cohorte CONSTANCES
Améliorer la santé de demain

The Biobank of the French CONSTANCES Cohort

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POPULATION-BASED EPIDEMIOLOGICAL COHORTS
INSERM-UVSQ UMS 011

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The CONSTANCES Cohort Study

- Main objective: an open general-purpose epidemiological infrastructure
- Specific objectives
  - Scientific: focus on chronic diseases, aging, occupational risks, social determinants and health inequalities, women's health
  - Public health: description of the French adult population health status and of exposures to major risk factors; description of the use of the health care system ; trajectories of prevention and health care

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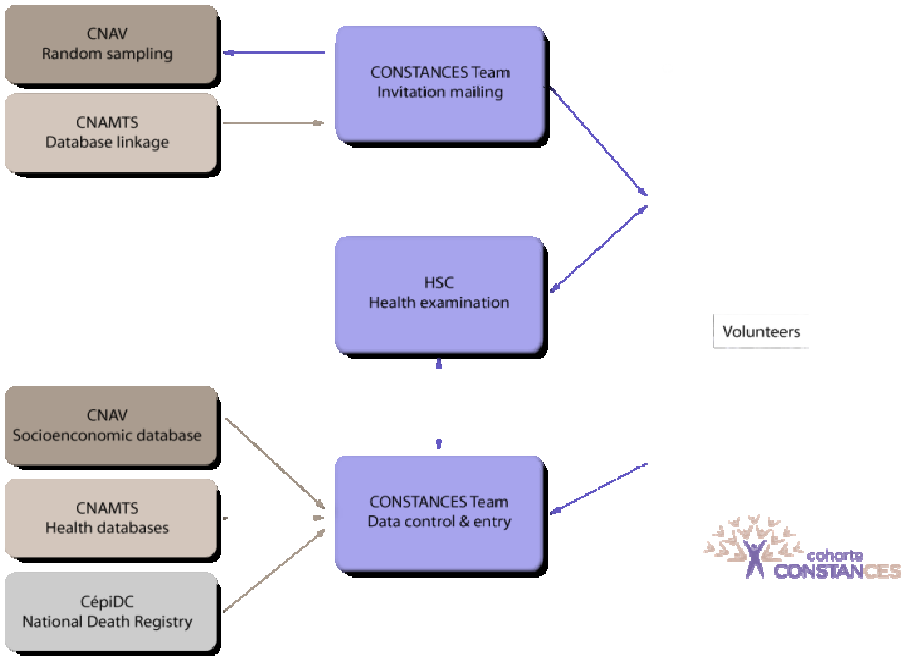
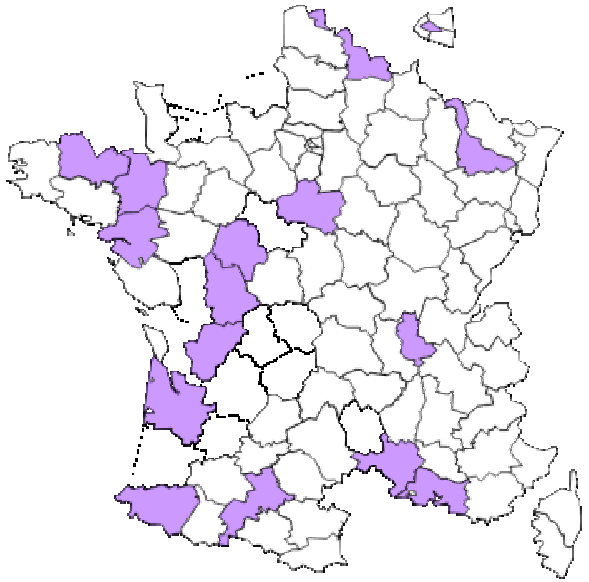
General overview of the design



Main features of the cohort

- Structure:
  - 18-69 years at inception
  - representative of the general population for age, gender and SES
- Size: 200,000 subjects
- Recruitment: in 17 Health Screening Centers
- Inclusion period: 5 years starting in January 2012



Data collected at inclusion

- Socioeconomic factors
- Occupational data
- Lifestyle
- Health
  - medical history, health scales
  - physical and biological screening: biometry, blood pressure, respiratory function, vision and audition, current diseases, main blood parameters
  - Specific health screening for the 45+: full cognitive and physical functioning work-up
- Biobank: blood and urine

Follow-up

- Annual mail questionnaire: occupational status, working conditions and exposures, housing, life habits, life events, health scales and disease incidence and treatment, social network and functioning…
- Regular visits to the HSC: every 5 years
- Regular linkage with national data bases
  - Mortality data base: vital status, cause of death
  - Retirement data base: detailed occupational status
  - Health data bases: hospitalization, serious diseases, health care system use (doctor visits, drugs…)
  - "La Poste": address follow-up and geocoding
- Control of selection and attrition effects
  - Random cohort of non-participants (n=400,000)
  - Follow-up in the same national data bases

CONSTANCES Biobank: Objectives

- Anticipating
  - Future research questions
  - Evolution of analytical and storage techniques

- Offering a high quality of the stored specimens and long-term integrity

In order to share the biological resources as large-scale data-pooling

Ensuring the integrity of the Biosamples (1)

Pre-storage phase: avoiding (minimizing) the artifacts due to cells lysis, cells metabolism and enzymatic degradation through harmonization and monitoring of collection steps

- Reduced time between sampling and centrifugation (45 mn max)
- Quick and complete separation of blood cells from serum/ plasma
- Storage after centrifugation at 4-8℃ in the dark
- Transportation from each collection sites to the aliquoting platform within 24 hours at 4-8℃
- Robotisation of the aliquoting
- Aliquoting the samples into aliquots of small volume (<= 0.5 mL for serum and plasma, 1,0 mL for urine) to avoid freeze-thaw cycles

Stability of analytes at 4-8°C

- Blood analytes
  - 345 analytes studied:
    - 15 are not stable within 2 days
    - 21 are not stable within 4 hours
- Urine analytes
  - 45 analytes studied:
    - 0 are not stable within 2 days
    - 4 are not stable within 4 hours

Recommendations of the WG on Preanalytical Quality of the German Society for Clinical Chemistry and Laboratory Medicine
3rd revised edition 2010

Ensuring the integrity of biosamples (2)

- Specific programs requiring special care during the pre storage phase:
  - Blood collection on ice
  - Immediate pre analytical treatment
  - Immediate freezing
  - Isolation of morphonuclear cells
  - Etc, …..

Will be placed on recruitment sites specially trained and equipped

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Biosamples

Basic program (whole cohort)

- *Serum:* proteins, hormones, nutrients, biomarkers (4 aliquots 0.3/0.5 mL)
- *Plasma (Lithium Heparine):* biomarkers (4 aliquots 0.3/0.5 mL)
- *Plasma (EDTA):* biomarkers (4 aliquots 0.3/0.5 mL)
- *Buffy-coat:* genomics, epigenetics (2 aliquots 0.5 mL)
- *Urine:* biomarkers (4 aliquots 1.0 mL)

In all: more than 4,000,000 aliquots

Optional program (on subsets of participants)

- *Washed erythrocytes*
- *RNA (Paxgene Blood RNA System)*
- *Proteins (P 100 tube)*
- *Mononuclear cells (+ cryoprotectant)*
- *Saliva*
- *Hair, nails, feces*

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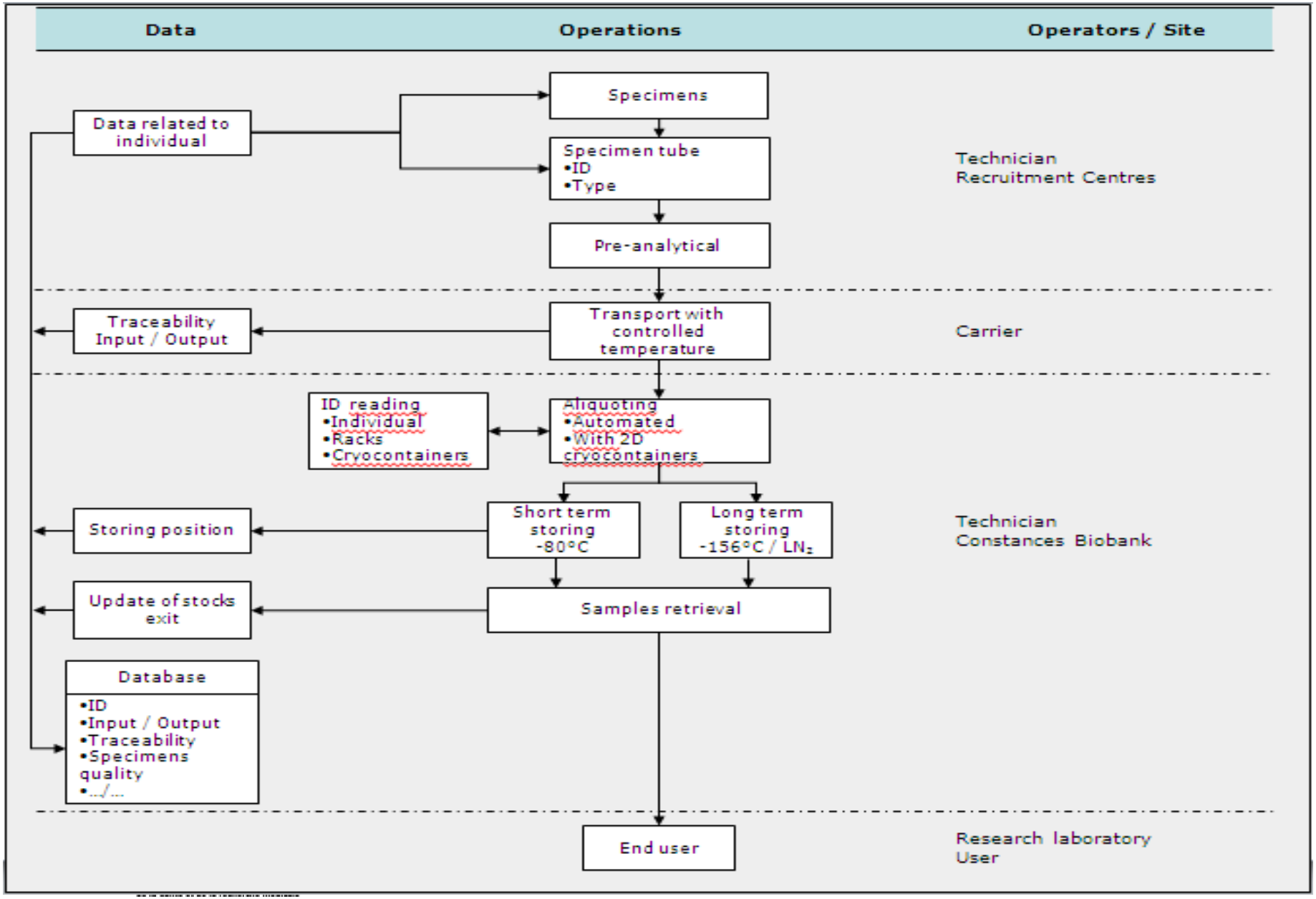
CONSTANCES Biobank: general design

The Biobank will divided into two separate parts:

- An "active" (working) Biobank for a short/middle term preservation and regular in-/ouputs (< 5years, -80℃).

- A "passive" (archive) Biobank for a long term preservation (> 10-15 years, -150/-196℃ in liquid nitrogen (or vapor phase)). This passive biobank will also work as back-up storage.

- For safety reasons both parts of the CONSTANCES biobank will be located on two different sites.


Data
Operations
Operators / Site
Specimens
Data related to individual
Specimen tube
•ID
•Type
Technician
Recruitment Centres
Pre-analytical
Transport with controlled temperature
Traceability Input / Output
Carrier
ID reading
•Individual
•Racks
•Cryocontainers
Aliquoting
•Automated
•With 2D cryocontainers
Short term storing -80°C
Long term storing -156°C / LN2
Storing position
Technician
Constances Biobank
Samples retrieval
Update of stocks exit
Database
•ID
•Input / Output
•Traceability
•Specimens quality
•.../...
End user
Research laboratory
User

Quality Assurance scheme

- Staff training scheme: staff's skills will be regularly improved and checked
- Standard Operating procedures (SOPs) for all the processes
- Maintenance scheme for:
    - Infrastructure
    - Buildings
    - Equipment (laboratory, storage devices, …)
    - Information System (equipment, data base)
    - 24h/a day; 7d/a week
- Quality audit (external and internal)
- Traceability of all the operations
- Certification / accreditation

Quality Control

- Scheduled controls will be implemented
  - Robots for aliquoting the biosamples
  - Temperature monitoring
  - Security devices
  - Regular control of the localization of each aliquot
  - Scheduled assessment of the specimens “biological” quality (eg: stability) for molecules of interest and DNA

Traceability

- Each “life event” of each biosample will be recorded in the Biobank Information System
  - Sampling
  - Pre analytical phase on the recruitment center
  - Transportation
  - Reception in the biobank
  - Aliquoting steps
  - Storage management: in- and outputs
  - Shipping to the final user

Examples

Date and hours

•Blood sampling
•centrifugation
•Shipping
•Arrival at the central repository
•Input in the central repository
• in the back-up repository
•Retrieval
•Shipping to the final user

Specimens

•Quality of the specimens (checked in the central lab’)
•Lipaemic, haemolized, icteric, ….
•Number of aliquots for each biological fluids

Biobank Information System (BIS)

- In-and output of specimens
- Location and traceability of samples
- Robots interfaced
- Risk assessment management: alarms, quality assurance scheme monitoring
- Back-up storage of the data
- ID number within the biobank DB different from ID used for the central DB of the cohort
- Password-secured interface for linkage of biological and epi data for the same individuals
- Interoperability of the Constances data base will facilitate its integration in national and international biobank networks

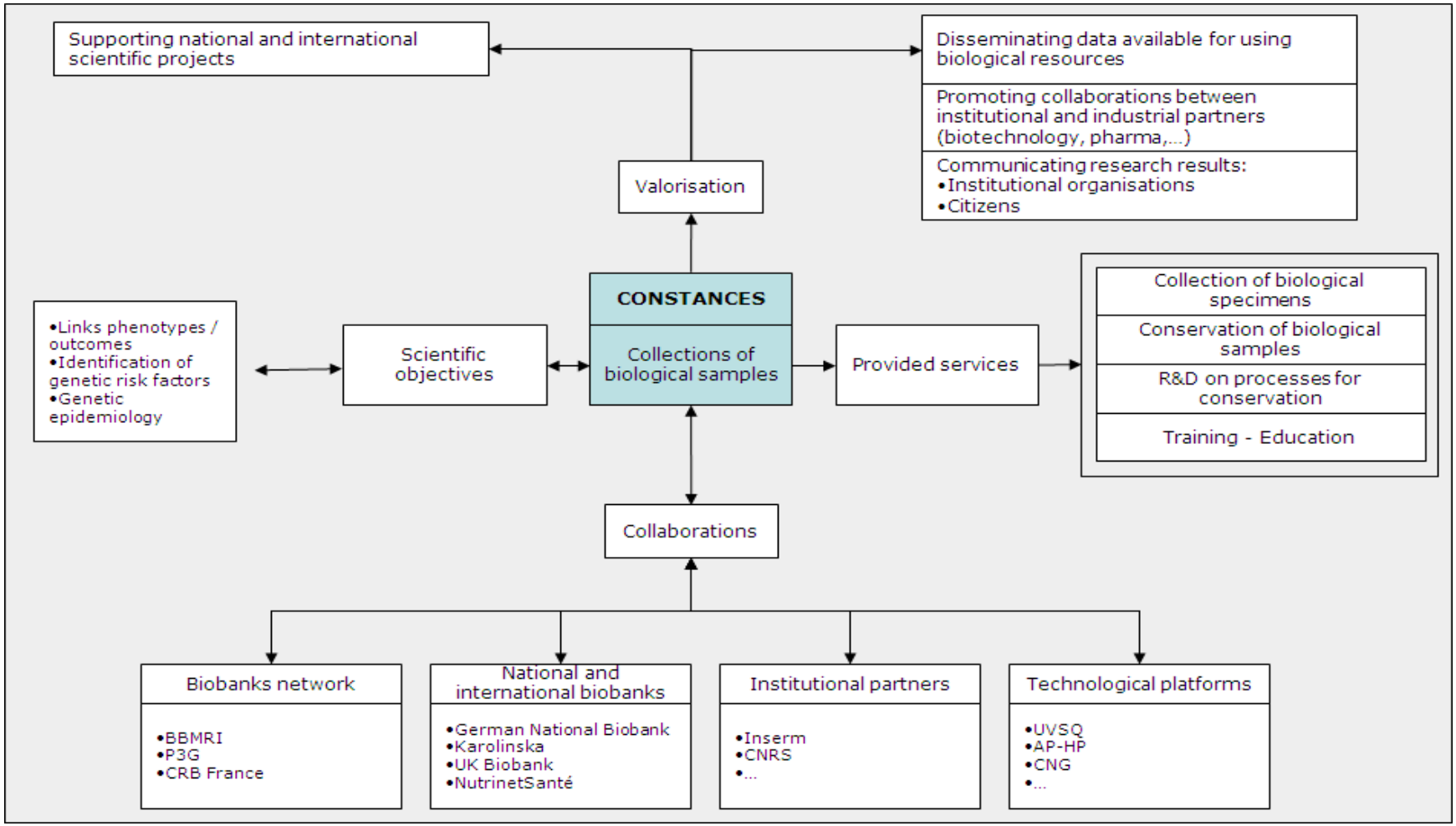
Certification

- According to the French Standard NF 96-600

  "Quality of Biological Resource Center"
- According to the recommendation of the OECD
- Approval as "Biological Resource Center" (BRC) by the French official bodies
- Compliant with the requirements of other countries (FDA: CFR 21 part 11, etc…)
- The CONSTANCES biobank is member of the French BIOBANQUES infrastructure, part of the BBMRI network

Governance

- International Scientific Committee of the Constances Cohort
- Institutional Steering Committee
- Scientific Advisory College



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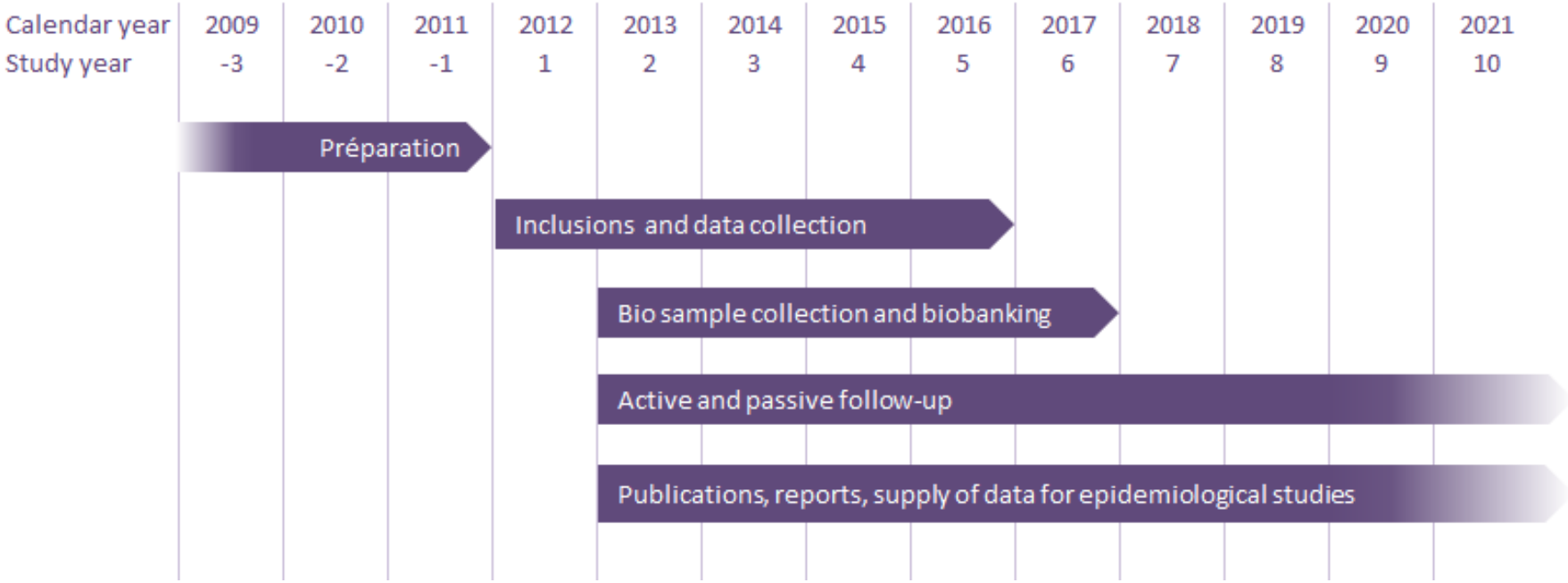
Timescale

TIME SCHEDULE



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