GENDER·NET Plus
Promoting gender equality in H2020 and the ERA

Final Dissemination Conference

13-14 February 2023

GOING-FWD

Gender Outcomes INternational Group: to Further Well-being Development

Diversity, Gender Expertise and Gender Equality Measures

Co-Principal Investigators

Louise Pilote — Centre universitaire de santé McGill · McGill University Health Centre

Colleen Norris — McGill · University of Alberta

Valeria Raparelli — Università degli Studi di Ferrara · Dipartimento di Medicina Traslazionale e per la Romagna

Monica Parry — Bloomberg Lawrence S. Bloomberg Faculty of Nursing, University of Toronto

Carole Clair — unisanté, Centre universitaire de médecine générale et santé publique · Lausanne

Co-Investigators

Canada

Karin Humphries
Ruth Sapir-Pichhadze
Michal Abrahamowicz
Khaled El Emam
Simon Bacon

Austria

Peter Klimek

Site Principal Investigators

Alexandra Kautzky-Willer — Medical University of Vienna

Karolina Kublickiene — Karolinska Institutet

Maria Trinidad Herrero — Universidad de Murcia

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GENDER OUTCOMES INTERNATIONAL GROUP: TO FURTHER WELL-BEING DEVELOPMENT

Early Career Investigators

Canada:
Y Zhou, Z. Azizi, R. Dev, C. Tadiri
Austria:
S. Linder, T Gisinger, J Harreiter
Sweden:
L. Ward, L Hernandez-Munoz
Spain:
A.M. Lucas

Other trainees

Canada (3)
Austria (2)
Rome (3)
Sweden (2)
Spain (5)

Scientific Advisory Committee

Vera Regitz-Zagrosek
Londa Schiebinger
Carole Claire
Rachel Dryer

Patient Partners (7)

Objectives of the Project

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GENDER OUTCOMES INTERNATIONAL GROUP: TO FURTHER WELL-BEING DEVELOPMENT

The overarching aims of this large consortium are to **integrate sex and gender dimensions** in applied health research, to evaluate their impact on **clinical** cost-sensitive outcomes and **patients reported outcomes** (PROMs) related to quality of life in **Non-Communicable Diseases** (NCD)

- ✓ **30 Cohorts**
- ~ **30 Million of patients**
- ✓ **30 Investigators**
- ✓ **5 Countries**
- ✓ **4 Main clinical areas**

Cardiovascular disease

Metabolic disease - Diabetes

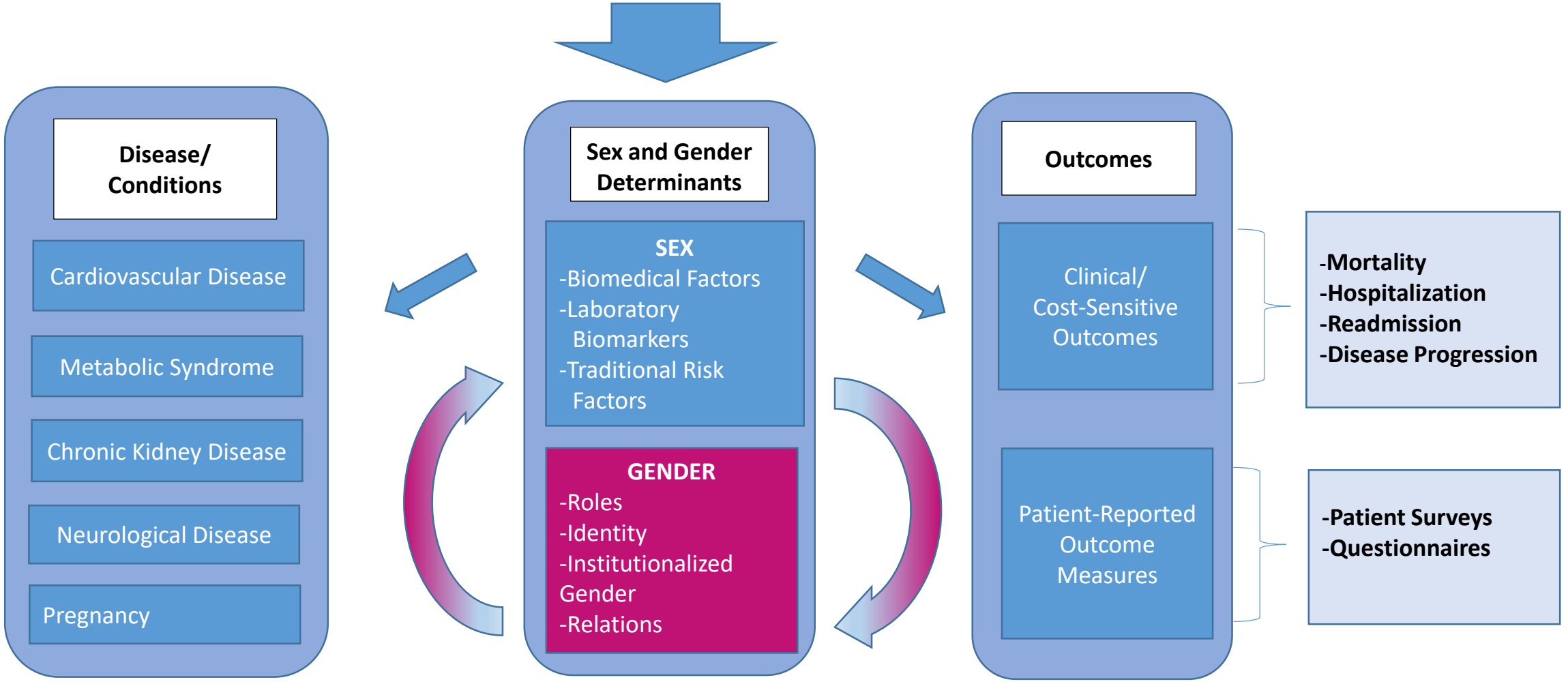
Chronic Kidney Disease

Neurological Disease

Conceptual Framework

GENDER OUTCOMES INTERNATIONAL GROUP: TO FURTHER WELL-BEING DEVELOPMENT

Equity + Diversity + Inclusion



Main Deliverables

- ✓ **Build capacity in the value of sex and gender science and knowledge translation**
- ✓ **Measure gender: the GOING-FWD Methodology**
- ✓ **Perform Big Data Analysis with Innovative Analytic Tools for comparison across datasets and countries**
- ✓ **Apply gender methodology to better understand non communicable chronic diseases (and COVID-19)**

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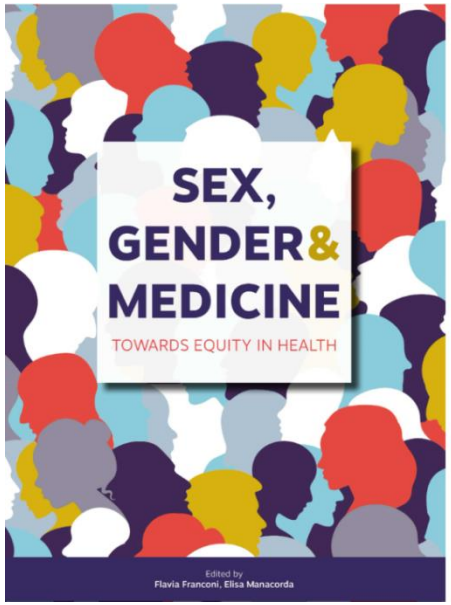
Building capacity in the value of sex and gender science

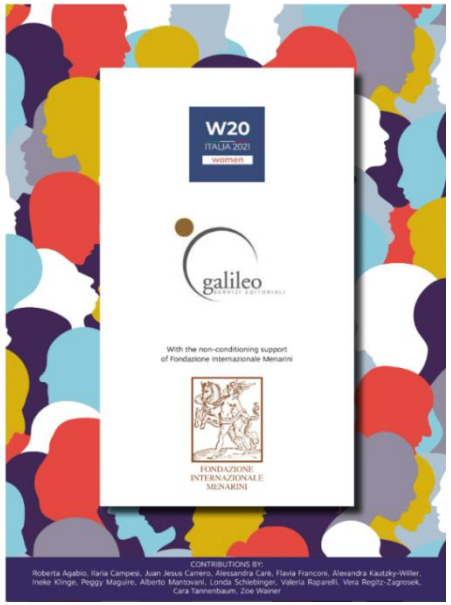
- GOING-FWD Investigators and Co-Investigators **(n=12)**
- POST-DOCTORAL FELLOWS/Early career research **(n=9)**
- Masters/PhD students **(n=15)**

Knowledge translation

- GOING-FWD Website (https://www.mcgill.ca/going-fwd4gender/)
- Social Media: YouTube, Twitter, Twitter Webinar and Facebook
- Over **50 abstracts;** Poster and Oral Presentations (National and International)
- **54 manuscripts published** in relation to Sex and Gender measurement
- **12 manuscripts** in relation COVID and Sex and Gender

GOING-FWD Framework and Methodologies and Innovative Analytic Techniques May ***INFLUENCE POLICY AND CLINICAL PRACTICE*** Fostering Sex and Gender Equity in Health





G20 meeting in Rome – Official Presentation to G20 Representatives/other Stakeholders at EU and country level

Issue 4 | July 2021

MEET THE METHODS SERIES:

METHODS FOR PROSPECTIVELY AND RETROSPECTIVELY INCORPORATING GENDER-RELATED VARIABLES IN CLINICAL RESEARCH

GOING-FWD Team: Louise Pilote, MD, MPH, PhD; Valeria Raparelli, MD, PhD; and Colleen M. Norris, RN GNP, PhD

Gender Outcomes INternational Group: to Further Well-being Development (GOING-FWD) is a data science and personalized medicine project funded by CIHR and GENDER-NET Plus, which uses data from over 30 million patients with chronic disease across Canada and four European countries. The project is led and coordinated by Louise Pilote, MD, MPH, PhD, a researcher at the McGill University Health Center Research Institute and a James McGill Professor of Medicine at McGill University. Co-leaders are Valeria Raparelli, MD, PhD, Assistant Professor of Internal Medicine at the University of Ferrara (Italy), and Colleen M. Norris, RN GNP, PhD, Professor of Nursing, Medicine and Public Health Science at the University of Alberta. In this Meet the Methods sheet, Louise Pilote, Colleen M. Norris, and Valeria Raparelli discussed methods for prospectively and retrospectively integrating gender-related variables in clinical research.

DECIDING WHICH GENDER-RELATED VARIABLES ARE RELEVANT TO YOUR CLINICAL STUDY

What is a gender-related variable?

A gender-related variable is a non-biological variable which differs in terms of magnitude, prevalence, and/or impact between people of different genders. Gender can be broken down into four dimensions: gender identity, relations, roles, and institutionalized gender[1]. A gender-related variable may fall under any of these domains. Researchers may want to focus their inquiries on a single dimension, or measure variables across multiple dimensions. Below are a few gender-related variables you may want to consider. Find more examples of gender-related variables here[2].

WHICH DIMENSION(S) OF GENDER ARE RELEVANT?

GENDER IDENTITY
How an individual self-identifies, including how they behave, express their gender, and are perceived by other people

GENDER RELATIONS
How individuals interact with and are treated by other people based on their perceived and/or expressed gender identity

GENDER ROLES
Social expectations and norms typically associated with a given gender

INSTITUTIONALIZED GENDER
The way power, resources, and opportunities are distributed in society based on gender

WHICH GENDER-RELATED VARIABLES ARE RELEVANT?

- Stress
- Personality traits
- Anxiety and depression
- Self-reported gender identity (e.g., woman, man, non-binary)

- Marital or relationship status
- Social support (e.g., ENRICHD Social Support Inventory[3])
- Family or local network (i.e., social capital)
- Experiences of gender-based violence
- Experience with healthcare providers (e.g., use of gender inclusive language)

- Household responsibilities
- Family caregiver or parental responsibilities
- Occupation or employment status
- Primary earner status
- Gender of healthcare providers

- Wage gap
- Education level
- Retirement eligibilities
- Gender inequality (e.g., Gender Inequality Index[4*])

*Note that this instrument uses only a binary definition of sex.

CIHR IRSC Institute of Gender and Health / Institut de la santé des femmes et des hommes

Pilote L, Norris CM and Raparelli V. Methods for Prospectively and Retrospectively Incorporating Gender-Related Variables in Clinical Research - https://cihr-irsc.gc.ca/e/52608.html

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Gender Wish List

Demographics

Age
Date of Birth (DOB)
Sex
Ethnicity
Language
Country of residence
Country of Origin
Province/Region
Ethnic background of parents
Rural/Urban Status
Country of Birth/ Birth place
Current living situation (with partner, parents, etc.)
Postal code
Address

Gender Roles

Primary earner status
Employment Status
Occupation
Work hours per week
Level of responsibility for disciplining children
Number of hours per week spent on housework
Status of household's primary responsibility
Number of children
Social status

Gender Relations

Marital/Relationship Status

Social support

ENRICHD social support instrument
Availability of Caregiver
Medical Outcomes Study (MOS)
Social Support Survey

Institutionalized gender

Educational Level
Number of years of schooling

SES/Income

Monthly finances
Household income
Investments (stocks, bonds etc.)
Perceived Social Standing
GII (Gender inequality index)
Type of maternity care

Gender Identity

Stress

14-Item Perceived stress scale (PSS)
Stress level at work
Stress level at home
Stress management
Wellness

Personality traits

Emotional intelligence
BEMS (instrument)
Marlowe-crowne question (assesses personality, temperament, and demeanor)

Depression/Anxiety

Patient Health Questionnaire-9
HAD Scale - Hospital Anxiety and Depression Scale
Anxiety/Depression
Anxiety sensitivity question
Beck depression inventory question
Pill question (?)
Tas questions (?)
State-Trait Anxiety Inventory (STAI) (quantifies adult anxiety)
Beck anxiety inventory question

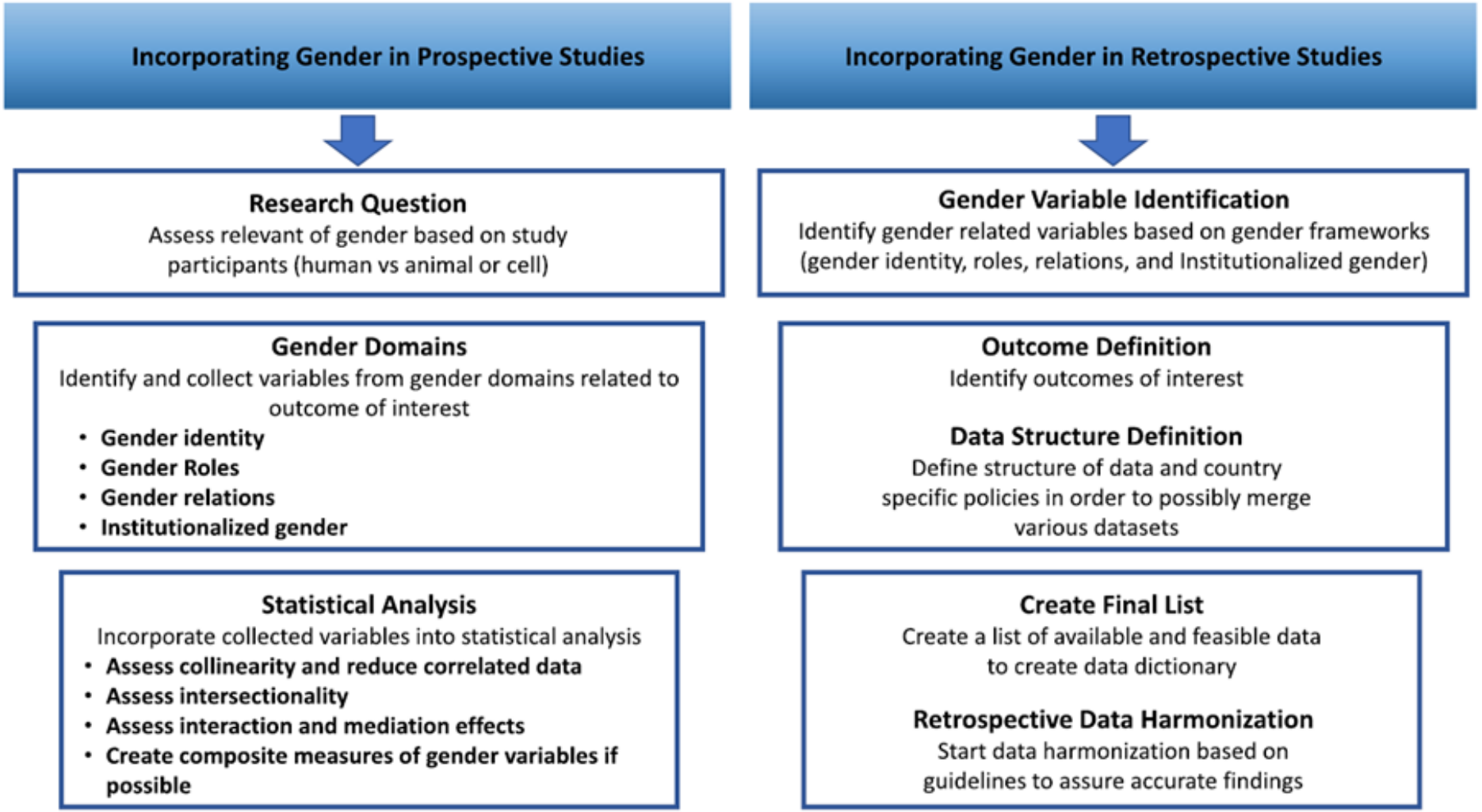
Other psychiatric questionnaires

Whiteley index questions (assesses hypochondria)

Discrimination

Day-to-day experiences

Incorporating Gender in Prospective and Retrospective Studies



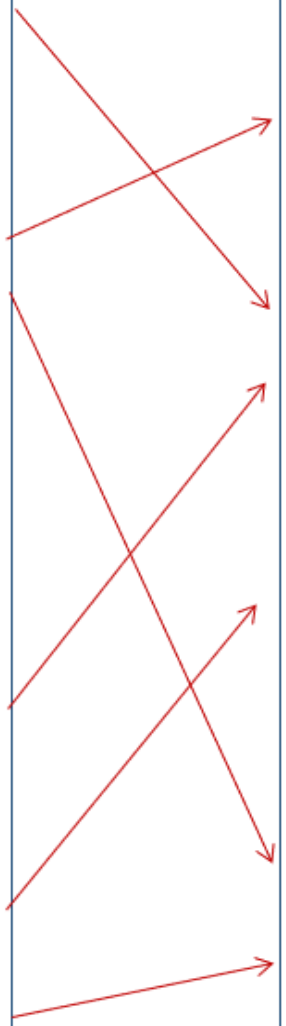
Tadiri et al. Methods for prospectively incorporating gender into health sciences research. Journal of Clinical Epidemiology. 2021 January 1; 129:191-197

Raparelli et al. and the GOING-FWD Collaborators. Identification and inclusion of gender factors in retrospective cohort studies: the GOING-FWD framework. BMJ Global Health 2021;6:e005413.

Methodology for Data Harmonization

Databases

- GENESIS PRAXY
- APPROACH
- EVA
- VIRGO
- ALBERTA HEALTH SERVICES
- REWARD
- DECADE
- MOSMI
- CPCSSN
- MAIN ASSOCIATION OF AUSTRIAN SOCIAL SECURITY INSTITUTIONS
- AT-HIS
- E-HIS
- IMPROVED
- HEALTH MURCIA SERVICE (SMS)
- HEALTH RIOJA SERVICE (HRS)
- DAC
- DAC2
- DALI
- MIA
- NJURBIOPSIPROJEKTET
- KOPIA
- HEARTIS
- MBDS
- OEDTR
- MS DATASET
- CCHS
- BIOBANK
- STEPS



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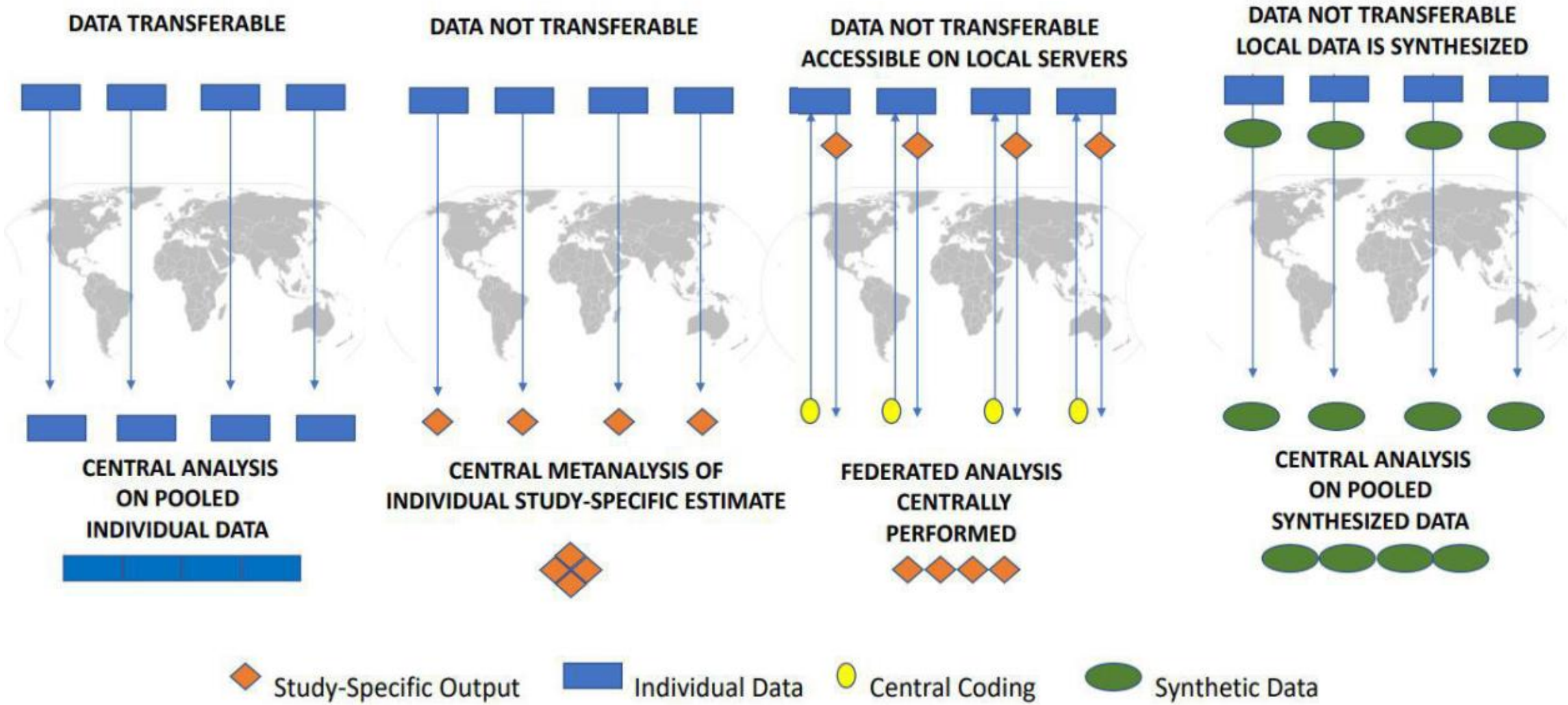
Data TRANSFERABILITY/PRIVACY WITHIN AND OUTSIDE COUNTRIES Requires Innovative Analytic Techniques



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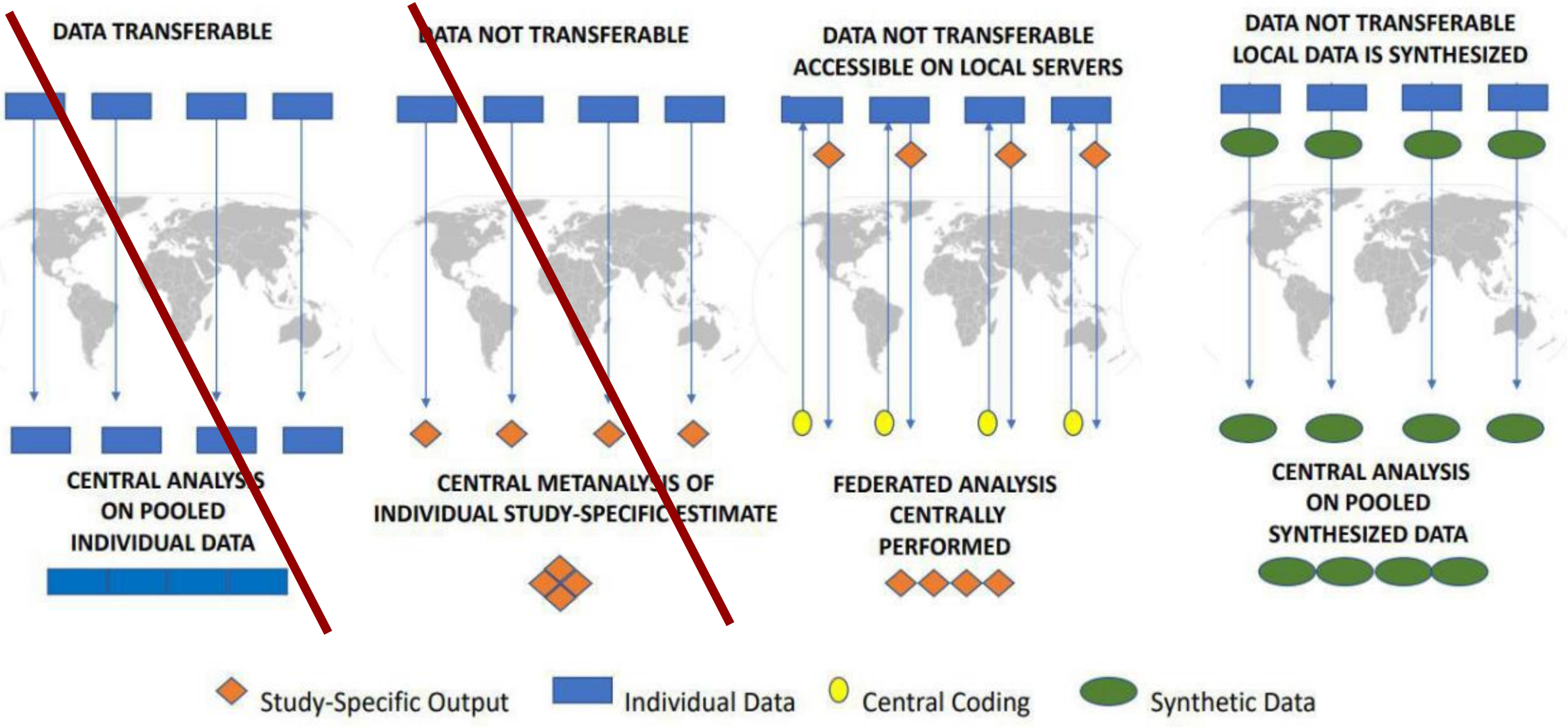
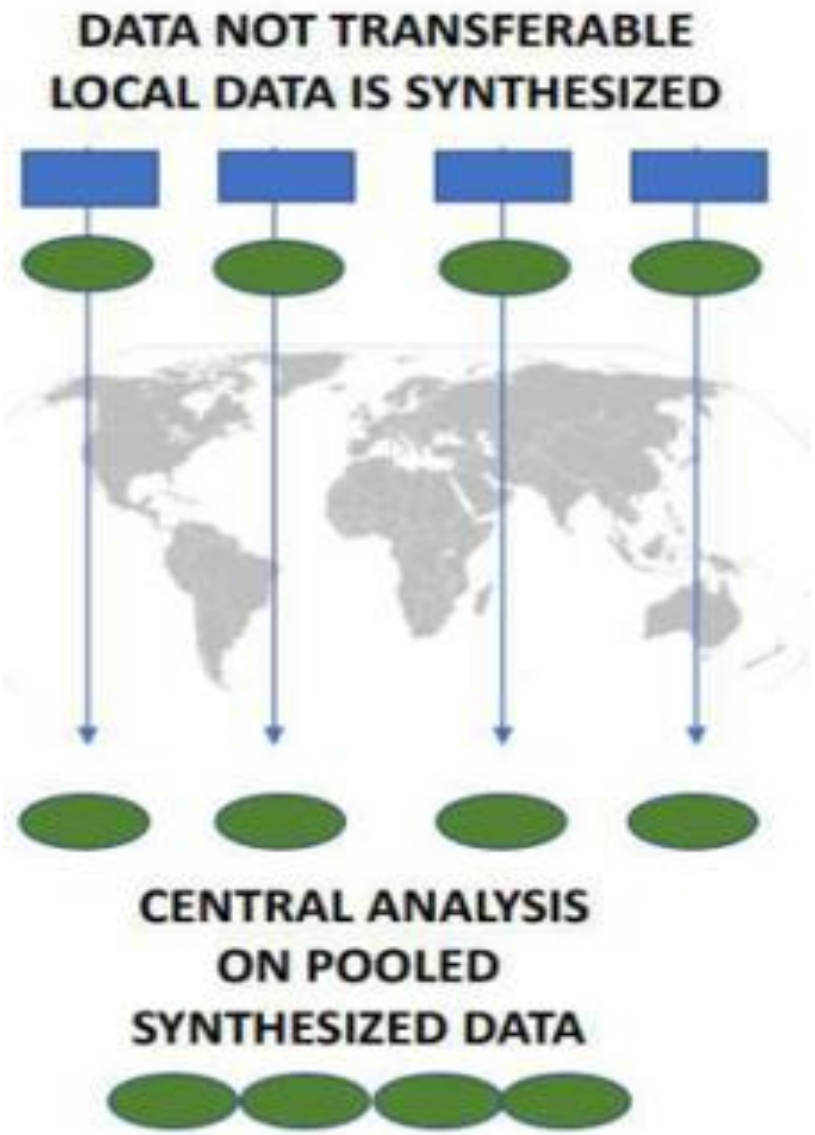


Methodologies for Using SYNTHETIC DATA



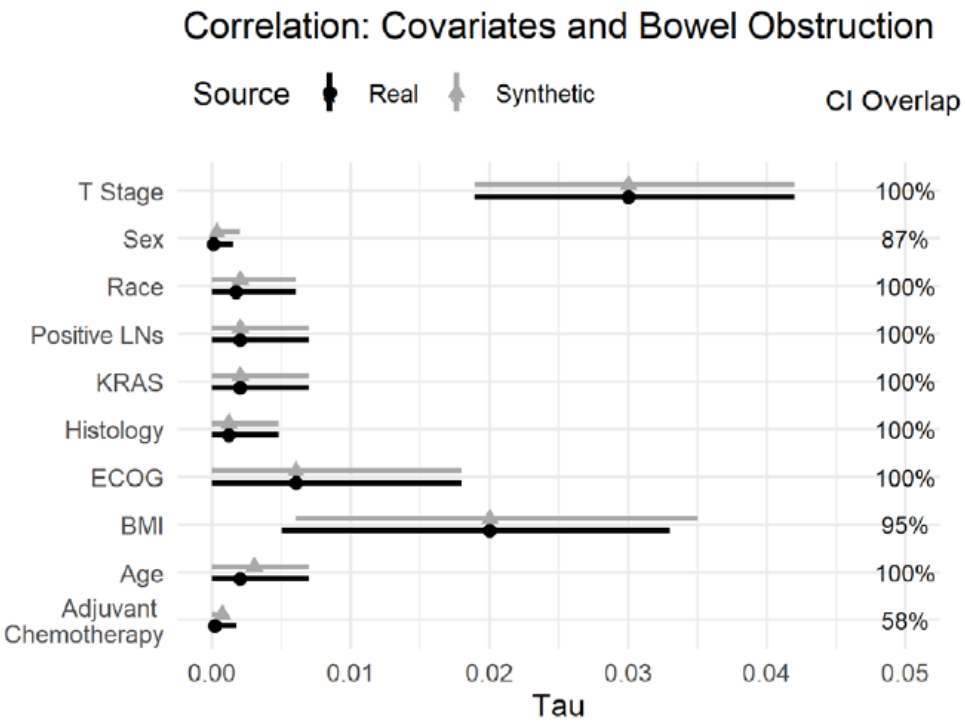


Figure 1 Tau coefficient for the real and synthetic data, and the CI overlap for the bivariate relationship with obstruction. BMI, Body Mass Index; ECOG, Eastern Cooperative Oncology Group; KRAS, Kirsten rat sarcoma virus; LNs, Lymph Nodes.

Can synthetic data be a proxy for real clinical trial data? A validation study. Azizi Z, Zheng C, Mosquera L, Pilote L, El Emam K. GOING-FWD Collaborators. BMJ open. 2021 Apr 1;11(4):e043497.

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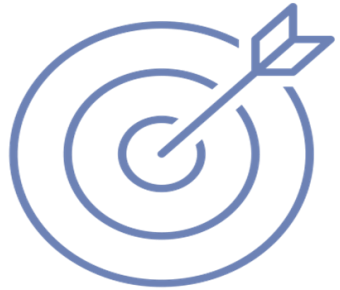

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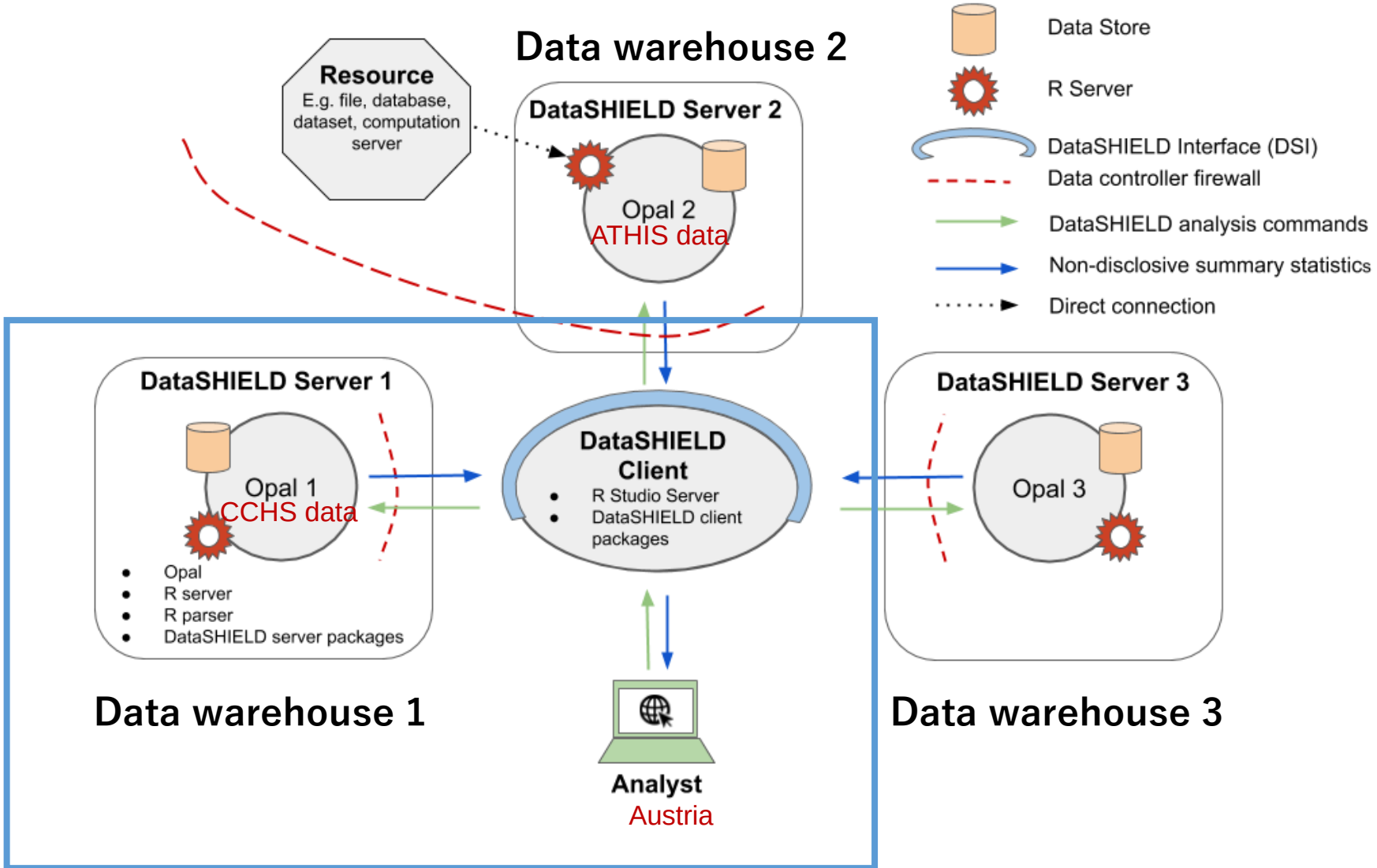
DataSHIELD Deployment Architecture for Federated Analyses



Sex ⟷ Gender

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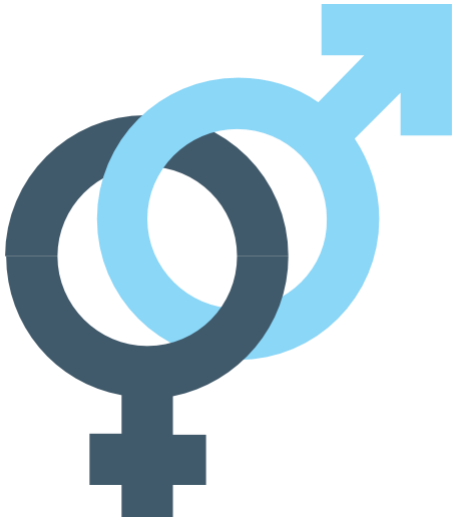
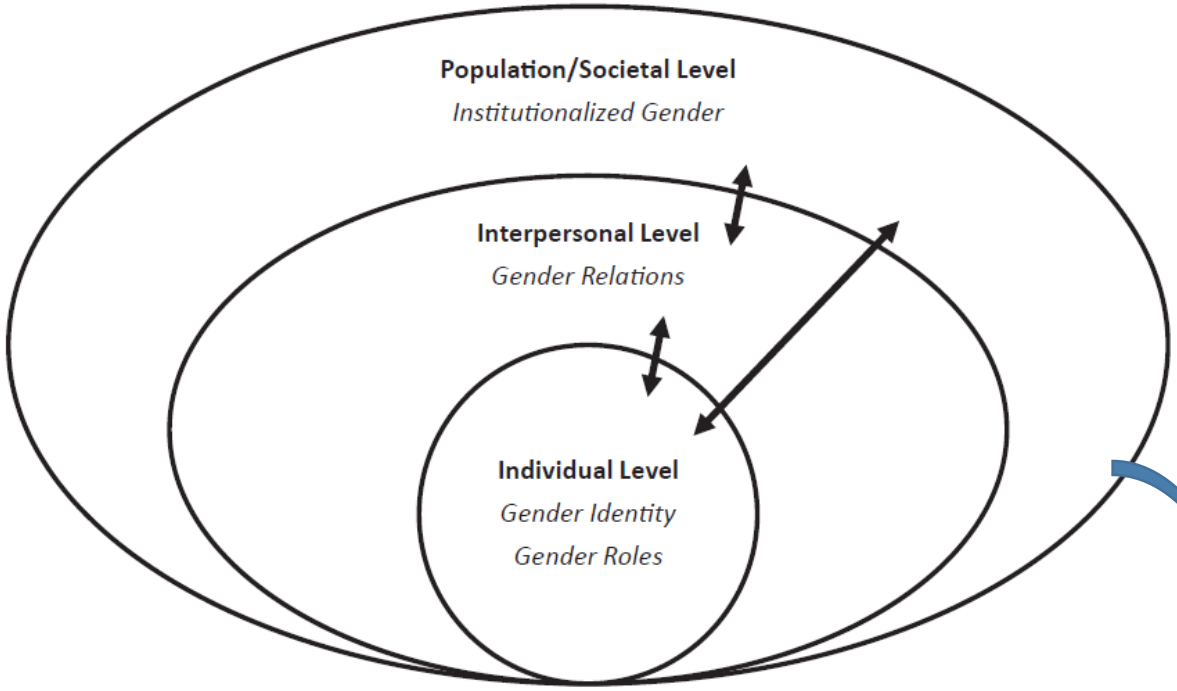




Sex disaggregated data identifies Biological differences between males and females that interact with GENDER Factors

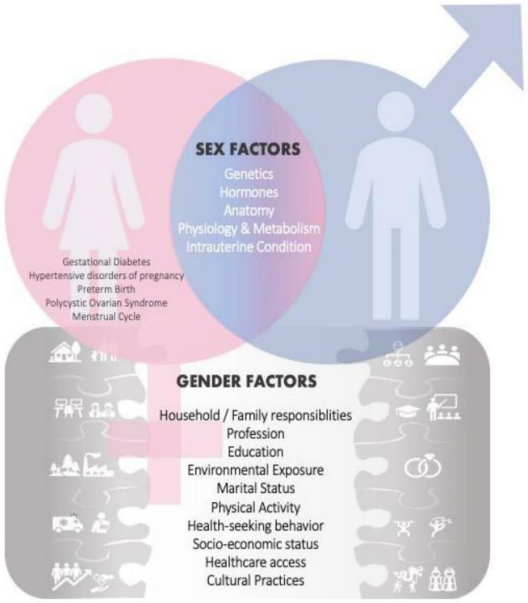
Gender is influenced by the social / environmental (individual, interpersonal, and Population/Societal) context, AND gender-related characteristics interact with EACH OTHER & SEX

frontiers | Frontiers in Cardiovascular Medicine

TYPE Review
PUBLISHED 08 August 2022
DOI 10.3389/fcvm.2022.916194

Gender dimension in cardio-pulmonary continuum

Leah Hernandez[1†], Agne Laucyte-Cibulskiene[1,2†], Liam J. Ward[1,3], Alexandra Kautzky-Willer[4], Maria-Trinidad Herrero[5], Colleen M. Norris[6,7], Valeria Raparelli[6,8,9], Louise Pilote[10], Peter Stenvinkel[1], Karolina Kublickiene[1]* and the GOING-FWD Consortium



Laucyte-Cibulskiene *et al. Biol Sex Differ* (2021) 12:50
https://doi.org/10.1186/s13293-021-00393-0

Biology of Sex Differences

RESEARCH Open Access

Role of GDF-15, YKL-40 and MMP 9 in patients with end-stage kidney disease: focus on sex-specific associations with vascular outcomes and all-cause mortality

Agne Laucyte-Cibulskiene[1,2†], Liam J. Ward[1†], Thomas Ebert[1], Giulia Tosti[3], Claudia Tucci[4], Leah Hernandez[1], Alexandra Kautzky-Willer[5], Maria-Trinidad Herrero[6], Colleen M. Norris[7,8], Louise Pilote[9], Magnus Söderberg[10], Torkel B. Brismar[11,12], Jonaz Ripsweden[11,12], Peter Stenvinkel[1], Valeria Raparelli[7,13†] and Karolina Kublickiene[1,14*†] on behalf of The GOING-FWD Consortium

Open access Original research

BMJ Open

Importance of sex and gender factors for COVID-19 infection and hospitalisation: a sex-stratified analysis using machine learning in UK Biobank data

Zahra Azizi,[1] Yumika Shiba,[2] Pouria Alipour,[1,3] Farhad Maleki,[4] Valeria Raparelli,[5,6] Colleen Norris,[6,7] Reza Forghani,[4] Louise Pilote ,[1,3,8] Khaled El Emam ,[9,10] The GOING-FWD investigators

CONCLUSIONS

Sex-specific risk patterns of COVID-19 test positivity exist, with gender-related factors being more relevant in females and biological factors in males.

Received: 25 January 2022 | Accepted: 31 March 2022
DOI: 10.1111/eci.13786

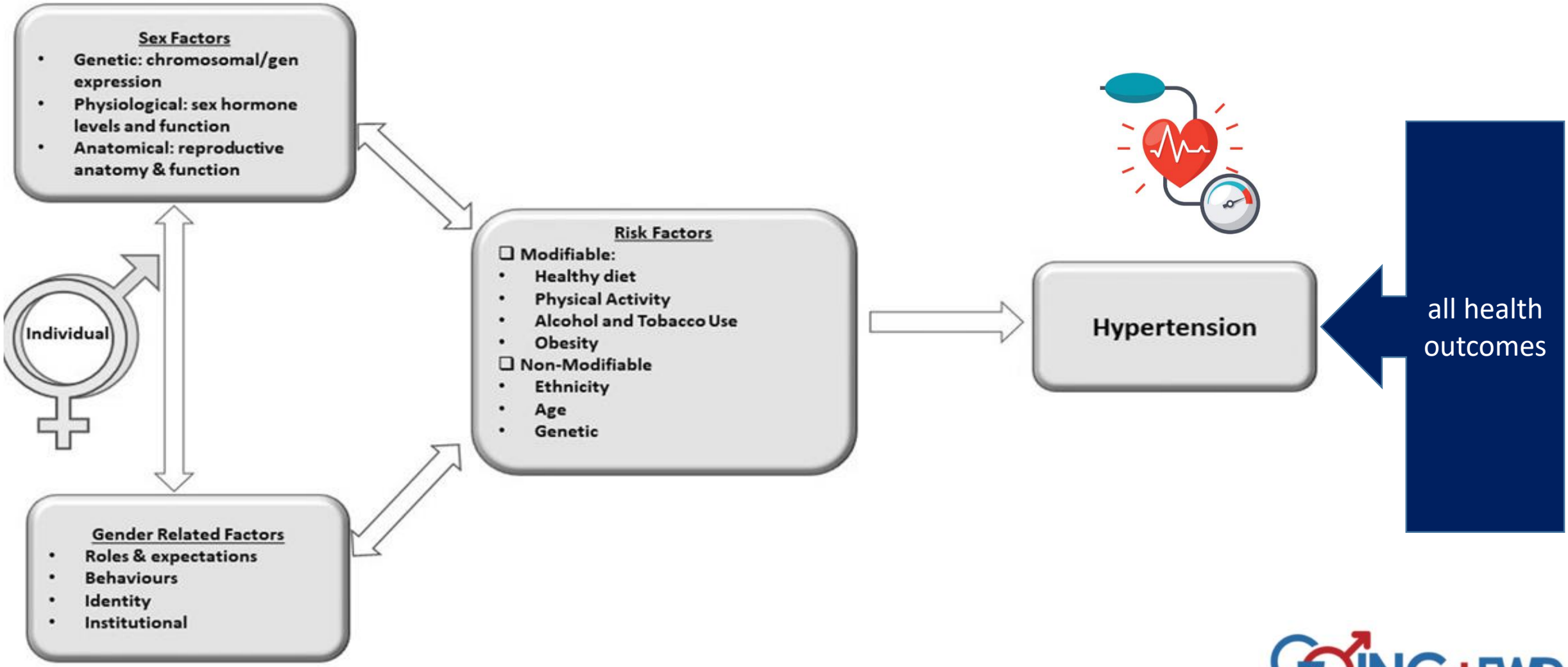
ORIGINAL ARTICLE

WILEY

Angiotensin-converting enzyme 2 and transmembrane protease serine 2 in female and male patients with end-stage kidney disease

Samsul Arefin[1] | Leah Hernandez[1] | Liam J. Ward[1,2] | Angelina Schwarz[1] | GOING-FWD Collaborators | Peter Barany[1] | Peter Stenvinkel[1] | Karolina Kublickiene[1]

Using GOING-FWD Methodologies to Identify SEX and GENDER Factors Associated with Outcomes



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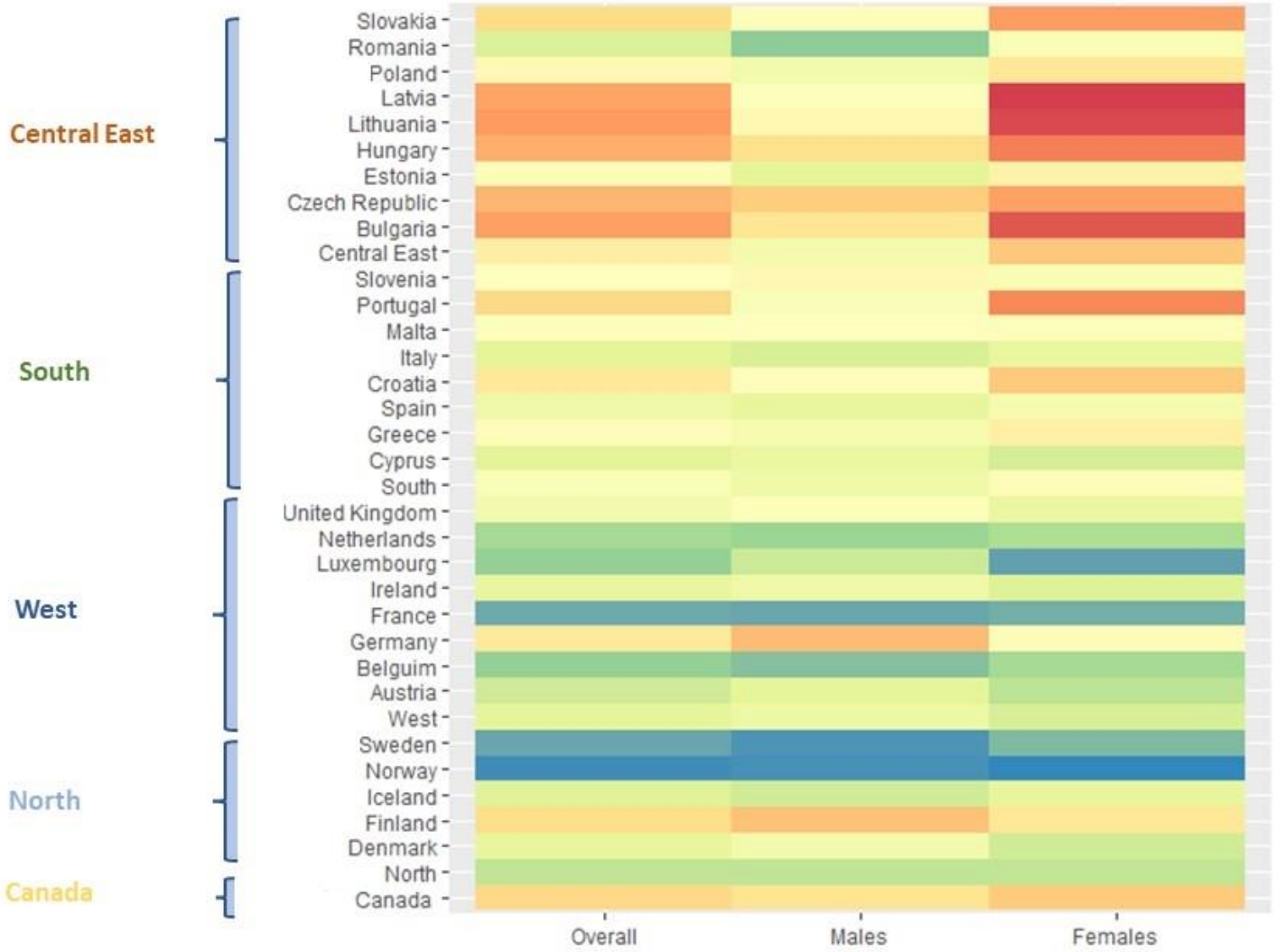
Heat Map Plot: Country- and Sex-related Differences in the Prevalence of HTN



Legend

Cold colours
Min: Dark Blue
indicate low prevalence

Hot colours
Max: Dark Red
indicate high prevalence

Women living in Central-East and Southern Europe had a greater prevalence of hypertension compared to Men

The Influences of Sex and Gender Aspects in the Prevalence of Hypertension. Zahra Azizi Z et al.

Country-Gender Interactions

Significant interaction between socioeconomic status (SES) and sex in country-stratified analysis

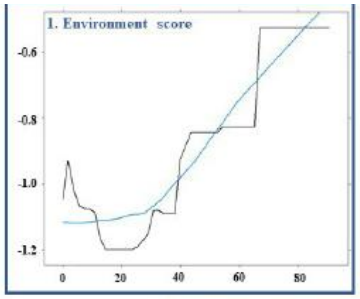
- More evident in **central-east** and **southern countries** vs **Northern, Western Nations and Canada**
- **Women** with **lower SES, income, education** > **HTN**
- **Women** who were **divorced** or **widowed** > **HTN, any country**
- **Immigrants** > **HTN**
- **Northern and Southern Europe** < **HTN** vs **central-east region**

Machine Learning-based Prediction Models for SARS-CoV-2 Positive Test

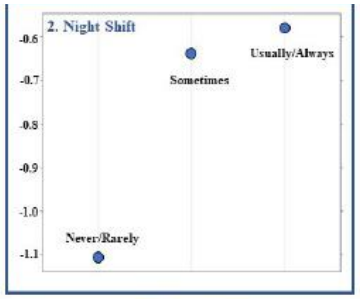
Five most influential variables

Females

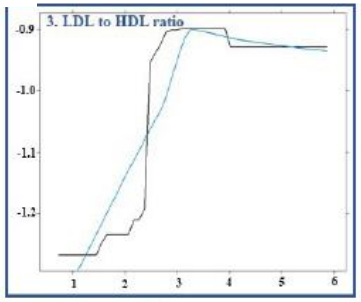
Environment



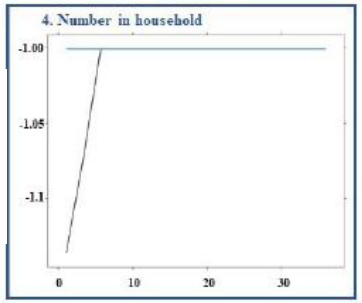
Night shift

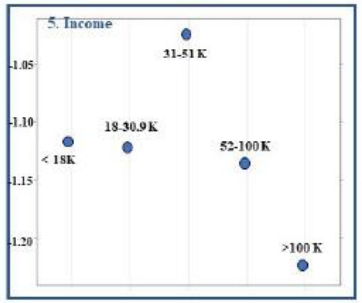


LDL to HDL ratio



Number in household

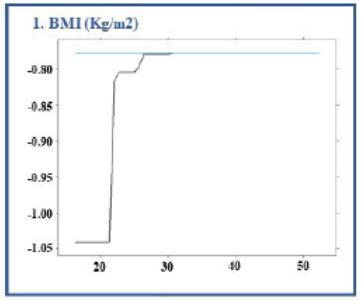




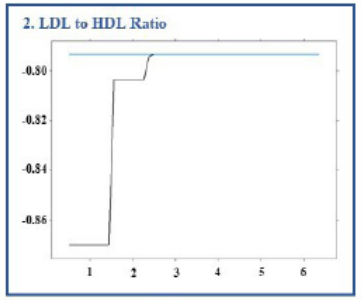
Income

Males

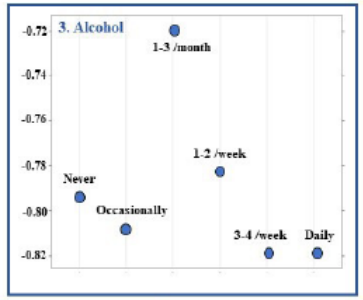
BMI



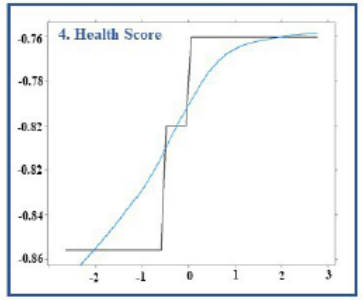
LDL to HDL ratio

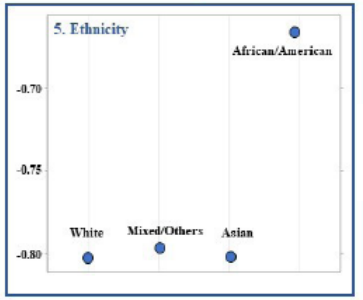


Alcohol



Health Score

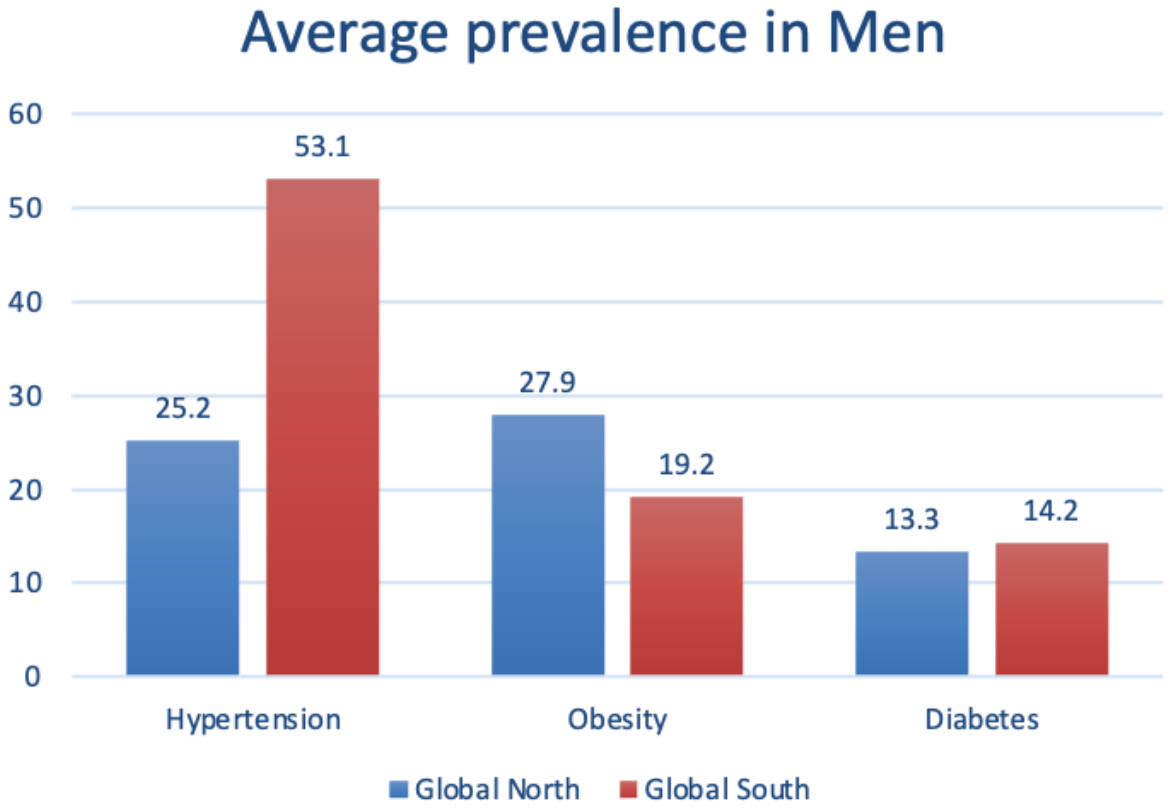


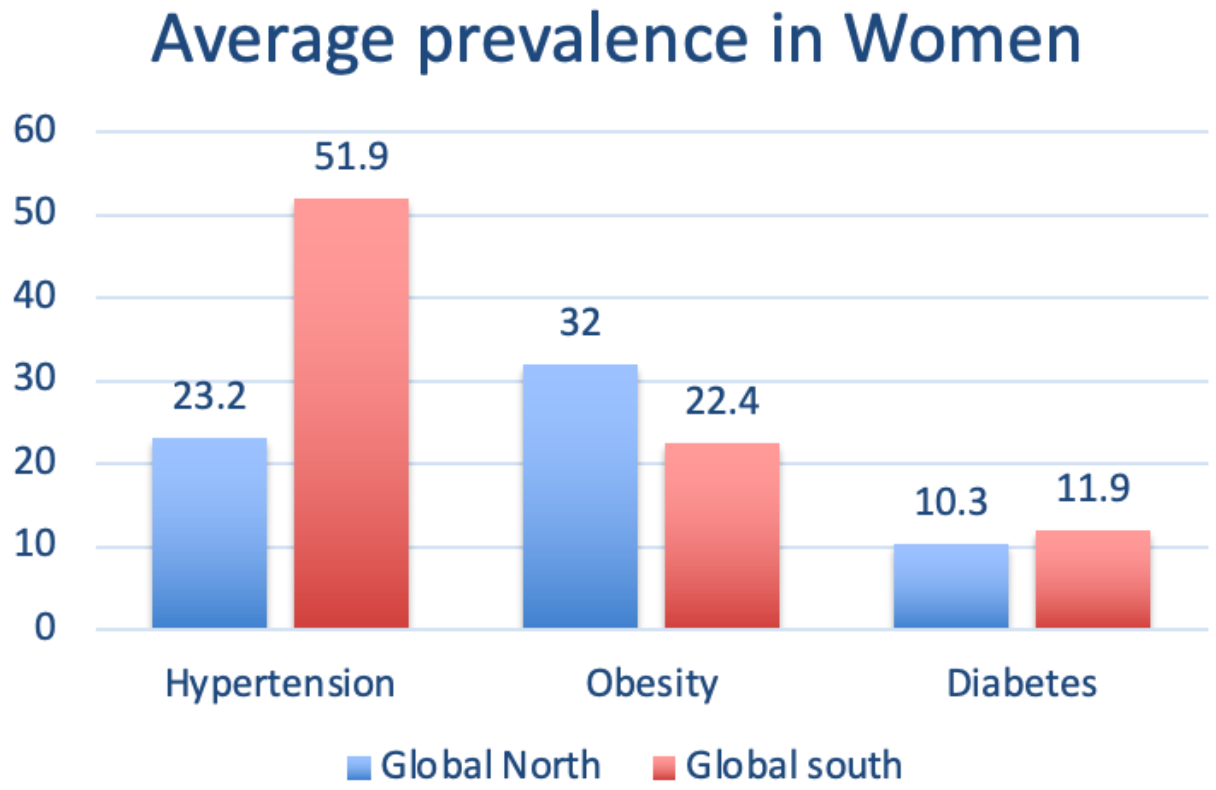


Ethnicity

Azizi Z, *et al.* Importance of sex and gender factors for COVID-19 infection and hospitalisation: a sex-stratified analysis using machine learning in UK Biobank data*BMJ Open 2022;12:e050450*

Prevalence of CVD Risk factors in Global North and South in Males and Females



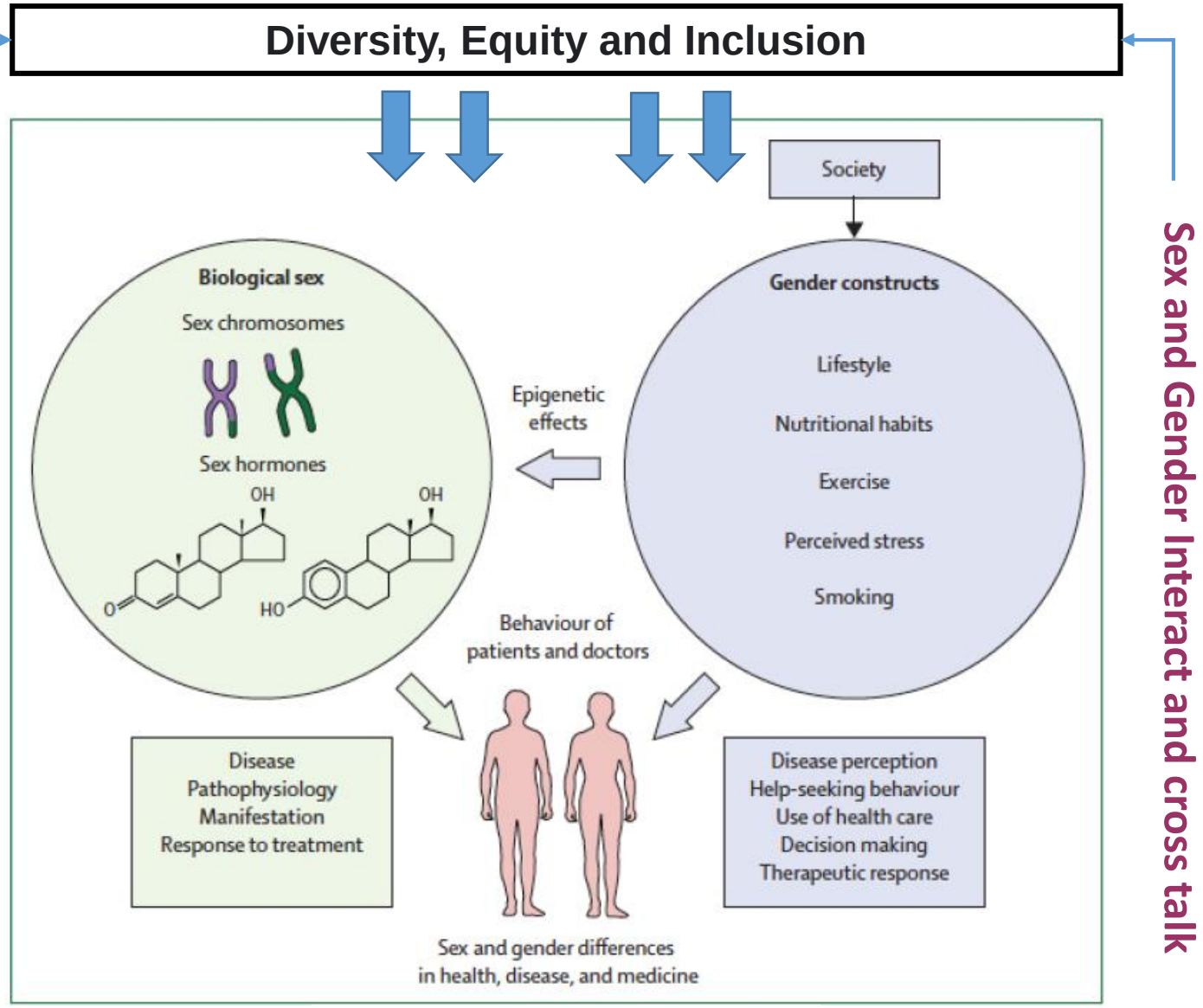


Dev R, Adams AM, Raparelli, V, Norris CM, Pilote L, & GOING-FWD Investigators. (2022)

PART “DEUX”- NEXT STEPS

- ✓ Tailored solutions to measure the unique sex and gendered factors of women, men and gender-diverse people
- ✓ Developing Sex and Gender tools for integration in health policy, clinical practice guidelines
- ✓ Moving to developing sex and gendered based interventions to improve outcomes
- ✓ Multidisciplinary and intersectional approach in providing clinically relevant solution to Canadian and European citizens

Conceptual Framework for GFW for Gender in Health



Mauvais-Jarvis et al. Lancet 2020; 396: 565–82

Precision Medicine/health/innovations for health care

GENDER·NET Plus
Promoting gender equality in H2020 and the ERA

Now this is not the end.

It is not even the beginning
of the end.

But it is, perhaps,
the end of the beginning.

Winston Churchill

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