Construyendo la cohorte IMPaCT-Spain

Marina Pollán
Centro Nacional de Epidemiología
Instituto de Salud Carlos III
CIBER de Epidemiología y Salud Pública (CIBERESP)

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1. Antecedentes

2. Medicina de Precisión

3. ¿Quiénes son nuestros modelos?

4. La cohorte IMPaCT: dónde estamos

Antecedentes

- **Año 2016**: Reunión con Director del Instituto de Salud Carlos III: Jesús Ferández Crespo

  Manolis Kogevinas
  Fernando Rodríguez Artalejo
  Miguel Delgado
  Marina Pollán

- **Año 2017**: Solicitud a las Áreas CIBER de un proyecto de investigación anclado en el ámbito de la Medicina de Precisión

Antecedentes

- **Año 2018**: Presentación de nuestro proyecto a la nueva Directora del ISCIII: Raquel Yotti:

- Elaboración de un documento más elaborado, inclusión de otras áreas CIBER

"CONAMIGOS" PROJECT

(COHORTE NACIONAL ABIERTA MULTIPROPÓSITO DE INVESTIGACIÓN E INNOVACIÓN GLOBAL PARA EL OBJETIVO SALUD)

A highway for biomedical research in Spain

A Proposal for a Large National Cohort of Adults Residing in Spain

CIBERESP
CIBEROBN
CIBERCV

Contexto: El paradigma médico

JOURNAL OF THE ROYAL SOCIETY OF MEDICINE Volume 88 November 1995

The need for evidence-based medicine

David L Sackett FRSC MD Msc Epid FRCPC William M C Rosenberg MA MB BS DPhil MRCP

J R Soc Med 1995;**88**:620–624

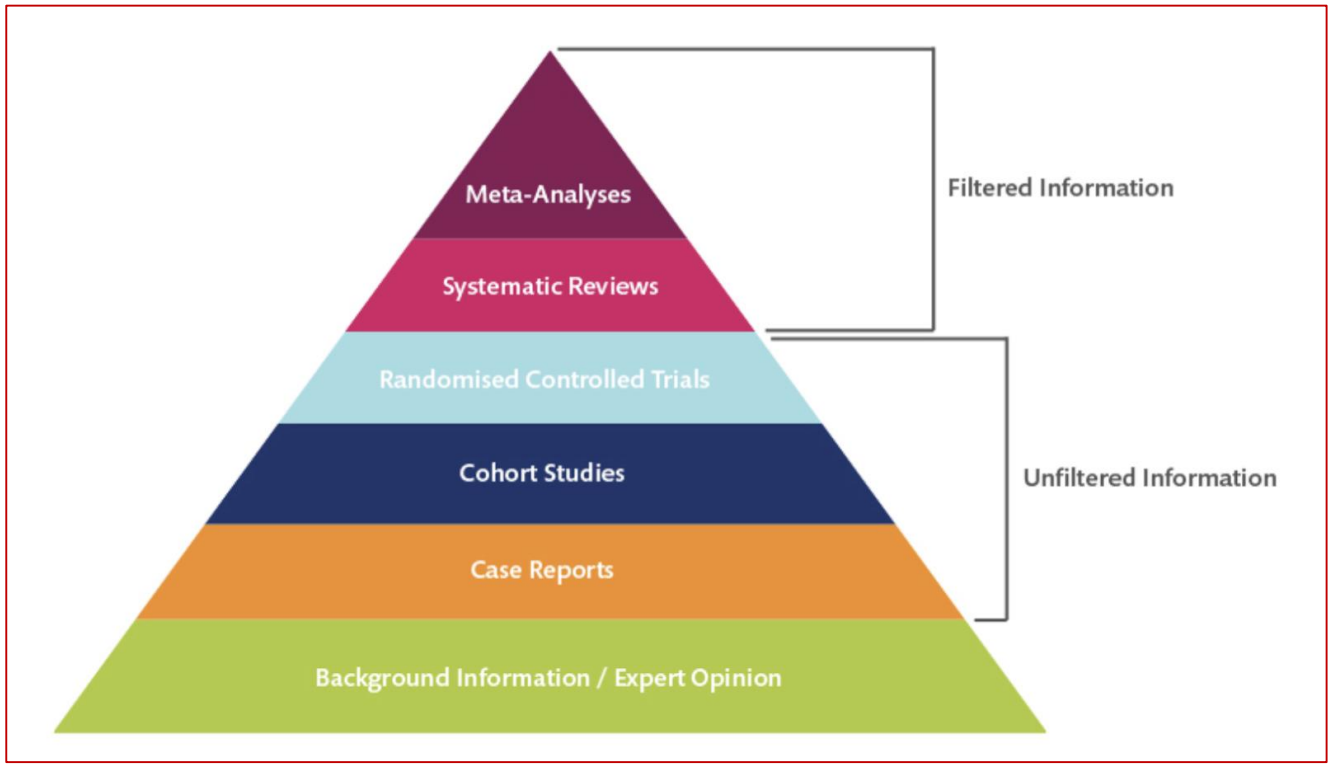
Keywords: *evidence-based medicine; continuing medical education; randomized trials*

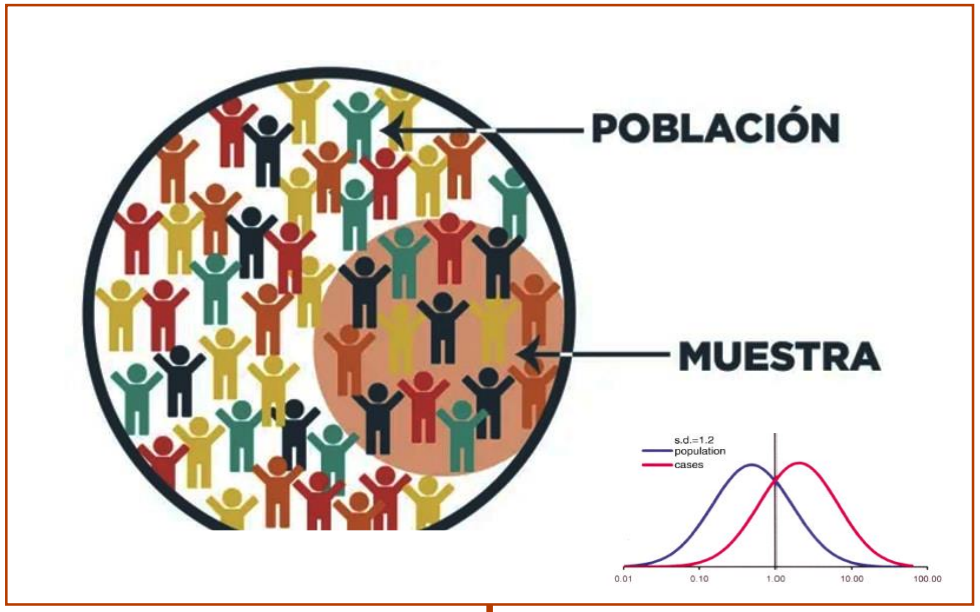
SUMMARY

As physicians, whether serving individual patients or populations, we always have sought to base our decisions and actions on the best possible evidence. The ascendancy of the randomized trial heralded a fundamental shift in the way that we establish the clinical bases for diagnosis, prognosis, and therapeutics. The ability to track down, critically appraise (for its validity and usefulness), and incorporate this rapidly growing body of evidence into one's clinical practice has been named 'evidence-based medicine'[5,6] (EBM).

Contexto: EBM

- Aplicación del **método científico**
- Comparación de **grupos**
- Conclusiones basadas en el "**resultado global**"





Contexto: La revolución genómica

NATURE | VOL 409 | 15 FEBRUARY 2001 | www.nature.com

Publication of human genomes sparks fresh sequence debate

Declan Butler

This week's publication of the human genome sequence by both Celera Genomics of Rockville, Maryland, and the publicly funded international Human Genome Project (HGP) has re-ignited the debate over the relative merits of the two teams' different strategies.

The two groups published their work simultaneously, as promised last summer, and held a cordial joint press conference in Washington on Monday to advertise the fact. At five more press conferences around the world, participants in the public project celebrated their achievement, which is published in *Nature* (see pages 860–921).

But in the run-up to these meetings, leading members of both teams had been working hard in an attempt to ensure that history — or

Cordial: Celera's Craig Venter (left) and the HGP's Francis Collins at Monday's press conference.

Medicina Personalizada:

IMPaCT

Personalized medicine has the potential to change the way we think about, identify and manage health problems. It is already having an exciting impact on both clinical research and patient care, and this impact will grow as our understanding and technologies improve.

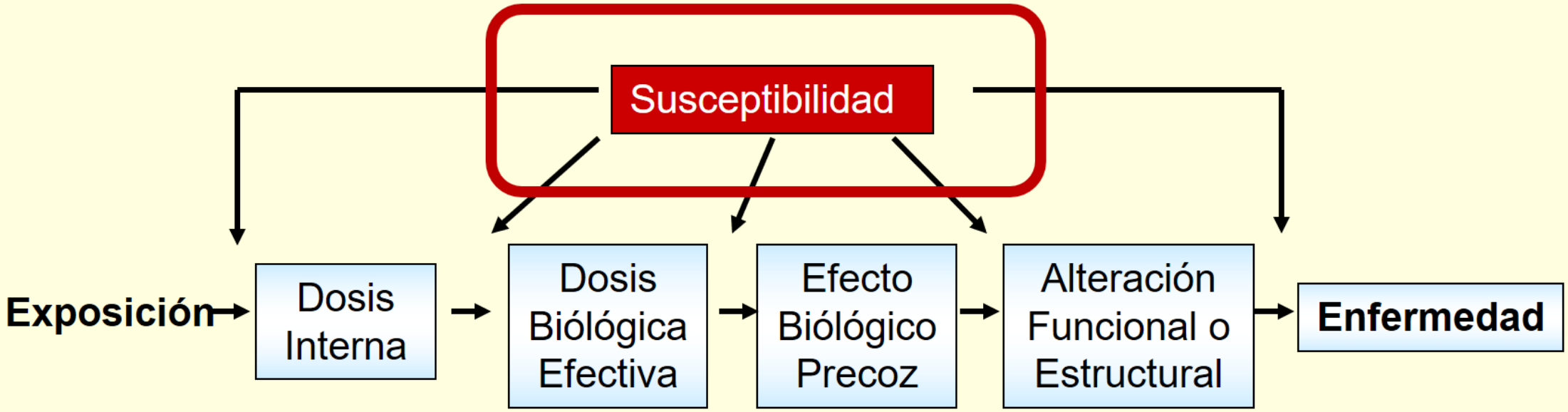
Traditional "One-Size-Fits-All" Approach
All patients with the same diagnosis receive same treatment

Personalized Medicine Approach
Treatment strategy based on patient's unique genetic profile

Genetic Profile A:
Targeted Therapy

Genetic Profile B:
Standard Therapy

¿Y en epidemiología?



Ciencia que trata de la contribución de factores genéticos y ambientales identificados a nivel molecular en la etiología distribución y control de la enfermedad en la población.

Susceptibilidad individual

Vol 447|28 June 2007|doi:10.1038/nature05887 nature

ARTICLES

Genome-wide association study identifies novel breast cancer susceptibility loci

Douglas F. Easton[1], Karen A. Pooley[2], Alison M. Dunning[2], Paul D. P. Pharoah[2], Deborah Thompson[1], Dennis G. Ballinger[3], Jeffery P. Struewing[4], Jonathan Morrison[2], Helen Field[2], Robert Luben[5], Nicholas Wareham[5], Shahana Ahmed[2], Catherine S. Healey[2], Richard Bowman[6], the SEARCH collaborators[2]*, Kerstin B. Meyer[7], Christopher A. Haiman[8], Laurence K. Kolonel[9], Brian E. Henderson[8], Loic Le Marchand[9], Paul Brennan[10], Suleeporn Sangrajrang[11], Valerie Gaborieau[10], Fabrice Odefrey[10], Chen-Yang Shen[12], Pei-Ei Wu[12], Hui-Chun Wang[12], Diana Eccles[13], D. Gareth Evans[14], Julian Peto[15], Olivia Fletcher[16], Nichola Johnson[16], Sheila Seal[17], Michael R. Stratton[17,18], Nazneen Rahman[17], Georgia Chenevix-Trench[19], Stig E. Bojesen[20], Børge G. Nordestgaard[20], Christen K. Axelsson[21], Montserrat Garcia-Closas[22], Louise Brinton[22], Stephen Chanock[23], Jolanta Lissowska[24], Beata Peplonska[25], Heli Nevanlinna[26], Rainer Fagerholm[26], Hannaleena Eerola[26,27], Daehee Kang[28], Keun-Young Yoo[28,29], Dong-Young Noh[28], Sei-Hyun Ahn[30], David J. Hunter[31,32], Susan E. Hankinson[32], David G. Cox[31], Per Hall[33], Sara Wedren[33], Jianjun Liu[34], Yen-Ling Low[34], Natalia Bogdanova[35,36], Peter Schürmann[36], Thilo Dörk[36], Rob A. E. M. Tollenaar[37], Catharina E. Jacobi[38], Peter Devilee[39], Jan G. M. Klijn[40], Alice J. Sigurdson[41], Michele M. Doody[41], Bruce H. Alexander[42], Jinghui Zhang[4], Angela Cox[43], Ian W. Brock[43], Gordon MacPherson[43], Malcolm W. R. Reed[44], Fergus J. Couch[45], Ellen L. Goode[45], Janet E. Olson[45], Hanne Meijers-Heijboer[46,47], Ans van den Ouweland[47], André Uitterlinden[48], Fernando Rivadeneira[48], Roger L. Milne[49], Gloria Ribas[49], Anna Gonzalez-Neira[49], Javier Benitez[49], John L. Hopper[50], Margaret McCredie[51], Melissa Southey[50], Graham G. Giles[52], Chris Schroen[53], Christina Justenhoven[54], Hiltrud Brauch[54], Ute Hamann[55], Yon-Dschun Ko[56], Amanda B. Spurdle[19], Jonathan Beesley[19], Xiaoqing Chen[19], kConFab[57]*, AOCS Management Group[19,57]*, Arto Mannermaa[58,59], Veli-Matti Kosma[58,59], Vesa Kataja[58,60], Jaana Hartikainen[58,59], Nicholas E. Day[5], David R. Cox[3] & Bruce A. J. Ponder[2,7]

Breast cancer exhibits familial aggregation, consistent with variation in genetic susceptibility to the disease. Known susceptibility genes account for less than 25% of the familial risk of breast cancer, and the residual genetic variance is likely to be due to variants conferring more moderate risks. To identify further susceptibility alleles, we conducted a two-stage genome-wide association study in 4,398 breast cancer cases and 4,316 controls, followed by a third stage in which 30 single nucleotide polymorphisms (SNPs) were tested for confirmation in 21,860 cases and 22,578 controls from 22 studies. We used 227,876 SNPs that were estimated to correlate with 77% of known common SNPs in Europeans at $r^2 > 0.5$. SNPs in five novel independent loci exhibited strong and consistent evidence of association with breast cancer ($P < 10^{-7}$). Four of these contain plausible causative genes (*FGFR2*, *TNRC9*, *MAP3K1* and *LSP1*). At the second stage, 1,792 SNPs were significant at the $P < 0.05$ level compared with an estimated 1,343 that would be expected by chance, indicating that many additional common susceptibility alleles may be identifiable by this approach.

Pequeños efectos de cada variante

Grandes estudios de asociación

Colaboración internacional

IMPaCT

THE PRECISION MEDICINE INITIATIVE

"Doctors have always recognized that every patient is unique, and doctors have always tried to tailor their treatments as best they can to individuals. You can match a blood transfusion to a blood type — that was an important discovery. What if matching a cancer cure to our genetic code was just as easy, just as standard? What if figuring out the right dose of medicine was as simple as taking our temperature?"

- President Obama, January 30, 2015

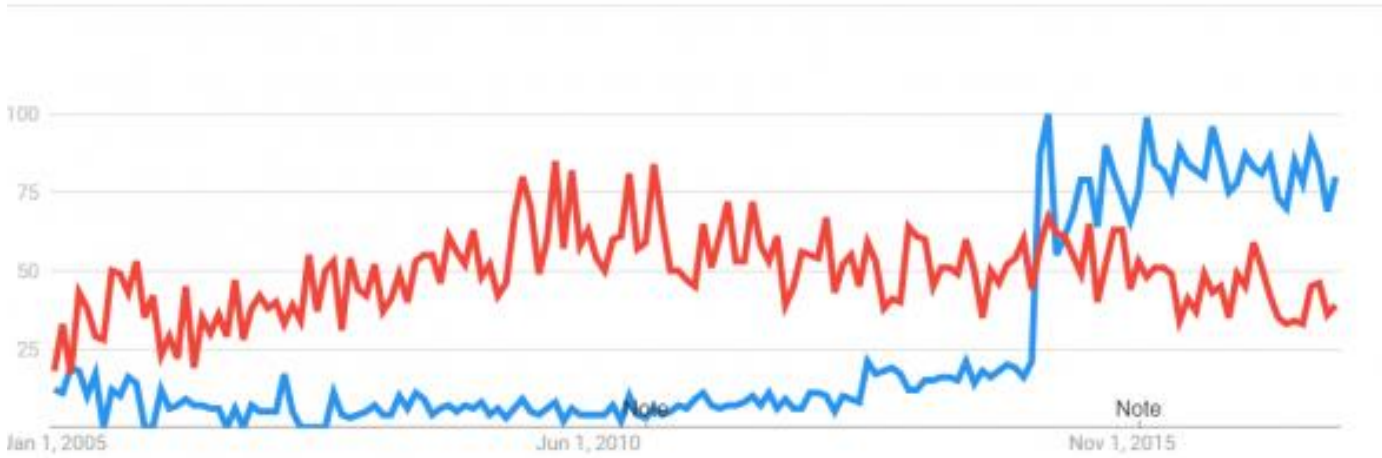
Medicina de Precisión:

Home / About Genomics / Talking Glossary of Genetic Terms / **Personalized Medicine**

NIH National Human Genome Research Institute

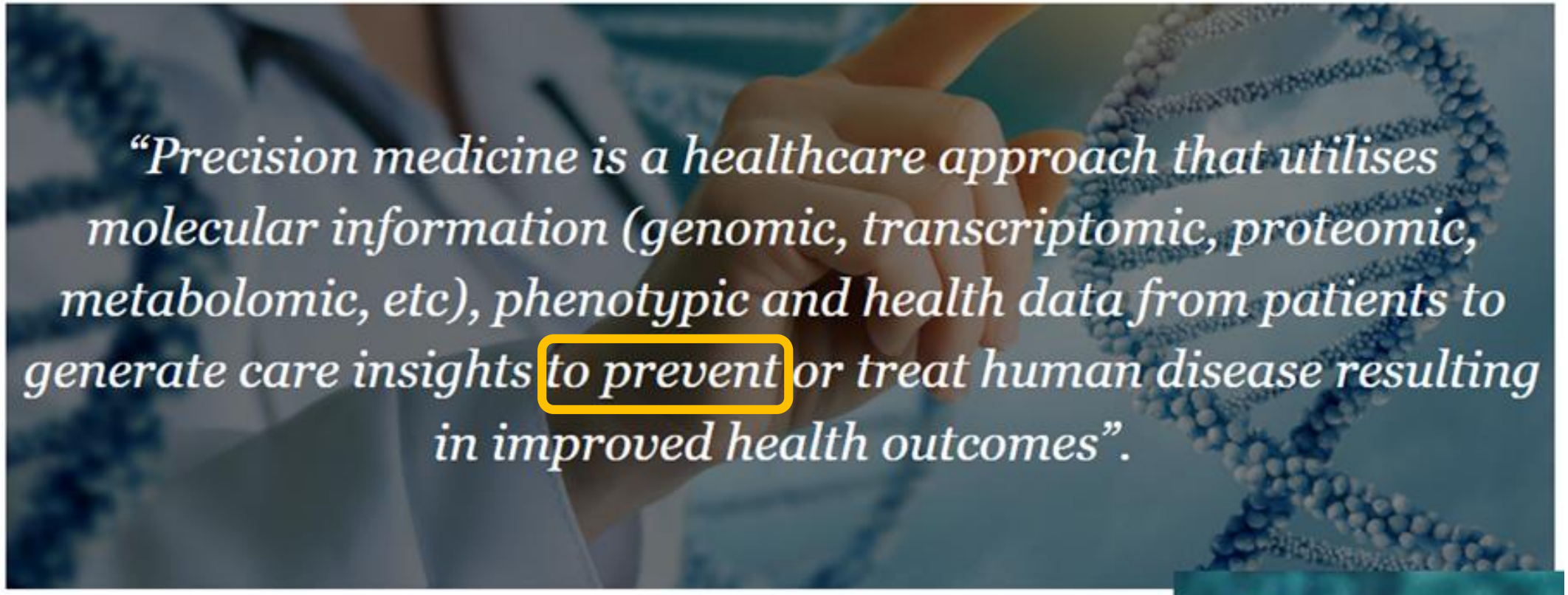
Personalized Medicine

Personalized medicine is an emerging practice of medicine that uses an individual's genetic profile to guide decisions made in regard to the prevention, diagnosis, and treatment of disease. Knowledge of a patient's genetic profile can help doctors select the proper medication or therapy and administer it using the proper dose or regimen. Personalized medicine is being advanced through data from the Human Genome Project.



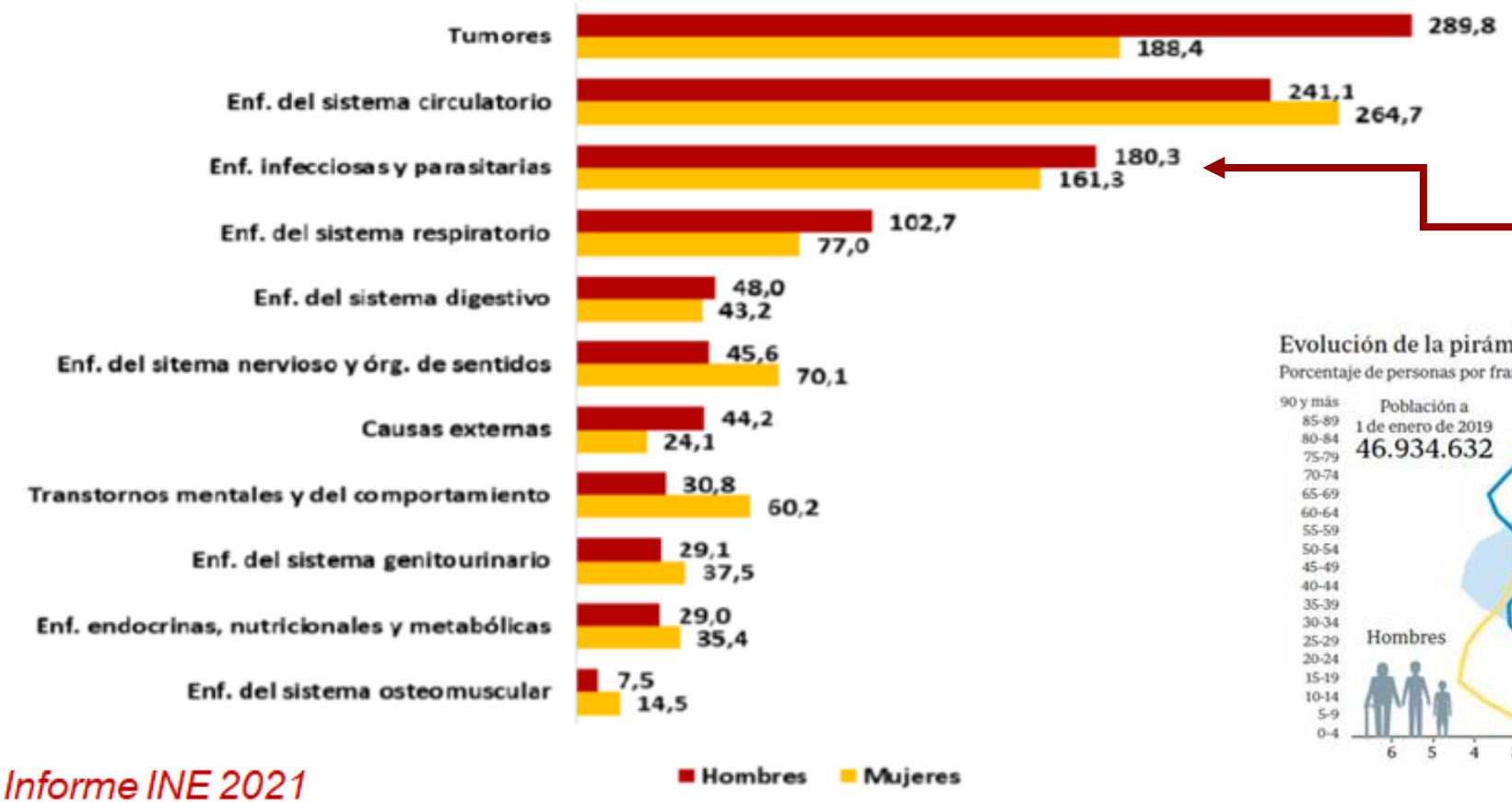
Searches through 2018 for "personalized medicine" are in red, while "precision medicine" results are in blue

Medicina de Precisión:



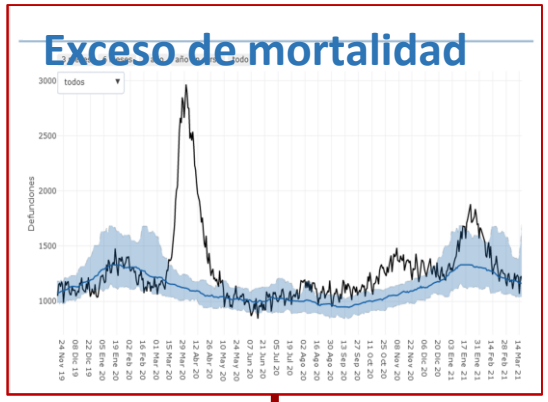
¿Y por qué incluir la prevención?

Defunciones según causa de muerte por capítulos de la CIE-10 y sexo. Año 2020
Tasas brutas por 100.000 habitantes

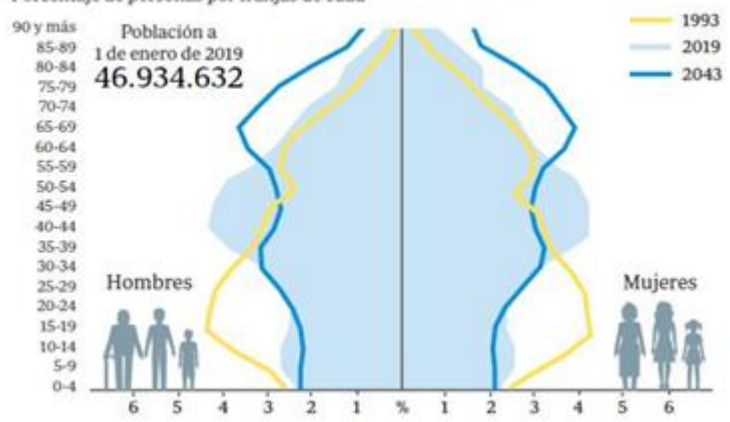


Informe INE 2021

Exceso de mortalidad



Evolución de la pirámide de población en España
Porcentaje de personas por franjas de edad



Publicado por ABC. Fuente: INE

Medicina Predictiva

nature portfolio

Predictive medicine is a branch of medicine that aims to identify patients at risk of developing a disease, thereby enabling either prevention or early treatment of that disease. Either single or more commonly multiple analyses are used to identify markers of future disposition to a disease.

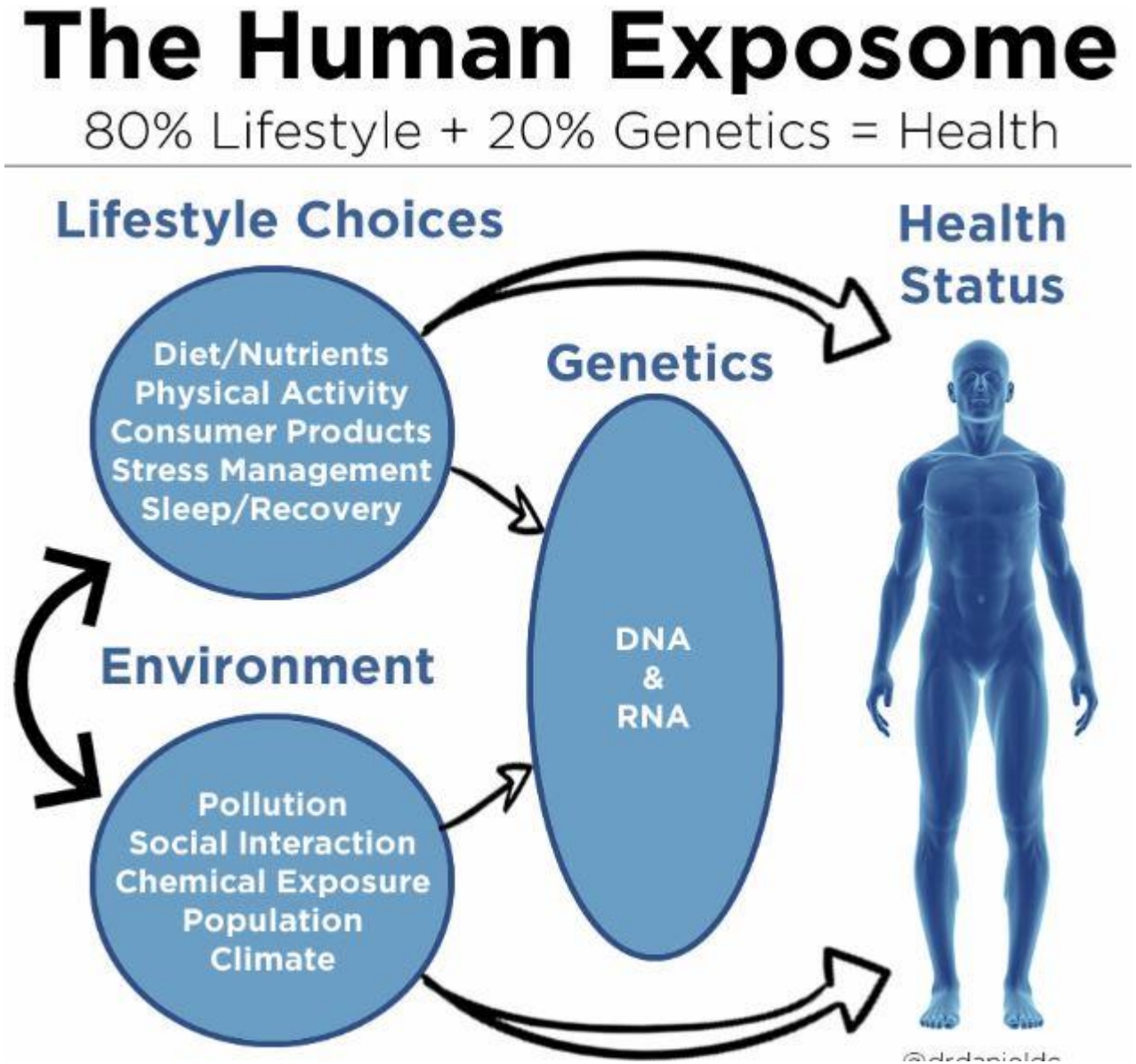
Predictive medicine

From Wikipedia, the free encyclopedia

Predictive medicine is a field of medicine that entails predicting the probability of disease and instituting preventive measures in order to either prevent the disease altogether or significantly decrease its impact upon the patient (such as by preventing mortality or limiting morbidity).[1]

While different prediction methodologies exist, such as genomics, proteomics, and cytomics, the most fundamental way to predict future disease is based on genetics. Although proteomics and cytomics allow for the early detection of disease, much of the time those detect biological markers that exist because a disease process has *already* started. However, comprehensive genetic testing (such as through the use of DNA arrays or full genome sequencing) allows for the estimation of disease risk years to decades before any disease even exists, or even whether a healthy fetus is at higher risk for developing a disease in adolescence or adulthood. Individuals who are more susceptible to disease in the future can be offered lifestyle advice or medication with the aim of preventing the predicted illness.

Pero los genes explican poco...

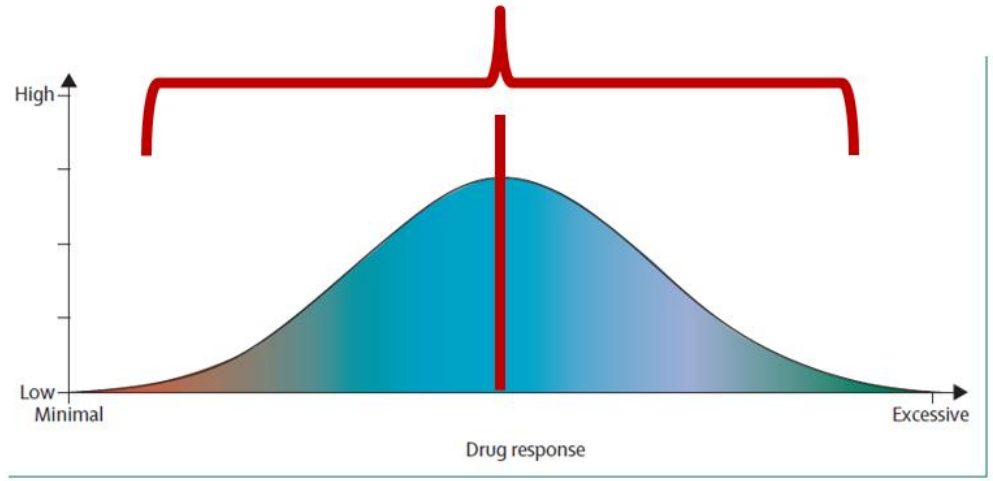


"Getting to the core of human exposome requires deep data on human environment and behavior"

Ville N Pimenoff

Karolinska Institute

Medicina Predictiva



Estimación

versus

Predicción

$$h_j(t/x_j) = h_0(t).\exp(\sum_i b_i x_{ij})$$

Predecir requiere:

- Gran tamaño muestral
- Posible sobre ajuste -> validación externa
- Calibración y validación en poblaciones diferentes
- Nuevas herramientas de análisis

Convocatoria IMPaCT

- Configurar una **infraestructura de servicios científico-técnicos** que vertebre y fortalezca las capacidades de I+D+I en Medicina de Precisión existentes y **facilite la implementación real de la Medicina de Precisión** en el SNS.

- Generar, a modo de reserva estratégica, **capacidad de análisis inmediato de datos, obtenidos en tiempo real**, que permita una respuesta coordinada e inmediata ante cualquier urgencia científica que afecte a la Salud Pública.

- **Orientar la investigación hacia los problemas de salud a través de la implementación real de la Medicina de Precisión** en el SNS.

- **Potenciar la participación y liderazgo de España** en proyectos, programas, plataformas e infraestructuras internacionales de I+D+I orientadas a **la Medicina de Precisión y la Ciencia de Datos.**

- **Fomentar la innovación** orientada a la implementación de la Medicina de Precisión como instrumento que **contribuye a la sostenibilidad y eficiencia** del SNS.

Funciones IMPaCT

EJE 1. MEDICINA PREDICTIVA – Aborda el diseño y establecimiento de una **cohorte de base poblacional representativa** de la población residente en España, su **variabilidad étnica, diversidad geográfica** y ambiental, con la **participación de todas las CC.AA**. y seguimiento prospectivo. Contribuir al diseño de estrategias de precisión y modelos predictivos en la prevención primaria, diagnóstico precoz y tratamiento temprano de las principales enfermedades.

EJE 2. CIENCIA DE DATOS – Se orienta al desarrollo y validación de un entorno de integración y análisis conjunto de datos, para el uso secundario de los datos clínicos, moleculares y genéticos, de forma coordinada con los ejes estratégicos 1 y 3. Generar un modelo que permita responder de forma eficiente a preguntas mediante modelos para orientado a generar conocimiento relevante para el SNS**.**

EJE 3. MEDICINA GENOMICA – Aborda el establecimiento de una infraestructura cooperativa distribuida de secuenciación de alta complejidad, orientada al diagnóstico de enfermedades, en las que el máximo esfuerzo disponible en el SNS no lo alcanza, atender las necesidades de la cohorte CIBER-SNS y cumplir los compromisos de secuenciación asumidos en “1M+ Million Genomes”

Cohorte IMPaCT: Antecedentes

Infraestructuras existentes en muchos de los países de nuestro entorno:

- UK Biobank
- All of US (EEUU)
- Francia: Constances
- Alemania: NAKO
- LifeGene (Suecia)

Experiencia reciente en nuestro país: ENE-COVID

Estudio Nacional de Sero-Epidemiología
ENE-COVID-19

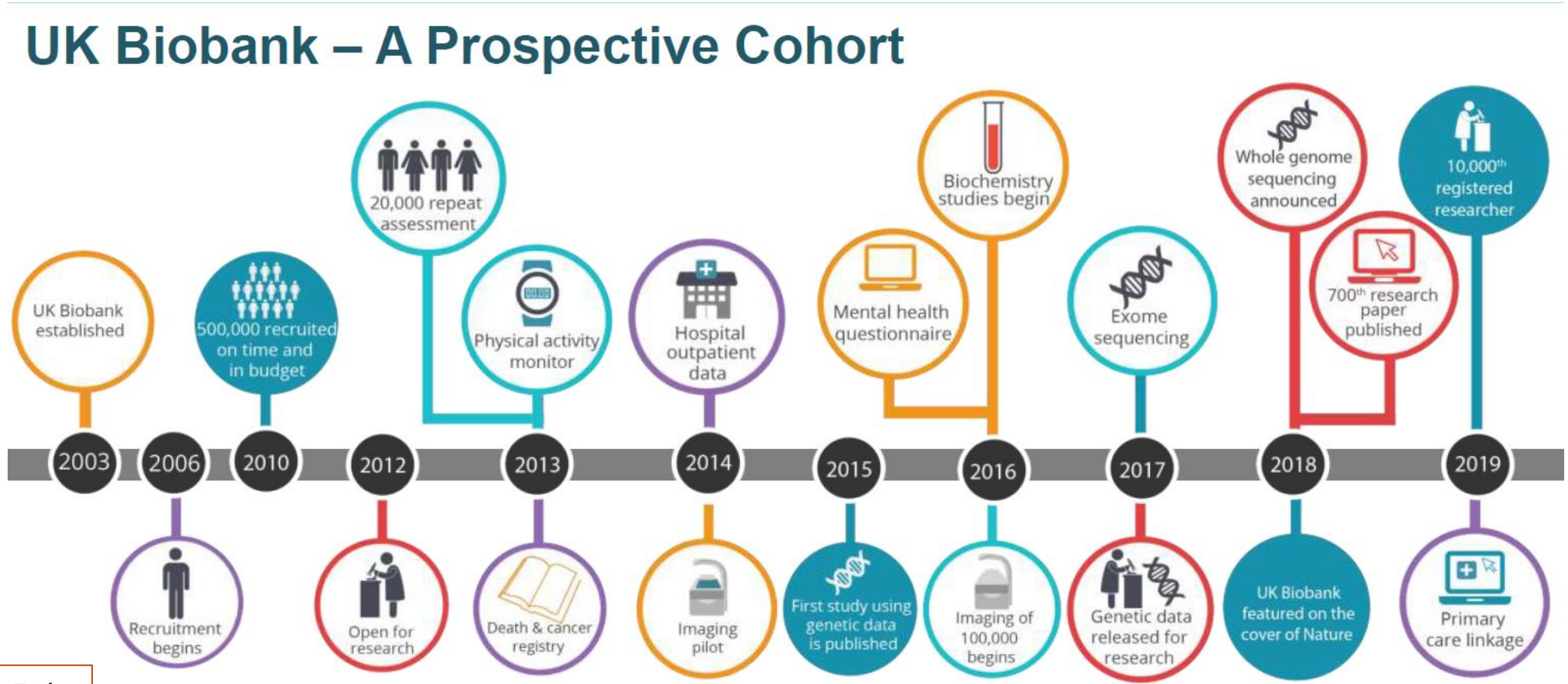
biobank uk

Improving the health of future generations

IMPaCT

UK Biobank is a large-scale biomedical database and research resource, containing in-depth genetic and health information from half a million UK participants. The database is regularly augmented with additional data and is globally accessible to approved researchers undertaking vital research into the most common and life-threatening diseases. It is a major contributor to the advancement of modern medicine and treatment and has enabled several scientific discoveries that improve human health.

500.000 participantes 40-69 años



Participation rate of 5.5%.

biobank uk

Improving the health of future generations

IMPaCT

biobank uk
Improving the health of future generations

IMPaCT

biobank uk

Nature
11 October 2018

nature
International journal of science

Article | OPEN | Published: 10 October 2018

The UK Biobank resource with deep phenotyping and genomic data

Clare Bycroft, Colin Freeman, Desislava Petkova, Gavin Band, Lloyd T. Elliott, Kevin Shar
Motyer, Damjan Vukcevic, Olivier Delaneau, Jared O'Connell, Adrian Cortes, Samantha
Young, Mark Effingham, Gil McVean, Stephen Leslie, Naomi Allen, Peter Donnelly & Jon
Marchini

Nature 562, 203–209 (2018) | Download Citation

Abstract

The UK Biobank project is a prospective cohort study
and phenotypic data collected on approximately 500,
from across the United Kingdom, aged between 40 a
recruitment. The open resource is unique in its size

UK Biobank adds the first tranche of data from a study into circulating metabolomic biomarkers to its biomedical database

March 22nd 2021

dataset 8,428 subjects). Here we show tha
imaging phenotypes
phenotypes are heritable. We identify 148 clusters of
ciations between single nucleotide polymorphisms and imaging
otypes that replicate at $P < 0.05$, when we would expect 21 to

"....The generosity of the United Kingdom in sharing this resource with the rest of the world is a shining example of the value of investing in the greater good."

NAKO Gesundheit studie

Special focus on occupational and environmental factors.

Cohort participants: Randomly selected sample of German adults aged 20–69 years at baseline

- Drawn from compulsory registries of residents in the study area

Aim: 200 000 participants (50% men/50% women)

main part of the overall budget. A total of 210 million Euros will be provided for the first 10 years of the project. This sum is complemented by considerable in-kind contributions of each of the recruitment centers.

Recruitment:

18 study centres (mainly urban/industrialized areas)
grouped into 8 clusters→10.000 x centre

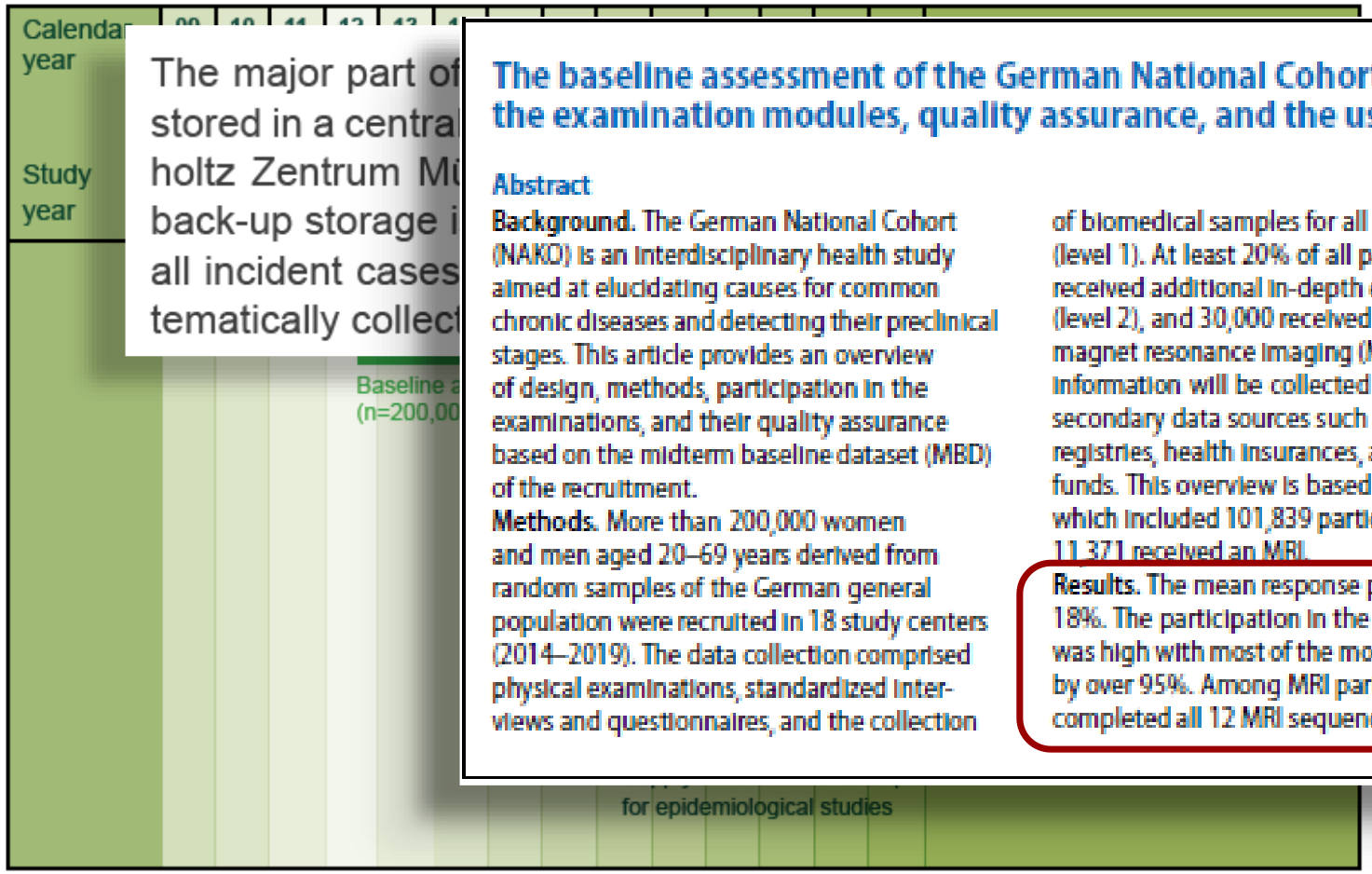
Estimated participation rate of 40-50%

A first outline of these plans was formally evaluated in April 2008 by an international review panel, in the context of a five-yearly scientific peer review of the Helmholtz Association. For the biomedical Helmholtz institutes, coordinated by the German Cancer Research Center [DKFZ] and Helmholtz Research Center München [HMGU], start-up funds at the level of 20 Mio Euro for the period 2009-2013 have been provided.

NAKO GESUNDHEITS-STUDIE

IMPaCT

The projected time schedule for the National Cohort covers a period of 25-30 years. However, the present application refers only to the first 10 years in which 5 years of baseline assessment will be followed by 5 years of re-assessment of the full cohort. Active follow-up by means of questionnaires is scheduled every 2-3 years. Use of data and material for epidemiological studies can start as soon as the baseline recruitment has been completed.



The major part of
stored in a centra
holtz Zentrum Mü
back-up storage i
all incident cases
tematically collect

The baseline assessment of the German National Cohort (NAKO Gesundheitsstudie): participation in the examination modules, quality assurance, and the use of secondary data

Abstract

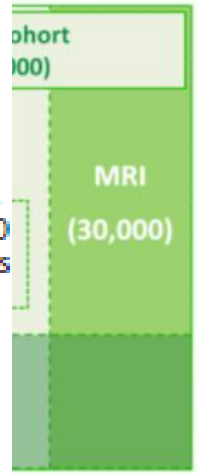
Background. The German National Cohort (NAKO) is an interdisciplinary health study aimed at elucidating causes for common chronic diseases and detecting their preclinical stages. This article provides an overview of design, methods, participation in the examinations, and their quality assurance based on the midterm baseline dataset (MBD) of the recruitment.

Methods. More than 200,000 women and men aged 20–69 years derived from random samples of the German general population were recruited in 18 study centers (2014–2019). The data collection comprised physical examinations, standardized interviews and questionnaires, and the collection of biomedical samples for all participants (level 1). At least 20% of all participants received additional in-depth examinations (level 2), and 30,000 received whole-body magnet resonance imaging (MRI). Additional information will be collected through secondary data sources such as medical registries, health insurances, and pension funds. This overview is based on the MBD, which included 101,839 participants, of whom 11,371 received an MRI.

Results. The mean response proportion was 18%. The participation in the examinations was high with most of the modules performed by over 95%. Among MRI participants, 96% completed all 12 MRI sequences. More than 90% of the participants agreed to the use of complementary secondary and registry data.

Discussion. Individuals selected for the NAKO were willing to participate in all examinations despite the time-consuming program. The NAKO provides a central resource for population-based epidemiologic research and will contribute to developing innovative strategies for prevention, screening and prediction of chronic diseases.

Bundesgesundheitsbl
https://doi.org/10.1007/s00103-020-03093-z



: 2,5 h

4 h

earch projects,

- MRI program, n=30.000, at 5 sites

Constances (Francia)

Special focus on occupational and environmental factors.

Cohort participants: Randomly selected sample of French adults aged 18–69 years at inception

- stratified on age, gender, socio-economic status (SES) and region of France
- restricted to persons living in one of the 20 CONSTANCES 'départements'
- affiliated to the National Health Insurance Fund →salaried workers (including active, retired & unemployed) & their families (85% French population)

Aim: 200 000 participants

Control of selection effects: To take into account non-participation and attrition, a random cohort of non-participants was set up and will be followed through the same national databases as participants.

Recruitment:

22 selected health screening centres (HSCs)located in 20 'départements' in the principal regions of France.

Participation rate of 7.3%.

Follow-up questionnaire : 80%

CONSTANCES

https://oem.bmj.com/content/oemed/74/1/66.full.pdf

Constances (Francia)

CONSTANCES

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CONSTANCES ASSETS

Due to its population size, the quality and diversity of data, and its monitoring methods, Constances is a **unique epidemiological research tool**. Constances, is a research platform broadly accessible to the scientific community that can be compared to the largest international cohorts.

Constances is also a **public health tool**, designed to support the public health objectives of the French National Health Insurance Fund for Employees (CNAMTS) and of the national government, owing to the collection of highly diverse data from multiple sources on a representative sample.

Constances is an **epidemiological surveillance tool**, implemented through a partnership with the French institute for public health surveillance. Its data covers multiple domains, such as the epidemiological surveillance of occupational hazards.

The Constances project, managed through the participation of French local health insurance funds and health clinics, is a partnership between INSERM, Versailles Saint Quentin University (UVSQ), the French national health insurance fund (CNAMTS), the French national retirement pension fund (Cnav) and the support of the French Ministry of health (Directorate general for health). Constances has received French government funding for an 8-year period (Investment for the Future Program).

Constances has received French government funding for an 8-year period (Investment for the Future

LifeGene

IMPaCT

LifeGene

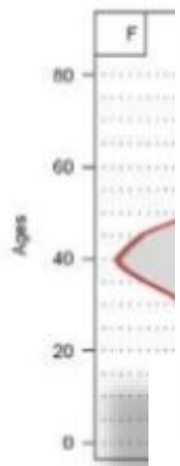
Targ

LifeGene is both a cohort and an infr

LifeGene

Cohort

- Index persons 18-45 years (random sample)
- Adult members of the household
- Their children (1/2 of the households)
- Twins as index persons



Infrastructure

- High throughput biobanking
- In person testing centers
- IT and data management system

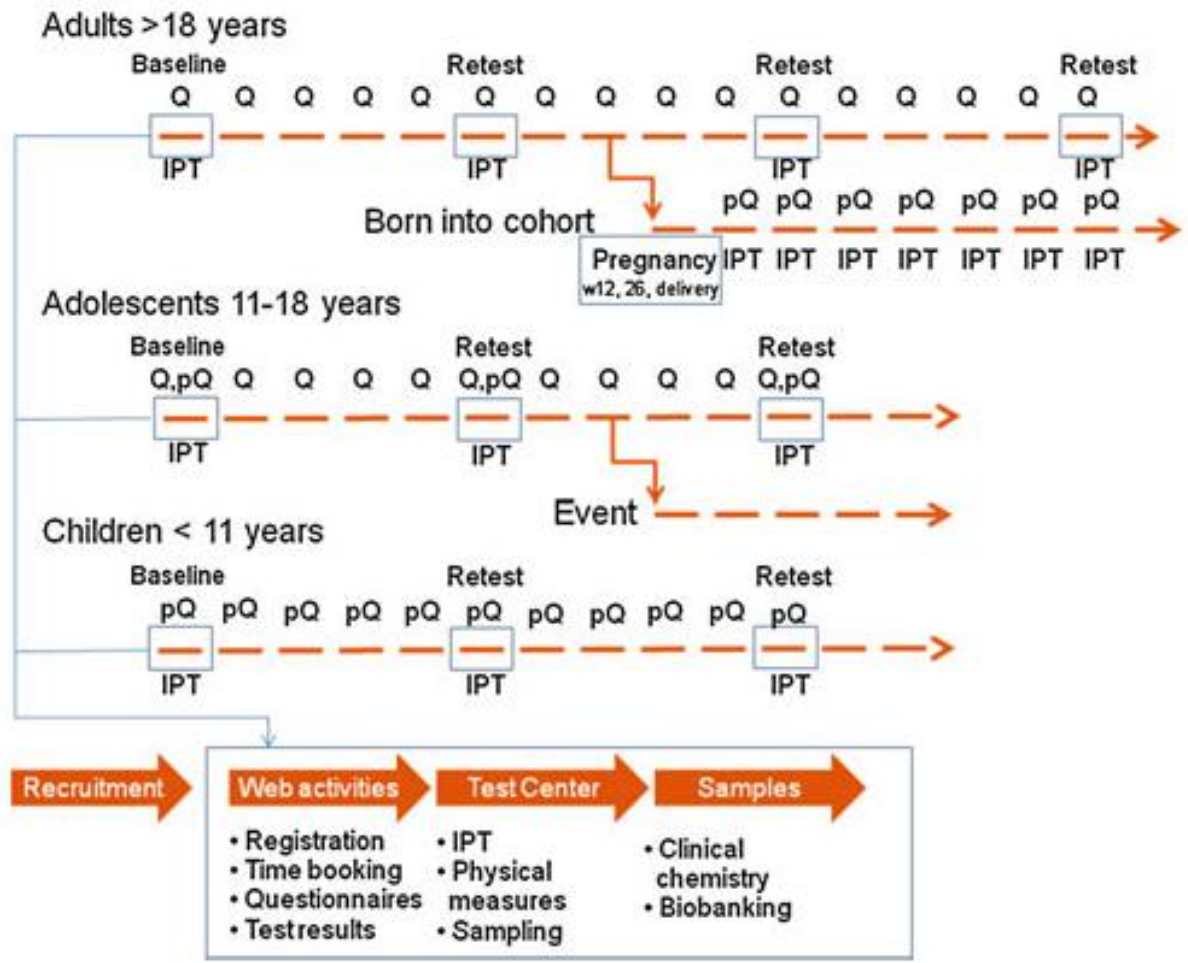


Fig. 1 Flow chart on the structure of the study. Questionnaires (Q), parental questionnaires (pQ) and In Person Testing (IPT) in adults, adolescents and children

https://lifegene.se/for-scientists/about-lifegene/

LifeGene

ABOUT US | ABOUT HARMONIZATION | WHAT WE OFFER | PARTNERSHIPS | CONTACT US | MAELSTROM CATALOGUE

IMPaCT

LifeGene Project

LifeGene

The objectiv
Study featur

- Ascer
- Repea
- Linka
- Collec
- Collec

Sources of Recruitment

General Population	Volunteer enrolment Selected sample
Supplementary Information	Index participants were randomly sampled from the general population from the supplier of addresses; SPAR or Skatteverket. Other persons interested in participating have the possibility to spontaneously register from the LifeGene website.

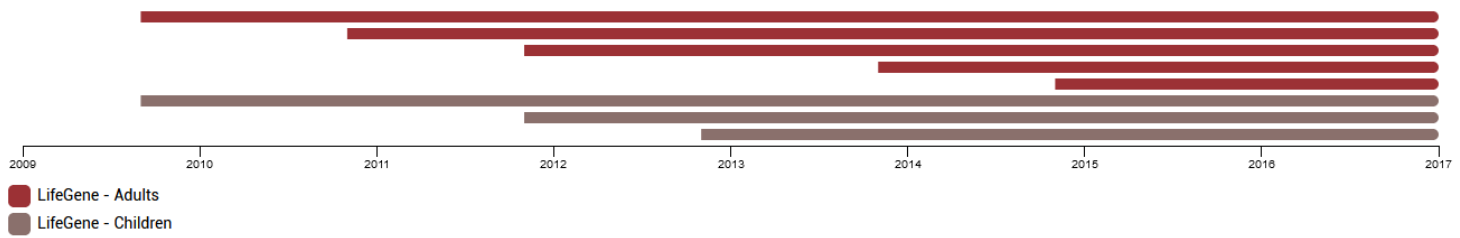
Overview

Acronym	LifeGene	
Website	LifeGene	
Investigators	Prof. Nancy Pedersen Karolinska Institutet	
Contacts	Prof. Nancy Pedersen Karolinska Institutet	Kicki Kjaergaard Karolinska Institutet

General Design

Study design	Cohort
Start Year	2009
General Information on Follow Up (profile, frequency)	Following baseline, participants and their family are prompted annually to respond a short, web-based questionnaire.
Recruitment Target	Individuals Families
Number of Participants	100,000
Number of Participants with Biological Samples	50,000

Timeline



Last Update: February 5, 2020

All of Us℠ The Precision Medicine Initiative

THE FUTURE OF HEALTH BEGINS WITH YOU

The future of health begins with you.

The *All of Us* Research Program is inviting one million people across the U.S. to help build one of the most diverse health databases in history. We welcome participants from all backgrounds. Researchers will use the data to learn how our biology, lifestyle, and environment affect health. This may one day help them find ways to treat and prevent disease.

JOIN NOW!

Launched with a **$215 million** investment in the Presiden

The Precision Medicine Initiative Cohort Program – Building a Research Foundation for 21st Century Medicine

Precision Medicine Initiative (PMI) Working Group Report to the Advisory Committee to the Director, NIH

September 17, 2015

Key Investments to La

Complementing robust ir
will provide a $215 millio
Administration (FDA), and
effort, including:

What Will Participants Do?

When you join the *All of Us* Research Program, you will be asked to enroll, give consent, and agree to share health records. You can do this online, or at one of our partner centers.

If you take part, you will be asked to complete health surveys. You may be asked for physical measurements and biosamples (blood and urine samples).

You may be invited to share more data in the future, through additional health surveys, health trackers, or other research studies.

- $130 million to NIH fo
  our understanding of health and disease and set the foundation for a new way of doing research through engaged participants and open, responsible data sharing.
- $70 million to the **National Cancer Institute (NCI), part of NIH, to scale up efforts to identify genomic drivers in cance**r and apply that knowledge in the development of more effective approaches to cancer treatment.
- $10 million to FDA to acquire additional expertise and advance the **development of high quality, curated databases to support the regulatory structure** needed to advance innovation in precision medicine and protect public health.
- $5 million to ONC to support the development of **interoperability standards and requirements** that address privacy and enable secure exchange of data across systems.

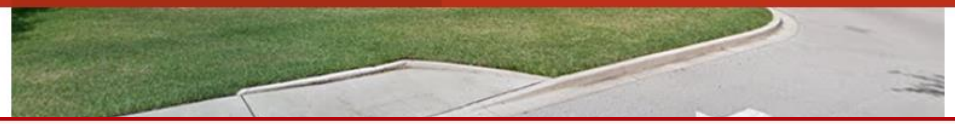
Source: https://obamawhitehouse.archives.gov/the-press-office/2015/01/30/fact-sheet-president-obama-s-precision-medicine-initiative

All of Us℠ The Precision Medicine Initiative®
THE FUTURE OF HEALTH BEGINS WITH YOU

IMPaCT

Healthcare IT News

GLOBAL EDITION TOPICS SIGN UP MAIN MENU



national biobank, run by the Mayo Clinic, where 35 blood and urine samples from each participant will one day be stored. To prepare for the national launch, Mayo doubled the size of its 35,000-square-foot facility in Minnesota and expanded a smaller bank in Florida, as a backup site to protect samples from any localized natural disasters.

Mayo Clinic will store 35 samples from each participant at the All of Us Research Program biobank at Mayo Clinic. The samples add up to 35 million biospecimens.

35 millones de muestras

All of Us℠ The Precision Medicine Initiative
THE FUTURE OF HEALTH BEGINS WITH YOU

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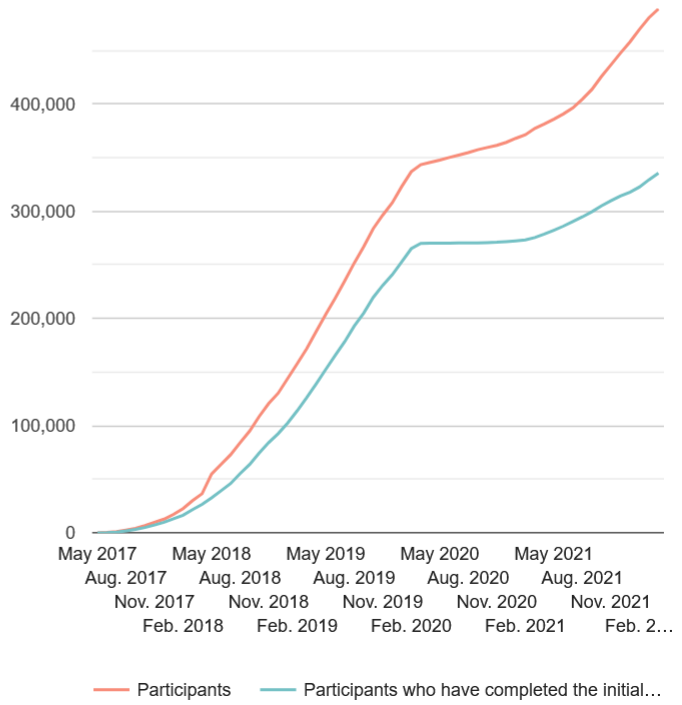
489,000+
Participants

335,000+
Participants who have completed initial steps of the program

Enrollment Numbers

This graph represents participants who have consented to join the program and those who have completed all initial steps of the program. The initial steps are consenting, agreeing to share electronic health records, completing the first three surveys, providing physical measurements, and donating at least one biospecimen to be stored at the biobank.

The following numbers are approximated to protect participants' privacy. Numbers are updated as of May 3, 2022.



https://www.researchallofus.org/data-tools/data-snapshots/

Table 1. Data Available to Researchers from the All of Us Cohort.*

Data Source	Details
Current sources	
Health surveys	Initial surveys include information on sociodemographic characteristics, overall health, lifestyle, and substance use, with subsequent modules covering personal and family medical history and access to health care.
Physical measurements	Per-protocol measurements include blood pressure, heart rate, weight, height, body-mass index, and hip and waist circumferences.
Biospecimens†	Blood and urine samples are tested for DNA, RNA, cell-free DNA, serum, and plasma. If blood specimens cannot be obtained, saliva specimens are obtained.
Electronic health records	Initial capture of structured data includes billing codes, medication history, laboratory results, vital signs, and encounter records from health care provider organizations. Records will be expanded to include narrative documents. Pilot studies are testing data collection through Sync for Science and other health data aggregators.
Digital health information	Data can be captured from compatible participant-owned devices such as Fitbit. Pilot studies of other devices and linkage to health apps are being explored.
Future sources	
Health surveys	Additional modules, including surveys regarding social behavioral determinants of health, are under development.
Bioassays	Pilot studies for genotyping and whole-genome sequencing are expected to begin by early 2020. Additional pilot studies of bioassays are planned.
Health care claims data	Systems for the use of claims data, including billing codes and medication data, are under development.
Geospatial and environmental data	These data include geospatial linkage to measures such as weather, air quality, pollutant levels, and census data. Assays and sensor-based measurements of exposure are under consideration.
Other sources	Voluntary contributions of data from social networks (e.g., Twitter feeds) and additional biospecimen collections are under consideration.

The All of Us Research Program NEJM 2019

ENE-COVID

Estudio Nacional de sero-Epidemiología de la infección por SARS-CoV-2 en España (ENECOVID)

https://portalcne.isciii.es/enecovid19/

ENE-COVID

IMPaCT

Formación

> 2.600 profesionales consultando y descargando protocolos desde la plataforma de formación

Protocolos

Necesidad de simplificar el proceso y especificar cada paso

Laboratorios

28 laboratorios de microbiología coordinados por el Centro Nacional de Microbiología, con el mismo equipamiento para las pruebas serológicas

Coordinación

17 CCAA y **2** ciudades autónomas

Logística

Envío del material necesario a **> 1.400 centros de salud** en todo el país

Sistema de Information único

Dando soporte a **más de 4.400 usuarios** e incorporando cambios y mejoras durante el proceso

Soporte Legal & Consideraciones Éticas

Acuerdo Ministerio de Sanidad - Instituto de Salud Carlos III, Instituto Nacional de Estadística y aprobación del Consejo Inter-territorial

Revisado por el Comité de Ética del ISCIII

Funciones IMPaCT

EJE 1. MEDICINA PREDICTIVA – Aborda el diseño y establecimiento de una **cohorte de base poblacional representativa** de la población residente en España, su **variabilidad étnica, diversidad geográfica** y ambiental, con la **participación de todas las CC.AA**. y seguimiento prospectivo. Contribuir al diseño de estrategias de precisión y modelos predictivos en la prevención primaria, diagnóstico precoz y tratamiento temprano de las principales enfermedades.

EJE 2. CIENCIA DE DATOS – Se orienta al desarrollo y validación de un entorno de integración y análisis conjunto de datos, para el uso secundario de los datos clínicos, moleculares y genéticos, de forma coordinada con los ejes estratégicos 1 y 3. Generar un modelo que permita responder de forma eficiente a preguntas mediante modelos para orientado a generar conocimiento relevante para el SNS**.**

EJE 3. MEDICINA GENOMICA – Aborda el establecimiento de una infraestructura cooperativa distribuida de secuenciación de alta complejidad, orientada al diagnóstico de enfermedades, en las que el máximo esfuerzo disponible en el SNS no lo alcanza, atender las necesidades de la cohorte CIBER-SNS y cumplir los compromisos de secuenciación asumidos en “1M+ Million Genomes”

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Plan Estratégico IMPaCT

El Plan Estratégico de IMPaCT se configura en torno a tres ejes estratégicos y dos líneas estratégicas transversales. Los ejes estratégicos responden a cada uno de los tres programas y, a su vez, se disponen en acciones y paquetes de trabajo específicos, con indicadores de cumplimiento que deberán permitir comprobar la efectividad del despliegue de la infraestructura. De forma complementaria, las dos líneas estratégicas transversales permiten aportar coherencia interna a aquellos aspectos tales como la ética de los datos y la internacionalización de la plataforma, que son comunes a los tres ejes estratégicos.

OBJETIVOS Cohorte IMPaCT

Establecimiento de una cohorte de **200,000 personas** representativas de la población española con implantación en todo el territorio e integrada en el SNS.

1) Mejorar la comprensión de **las causas de las principales enfermedades y condiciones de salud**, incluidos el deterioro funcional asociado a la edad, las lesiones y la discapacidad.

2) **Monitorizar el estado de salud** de los residentes en España, con especial atención a las desigualdades en salud (**salud pública de precisión**)

3) **Predecir el riesgo de enfermedad** y de otras condiciones de salud, incluidos el deterioro funcional asociado a la edad, las lesiones y la discapacidad (**medicina preventiva de precisión**)

4) **Identificar biomarcadores de enfermedad subclínica o en fases iniciales**, así como biomarcadores de fenotipos específicos útiles en clínicas (**medicina clínica de precisión**)

INSTITUCIONES IMPLICADAS

Entidad solicitante: CIBER

- Coordinación desde el área transversal CIBERESP
- Aportación específica de cada una de las áreas CIBER

Entidades colaboradoras:

- Servicio de Salud (AP) de todas las CCAA y Ciudades Autónomas
- Instituto Nacional de Estadística (INE)

PAQUETES DE TRABAJO

- WP-1: **Coordinación**
- WP-2: **Diseño** y estrategia de reclutamiento y selección
- WP-3: Definición y **medida de las variables de interés**
- WP-4: **Muestras biológicas**
- WP-5: **Seguimiento activo** y fidelización
- WP-6: Metodología y análisis: Plan de **análisis estadístico**
- WP-7: **Gestión de datos** y **control de calidad**
- WP-8: **Aspectos éticos y legales**
- WP-9: Logística y **trabajo de campo**
- WP-10: **Enlace de registros (linkage)** con información existente
- WP-11: **Comunicación**

GOBERNANZA

IMPaCT

Coordinación Programa IMPaCT

Comité Científico Asesor Externo

Comité Científico Asesor Interno

Representantes de todas las áreas CIBER

Investigadora Principal

Comité Ejecutivo

Comité de Participación Operativa

Dirección de Gestión del Programa

Comité de ética

Entidad solicitante

ciber

Centro de Investigación Biomédica en Red

Entidades colaboradoras

INE

Instituto Nacional de Estadística

Servicios de Salud

Puesta a punto

Diseño de selección y reclutamiento

Diseño de seguimiento y estrategias de adherencia

Estrategia de comunicación

Examen de salud

Cuestionarios

Pruebas complementarias

Muestras biológicas

Monitores personales

APPs

Fuentes complementarias

Trabajo de Campo

Call center

Centros de salud

Exploraciones complementarias

Plan de análisis de datos

Plan de difusión de resultados y acceso de datos

Plataforma de información

Biobanco

Linkage de datos clínicos y no clínicos

Comité Ejecutivo (Programa 1)

IMPaCT

CIBER de Epidemiología y Salud Pública

- Marina Pollán
- Fernando Rodríguez Artalejo
- Beatriz Pérez Gómez
- Miguel Delgado
- Manolis Kogevinas
- Jordi Alonso

Otras áreas CIBER

- Miguel Ángel Martínez (CIBEROBN)

Sistema Nacional de Salud

- Isabel del Cura (Madrid)
- Maria José Sánchez (Andalucía)
- Oscar Zurriaga (Comunidad Valenciana)
- Sinda Blanco (Galicia)
- Itziar Vergara (País Vasco)












Grupo de diseño

COORDINATION

Miguel A. Martínez-González, Univ. Navarra, HSPH, CIBEROBN
Beatriz Pérez Gómez, Centro Nacional de Epidemiología-ISCIII, CIBERESP

CIBERESP

Roberto Pastor Barriuso, Centro Nacional de Epidemiología-ISCIII, MADRID
Miguel Delgado-Rodríguez, Univ. Jaén, ANDALUCÍA
Victor Moreno, IDIBELL, I. Catalán Oncología, Univ. Barcelona, CATALUÑA
Mònica Guxens, ISGLOBAL, INMA cohort, Erasmus University, CATALUÑA

CONTRIBUTING ENTITITIES

NHS

Isabel del Cura, Salud Madrid-Investigación APS, REDISSEC, Univ. Rey Juan Carlos. MADRID
Itziar Vergara, Osakidetza-Invest. APS, Biodonostia, REDISSEC. PAÍS VASCO
Francisco Gude, IDIS, Hospital Univ. Santiago, Univ. Santiago Compostela. GALICIA
Joan Llobera, IB-Salut Investigación APS, IdiSBa, redIAPP. BALEARES
María José Sánchez-Pérez, EASP, EPIC, ibs.Granada, Univ. Granada, CIBERESP. ANDALUCÍA

National Institute of Statistics

Carlos Ballano, Instituto Nacional de Estadística. MADRID

OTHER CIBERS

Gemma Rojo-Martínez, IBIMA, Hosp. Regional Universitario Málaga, CIBERDEM

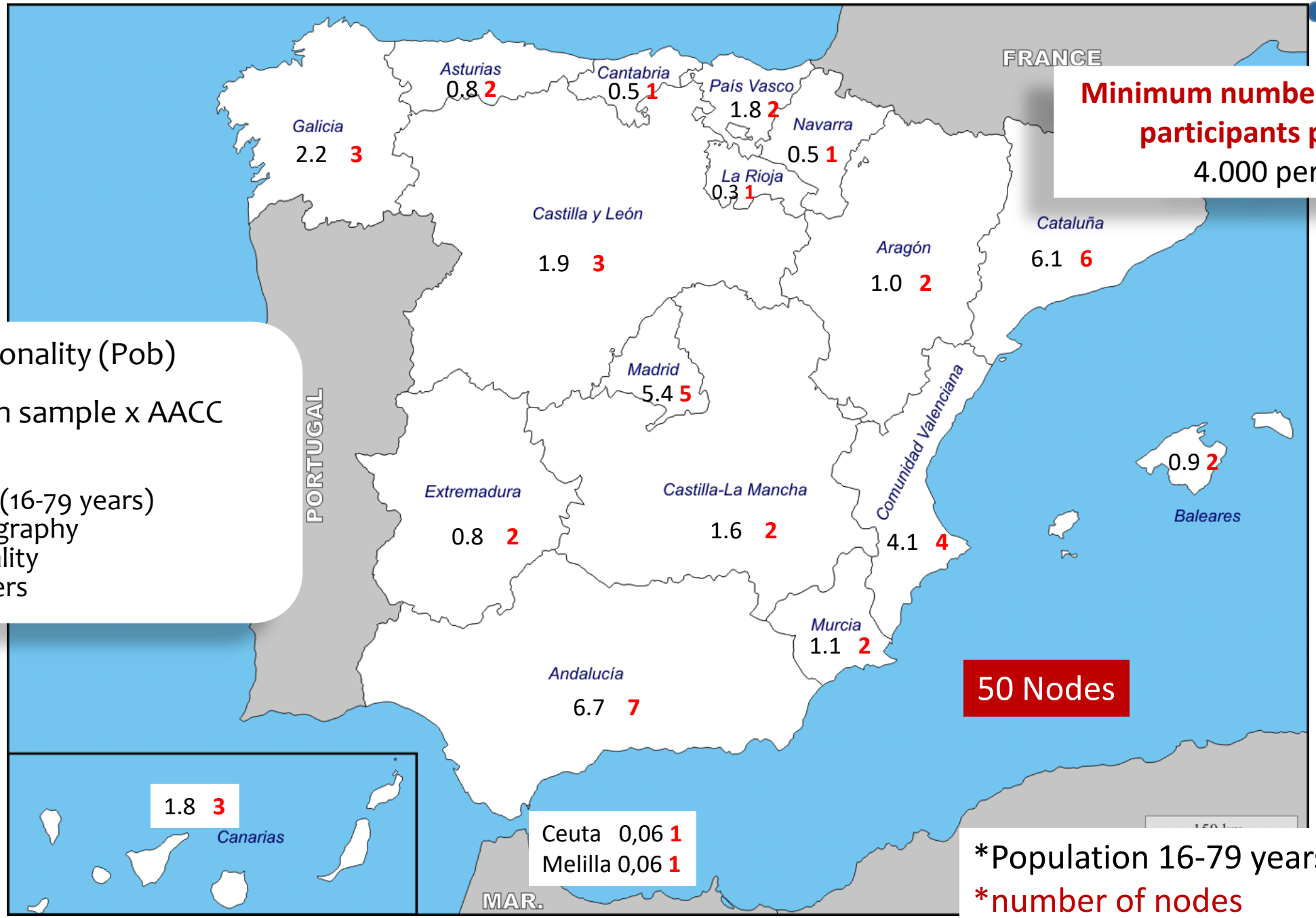
Secretary *(adjunct to MA M-G):* ***Nerea Martín-Calvo****, Univ. Navarra, CIBEROBN*

PROGRAMA DE MEDICINA PREDICTIVA

Cohorte IMPaCT

Protocolo 1. Diseño del estudio

ciber isciii



Minimum number of expected participants per AACC

4.000 persons

- Proporcionality (Pob)
- Minimum sample x AACC
- Diversity
  - Age (16-79 years)
  - Geography
  - Rurality
  - Others

*Population 16-79 years (in millions)

*number of nodes

AACC

IMPaCT at regional level

Support

Information system
Primary care management

IMPaCT Coordination

IMPaCT

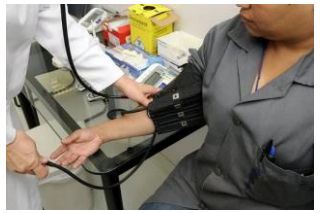
Regional IP+ IMPaCT support

Node 1	Node 2	Node 3
50.000 pp	50.000 pp	50.000 pp
Local team	**Local team**	**Local team**

IMPaCT Center	IMPaCT Center	IMPaCT Center
		
 4.000	 4.000	 4.000

Grupo de trabajo: cuestionarios y exploración física

Fernando Rodríguez-Artalejo
Manolis Kogevinas

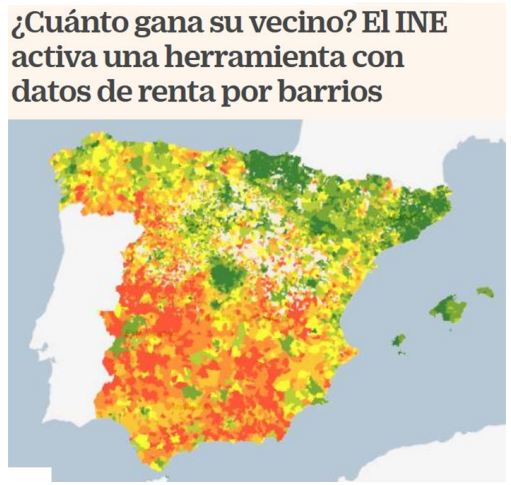


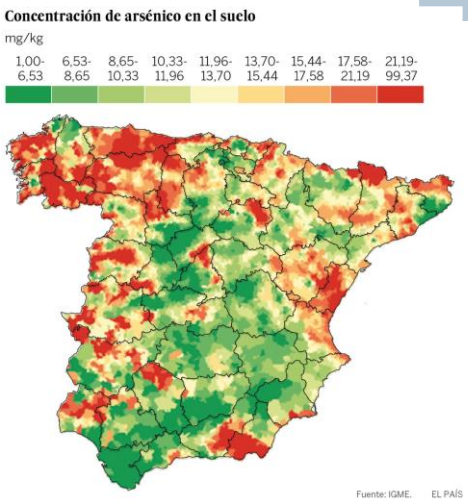
… & more than 60 CIBER & CCAA researchers (with their teams)!!!

Health dimensions to be initially assessed in the IMPaCT cohort		
Basic questionnaire	**Specific questionnaires**	**Physical exam**
Affiliation data	Neurological and psychiatric factors	Cardiovascular system
Demographic variables	Psychosocial factors	Diabetes (glucose tolerance)
Socio-economic level, social class	Immune status and past infections	Cognitive function
Personal medical history	Chronic pain	Lung function
Family medical history	Oral health	Musculoskeletal system
Medication of the last 7 days	Functioning of the sense organs	Oral health
Participation in preventive programmes	Physical activity, sedentary lifestyle	Ophthalmological examination
Sexual and reproductive health	Diet & nutrition	Hearing
Tobacco use & passive exposure	Factors of the built environment	Smell
Alcohol consumption patterns	Characteristics of the house	Physical activity and function
Use of other drugs	Characteristics of the neighborhood	Anthropometry
Addictions	Barriers to healthy lifestyles	
Health-related quality of life	Occupation	
Disability	Use of health services	
(daily life instrumental & basic activities ≥ 60 years of age).	Ionizing & non-ionizing radiation	
	Exposure to water	

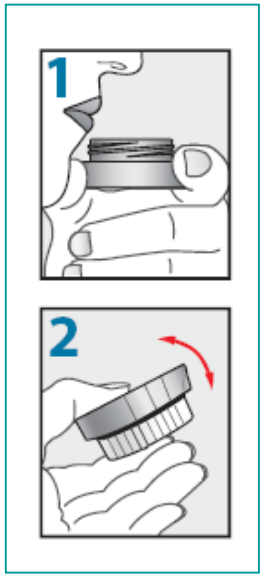
Información contextual

- Nivel de renta
- Contaminación ambiental
- Ruido
- Tráfico
- Radiación solar
- Radiación ionizante natural
- Densidad de población
- Cercanía a industrias contaminates

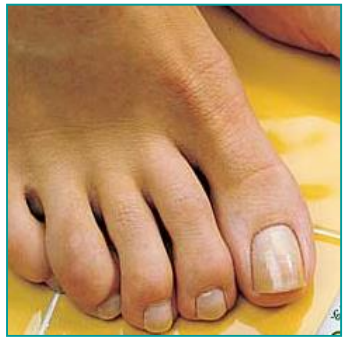




Grupo de muestras biológicas



- Cristina Villena (CIBERES)
- Javier Llorca (CIBERESP)
- Eva Bermejo (Biobanco ISCIII)
- Nerea Fernández de Larrea (CIBERESP & CT Biobanco ISCIII)
- Cristina Razquín Burillo (CIBEROBN)
- Mª Jesús Pareja (Andalucía)
- Jacobo Martínez Santamaría (Comunidad Valenciana)
- Beatriz Sobrino (Galicia: Programa Genómica)
- Silvia Calabuig (CIBERONC)
- Ady Castro (IMPaCT)



- Protocolo de recogida
- Preprocesamiento
- Alicuotado
- Etiquetado
- Almacenamiento
- Transporte
- Trazabilidad y control de calidad

GT: Recuperación de información clínica

- **Boni Bolivar (Cataluña)**
- **Ana Clavería (Galicia)**

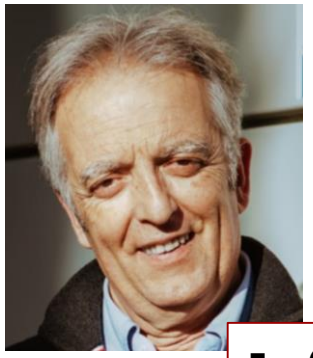
Andalucía	Román Villegas
Madrid	Pablo Serrano
Valencia	Oscar Zurriaga
Baleares	Oana Buliliete
Euskadi	Alvaro Sánchez
Castilla y León	César Alameda González

Secretaria	*Maria Aragón (Cataluña)*

- Información a recoger de la historia clínica
- Requerimientos clínicos

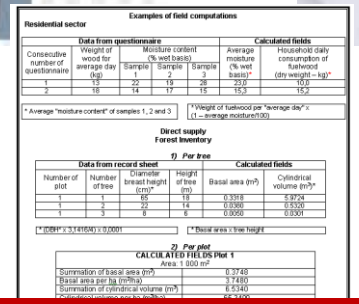
GT Estudio Piloto

- **Isabel del Cura (Madrid)**
- **Joan Llobera (Baleares)**
- Ignacio Párraga (Castilla la Mancha)
- Itziar Vergara (País Vasco)
- Carmen Chaverri (Aragón)
- Ana Garzón Sánchez (apoyo Madrid)
- Cristina Villena (Responsable Grupo Muestras Biológicas)



- Characteristics of IMPaCT centers
- Invitation and registration of participants
- Flow-chart of the basal visit
- Tracking the process

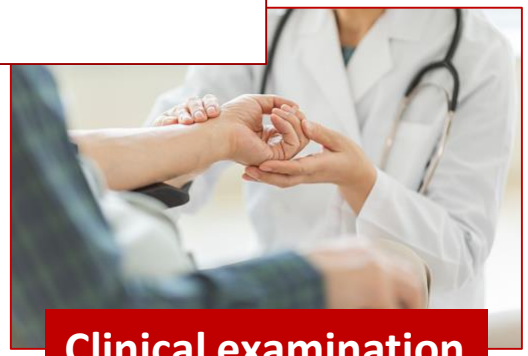
Invitation



Basal quiestionnaire

Blood extraction

Other samples

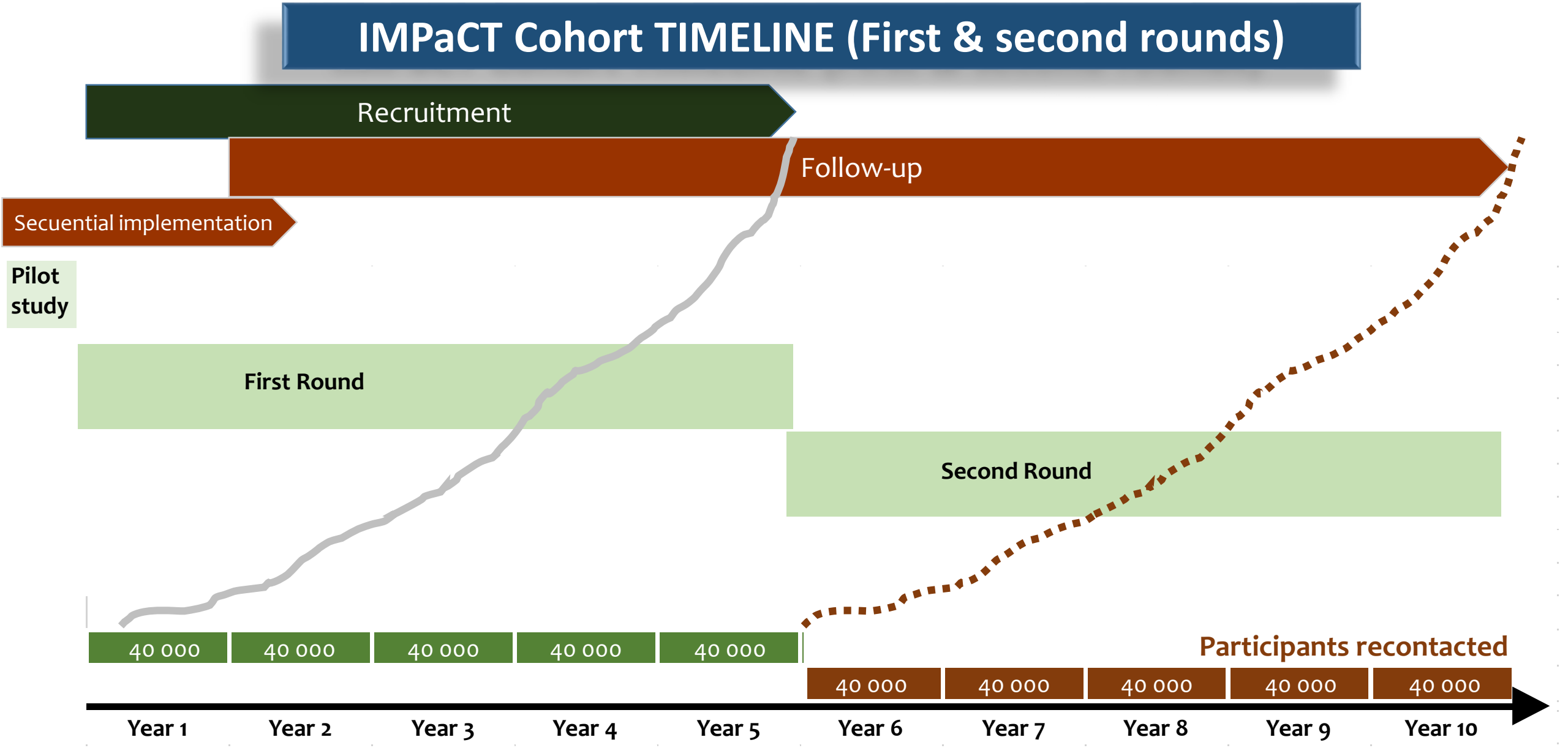


Clinical examination

Sample processing

Other questionnaire

COHORTE IMPaCT



COHORTE IMPaCT

Roberto Pastor Barriuso

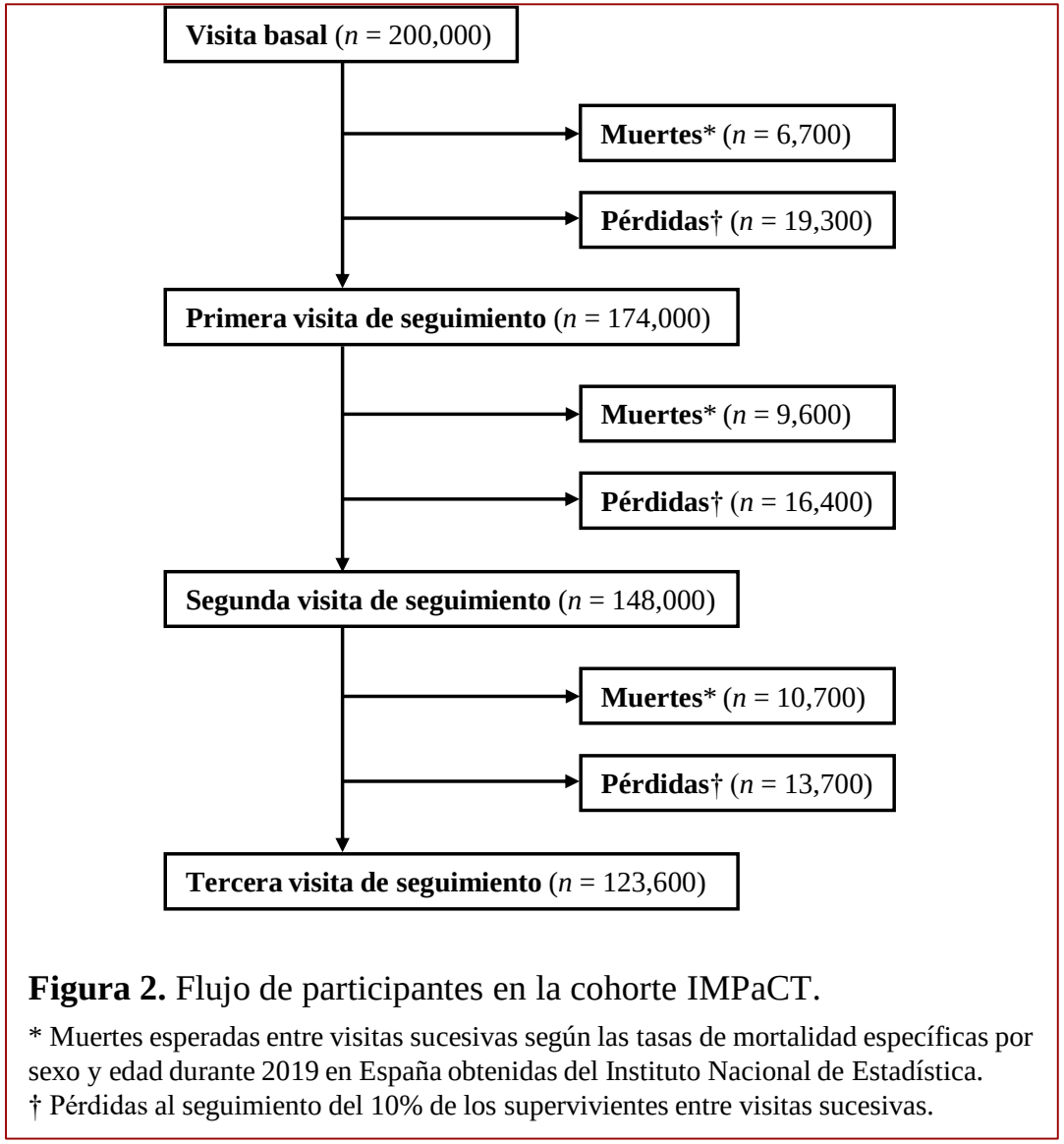


Figura 2. Flujo de participantes en la cohorte IMPaCT.

* Muertes esperadas entre visitas sucesivas según las tasas de mortalidad específicas por sexo y edad durante 2019 en España obtenidas del Instituto Nacional de Estadística.
† Pérdidas al seguimiento del 10% de los supervivientes entre visitas sucesivas.

COHORTE IMPaCT

	Año 5†			Año 10†			Año 15†			Año 20†		
	Hombre	Mujer	Total	Hombre	Mujer	Total	Hombre	Mujer	Total	Hombre	Mujer	Total
Cáncer‡	2,000	1,200	**3,200**	5,900	3,700	**9,600**	9,800	6,100	**15,900**	13,500	8,400	**21,900**
Cav. oral, faringe	90	20	**110**	270	70	**340**	450	120	**570**	620	170	**790**
Esófago	30	10	**40**	100	20	**120**	170	30	**200**	230	40	**270**
Estómago	80	40	**120**	250	130	**380**	430	220	**650**	600	310	**910**
Colorrectal	340	190	**530**	1,050	590	**1,640**	1,770	1,010	**2,780**	2,470	1,420	**3,890**
Hígado	70	20	**90**	200	60	**260**	340	110	**450**	470	160	**630**
Páncreas	60	40	**100**	160	120	**280**	280	220	**500**	390	310	**700**
Laringe	60	0	**60**	180	10	**190**	290	20	**310**	390	20	**410**
Pulmón	350	70	**420**	1,040	210	**1,250**	1,740	340	**2,080**	2,420	470	**2,890**
Melanoma	40	40	**80**	110	110	**220**	180	180	**360**	250	240	**490**
Mama	0	370	**370**	0	1,090	**1,090**	0	1,780	**1,780**	0	2,410	**2,410**
Cuerpo útero	0	90	**90**	0	270	**270**	0	450	**450**	0	620	**620**
Ovario	0	50	**50**	0	140	**140**	0	220	**220**	0	310	**310**
Próstata	480	0	**480**	1,440	0	**1,440**	2,420	0	**2,420**	3,360	0	**3,360**
Riñón	60	30	**90**	190	80	**270**	310	130	**440**	420	180	**600**
Vejiga	240	40	**280**	750	130	**880**	1,270	220	**1,490**	1,780	320	**2,100**
Cerebro, SNC	30	30	**60**	100	80	**180**	160	130	**290**	220	170	**390**
Tiroides	10	40	**50**	40	120	**160**	60	190	**250**	80	250	**330**
Linf. no Hodgkin	60	50	**110**	180	140	**320**	300	240	**540**	410	330	**740**
Mieloma múltiple	20	20	**40**	80	60	**140**	130	100	**230**	170	140	**310**
Leucemia	40	30	**70**	130	90	**220**	230	140	**370**	320	200	**520**
ECV§	3,100	2,100	**5,200**	9,100	6,500	**15,600**	14,900	11,000	**25,900**	20,200	15,500	**35,700**
IAM	570	200	**770**	1,720	610	**2,330**	2,850	1,070	**3,920**	3,920	1,530	**5,450**
EIC	1,120	390	**1,510**	3,320	1,200	**4,520**	5,490	2,060	**7,550**	7,530	2,930	**10,460**
IC	370	270	**640**	1,210	970	**2,180**	2,210	1,900	**4,110**	3,240	2,910	**6,150**
ECBV	760	520	**1,280**	2,320	1,650	**3,970**	3,940	2,920	**6,860**	5,520	4,230	**9,750**
EPOC§	890	320	**1,210**	2,760	1,000	**3,760**	4,760	1,720	**6,480**	6,760	2,440	**9,200**
Mortalidad‖	2,200	1,300	**3,500**	7,100	4,700	**11,800**	12,700	9,300	**22,000**	18,500	14,300	**32,800**

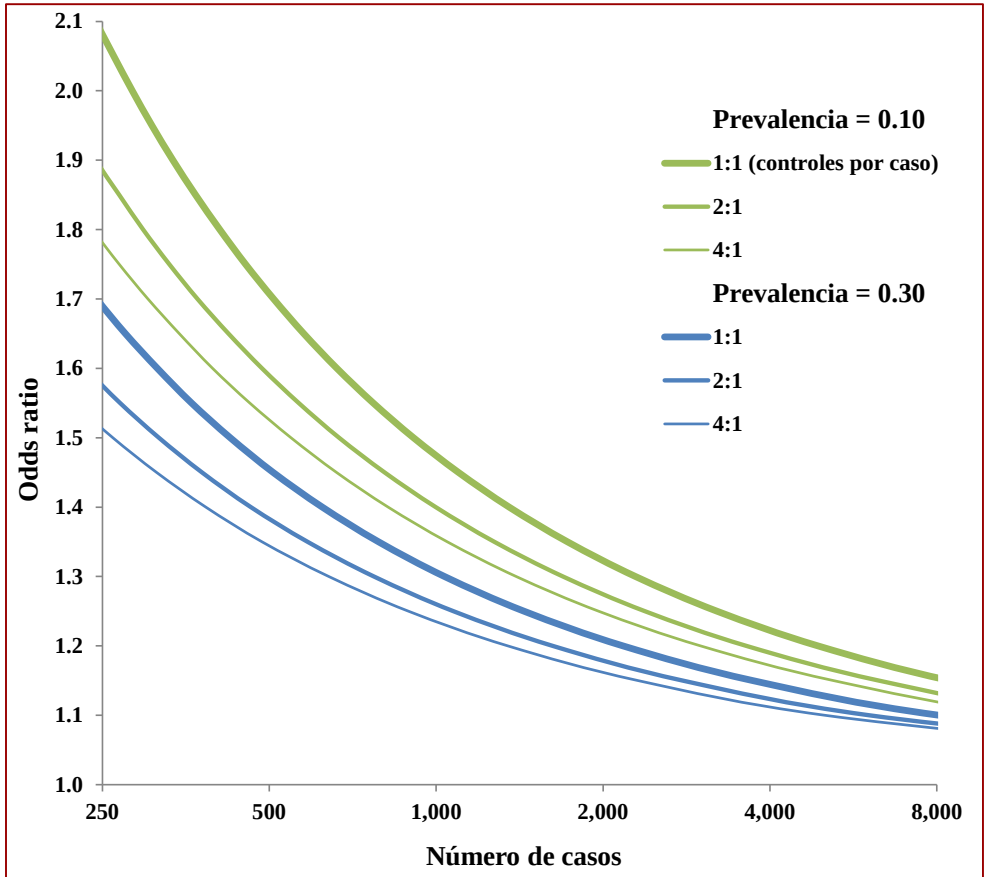


Figura 3. Odds ratio mínimo detectable en función del número de casos, la razón de controles a casos y la prevalecia poblacional de exposición.

CONCLUSIÓN

FORTALEZAS de la Cohorte IMPaCT

- Institución solicitante: **CIBER** (más de 400 grupos de investigación)
- Inclusión de **todas las CCAA y ciudades autónomas**
- Implantación en **Atención Primaria**
- Protocolos establecidos por grupos de expertos: **colaboración desde el inicio**
- Mucho **camino ya recorrido por otros**
- Desarrollo conjunto con los **Programas de Genómica** y **Ciencia de Datos**

INCERTIDUMBRES

- **Implantación acelerada**
- **Horizonte** (financiación) a 3 años
- **Representatividad** versus Exhaustividad
- **Número de centros** (nodos)
- **Pruebas complementarias** imprescindibles
- **Integración de la información** (enriquecimiento de la cohorte y seguimiento)

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Beatriz Pérez Gómez y Fernando Rodríguez Artalejo

Nuestra **Gestora de Proyecto:** Ady Castro

Los otros miembros de la **Comisión Permanente**:

CIBER: Margarita Blázquez, Raquel Campo, Iria Regueira

ISCIII: Maria Pilar Gayoso

Los responsables de todas las **Comunidades y Ciudades Autónomas e INE**

Al **Comité Ejecutivo**

A los coordinadores y a los miembros de los **Grupos de trabajo**

Al **Comité de Ética** del Instituto de Salud Carlos III

Y a todos los investigadores que han contribuido y siguen contribuyendo para poder poner esta infraestructura en marcha