Instituto de Salud Carlos III

IMPaCT

Cohorte IMPaCT-Spain: Diseño y Puesta en Marcha

Prof. Marina Pollán

Índice

1. Introducción: Contexto

2. ¿Quiénes son nuestros modelos?

3. La cohorte IMPaCT: dónde estamos

Contexto: EBM

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

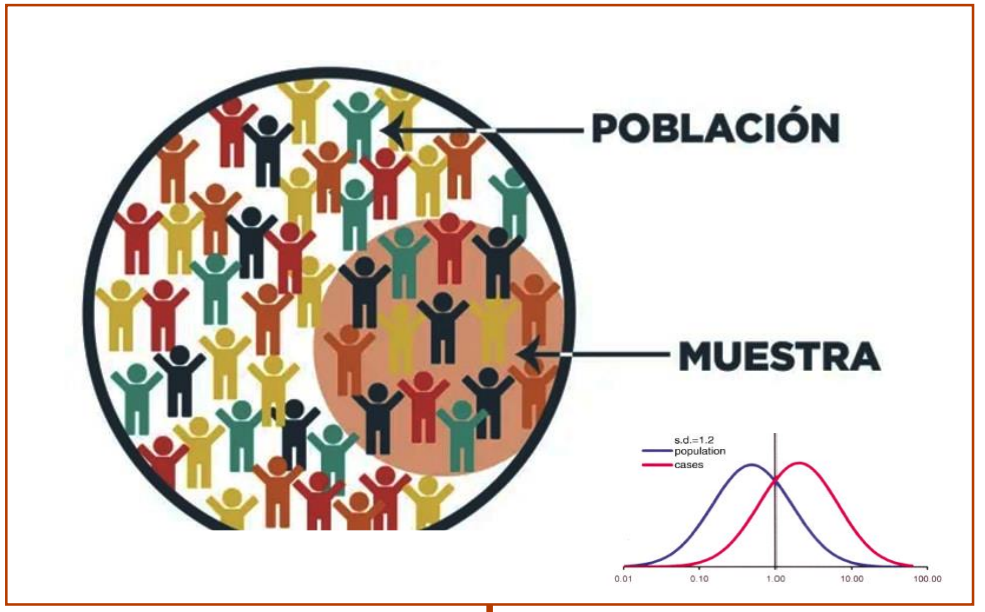
J R Soc Med 1995;**88**:620–624

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



Revolución genómica

Instituto de Salud Carlos III

Publication of human genomes sparks fresh sequence debate

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

Declan Butler

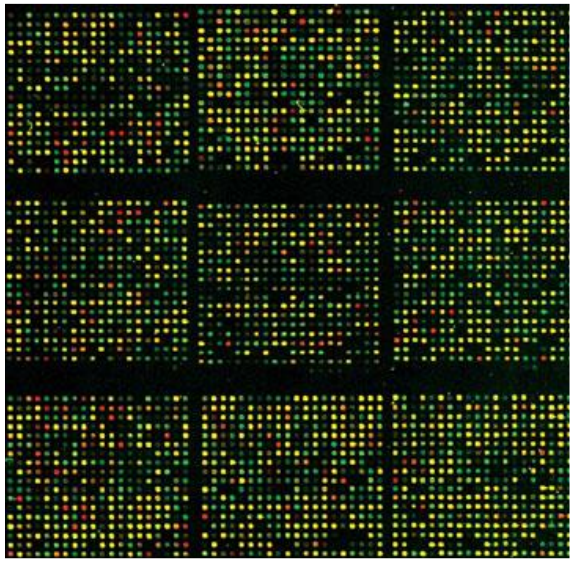
This week's publication of the human genome sequence by both Celera Genomics of Rockville, Maryland, and the publicly funded international Human Genome Project (HGP) has re-ignited the debate over the relative merits of the two teams' different strategies.

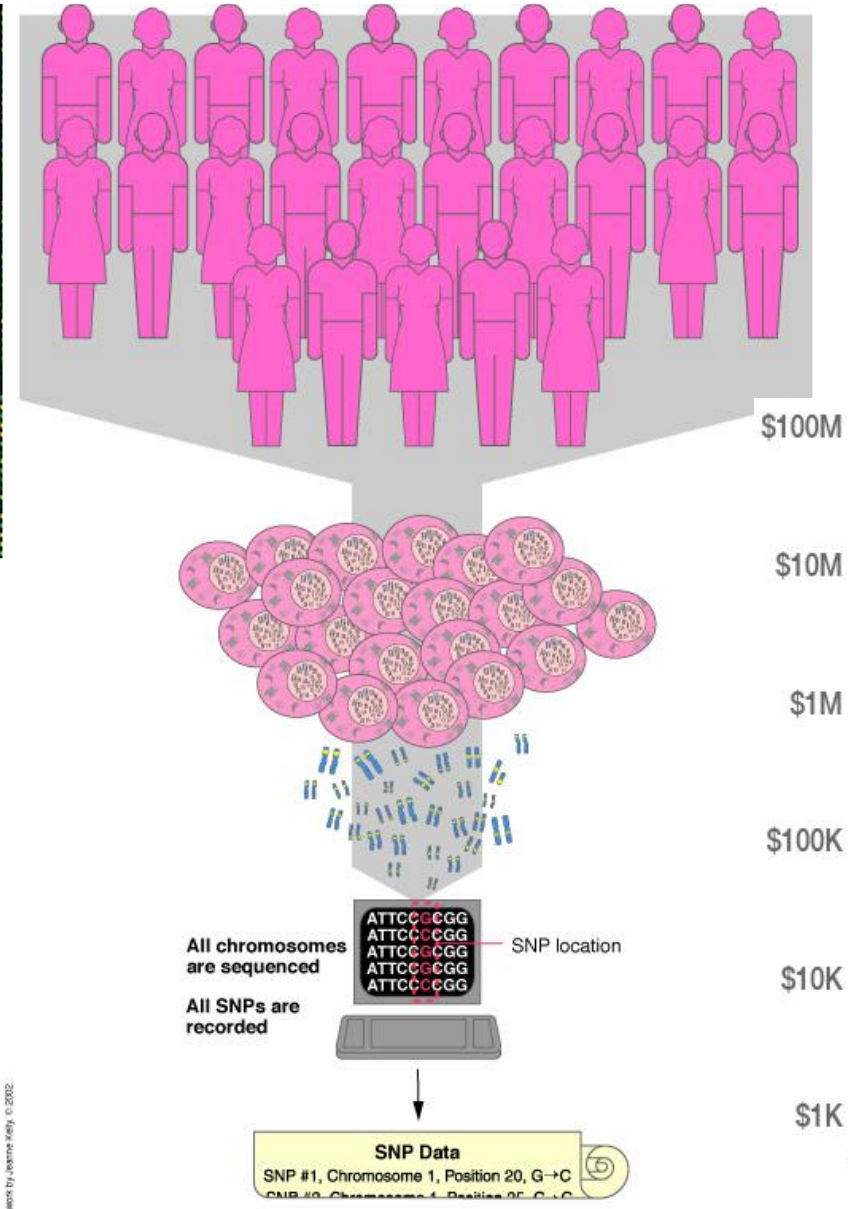
The two groups published their work simultaneously, as promised last summer, and held a cordial joint press conference in Washington on Monday to advertise the fact. At five more press conferences around the world, participants in the public project celebrated their achievement, which is published in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

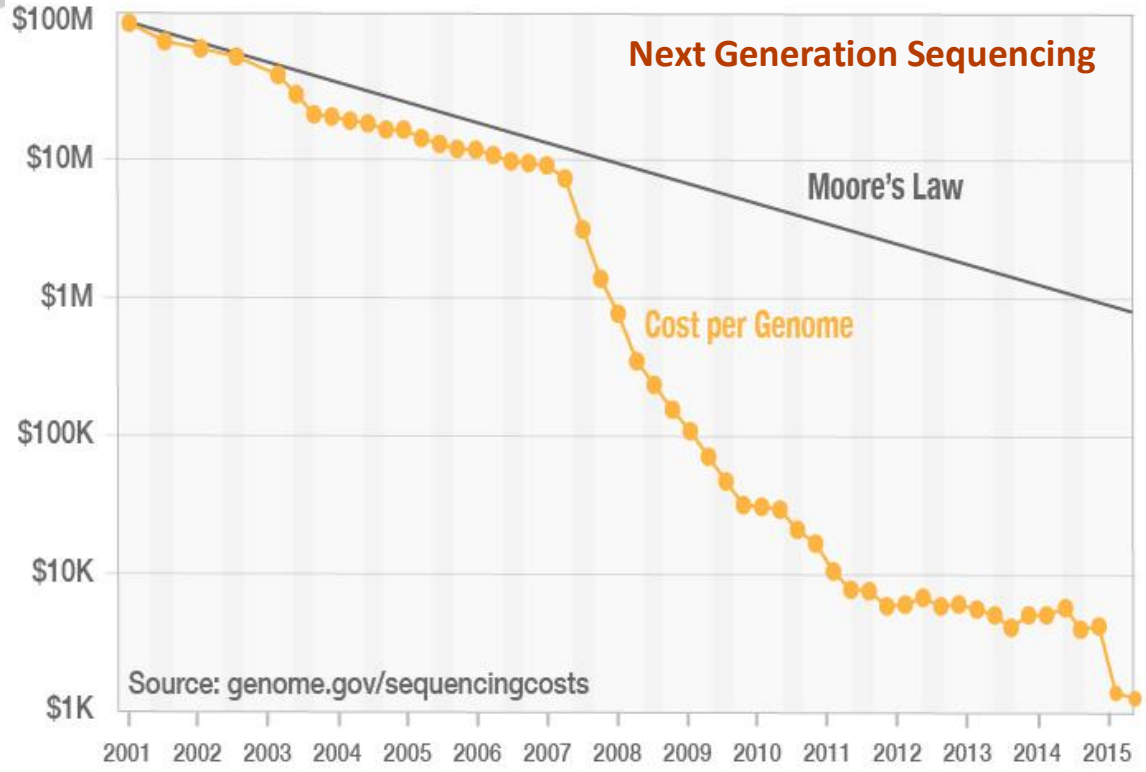
But in the run-up to these meetings, leading members of both teams had been working hard in an attempt to ensure that history — or

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

Revolución tecnológica







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

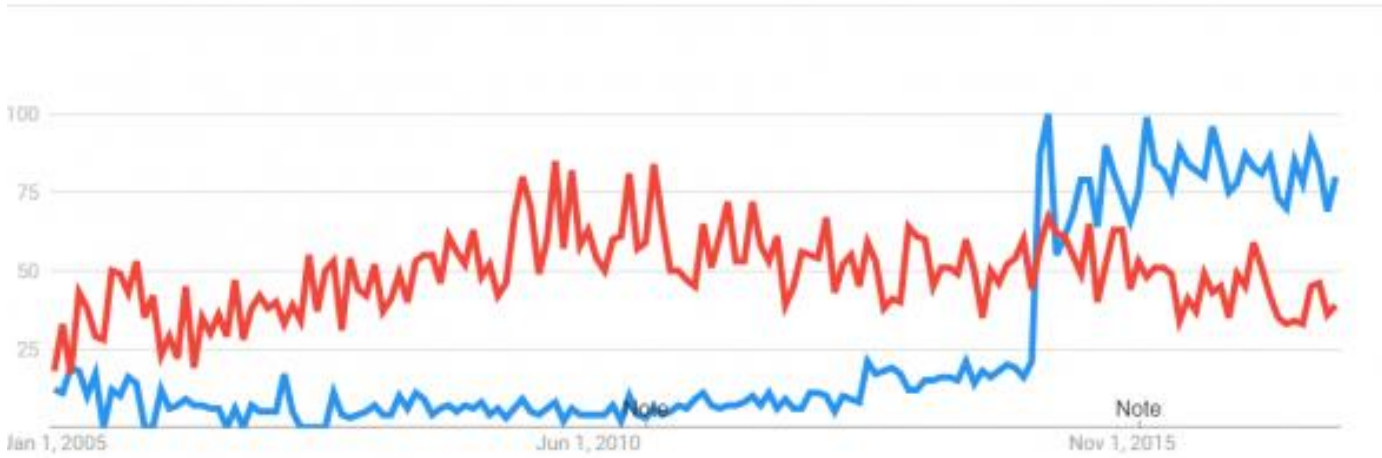
Medicina de Precisión:

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

NIH National Human Genome Research Institute

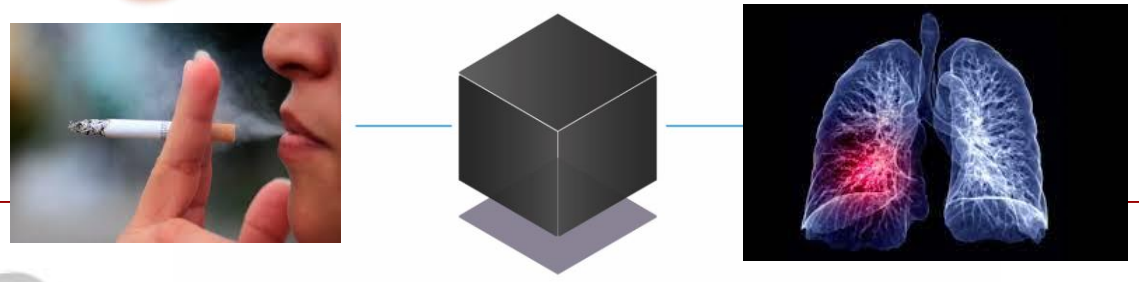
Personalized Medicine

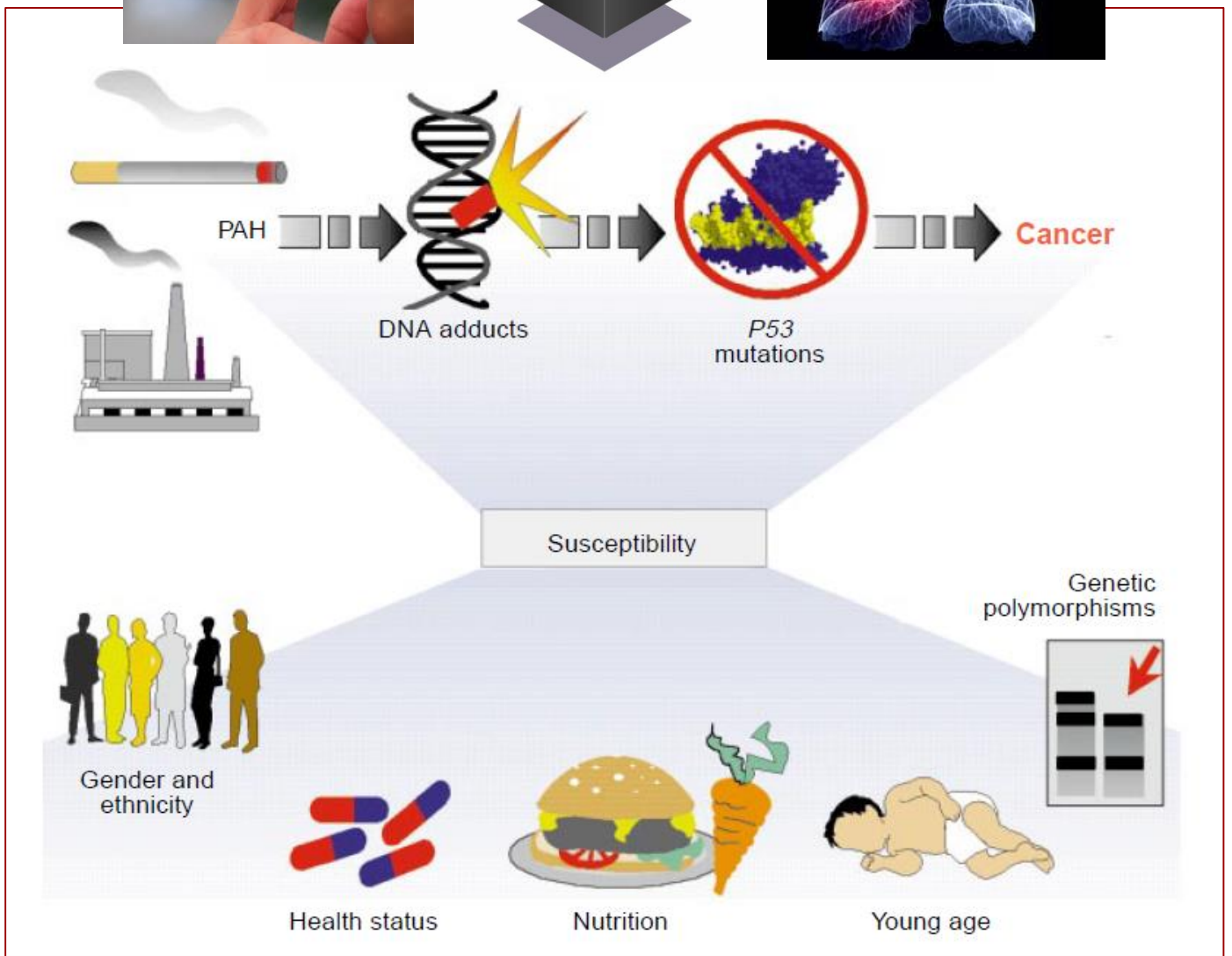
Personalized medicine is an emerging practice of medicine that uses an individual's genetic profile to guide decisions made in regard to the prevention, diagnosis, and treatment of disease. Knowledge of a patient's genetic profile can help doctors select the proper medication or therapy and administer 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

Epidemiología de Precisión





Perera F.P. Science 1997

Funciones 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

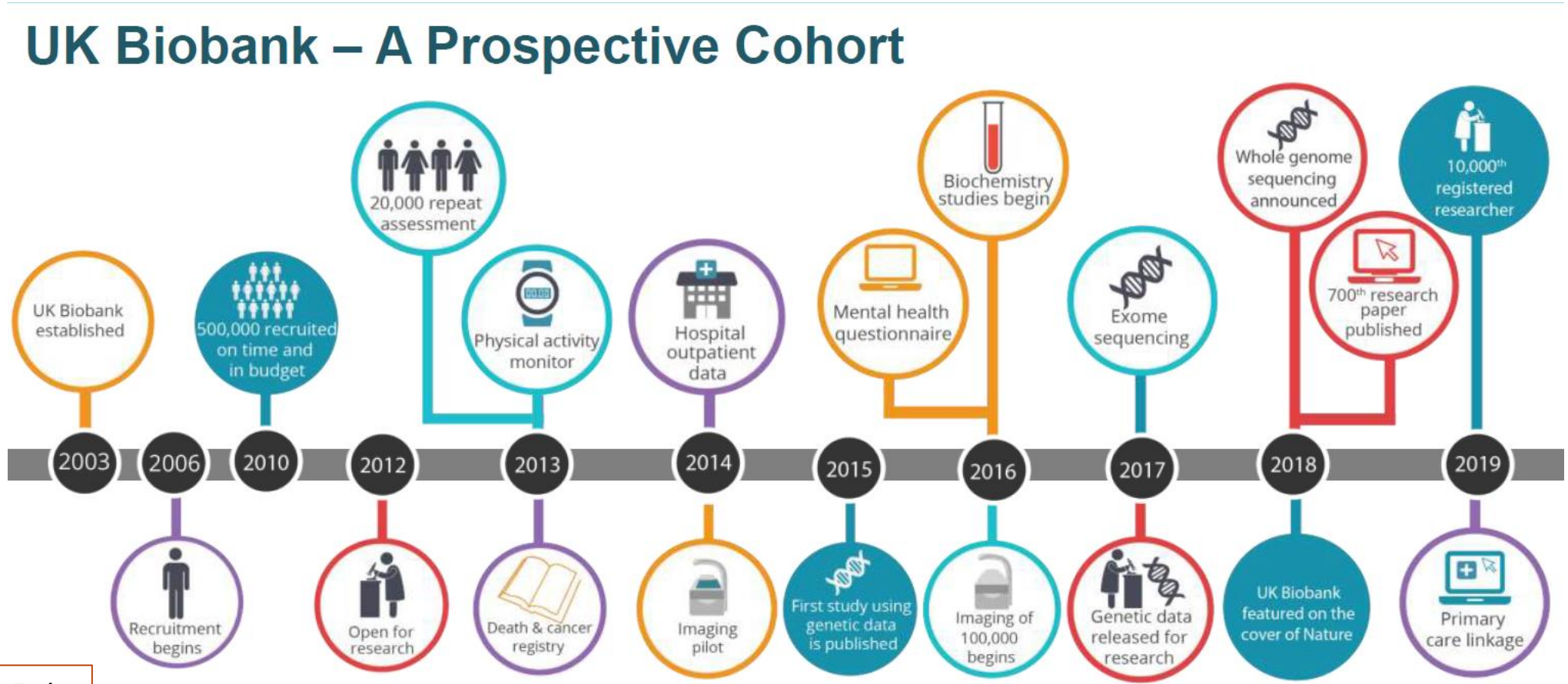
biobank uk

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%.

Touch-screen stations (x 15-20)
Consent
Touch-screen questions
Hearing test
Cognitive function tests

Interview stations (x 3)
Interview
Blood pressure (x 2)
Arterial stiffness

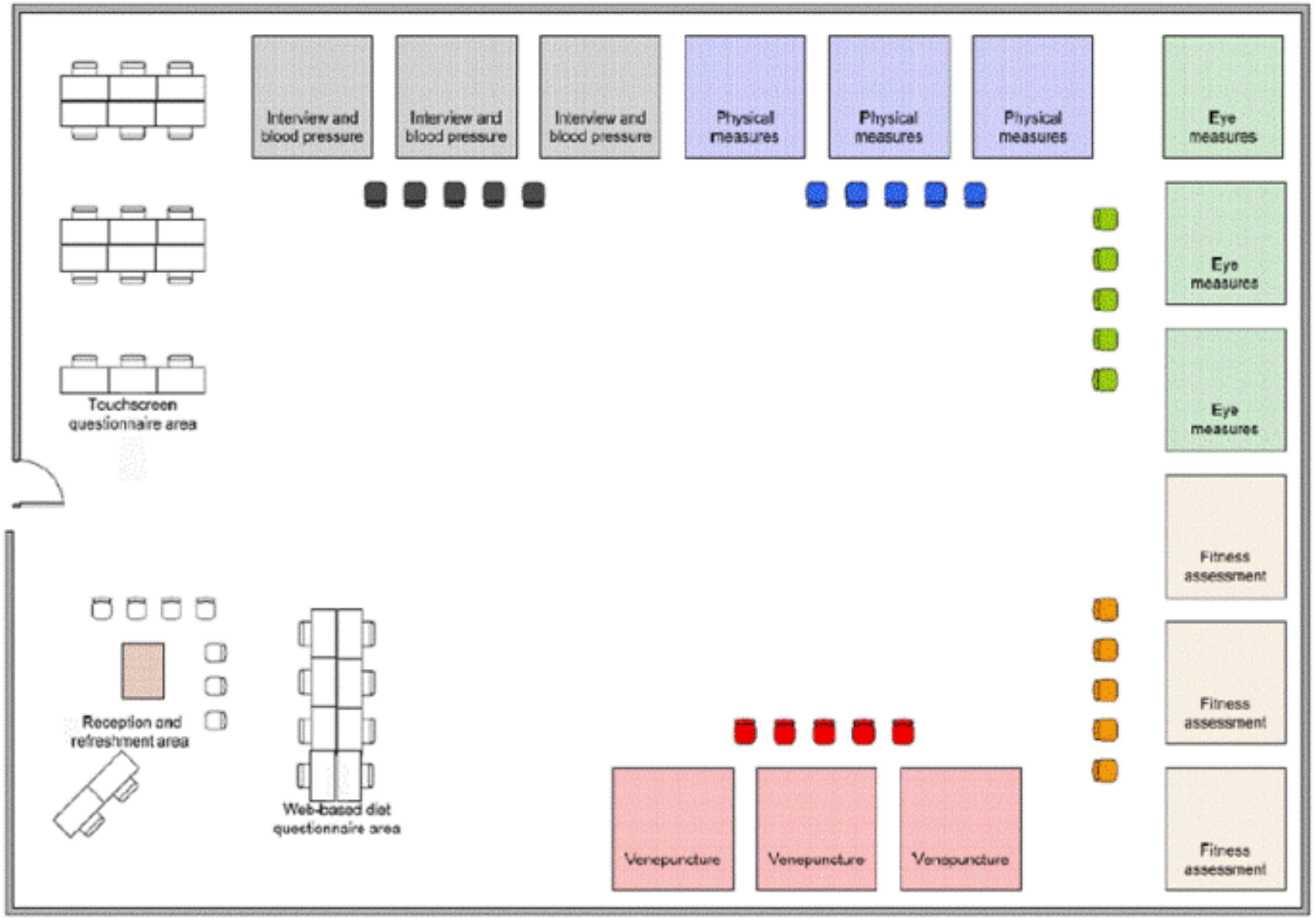
Physical measures stations (x 3)
Hand grip strength (R & L)
Height (standing & sitting)
Waist/hip circumference
Weight/impedance
Spirometry
Heel ultrasound (L/*R*)

Sample collection stations (x 3)
Blood (45 ml; 6 tubes)
Urine (9 ml; 1 tube)

Web diet questionnaire

biobank uk
Improving the health of future generations

IMPaCT



biobank uk

Improving the health of future generations

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Improving the health of future generations

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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

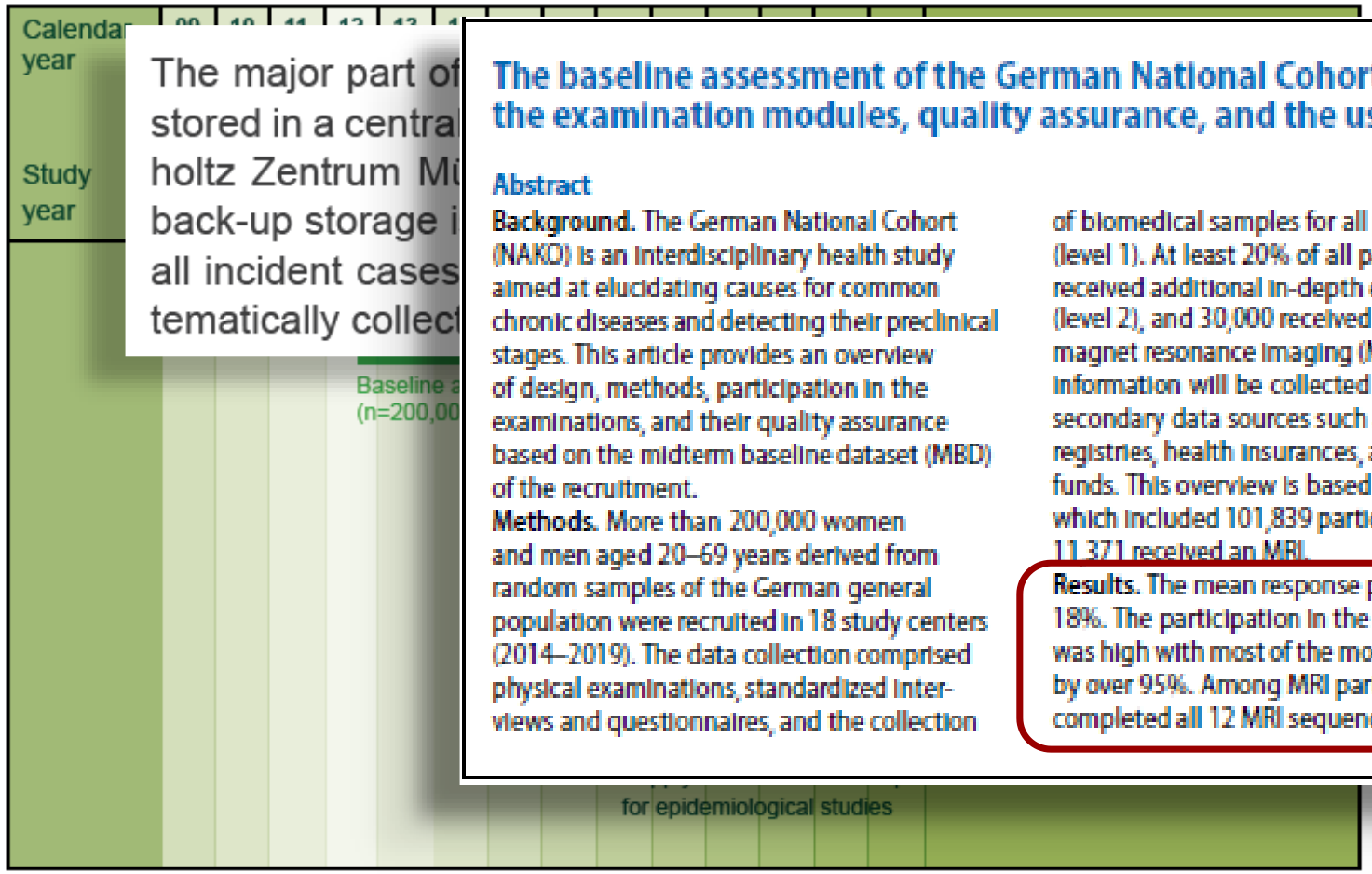
Estimated participation rate of 40-50%

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

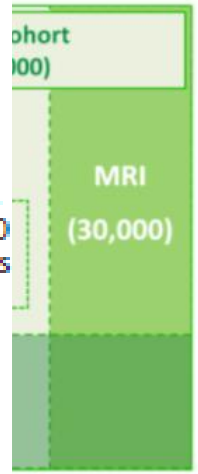
Background. The German National Cohort (NAKO) is an interdisciplinary health study aimed at elucidating causes for common chronic diseases and detecting their preclinical stages. This article provides an overview of design, methods, participation in the examinations, and their quality assurance based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

200.000 participantes 18-69 años

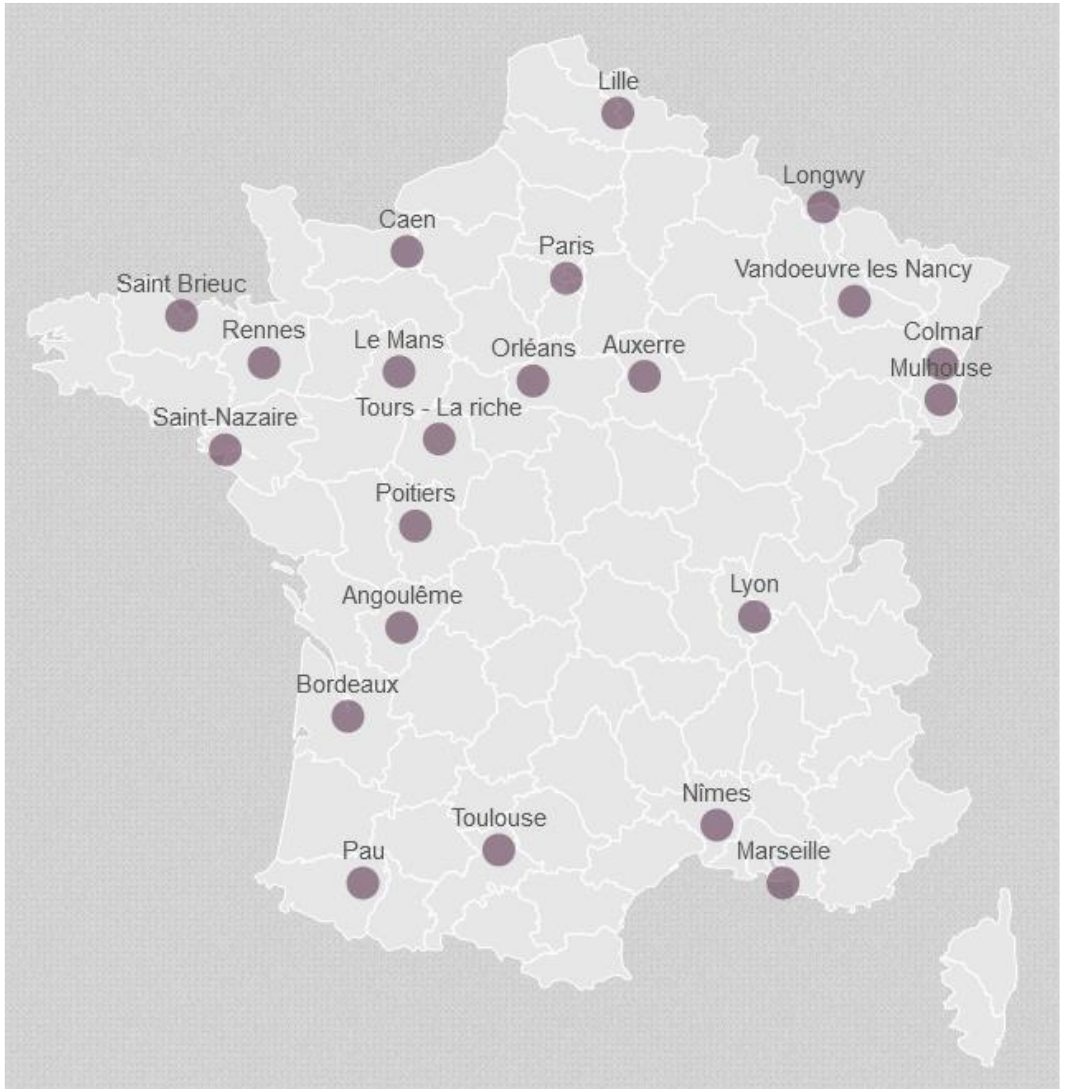
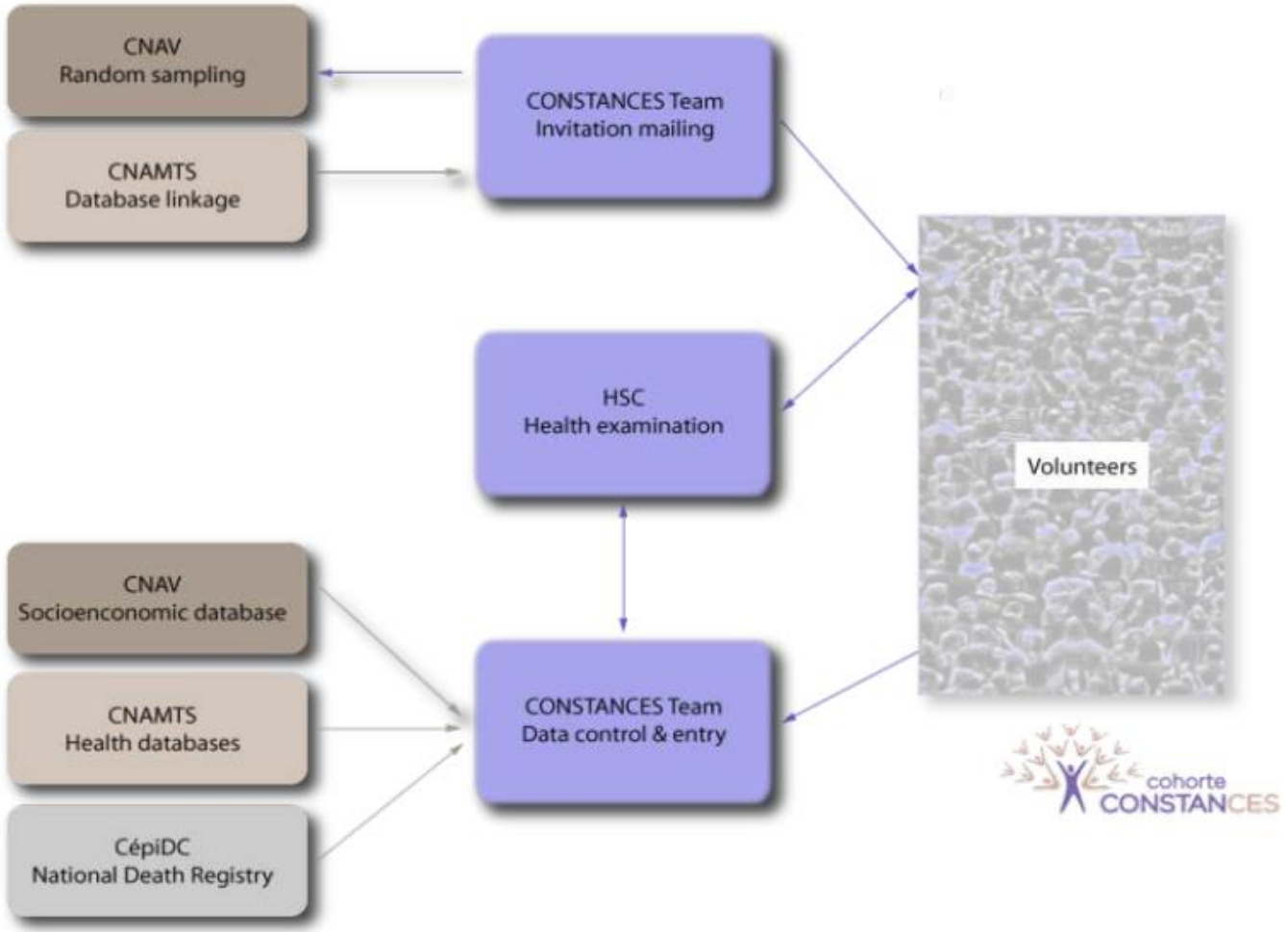


Figure 1. General overview of the design



LifeGene

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LifeGene

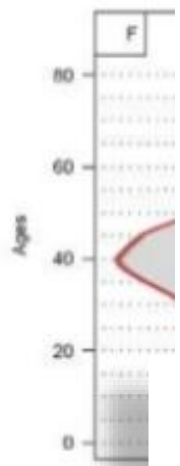
Targ

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

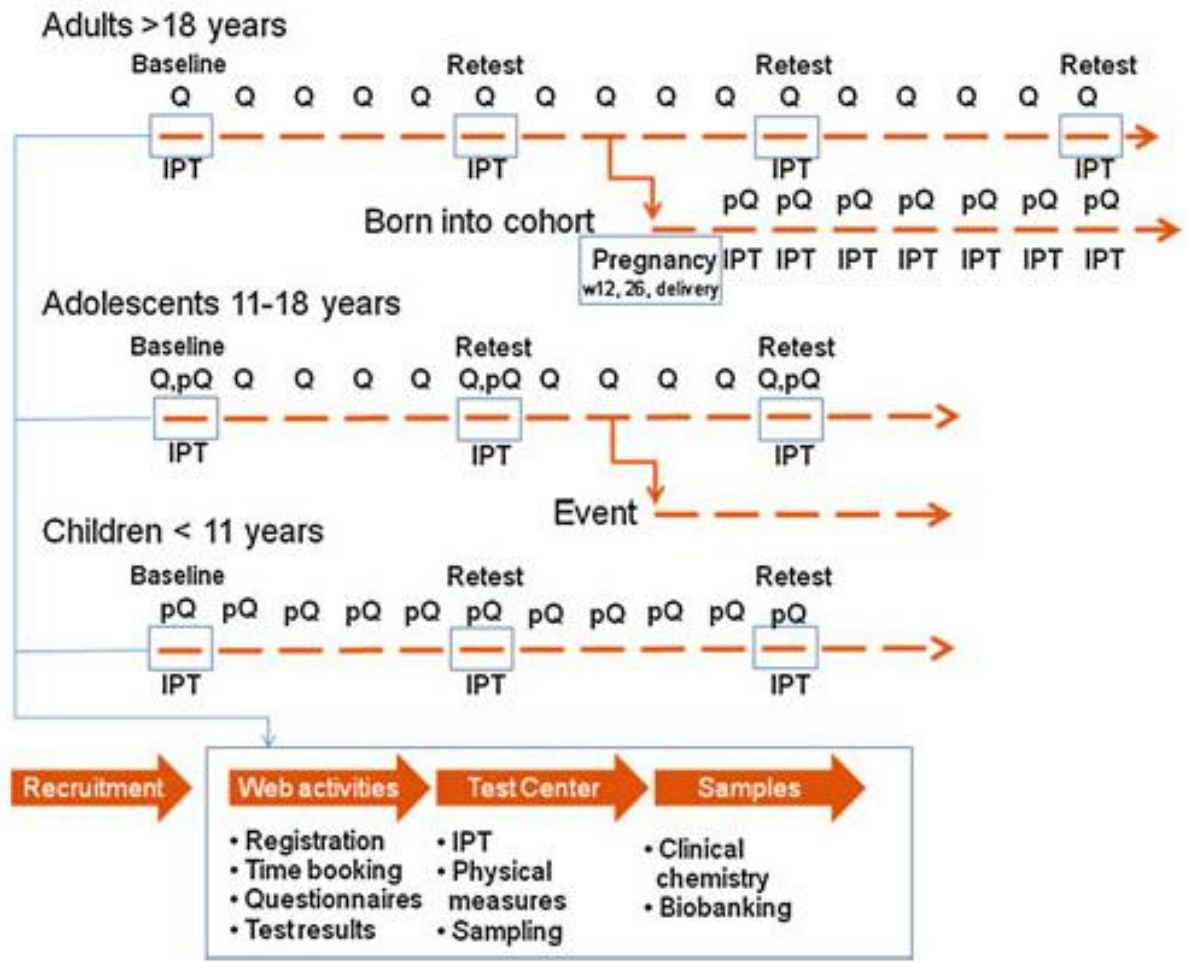


Fig. 1 Flow chart on the structure of the study. Questionnaires (Q), parental questionnaires (pQ) and In Person Testing (IPT) in adults, adolescents and children

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

LifeGene

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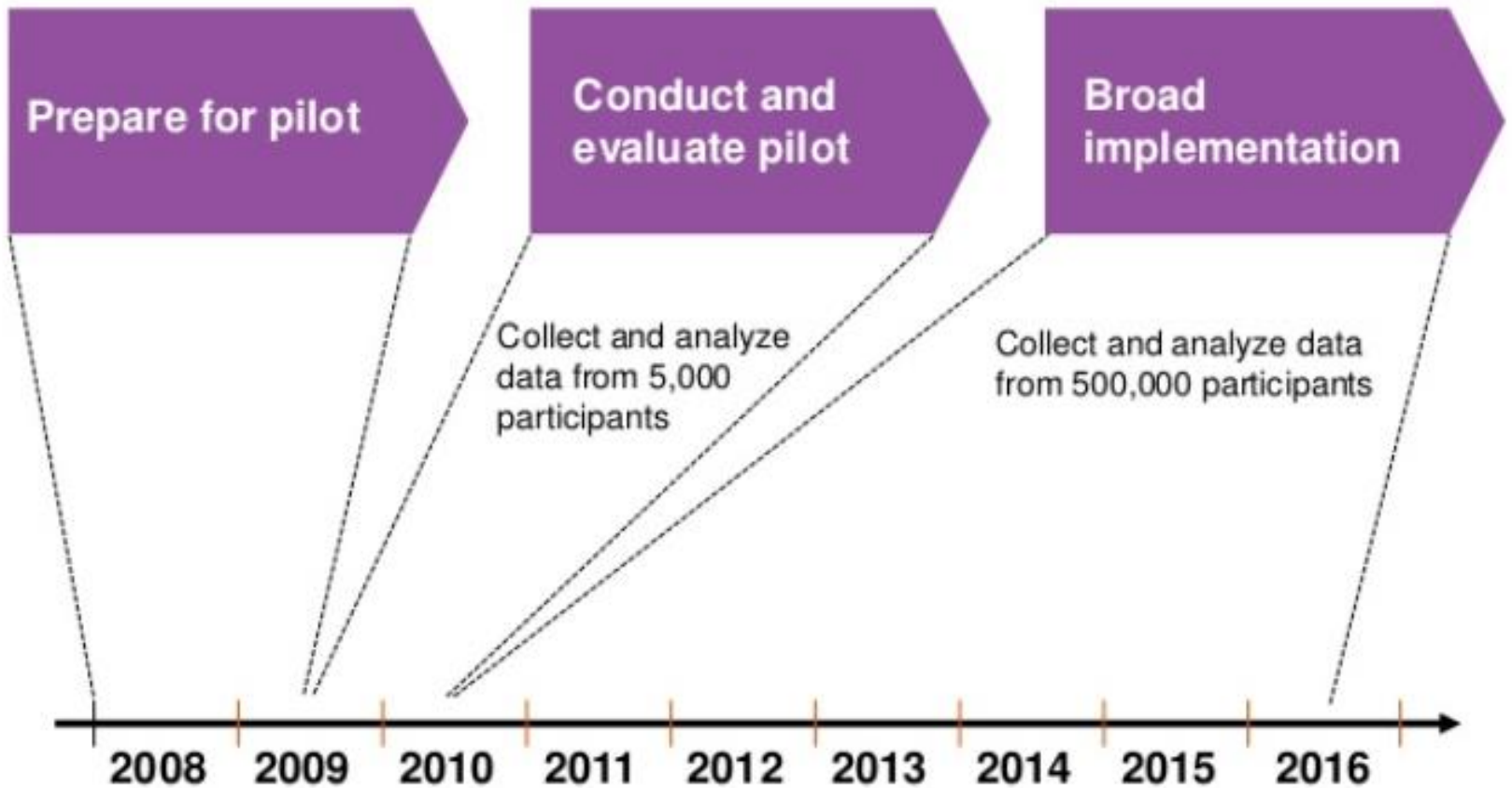
The **timeline** is geared for an industrial scale roll-out in 2010



LifeGene

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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.

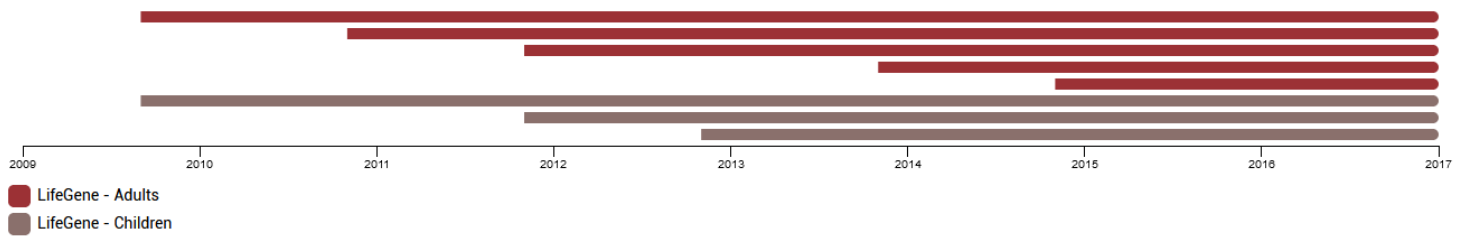
Overview

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

Building out the infrastructure necessary to collect so much data on such a huge cohort has taken time and some serious cash. Last year alone, the All of Us budget was $230 million. For the full project, which will run for a decade, Congress has authorized a whopping $1.455 billion. In addition to the 298 enrollment sites NIH hopes to launch by the end of this year (120 are online so far), that money will go toward a 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.

Those samples contain the DNA that researchers will sequence, and in a rare first for a research project of this magnitude, they will also return the results to participants. But none of this will happen right away. The first sequencing will begin later this year, beginning with a small, 20,000 person pilot. Before everyone else can get the same treatment, someone has got to build a *lot* more sequencing machines. "There's not enough capacity in the US to even begin to do a million people," says Eric Dishman, director of All of Us. In addition to genotyping—the technique companies like 23andMe uses to create its limited health reports—All of Us will also be doing whole genome sequencing, which requires much more machinery. "It'd be like saying, "Hey, let's all take a high speed train trip across the US. There just aren't enough of them right now to do

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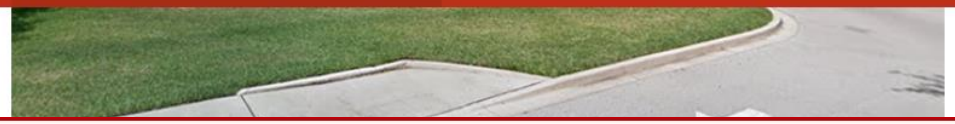


national biobank, run by the Mayo Clinic, where 35 blood and urine samples from each participant will one day be stored. To prepare for the national launch, Mayo doubled the size of its 35,000-square-foot facility in Minnesota and expanded a smaller bank in Florida, as a backup site to protect samples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

Participants at a Glance

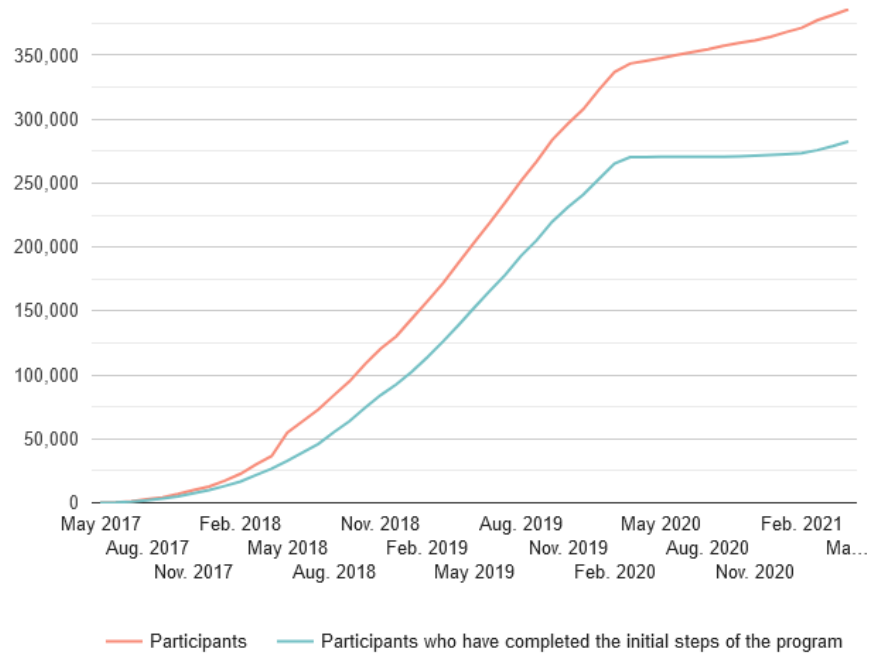
389,000+
Participants

285,000+
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 June 24, 2021.



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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

¿Estas infraestructuras han sido útiles durante la pandemia?

biobank uk
Improving the health of future generations

IMPaCT

Final results

The 20,000 volunteers, a combination of existing UK Biobank participants and their children and grandchildren aged over 18, helped produce results that are representative of the UK population.

One of the most significant findings of the study is that **99% of participants who had tested positive for previous infection retained antibodies to SARS-CoV-2 for 3 months after being infected, and 88% did so for the full 6 months of the study.** This discovery provides an early indication that the antibodies produced following natural infection may protect most people against subsequent infection for at least 6 months.

Overall in the study, 6.6% of the participants had been infected previously in May/June 2020 and this rose to 8.8% by the end of November 2020. These rates did not differ in men and women. However the rates were higher in younger people, ranging from 13.5% in those under 30 to 6.7% in those over 70.

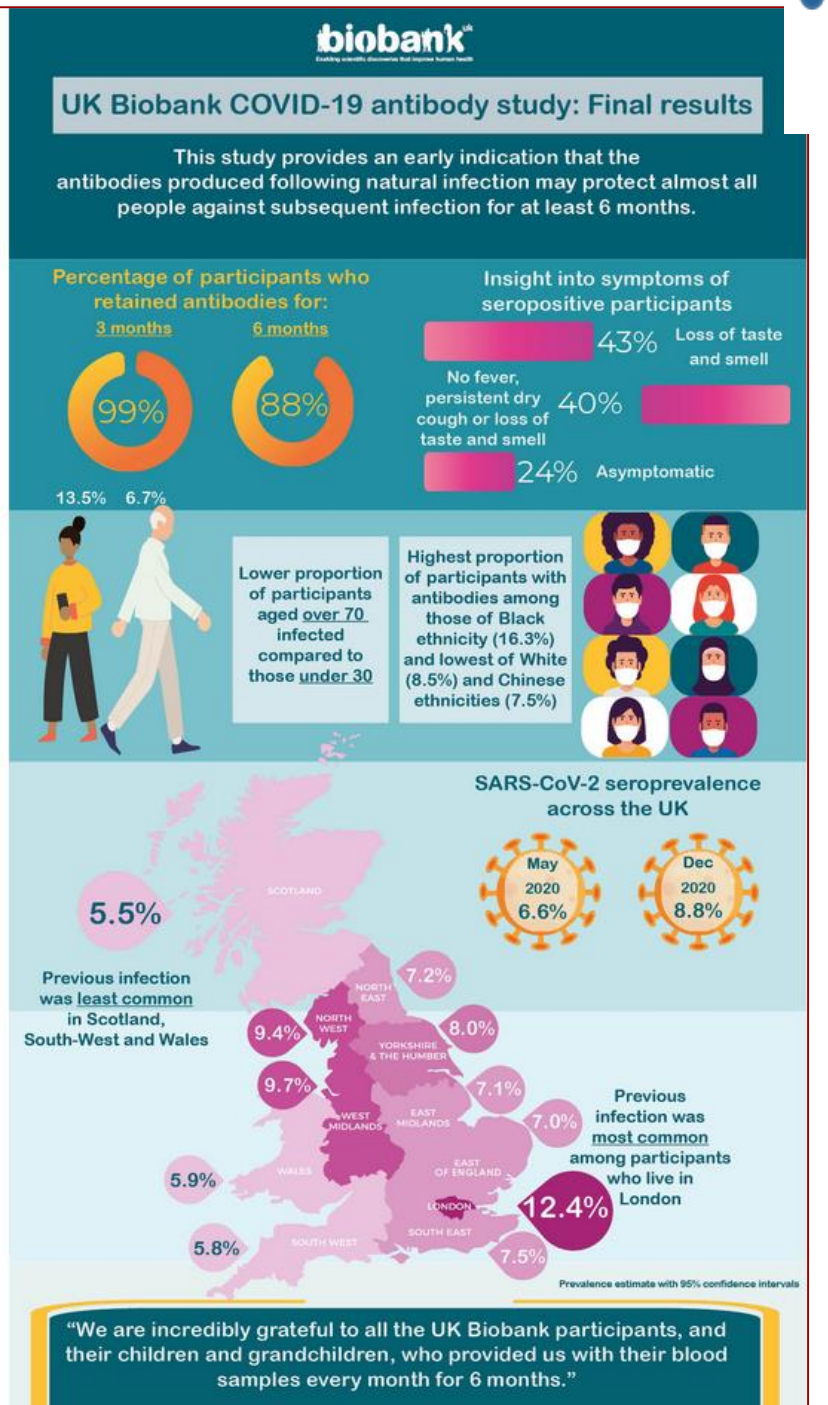
SARS-CoV-2 seroprevalence was most common in London (12.4%) and least common in Scotland (5.5%) and highest among participants of Black ethnicity (16.3%) and lowest among those of White (8.5%) and Chinese ethnicities (7.5%).

These data will be added to the UK Biobank database and research resource, enabling scientists globally to conduct further research into how SARS-CoV-2 infection affects health over the longer-term. You can find out more about these results by watching on-demand content for a participant event we held on 17th February. Please follow this link .

Thank you to everyone taking part.

Thank you to the 88,000 participants and their 15,000 family members who volunteered for the study to test antibodies. We were over-whelmed by the response and sorry that we could not include everybody – but your support at this time of crisis is very much appreciated

Professor Sir Rory Collins, UK Biobank Principal Investigator



Original Article

The Impact of the COVID-19 Pandemic on Self-Reported Health

Early Evidence From the German National Cohort

Annette Peters, Susanne Rospleszcz, Karin H. Greiser, Marco Dallavalle, Klaus Berger*

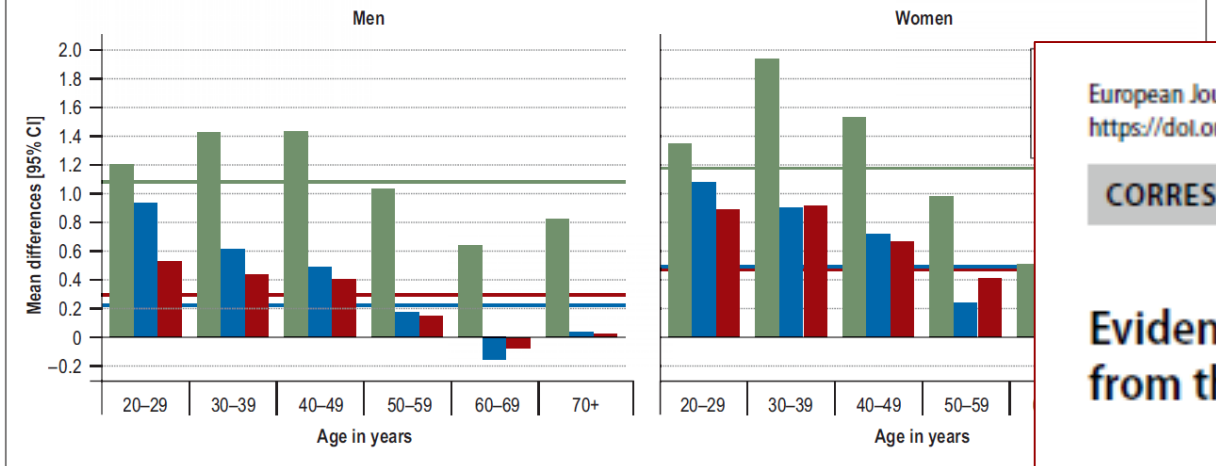
NAKO GESUNDHEITS-STUDIE

IMPaCT

Peters A et al.: The impact of the COVID-19 pandemic on self-reported health—early evidence from the German National Cohort. Dtsch Arztebl Int 2020; 117: 861–7. DOI: 10.3238/arztebl.2020.0861

CONSTANCES

FIGURE 1



Mean differences in mental health summary scores between the time of the COVID-NAKO questionnaire and the NAKO baseline examination and sex
PHQ-stress; PHQ-9, depressive symptoms; GAD-7, anxiety symptoms; CI, confidence interval

European Journal of Epidemiology (2021) 36:219–222
https://doi.org/10.1007/s10654-020-00716-2

CORRESPONDENCE

Evidence of early circulation of SARS-CoV-2 in France: findings from the population-based "CONSTANCES" cohort

Fabrice Carrat[1] · Julie Figoni[2] · Joseph Henny[3,4] · Jean-Claude Desenclos[2] · Sofiane Kab[3,4] · Xavier de Lamballerie[5] · Marie Zins[3,4]

Abstract

Using serum samples routinely collected in 9144 adults from a French general population-based cohort, we identified 353 participants with a positive anti-SARS-CoV-2 IgG test, among whom 13 were sampled between November 2019 and January 2020 and were confirmed by neutralizing antibodies testing. Investigations in 11 of these participants revealed experience of symptoms possibly related to a SARS-CoV-2 infection or situations at risk of potential SARS-CoV-2 exposure. This suggests early circulation of SARS-CoV-2 in Europe.

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

IMPaCT

Tuesday, June 16, 2020

All of Us Research Program launches COVID-19 research initiatives

NIH effort expands data collection to shed light on pandemic's spread and impact.

The *All of Us* Research Program, today announced that it is levera base to seek new insights into C on the pandemic's impacts and information.

All of Us will make data gathered to approved researchers over tim Researcher Workbench, now in origins of entry, spread and impa

"With our nearly 350,000 partici will enable the research commu questions and inform future pre *of Us*'s chief executive officer.

Antibody Testing

All of Us will test blood samples March 2020 and working backward until positive tests are no longer found. The tests will show the prevalence of novel coronavirus exposure among *All of Us* participants, and help researchers assess varying rates across regions and communities.

Study collaborators include the Frederick National Laboratory for Cancer Research, supported by the National Cancer Institute; the National Institute of Allergy and Infectious Diseases; the Centers for Disease Control and Prevention; and Quest Diagnostics.

Antibody testing, which uses blood samples, is different than the nasal swab tests health care providers commonly use to detect active infection. Antibody tests are generally done with people who do not currently have symptoms, to find out if they had the virus in the past.

› Clin Infect Dis. 2021 Jun 15;ciab519. doi: 10.1093/cid/ciab519. Online ahead of print.

Antibodies to SARS-CoV-2 in All of Us Research Program Participants, January 2-March 18, 2020

Keri N Althoff [1], David J Schlueter [2], Hoda Anton-Culver [3], James Cherry [4], Joshua C Denny [5], Isaac Thomsen [6], Elizabeth W Karlson [7], Fiona P Havers [8], Mine S Cicek [9], Stephen N Thibodeau [9], Ligia A Pinto [10], Douglas Lowy [4], Bradley A Malin [6], Lucila Ohno-Machado [11], Carolyn Williams [12], David Goldstein [13], Aymone Kouame [6], Andrea Ramirez [5], Adrienne Roman [6], Norman E Sharpless [4], Kelly A Gebo [14], Sheri D Schully [5]

Affiliations + expand

PMID: 34128970 DOI: 10.1093/cid/ciab519

ENE-COVID

IMPaCT

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”

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

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

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

CRONOGRAMA

	2021				2022				2023			
Mes	**3**	**6**	**9**	**12**	**15**	**18**	**21**	**24**	**27**	**30**	33	36
P1. Coordinación.		E0	E0	E0	E0	E0	E0	E0	E0	E0	E0	E0
P2. Elaboración de estrategia de selección y reclutamiento de los participantes en el estudio.		E1										
P3. Definición y medida de las variables de interés		E2 E3										
P4. Definición de procedimientos del biobanco.		E4										
P5. Elaboración de estrategia seguimiento activo de los participantes en la cohorte.						E5						
P6. Plan de análisis de datos.				E6								
P7. Elaboración de procedimientos de recogida y transmisión automatizada de la información, gestión y depuración centralizada de la base de datos, control de calidad.				E7	E8							
P8. Aspectos éticos y legales.				E9 E10								
P9.Trabajo de campo												
Manual operacional				E11								
Entrenamiento profesionales estudio piloto												
Estudio piloto						E12						
Entrenamiento de profesionales para reclutamiento y recogida datos												
Reclutamiento y recogida datos de la cohorte							E13	E13	E13	E13	E13	E13
P10. Enlace (linkage) de información obtenida de los participantes con información historia clínicas electrónicas y otras bases de datos sanitarias y no sanitarias												
Definición de los procedimientos								E14				
Actividades de linkage												
P11. Comunicación con los participantes en el estudio y la ciudadanía.												
Definición de los procedimientos					E15	E16		E17				
Actividades de comunicación												

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

- Beatriz Pérez Gómez (CIBERSP)
- Miguel Ángel Martínez (CIBEROBN)
- Mª José Sánchez (Andalucía y CIBERESP)
- Roberto Pastor Barriuso (CIBERESP)
- Miguel Delgado (CIBERESP)
- Mónica Guxens (CBIERESP)
- Víctor Moreno (CIBERESP)
- Isabel del Cura (Madrid)
- Joan Llobera (Baleares)
- Itziar Vergara (País Vasco)
- Gema Rojo (CIBERDEM)
- Nerea Martín Carlo (CIBEROBN)
- Francisco Gude (Galicia)
- Carlos Ballano (INE)

PROPUESTA DE DISEÑO

- Número de centros (Atención Primaria)
- Características mínimas requeribles a los centros
- Criterios de selección de los participantes
- Forma de selección de los participantes
- Eventos de particular interés
- Estimación de eventos esperados
- Diseño del Estudio Piloto
- Otras propuestas para los GT

Grupo cuestionarios y Exploración física

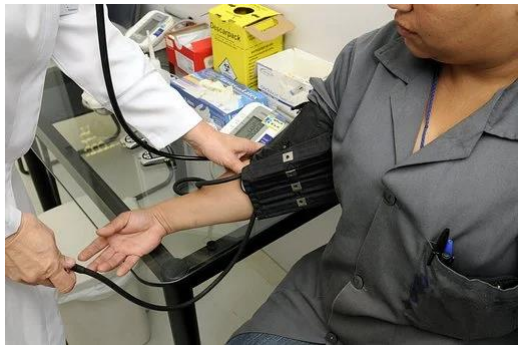
- Fernando Rodríguez Artalejo (CIBERSP)
- Manolis Kogevinas (CIBERESP)
- **Y más de 60 expertos de CIBER y CCAA con sus equipos**

Cuestionario básico
Dato de filiación (que faciliten el seguimiento)
Variables demográficas
Nivel socieconómico, clase social
Historial médico personal
Historial médico familiar
Medicación de los últimos 7 días
Participación en programas de detección precoz de enfermedades
Salud sexual y reproductiva en hombres/mujeres
Consumo de tabaco
Exposición al humo ambiental de tabaco
Consumo de bebidas alcohólicas, patrones de consumo de alcohol
Consumo de otras drogas
Adicciones sin sustancias
Calidad de vida relacionada con la salud
Discapacidad en actividades instrumentales de la vida diaria (mayores de 60 años).
Discapacidad en actividades básicas de la vida diaria (mayores de 60 años).

Cuestionarios específicos
Factores neurológicos y psiquiátricos
• síntomas de depresión
• trastornos de ansiedad
• sueño y alteraciones ciclo circadiano
Factores psicosociales
• personalidad
• estrés crónico
• estrés laboral
• red social
• conflictos en el trabajo y en la familia
• inseguridad laboral
Situación inmunitaria e infecciones pasadas
Dolor crónico
Salud oral
Funcionamiento de los órganos de los sentidos
• Vista
• Oído
• Olfato/Gusto
Actividad física, sedentarismo
Alimentación
• consumo de alimentos
• preferencias y hábitos alimentarios
Factores del medio ambiente construido
Características de la vivienda
Características del barrio
Barreras a los estilos de vida saludables
Ocupación (exposiciones especiales en el trabajo)
Utilización de servicios sanitarios
Radiación ionizante (asociada también a aspectos clínicos) y non-ionizante
Exposición al agua

Exploración física

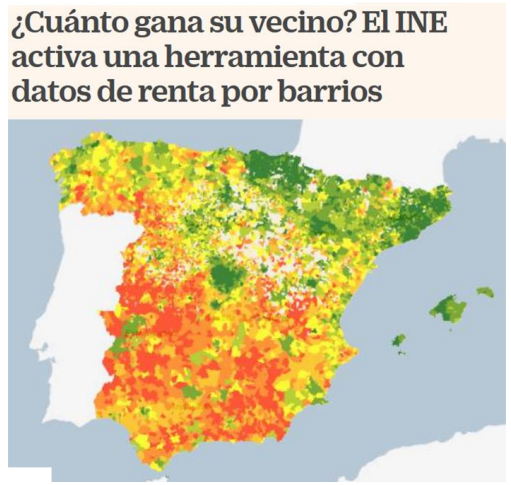
Examen físico
1) Sistema cardiovascular
• Presión arterial y frecuencia cardíaca
• Electrocardiografía
• Ecocardiografía 3D
• Índice tobillo-brazo
• Medidas de rigidez arterial (onda de pulso).
2) Diabetes
• Prueba de tolerancia oral de glucosa.
3) Función cognitiva
• memoria (semántica, episódica, de trabajo)
• atención / función ejecutiva,
• coordinación motriz
• razonamiento numérico (inteligencia fluida)
• vocabulario
4) Función pulmonar
• espirometría
• difusión de CO
• óxido nítrico en el aire exhalado.
5) Sistema musculoesquelético
• examen médico para identificar artrosis y artritis reumatoide.
• cadera
• mano
• rodilla
6) Salud bucal
• caries, enf. periodontal, número de dientes, trastornos de la articulación temporomandibular

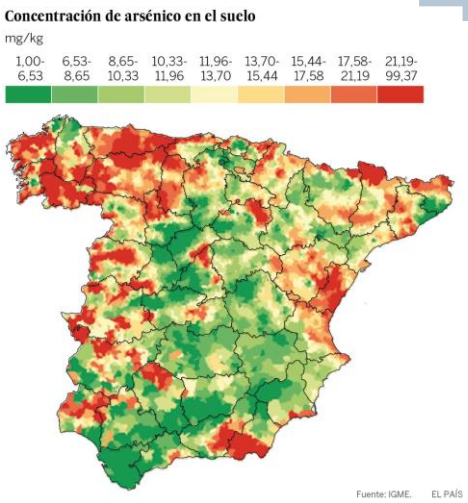


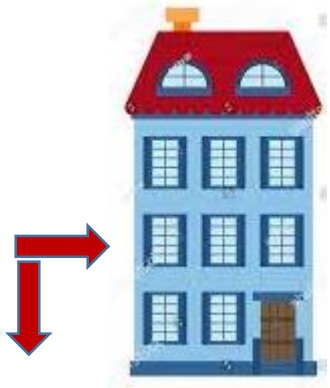
7) Exploración oftalmológica
• fotografía de retina
• prueba de agudeza visual
8) Audición
• comprensión verbal mediante prueba de los tres dígitos
• audiometría tonal
9) Olfato
• Tiras olfativas
10) Actividad y función física
• acelerometría de 7 días
• ergometría submáxima en bicicleta
• fuerza de agarre de la mano
• velocidad de la marcha
• Short Physical Performance Battery (mayores de 60 años)
11) Antropometría
• peso, talla, circunferencia de cintura y cadera, ……..
• bioimpedancia eléctrica
• DEXA

Información contextual

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

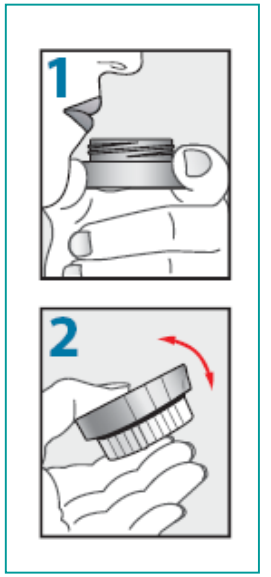


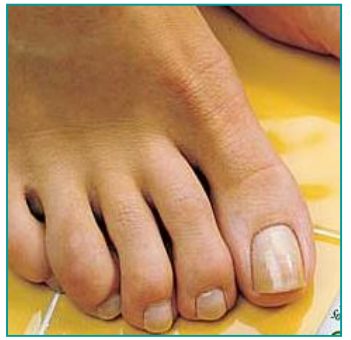




Grupo de muestras biológicas

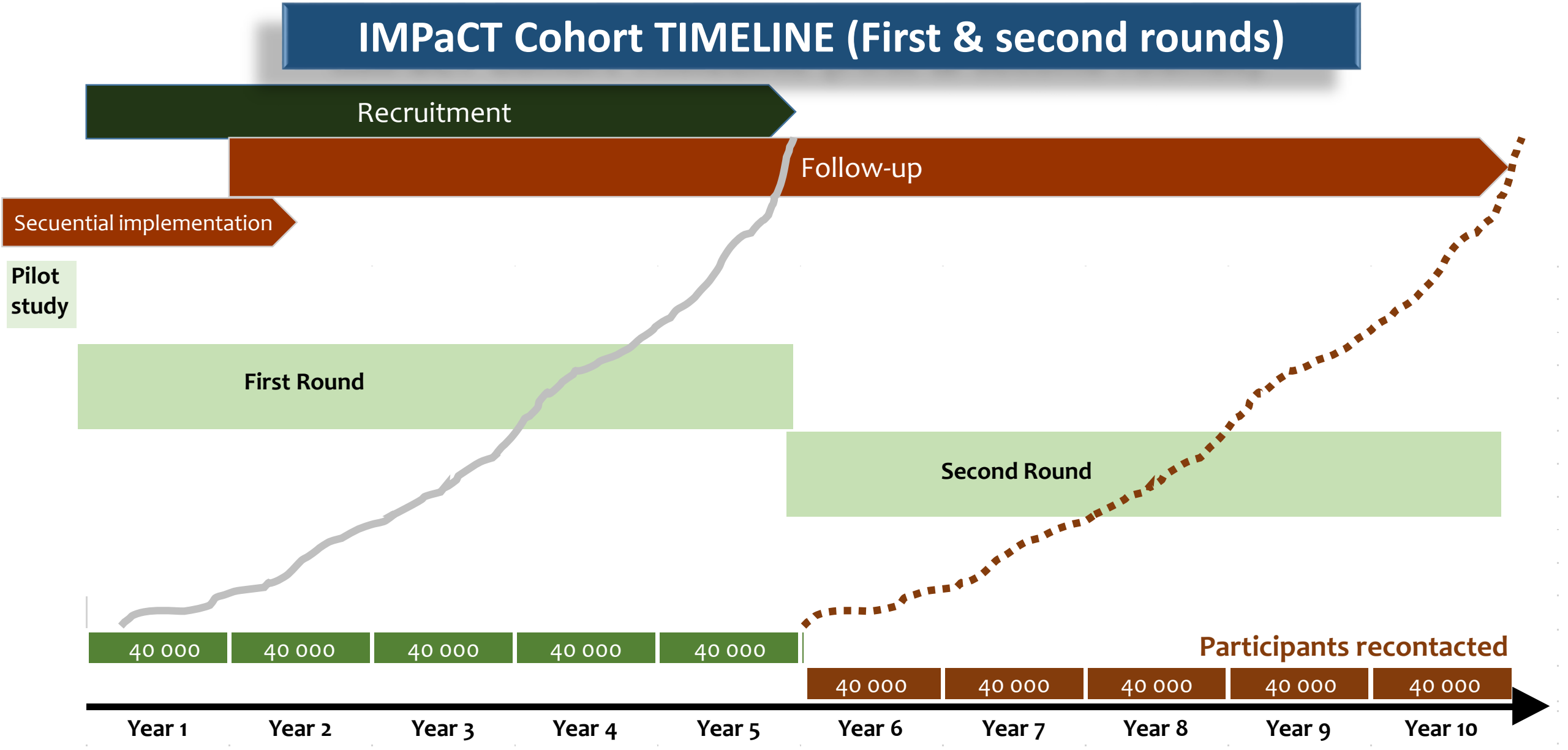
- Cristina Villena (CIBERES)
- Javier Llorca (CIBERESP)
- Eva Bermejo (Biobanco ISCIII)
- Nerea Fernández de Larrea (CIBERESP & CT Biobanco ISCIII)
- Cristina Razquín Burillo (CIBEROBN)
- Mª Jesús Pareja (Andalucía)
- Jacobo Martínez Santamaría (Comunidad Valenciana)
- Beatriz Sobrino (Galicia: Programa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





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

COHORTE IMPaCT



COHORTE IMPaCT

Roberto Pastor Barriuso

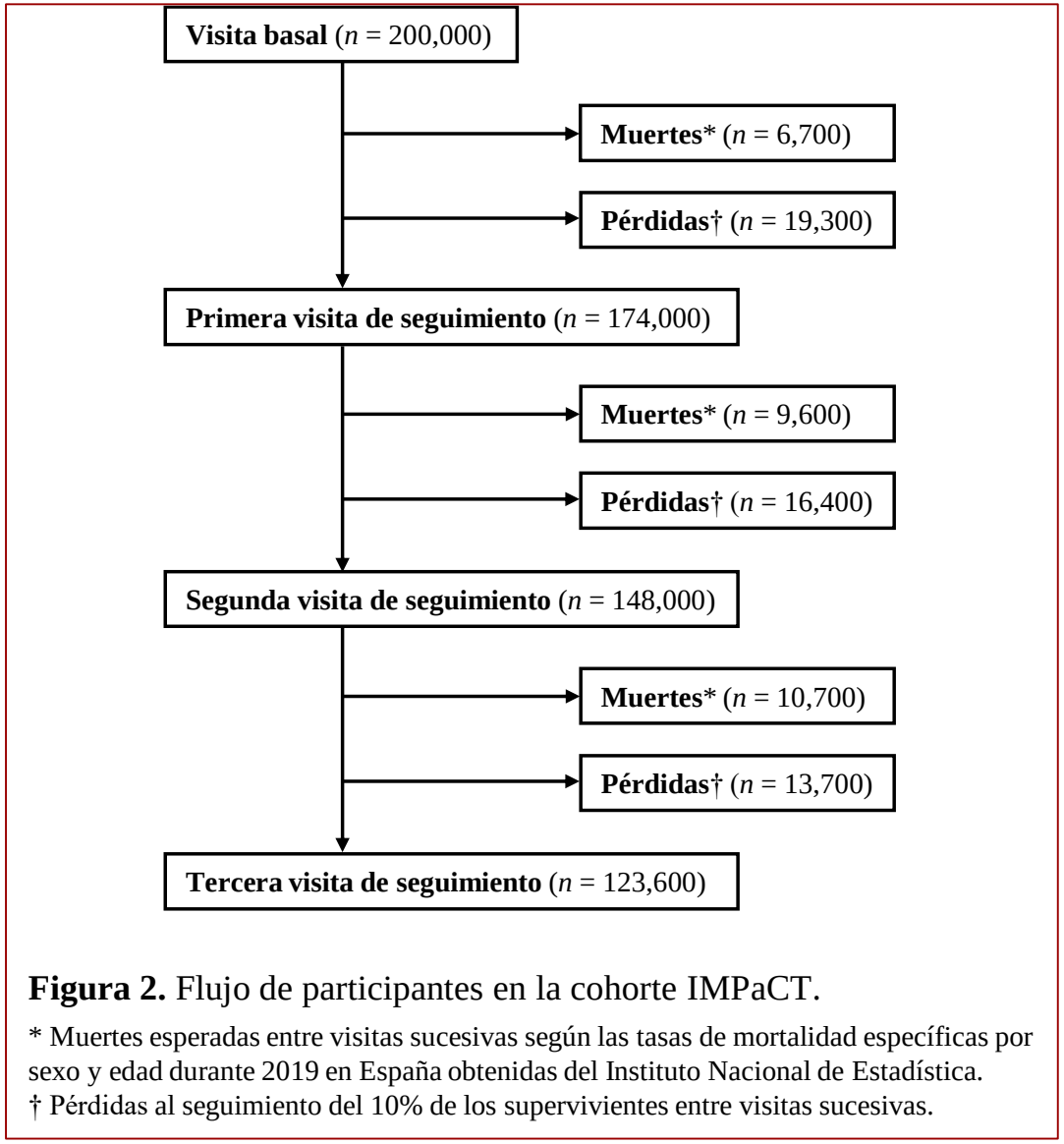


Figura 2. Flujo de participantes en la cohorte IMPaCT.

* 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**

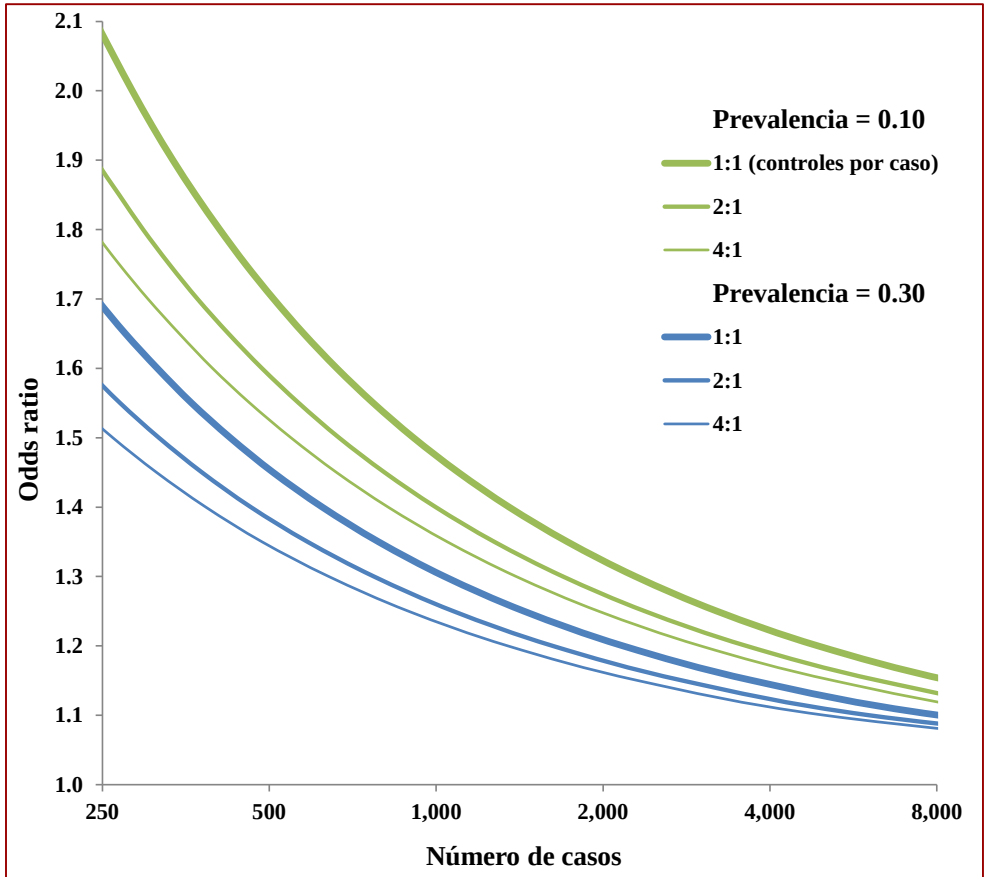


Figura 3. Odds ratio mínimo detectable en función del número de casos, la razón de controles a casos y la prevalecia poblacional de exposición.

CRONOGRAMA

	2021				2022				2023			
Mes	**3**	**6**	**9**	**12**	**15**	**18**	**21**	**24**	**27**	**30**	33	36
P1. Coordinación.		E0	E0	E0	E0	E0	E0	E0	E0	E0	E0	E0
P2. Elaboración de estrategia de selección y reclutamiento de los participantes en el estudio.		E1										
P3. Definición y medida de las variables de interés		E2 E3										
P4. Definición de procedimientos del biobanco.		E4										
P5. Elaboración de estrategia seguimiento activo de los participantes en la cohorte.						E5						
P6. Plan de análisis de datos.				E6								
P7. Elaboración de procedimientos de recogida y transmisión automatizada de la información, gestión y depuración centralizada de la base de datos, control de calidad.				E7	E8							
P8. Aspectos éticos y legales.				E9 E10								
P9.Trabajo de campo												
Manual operacional				E11								
Entrenamiento profesionales estudio piloto												
Estudio piloto						E12						
Entrenamiento de profesionales para reclutamiento y recogida datos												
Reclutamiento y recogida datos de la cohorte							E13	E13	E13	E13	E13	E13
P10. Enlace (linkage) de información obtenida de los participantes con información historia clínicas electrónicas y otras bases de datos sanitarias y no sanitarias												
Definición de los procedimientos								E14				
Actividades de linkage												
P11. Comunicación con los participantes en el estudio y la ciudadanía.												
Definición de los procedimientos					E15	E16		E17				
Actividades de comunicación												

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)