Cómo poner puertas al campo:
tres **revisiones panorámicas** sobre el uso de **biomarcadores en prevención personalizada** de enfermedades **crónicas**

Ponentes: Plans-Beriso E.[1], Barahona-López C.[2], Diez-Echave P.[2], Hernandez O.R[2]

Filiación: [1] ISCIII, [2] CIBER

Centro Nacional de Epidemiología. Instituto de Salud Carlos III. Madrid. 14 de diciembre, 2023

Funded by the European Union

HORIZON-HLTH-2021-STAYHLTH-01-04 101057721

Autores

Plans-Beriso E., Babb-de-Villiers C., Barahona-López C., Diez-Echave P., Turner H., Hernandez O.R., Fernández de Larrea N., Cierco-Jiménez R., Erady C., Petrova D., Wilson H., Fernández-Martínez N., García-Ovejero E., Craciun O., Arruabarrena-Blanco E., Granero B., García-Esquinas E., Kuhn I., Jiménez-Planet V., Moreno V., Rodríguez-Artalejo F., Sánchez M.J., Pollan M, Blackburn L.

Project leaders: Pérez-Gómez B. & Kroese M.

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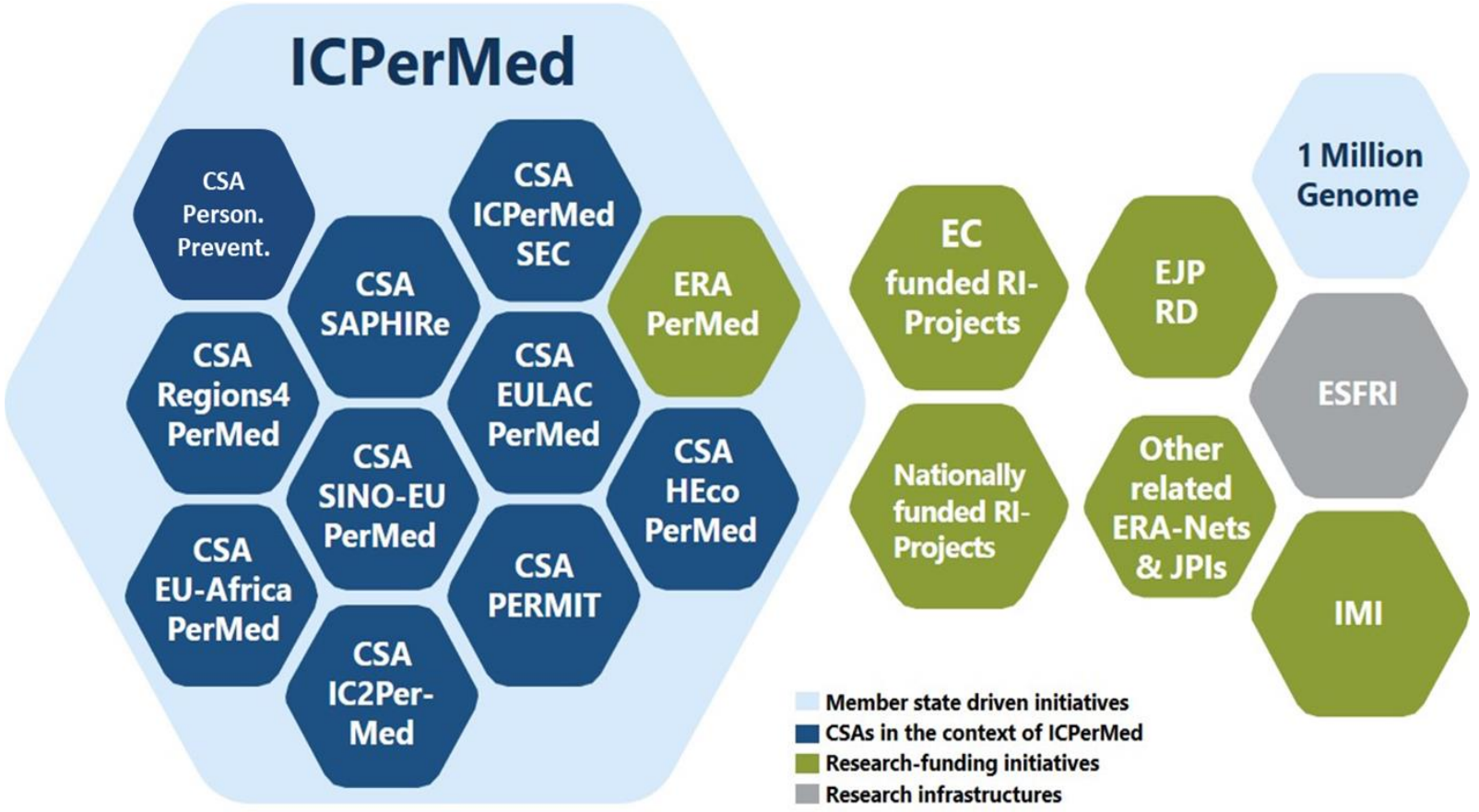
ICPerMed
CSA Person. Prevent.
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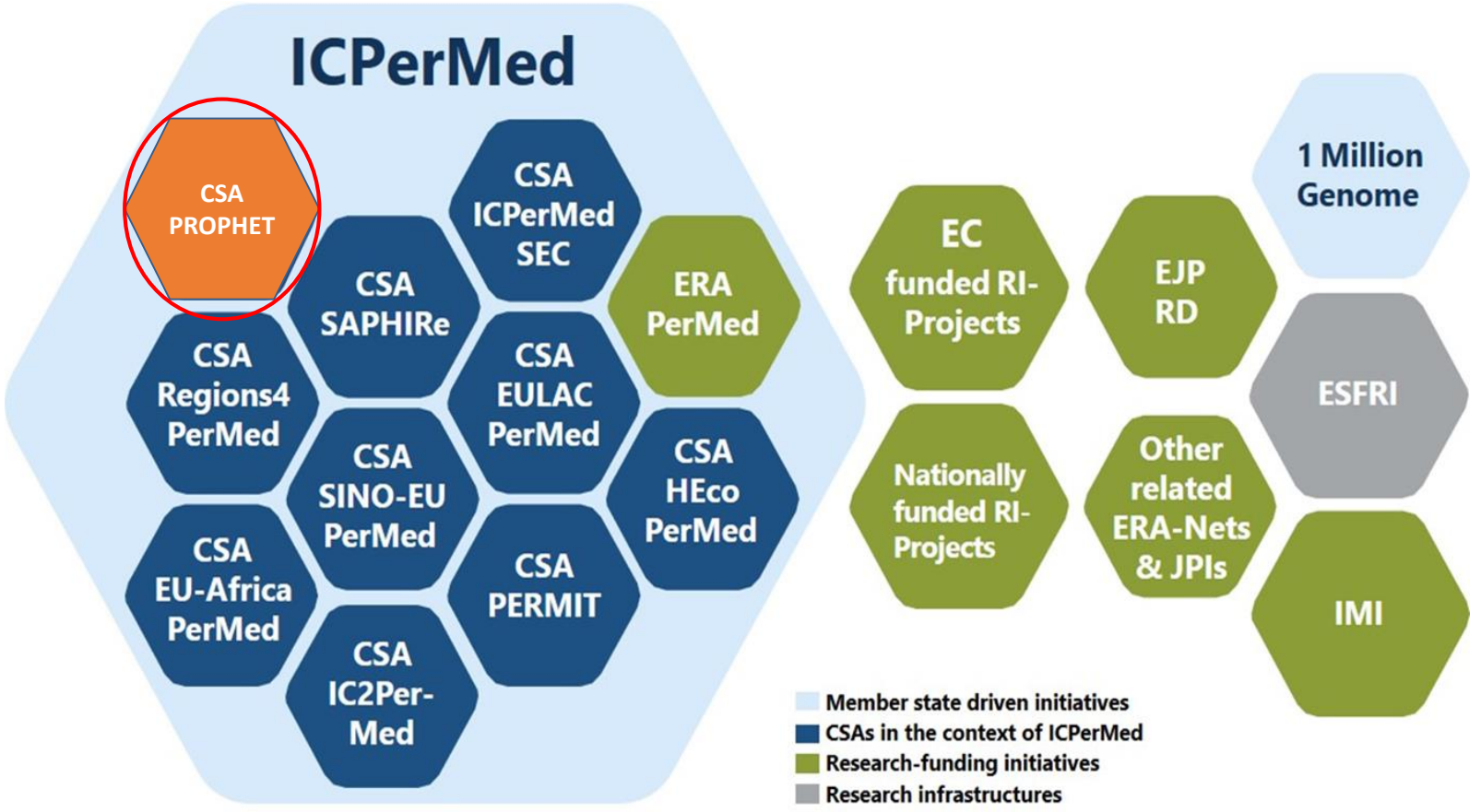
CSA SAPHIRe
ERA PerMed
CSA Regions4 PerMed
CSA EULAC PerMed
CSA SINO-EU PerMed
CSA HEco PerMed
CSA EU-Africa PerMed
CSA PERMIT
CSA IC2Per-Med
EC funded RI-Projects
EJP RD
1 Million Genome
Nationally funded RI-Projects
Other related ERA-Nets & JPIs
ESFRI
IMI
Member state driven initiatives
CSAs in the context of ICPerMed
Research-funding initiatives
Research infrastructures


ICPerMed
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CSA ICPerMed SEC
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European Union: Horizon - CSA Staying Healthy (2021) (HORIZON-HLTH-2021-STAYHLTH01) of ICPerMed

ICPerMed

CSA PROPHET

International Consortium on PM: 18 partners

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ICPerMed

CSA PROPHET

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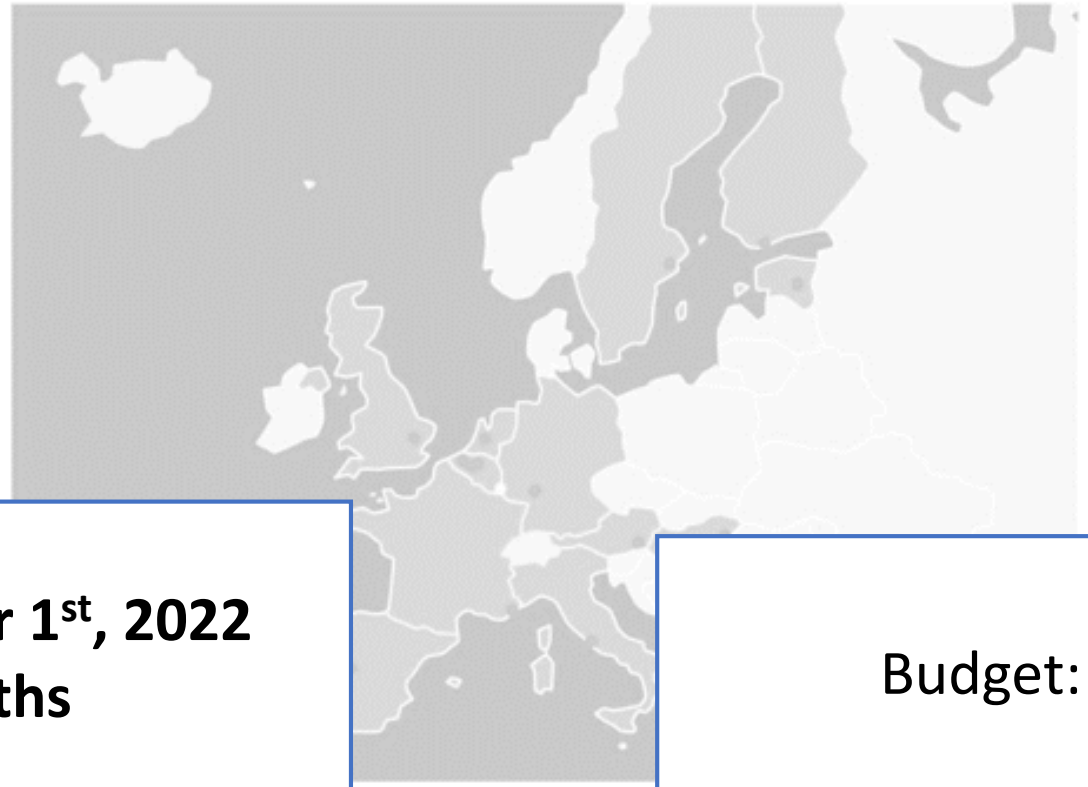

Starting Date : **September 1st, 2022**
Duration : **48 months**

Budget: **€3,000,000**

"Hoja de ruta para la **prevención personalizada** en el futuro de la **atención médica**"

A través de SRIA:

Strategic **R**esearch and **I**nnovation **A**genda

WP2 (mapeo) coordinado por

ciber | ESP

25 YEARS making science work for health | PHG FOUNDATION

T2.1.1 - Mapping available **biomarkers** including genetics, for **risk prediction** and **stratification**, and their potential integration with digital technologies

Pregunta	¿Qué **biomarcadores** hay disponibles o en desarrollo para la **prevención personalizada** de **enfermedades crónicas** en la población general?

PROPHET
a PeRsOnalized Prevention roadmap for the future HEalThcare

4 meses

ROPHET
a PeRsOnalized Prevention roadmap for the future HEalThcare

QUALITY CONTROL

- Consulta a **expertos** → In each area **Librarians**
- **Entrenamiento personal** → 

- **Comunicación** permanente → slack Gmail zoom
- **Cursos** and **seminarios** → iSC
- **Estudio piloto** → covidence Prophet Trial and Error

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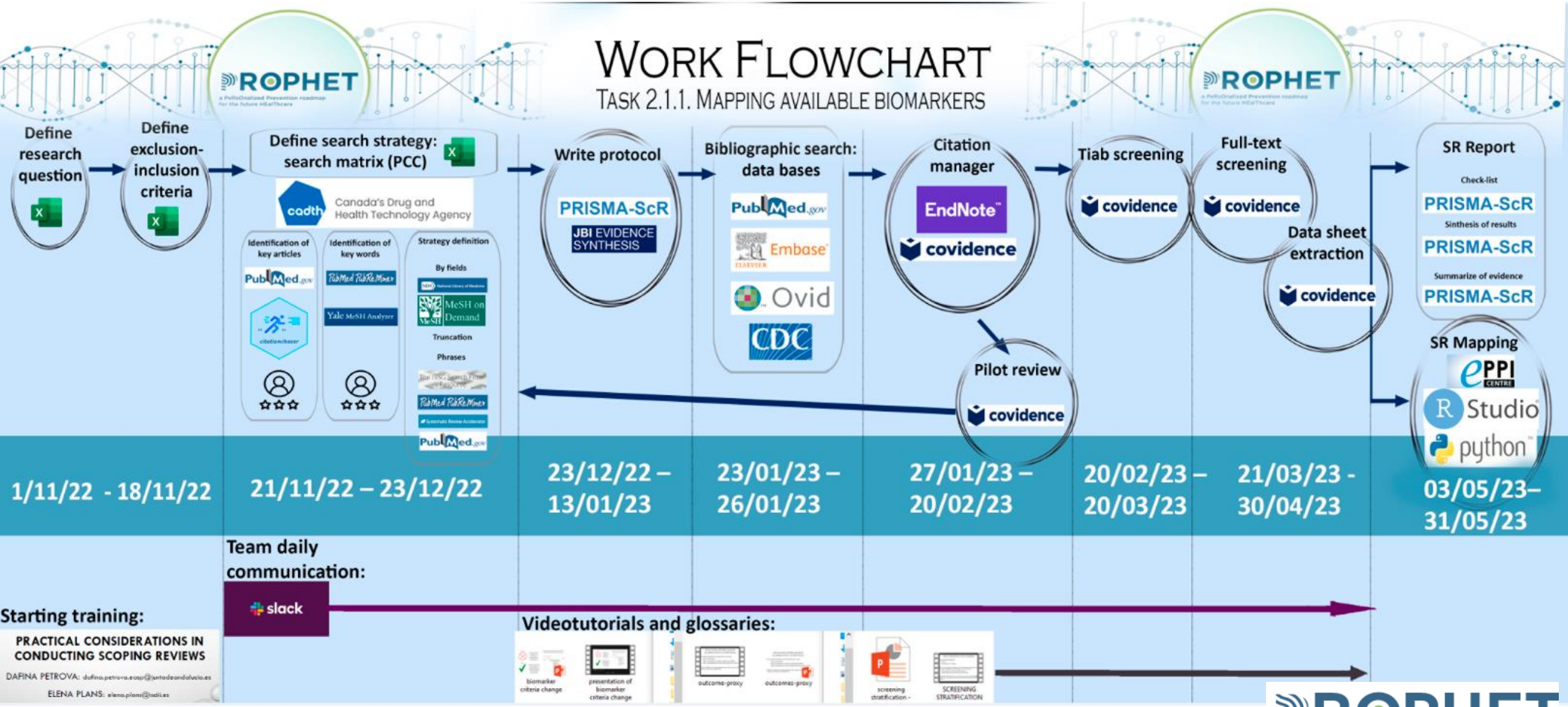
WORK FLOWCHART

TASK 2.1.1. MAPPING AVAILABLE BIOMARKERS



ROPHET
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Tres revisiones panorámicas **rápidas:** **2020-2023**

Prevención PRIMARIA

ADULTOS

Prevención SECUNDARIA

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a PeRsOnalized Prevention roadmap for the future HEalThcare

SCOPING REVIEW PROTOCOL: Search Matrix

BIOMARKERS
(exp Biological factors/ or ("biological factor*" or biomarker* or "bio* marker*").ti,ab,kw,kf.)
(exp *carbohydrates/ or exp *lipids/ or exp *amino acids/ or exp *proteins/ or exp *vitamins/ or exp *steroids/ or exp *Hormones/ or exp *Enzymes/)
(exp genetic markers/ or exp genotype/ or exp genetics/ or exp genomics or ("genetic marker*" or "genotype" or "germline biomarker*" or "genetic*" or "genomic*" or "epigen*" or "epigenetic mark*").ti,ab,kw,kf.)
(exp Microchip Analytical Procedures/) or (Microarray*).ti,ab,kw,kf.
(exp Metabolomics/ or exp Proteomics/ or ("metabolomic*" or "proteomic*" or "lipidomic*" or "immunomic*" or "nutriomic*" or "transcriptomic*" or "radiomic*").ti,ab,kw,kf.)
(exp Carcinogens / or exp Oncogenes/ or ("carcinogen*" or "oncogen*" or "tumor initiator*" or "tumor promoter" or "tumour initiator*" or "tumour promoter*").ti,ab,kw,kf.)
(exp *"Diagnostic Imaging"/ or (imag*).ti,ab,kw,kf.)

DISEASES
(exp Breast Neoplasms / or ("breast cancer*" or "breast neoplasm*" or "breast carcinoma*").ti,ab,kw,kf.)
(exp Lung Neoplasms / or ("lung cancer*" or "lung carcinoma*" or "lung neoplasm*").ti,ab,kw,kf.)
(exp Prostatic Neoplasms / or ("prostatic neoplasm*" or "prostatic cancer*" or "prostate cancer*").ti,ab,kw,kf.)
(exp Stomach Neoplasms / or ("stomach neoplasm*" or "gastric cancer*" or "stomach cancer*" or "gastric carcinoma*").ti,ab,kw,kf.)
(exp Colorectal neoplasms/ or ("colorectal neoplasm*" or "colorectal cancer*").ti,ab,kw,kf.)
(exp Uterine Neoplasms / or ("uterine cancer*" or "uterine neoplasm*" or "uterus cancer*").ti,ab,kw,kf.)
(exp Uterine Cervical Neoplasms / or ("cervical cancer*" or "uterine cervical neoplasm*" or "uterine cervix cancer*").ti,ab,kw,kf.)
(exp Urinary Bladder Neoplasms/ or ("bladder cancer*" or "Urothelial carcinoma*" or "Transitional cell carcinoma*" or "urinary bladder neoplasm*").ti,ab,kw,kf.)
(exp Pancreatic Neoplasms/ or ("pancreatic cancer*" or "pancreatic neoplasm*" or "pancreas cancer*").ti,ab,kw,kf.)
(exp Kidney Neoplasms/ or ("kidney cancer*" or "kidney neoplasm*").ti,ab,kw,kf.)
(exp Liver Neoplasms/ or ("liver cancer*" or "hepatic cancer*").ti,ab,kw,kf.)

PREVENTION
(exp Primary Health Care/ or ("public health service*" or "primary health care" or "primary care").ti,ab,kw,kf.)
(exp Primary prevention/ or ("primary disease prevent*" or "preventable disease*").ti,ab,kw,kf.)
(exp Preventive Medicine/ or ("preventive medicine*" or "medical prevent*").ti,ab,kw,kf.)
("protective factor*".ti,ab,kw,kf.)
(susceptibil*.ti,ab,kw,kf.)
(exp *smoking/)
(exp *exercise/ or exp *sedentary behavior/)
(exp *"Diet, food, and nutrition"/ or exp *Overweight/)
(exp *Alcohol Drinking/)
(exp *Type 2 Diabetes Mellitus/)
(exp *HIV/)
(exp*Human Papillomavirus Viruses/)
(exp *Helicobacter pylori/)
(exp *air pollution/)
(exp *Immunization /)
("cancer prevent*" or "cancer vaccin*" or "cancer immuniz*".ti,ab,kw,kf.)
(exp Chemoprevention / or ("chemoprevent*" or "chemoprophylax*").ti,ab,kw,kf.)
(exp Prophylactic Surgical Procedures / or ("surgical prevent*").ti,ab,kw,kf.)
(exp *Community Health Planning/ or ("community setting*" or "health care plan*" or "community health plan*").ti,ab,kw,kf.)
(exp *Preventive health service/ or "preventive health service*".ti,ab,kw,kf.)
(exp *Community Health Center/ or ("community health center*" or "community health centre*" or "community care").ti,ab,kw,kf.)
(exp *Health Education/ or ("health educat*" or "health promot*").ti,ab,kw,kf.)
(exp Mass Screening/ or exp Secondary Prevention/ or ("secondary prevent*" or "screening*").ti,ab,kw,kf.)
(exp Population Surveillance/ or ("population surveillance*" or "population screening*").ti,ab,kw,kf.)
(exp Early Diagnosis/ or ("early diagnos*").ti,ab,kw,kf.)

PERSONALIZED
(exp Precision medicine/ or ("personalized medicine*" or "precision medicine*" or "predict*" or "individualized medicine*" or "personalised medicine*" or "individualised medicine*").ti,ab,kw,kf.)
(exp Risk assessment/ or exp Risk adjustment/ or ("risk stratifi*" or "risk scor*" or "risk assess*" or "risk adjust*").ti,ab,kw,kf.)
(exp Machine learning/)

Common cells

Specific cells

- **Cancer**
- **Cardiovascular diseases**
- **Neurodegenerative diseases**

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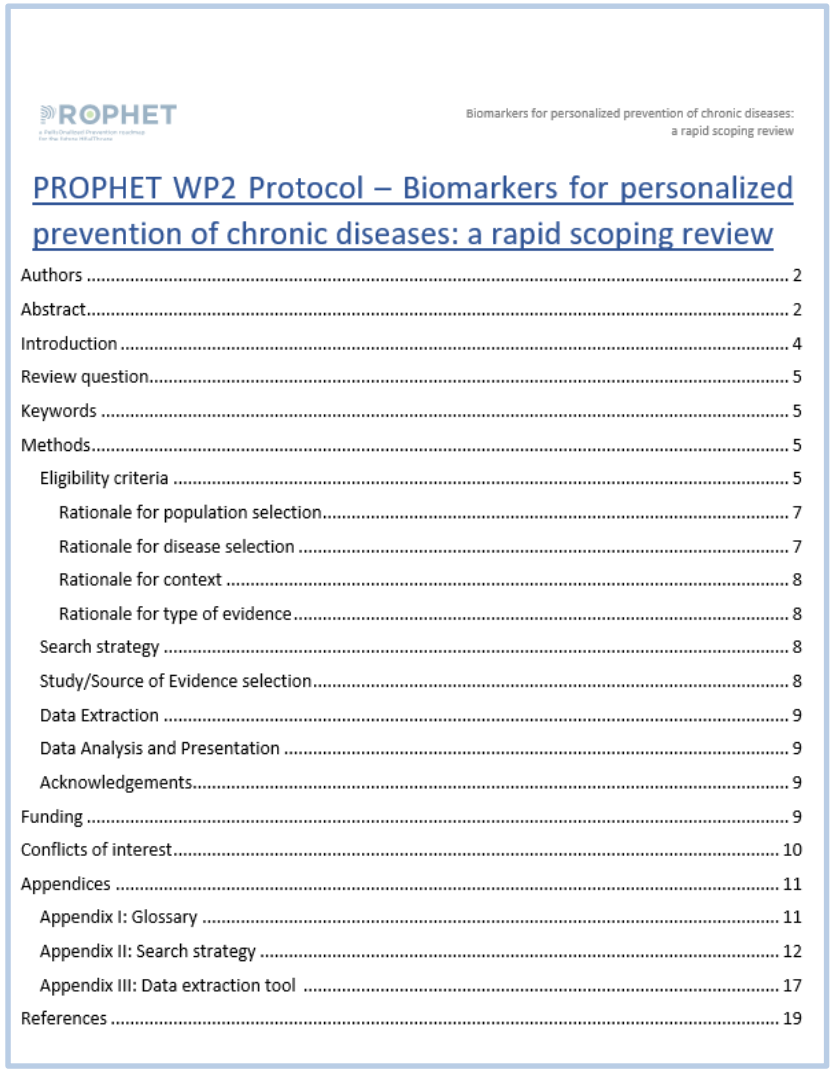
Protocolo de la Revisión panorámica



PROPHET

Biomarkers for personalized prevention of chronic diseases: a rapid scoping review

PROPHET WP2 Protocol – Biomarkers for personalized prevention of chronic diseases: a rapid scoping review

Open Science Framework

	Inclusion	Exclusion
Context	✓ Clinical or Public Health settings. ✓ English language only. ✓ Any geographical setting.	× Studies published before 2020.
Type of evidence	✓ **Reviews**: Umbrella review, systematic review, meta-analysis, scoping review. ✓ **Experimental and quasi-experimental study designs:** Randomized controlled trials, non-randomized controlled trials, before and after studies, interrupted time-series studies. ✓ **Analytical observational study designs:** Prospective and retrospective cohort studies, case-control studies, and analytical cross-sectional studies. ✓ **Descriptive observational study designs:** Descriptive cross-sectional studies.	× Editorials and opinion pieces. × Narrative reviews. × Protocols. × Qualitative study designs. Delphi studies. × Conference abstracts, conference reports. × Clinical practice guidelines. × Basic research (i.e., laboratory research in animals, human tissues, and cell lines). × Data simulation or modelling studies. × Case reports and case series.
Sources	✓ **MEDLINE** via Ovid. ✓ **Embase** via Ovid. ✓ **Embase preprints** via Ovid.	

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¿Qué y cómo se usan los **biomarcadores** en prevención **primaria**? Quizás el interés en radique en cómo **interaccionan** con el ambiente…

¿Qué es **personalizar**? Porque la definición es diferente en prevención **primaria** que en prevención **secundaria**…

Por cierto, ¿Cómo **clasificamos** los biomarcadores?

Más allá de los **genes**, ¿Qué biomarcadores personalizan?

¿Pero a qué consideramos un biomarcador **conocido**?

Cuando es un biomarcador conocido, no lo incluimos, pero se combina con otros biomarcadores de forma novedosa entonces, sí lo incluimos

ROPHET
a PeRsOnalized Prevention roadmap for the future HEalThcare

Data Extraction Sheet

DATA EXTRACTION

Data Extraction

Methods

Study Design

- ○ Umbrella review
- ○ Systematic review + meta-analysis
- ○ Systematic review (without meta-analysis)
- ○ RCT
- ○ Cohort study
- ○ Case-control study
- ○ Other Design

Clear above selection

Biomarker(s)

Name of Biomarker(s)

Enter the names separating them with the ampersand "&". DO NOT USE commas
Example: miR-221 & miR-222 & miR-340

Molecular Biomarker(s)

- ☐ Genetics/Genomics
- ☐ Epigenetics/Epigenomics
- ☐ Transcriptomics
- ☐ Metabolomics
- ☐ Proteomics
- ☐ Microbiomics/Microbiology
- ☐ Biochemistry
- ☐ Other molecular biomarker
- ☐ N/P (Not Provided)

Clear above selection

Celular Biomarker(s)

- ☐ Hystology
- ☐ Cytology
- ☐ Other celular biomarker
- ☐ N/P

Clear above selection

Image Biomarker(s)

- ☐ X-Rays
- ☐ Ultrasound
- ☐ CT Scan
- ☐ PET/SPECT
- ☐ Spectrometry
- ☐ MRI
- ☐ Scintigraphy (Gamma)
- ☐ Mammography
- ☐ Other image biomarker
- ☐ N/P

Clear above selection

Physiological Biomarker(s)

- ☐ Blood Pressure
- ☐ Ankle-brachial Index
- ☐ ECG
- ☐ EEG
- ☐ Electromyography
- ☐ Other physiological biomarker
- ☐ N/P

Clear above selection

Anthropometric Biomarker(s)

- ☐ BMI
- ☐ Body perimeters
- ☐ Other anthropometric biomarker
- ☐ N/P

Clear above selection

Mendelian Randomization

Has mendelian randomization been used in the study?

- ○ Yes
- ○ No

Clear above selection

Clinical Utility

Does the article mention the clinical utility of the biomarker? (explicitly)

- ○ Yes
- ○ No

Clear above selection

AI

Did they use AI technology or methods related to AI? (Deep learning, machine learning, clinical trial simulation, etc)

- ○ Yes
- ○ No

Clear above selection

Radiomics

Does the article mention radiomics?

- ○ Yes
- ○ No

Clear above selection

Technology

Did they use a new technology/wearable to measure the biomarker?

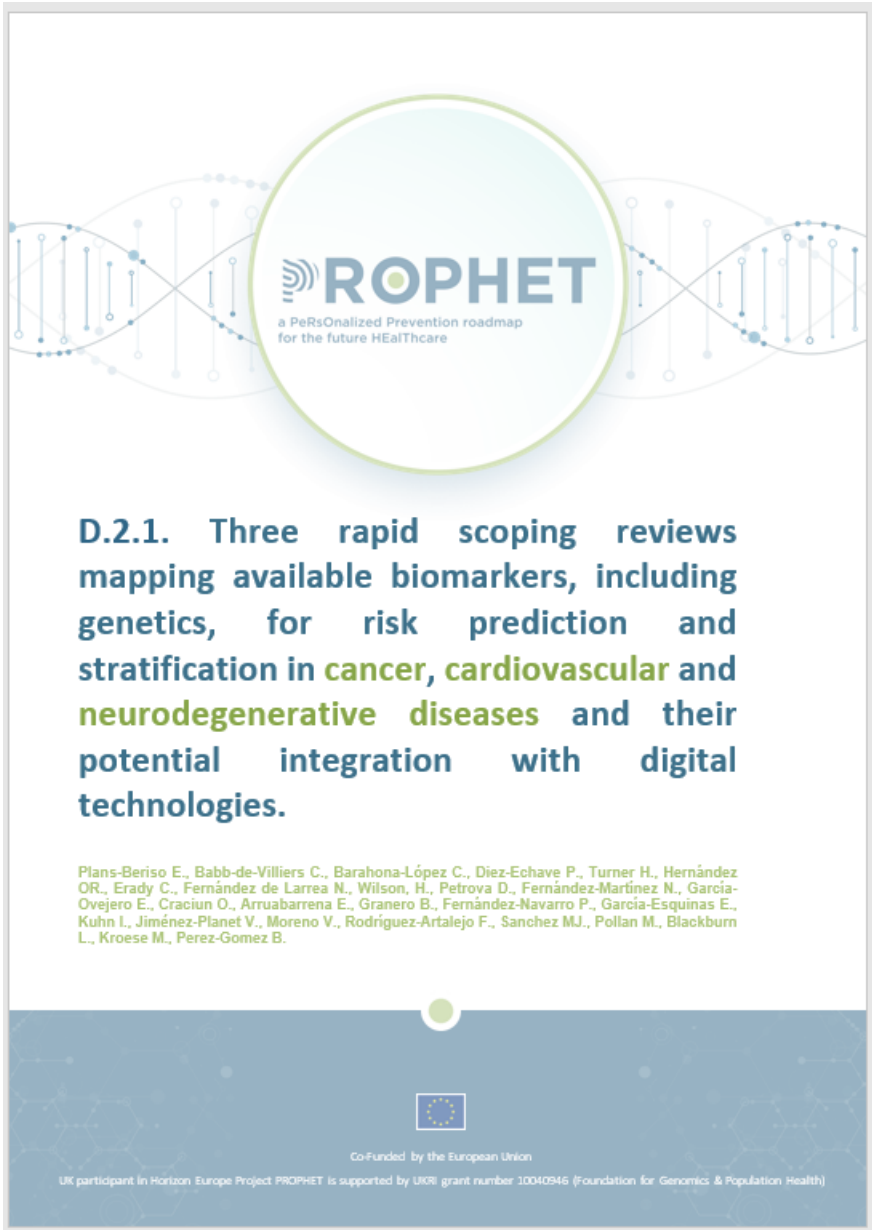
- ○ Yes
- ○ No

Clear above selection

If they used a new technology/wearable to measure the biomarker, specify which one

- ☐ Smart Watch
- ☐ Pulsioximetry
- ☐ Infrared Cameras
- ☐ Other

Clear above selection



PROPHET
a PeRsOnalized Prevention roadmap for the future HEalThcare

D.2.1. Three rapid scoping reviews mapping available biomarkers, including genetics, for risk prediction and stratification in cancer, cardiovascular and neurodegenerative diseases and their potential integration with digital technologies.

Plans-Beriso E., Babb-de-Villiers C., Barahona-López C., Diez-Echave P., Turner H., Hernández OR., Erady C., Fernández de Larrea N., Wilson, H., Petrova D., Fernández-Martínez N., García-Ovejero E., Craciun O., Arruabarrena E., Granero B., Fernández-Navarro P., García-Esquinas E., Kuhn I., Jiménez-Planet V., Moreno V., Rodríguez-Artalejo F., Sanchez MJ., Pollan M., Blackburn L., Kroese M., Perez-Gomez B.

Co-Funded by the European Union

UK participant in Horizon Europe Project PROPHET is supported by UKRI grant number 10040946 (Foundation for Genomics & Population Health)

Project acronym	PROPHET
Project title	A Personalized Prevention roadmap for the future Healthcare (PROPHET)
Thematic priority	HORIZON-HLTH-2021-STAYHLTH-01
Type of action	CSA
Grant Agreement	101057721
Deliverable number and title	D.2.1. Three rapid scoping reviews mapping available biomarkers, including genetics, for risk prediction and stratification in cancer, cardiovascular and neurodegenerative diseases, and their potential integration with digital technologies.
Work package	WP2
Due date:	31/07/2023
Submission date	
Start date of project	01/09/2022
Duration of project (End Date)	31/08/2026
Organisation responsible of deliverable	CIBER
Version	1
Status	Finished
Author name(s)	Plans-Beriso E., Babb-de-Villiers C., Barahona-López C., Diez-Echave P., Turner H., Hernández OR., Erady C., Fernández de Larrea N., Wilson, H., Petrova D., Fernández-Martínez N., García-Ovejero E., Craciun O., Arruabarrena E., Granero B., Fernández-Navarro P., García-Esquinas E., Kuhn I., Jiménez-Planet V., Moreno V., Rodríguez-Artalejo F., Sanchez MJ., Pollan M., Blackburn L., Kroese M., Perez-Gomez B.
Contributing partners	CIBER/ISCIII PHG
Reviewer(s)	
Document type:	R – Report
Dissemination level:	PU – Public

Rapid scoping reviews on biomarkers for risk prediction and stratification in cancer, cardiovascular and neurodegenerative

Rapid scoping reviews on biomarkers for risk prediction and stratification in cancer, cardiovascular and neurodegenerative

PROPHET
a PeRsOnalized Prevention roadmap for the future HEalThcare

Cáncer	***Paul Diez Echave***
Enfermedades Cardiovasculares	***Orlando Hernández***
Enfermedades neurodegenerativas	***Cristina Barahona López***

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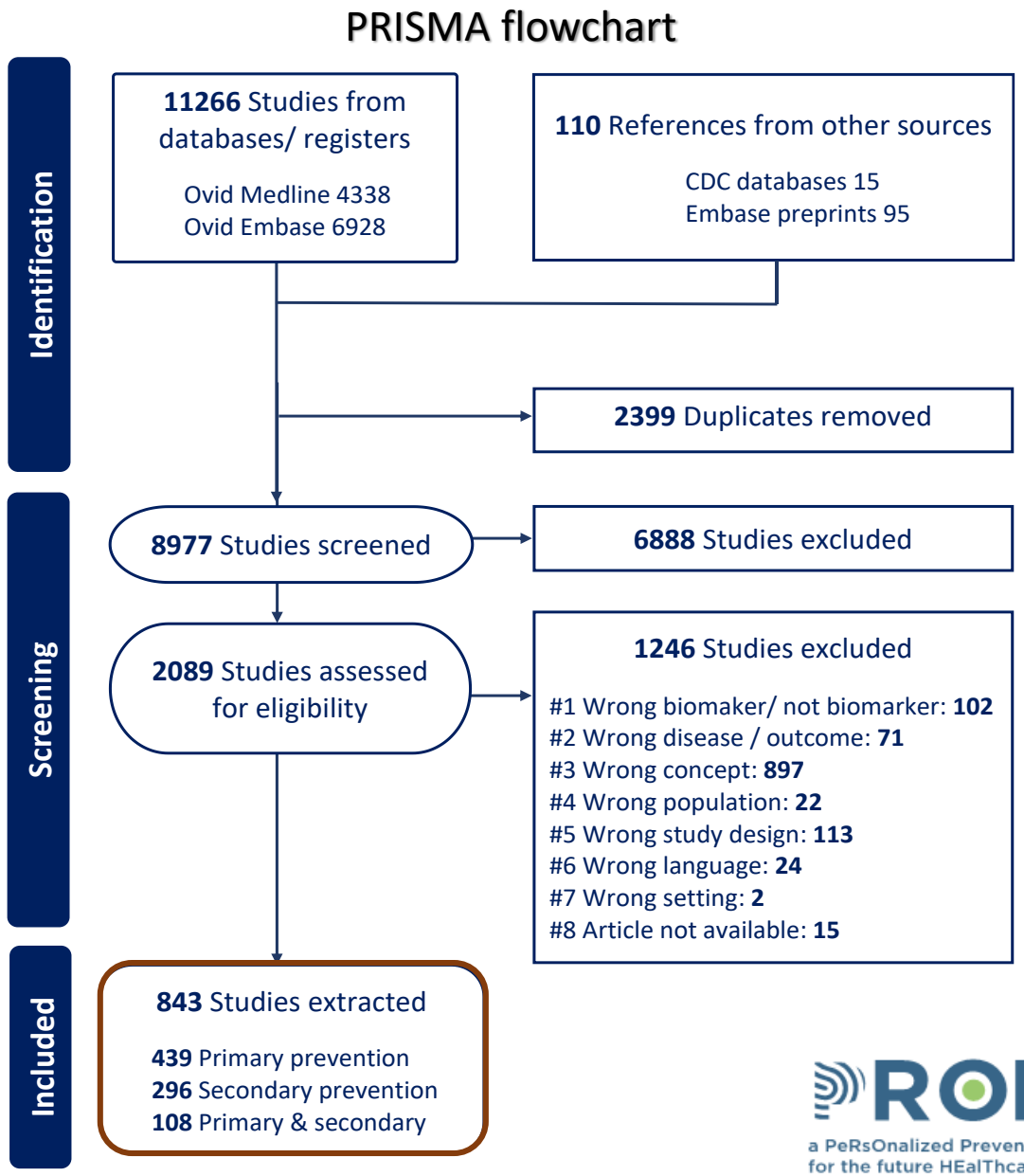
a PeRsOnalized Prevention roadmap for the future HEalThcare

Cáncer

- Cáncer de **mama**
- Cáncer de **próstata**
- Cáncer de **pulmón**
- Cáncer **colorrectal**
- Cáncer **gástrico**
- Cáncer **pancreático**
- Cáncer de **hígado**
- Cáncer de **cuello uterino**
- Cáncer **cervical**
- Cáncer de **riñón**
- Cáncer de **vejiga**



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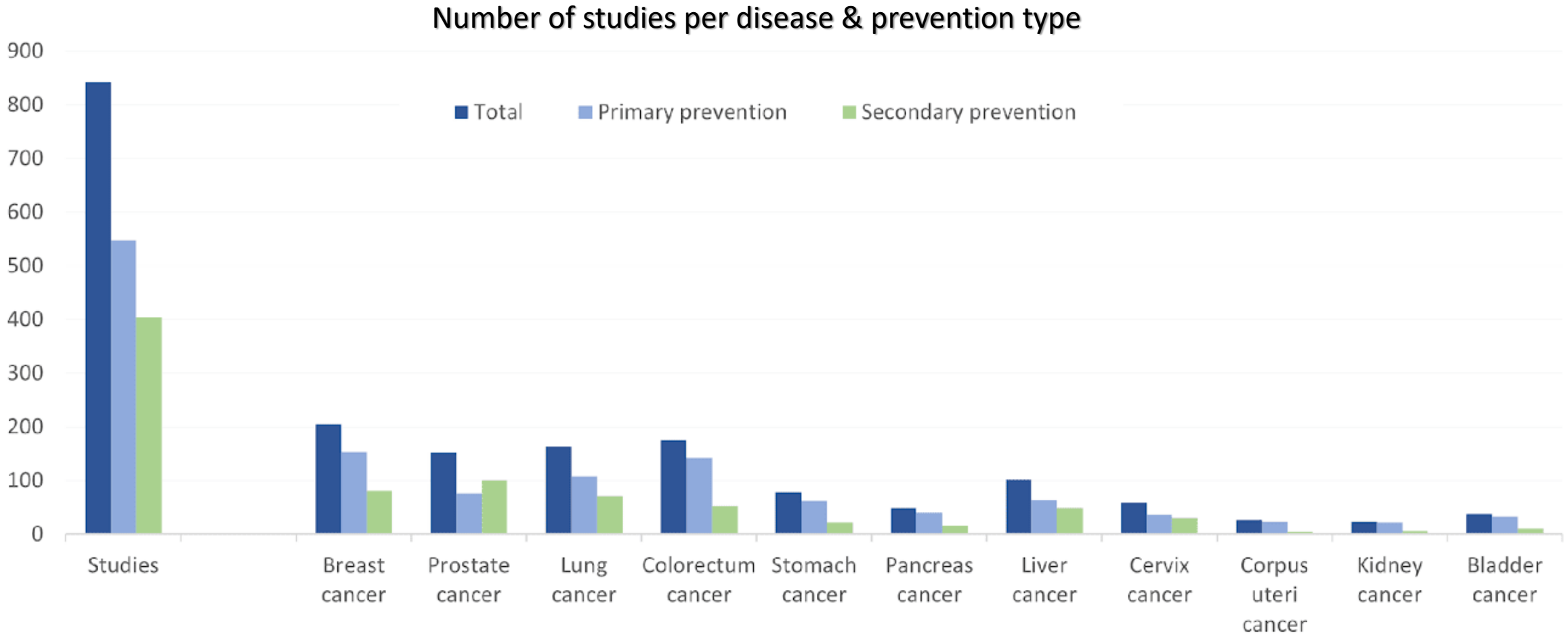
Cáncer



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Cáncer

Number of studies per disease, prevention type & biomarker category

Prevención primaria

	Breast cancer	Prostate cancer	Lung cancer	Colo-rectum cancer	Gastric cancer	Pancreatic cancer	Liver cancer	Corpus uteri cancer	Cervical cancer	Kidney cancer	Bladder cancer
Molecular	138	73	101	141	61	39	62	22	36	21	31
Cellular	9	7	4	6	3	0	6	3	4	1	1
Imaging	17	2	6	3	2	2	4	1	1	0	0
Physio-logical	0	2	1	5	2	2	2	1	0	0	1
Anthropo-metric	27	7	12	32	9	6	9	5	2	4	2

Prevención secundaria

	Breast cancer	Prostate cancer	Lung cancer	Colo-rectum cancer	Gastric cancer	Pancreatic cancer	Liver cancer	Corpus uteri cancer	Cervical cancer	Kidney cancer	Bladder cancer
Molecular	46	94	48	52	19	13	46	5	26	6	11
Cellular	2	21	3	7	0	0	11	1	17	0	1
Imaging	44	34	30	2	2	4	11	0	4	0	1
Physio-logical	1	5	3	2	0	0	0	0	0	0	0
Anthropo-metric	15	17	3	6	0	3	4	2	0	1	0

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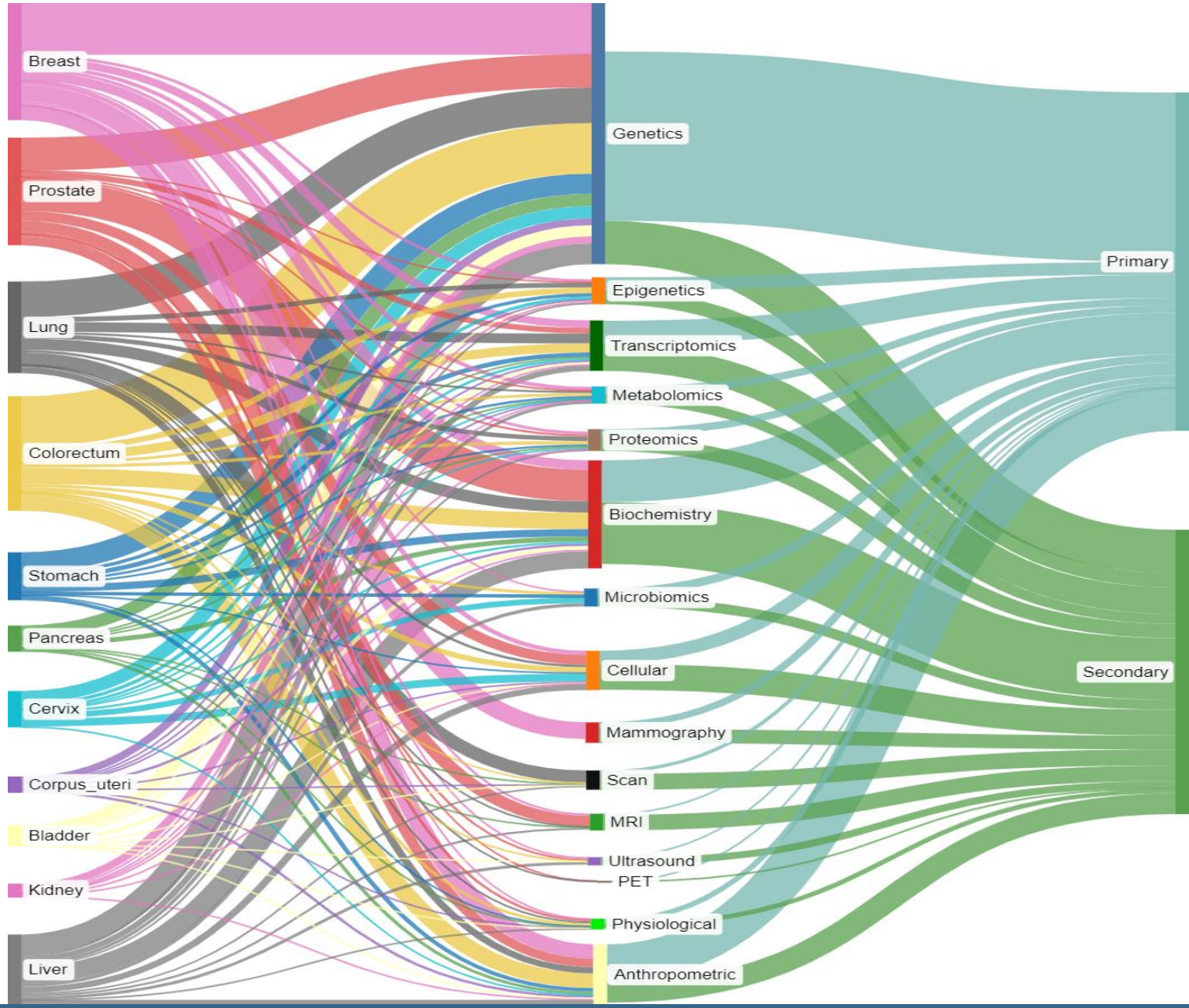
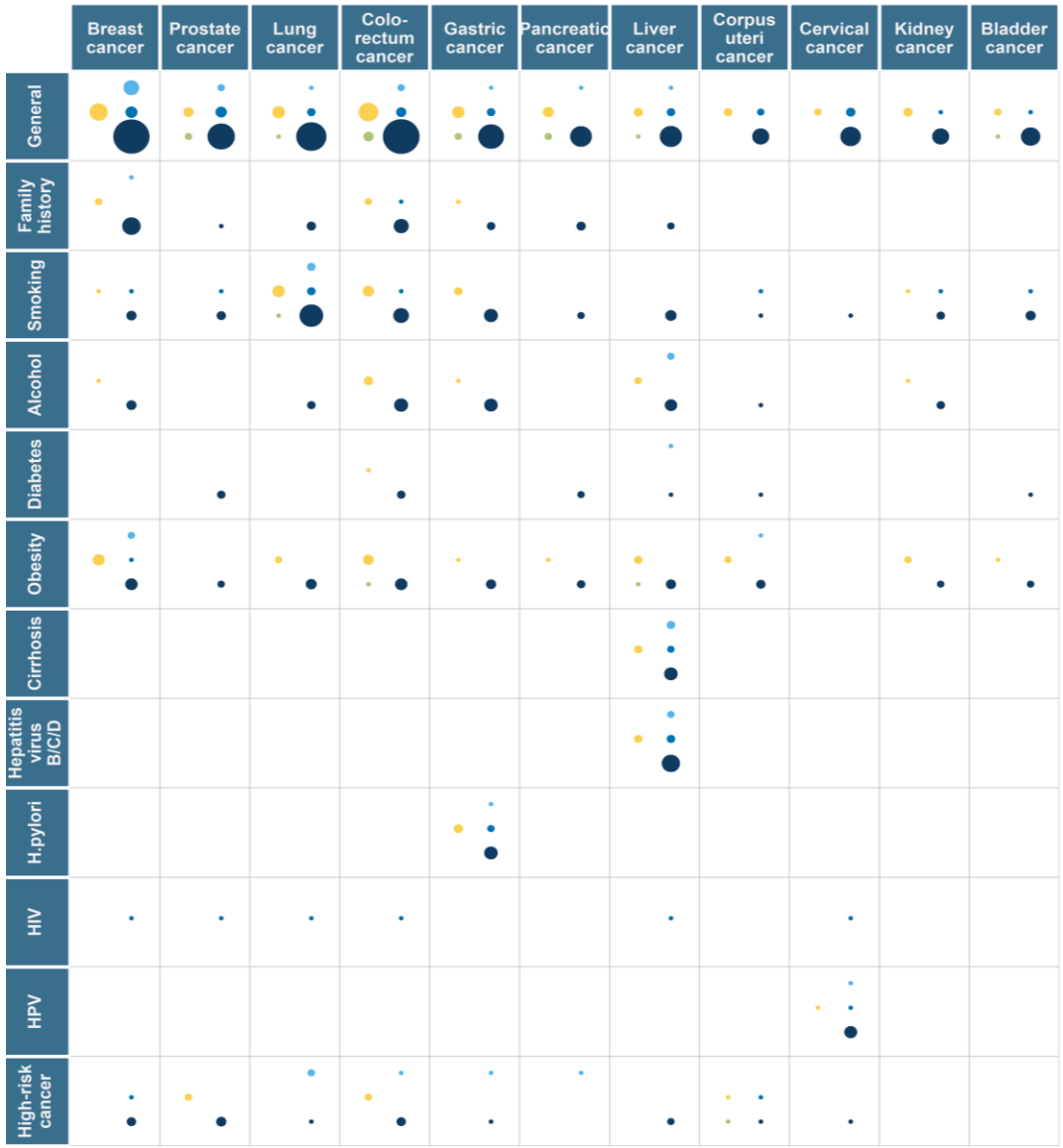
Cáncer

- Biomarcadores moleculares (principalmente genéticos)
- El uso de otras -omicas, como la epigenomica, transcriptómica, metabolómica y proteómica, tiene resultados limitados
- En prevención secundaria, predomina el uso de biomarcadores de imagen, tecnologias multi-omicas y inteligencia artificial



Cáncer

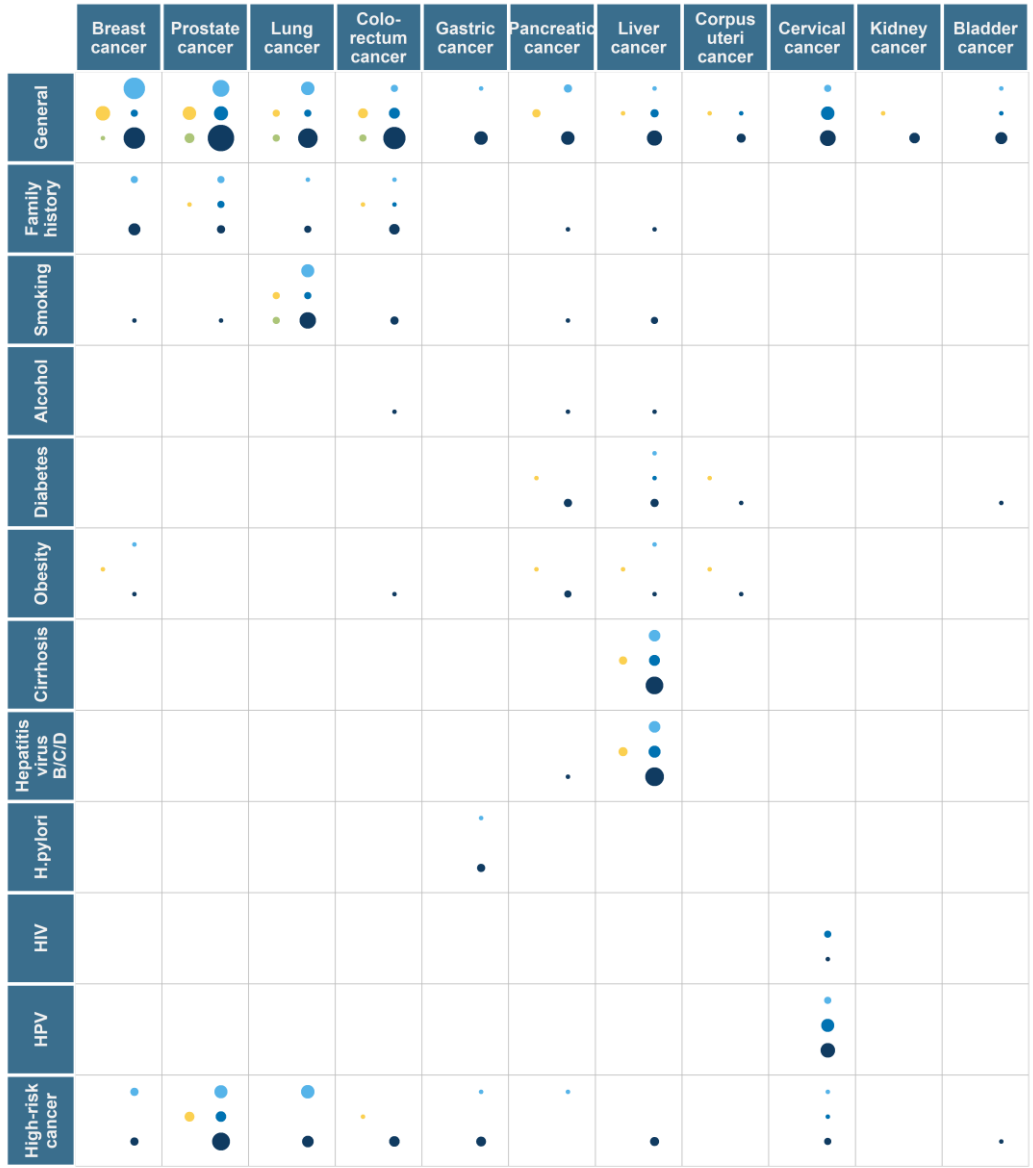


Prevención primaria

Type of biomarkers
- Molecular
- Cellular
- Imaging
- Physiological
- Anthropometric

Number of studies
- 1
- 50
- 100
- 150

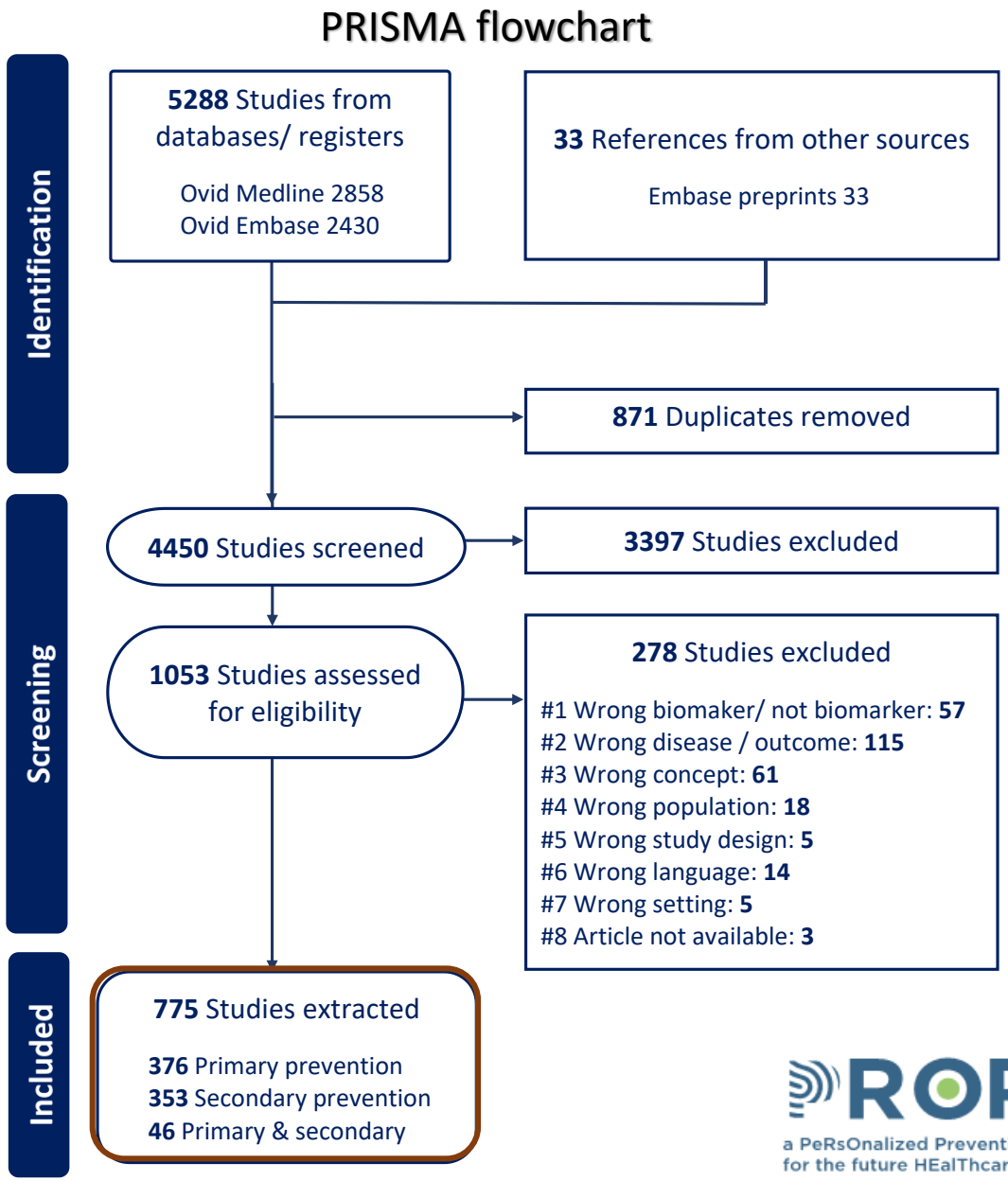
Prevención secundaria



Enfermedades Cardiovasculares

- Enfermedad cardiaca isquémica
- Accidente cerebro vascular
- Cardiomiopatía y miocarditis
- Fibrilación auricular y aleteo auricular
- Aneurisma aórtico
- Valvulopatía cardíaca no reumática
- Enfermedad arterial periférica

Eventos cardíacos adversos mayores (MACE)



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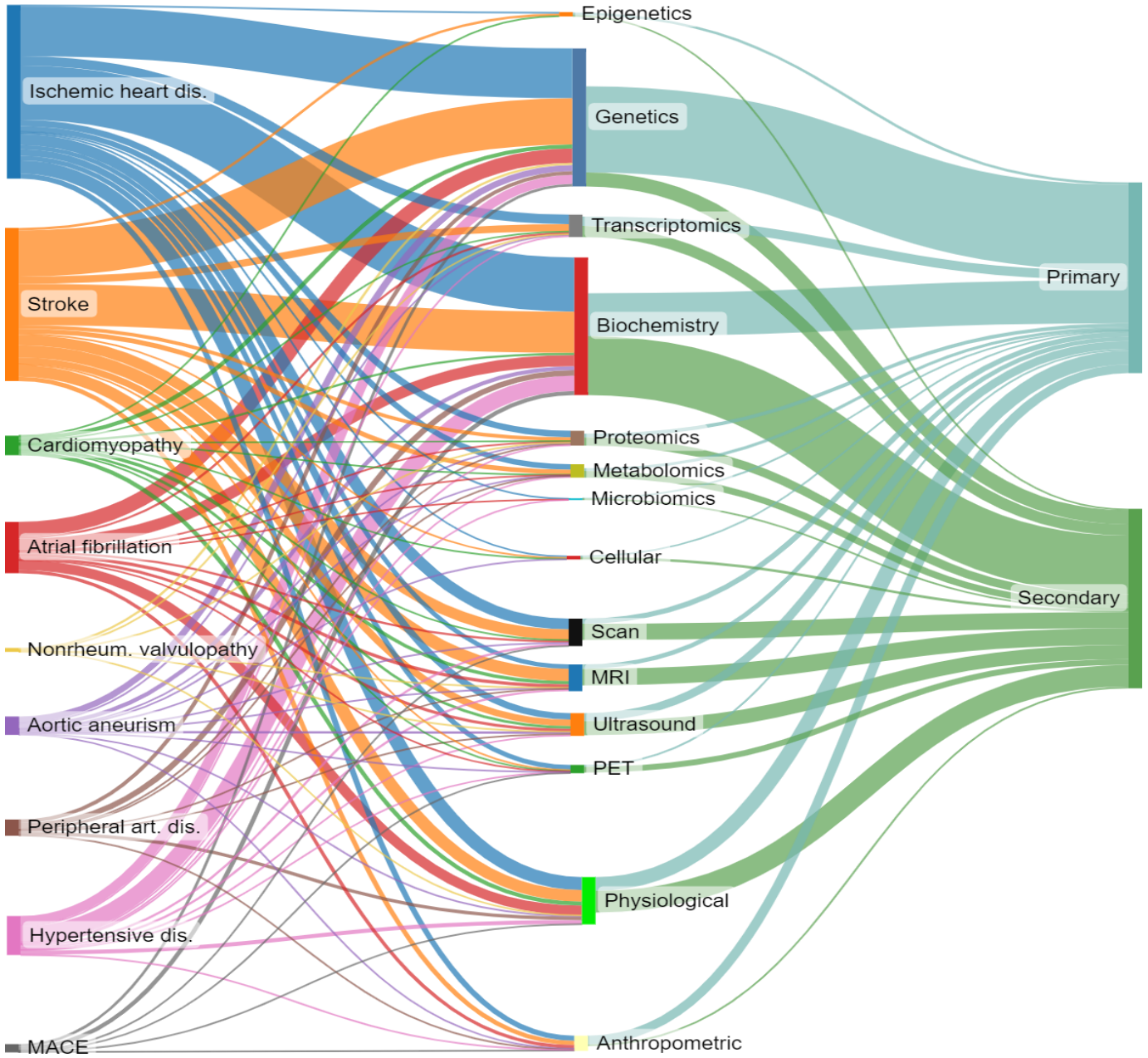
Enfermedades Cardiovasculares

- ECI y ACV son la mayoria
- Prevención primaria la mayoría son moleculares
- El uso de imágenes, tecnologías multi-ómicas e IA predominan en la prevención secundaria
- Los biomarcadores moleculares (principalmente genéticos)
- Los biomarcadores bioquímicos también son relevantes



Enfermedades neurodegenerativas

DEMENCIAS

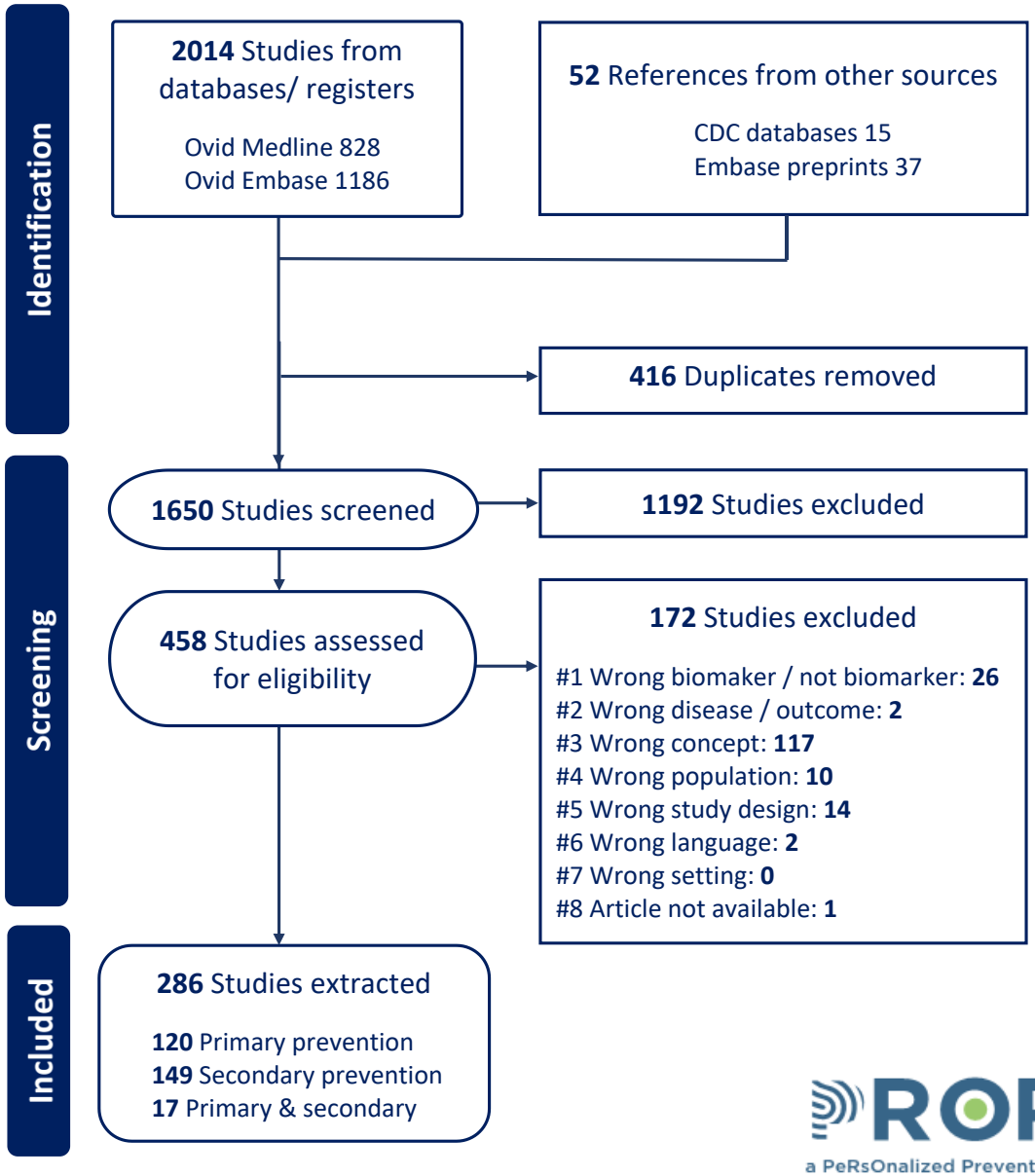
- Alzheimer
- Demencia vascular
- Demencia por cuerpos de Lewy
- Demencia frontotemporal

ENFERMEDADES DESMIELINIZANTES

- Esclerosis múltiple
- Esclerosis lateral amiotrófica

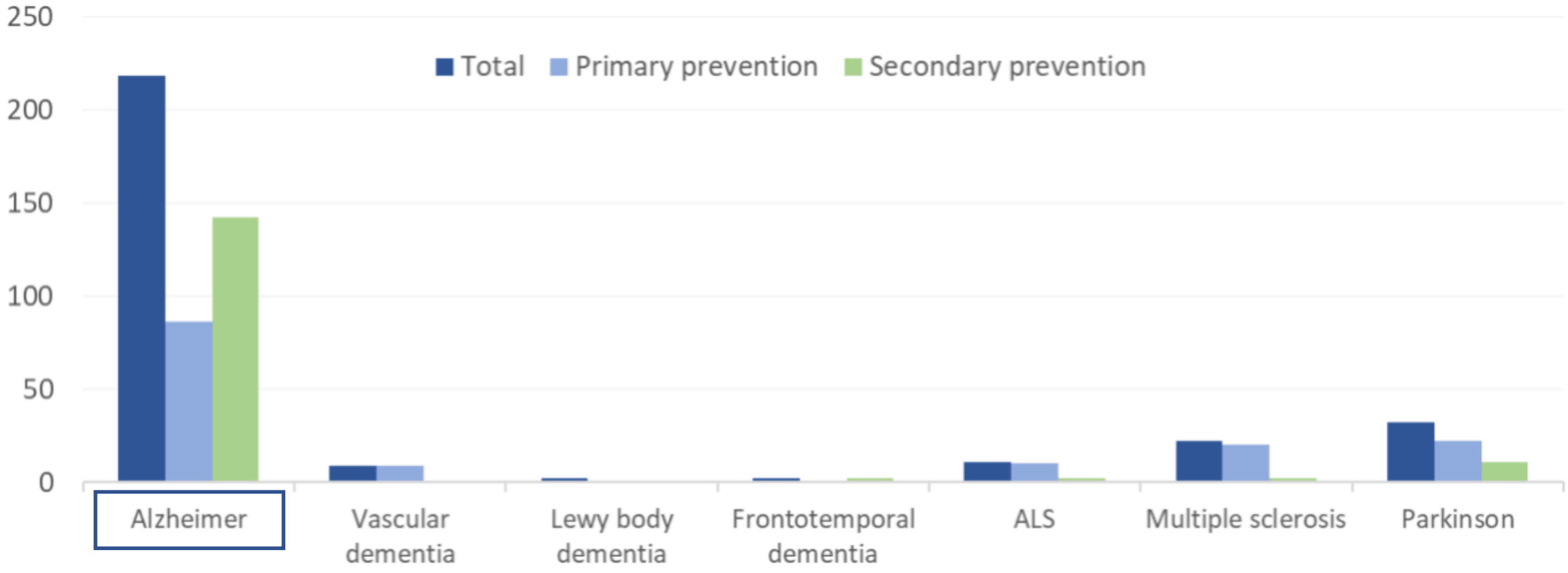
SINUCLEOPATÍAS

- Parkinson



ROPHET
a PeRsOnalized Prevention roadmap for the future HEalThcare

Enfermedades neurodegenerativas



PROPHET
a PeRsOnalized Prevention roadmap for the future HEalThcare

Enfermedades neurodegenerativas

Prevención primaria

	Alzheimer	Vascular dementia	Lewy body disease	Frontotemporal dementia	Amyotrophic lateral sclerosis	Multiple sclerosis	Parkinson
Molecular	77	7	0	0	10	21	22
Cellular	1	0	0	0	0	0	0
Imaging	22	3	1	0	1	1	3
Physiological	16	4	0	0	1	1	3
Anthropometric	10	4	0	0	2	2	3

Prevención secundaria

	Alzheimer	Vascular dementia	Lewy body disease	Frontotemporal dementia	Amyotrophic lateral sclerosis	Multiple sclerosis	Parkinson
Molecular	86	1	0	2	1	2	7
Cellular	1	0	0	0	0	1	0
Imaging	83	0	1	0	1	1	5
Physiological	15	0	0	0	0	0	4
Anthropometric	7	0	0	0	0	1	1

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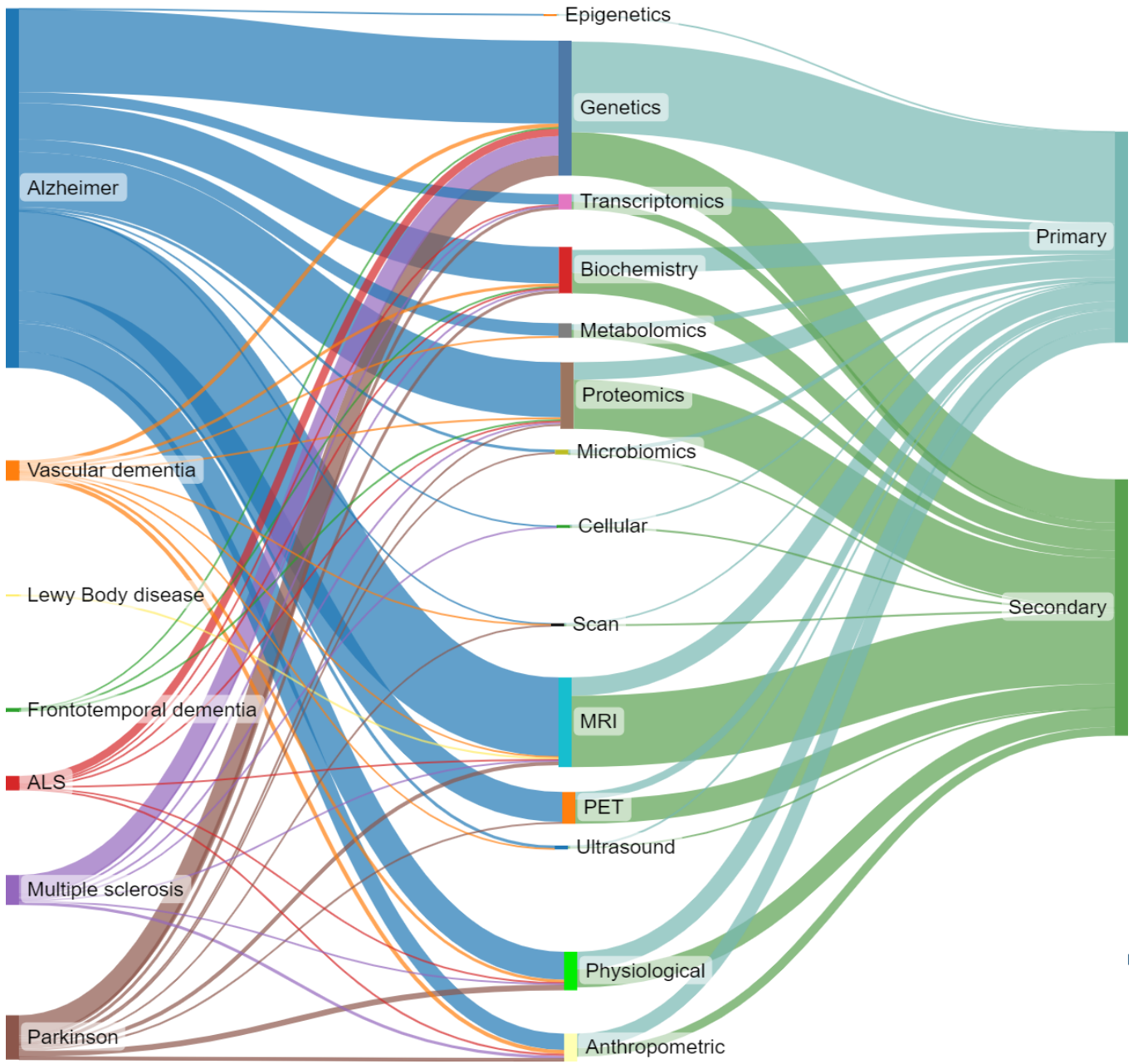
Enfermedades neurodegenerativas

El Alzheimer es la única enfermedad con resultados para todos los biomarcadores.

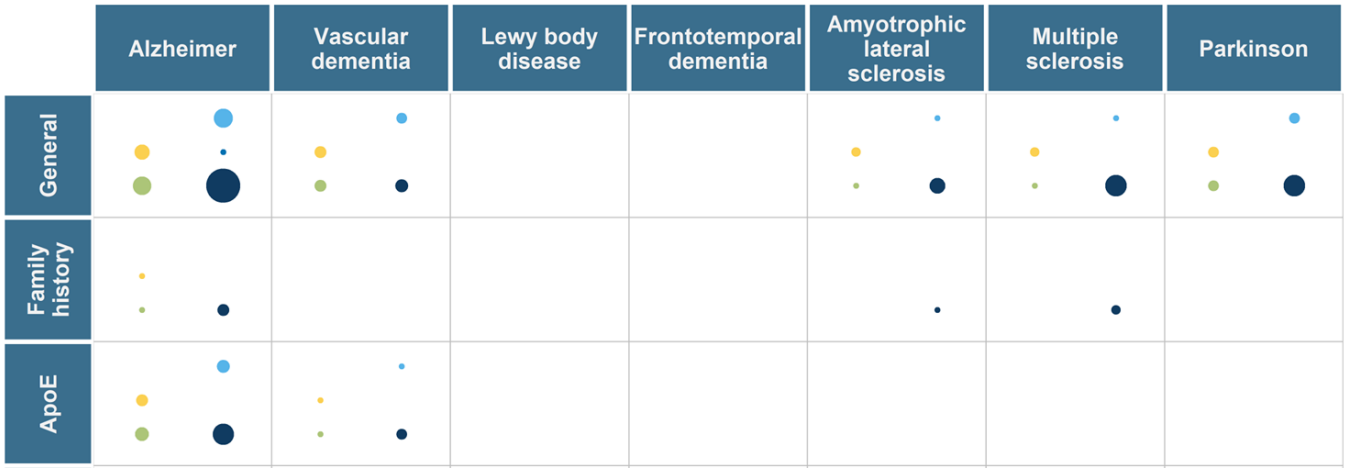
Los biomarcadores basados en proteínas están bastante bien representados:

Múltiples estudios que utilizan tipos y fracciones de amiloide en muestras de sangre (sustituto de pruebas más caras o invasivas).

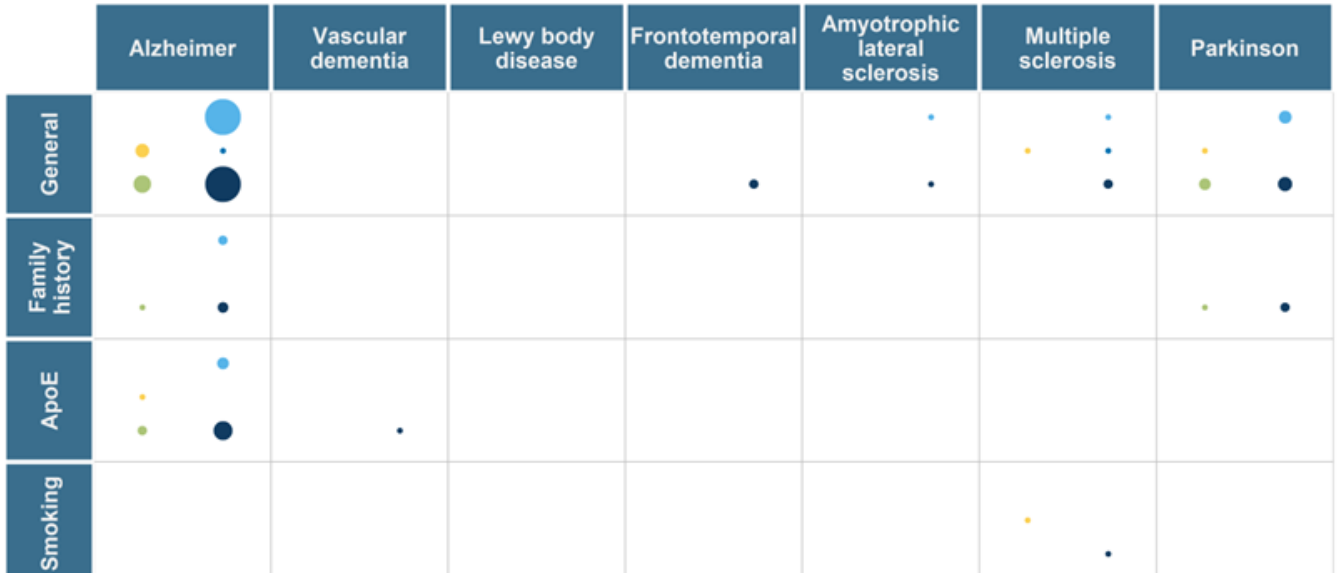
Imágenes (especialmente MRI y PET/SPECT).



Enfermedades neurodegenerativas

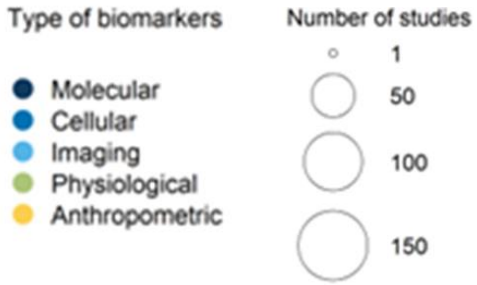


Prevención primaria



Prevención secundaria

Individuos con deterioro cognitivo leve



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CONCLUSIONES GENERALES

Estas revisiones resumen las principales características y conclusiones de la bibliografía sobre este tema.

Abarca los tres principales grupos de enfermedades crónicas:

11 cánceres

9 enfermedades cardiovasculares

7 enfermedades neurodegenerativas

Fortalezas

- ✓ Protocolo común y cuidadoso control de calidad
- ✓ Diferentes formas de presentar los resultados: informe + mapas interactivos

Limitaciones

- ✓ No se evalúa la calidad ni los sesgos de los estudios

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CONCLUSIONES GENERALES

- Ha resultado muy compleja la categorización y clasificación

  → Prevención primaria vs prevención secundaria (vs prevención terciaria)
  i.e. susceptibilidad genética (SNP, PRS…)

  → Personalización: incorporar o considerar características de los individuos que puedan permitir una mejor estratificación de riesgo

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CONCLUSIONES GENERALES

→ El **cáncer** es el área con más investigación, seguida de las ECV. Escasa investigación en neurodegenerativas.

→ Los **biomarcadores** se utilizan de manera **individual**, **combinados** con otros biomarcadores y/o factores de riesgo (por ejemplo, como parte de un modelo), y/o en combinación con nuevas **tecnologías digitales**.

- La IA se utiliza con mayor frecuencia con imágenes BM o grandes cantidades de datos

  → **modelos predictivos / detección precoz**

- Baja integración de tecnologías *"wearables"* (i.e. Acelerómetro, Smart Watch)

- Utilización de grandes bases de datos disponibles: oportunidad/riesgo

(i.e. UK Biobank, Gene Expression Omnibus, MEGASTROKE, The Cancer Genome Atlas (TCGA) or Alzheimer's Disease Neuroimaging Initiative (ADNI))

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CONCLUSIONES GENERALES

→ Los biomarcadores deberían añadirse a lo que ya sabemos en materia de prevención, y sabemos mucho....

Biomarcadores genómicos/genéticos:

La categoría de biomarcadores **más investigada en prevención primaria**

La **segunda** categoría (después de los biomarcadores de imagen) más investigada en **prevención secundaria**.

Permiten identificar a un número reducido de personas con alto riesgo

↓

En la mayoría de los casos, la prevención primaria consiste en

- Recomendaciones generales sobre un estilo de vida saludable
- Control de los factores de riesgo conocidos

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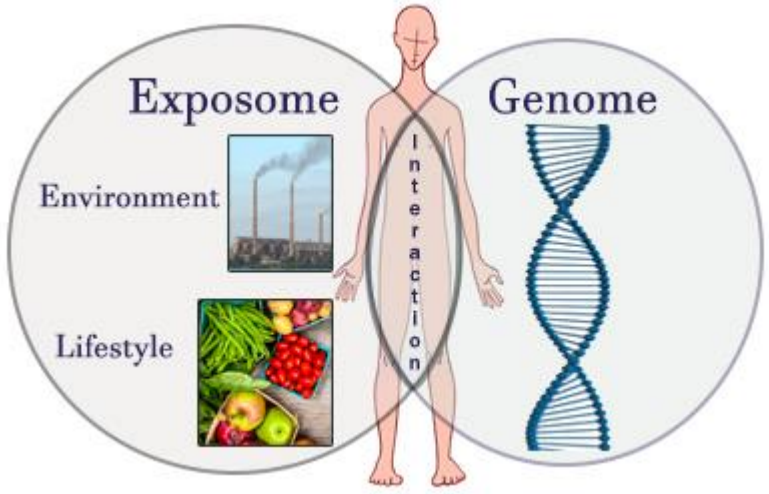
CONCLUSIONES GENERALES

Biomarcadores genómicos/genéticos:

El potencial de la personalización basada en la población



https://blogs.cdc.gov/genomics/2022/09/06/from-the-genome-to-the-exposome/

→ Algunos buenos ejemplos de **interacciones gen-ambiente**, pero, en general, la bibliografía es relativamente escasa.

→ **Biomarcadores epigenéticos** actualmente en investigación
(papel crucial en la comprensión de los factores ambientales/de estilo de vida)

→ Otras **ómicas** (i.e. microbiota)

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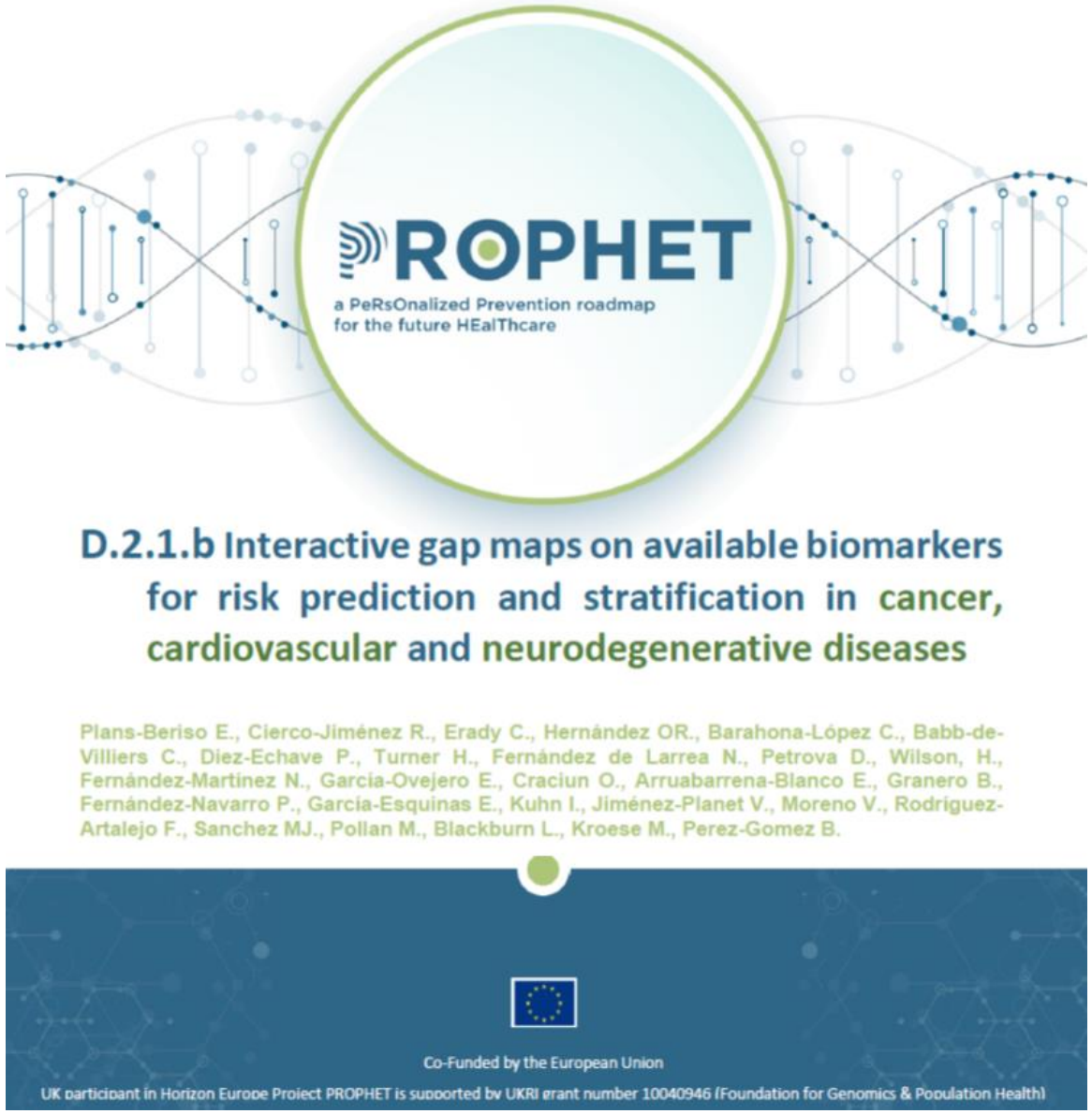

✓ Desarrollo de **scripts** que ayudarán a traducir las variables de Covidence a Evimap

RStudio®

Eppi-mapper

ePPI REVIEWER

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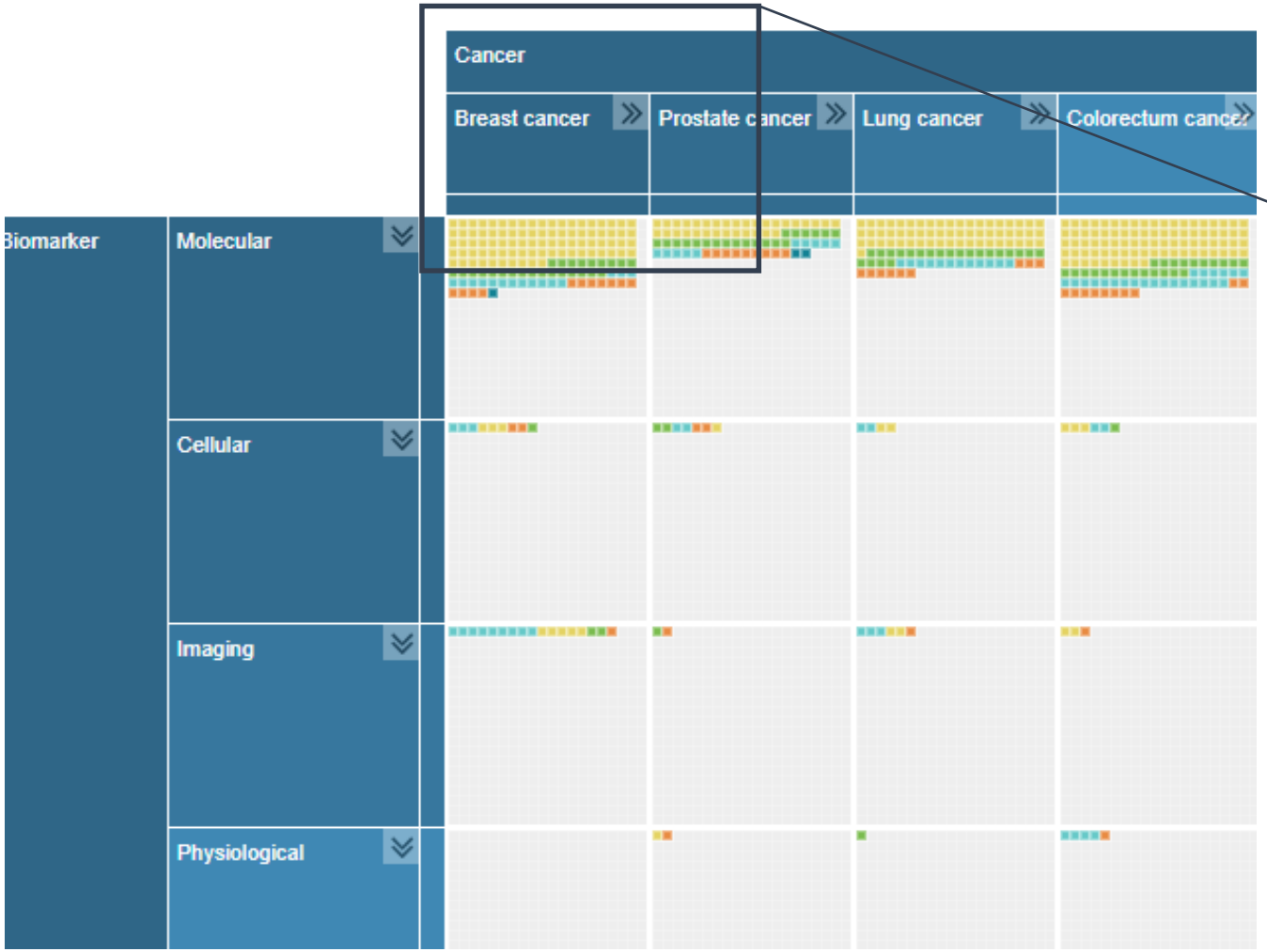

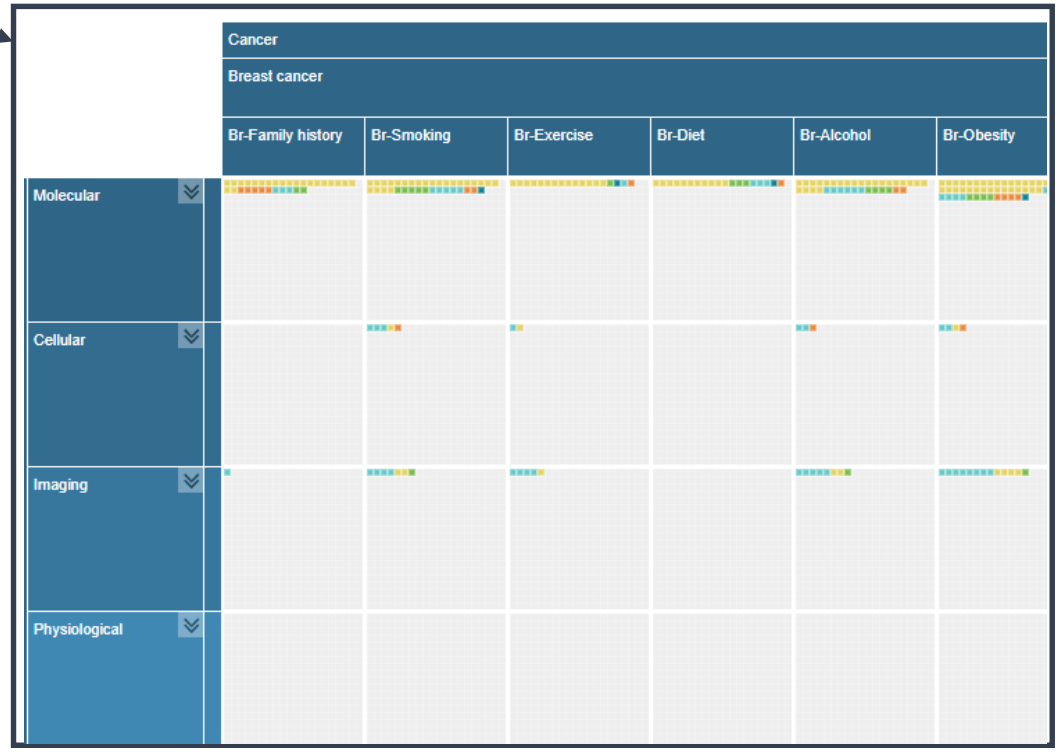

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Mapas interactivos

	Prevención primaria		Prevención secundaria
	Factores relacionados con el estilo de vida/riesgo familiar	Población de estudio	Población de estudio
Cáncer			
ECV			
Enfermedades neurodegenerativas			

https://biodama.isciii.es/prophet/

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