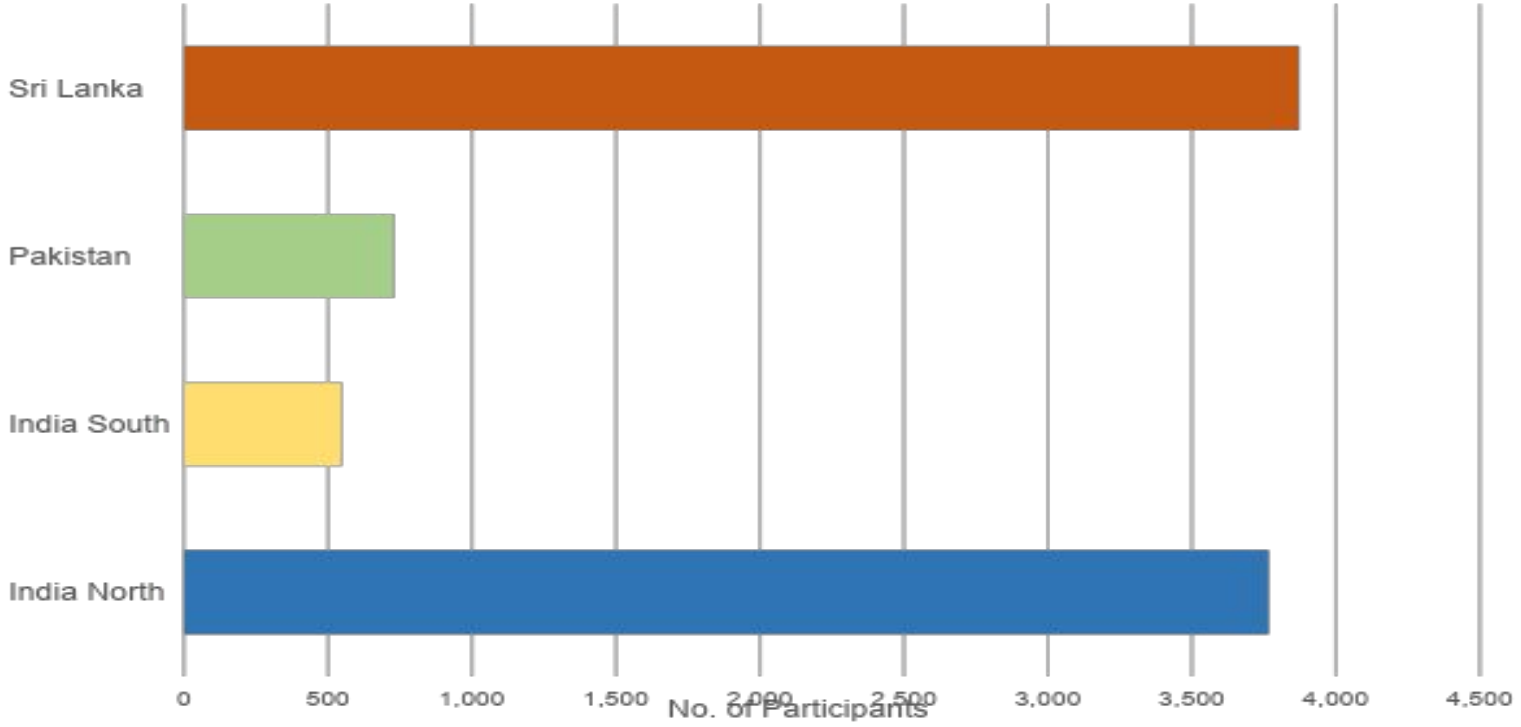
ii. Severe: COVID-19 (hospital admission or main / contributory cause for death)

iii. Prolonged: persistent symptoms after 6 weeks.

Outcomes identification

- **WS1: Clinical follow-up**
  - Evaluate 30,000 South Asians for COVID-19
  - Three existing cohorts:
    - **LOLIPOP study** (UK; N=19,000)
    - **iHealth-T2D** (UK and South Asia; N=24,000)
    - **GHRU Surveillance study** (South Asia, N=53,000)
  - Questionnaire: adapted from WT/IHCC template
  - Blood sample: COVID-19 serology

Progress on Clinical Follow-up



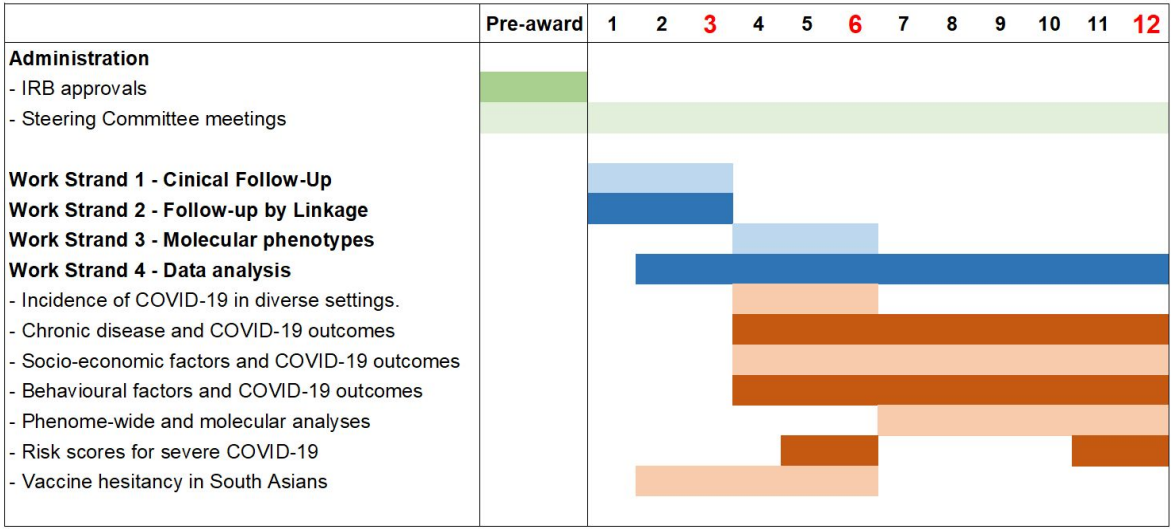
Analysis

- **WS2: Record linkage**
  - UK: NHS and mortality data
  - India: ICMR COVID-19 registry

- **WS3: Molecular phenotyping**
  - Collate existing molecular data
  - New GWAS on 2,500 COVID cases / controls

- **WS4: Analysis**
  - Incidence in UK and SA communities
  - Risk factors for COVID-19 outcomes: Environmental, behavioural & molecular factors.
  - Primary determinants of the ‘excess risk’ in SA

Timelines


Pre-award
1
2
3
4
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10
11
12
Administration
- IRB approvals
- Steering Committee meetings
Work Strand 1 - Cinical Follow-Up
Work Strand 2 - Follow-up by Linkage
Work Strand 3 - Molecular phenotypes
Work Strand 4 - Data analysis
- Incidence of COVID-19 in diverse settings.
- Chronic disease and COVID-19 outcomes
- Socio-economic factors and COVID-19 outcomes
- Behavioural factors and COVID-19 outcomes
- Phenome-wide and molecular analyses
- Risk scores for severe COVID-19
- Vaccine hesitancy in South Asians

Funding

CHAN ZUCKERBERG INITIATIVE

MRC Medical Research Council

Department of BioTechnology, Government of India

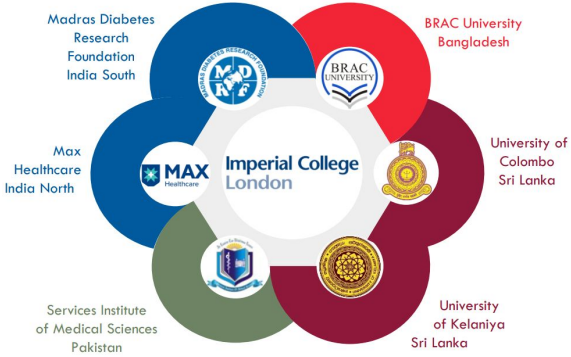
सत्यमेव जयते

The collaboration

Imperial College London

NIHR Global Health Research Unit

on Diabetes and Cardiovascular Disease in South Asia



LOLIPOP

The London Life Sciences Population Study

i HEALTH T2D

Rhoda Au, PhD

Professor
Boston University Schools of Medicine and Public Health

Senior Investigator/Director of Neuropsychology
Framingham Heart Study

USA

November 3, 2021

Foundational Phase Update

Davos Alzheimer's Collaborative

Rhoda Au

Objectives of Global Cohort Development

Davos Alzheimer's Collaborative

01

Build a global cohort that is representative of the world population

02

Empower LMICs to contribute as meaningfully as HICs

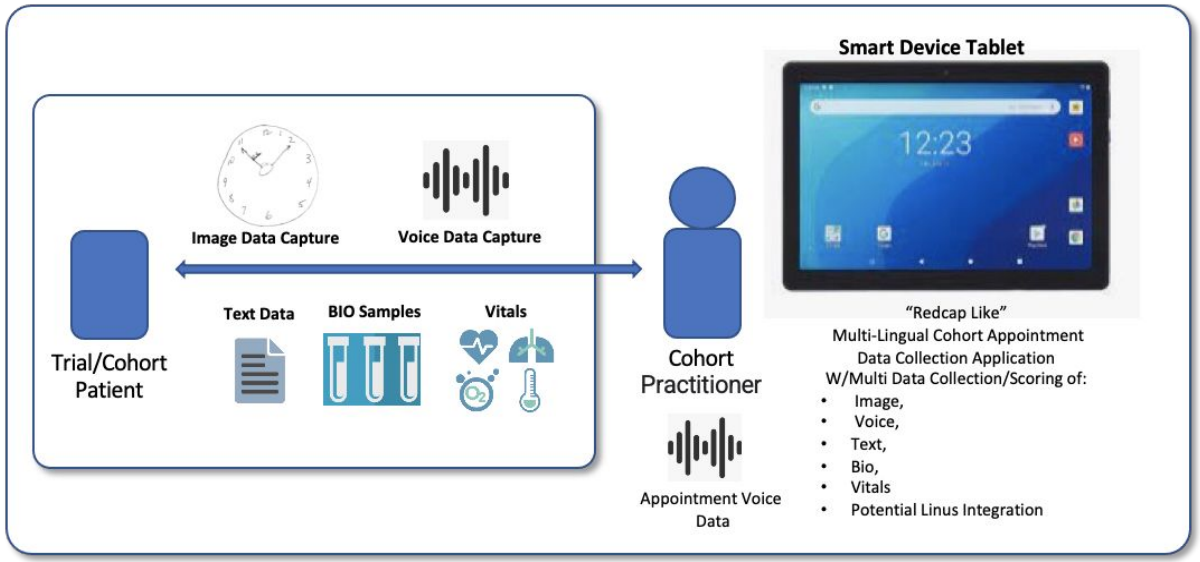
03

Accelerate discovery science by decentralizing data access and facilitating worldwide use

Clinician-free Digital Phenotyping System

Reliable Assessments without Highly-Trained Clinical Staff

Davos Alzheimer's Collaborative



ADDI Global Cohort Administration Services

- ***Cohort Management***
- L1 / L2 Admin Management
- User Management
- Tools Management
- Reporting
- Statistics

In partnership with:

LINUS HEALTH

ADDI Alzheimer's Disease Data Initiative

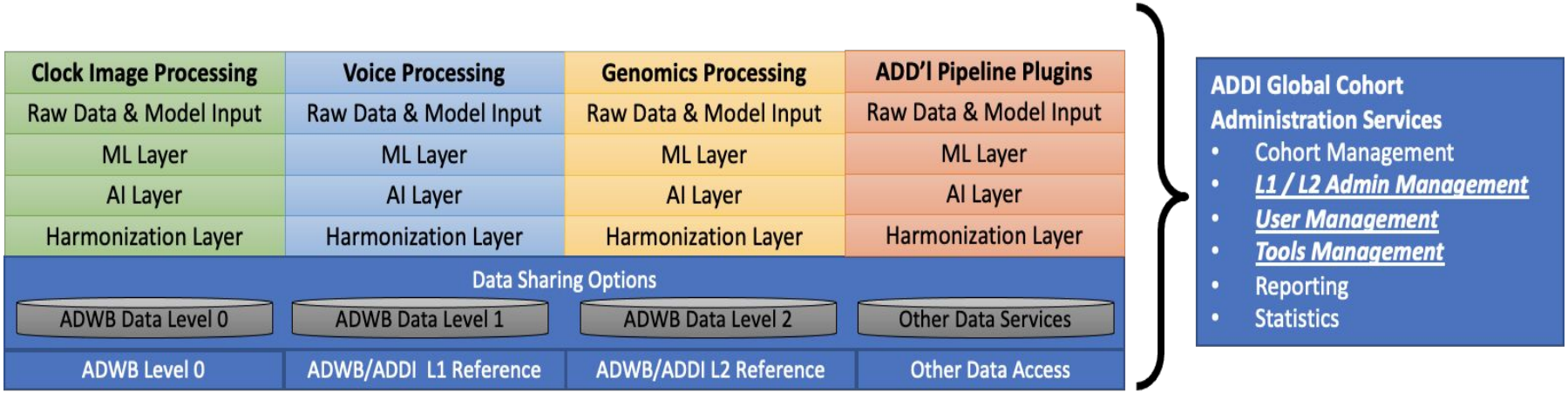
GLOBAL CEOINITIATIVE

WORLD ECONOMIC FORUM

Straightforward Data Processing Pipeline

High Quality Data Analysis without Domain Specific Expertise

Davos Alzheimer's Collaborative



Features

- Set of ADDI and third-party data plugins
- Distributed design enables data organizations to run/operate/maintain the pipeline in their own clouds/environments
- Includes sets of Administration Services to enable/manage/operate the pipelines

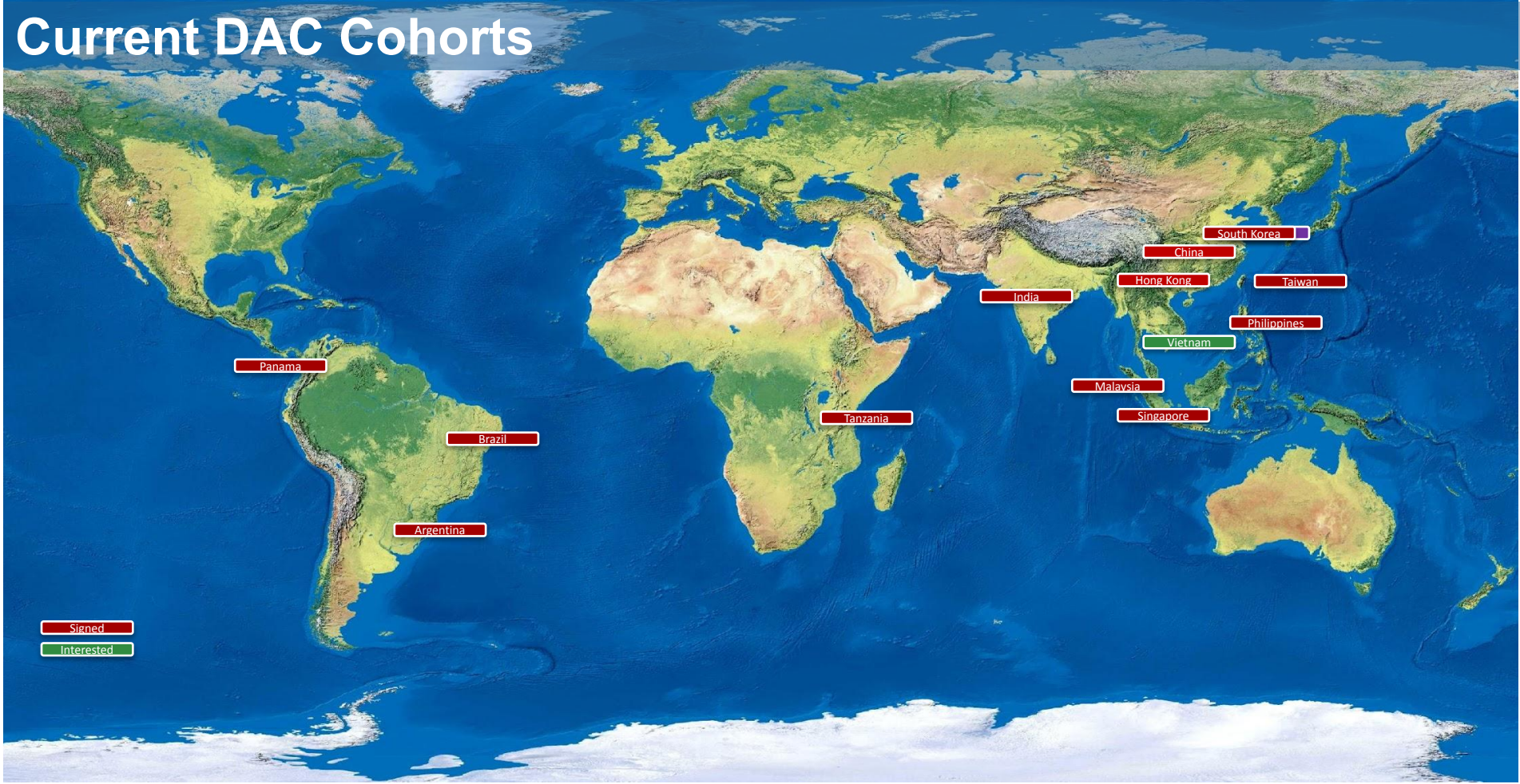
In partnership with:

ADDI Alzheimer's Disease Data Initiative

GLOBAL CEOINITIATIVE

WORLD ECONOMIC FORUM

Current DAC Cohorts



FLENI Cohort (Buenos Aires)

Primary Investigator	Ricardo Allegri		
Country	Argentina		
Participant count	1,284	Gender	Not specified
Start date	2011	Cadence	Not specified
Study type	Hospital-based (Instituto de Investigaciones Neurológicas (FLENI))		
Ages	Not specified		
Ethnic representation	Not specified		
Existing data	Partial APOE genotyping, stored plasma & CSF, Brain MRI, PET imaging		

AGELESS 1 - LRGS TUA Neuroprotective Model for Healthy Longevity among Malaysian Older Adults

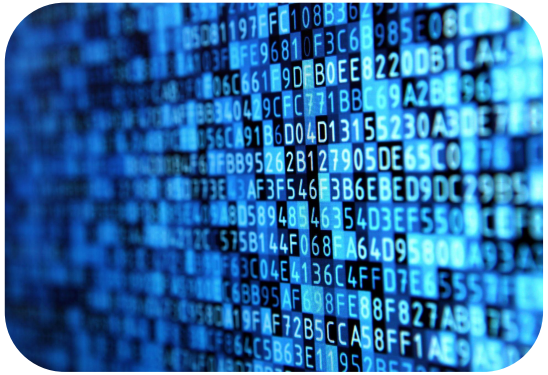
Davos Alzheimer's Collaborative

Primary Investigator	Dr. Tan Maw Pin, Dr. Suzana Shahar		
Country	Malaysia		
Participant count	2,322	Gender	48.1% Male 51.9% Female
Start date	2012-2013	Cadence	18 & 36 months, 5 years
Study type	Population/Community-Based		
Ages	60 or older		
Ethnic representation	60.5% Malay, 34.3% Chinese, 5% Indian		
Existing data	Health and lifestyle factors, stored whole blood samples, buccal, toenail, hair		

GLOBAL CEOINITIATIVE

WORLD ECONOMIC FORUM

Customized Benefits: Value Proposition for Cohorts



Expansive dataset and open-source analytic tools

- Accessed through the free Alzheimer's Disease Data Initiative (ADDI) tool

International network of collaborators

Participation in XPRIZE style challenges builds local analytic capabilities

- Motivate change, inspire ideas

Customized Benefits: Low-income Countries

Davos Alzheimer's Collaborative

Targeted penetration strategy

- Find motivators for low-income countries, especially for ones with younger populations.
- Piggy-back on current priority programs such as worm eradication
- Help developing economies bypass the "mistakes" of developed economies

Align with current health priorities & economic development interests

Prevention focus from a lifespan approach reduces later life risk

Customized Benefits: Budget Stretching

Pilot data needed for traditional grants

Use the connections and credibility of DAC to secure funding for denser omics & phenotypic characterization

- Co-funded government grants (FNIH, NNSF, HK I&T, etc.)
- Attract private capital investment (e.g., pharma, private equity, VC)

Making-The-Leap Solutions

Turning "Can't…" into "Can!"

Davos Alzheimer's Collaborative

Digital Phenotyping

- Reliable/consistent collection without need for highly trained clinicians/staff
- Push data directly into automated QC, data harmonization
- Generate common data elements in real time

Expertise Gap Solutions

- Build community-based cohorts to get true population level estimates
- Identify/validate digital surrogates for imaging biomarkers
- Identify/validate digital surrogates for clinical diagnosis

Global Data Access

- Analysis ready curated and representative data resource
- Biospecimen bank inventory
- Free analytic workbench
- Data analytic challenge program to create scientific precedent where none currently exist

THANK YOU

WORLD ECONOMIC FORUM

GLOBAL CEOINITIATIVE ON ALZHEIMER'S DISEASE

Davos Alzheimer's Collaborative

Patrick Sleiman, PhD

Lead Analytical Scientist
Center for Applied Genomics

Associate Professor
Perelman School of Medicine,
University of Pennsylvania

USA

IHCC/DAC AD PRS

Patrick Sleiman

Development of transethnic AD PRS

- Score based on summary stats from stage I of Jun et al., transethnic GWAS
  - **2 stage design Stage 1 ADGC European Ancestry, African-Americans, Japanese, and Israeli-Arabs (26,320 EAs, 4983 AAs, 1845 JPN, and 115 IAs)**
  - **Stage 2 International Genomics Alzheimer's Project (EA)**

- Supplemented with Bellenguez et al., stage I data excluding UKB proxy-ADD
  European Alzheimer's Disease BioBank (EADB) consortium (&UKBB) 20,464 cases and 22k controls.
  Phase I EADB 39,106 AD cases & 46,828 UKBB proxy-ADD (n= 85,934 cases)
  Phase II ADGC, Finngen, CHARGE 25,392 cases
  75 independent loci, 33 previously reported, 42 novel

- Multi-allelic variants, indels and rare SNPs with MAF < 3% were excluded from analysis
- Remaining variants from the combined summary stats were LD pruned using an R^2 threshold of 0.3 resulting in a final list of 74 variants
- Validation was carried out in the eMERGE consortium Phase I-III dataset

Development of PRS in early onset dementia

- Like other published AD PRS studies the APOE region has been omitted from the score and will be incorporated as a covariate in the full model

APOE risk varies by ancestry

- The effect of APOE genotype on AD risk is highly variable across populations
- The ε4 frequency is lower in Asians and associated with higher AD risk among Japanese (JPN) compared with EAs.
- Effect of ε4 on AD risk is lower in African-Americans (AAs) among whom the ε4 frequency is about 50% higher than in EAs

- Other covariates include age, sex and the first 3 principal components for genetic ancestry correction.

PRS Implementation / metrics

- As all groups may not have accurate age at onset data we are requesting odds ratios (rather than hazard ratios)
  - 1) Sites will return odds ratio per standard deviation of the PRS distribution with 95% CI
  - 2) We estimate a model discrimination (AUC) with CI of A) the PRS alone B) the PRS and APOE status C) The non-genetic predictors alone D) the full model
  - 3) Tail discrimination: We're proposing to set the cutoff for the high risk group at the 97.5% of the PRS. Provide the ORs and 95% CI (and the P-value for the OR) for the high risk group vs everybody else. i.e the subjects in the top 2.5% of the PRS vs the bottom 97.5%.
  - 4) Provide the sensitivity / specificity as well as negative (NPV) and positive (PPV) predictive values at the proposed cutoff (split by ancestry if appropriate for your cohort)
- For the NPV/PPV please use prevalence adjusted metrics, i.e. PPV = (Sn * Pr) / [(Sn * Pr) + ((1 – Sp) * (1 – Pr))] and NPV = (Sp * (1 – Pr)) / [(Sp * (1 – Pr)) + ((1 – Sn) * Pr)] where Sn = sensitivity, Sp = specificity, and Pr = population based prevalence reflective of your study population.

Site	Genetic ancestry	Phenotypic outcome	# case:control	Age range (if restricted)
Dementia Endpoints				
NCGG	Japanese (East Asian)	AD, MCI	Case:1000 Normal Cognitive:1000	77(32-100)
East London Genes and Health cohort	British-Pakistani/British-Bangladeshi (South asian)	All-cause dementia (from secondary/primary care records); MCI/cognitive decline cases excluded	104 cases; 614 controls	Cases >40 years; healthy controls >70 years old
Korean Biobank Project	Korean (East Asian)	Phenotype 1: Cortical amyloid positivity (by Flutemetamol PET imaging) (Control: Cortical amyloid negativity)	191:337 (total 528)	
		Phenotype 2: Clinical Dementia Rating (CDR) global Score 1 or over (Control: CDR global 0.5 or less)	157:539 (total 696)	
Intermediate phenotypes / biomarkers				
AWI-Gen	African (Different ethnolinguistic and geographic groups)	NA		
ELSA	Brazilian (Admixed)	Neuro-cognitive endophenotypes	2844	
INTERVAL (UK Blood Donors)	European (White British)	Stroop Test (attention and reaction times), Trail Making Test (executive function), Pairs Test (Episodic Memory), Reasoning Tests (intelligence), >3K proteins on the SomaLogic proteomics platform	~9k Cognitive measure; 1140 proteomics	

Sites with AD phenotype endpoints

NCGG, East London, Korea Biobank

Phenotype 1: Cortical amyloid positivity (by Flutemetamol PET imaging) (Control: Cortical amyloid negativity)
Phenotype 2: Clinical Dementia Rating (CDR) global Score 1 or over (Control: CDR global 0.5 or less)

Cohort	Odds ratio per SD	Estimate of model discrimination (AUC) with CI of PRS score only	Estimate of model discrimination (AUC) with CI for genetic predictors ie PRS and APOE counts	Estimate of model discrimination (AUC) with CI of the non-genetic covariates only	Estimate of model discrimination (AUC) with CI of the full model (i.e. with genomic predictor and non-genetic covariates)
Korea pheno1	1.1857 (0.9917,1.4177)	0.5482 (0.4968,0.5997)	0.6770 (0.6282,0.7259)	0.6266 (0.5762,0.6770)	0.7505 (0.7053,0.7957)
Korea pheno2	1.0403 (0.8709,1.2426)	0.5074 (0.4559,0.5589)	0.6122 (0.5604,0.6640)	0.5451 (0.4931,0.5970)	0.6372 (0.5858,0.6886)
EastLondon	1.11 (95% CIs: 0.94-1.33)	0.53 (95% CIs: 0.47-0.59)	0.54 (95% CIs: 0.48-0.60)	0.68 (95% CIs: 0.61-0.75)	0.69 (0.62-0.76)
Japan	1.120	0.545 (0.5198-0.5702)	0.6071 (0.5824-0.6318)	0.61575 (0.5907-0.6408)	0.6254 (0.6005-0.6503)

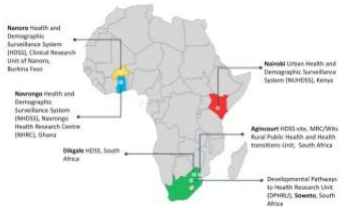
Random effects restricted maximum likelihood (REML) meta-analysis of AUC and variance 0.674 (0.643-0.706)

Neuro-cognitive endophenotypes / Proteomics

ELSA Brazil 2844 admixed individuals w/neurocognitive assessments

Trait	Unadjusted Model		PC adjusted		PCs + ApoE	
	P value	Beta (SE)	P value	Beta (SE)	P value	Beta (SE)
Common mental disorders score	5.5e-09	13.3 (2.2)	1.2e-06	11 (2)	1.2e-06	11.2 (2.3)

AWI-Gen
10603 participants
Genotyped on H3A chip
Imputed using Sanger AFR panel



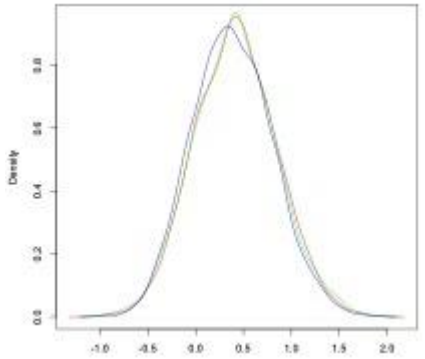
INTERVAL (UK Blood Donors)

Assayed 3K proteins on the SomaLogic proteomics platform

PRS + APOE SNPs

Correlation with blood APOE protein levels

	APOE.2937.10.2	APOE.5312.49.3
R2	6.55E-03	0.00475
P	0.0057	0.0194
BETA	16.9	15.03
SE	6.11	6.42



Conclusions and Further work

- Developed a transethnic AD PRS based on 74 variants
- Effect estimates derived from studies including individuals of European Ancestry, African-Americans, Japanese, and Israeli-Arabs
- Performance of score evaluated across dementia, neurocognitive and proteomic endpoints in diverse ancestries
- Performance varied by endpoint over ancestry
- Positive association with neurocognitive endpoint in ELSA and circulation APOE levels in INTERVAL study
- **Future work includes:**
- Evaluation of score in a large European ancestry cohort from UKB
- Evaluate inclusion of ancestry dependent APOE estimates

Acknowledgments

- **CHOP**
  - Hakon Hakonarson
  - John Connolly
- **NCGG**
  - Kouichi Ozaki
- **East London Genes and Health cohort**
  - Charlie Marshall
- **Korean Biobank Project**
  - Jae Pil
- **AWI-Gen**
  - Michele Ramsay
  - Ananyo Choudhury
- **ELSA**
  - Alexandre Pereira
- **INTERVAL (UK Blood Donors)**
  - **Adam Butterworth**

Live Panel Discussion

Please put your questions in the chat

Returning at 12:40 UTC

Working Group High Level Overviews

Scott Sundseth, PhD

Associate Director
International HundredK+ Cohorts Consortium

USA

Session Overview

Session Topics:

- Training and Workforce Working Group
- Data Interoperability and Infrastructure Working Group
- Policy and Systems Working Group
- Scientific Strategy and Cohort Enhancement Working Group

Session Speakers:

- Paballo Chauke, MSc & Albert Tenesa, PhD
- Philip Awadalla, PhD & Thomas Keane, PhD
- Laura Lyman Rodriguez, PhD & Nicki Tiffin, PhD
- Hákon Hákonarson, MD, PhD & Adam Butterworth, PhD

Paballo Chauke, MSc

Training and Outreach Coordinator,
H3ABioNet
South Africa

Albert Tenesa, PhD

Group Leader, Roslin Institute and the Medical Research Council Human Genetics Unit, The University of Edinburgh
UK

3 November 2021

Training and Workforce Working Group

Co-Chair Names: Paballo Chauke and Albert Tenesa

International 100K Cohort Consortium

Outline

- Working Group Action Plan
- Proposed Goals
- Action Plan
- Job Opportunity

Working Group Action Plan

Working Group Action Plan

Strategic Purpose: This NEW Working Group will support the IHCC Strategic Directive “Make it Possible for ALL Cohorts to Contribute to IHCC Science Challenges” by:

- Assessing cohort workforce capabilities and competencies and designing activities to address identified needs
- Coordination with other working groups to address workforce needs related to scientific challenges
- Training the next generation of cohort leaders

Proposed Goals: **5-year Goal - For the IHCC to be viewed as THE go-to resource for large cohort research.**

- 1-3 year Goals:

  - Establish Cross-Cohort Exchange Program
  - Establish Mentorship Activities for Young Investigators (including educational career development opportunities)
  - Establish an ongoing Cohort Educational Webinar Series, with additional hands-on workshops and/or forum discussions as needed

Action Planning

- DONE: Nominate/recruit (2) L&S co-chair leaders
- DONE??: “Brand” the L&S working group – **rename the group (?)**
- Define the appropriate scope and boundaries for the work to be undertaken
- Develop processes to define and understand gaps in cohort resources
- Identify resources to fill gaps to support ongoing success
- Build Knowledge, Skills and Attitudes (KSA) needed to do population research using cohort data

Action Plan

- Had a meeting as the Training and Sharing Working Group- not well attended
- We are recruiting new members
- We need sub-committee chairs for our work i.e webinars, cohort exchange program etc

Job opportunity alert!

Global Genomic Medicine Collaborative
Project Manager, International Hundred K+ Cohorts Consortium (IHCC)
contract position, hourly, 20% FTE, 8 hrs/week

The Global Genomic Medicine Collaborative (G2MC - http://g2mc.org) is hiring a part-time Project Manager to work with the International HundredK+ Cohorts Consortium (IHCC) Program Team to implement the activities of the IHCC (https://IHCCGlobal.org) - specifically providing support to the identified working groups described. The G2MC Secretariat has its headquarters in Durham, NC; relocation is not required as the G2MC is a virtual global organization. This position is expected to be conducted remotely.

The IHCC project manager will report to the IHCC Associate Director and work directly with IHCC Program manager and other support staff. This position will have close interaction with and direction from the Leads of the IHCC Working Groups identified below, and interact with the IHCC Scientific Steering Committee and IHCC member cohorts.

Work Performed

The IHCC project manager will generally provide the following support to the identified working groups, in addition to the items listed specifically for each working group. Knowledge of genomics, policy and education is desired:

General Project Manager responsibilities:

- Ensure Communication to Working Group members on behalf of the Leads
- Schedule / convene working group members on a regular basis, prepare agendas for Lead approval, prepare meeting minutes, and follow up on action items
- Research and prepare information for proposed working group projects
- Engage in regular contact and regular teleconferences with IHCC Secretariat members for coordination of work across working groups
- Support activities required for working group preparations for workshops, steering committee meetings and annual summits

Working Group specific responsibilities:
Policies & Systems Working Group (https://ihccglobal.org/teamc/)

- Develop a policy agenda to facilitate and optimize the impact of assembling cohorts; address challenges and identify common needs. By: 1. Assessing external policy and system level needs, gaps, and challenges and design activities to address identified needs. 2. Coordinating with other working groups to address policy and systems level needs related to science challenges. 3. Ensuring IHCC is promoting good work of other groups (e.g., GA4GH, GDPR, G2MC, FAIR Principles)
-

Education, Training & Capacity Development Working Group (https://ihccglobal.org/teamd/)

- Making it possible for ALL cohorts to contribute to IHCC science challenges through collaboration enhancement, training, education, and knowledge sharing. By: 1. Assessing cohort workforce capabilities and competencies and design activities to address identified needs. 2. Coordinating with other working groups to address workforce needs related to scientific challenges. 3. Training the next generation of cohort leaders.

Education/Experience:
Work requires analytical, communications, writing, and organizational skills generally acquired through completion of a Master's degree program or equivalent experience, and experience in program administration and project management to acquire skills necessary to coordinate a variety of activities.
Experience and knowledge of research cohorts, genetics and genomics research highly preferred. Experience and knowledge gained from working with international projects is highly desired, as is grant writing expertise.
Flexibility in schedule to allow for scheduling of international conference calls (early morning or late evening) required.
Salary or Hourly rate commensurate with experience.
Job duties may include international travel for the Annual Summit (post COVID-19 Pandemic).


“If you want to go fast, go alone. If you want to go far, go together” – African proverb

Thank You All and Questions/Discussion

Thanks for listening, any questions?

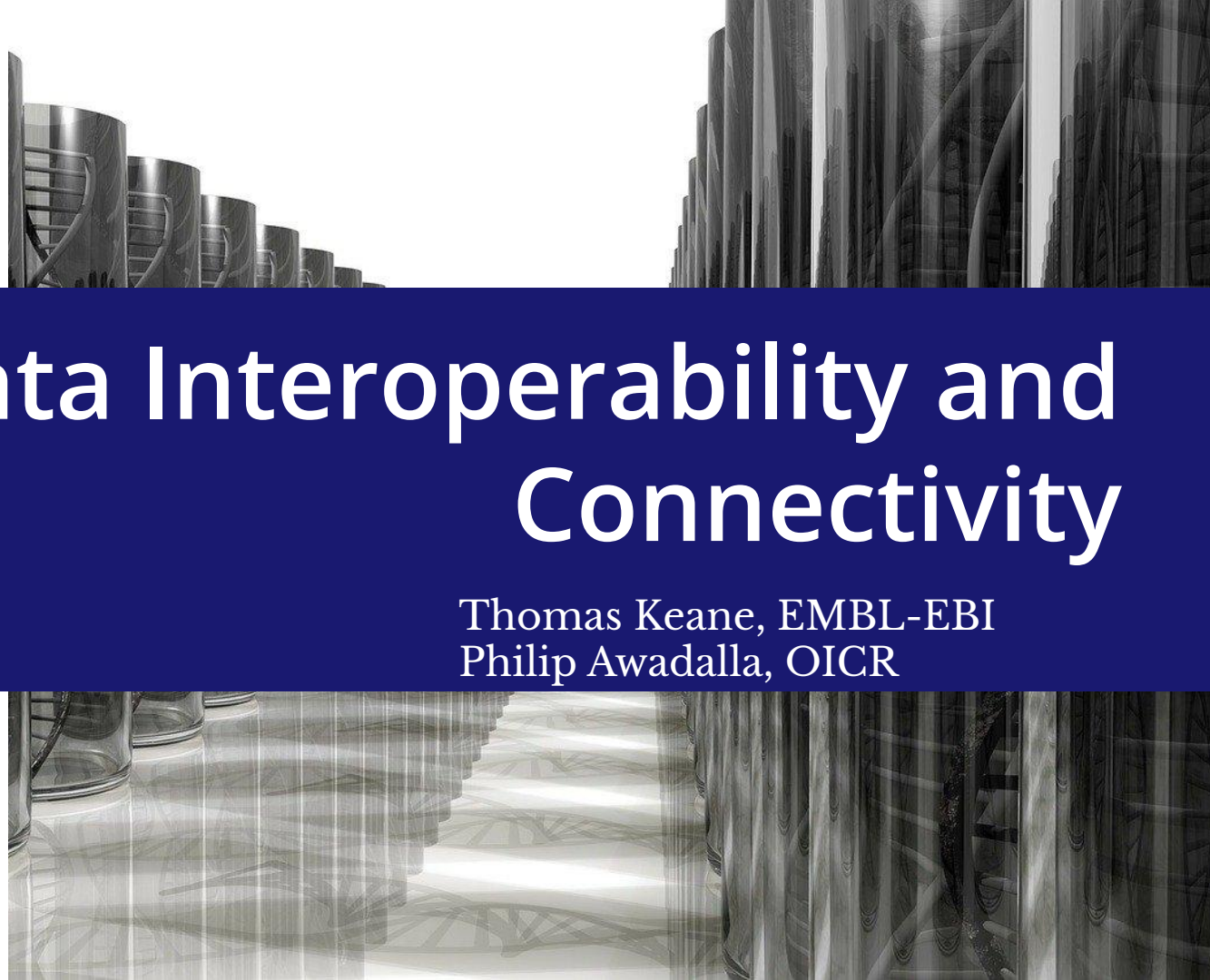
Philip Awadalla, PhD

Director of Computational Biology,
Ontario Institute for Cancer Research
Canada

Thomas Keane, PhD

Team Leader, European Bioinformatics Institute
UK

November 2021



Data Interoperability and Connectivity

Thomas Keane, EMBL-EBI
Philip Awadalla, OICR

Data Interoperability and Connectivity Team

"Deliver interoperable cross cohort infrastructure to enable population scale biomolecular data to be accessible across international borders accelerating research and improving the health of individuals resident across continents."

Aims

- Increase cohort data re-use and sharing (FAIR)
- Create a global platform for cross cohort scientific research
- Align with emerging global standards to maximise interoperability

Challenges

Challenge 1: Common framework for cohort metadata integration

Challenge 2: Cohort data discovery

Challenge 3: Cohort access and authorization

Challenge 4: Federated analysis interoperability for research

5 Year Implementation

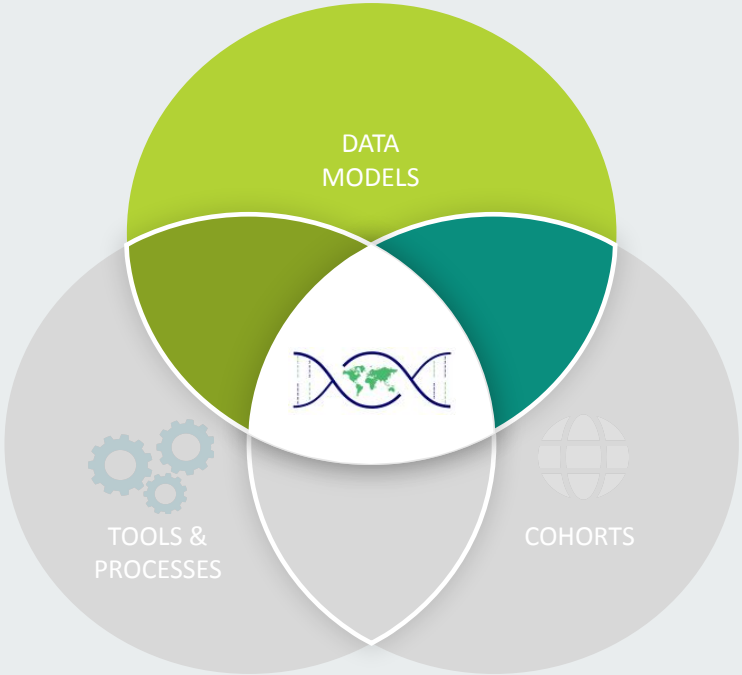
1. Common framework for cohort metadata integration

Data models to represent both access conditions and cohort data

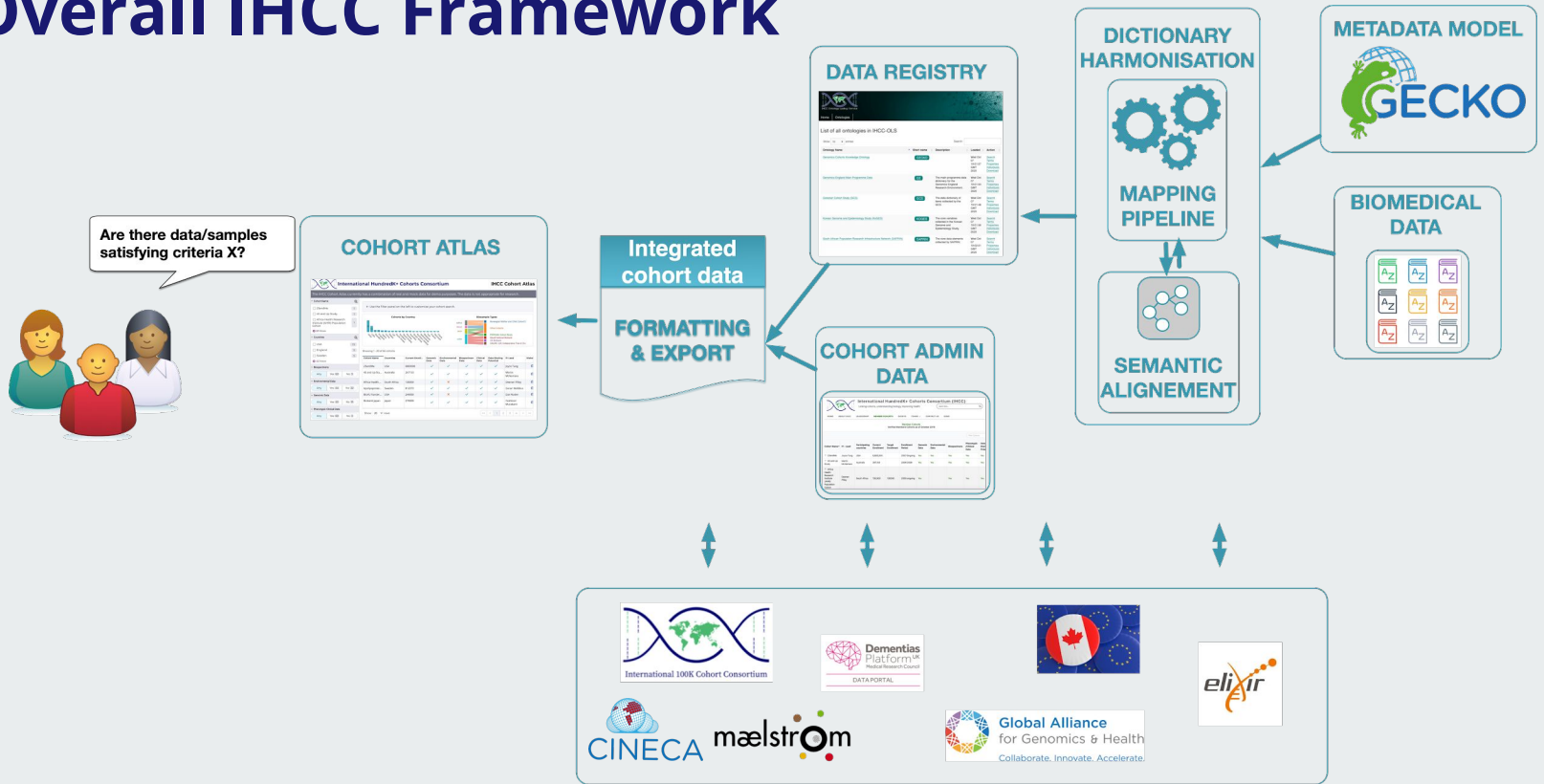
Tools and processes for implementations

Genomics Cohort Knowledge Ontology (GECKO)

- Commonly used attributes to describe cohort metadata
- “Medication”, “sample type”, “genomics datatypes”...



Overall IHCC Framework



5 Year Implementation

2. Cohort data discovery

IHCC Cohort Atlas

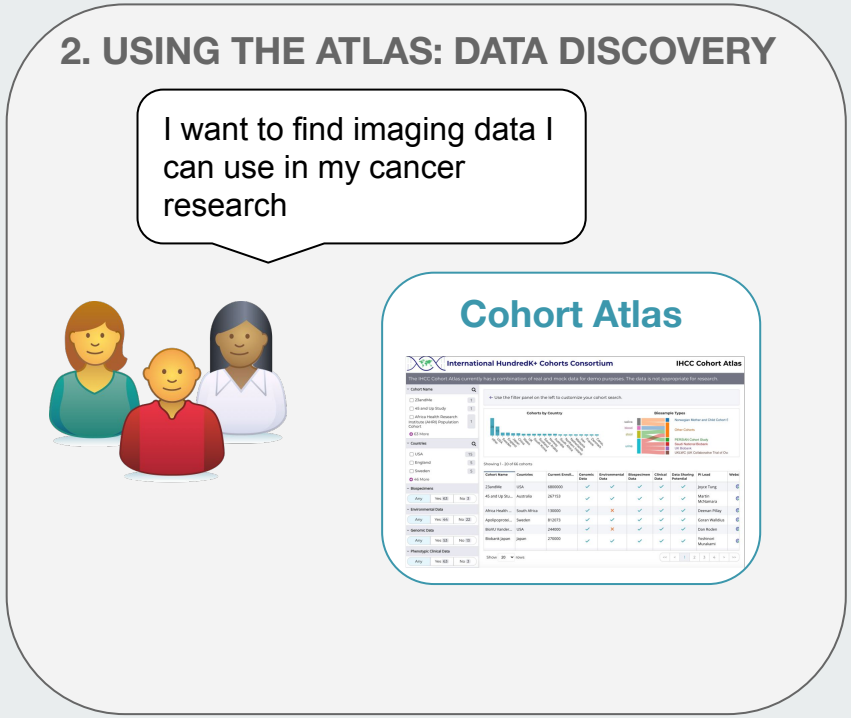
- Enables researchers to search across IHCC cohort metadata
- 13 cohorts, >100 variables harmonised

Davos Alzheimer's Collaborative

- Example of disease specific expansion of the atlas

Future vision for atlas

- Cornerstone of future IHCC data science platform



5 Year Implementation

3. Cohort access and authorization

Access individual level human cohort data is difficult

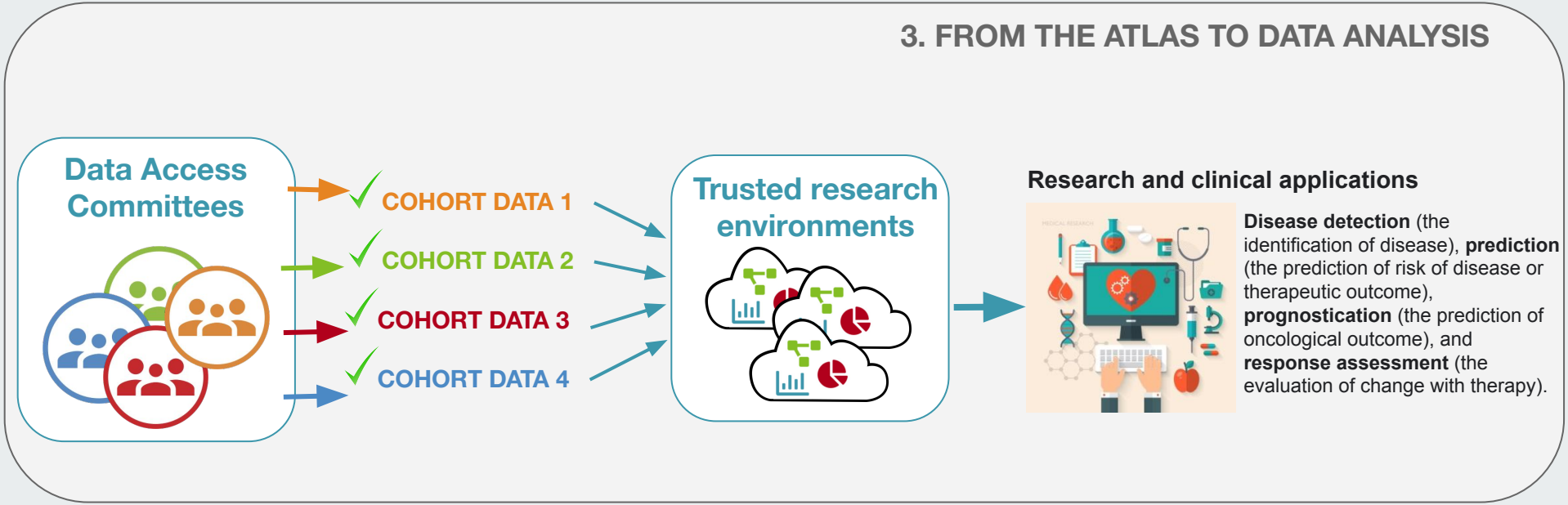
- Heterogeneity of access systems, criteria, processes

Encourage and support cohorts to adopt emerging standards and best practices

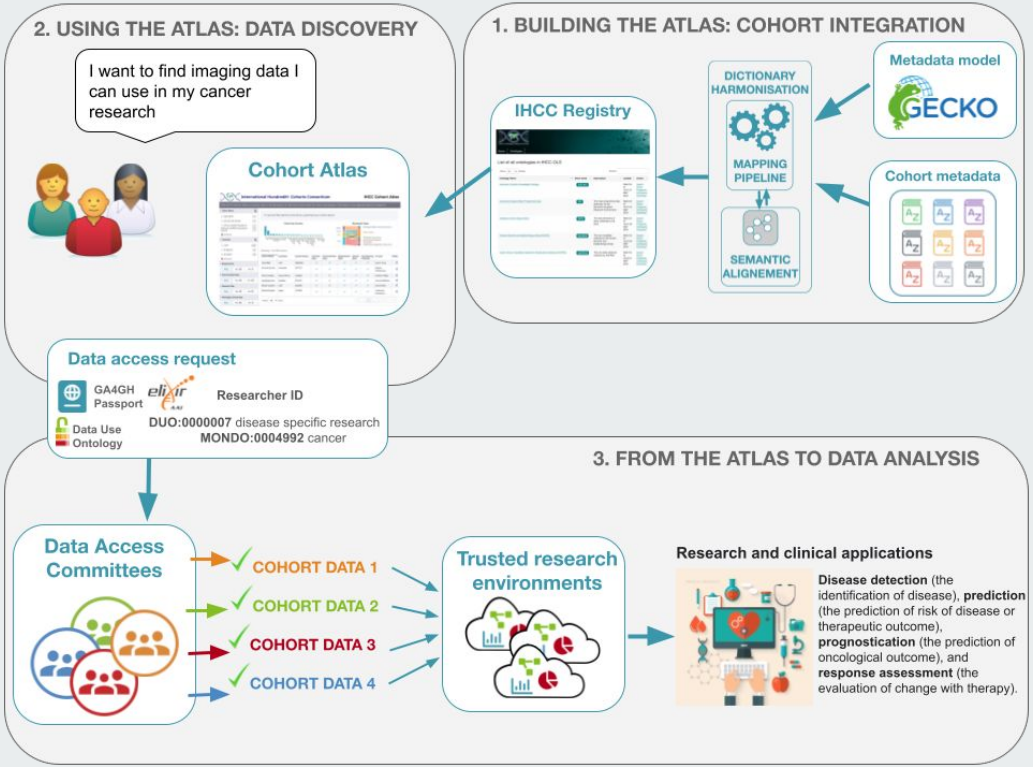
- Data Use Ontology, Researcher Passports, common AAI
- Build demonstrators with cohorts and access platforms

5 Year Implementation

4. Federated analysis interoperability for research



5 Year Implementation



Global Standards

Cohort interoperability standards are emerging

Global Alliance for Genomics and Health (GA4GH)

- 8 workstreams (e.g. Discovery, Data Use, Clinical and phenotypes, Ethics, Security)
- Clinical metadata standards (e.g. HL7/FIHR, OMOP etc)

IHCC Data team and GA4GH

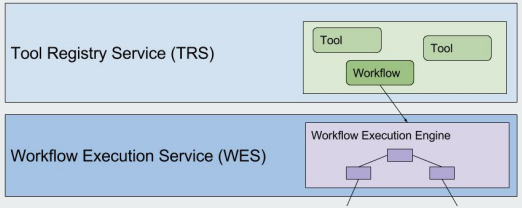
- Foundation for all IHCC products to interop with other cohorts
- e.g. IHCC cohort atlas cross queries with other aggregate resources

Global Alliance for Genomics & Health
Collaborate. Innovate. Accelerate.

Data Use Ontology

Phenopackets
Open and Computable Bioinformation

Beacon Network



IHCC Atlas Workshop

1st workshop held Oct 27th 2021

- 23 attendees
- Tutorials on metadata harmonisation best practices
- Practical demonstration of adding new coh to the IHCC Atlas

Recording is available

- https://ihccglobal.org/ihcc-data-atlas-workshop/

Plan to re-run the workshop in early 2022

Program Overview

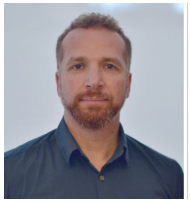
October 27 – Session for America & Europe, Africa | Time Zone Converter

Time (UTC)	Subject	Presenter
15:00 – 15:10	IHCC project and data team overview	Thomas Keane (EMBL-EBI)
15:10 – 15:20	IHCC Cohort Atlas overview	Melanie Courtot (EMBL-EBI) / Rosi Bajari (OICR)
15:20 – 15:35	IHCC Cohort Atlas Data harmonization	Melanie Courtot (EMBL-EBI)
15:50 – 17:00	Live demo for cohort metadata harmonization	Carles (EMBL-EBI) / Isuru (EMBL-EBI)

Contact us! ihcc-browser@googlegroups.com

Acknowledgements

Thomas Keane



Philip Awadalla

Christina Yung

Rosi Bajari

Giselle Kerry

Melanie Courtot

Eric Plummer

KNOCEAN

James Overton

Rebecca Jackson

Nicolas Matentzoglu

Minh Ha

Brandon Chan

Carles Garcia

Isuru Liyanage

Dan Brake

Chris Lunt

elixir

CINECA

OICR Ontario Institute for Cancer Research

EMBL-EBI

NIH National Institutes of Health Turning Discovery Into Health

Global Genomic Medicine Collaborative

This project has received funding from the European Union's Horizon 2020 Research and Innovation Programme under grant agreement No. 825775.

Laura Lyman Rodriguez, PhD
Interim Chief Program Support Officer,
Senior Advisor to the Executive Director
Patient-Centered Outcomes Research
Institute (PCORI)
USA

Nicki Tiffin, PhD, MPH
Associate Professor, University of Cape
Town
South Africa

November 3, 2021

Policy & Systems Working Group

Laura Lyman Rodriguez, USA
Nicki Tiffin, South Africa

International 100K Cohort Consortium

Disclaimer

All statements, opinions, or discussions by LLR are solely representative of my personal views and are not reflective of any positions of the Patient-Centered Outcomes Research Institute (PCORI)

Taking our Cue from the Big Picture

Vision

A global community of cohorts working together to advance science and improve health for all.

Mission

To forge cohort connections that revolutionize population health science by providing sustainable data infrastructure, cultivating a collaborative research environment, and **promoting policies and best practices that foster connectivity, interoperability, and reciprocity**.

Action Plan – Pragmatic Framework

“Coordinate with other working groups”

Local Collaborate with & facilitate progress in IHCC Projects

Community

Enterprise

IHCC Funded Projects – August 2021

Project	PI/PM	Institution	Funders	Year	# cohorts	# LMIC cohorts
Polygenic risk scores (PRS)	Hakon Hákonarson (USA)	Children's Hospital of Philadelphia (CHOP)	NIH/WT	2020	6	2
Exploring the role of genetically determined BMI in infancy, childhood, and early adulthood on colorectal cancer development in later life	David J. Hughes (Ireland)	University College Dublin, International Agency for Research on Cancer (IARC), University of Texas	NIH/WT	2021	4	1
High-Throughput Metabolomic Biomarker Measures in Diverse Ancestries	Hakon Hákonarson (USA)	Children's Hospital of Philadelphia (CHOP)	NIH/WT	2021	4	2
Opioid cohort consortium (OPICO) to investigate the effects of regular opioid use on mortality and on cancer development	Paul Brennan (France)	International Agency for Research on Cancer (IARC)	NIH/WT	2021	10	4
Global Mental Health Impact of the COVID-19 Pandemic	Jordan Smoller (USA) Sarah Bauermeister (UK) & Andre Brunoni (Brazil)	Massachusetts General Hospital, Oxford University, University of Sao Paulo Medical School	NIH/WT	2021	12	3
Novel coronavirus host susceptibility study in South Africa (COVIGen-SA)	Michele Ramsay (S. Africa)	Wits Health Consortium	NIH/WT	2021	3	3
Strengthening biospecimen collection for Global Longitudinal Population Studies in the COVID-19 era	John Chambers (Singapore)	Nanyang Technological University	CZI	2021	4	3
Davos Alzheimer's Collaborative - Pilot PRS	Davos Alzheimer's Collaborative - Pilot	Children's Hospital of Philadelphia (CHOP)	DAC	2021	7	4

https://ihccglobal.org/ihcc-funded-projects/

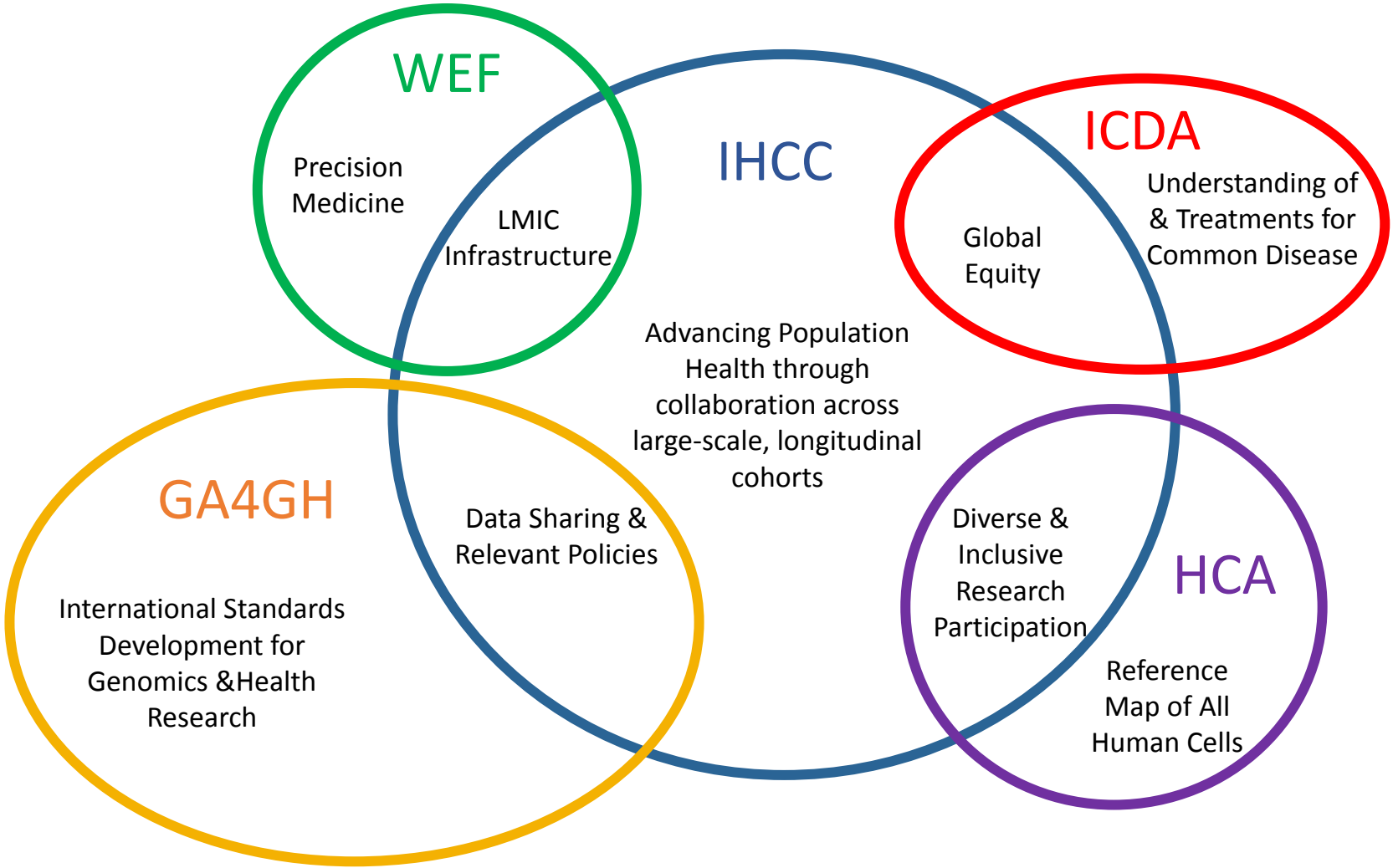
Action Plan – Pragmatic Framework

“Coordinate with other working groups”

Local Collaborate with & facilitate progress in IHCC Projects

Community Topic specific advancement with & through other consortia

Enterprise

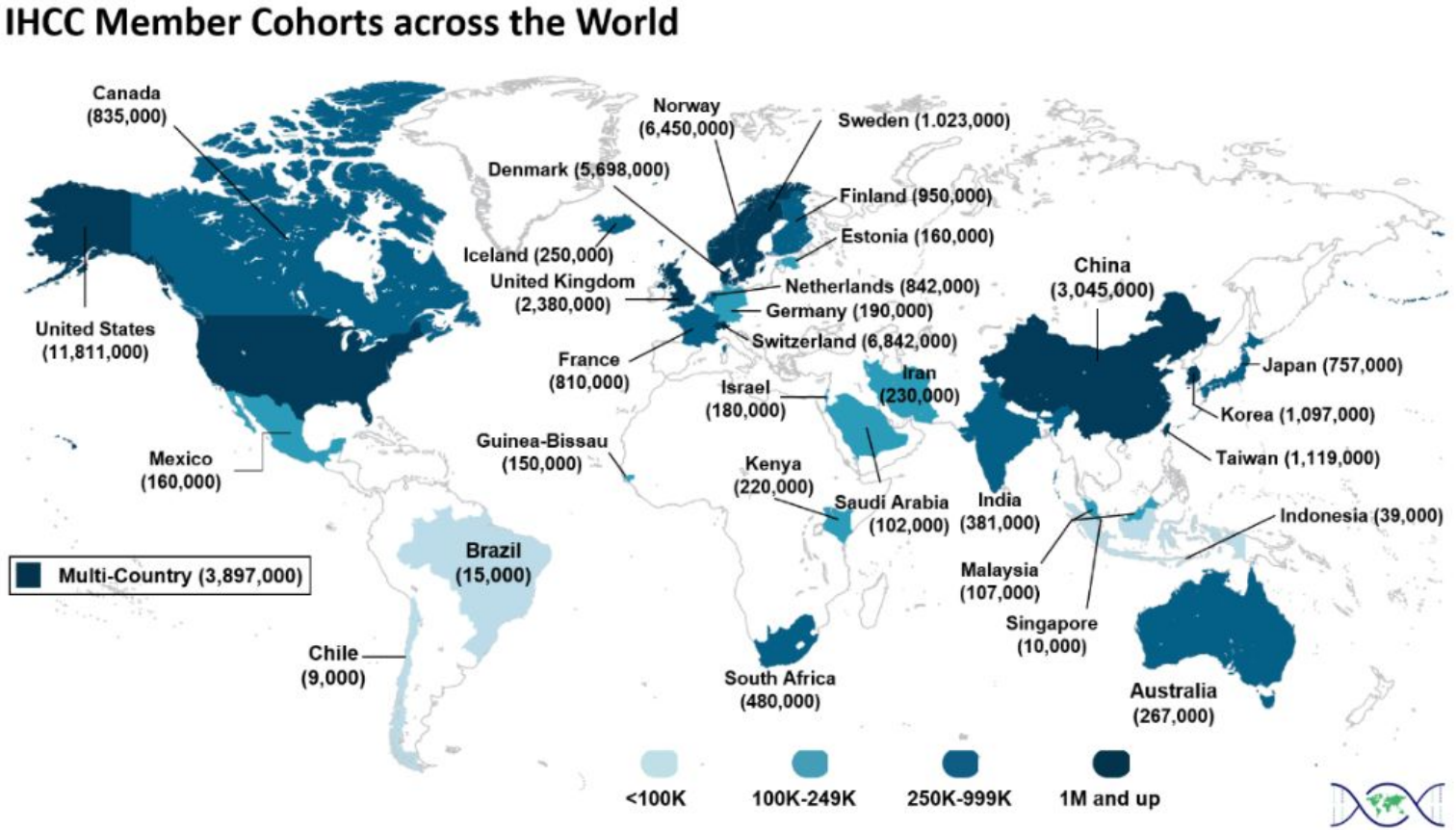

WEF
Precision Medicine
LMIC Infrastructure
IHCC
Advancing Population Health through collaboration across large-scale, longitudinal cohorts
ICDA
Global Equity
Understanding of & Treatments for Common Disease
GA4GH
Data Sharing & Relevant Policies
International Standards Development for Genomics &Health Research
HCA
Diverse & Inclusive Research Participation
Reference Map of All Human Cells

Action Plan – Pragmatic Framework

“Coordinate with other working groups”

Local	Collaborate with & facilitate progress in IHCC Projects
Community	Topic specific advancement with & through other consortia
Enterprise	Building resources and disseminating experience

Power and Potential of IHCC for Research



~110 cohorts, ~60M participants

Proposed 1-3 Year Goals (May Summit)

- Collaborate with other Working Groups to develop project policies and policy frameworks to streamline and promote collaboration and data sharing across IHCC activities
- Interface with and contribute to international efforts to address IHCC policy interests, *e.g.*, data access procedures, policy interoperability, pathways to address privacy regulations, etc.
- Assemble a “tool box” to promote capacity in IHCC cohorts and others around the globe to share data and collaborate to advance science and improve health for all

Draft Goals for Discussion and Prioritization

- Create a prioritized list of *specific* challenges for IHCC projects & **develop guidelines/resources** for broader application as issues are identified & worked through
  - Idea: Work with the Metabolomics project to support data sharing and publication activities for meta-analysis; work iteratively to test with other projects and work toward generalised guidelines
- Establish a reliable source for vetted resources (a "**toolbox**") based on needs and priorities of IHCC members
  - Area for collaboration with other consortia 'ELSI' groups; identified gaps could become targets for focused work
  - Idea: Could such a centralised repository with supporting documents, white papers, etc. be leveraged to support IHCC Member cohorts' policy work or discussions with funders?
- Create **policy consult/helpdesk** to capture needs/requests for assistance from cohort members
  - Idea: Perhaps establish an online form/centralised email address to contact for consults/assistance
- Develop **relationships with regional and global cohort alliances** (on-going)
- Work with Education & Training WG: **integrate training** into ongoing programmes as needed

We are Hiring!

IHCC Working Group Project Manager!

Provide the support to 2 working groups: Policies & Systems and Training & Workforce
Estimated 8 hours a week (contract position)

Project Manager responsibilities:

- Communicate with Working Group (WG) members
- Schedule WG meetings and related actions
- Participate to monthly IHCC Secretariat meetings
- Support the WG co-leads in WG specific activities, projects and presentations (to steering committee meetings and summits).

Knowledge of genomics, policy and education is desired. International experience is a plus!

Go to the *"IHCC Job Opening!"* tab in Socio for the full job description and details to apply

Hákon Hákonarson, MD, PhD

Director of the Center for Applied Genomics, CHOP
USA

Adam Butterworth, PhD

Reader in Molecular Epidemiology,
University of Cambridge
UK

November
03, 2021

Scientific Strategy and Cohort Enhancement Working Group

Adam Butterworth
Hákon Hákonarson

Outline

5-Year Strategic Plan

- Review action items from May Summit
  - IHCC Members' Survey
- Goals for the Workshop
  - Review strategic direction
  - Review Responsibilities
  - Revisit Action Ideas
  - Preview Breakout Questions
- Program Updates
  - Five IHCC Pilot Projects
  - Davos Alzheimer's Collaborative

Action Items from May Summit

Action Items

- Collect info from cohorts on research interests/priorities to enable matchmaking for future joint funding proposals.
  ACTION: Create survey for respective cohorts
    - Dementia
    - PRS
    - Conditions of interest – LoF, PGx, Items from previous Summit outcomes
    - Dovetail with ‘Survey Day’ at Secretariat (Ricardo, Chile – PGx; Education, Sample requirements, Education etc.)
    - Reach out to currently-funded pilots to supplement survey items

- Use this info for catalogue of cohort interests to share with funders. Create similar catalog of industry/funder interests to share with cohorts. Matchmaker for cohorts <--> funders/industry. Include local funders when possible.
  ACTION: Explicitly target industry funders:
    - Secretariat has a list of funders – discussion and webinar with industry members planned
    - Tailored survey to industry/funders – Need to solicit the proposition value for industry

SHARED Action Items

- Plan and propose funding for large-scale collaborative project with high-tech element to improve capacity in LRS cohorts.
  ACTION:
  - Capitalize on Nightingale project
  - Specifically focus on integrating LRS
  - Assay providers may model this approach
- Establish process to assemble cohorts and negotiate with vendors for bulk rates.
  ACTION:
  - Difficult to form a conglomerate with individual agreements needed
  - Need a lead institution
  - Discuss capacity of sites to share samples
- Survey membership for who has samples that need conversion to genotype data; use for bulk negotiation.
  ACTION:
  - Add to survey – assess plans to capture various OMICS in next 18-24 months
- Establish a pre-competitive environment for venture capital and industry funders to have limited, time-stamped, or non-exclusive access to cohorts
  ACTION:
- Address in planned survey of funders, as well as webinars

Collect info from cohorts on research interests/priorities to enable matchmaking for future joint funding proposals.

ACTION: Create Survey for Respective Cohorts

Relevant Items Include:

- Cohort overview
- Research Priorities incl. previous Summit
  - Dementia PRS
  - Phenotypes
  - LoF
  - PGx
- Data & Sharing
- Collaboration expectations
  - Industry
  - Academia
- Biosamples
  - Availability
- Environmental Data
- Workplace Dev/Education

Survey Outcome – Matchmaking

- Use survey date to catalog of cohort interests
- Align with Data Atlas and Secretariat catalog
- Share and matchmake with other cohorts
- Share and matchmake with industry/funder interests

Survey Outcome – Funding & Support

- Examine funding for large-scale collaborative project with high-tech element to improve capacity in LRS cohorts.

- Identify survey membership with samples that need conversion (e.g. genotype/sequencing) use for bulk negotiation.

- Assess appetite for a pre-competitive environment between funders/cohorts

Goals for workshop

Strategic Directions

- **Demonstrate that IHCC generates impactful science** - Provide "proof of concept" that IHCC generates impactful science through ambitious scientific projects that require scale and diversity and improve health for all

- **Make it possible for all cohorts to contribute to IHCC scientific challenges** - Promote the development and/or adoption of policies and best practices and enhance cohort capabilities and competencies to improve the practice of collaboration

Specific Responsibilities

1. Oversee launch, execution, and close-out of scientific challenges

2. Design implementation protocol for scientific strategies

3. Coordinate with other working groups to address cohort capability/competency/policy/system gaps related to specific challenges

Action Ideas

- Facilitate existing pilot projects to completion
- Capture and learn from pilot project outcomes, including impact, collaborations, added value, capacity building, challenges/barriers
- Progress the IHCC-DAC collaboration
- Generate funding to (a) launch new projects and (b) extend pilot projects
- Engage LRS/under-resourced cohorts to enhance participation
- Cross-linking of WGs to enable closer alignment

Breakout questions

1. How can we develop scientific project ideas that allow inclusion of a broader, more diverse set of cohorts?

2. How can we empower IHCC members to develop project ideas and apply for ‘bottom-up’ funding?

3. How can we capitalise on the industrial links that IHCC has built (e.g. assay providers, pharma partners etc)?

Program Updates

IHCC Pilot Projects

Competitive funding from IHCC to advance scientific progress and establish collaborations – Five projects funded and already presented

IHCC Pilot Projects:

Project	Contact PI
Exploring the role of genetically determined BMI in infancy, childhood, and early adulthood on colorectal cancer development in later life	David Hughes
High-Throughput Metabolomic Biomarker Measures in Diverse Ancestries	Hakon Hákonarson
Opioid cohort consortium (OPICO) to investigate the effects of regular opioid use on mortality and on cancer development	Paul Brennan
Global Mental Health Impact of the COVID-19 Pandemic	Jordan Smoller
Novel corona virus host susceptibility study in South Africa (COVIGen-SA)	Michele Ramsay
Strengthening biospecimen collection for Global Longitudinal Population Studies in the COVID-19 era	John Chambers

Davos Alzheimer's Collaborative

Develop a transethnic Alzheimer Disease (AD) polygenic risk score (PRS) to enable detection of individuals at high risk of developing the disease

Opportunity based on:

- Genetic based risk scores have the advantage of identifying AD-risk individuals before the onset of any symptoms.
- The disadvantage of PRS, to date, has been the limited transferability of the scores across ethnic groups (GWAs data in non-Europeans)
- Need for novel PRS based on a transethnic AD GWAs data
- Program already presented by Dr. Sleiman

DAC – Participating Sites

Site	Genetic Ancestry	Phenotypic Outcome	# Case:Control
NCGG	Japanese (East Asian)	AD, MCI	Case:1000 Normal Cognitive:1000
East London Genes and Health cohort	British-Pakistani/British-Bangladeshi (South Asian)	All-cause dementia (from secondary/primary care records); MCI/cognitive decline cases excluded	104 cases; 614 controls
Korean Biobank Project	Korean (East Asian)	Phenotype 1: Cortical amyloid positivity (by Flutemetamol PET imaging) (Control: Cortical amyloid negativity)	191:337 (total 528)
		Phenotype 2: Clinical Dementia Rating (CDR) global Score 1 or over (Control: CDR global 0.5 or less)	157:539 (total 696)
AWI-Gen	African (Different ethnolinguistic and geographic groups)	Cognitive phenotyping is ongoing	
ELSA	Brazilian (Admixed)	Cognitive phenotyping is ongoing	
INTERVAL (UK Blood Donors)	European (White British)	Stroop Test (attention and reaction times), Trail Making Test (executive function), Pairs Test (Episodic Memory), Reasoning Tests (intelligence), >3K proteins on SomaLogic proteomics platform	~9k Cognitive measure; 1140 proteomics

Summary

- Significant progress made since May 2021
- IHCC successful with funding to grow staff support and cover pilot programs and new scientific direction
- Pilot programs highly successful – new programs under consideration
- IHCC-DAC collaboration on target
- Five year vision to be further expanded via break out sessions at this meeting

Working Group Strategic Planning Implementation Breakouts

Working Group Breakout Instructions

- Go back to the agenda
- Select the breakout, from the agenda, you wish to join
- Click on the Zoom link in the description
- A Zoom window will open, and you will be granted access to join the breakout session

If you have any difficulties, email idonner@palladianpartners.com

Working Group Report Back

Scott Sundseth, PhD

Associate Director
International HundredK+ Cohorts Consortium

USA

Session Overview

Session Topics:

- Training and Workforce Working Group
- Data Interoperability and Infrastructure Working Group
- Policy and Systems Working Group
- Scientific Strategy and Cohort Enhancement Working Group

Session Speakers:

- Paballo Chauke, MSc & Albert Tenesa, PhD
- Philip Awadalla, PhD & Thomas Keane, PhD
- Laura Lyman Rodriguez, PhD & Nicki Tiffin, PhD
- Hákon Hákonarson, MD, PhD & Adam Butterworth, PhD

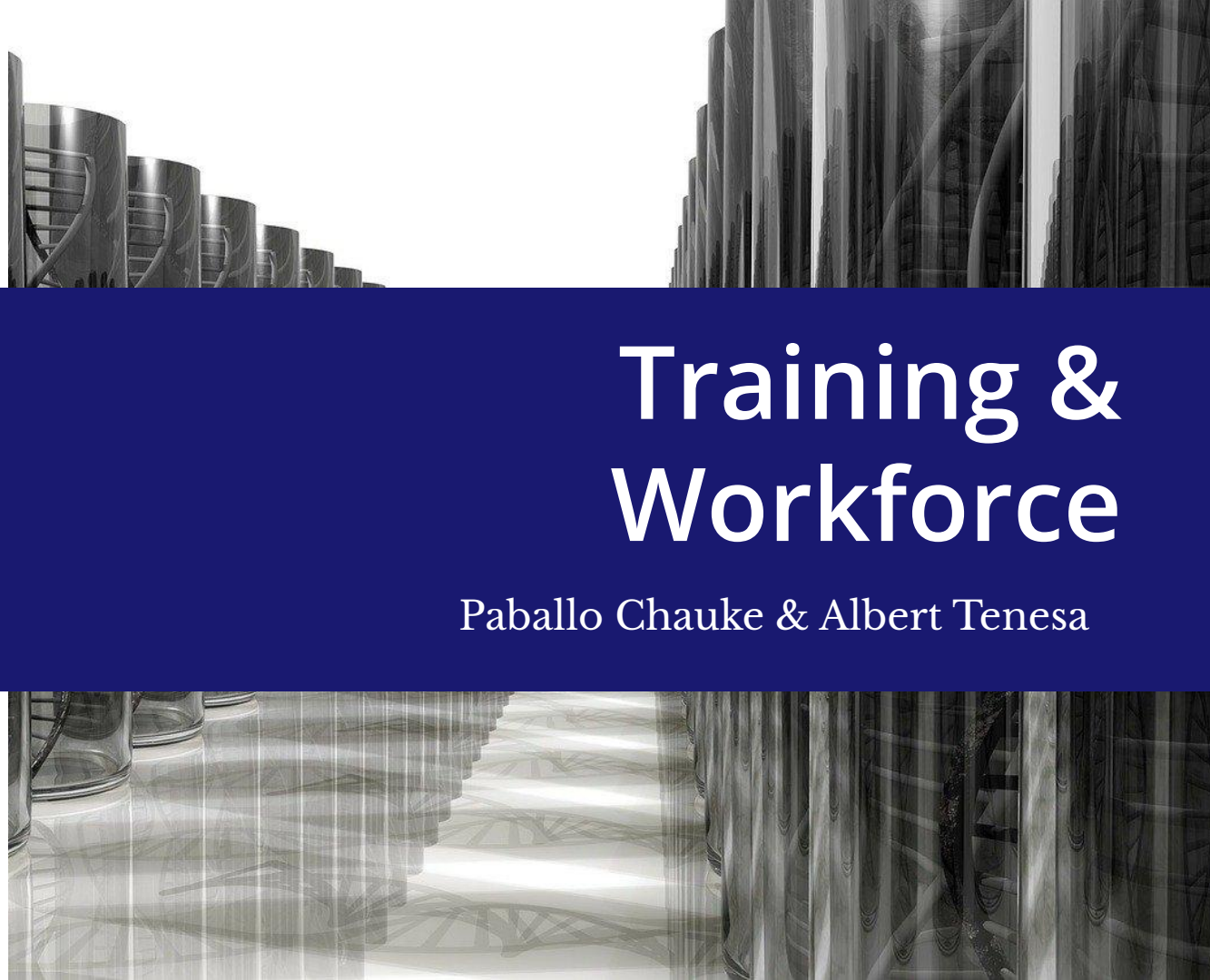
Paballo Chauke, MSc

Training and Outreach Coordinator,
H3ABioNet
South Africa

Albert Tenesa, PhD

Group Leader, Roslin Institute and the Medical Research Council Human Genetics Unit, The University of Edinburgh
UK

< Date >



Training & Workforce

Paballo Chauke & Albert Tenesa

Points of discussion

Cohort exchange programme (Aleksandra Gentry-Maharaj)

Mentorship activities for junior investigators (Aleksandra Gentry-Maharaj)

Educational webinar series (Ananya Gupta)

Forum for discussion (Slack channel)

Points of discussion

Identify training needs and expertise (Questionnaire)

In the long term to achieve accreditation

Link your institutions training programmes through a web link at IHCC

Contact training leads from Cohorts to engage and work together

Points of discussion

Altlas to include in cohort information whether they will offer mentorship and and exchanges

Philip Awadalla, PhD

Director of Computational Biology,
Ontario Institute for Cancer Research
Canada

Thomas Keane, PhD

Team Leader, European Bioinformatics Institute
UK

Discussion Topics

Cohort atlas functionality

- How to link the atlas to the cohorts themselves, getting access to the cohorts
- Level of detail in the Atlas
  - Currently based on 1) data dictionary 2) high level descriptors from IHCC website
  - Increase the depth of information
  - Consider high level descriptors that we collect
  - Option to work with cohorts to represent their data model in terms of OMOP or other common data models
  - Provide specific information about cohorts: access, recruitment status…
- Work with policy group regarding data access policies for the cohorts
  - Consider if individual data would be in the Atlas, or if Atlas would provide access to it through the cohort site
  - Until new resources arrive, link in the cohort site is the current best option
- How to integrate environmental data
  - Efforts to validate questionnaires that apply internationally
  - Efforts to build tools to pull geospatial exposures assessment using addresses
  - This info could be added into the Atlas
  - We could get those mapped into the GECKO ontology
  - Collaboration on phenX toolkit / environmental questionnaires mapping into GECKO?
  - Occupation
    - Example in France (Marcel Goldberg), they

Suggested Topics

5 year roadmap discussion

- Does the order make sense?
  - Discovery, cohort access, federated analysis platforms
- What are we missing

Status and expansion of the Atlas

- Current status:
- Workshop ran in late October
- How to get quantitative data into the Atlas
- Strategies to expand granularity of GECKO terms
- Strategies to update data from cohorts in the Atlas
- Inclusion of the cohort data harmonisation/gathering

Discovery of ‘return of results…

- Scientific programs are enriching cohorts through new data generation and creation of derived variables - how to enrich the IHCC and which to prioritize or start with?
- Familiarity with genomics, but what about metabolites or proteomic markers? How to harmonize say mass spec vs. targeted panels? Imaging? Availability - Interpreted vs raw?
- Medication usage? How to harmonize? Whose tools?
- High level results, GRS/PRS scores captured by various projects/cohorts - useful for replication? Different communities/ethnicities?
- Digital phenotyping?

Covid-19 results

- Infection status- and where available sequence data?
- Vaccination information - type, frequency ie, boosters?
- Antibody responses - where available?
- Mental health impacts - variables
- Long term impact - long haulers.

Environmental exposures

- How to partner with other programs/govt data assets? At what level of resolution is possible in different regions or

Enabling AI/ML/SL applications? Federated analysis of interoperability - hybrid models of data safe havens.

Funding status

- NIH U24 data resource (submitted)
- Wellcome discretionary award (planned)
- Other opportunities/ideas?

Laura Lyman Rodriguez, PhD
Interim Chief Program Support Officer,
Senior Advisor to the Executive Director
Patient-Centered Outcomes Research
Institute (PCORI)
USA

Nicki Tiffin, PhD, MPH
Associate Professor, University of Cape
Town
South Africa

November 3, 2021

Policy & Systems Working Group

Laura Lyman Rodriguez, USA
Nicki Tiffin, South Africa

International 100K Cohort Consortium

Breakout Discussion

1. Establishing links between WG and the projects (help desk, needs-based interactions as the projects get going)
2. Need to interact with the other WGs, and to build some processes based on those interactions – with facilitation by the Secretariat
3. Recognise the diversity of the IHCC members and their policy and data-sharing contexts
4. Retain flexibility so that we can provide generalized policy and guideline elements, that can be used to compile customized solutions for cohorts and IHCC projects
5. Articulate opportunities to share benefits and resource developments/enhancements with cohorts and IHCC members, especially where IHCC has supported resource generation

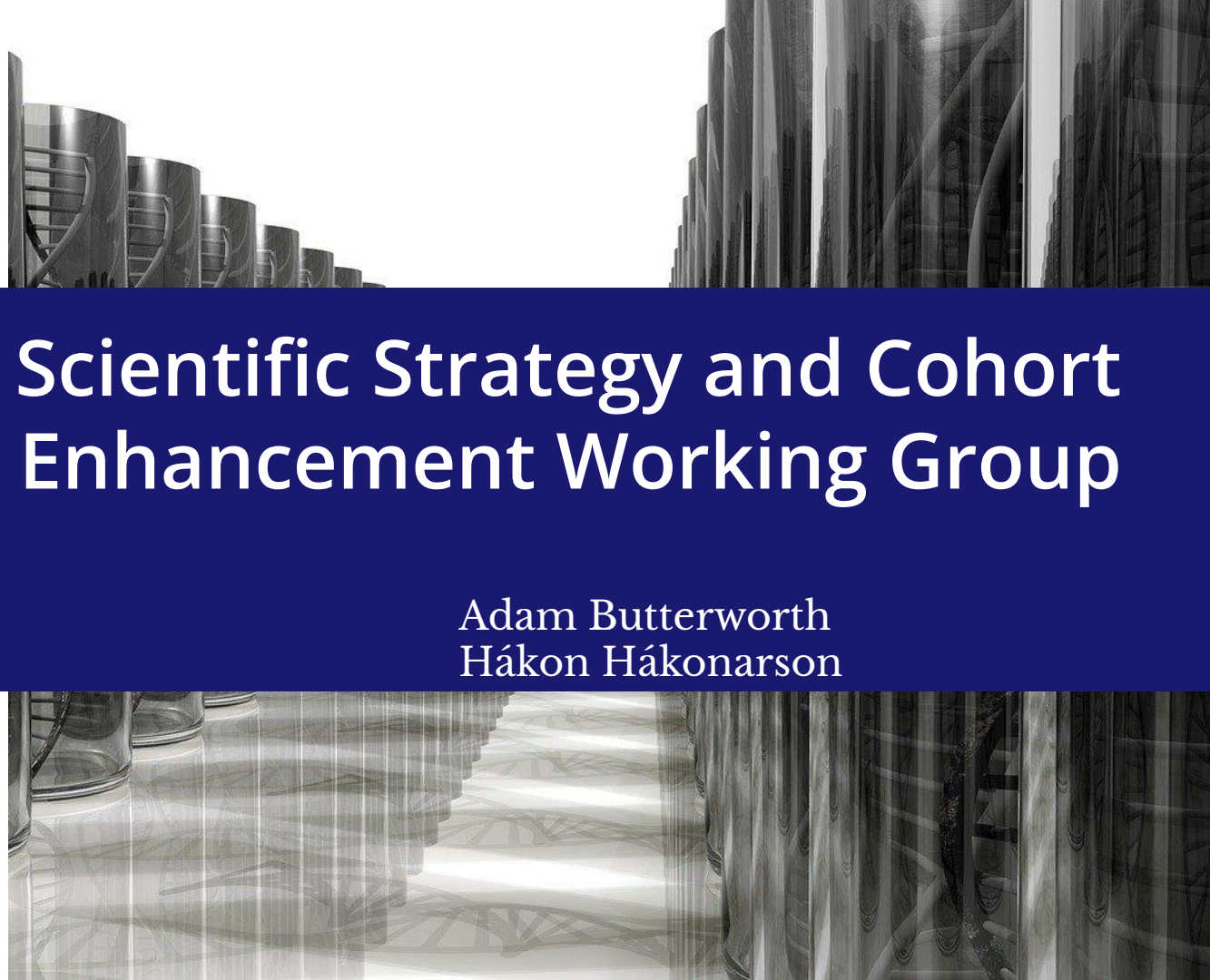
Hákon Hákonarson, MD, PhD

Director of the Center for Applied Genomics, CHOP
USA

Adam Butterworth, PhD

Reader in Molecular Epidemiology,
University of Cambridge
UK

3rd November



Scientific Strategy and Cohort Enhancement Working Group

Adam Butterworth
Hákon Hákonarson

Survey of cohort members

- Critical information -> important to capitalise on this and use as foundation for next steps
- Use to enhance existing pilot projects
- Identify gaps where cohort enhancement could help (e.g. could participate in pilot projects if GWAS data could be generated), particularly in LRS/LMIC settings
- “Match-make” between cohorts, industry partners, assay providers & funding agencies

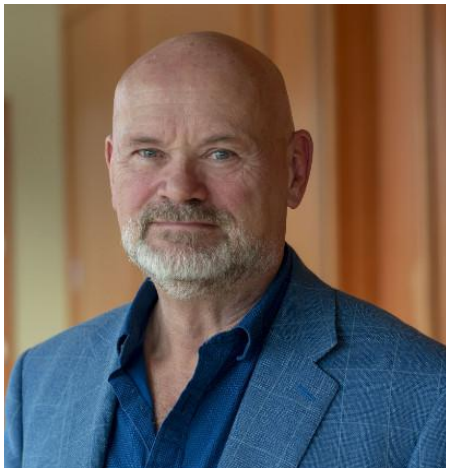
Challenges & opportunities

- Regulations & restrictions of specific cohorts (e.g. data-sharing): work with Policy WG to collate and address
- Integrating data is still a major challenge that IHCC can help to address
- Can existing external projects be extended into IHCC cohorts (e.g. G2MC Undiagnosed Rare Diseases)?

Working with industry

- IHCC has sample size & diversity -> key strengths of interest to industry
- Need to capitalise on the feasibility demonstrated through the pilot projects & build on work with industry partners in individual cohorts
- Understand the interests & needs of different industry partners to inform collaborative proposals (e.g. specific diseases? Capitalise on large sample size for rare diseases, healthy centenarians etc)

Day 1 Summary



Peter Goodhand

CEO
Global Alliance for Genomics and Health (GA4GH)

Co-Chair
International HundredK+ Cohorts Consortium

Canada

Day 1 Summary

IHCC Funded Project Presentations

Project 1: BMI and Colorectal Cancer Development
David Hughes, BSc, PhD, PGDE (University College Dublin, Ireland)

Project 2: High-Throughput Metabolomic Biomarker Measures in Diverse Ancestries
John Connolly, PhD (Center for Applied Genomics, USA)

Project 3: Opioid Cohort Consortium (OPICO) to Investigate the Effects of Regular Opioid Use on Mortality and on Cancer Development
Mahdi Sheikh, MD, PhD (International Agency for Research on Cancer, World Health Organization, France)

Project 4: Global Mental Health Impact of the COVID-19 Pandemic
Sarah Bauermeister, MSc, PhD (University of Oxford, UK)

Project 5: Novel Coronavirus Host Genomic Study - South Africa COVIGen-SA
Michèle Ramsay, PhD (University of the Witwatersrand, Johannesburg, South Africa)

Day 1 Summary

IHCC Funded Project Presentations

Project 6: COVID Biospecimen Collection Asia
Ananya Gupta, PhD (Imperial College London, UK)

Project 7: Davos Alzheimer's Collaborative (DAC) — Foundational Phase
Rhoda Au, PhD (Boston University Schools of Medicine and Public, USA)

Project 8: Polygenic Risk Scores (PRS) Projects for IHCC and DAC
Patrick Sleiman, PhD (Center for Applied Genomics, USA)

Day 1 Summary

Working Groups

- Working Group High Level Overviews
  - Reviewed action plans, goals, and program updates
- Working Group Strategic Planning Implementation Breakouts
  - Got to work with members to brainstorm
- Working Group Report Back and Day 1 Summary

Working Groups:

- Training and Workforce
- Data Interoperability and Infrastructure
- Policy and Systems
- Scientific Strategy and Cohort Enhancement

Day 2 Outline

November 4 @ 11:30 UTC

- NIH DS-I Africa Grant Presentation
- Race, Ethnicity, and Ancestry Presentations
  - Live panel discussion
- Environmental and Climate Data Capture Presentations
  - Live panel discussion
- Funding Opportunities/ Resource Presentations and Workshop Summary
  - Live panel discussion

Thank you and see you tomorrow!