BORDEAUX POPULATION HEALTH

Research Center - U1219

YEAR BOOK 2021

université de BORDEAUX

RÉPUBLIQUE FRANÇAISE
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Inserm
La science pour la santé
From science to health

Created in January 2016, under the direction of Prof. Christophe Tzourio, the Bordeaux Population Health Research Centre is a Mixed Research Unit (UMR) affiliated to the National Institute of Health and Medical Research INSERM and the University of Bordeaux. The Centre and its teams are evaluated for renewal every five to six years on the basis of the quality of their activity and the relevance of their scientific projects.

Since January 2022, the centre is directed by Prof. Stéphanie Debette.

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FOREWORD

FROM THE DIRECTION

Stéphanie Debette

Director, Bordeaux
Population Health research center, 2022-2027

Stéphanie Debette, MD PhD, is Professor of Epidemiology at University of Bordeaux and practicing Neurologist at Bordeaux University Hospital. She serves as current director of the BPH. Prof. Debette has been coordinating large genomic and epidemiological studies on stroke, cognitive traits, and imaging markers of brain aging, especially cerebral small vessel disease, aiming to decipher underlying molecular mechanisms and to improve prevention and treatment of stroke and dementia. Prof. Debette leads an ERC grant, is PI of a national investment for the future grant (RHU-SHIVA) and has been coordinating the EU-JPND BRIDGET initiative. She received the Claude Pompidou Foundation prize for dementia research, and the scientific excellence award of the European Stroke Organization. A former Fulbright and Bettencourt-Schueller fellow and adjunct associate professor at Boston University, she was a visiting professor at Kyoto University. She serves in the research steering committee of the Cohorts for Heart and Aging Research in Genomic Epidemiology (CHARGE) consortium and chaired the International Stroke Genetics Consortium (ISGC, 2017-2019). As former vice-president for external relations at the University of Bordeaux (2018-21) she led a H2020 program to establish a joint research and innovation agenda within the ENLIGHT European University Alliance.

It is an honor and privilege to draft these few lines to inaugurate the first Yearbook of the Bordeaux Population Health research center (BPH). As such, besides a presentation of the research teams and 2021 research highlights, the following pages also include a few facts and figures describing the center and its environment.

Co-hosted by the University of Bordeaux and INSERM, the BPH brings together over 500 staff members with a common goal: to explore and address major public health challenges and priorities with a multidisciplinary perspective and robust methodological approaches. Our mission is to generate high-quality scientific evidence to better understand disease mechanisms, prevent disease occurrence in the population and provide optimal care to patients.

The center comprises 10 research teams, as well as a scientific coordination across teams covering (i) brain health across the lifecourse, (ii) data science (AI, omics, longitudinal data, real world health data research), (iii) infectious diseases and preparedness, (iv) aging and resilience, and (v) environmental and social determinants of health, with research objects ranging from observational studies to interventions.

The BPH (previously named Research Centre in Epidemiology and Biostatistics) was established in 2008 under the leadership of Prof. Roger Salamon and directed since 2015 by Prof. Christophe Tzourio. The center was successfully renewed in January 2022, when I stepped in as the new director.

I would like to seize the opportunity of these introductory words to thank Prof. Tzourio, as well as deputy director Prof. Rodolphe Thiébaut, for their enormous investment for the BPH community over the past years and their outstanding leadership. During Prof. Tzourio's term the BPH literally doubled in size, growing from 250 to more than 500 staff members and further increased its international visibility and recognition. Several world-class researchers and their teams joined the center and the research spectrum was expanded, strengthening its interdisciplinary component. Last but not least, they skilfully guided us through the pandemic.

At the same time, I would like to thank Dr. Hélène Jacqmin-Gadda, who worked closely with me between 2019 and 2021 to set up the new team structure and scientific program for the evaluation by the HCERES committee and host institutions. Her support and wise insight have been key.

In this new term, I am grateful to be supported by a steering committee comprising 5 team directors, Dr. Carole Dufouil, Dr. Hélène Jacqmin-Gadda, Dr. Olivier Marcy, Prof. Antoine Pariente, Dr. David-Alexandre Tregouët, advising me on various leadership aspects and taking on specific tasks to prepare the monthly board of directors.

I would also like to thank the BPH administrative team, directed by Isabelle Bely, whose daily support and efficient work, including particular efforts throughout the pandemic and constructions in our building, are much appreciated. Special thanks to Valérie Garcia for her help in preparing this first edition of the BPH yearbook.

BPH IDENTITY

Organisation
Research areas
Cross-cutting themes
Key figures
The BPH within the community

ORGANISATION

Director: Prof. Stéphanie Debette
Secretary General: Isabelle Bely

The BPH brings together over 500 staff members with a common goal: to explore and address major public health challenges and priorities with a multidisciplinary perspective and robust methodological approaches. As one of the largest public health research centers in France, the BPH is internationally recognized for its cutting-edge research, the unique, deeply phenotyped cohorts it has created and followed for up to 30 years, the seamless collaboration between data scientists, epidemiologists and clinicians, its leadership role in international consortia, and strong partnerships with the Global South.

Research organisation

The BPH is devoted to producing innovative research based on robust methodology to address a wide range of public health challenges. The Center is composed of 10 complementary research teams gathering basic and clinician scientists, healthcare professionals, technicians and engineers, post-doctoral fellows, PhD and undergraduate students who work together towards a common goal.

DOMAINS OF RESEARCH

The 10 BPH research teams cover a wide array of research domains. "Historical" topics covered since inception include biostatistics, neuroepidemiology, epidemiology of infectious diseases, cancer, aging, nutrition, and trauma prevention. Subsequently this focus was broadened to encompass public health data science with artificial intelligence dimensions, real world data in pharmacoepidemiology and beyond, genetic and molecular epidemiology, global health including for non-communicable diseases, social determinants of health, health economics, and methodological research in prevention.

Scientific coordination across research teams

Weekly scientific seminars are organised across the 10 research teams along 5 themes representing a major focus of BPH research. BPH research, under the overall coordination of Dr. Hélène Jacqmin-Gadda These are also aligned with strategic topics of Horizon Europe and aim at contributing to the United Nations' sustainable development goals.

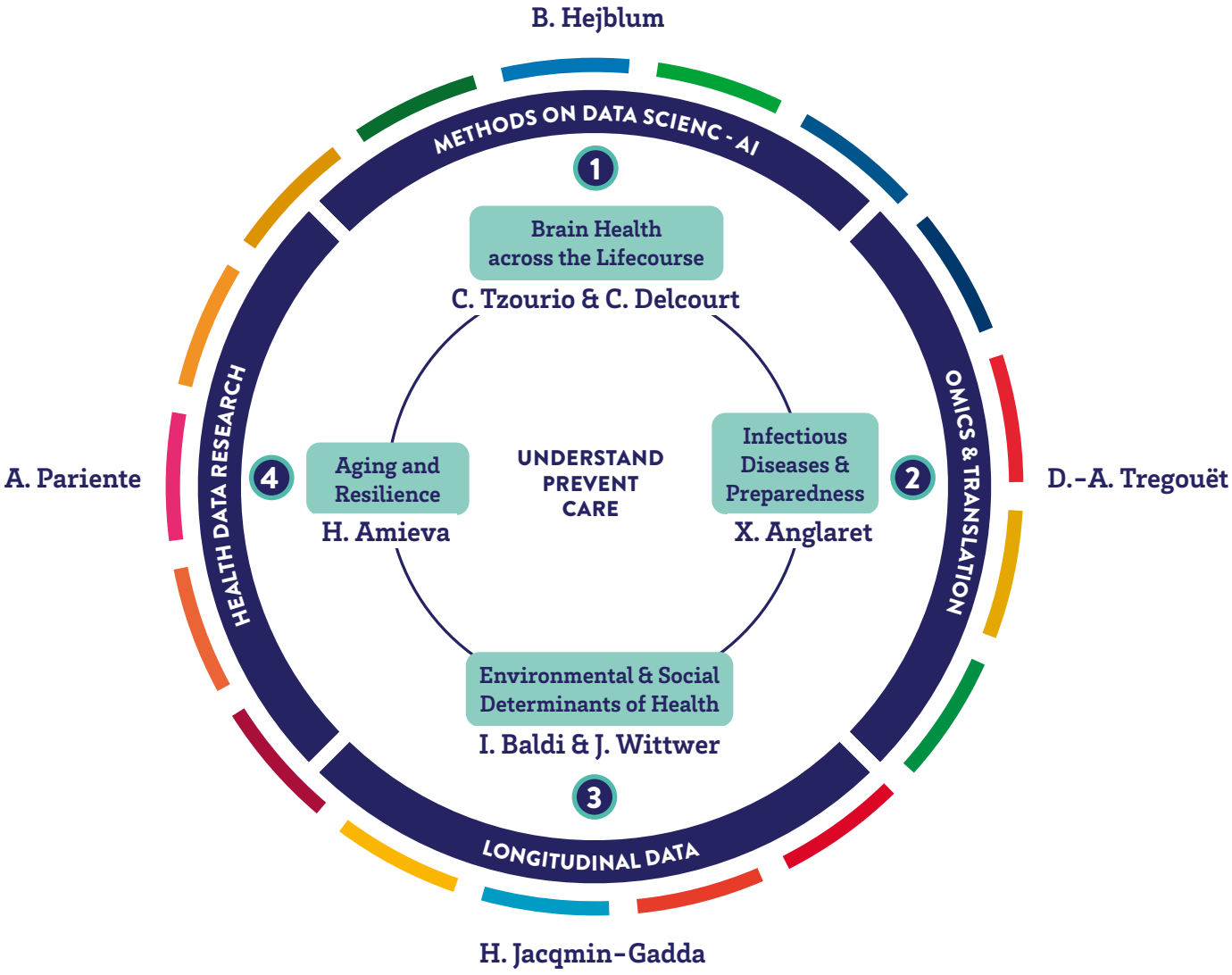
H. Jacqmin-Gadda
Overall coordinator

4 applied cross-cutting themes

1. Brain health across the life course, co-led by Christophe Tzourio & Cécile Delcourt
2. Infectious diseases and preparedness, led by Xavier Anglaret
3. Environmental and social determinants of health, co-led by Isabelle Baldi & Jérôme Wittwer
4. Ageing and resilience, led by Hélène Amieva

1 data science cross-cutting theme with 4 sub-themes:

1. Artificial intelligence, led by Boris Hejblum
2. Omics, led by David-Alexandre Tregouët
3. Longitudinal data, led by Hélène Jacqmin-Gadda
4. Health data research, led by Antoine Pariente



KEYS FIGURES

RESEARCH OUTCOMES DURING THE PAST 5 YEARS

2958
Scientific papers (2015-2020)

21%
TOP 10
Percentage of publications by our teams within the top 10% of the most cited worldwide.

3,04
Normalised citation index for the 2013-19 period

300
Others outcomes

- **>120** Scientific books or monographs
- **42** Software contributions
- **13** Patents
- **3** Start-ups
- **>120** General public communications

NATIONAL OR INTERNATIONAL GRANTS & RESEARCH INCOMES DURING THE PAST 5 YEARS

36
International grants (outside Europe), among which 15 in coordination

28
European grants (ERC, H2020, etc.), among which 7 in coordination

157
National public grants (ANR, PHRC, FUI, INCA, etc.), among which 102 in coordination

9
National investment for the future initiative grants (PIA), among which 3 in coordination

42
Local grants (regional government, etc.), among which 30 in coordination

68
Grants from foundations and charities (ARC, FRM, etc.), among which 56 in coordination

24
Covid projects

> 25
Prizes and/or distinctions

KEY FIGURES FOR 2021

680
Scientific papers in 2021

ONGOING RESEARCH CONTRACTS

122
Contracts including...

- **106** National public grants
- **6** European grants
- **4** International grants (outside Europe)
- **6** Grants from foundations and charities or private entities (ARC, FRM, etc.)

STAFF MEMBERS

10
Research teams

491
Staff including

- **99** Researchers or teacher/clinician-researchers
- **28** Hospital practitioners
- **42** Permanent supporting staff (study and research engineers, technicians and administrative staff)
- **165** Non-permanent supporting staff
- **120** PhD students
- **17** Post-docs

THE BPH WITHIN COMMUNITY

The BPH is co-hosted by Inserm and the University of Bordeaux. Two BPH research teams have a third host institution, INRIA (SISTM team) and IRD (GHiGS team). The center is located within the University of Bordeaux campus, one of the largest university campuses in Europe, and specifically on the Carreire biomedical campus. The BPH is situated within walking distance from Bordeaux University Hospital, with which it entertains strong connections.

RESEARCH-BASED TEACHING

The University of Bordeaux was one of the first four universities in France to receive the Initiative of Excellence label from the Investments for the Future scheme (PIA). It is identified as a world-class cluster of excellence in higher education and scientific research.

Public health teaching

We are located next to the teaching premises of the ISPED Bordeaux School of Public Health, directed by Prof. Simone-Mathoulin-Pelissier, also a researcher at the BPH. All ISPED teachers conduct their research in a BPH team and 51 researchers from the BPH teach at the ISPED on a regular basis. ISPED delivers training courses in areas such as epidemiology, biostatistics, health promotion, occupational and environmental health, global health, management of medical and medico-social organisations, public health data science, and medical informatics.

Graduate programs and summer schools

BPH researchers developed an international research-based teaching offer supported by PIA3 funding (EUR), including the Digital Public Health Graduate Program (DPH) and an interdisciplinary graduate program to address current and future public health challenges in Africa (EUR@ AFRICA). Moreover, BPH researchers co-lead several international summer school programs (e.g. Neurepiomics) and methodological seminars (e.g. Melodem), and contribute to the ISPED summer school programs.

Health sciences and medical curriculum

BPH researchers also make significant contributions to university curricula by teaching (research-based) courses in various disciplines: Health Sciences (Medical Science Faculty, Pharmaceutical Science Faculty) and Social Sciences (Psychology Faculty, Social sciences, Anthropology and Ethnology Faculty).

CLINICAL RESEARCH

The link with the clinical sector of the University Hospital of Bordeaux (CHUB) is reinforced by the strong involvement of many BPH researchers as leaders in the main methodological and operational structures for clinical and epidemiological research.
Many clinicians (neurologists, psychiatrists, infectious disease specialists, oncologists, emergency medicine specialists, etc.) are also involved in BPH research projects, some of them as directors or deputy directors of the research teams.

Methodological structures

- CIC-EC (Centre for Clinical Investigations – Clinical Epidemiology)
- Population-based cancer registries
- Clinical trial units in various domains:
  - EUCLID (EUropean CLInical Trials Platform & Development) F-CRIN (French Clinical Research Infrastructure Network) platform for international trials
  - USMR (Methodological support unit for clinical and epidemiological research) for clinical research at Bordeaux University Hospital.
  - CMG-EC (Methodology and Clinical Trial Management Centre) for HIV and hepatitis research (with ANRS)
  - MEREVA (Methodology and monitoring of clinical research on HIV and other infectious diseases in developing countries) for clinical research in low-income countries.

Hospital units led by BPH researchers

- Departments of Medical Informatics
- Occupational health unit for research organisations
- Hospital Unit for Innovation in Prevention (UHIP) at CHU Saint André.

CHU BDX CENTRE HOSPITALIER UNIVERSITAIRE BORDEAUX

Bordeaux Universiy Hospital (CHUB) is one of the largest French University Hospitals in terms of activity, with a total capacity of 3,000 beds.

LARGE-SCALE PROJECTS AND PARTNERSHIPS

BPH researchers lead several ambitious research projects funded by the "Investment for the Future" program of the French Government (PIA3) as well as various other large competitive programs funded at the national, European, or international level. Some of these (as of 2021) are listed below.

"Investment for the Future" program (PIA3)

- BCube, the Bordeaux Biobank for Brain Health Cohort
- RHU SHIVA "Recherche Hospitalo-Universitaire en santé" on cerebral small vessel disease

Large competitive research programs funded by the University of Bordeaux Initiative of Excellence

- Large research program (GPR) IPORA (coordinator): Interdisciplinary Policy-Oriented Research on Africa.
- Large research program (GPR) HOPE (WP lead): Understanding Human Well-being and Behavior for better Policies & Societies
- Impulse program PHDS (coordinator): Public Health Data Science Bordeaux Network
- Impulse program (WP lead on the impact of the environment): Tackling global change, integrated approaches for people and environment

European programs with a coordinating role

- EBOVAC-2 (IMI H2020), phase 2 trial for an Ebola vaccine
- BRIDGET (JPNDcoFUND), (epi)genomic determinants of brain aging
- Drug-Safe 2 (ANSM), risks of medical drugs-administrative databases
- TB-speed (UNITAID), to increase TB diagnosis in children
- NIH, International epidemiology Databases to Evaluate AIDS (IeDEA) in Western Africa

Department of Public Health / Université de BORDEAUX

Research at the University of Bordeaux is divided into 11 departments, each bringing together different research structures (joint research units, university teams, platforms, etc.). The department of Public Health, directed by Prof. Antoine Pariente, comprises the Bordeaux Population Health Research Centre with its 10 research teams, the Clinical Investigation Centre (CIC 14.01), and, since September 2022, the service unit MART (Methods and Applied Research for Trial).

RESEARCH

RESEARCH TEAMS
RESEARCH HIGHLIGHTS
IN 2021

AGING, CHRONIC DISEASES, TECHNOLOGY, DISABILITY, AND ENVIRONMENT

BPH RESEARCH TEAM ACTIVE

Pr. Hélène Amieva

PhD, ACTIVE Director

Hélène Amieva has a PhD in neurosciences. After one year of post-doctoral fellowship at the Psychology Department of Aberdeen University (UK), she has been working at the CNRS as a permanent researcher for nine years. She is currently Professor of psychogerontology at Bordeaux University.
Her main expertise is in the field of epidemiology and neuropsychology of aging, dementia and Alzheimer's disease, in particular psychosocial factors modulating clinical trajectories and cognitive decline in aging. She has also been involved in clinical studies assessing non-drug treatments. She has conducted the ETNA3 study, a national trial assessing the efficacy of non-pharmacological therapies in Alzheimer's disease, involving 653 patients followed up for three years in 40 French hospital centers. Currently, she is the principal investigator of the study assessing the impact of the French Alzheimer Village in South-western France, an innovative experiment for people suffering from Alzheimer's disease.
She is the author or co-author of about 190 articles published in international journals.
She is co-director of the Master of "Psychogerontology and Public Health" at Bordeaux University. Since 2021, she is the general secretary of the French speaking society of Neuropsychology relying on a community of physicians, psychologists, speech therapists and researchers working in French-speaking countries and actively involved in the field of neuropsychology.

The ACTIVE team is composed of epidemiologists,psychologists, cognitive scientists, geriatricians, physical therapists, neurologists and a psychiatrist, with the aim of studying: (1) intrinsic capacities of individuals and environmental factors contributing to develop/maintain/ reduce functional capacity in the context of acute/chronic disease, disability, and/or old age; and (2) innovative strategies based on the optimization of such factors.

The first research axis investigates to what extent intrinsic capacity and environments contribute to develop/ maintain/ reduce functional ability (coordinated by Karine Pérès):
Functional trajectories of aging process are studied through a continuum distinguishing robustness, pre-frailty, frailty, and activity limitation. We examine their determinants through a multidimensional approach considering intrinsic capacities (cognition, depression,sensory impairments, personality trait…) and environmental factors (family support, social network, (un)adapted home, professional assistance, digital technologies) that may influence the sequence and speed of functional deterioration. The heterogeneity of these trajectories is explored in several prospective population-based and clinical studies: PAQUID, AMI, 3C, CONSTANCES, COGLOC…
Taking advantage of the ongoing cohort studies, the PA-COVID sub-study, set up very shortly after the first COVID-19 lockdown in France, aims at providing valuable knowledge on older adults' social and psychological experiences of the COVID-19 crisis and their impact on cognitive, mental and functional health.

The second research axis focuses on innovative strategies based on the optimization of individuals' intrinsic capacity and/or environments (coordinated by Hélène Sauzéon):
As an example of strategies based on optimised environments, the French Alzheimer village (opened in 2020 in the city of Dax) is an experimental village hosting 120 persons with Alzheimer's disease. Built like a traditional village with a historic centre, medical institution stigmas are avoided to make the environment feel home-like. Equipped with places to live (restaurant, hair salon, grocery, library…), it aims at providing a home-like environment, optimizing the opportunities to participate in daily activities and social life with other people. A 5-year research program evaluating whether this model is successful compared to traditional nursing homes is ongoing.

Le village Alzheimer de Dax

Our research program that involves interventions relying on digital technologies addresses two significant health issues: rehabilitation access and patient agentivity (i.e., active role of the patient). Good candidates for interventions with digital technologies are patients who are not care-compliant due to their geographical distance from specialized rehabilitation centres. A 3-year research project is being conducted on patients with vascular aphasia to evaluate the benefits of tele-rehabilitation compared to a conventional face-to-face condition.
Another research component stresses the role of self-determination in rehabilitation by leveraging recent technological advances. The program includes a large panel of individuals of various ages and with various disability conditions. The goal is to study the impact of the technology properties of adaptability (self-configuration of objectives/contents of the intervention by the care recipient) and/or adaptivity (self-configuration of intervention by machine-learning algorithms) on rehabilitation results.

2021 Key publications

. Knopman DS, Amieva H, Petersen RC, Chételat G, Holtzman DM, Hyman BT, Nixon RA, Jones DT. Alzheimer disease. Nat Rev Dis Primers. 2021 May 13;7(1):33.

. Zamudio-Rodríguez A, Dartigues JF, Amieva H, Pérès K. A Literature Review of Healthy Aging Trajectories through Quantitative and Qualitative Studies: A Psycho-epidemiological Approach on Community-dwelling Older Adults. J Frailty Aging. 2021;10(3):259-271

. Hernández-Ruiz V, Meillon C, Avila-Funes JA, Bergua V, Dartigues JF, Koleck M, Letenneur L, Ouvrard C, Pérès K, Rascle N, Tabue-Teguo M, Amieva H. Older Adults and the COVID-19 Pandemic, What About the Oldest Old? The PACOVID Population-Based Survey. Front Psychiatry. 2021 Aug 20;12:711583.

. Pérès K, Ouvrard C, Koleck M, Rascle N, Dartigues JF, Bergua V, Amieva H. Living in rural area: A protective factor for a negative experience of the lockdown and the COVID-19 crisis in the oldest old population? Int J Geriatr Psychiatry. 2021 Dec;36(12):1950-1958.

. Pech M, Sauzeon H, Yebda T, Benois-Pineau J, Amieva H. Falls Detection and Prevention Systems in Home Care for Older Adults: Myth or Reality? JMIR Aging. 2021 Dec 9;4(4):e29744.

. David R, Cassoudesalle H, Chhun H, Compagnat M, Amaghnouj K, Leclère FM, Moucheboeuf G, Glize B, De Seze M. Informative booklet enhances adherence to brace in young people with idiopathic scoliosis. Ann Phys Rehabil Med. 2021 Jul;64(4):101420.

. Arheix-Parras S, Barrios C, Python G, Cogné M, Sibon I, Engelhardt M, Dehail P, Cassoudesalle H, Moucheboeuf G, Glize B. A systematic review of repetitive transcranial magnetic stimulation in aphasia rehabilitation: Leads for future studies. Neurosci Biobehav Rev. 2021 Aug;127:212-241.

. Cassoudesalle H, Petit A, Chanraud S, Petit H, Badaut J, Sibon I, Dehail P. Changes in resting-state functional brain connectivity associated with head impacts over one men's semi-professional soccer season. J Neurosci Res. 2021 Feb;99(2):446-454.

. Hucteau E, Noize P, Pariente A, Helmer C, Pérès K. ADL-dependent older adults were identified in medico-administrative databases. J Clin Epidemiol. 2021 Nov;139:297-306.

. Mazon C, Etchegoyhen K, Saint-Supery I, Amestoy A, Bouvard M, Consel C, Sauzéon H. Fostering parents-professional collaboration for facilitating the school inclusion of students with ASD: design of the "ToGather" web-based prototype. Educ Technol Res Dev. 2021 Dec 2:1-32.

ASSESSING HEALTH IN A DIGITALIZING REAL-WORLD SETTING PHARMACOEPI & BEYOND

BPH RESEARCH TEAM AHEAD

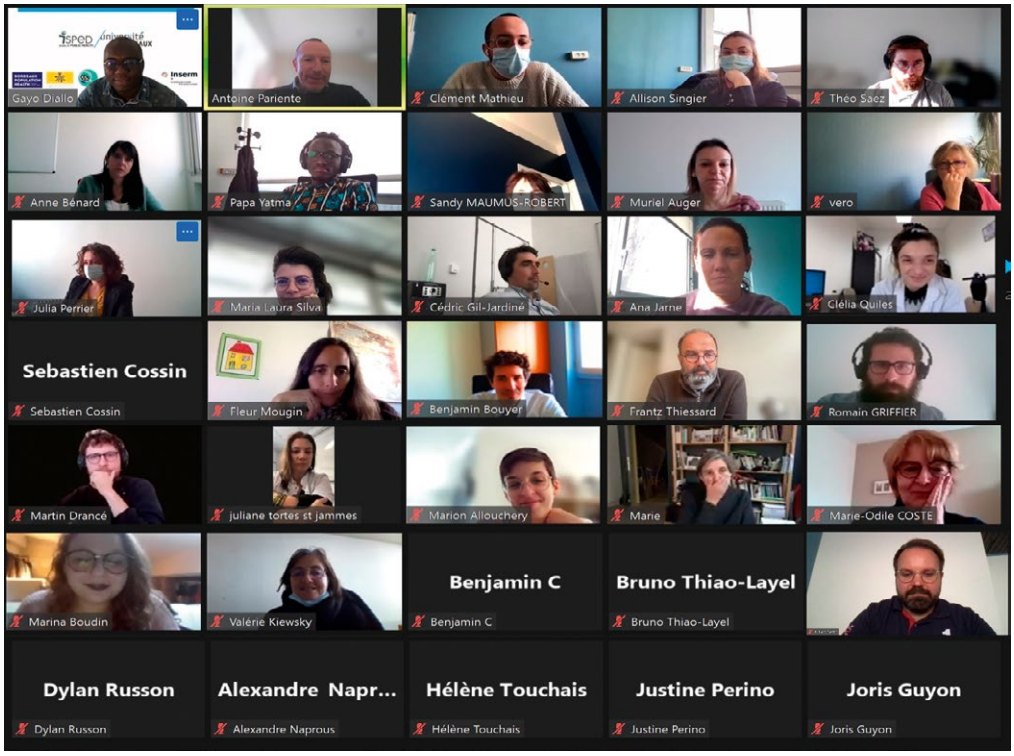
Pr. Antoine Pariente

MD, PhD, AHEAD Director

Dr. Antoine Pariente did his MD in Pharmacology and Public Health and completed his training with a PhD in Pharmacoepidemiology focusing on population impact of drugs in dementia.
From 2016 to 2021, he headed the Bordeaux Pharmacovigilance Centre; from 2018 to 2021, he was appointed as a scientific independent expert towards the European Medicines Agency Pharmacovigilance Risk Assessment Committee (PRAC), where he was selected to chair the Interest Group for Impact of Pharmacovigilance regulatory Actions Assessment.
During the 2015-2019 period, he coordinated the French national academic platform for pharmacoepidemiology DRUGS-SAFE (Drugs Systematized Assessment in real-life environment). After being selected through a national call emitted by the French Drug Agency, this was transformed into the DRUGS-SAFER Centre. Antoine Pariente also coordinates this academic centre, which has been appointed by the authorities to provide real-world evidence supporting decision-making regarding the use and safety of drugs.
From 2016 to 2020, he chaired the Bordeaux Population Health research team "Pharmacoepidemioloy-Drugs and Population Health".
He is now the director of the BPH AHeaD team, created from the merging of the Pharmaco, ERIAS (headed by Gayo Diallo), and IETO (headed by Emmanuel Lagarde) teams.

We are interested in better understanding healthcare in a real-world setting and better assessing medicines in this observational environment. We aim to investigate trajectories of care and their determinants, with a specific interest in emergency care use on the one hand, and trajectories of care for patients with chronic diseases relating to cardiovascular health or mental health on the other hand.

Over the past five years, we belonged to three different teams ("Pharmacoepidemiology-Pharmacoepi"; "Injuries-IETO"; "Informatics in Health-ERIAS"). The collaborations we developed ultimately concentrated most of our teams' research efforts around the secondary use of electronic databases for the study of health and medicines in a real-world setting.
In anticipation of the research challenges that will emerge from the multiplication, diversification, and complexification of digital health data, we decided to join forces with the AHeaD team project.
This will combine our originating teams' expertise in electronic health records databases (HERs), hospital data warehouses, ontologies, data visualization, knowledge representation, and machine learning and natural language processing for health research, thus constituting a tremendous research opportunity. Indeed, while the questions and needs for health assessment in real-world settings will remain, the way to answer these questions is likely to change dramatically. In the coming years, the use of electronic health databases, that developed tremendously over the past 30 years, will need to be complemented using information from other sources that will help strengthen and substantiate the real-world evidence provided. Building bridges between applied health research, already widely using EHRs, and informatics appears as a necessity when envisioning the future development of health assessment in real-world settings.
The research will divide into three axes corresponding to different objectives and methods:



The research will divide into three axes corresponding to different objectives and methods:

1. Data & Signals: Structuring and bridging data for hypothesis-generating in real-world assessment

Safety signal or repurposing hypotheses are mostly presented or generated from the results obtained from one data source/ type of information analysis. We intend to go further by developing approaches that will combine various types/sources of information for hypothesis-generating research from real-world data.

2. Use & Effectiveness: Stay focused, remain global

Medicine & health determinants assessment is better performed when closely focusing on one type of medicine or care. The downside is to risk losing sight of the overall care environment (therapeutic alternatives; healthcare trajectories).

We intend to develop research that will contextualize and characterize overall healthcare surrounding targeted research regarding the use or effectiveness of a given type of medicine or care.

3. Policies & Impact: Assessing the public health impact of regulatory actions

The hypotheses generated/confirmed within the two first research axes can result in official recommendations or regulatory actions aiming to optimize healthcare strategies. Here, our research will assess to what extent these strategies are successfully adopted and beneficial to health, thereby completing our research path from generating a hypothesis to applying it in society.

2021 Key publications

COVID-19 related publications

. Nair G, Robblee J, Drici MD, Valnet-Rabier MB, Micallef J, Salvo F, Treluyer JM, Liu PP. Features of inflammatory heart reactions following mRNA COVID-19 vaccination at a global level. Clin Pharmacol Ther. 2021. doi: 10.1002/cpt.2499. Epub.

. Gil-Jardiné C, Chenais G, Pradeau C, Tentillier E, Revel P, Combes X, Galinski M, Tellier E, Lagarde E. Surveillance of COVID-19 using a keyword search for symptoms in reports from emergency medical communication centres in Gironde, France: a 15-year retrospective cross-sectional study. Intern Emerg Med. 2021. doi: 10.1007/s11739-021-02818-5. Epub.

. Ramiz L, Contrand B, Rojas Castro MY, Dupuy M, Lu L, Sztal-Kutas C, Lagarde E. A longitudinal study of mental health before and during COVID-19 lockdown in the French population. Global Health. 2021;17:29. doi: 10.1186/s12992-021-00682-8.

. Gil-Jardiné C, Chenais G, Pradeau C, Tentillier E, Revel P, Combes X, Galinski M, Tellier E, Lagarde E. Trends in reasons for emergency calls during the COVID-19 crisis in the department of Gironde, France using artificial neural network for natural language classification. Scand J Trauma Resusc Emerg Med. 2021;29:55. doi: 10.1186/s13049-021-00862-w.

. Létinier L, Jouganous J, Benkebil M, Bel-Létoile A, Goehrs C, Singier A, Rouby F, Lacroix C, Miremont G, Micallef J, Salvo F, Pariente A. Artificial Intelligence for Unstructured Healthcare Data: Application to Coding of Patient Reporting of Adverse Drug Reactions. Clin Pharmacol Ther. 2021;110:392-400. doi: 10.1002/cpt.2266.

. Klann JG, Estiri H, Weber GM, Moal B, Avillach P, Hong C, Tan ALM, Beaulieu-Jones BK, Castro V, Maulhardt T, Geva A, Malovini A, South AM, Visweswaran S, Morris M, Samayamuthu MJ, Omenn GS, Ngiam KY, Mandl KD, Boeker M, Olson KL, Mowery DL, Follett RW, Hanauer DA, Bellazzi R, Moore JH, Loh NW, Bell DS, Wagholikar KB, Chiovato L, Tibollo V, Rieg S, Li ALLJ, Jouhet V, Schriver E, Xia Z, Hutch M, Luo Y, Kohane IS; Consortium for Clinical Characterization of COVID-19 by EHR (4CE) (CONSORTIA AUTHOR), Brat GA, Murphy SN.

. Validation of an internationally derived patient severity phenotype to support COVID-19 analytics from electronic health record data. J Am Med Inform Assoc. 2021;28:1411-20. doi: 10.1093/jamia/ocab018.

Mental health, psychotropics and dementia related publications

. Linard M, Bezin J, Hucteau E, Joly P, Garrigue I, Dartigues J-F, Pariente A, Helmer C. Antiherpetic drugs: a potential way to prevent Alzheimer's disease? Alzheimers Res Ther. Accepted Tournier M, Pambrun E, Maumus-Robert S, Pariente A, Verdoux H. The risk of dementia in patients using psychotropic drugs: Antidepressants, mood stabilizers or antipsychotics. Acta Psychiatr Scand. 2021. doi: 10.1111/ acps.13380. Epub.

Data & signals developments non-COVID related publications

. Osman I, Ben Yahia S, Diallo G: Ontology Integration: Approaches and Challenging Issues. Information Fusion. 2021; 71: 38-63. https:// doi. org/10.1016/j.inffus.2021.01.007.

. Altman MC, Rinchai D, Baldwin N, Toufiq M, Whalen E, Garand M, Syed Ahamed Kabeer B, Alfaki M, Presnell SR, Khaenam P, Ayllón-Benítez A, Mougin F, Thébault P, Chiche L, Jourde-Chiche N, Phillips JT, Klintmalm G, O'Garra A, Berry M, Bloom C, Wilkinson RJ, Graham CM, Lipman M, Lertmemongkolchai G, Bedognetti D, Thiebaut R, Kheradmand F, Mejias A, Ramilo O, Palucka K, Pascual V, Banchereau J, Chaussabel D. Development of a fixed module repertoire for the analysis and interpretation of blood transcriptome data. Nat Commun. 2021;12:4385. doi: 10.1038/s41467-021- 24584-w.

BIOSTAT

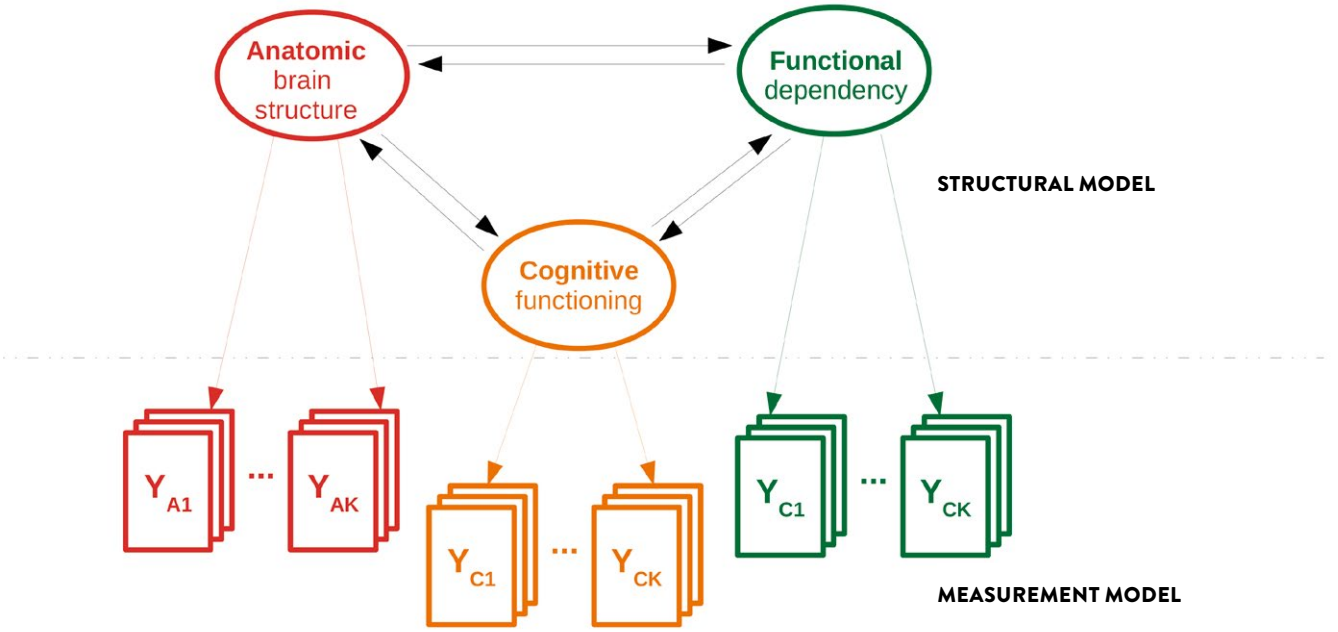
BPH RESEARCH TEAM BIOSTATISTICS

Dr. Hélène Jacqmin-Gadda
PhD, BIOSTAT Director

Hélène Jacqmin-Gadda obtained the "Habilitation à Diriger des Recherches" (HDR) in Biostatistics in 2002 at Bordeaux University (France). She is Director of Research at the French National Institute of Health and Medical Research (Inserm) and head of the Biostatistics team at the BPH since 2014. Her research focuses on statistical methods for the analysis of longitudinal data with complex observation schemes and especially, models for multivariate longitudinal data and joint models for longitudinal data and time-to-event, as well as evaluation of predictive abilities of these models. Her main motivation is the study of cognitive aging and dementia. Other fields of application are HIV and cancer. She has advised 23 master students and 10 PhD students. She has co-authored about 130 publications in peer-review journals and two books about biostatistical models in epidemiology published in 2015. She is currently associate editor of *Statistics in Medicine and the International Journal of Biostatistics* and she was associate editor of Biometrics from 2003 to 2014.

The main objective of the team is the development of statistical methods for time-dependent data coming from either observational cohort studies, clinical trials or case-control studies, with the aim of answering clinical and public health questions regarding chronic diseases: future burden, risk factors, individual prediction, underlying pathological mechanisms, and treatment effects.

Over the past five years the team has worked on two main topics: multivariate models for time-dependent data and model-based estimation of public health indicators. Our main domain of research focuses on the development of multivariate dynamic models for the analysis of censored time-to-events and/or repeated measures of longitudinal data accounting for complex observation schemes. These works are motivated by the study of the natural history of chronic diseases such as Alzheimer's disease or Multi-System Atrophy, the investigation of the impact of time-dependent exposures, or the validation of surrogate markers for clinical trials in cancer research. Parametric and semiparametric estimation procedures for frailty models for correlated time-to-events, clustered data and/or recurrent events as well as joint models for event times and longitudinal markers were implemented in the R-package Frailtypack. Another field of research is the extension of mixed models using latent classes and/ or latent processes for the analysis of multiple longitudinal outcomes with non-standard distributions in heterogeneous populations. We proposed the R-package LCMM, which enables the estimation of latent class mixed models, joint latent class mixed models and mixed models for curvilinear univariate or multivariate longitudinal outcomes. These models were motivated by the analysis of cognitive decline in cohort studies. They account for population heterogeneity and issues raised by the metrologic properties of measurement tools of cognition and autonomy (high correlation between markers measuring one or several underlying processes, ordinal data, non-standard asymmetric distributions with floor and/or ceiling effects and unequal sensitivity to changes). We also designed methods for the estimation of Illness-Death model accounting for interval-censoring (Package SmoothHazard). Tools for computing individual prediction and evaluating predictive abilities of these models were also developed. Relying on multi-state methodology, we propose several approaches to forecast the future burden of neurologic diseases



and assess the expected impact of intervention scenarios, targeting their modifiable risk factors. Depending on the complexity of the investigated scenarios, the indicators for the future burden of the disease are computed analytically or using micro-simulations.

Our current projects particularly focus on causal questions and big-data issues in the framework of dynamic models. On the one hand, causal questions are related to our research about the mechanism underlying pathological processes in chronic diseases, the role of long-term exposure and the impact of social inequalities in health. We plan on investigating the causal interpretation of the multivariate models we developed and we will propose new methods for studying causality for censored time-to-events and/or time-dependent risk factors. On the other hand, as technological progress helps collect large amounts of data (genetics, biology, imaging, IoT data), we will investigate new approaches that tackle high-dimensionality issues with respect to the number of time-dependent predictors, markers and outcomes.

2021 Key publications

. Ben-Hassen, C., Helmer, C., Berr, C., Jacqmin-Gadda, H. 5-year dynamic prediction of dementia using repeated measures of cognitive tests and a dependency scale. Am J Epidemiol, 2021 (online 9/11/2021) https://doi.org/10.1093/aje/kwab269

. Carles, S., Taddé, B. O., Berr, C., Helmer, C., Jacqmin-Gadda, H., Carrière, I., Proust-Lima, C. Dynamic reciprocal relationships between cognitive and functional declines along the Alzheimer's disease continuum in the prospective COGICARE study. Alz Res Therapy 2021, 13(1), 1-12. https://doi.org/10.1186/ s13195-021-00887-4

. Castel C, Sommen C, Le Strat Y, Alioum A. A multi-state Markov model using notification data to estimate HIV incidence, number of undiagnosed individuals living with HIV, and delay between infection and diagnosis: illustration in France, 2008-2018. Stat Methods Med Res. 2021 Nov;30(11):2382-2398. https://doi.org/10.1177%2F09622802211032697

. De Courson H, Ferrer L, Barbieri A, Tully PJ, Woodward M, Chalmers J, Tzourio C, Leffondré K. Impact of Model Choice When Studying the Relationship Between Blood Pressure Variability and Risk of Stroke Recurrence. Hypertension. 2021;78(5):1520-1526. https://doi.org/10.1161/ HYPERTENSIONAHA.120.16807

. Dinart D, Bellera C, and Rondeau V. Sample size estimation for cancer randomized trials in the presence of heterogeneous populations. Biometrics, 2021; https://doi.org/10.1111/biom.13527

. Emura T., Sofeu C., and Rondeau V. Conditional copula models for correlated survival endpoints: individual patient data meta-analysis of randomized controlled trials. Stat Methods Med Res, 2021, 30(12); https://doi.org/10.1177%2F09622802211046390

. Kaboré R, Ferrer L, Couchoud C, Hogan J, ..., Harambat J, Leffondré K. Dynamic prediction models for graft failure in pediatric kidney transplantation. Nephrol Dial Transplant 2021; 36(5):927-935. https://doi.org/10.1093/ndt/gfaa180

. Philipps V, Hejblum BP, Prague M, Commenges D, Proust-Lima C. Robust and Efficient Optimization Using a Marquardt-Levenberg Algorithm with R Package marqLevAlg. The R Journal 2021; http://arxiv.org/abs/2009.03840

. Rouanet A, Avila-Rieger J, Dugravot A, Lespinasse J, Stuckwisch R, Merrick R, Anderson A, Long L, Helmer C, Jacqmin-Gadda H, Dufouil C, Judd S, Manly J, Sabia S, Gross A, Proust-Lima C. How selection over time contributes to the inconsistency of the association between sex/gender and cognitive decline across cognitive aging cohorts. Am J Epidemiol 2021; https://doi.org/10.1093/aje/ kwab227

. Wagner M, Grodstein F, Leffondre K, Samieri C, Proust-Lima C. Time-varying associations between an exposure history and a subsequent health outcome: a landmark approach to identify critical windows. BMC Med Res Methodol 2021;21(1):266; https://doi.org/10.1186/s12874-021-01403-w

MOLECULAR EPIDEMIOLOGY OF VASCULAR AND BRAIN DISORDERS

BPH RESEARCH TEAM ELEANOR

Dr. David-Alexandre Trégouët

PhD, ELEANOR director

Holder of a PhD in Public Health (1999), with strong emphasis on genetic epidemiology, his research career started with the development of statistical methods to analyze family data as well as genetic polymorphisms in the context of candidate association studies. He then turned to the development and application of statistical/bioinformatics tools for the analysis of high-throughput microarray and next generation sequencing data. In parallel to these methodological developments, he is participating in the design and the analysis of several epidemiological studies aiming at identifying molecular determinants of cardiovascular diseases, his specialty being venous thrombosis (VT). He is joint coordinator of the French EOVT, FARIVE, MARTHA, MARFAST and PILGRIM studies, and joint convener of the International Network of Venous Thrombosis (INVENT) consortium, aimed at identifying genetic factors for VT. Within the F-CRIN supported INNVOTE network that brings together all French clinicians working in the field of VTE, he supervises the re search programs on VT genomics. Over recent years, his interests have extended to molecular epidemiology integrating epigenetics marks, microRNA and proteomic profiling in order to develop a research program on precision medicine in thrombotic disorders.

Pr. Stéphanie Debette

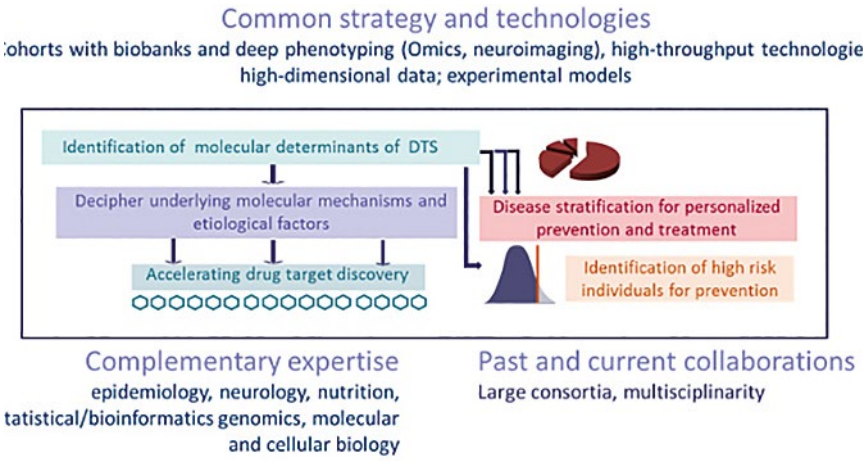
MD, PhD, BPH Director,
ELEANOR Deputy Director

The purpose of our research is to identify groups of individuals who are at high risk of developing three common and tightly linked neurological and vascular conditions: (dementia, stroke and venous thrombosis), to discover novel etiological factors and therapeutic targets, and to propose more personalized preventive strategies through improved risk stratification.

Our research program relies on major components:
(1) large-scale epidemiological and clinical cohorts coupled with biosamples; (2) the deployment of cutting-edge high-throughput technologies for deep molecular phenotyping;
(3) the application of advanced statistical methodologies;
(4) a group of experts in molecular-clinical epidemiology and
(5) a widespread network of collaborators that enables us to contribute to the functional characterization of the identified biomarkers.
Our project focuses on three interrelated clinical outcomes: cognitive impairment / dementia, stroke, and thrombosis, and is organised around 4 themes:

Molecular epidemiology of vascular brain aging, (PI: Stéphanie Debette)
Using collaborative genome-wide association study, meta-analyses and next-generation sequencing data, we are studying the genetic underpinnings of stroke and MRI-markers of covert cerebral small vessel disease (SVD). We have a growing interest in cross-ancestry studies, as these are crucial to enhance genomic discovery and make results more representative. Through the ERC SEGWAY, we are taking a lifespan approach to explore early determinants of brain aging and the impact of genetic predisposition to stroke, dementia and SVD on brain microstructure in young adults (i-Share cohort). In the RHU SHIVA project (national investment for the future funding), following up on efforts that we initiated in the EUJPND BRIDGET program, we are now expanding our explorations to other omics approaches (epigenomics, transcriptomics, proteomics and metabolomics), focusing in particular on deciphering the molecular underpinnings of covert SVD and its contribution to stroke and dementia. Finally, we are engaged in leveraging these molecular epidemiology studies to accelerate drug discovery and improve risk prediction/stratification for targeted prevention. Our group is also involved in European therapeutic guideline coordination.

INTEGRATIVE RESEARCH:
MOLECULAR EPIDEMIOLOGY OF DEMENTIA, STROKE AND VENOUS THROMBOSIS



Exposome of brain aging and dementia (PI: Cécilia Samieri)
The network and dynamics of environmental factors leading to age-related brain diseases has yet to be elucidated, in order to identify the most impactful targets for prevention. This exposome research axis leverages molecular epidemiology, brain imaging and advanced statistical approaches deployed to population-based cohorts with biobanks in order to investigate:
(1) the exposome of brain health at key ages, and
(2) the underlying pathways and life-course dynamics.
The general aims are to: refine assessment of already-known exposures (e.g., diet biomarkers); explore novel exposures (e.g., chemical mixtures); investigate beyond individual exposures (e.g., microbiome interactions); and eventually model the global exposome network, to improve etiological modeling of age-related brain diseases. We aim to capitalise on existing data (e.g., the 3C cohort) and target younger populations, building a new population-based cohort of 2,000 participants aged 55-80 years from the community living in the Bordeaux metropole, the B cube (Biobank and Brain Health in Bordeaux) study.

Precision Medicine for better prophylaxis & better knowledge on venous thrombosis (PI:David-Alexandre Trégouët)
After spending several years identifying common genetic factors of venous thrombosis (VT) in the general population, we are now embarking into a more integrative analysis of various molecular determinants (genes; epigenetic marks, proteins,...) on specific subgroups of individuals at higher risk of VT, including women under oral contraceptives, patients with a previous history of VT and patients with viral infections.
In parallel, building on our recent successes, we will continue our genetic investigations of rare forms of unexplained inherited VT through the application of whole exome/genome sequencing in familial cases.

Integrative approach for vascular and brain disorders (all PIs)
The deep characterisation and understanding of the biology of a complex disease requires to integrate results/data from other diseases as they very often share common risk factors and pathophysiological mechanisms. By capitalising on the existence of complementary and synergistic expertise and bioresources brought by ELEANOR's PIs in different yet interrelated diseases, we are implementing an integrative research strategy to optimize the identification and the characterisation of molecular determinants associated with some of the most common age-related diseases.

2021 Key publications

. Arsandaux J, Montagni I, Macalli M, Texier N, Bordes C, Sargurupremraj M, Mishra A, Debette S. Genetics of common cerebral small vessel disease. Nat Rev Neurol, in press Goumidi L, Thibord F, [...], Debette S, [...], Trégouët DA, Morange PE. Association between ABO haplotypes and the risk of venous thrombosis: impact on disease risk estimation. Blood. 2021;137(17):2394-2402.

. Harris WS, [...], Samieri C, [...], Mozaffarian D, on behalf of the Fatty Acids and Outcomes Research Consortium (FORCE). Circulating n-3 fatty acid levels and total and cause-specific mortality: A de novo pooled analysis from 17 prospective studies. Nat Commun. 2021 Apr 22;12(1):2329.

. Le Grand Q, Satizabal CL, Sargurupremraj M, Mishra A, Soumaré A, Laurent A, Crivello F, Tsuchida A, Shin J, Macalli M, Singh B, Beiser AS, DeCarli C, Fletcher E, Paus T, Lathrop M, Adams HHH, Bis JC, Seshadri S, Tzourio C, Mazoyer B, Debette S. Genomic studies across the lifespan point to early mechanisms determining subcortical volumes. Biol Psychiatry Cogn Neurosci Neuroimaging. 2021: S2451-9022(21)00286-X.

. Lefèvre-Arbogast S, Hejblum BP, Helmer C, Klose C, Manach C, Low DY, Urpi-Sarda M, Andres-Lacueva C, González-Domínguez R, Aigner L, Altendorfer B, Lucassen PJ, Ruigrok SR, De Lucia C, Du Preez A, Proust-Lima C, Thuret S, Korosi A, Samieri C. Early signature in the blood lipidome associated with subsequent cognitive decline in the elderly. eBio-Med. 2021 Jan 25;64:103216.

. Mishra A, Duplaà C, Vojinovic D, Suzuki H, Sargurupremraj M, Zilhão NR, [...], Soumare A, Smith JA, Knopman DS, Morris Z, Zhu Y, Rotter JI, Dufouil C, Valdés Hernández M, Muñoz Maniega S, Lathrop GM, [...], Seshadri S, Matthews PM, Longstreth Jr WT, Couffinhal T, Debette S. Gene-mapping study of extremes of cerebral small vessel disease reveals TRIM47 as a strong candidate. Brain, in press

. Morange PE, Peiretti F, Gourhant L, Proust C, Soukarieh O, Pulcrano-Nicolas AS, Saripella GV, Stefanucci L, Lacroix R, Ibrahim-Kosta M, Lemarié CA, Frontini M, Alessi MC, Trégouët DA, Couturaud F. A rare coding mutation in the MAST2 gene causes venous thrombosis in a French family with unexplained thrombophilia: The Breizh MAST2 Arg-89Gln variant. PLoS Genet. 2021;17(1):e1009284

. Razzaq M, [...], Soukarieh O, Proust C, [...], Trégouët DA. An artificial neural network approach integrating plasma proteomics and genetic data identifies PLXNA4 as a new susceptibility locus for pulmonary embolism. Sci Rep. 2021;11(1):14015.

Samieri C, Yassine HN, Melo van Lent D, Lefèvre-Arbogast S, van de Rest O, Bowman GL, Scarmeas N. Personalized nutrition for dementia prevention. Alzheimers Dement. 2021 Nov 10. Online ahead of print.

. Sargurupremraj M, Suzuki H, [...], Mishra A, Saba Y, [...], Schilling S, Sigurdsson S, [...], Bordes C, Le Grand Q, Duperron MG, Smith AV, [...], Soumaré A, Boerwinkle E, Sidney S, [...], Trégouët DA, [...], Lathrop M, Seshadri S, Tzourio C, Adams HH, Matthews PM, Fornage M, Debette S. Cerebral small vessel disease genomics and its implications across the lifespan. Nat Commun. 2020 Dec 8;11(1):6285. doi: 10.1038/s41467-020-19111-2.

. Thomas A, Crivello F, Mazoyer B, Debette S, Tzourio C, Samieri C. Fish Intake and MRI Burden of Cerebrovascular Disease in Older Adults. Neurology. 2021 Nov 30;97(22):e2213-e2222. Epub 2021 Nov 3.

EPIDEMIOLOGY OF CANCERS AND ENVIRONMENTAL EXPOSURES

BPH RESEARCH TEAM EPICENE

Pr. Isabelle Baldi

MD, PhD, EPICENE Director

Isabelle Baldi is a Professor in Occupational Health at Bordeaux University, and a member of the Environmental and Occupational Health department at Bordeaux University Hospital. Her research aims at assessing long-term effects of occupational & environmental pesticide exposure through epidemiological studies (especially on cancer and neurological outcomes). She has developed new tools for pesticide exposure assessment, such as crop exposure matrices (PESTIMAT, PESTIPOP) and algorithms (PESTEX-PO, CANEPA) based on field observations, using several epidemiological projects. She is co-leader of the AGRICAN cohort (https://www.agrican.fr/) and responsible for the neurological subgroup of the AGRICOH international consortium (https:// agricoh.iarc.fr/). She is involved in the European SPRINT program (https://sprint-h2020.eu/). She also heads the Registry of Central nervous system tumors, implemented in Gironde in 1999.

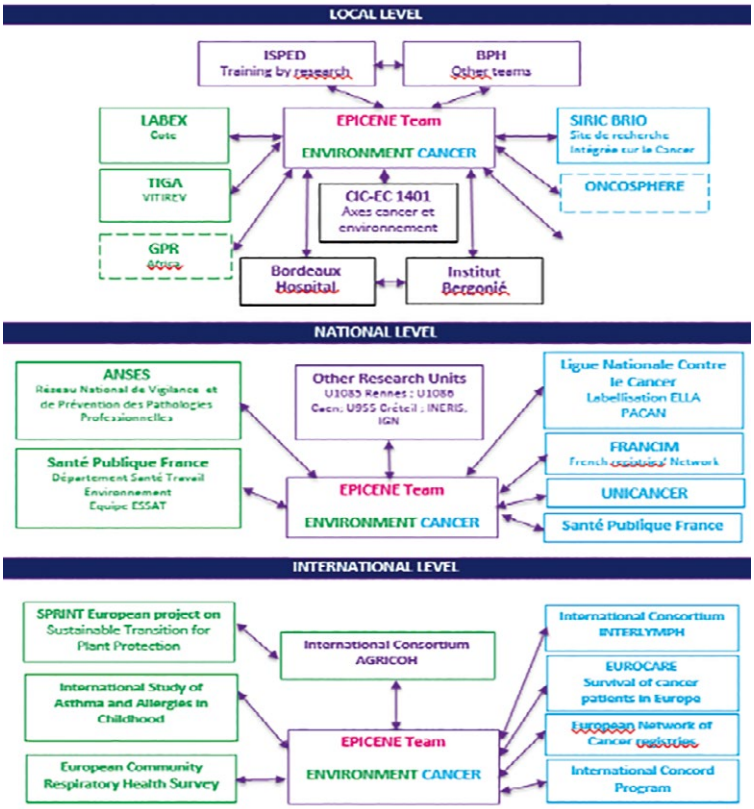
Dr. Alain Monnereau

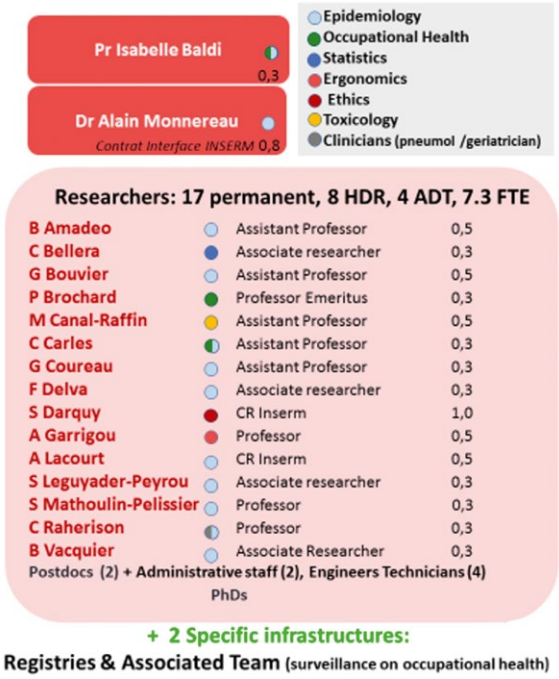
MD, PhD, EPICENE Deputy director

Alain Monnereau is a senior medical doctor specialized in epidemiology with significant research and leadership experiences within global organizations in cancer surveillance, epidemiology and public health. He has created and headed a population-based cancer registry in South-west France on hematological malignancies. He has also coordinated the French network of cancer registries and managed the cancer surveillance program of the French Cancer Plan. His experience in research on cancer epidemiology include cancer surveillance, behavioral and environmental risk factors but also clinical epidemiology, geographical epidemiology and cancer cohorts. He was member or investigator in several initiatives InterLymph international Consortium, which he chaired from 2016 to 2018. In 2022 he became Research Program Director of the Cancer Registry of California –United States.

EPICENE's research is focused on cancers and their environmental and occupational determinants. Our projects address methodological challenges in a multidisciplinary approach with the aim of expanding knowledge on cancer survival and its determinants, developing new approaches to estimate life-long environmental exposures (Exposome concept), understanding the role of the environment and the occurrence of certain cancers.

Theme 1: Cancer survival: improving knowledge, detecting frail individuals, identifying surrogate endpoints
Although survival rates have improved for the main cancers over the past decades, they remain highly variable depending on the cancer site and many more parameters. We strive to better understand the factors associated with better survival for cancer patients. Thanks to our involvement in population-based cancer registries, we generate new data on cancer survival and its determinants (treatments, comorbidities, care practices, palliative care) for several cancer types (chronic myeloid leukemia, breast cancer, lymphoma through the REALYSA cohort study...).We pay particular attention to frail people, for whom efforts of detection and prevention are strongly needed, including elderly people whose number will rapidly increase in the coming decades. We develop new tools for detection programs and we investigate cancer literacy in elderly cancer patients. Our efforts also focus on improving cancer screening strategies (organised mass screening and others). We also develop new biostatistical approaches to assess treatment efficacy and patient survival in randomized controlled trials and in real-life settings.
Theme 2: Methods in environmental and occupational exposures: the exposome concept
Our research aims to improve the knowledge of levels and determinants of exposure to major contaminants with field measurements in order to identify the main determinants of exposure (usable in retrospective questionnaires and in large population cohorts). Our research on pesticide exposures started 25 years ago and continues to provide many original data through the PESTEXPO program. We now aim to document baseline levels for "everyday" contamination on a farm and explore pesticide exposures in non-farming jobs (i.e., gardening, wood industry...). We also explore the exposures of the general population living near treated fields. We combine field measurements and ergonomic observations. Levels and determinants of exposures to other pollutants are also studied,





such as nanoparticles in the occupational and environmental settings, antineoplastic drugs in healthcare workers, electromagnetic fields... We also develop indirect exposure assessment tools, such as Job Exposure Matrices (PESTIMAT, MATPUF) and spatial modeling. Usable retrospectively in large populations with minimal collection of data (job or residential calendars), they are very useful to our epidemiological studies.

Theme 3: Environmental Etiology of Cancer

For more than 20 years, we have studied the etiology of CNS tumors, hematological malignancies and mesothelioma thanks to registries that we set up in this domain and our collaborations at both national and international levels. Recently, we also developed studies on sarcomas. As etiological research, including the role of the environment, remains scarce for most rare cancers, we intend to analyze the role of environmental determinants in the occurrence of these cancers, for which the role of environmental factors is suspected. Our efforts rely on cohorts (AGRICAN, LUCSO, REALYSA), case-control studies (CERENAT, ETIOSARC), and data from international consortia (AGRICOH, INTERLYMPH). We attempt to better understand cancer risks in specific populations, suspected to be more vulnerable because of individual conditions or comorbidities (e.g., allergies, immunological disorders), genetic characteristics (polymorphisms of detoxification genes,...) or specific exposures (women, smokers...)

2021 Key publications

. Baldi I, Carles C, Blanc-Lapierre A, Fabbro-Peray P, Druet-Cabanac M, Boutet-Robinet E, Soulat JM, Bouvier G, Lebailly P. A French crop-exposure matrix for use in epidemiological studies on pesticides: PESTIMAT. J Expo Sci Environ Epidemiol. 2017;27:56-63.

. Carles C, Bouvier G, Esquirol Y, Piel C, Migault L, Pouchieu C, Fabbro-Peray P, Lebailly P, Baldi I. Residential proximity to agricultural land and risk of brain tumor in the general population. Environ Res. 2017;159:321-30.

. Piel C, Pouchieu C, Tual S, Migault L, Lemarchand C, Carles C, Boulanger M, Gruber A, Rondeau V, Marcotullio E, Lebailly P, Baldi I, group A. Central nervous system tumors and agricultural exposures in the prospective cohort AGRICAN. Int J Cancer. 2017;141(9):1771-82.

Bellera C, Proust-Lima C, Joseph L, Richaud P, Taylor J, Sandler H, Hanley J, Mathoulin-Pelissier

. S. A two-stage model in a Bayesian framework to estimate a survival endpoint in the presence of confounding by indication. Stat Methods Med Res. 2018;27(4):1271-81.

. Galvin A, Helmer C, Coureau G, Amadeo B, Joly P, Sabathe C, Monnereau A, Baldi I, Rainfray M, Soubeyran P, Delva F, Mathoulin-Pelissier S. Determinants of cancer treatment and mortality in older cancer patients using a multi-state model: Results from a population-based study (the IN-CAPAC study). Cancer Epidemiol. 2018;55:39-44.

. Piel C, Pouchieu C, Migault L, Beziat B, Boulanger M, Bureau M, Carles C, Gruber A, Lecluse Y, Rondeau V, Schwall X, Tual S, Lebailly P, Baldi I, group AGRICAN. Increased risk of central nervous system tumours with carbamate insecticide use in the prospective cohort AGRICAN. Int J Epidemiol. 2019;48(2):512-26.

. Amadeo B, Penel N, Coindre JM, Ray-Coquard I, Ligier K, Delafosse P, Bouvier AM, Plouvier S, Gallet J, Lacourt A, Coureau G, Monnereau A, Mathoulin-Pélissier S, Desandes E. Incidence and time trends of sarcoma (2000-2013): results from the French network of cancer registries (FRANCIM). BMC Cancer. 2020 Mar 6;20(1):190.

. Frasca M, Sabathe C, Delaloge S, Galvin A, Patsouris A, Levy C, Mouret-Reynier MA, Desmoulins I, Vanlemmens L, Bachelot T, Goncalves A, Perotin V, Uwer L, Frenel ..., Mathoulin-Pelissier S. Palliative care delivery according to age in 12,000 women with metastatic breast cancer: Analysis in the multicentre ESME-MBC cohort 2008-2016. Eur J Cancer. 2020 Sep;137:240-249.

. Allemani C, Matsuda T, Di Carlo V, Harewood R, Matz M, Nikšić M, Bonaventure A, Valkov M, Johnson CJ, Estève J, Ogunbiyi OJ, Azevedo E Silva G, Chen WQ, Eser S, Engholm G, Stiller CA, Monnereau A, Woods RR, Visser O, Lim GH, Aitken J, Weir HK, Coleman MP; CONCORD Working Group. Global surveillance of trends in cancer survival 2000-14 (CONCORD-3): analysis of individual records for 37 513 025 patients diagnosed with one of 18 cancers from 322 population-based registries in 71 countries. Lancet. 2018 Mar 17;391(10125):1023-1075.

. Ghesquières H, Rossi C, Cherblanc F, Le Guyader-Peyrou S, Bijou F, Sujobert P, Fabbro-Peray P, Bernier A, Belot A, Chartier L, Fornecker LM, Baldi I, Bouabdallah K, Laurent C, Oberic L, Morineau N, Le Gouill S, Morschhauser F, Haioun C, Damaj G, Guidez S, Labouré G, Fitoussi O, Lebras L, Gressin R, Salles G, Ysebaert L, Monnereau A. A French multicentric prospective prognostic cohort with epidemiological, clinical, biological and treatment information to improve knowledge on lymphoma patients: study protocol of the "REal world dAta in LYmphoma and survival in adults" (REALYSA) cohort. BMC Public Health. 2021;21(1):432.

HEALTH, WELLBEING AND ACHIEVEMENT IN THE YOUNG

BPH RESEARCH TEAM HEALTHY

Pr. Cédric Galera

MD, PhD, HEALTHY Director

Cédric Galera is a pediatric psychiatrist and epidemiologist. He was resident in child psychiatry at the University of Bordeaux between 2000 and 2004. He did a research fellowship in Montreal (Canada) in 2003 and a clinical fellowship in Montevideo (Uruguay) in 2005. He is professor of Child and Adolescent Psychiatry at the University of Bordeaux and hospital practitioner at Charles Perrens hospital and at Bordeaux University Hospital. He has been a researcher at the BPH since 2008 and an associate researcher at the Research Unit on Children's Psychosocial Maladjustment (Cana da) since 2017.

Pr. Christophe Tzourio

MD, PhD, HEALTHY Deputy Director

Christophe Tzourio is a neurologist and epidemiologist. He is the immediate past director of the BPH. Prof. Tzourio trained as a resident at the Paris Hospitals and Chief of Clinic in Neurology at the Lariboisière Hospital. He joined INSERM in 1994 as a Research Associate and was promoted to Research Director in 2000. In 2005, he became Director of a new INSERM U708 research unit at the Pitié-Salpêtrière Hospital in Paris. In 2013, he was appointed Professor of Epidemiology at the University of Bordeaux and hospital practitioner at the Bordeaux University Hospital. From 2013 until 2021 he was director of the Bordeaux Population Health research center, Inserm U1219, at the University of Bordeaux.

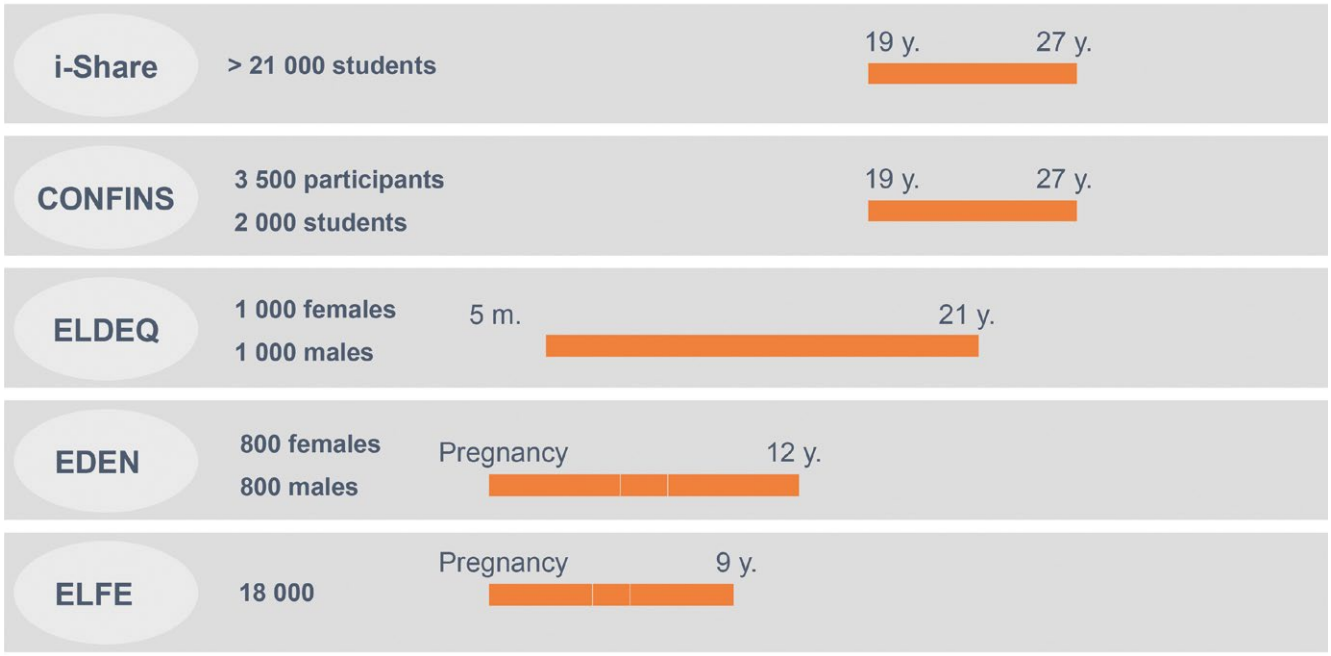
The research focus of our team is to understand and prevent mental health problems in youths.
We aim to:

1. **Investigate the risk and protective factors of Mental, Neurological and Substance use (MNS) problems in young people using a lifespan perspective**
2. **Test the efficacy of strategies to prevent Mental, Neurological and Substance use problems and build resilience to stressors in youths / parents**

Over the past five years, our team has provided relevant evidence on the early contribution of social environment and biological factors on youth mental health (cognition, externalizing behaviors, internalizing problems, ADHD and risk for suicide). Team members have studied the modulation of biological factors by the social environment in relation to externalizing problems and ADHD and the relative contributions of genes and environment on the developmental course of the ADHD phenotype and suicide risk, from the peri-conceptional period to adolescence. Team members have also found that cytokine patterns in the cord blood are associated with childhood anxiety/depression symptoms. Regarding interventions aiming at improving mental health, cognitive development and social outcomes, the team has shown the benefits of early non-parental care and evidenced the moderate efficacy of a multicomponent early intervention program on behavior, cognition and health, in an Irish sample. Team members have developed eHealth tools to be used for MNS in youths, particularly in students. These findings provide key elements to inform public policies and tailor our experimental interventions. Research of our team members takes advantages of various cohorts, including birth cohorts (ex: ELFE and ELDEQ) and young adult cohorts (iShare and CONFINS).

Our future research will rely on 3 axes:
Axis 1 Mental health epidemiology in the youths: understanding the risk and protective factors underlying MNS problems (Cédric Galera)
The HEALTHY team is particularly interested in quantifying (1) the putatively protective role that psychosocial services play on the prevention of MNS problems; (2) the impact of MNS problems on individual functioning, including educational and professional achievement; and (3) the biological and social

COHORTS USED TO INVESTIGATE MECHANISMS UNDERLYING MNS AND THEIR SEQUELAE



mechanisms underlying specific mental health disorders and problems like ADHD, depression, suicidality, pathological low levels of self-esteem, etc.

Axis 2 Exploring social and behavioral features of mental health in the youths (Ilaria Montagni, Christophe Tzourio)
This axis will aim at describing and analyzing health behaviors/lifestyle, health representations, and health literacy of young people, relying on sociological and communication approaches (Humanities and Social Sciences) and mixed-methods studies.

Axis 3 Designing, testing and evaluating interventions preventing MNS problems and promoting mental health in the youths (Cédric Galera, Ilaria Montagni, Christophe Tzourio)
We will conduct (1) specific interventions focusing on a defined mental health problem or disorder (selective and indicated interventions); and (2) general-population interventions targeting health behaviours, e.g., health literacy, healthy lifestyles, life-skills training, psycho-education (universal interventions).

2021 Key publications

. Arsandaux J, Montagni I, Macalli M, Texier N, Pouriel M, Germain R, Mebarki A, Kinouani S, Tournier M, Schuck S, Tzourio C. Mental health condition of college students compared to non-students during COVID-19 lockdown: the CONFINS study. BMJ Open. 2021 Aug 19;11(8):e053231.

. Galéra C, Cortese S, Orri M, Collet O, van der Waerden J, Melchior M, Boivin M, Tremblay RE, Côté SM. Medical conditions and Attention-Deficit/Hyperactivity Disorder symptoms from early childhood to adolescence. Mol Psychiatry. 2021 Oct 26.

. Galera C, Barbosa S, Collet O, Khalfallah O, Aouizerate B, Sutter-Dalley AL, Koehl M, Capuron L, Van der Waerden J, Melchior M, Côté S, Heude B, Glaichenhaus N, Davidovic L; EDEN Mother–Child Cohort Study Group. Cord Serum Cytokines at Birth and Children's Anxiety-Depression Trajectories From 3 to 8 Years: The EDEN Mother-Child Cohort. Biol Psychiatry. 2021 Mar 15;89(6):541-549.

. Macalli M, Texier N, Schück S, Côté SM, Tzourio C. A repeated cross-sectional analysis assessing mental health conditions of adults as per student status during key periods of the CO VID-19 epidemic in France. Sci Rep. 2021 Nov 9;11(1):21455.

. Macalli M, Orri M, Tzourio C, Côté SM. Contributions of childhood peer victimization and/or maltreatment to young adult anxiety, depression, and suicidality: a cross-sectional study. BMC Psychiatry. 2021 Jul 14;21(1):354.

Macalli M, Navarro M, Orri M, Tournier M, Thiébaut R, Côté SM, Tzourio C. A machine learning approach for predicting suicidal thoughts and behaviours among college students. Sci Rep. 2021 Jun 15;11(1):11363.

. Monnier M, Moulin F, Thierry X, Vandentorren S, Côté S, Barbosa S, Falissard B, Plancoulaine S, Charles MA, Simeon T, Geay B, Marchand L, Ancel PY, Melchior M, Rouquette A; SAPRIS study group, Galera C. Children's mental and behavioral health, schooling, and socioeconomic characteristics during school closure in France due to COVID-19: the SAPRIS project. Sci Rep. 2021 Nov 17;11(1):22373.

. Montagni I, Roussel N, Thiébaut R, Tzourio C. Health Care Students' Knowledge of and Attitudes, Beliefs, and Practices Toward the French COVID-19 App: Cross-sectional Questionnaire Study. J Med Internet Res. 2021 Mar 3;23(3):e26399.

. Moulin F, El-Aarbaoui T, Bustamante JJH, Héron M, Mary-Krause M, Rouquette A, Galéra C, Melchior. Risk and protective factors related to children's symptoms of emotional difficulties and hyperactivity/inattention during the COVID-19-related lockdown in France: results from a community sample. M. Eur Child Adolesc Psychiatry. 2021 Mar 9:1-12.

. Queroue M, Pouymayou A, Pereira E, Tzourio C, González-Caballero JL, Montagni I. An interactive video increasing French students' mental health literacy: a mixed-methods randomized controlled pilot study. Health Promot Int. 2021 Dec 13:daab202

GLOBAL HEALTH IN THE GLOBAL SOUTH

BPH RESEARCH TEAM GHiGS

Dr Olivier Marcy

MD, PhD, GHiGS Director

Olivier Marcy is a clinical epidemiologist and researcher at the University of Bordeaux and research director at the IRD (French Institute for Research and Sustainable Development). He worked for more than 10 years as a clinician and public health program manager in sub-Saharan Africa (Republic of Congo) and South East-Asia (Cambodia). His research focuses on diagnosis of tuberculosis (TB) in children and TB-HIV co-infection in adults and children. He is the project leader of the Unitaid-funded TB-Speed project on childhood TB diagnosis with research ranging from decentra lisation and implementation challenges to accuracy of diagnostic algorithms for vulnerable children. He is the current chair of the NIAID-funded TB-SRN international cohort on pulmonary TB in adults. He is also involved in the IPORA interdisciplinary and policy-oriented research platform where he is developing research on impact of air-pollution on respiratory health in urban settings in Africa.

Dr Renaud Becquet

PHD, GhiGS Deputy director

Renaud Becquet, senior scientist at Inserm, has a PhD and a HDR in epidemiology (University of Bordeaux). After his PhD in Abidjan, Côte d'Ivoire, and a two-year post-doctoral fellowship at the University of KwaZulu Natal, South Africa, he was recruited in 2008 as senior scientist at the Bordeaux Population Health Research Centre. His early research focused on the prevention of mother-to-child transmission of HIV in Africa. He later created a research platform with humanitarian organisation ALIMA to develop innovative and transformative research in sub-Saharan Africa, focusing on improving maternal and child health outcomes in complex situations. He authored and co-authored about 100 articles published in internatio nal journals. He has served as an expert in various committees and guideline development groups (WHO, UNICEF, UNAIDS). He is currently the coordinator of the Master Global Health in the Global South at the Bordeaux School of Public Health.

The objectives of the GHiGS team are:

- **to produce data on diseases affecting the Global South, their epidemiology, risk factors and consequences;**
- **to use these findings to design and evaluate innovative interventions at both individual and population levels, which are effective, equitable and sustainable, and contribute to the advancement of global health.**

Per the definition of Koplan et al. (The Lancet 2009; 373(9679): 1993-5), global health is an area for study, research, and practice that places a priority on improving health and achieving equity in health for all people worldwide. Global health emphasizes transnational health issues, determinants, and solutions; it involves many disciplines within and beyond health sciences and promotes interdisciplinary collaboration; and it is a synthesis of population-based prevention with individual-level clinical care.

Per the definition of the World Bank, the Global South is made up of Africa, Latin America and the Caribbean, Pacific Islands, and the developing countries in Asia, including the Middle East.

Scientific orientations of the research team

The GHiGS team aims to contribute to improving health at both individual and population levels in countries from the Global South and to contribute to reducing health inequities between and within countries. Low-and middle-income countries, particularly in Sub-Saharan Africa, are going through major changes including epidemiologic, sociodemographic, economic, agronomic, technological and climatic transitions. At the same time, they are carrying the triple burden of:
1/ infectious disease (including HIV), tuberculosis, malaria, hepatitis and a number of other emerging infectious disease threats (including hemorrhagic fevers and other epidemics);
2/ growingly prevalent non-communicable diseases (NCDs; diabetes, cancers, hypertension, obesity),
and 3/ unprecedented outdoor pollutions and environmental threats. The GHiGS team aims to respond to these major transitions and new challenges through integrated, multi-level and inter-disciplinary research approaches in the context of the Global South.
Among the key highlights of the past five years, the GHiGS team contributed to a major revision in the international HIV treatment guidelines issued by the World Health Organisation and was among the rare research teams worldwide to have conducted a treatment trial to reduce mortality during the Ebola epidemic in West Africa.
In the coming years, the GHiGS team will strengthen and expand two key research themes, i.e., infectious diseases and mother and child health issues, to address new challenges in the field of diagnosis, care, and treatment. NCD research, previously addressed by the team in relation with infectious diseases (HPV-and HBV-related cancers, cardiovascular and metabolic HIV-comorbidities), will become a standalone research theme. Major challenges in implementing evidence-based interventions will be addressed within a cross-sectional and structural research axis on "Models of care, implementation and health systems". Finally, beyond the

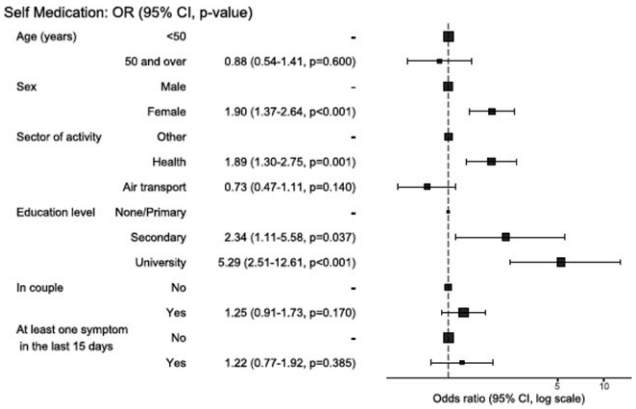


FIGURE 1 shows factors associated with self-medication to prevent the infection to SARS-CoV-2 in high-risk populations, Lomé, Togo in a binary logistic multivariable model. These associations were expressed as adjusted odds ratios.
Self-medication was coded as a binary variable (=1 if intake of at least one product and = 0 if not)

Source: Sadio AJ et al. BMC Public Health (2021) 21:58.
A study including around 1,000 participants from five sectors (healthcare, air transport, police, road transport and informal sectors) who were invited to provide information about their self-medication practices to prevent COVID-19. Health professionals, women and people with a high level of education were the most likely to practice self-medication.

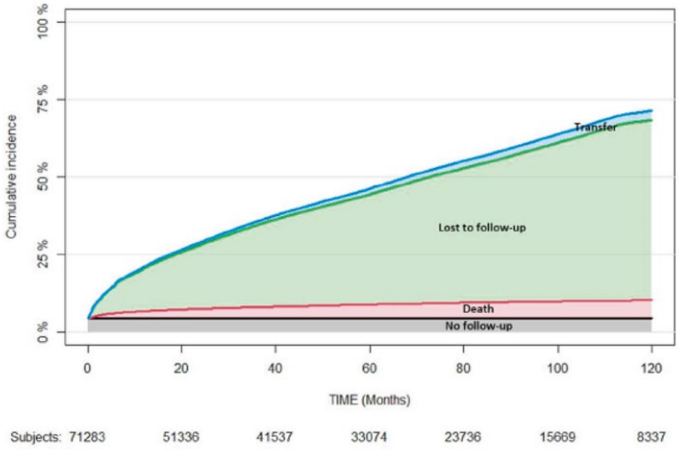


FIGURE 2. Ten-year stacked plot of cumulative incidence function of attrition by attrition types. IeDEA West Africa Collaboration, 2002to.

Source: Tiendrebeogo T et al. J Int AIDS Soc. 2021;24(5):e25723.
A cohort analysis of more than 70,000 patients initiated on Antiretroviral Treatment (ART) followed for 10 years in 8 West-African countries showed that overall attrition was as high as 21%, 45% and 71% at 12, 60 and 120 months following ART initiation, respectively. Overall, patients lost to follow-up accounted for 85% of patients lost to care.

individual and health system levels, the GHiGS team will explore the impact on health (NCDs, emerging epidemics,...) of global forces and environmental changes (climate change, bacterial ecosystem, resistance to antimicrobials, pollution...), as part of the "People in their environment" axis. Research by the GHiGS team will be built on equal partnership and co-construction with scientific partners, clinicians, policy-makers from the Global South countries. Through its expanded research program and strengthened collaborations and partnerships, the ambition of the GHiGS team is to contribute to the achievement of the Sustainable Development Goal #3 on Health and Well-Being.
Structuration of the research team The GHiGS activities will be organised around 3 research themes (infectious diseases; maternal and child health; non-communicable diseases) which correspond to major global health challenges; and 3 cross-sectional axes (Prevention, diagnosis and treatment; models of care, implementation, and health systems; people in their environment) that will structure research efforts, collaborations, and development of methods and scientific engineering capacities.

2021 Key publications

. Martin C, Kinda M, Lang HJ, Bangaly Sako F, Amara Traoré F, Koumbem E, Tinto H, Sanou A, Sondo A, Kaboré F, Donamou J, Guilavogui JP, Velardo F, Bicaba B, Marcy O, Augier A, Sayadi S, Poda A, Keita S, Anglaret X, Malvy

. D. Clinical presentation, outcomes and factors associated with mortality: A prospective study from three COVID-19 referral care centres in West Africa. Int J Infect Dis. 2021 Jul;108:45-52.

. Tiendrebeogo T, Messou E, Arikawa S, Ekouevi DK, Tanon A, Kwaghe V, Balestre E, Zannou MD, Poda A, Dabis F, Jaquet A, Minga A, Becquet R. Ten-year attrition and antiretroviral therapy response among HIV-positive adults: a sex-based cohort analysis from eight West African countries. J Int AIDS Soc. 2021;24(5):e25723.

. Bernard C, Seydi M, Tanon A, Messou E, Minga A, Font H, Dabis F. Barriers influencing task-shifting for the management of depression in people living with HIV: a study from West Africa IeDEA cohort collaboration. AIDS Care. 2021 Mar;33(3):352-356.

. Jafari-Guemouri S, Courtois L, Mama A, Rouas B, Neto Braga G, Accrombessi M, Massougbodji A, Ding XC, Tuikue Ndam N, Fievet N, Briand V. A Genotyping Study in Benin Comparing the Carriage of Plasmodium falciparum Infections Before Pregnancy and in Early Pregnancy: Story of a Persistent Infection. Clin Infect Dis. 2021 Jul 15;73(2):e355-e361.

. Duvignaud A, Jaspard M, Etafo IC, Gabillard D, Serra B, Abejegah C, le Gal C, Abidoye AT, Doutchi M, Owhin S, Séri B, Vihundira JK, Bérerd-Camara M, Schaeffer J, Danet N, Augier A, Ogbaini-Emovon E, Salam AP, Ahmed LA, Duraffour S, Horby P, Günther S, Adedosu AN, Ayodeji OO, Anglaret X, Malvy D. Lassa fever outcomes and prognostic factors in Nigeria (LASCOPE): a prospective cohort study. Lancet Glob Health. 2021 Apr;9(4):e469-e478.

. Tchankoni MK, Bitty-Anderson AM, Sadio AJ, Gbeasor-Komlanvi FA, Ferré VM, Zida-Compaore WIC, Dorkenoo AM, Saka B, Dagnra AC, Charpentier C, Ekouevi DK. Prevalence and factors associated with trichomonas vaginalis infection among female sex workers in Togo, 2017. BMC Infect Dis. 2021 Aug 9;21(1):775.

. Jaquet A, Boni SP, Boidy K, Tine J, Tchounga B, Touré SA, Koffi JJ, Dial C, Monnereau A, Diomande I, Tanon A, Seydi M, Dabis F, Diop S, Koffi G. Chronic viral hepatitis, HIV infection and Non-Hodgkin lymphomas in West Africa, a case-control study. Int J Cancer. 2021 Oct 15;149(8):1536-1543.

. Vessière A, Font H, Gabillard D, Adonis-Koffi L, Borand L, Chabala C, Khosa C, Mavale S, Moh R, Mulenga V, Mwanga-Amumpere J, Taguebue JV, Eang MT, Delacourt C, Seddon JA, Lounnas M, Godreuil S, Wobudeya E, Bonnet M, Marcy O. Impact of systematic early tuberculosis detection using Xpert MTB/RIF Ultra in children with severe pneumonia in high tuberculosis burden countries (TB-Speed pneumonia): a stepped wedge cluster randomized trial. BMC Pediatr. 2021 Mar 20;21(1):136.

. Fiorentino M, Nishimwe M, Protopopescu C, Iwuji C, Okesola N, Spire B, Orne-Gliemann J, McGrath N, Pillay D, Dabis F, Larmarange J, Boyer S. Early ART Initiation Improves HIV Status Disclosure and Social Support in People Living with HIV, Linked to Care Within a Universal Test and Treat Program in Rural South Africa (ANRS 12249 TasP Trial). AIDS Behav. 2021 Apr;25(4):1306-1322.

. Becquet V, Nouaman M, Plazy M, Agoua A, Zébago C, Dao H, Montoyo A, Jary A, Coffie PA, Eholié S, Larmarange J. A community-based healthcare package combining testing and prevention tools, including pre-exposure prophylaxis (PrEP), immediate HIV treatment, management of hepatitis B virus, and sexual and reproductive health (SRH), targeting female sex workers (FSWs) in Côte d'Ivoire: the ANRS 12381 PRINCESSE project. BMC Public Health. 2021 Dec 4;21(1):2214

LIFELONG EXPOSURES, HEALTH AND AGING

BPH RESEARCH TEAM LEHA

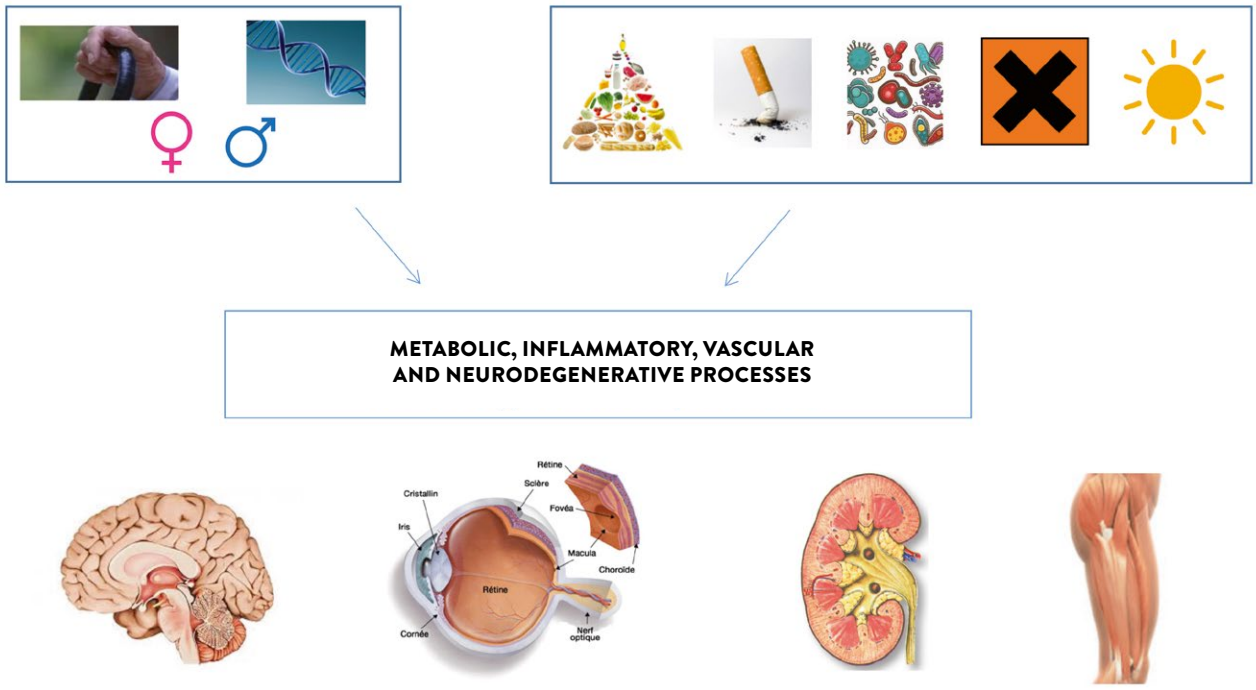
Dr Cécile Delcourt

PhD, LEHA Director

Cécile Delcourt has a PhD in statistics and public health and is a senior researcher at Inserm U1219-Bordeaux Population Health Research Centre, where she leads the LEHA (Lifelong Exposures, Health and Aging) research group. She has a strong expertise in the epidemiology of eye diseases (in particular AMD, cataract and glaucoma). She is internationally renowned in the identification of risk factors for major eye diseases (in particular smoking, light exposure and nutrition). She has led two major population-based epidemiological studies in the field, since 1995 (POLA and Alienor studies). She has founded and led from 2011 to 2018 the "European Eye Epidemiology" consortium, gathering 32 teams from 12 European countries, and has been workpackage leader in two European projects (Eye-Risk and Sense-Cog), granted in the Horizon 2020 framework. She has published more than 200 scientific articles, with a Factor H of 41. She received the Achievement Award of the American Academy of Ophthalmology in 2019.

The objective of team LEHA is to study age-related diseases, in particular those of the brain (dementia, Alzheimer's disease) and of the eye (age-related macular degeneration, glaucoma), using a lifelong approach and focusing on shared mechanisms and exposures, in order to define strategies for the prevention of age-related functional loss and the promotion of healthy aging.

We study populations of different ages (elderly, middle-aged, young) in prospective designs allowing for the study of slow long-term processes, using early biomarkers (in particular eye and brain imaging) allowing for the early detection of health-related effects of exposures. As age-related diseases share common mechanisms and consequences and interact with each other, aging is considered as a global state promoting the occurrence of diseases. Models of aging are mainly neurological diseases (cognitive decline and dementia/ Alzheimer's) and eye diseases (mainly age-related macular degeneration (AMD) and glaucoma), but also extend to other health endpoints, such as diabetes, kidney disease or physical performance.
Our research is based on population-based cohorts that we have been conducting in elderly populations for more than 30 years: the PAQUID cohort (n=3777, followed since 1988) and the 3C Study (n=9294 including 2104 in Bordeaux, followed since 1999), and its ancillary ophthalmological study in Bordeaux Alienor (n=963, followed since 2006). We also participate in population-based cohort studies (i-Share, 20,000 students, PI C. Tzourio), Constances (220,000 adults aged 18-69 years, followed since 2012, PI M. Zins, Inserm U1018, Villejuif) and B cube (planned 2000 aged 55-80 years in Bordeaux, PI C Samieri), in particular by generating cutting edge ophthalmological phenotypic information and several ranges of biomarkers. Finally, we collaborate with European and American cohorts, individually or within collaborative projects. Overall, these studies collect information on many aspects of aging (functions, chronic and degenerative diseases, disability) and their determinants (clinical factors, nutrition, environmental exposures, genetics), which allow a very comprehensive study of the epidemiology of health and aging in older adults, but also offer tscope for a broader lifelong approach, thanks to the epidemiological and clinical studies conducted in younger individuals.



Our research activity is divided in 3 axes:

- Burden of age-related and chronic disorders, which aims at documenting the frequency of age-related and chronic diseases and characterise their burden, in terms of loss of autonomy, impaired quality of life, as well as medical and non-medical costs.
- Mechanisms and processes of age-related diseases, which aims at finely characterising aging processes, by collecting detailed clinical, imaging and functional data over long periods of time, with major interest in degenerative and vascular processes as well as inflammatory mechanisms.
- Determinants of healthy aging, which focuses mainly on the role of nutrition and lifestyle, as well as environmental exposures (sunlight exposure, air pollution...). With regard to nutrition, our approach combines interest in specific dietary intakes and patterns with the use of innovative measurements (lipidomics, metabolomics, gut microbiota...).

2021 Key publications

. Ajana S, Cougnard-Gregoire A, Colijn JM, Merle BMJ, Verzijden T, de Jong P, Hofman A, Vingerling JR, Hejblum BP, Korobelnik JF, Meester-Smoor MA, Ueffing M, Jacqmin-Gadda H, Klaver CCW, Delcourt

C. Predicting Progression to Advanced Age-Related Macular Degeneration from Clinical, Genetic, and Lifestyle Factors Using Machine Learning. Ophthalmology. 2021;128(4):587-97.

Andre P, Pais de Barros JP, Mj Merle B, Samieri C, Helmer C, Delcourt C, Feart C. Mediterranean diet and prudent diet are both associated with low circulating esterified 3-hydroxy fatty acids, a proxy of LPS burden, among older adults. Am J Clin Nutr. 2021;114(3):1080-91.

Linard M, Baillet M, Letenneur L, Garrigue I, Catheline G, Dartigues JF, Peres K, Helmer C. Herpes simplex virus, early neuroimaging markers and incidence of Alzheimer's disease. Translational psychiatry. 2021;11(1):414.

Acar N, Merle BMJ, Ajana S, He Z, Gregoire S, Hejblum BP, Martine L, Buaud B, Bron AM, Creuzot-Garcher CP, Korobelnik JF, Berdeaux O, Jacqmin-Gadda H, Bretillon L, Delcourt C. BLISAR Study Group. Predicting the retinal content in omega-3 fatty acids for age-related macular-degeneration. Clin Transl Med. 2021;11(7):e404.

Merle BMJ, Cougnard-Gregoire A, Korobelnik JF, Schalch W, Etheve S, Rougier MB, Feart C, Samieri C, Delyfer MN, Delcourt C. Plasma Lutein, a Nutritional Biomarker for Development of Advanced Age-Related Macular Degeneration: The Alienor Study. Nutrients. 2021;13(6).

Morillon C, Le Goff M, Gattoussi S, Korobelnik JF, Rougier MB, Schweitzer C, Delcourt C, Delyfer

MN. Incidence, Progression, and Risk Factors of Epiretinal Membranes in the Elderly. Retina. 2021;41(3):495-504.

Chuy V, Gentreau M, Artero S, Berticat C, Rigalleau V, Pérès K, Helmer C, Samieri C, Féart C. Simple carbohydrate intake and higher risk for physical frailty over 15 years in community-dwelling older adults. J Gerontol A Biol Sci Med Sci. 2021.

Prezelin-Reydit M, Madden I, Macher MA, Salomon R, Sellier-Leclerc AL, Roussey G, Lahoche A, Garaix F, Decramer S, Ulinski T, Fila M, Dunand O, Merieau E, Pongas M, Zaloszyc A, Baudouin V, Bérard E, Couchoud C, Leffondré K, Harambat J. Preemptive Kidney Transplantation is Associated With Transplantation Outcomes in Children: Results From the French Kidney Replacement Therapy Registry. Transplantation. 2021.

POPULATION HEALTH TRANSLATIONAL RESEARCH

BPH RESEARCH TEAM
PHARes

Dr. Carole Dufouil

PhD, PHARes director

Carole Dufouil is a research director at Inserm Centre UMR1219 (Bordeaux Population Health) in Bordeaux, and director of the PHARes team (Population Health trAnslational Research). She is also deputy director for international and overseas relations at Bordeaux School of Public Health (ISPED). She has received training in biostatistics and public health. Her early publications were on methods to handle missing data in longitudinal studies. More recently, her research has focused on the determinants of neurological diseases, including Alzheimer's disease. She is particularly interested in the role of vascular risk factor exposure and cognitive stimulating activities, and imaging markers (PET, MRI) of brain aging and disease. She is co-PI of the 3C-Dijon study and co-PI of the MEMENTO study, a national clinical cohort, which was set up in the context of the French Alzheimer Plan 2008-2013, and aims to improve the understanding of the natural course of Alzheimer's disease and related disorders. She is also strongly involved in international scientific programs, through, among others, collaborations in the Framingham Heart study, or co-leading of the Melodem initiative which aims at harmonizing analytical approaches in longitudinal studies on dementia (www. melodem.org).

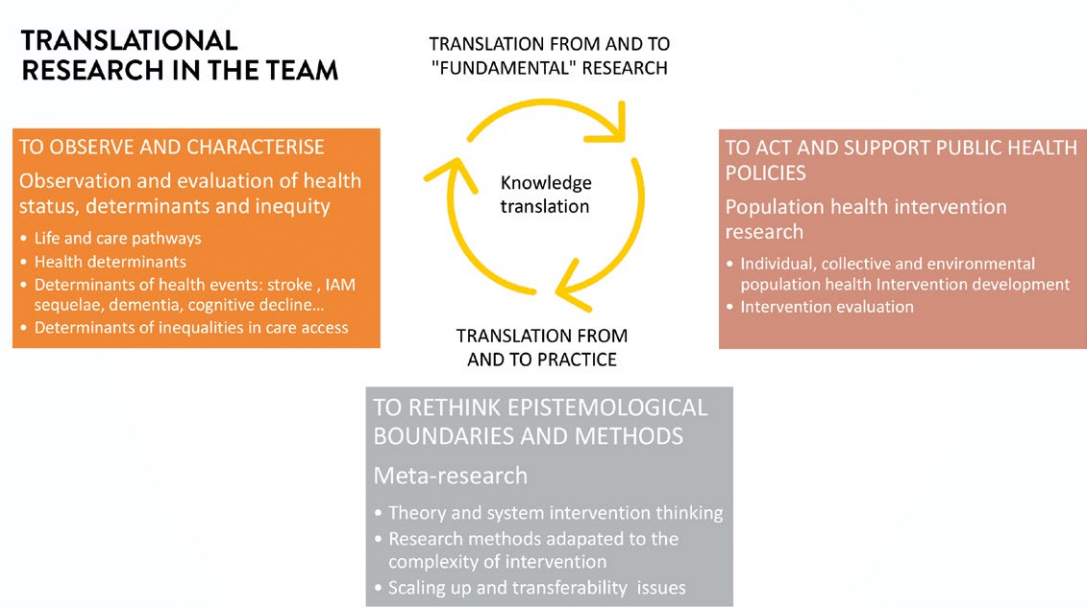
The PHARes Team aims to improve our understanding of and act upon the greatest risks and threats to population health, representing a large share of morbidity and mortality. Our research also examines social determinants of health and healthcare expenditure.
Through this translational approach, we seek to reduce the impact of these risks and threats (taking into account social and environmental inequalities, including inequalities in access to healthcare) by:

- **improving the measurement of risk factors and inequalities with real-world data and methods developed for and applied to observational studies, thus providing the evidence based for a critical building block for action,**
- **developing innovative methods (observational and experimental) for the development and evaluation of complex population health interventions,**
- **analysing the social and political processes underlying the unequal distribution of risks and health inequities in order to influence decision-making.**

The team works on five topics:
1. Methods for population health intervention research (Linda Cambon) This topic involves conducting research on research (meta-research), on concepts and methods for the evaluation of prevention and health promotion interventions. The questions cover all stages of the approach, from the development to the scaling-up of interventions.
2. Social determinants, migration dynamics, environment & health (Stéphanie Vandentorren, Laurence Kotobi)
This research theme relies on a strong interdisciplinary convergence on the cross-cutting themes of social inequalities, deprived populations, environmental risks and their relation to population health and health inequalities. Our research addresses the following issues:
   - Social determinants of maternal, child, sexual & reproductive health among vulnerable populations
   - Health status and healthcare access of vulnerable populations.
   - Innovative approaches to improve health and health equity in decision-making processes at the territorial level.

3. Pathways and determinants of health (Florence Saillour) The concept of pathway has been developed to respond to the need to make our health system and society evolve in the face of increased life expectancy, chronic illnesses and the complexity of managements. The identification of interventions to improve pathways and reduce inequalities in access to care is another major issue, leading to significant improvements in population health and focusing on three main goals :
   - Characterization of pathways
   - Identification of determinants of health
   - Optimisation of care pathways and reduction of health inequalities,

4. Innovations for prevention in the healthcare system (François Alla) The growing prevalence of chronic diseases is a major challenge for the sustainability of health systems. There is a need to transform health systems by increasing prevention and by implementing innovative organisations in



the management of these diseases. This transformation will require the development and the analysis of research-and field-based interventions. Transforming the health system also requires transferring innovative models into public decisions and practice. The objective of this theme is to identify, develop and/or evaluate technological (such as mobile health in prevention strategies) and organisational innovations (such as interprofessional collaboration to improve professional practice and health-care outcomes) in terms of prevention (or "preventive clinical practices "), at the hospital or in outpatient healthcare. Research covers all stages of innovation, from development to scale-up.

5. Economics and management of healthcare organisations (Jérôme Wittwer). Our aim is to conduct research projects that evaluate health policies and interventions using an applied and multidisciplinary approach, involving economists, management researchers, health professionals (doctors and nurses and other social science researchers with expertise in health services. This research addresses questions related to the evaluation of health systems and policies from a variety of perspectives, depending on the object studied (healthcare utilisation, healthcare pathways, technological or organisational innovations ...), the relevant evaluation outcome (take-up of public programs, efficiency, healthcare access inequalities, staff turnover, rehospitalisation...), the available data and the appropriate methods (econometrics using administrative data, expe rimental studies, medico-economic modelling of clinical data and registry data, qualitative interviews...).

Our team conducts research that takes into account:

- the characteristics of surveillance of health determinants (including social, environmental and cultural factors),
- the system in which the interventions are implemented, whether they are in or out of the health care environment (public domain: media, opinions, policies, professional practices, etc.),
- the complex nature of population health interventions (individual, ecological, collective, regulatory). Within this framework, our team focuses on 3 research objects that we believe to be at the heart of translational population health research:

1. Health status, health determinants and social inequalities (Research object "TO OBSERVE AND CHARACTERISE")
2. Population health interventions, whether they be policy, outreach, or organisations within and outside the healthcare setting (Research object "TO ACT ON AND SUPPORT PUBLIC HEALTH POLICIES")
3. Methodological research to better apprehend the complexity of the two first objects (Research object "TO RETHINK EPISTEMOLOGICAL BOUNDARIES AND METHODS")

The association of these three research objects (observational, interventional and meta-research) is fundamental to the development of translational research and mobilizes the principles of knowledge transfer between disciplines and between researchers and decision-makers to make it work.

2021 Key publications

.Cambon L, Alla F. Understanding the complexity of population health interventions: assessing intervention system theory (ISyT). Health Res Policy Syst. 2021 Jun 19;19(1):95. doi: 10.1186/s12961-021-00743-9. PMID: 34147105; PMCID: PMC8214800.

Cambon L, Schwarzinger M, Alla F. Increasing acceptance of a vaccination program for coronavirus disease 2019 in France: A challenge for one of the world's most vaccine-hesitant countries. Vaccine, Elsevier, 2021, 40 (2), pp.178-182. (10.1016/j.vaccine.2021.11.023). (hal-03524174)

Schwarzinger M, Watson V, Arwidson P, Alla F, Luchini S. COVID-19 vaccine hesitancy in a representative working-age population in France: a survey experiment based on vaccine characteristics. Lancet Public Health. 2021 Apr;6(4):e210-e221. doi: 10.1016/S2468-2667(21)00012-8. Epub 2021 Feb

6.PMID: 33556325

Frison E, Proust-Lima C, Mangin JF, Habert MO, Bombois S, Ousset PJ, Pasquier F, Hanon O, Paquet C, Gabelle A, Ceccaldi M, Annweiler C, Krolak-Salmon P, Béjot Y, Belin C, Wallon D, Sauvee M, Beaufils E, Bourdel-Marchasson I, Jalenques I, Chupin M, Chêne G, Dufouil C; Diabetes Mellitus and Cognition: Pathway Analysis in the MEMENTO Cohort. MEMENTO Cohort Study Group.Neurology. 2021 Aug 24;97(8):e836-e848. doi: 10.1212/WNL.0000000000012440.

Chamberlain JD, Rouanet A, Dubois B, Pasquier F, Hanon O, Gabelle A, Ceccaldi M, Krolak-Salmon P, Béjot Y, Godefroy O, Wallon D, Gentric A, Chêne G, Dufouil C; Memento Study group.Investigating the association between cancer and the risk of dementia: Results from the Memento cohort. Alzheimers Dement. 2021 Sep;17(9):1415-1421.

Premiers Pas, programme de recherche sur l'accès aux droits et aux soins des immigrés sans papier

(ANR, Laurence Kotobi et Jérôme Wittwer) -publication des premiers résultats sur support de l'Irdes (QES).

Motreff Y, Pirard P, Vuillermoz C, Rabet G, Petitclerc M, Stene LE, Baubet T, Chauvin P, Vandentorren S. Mental health care utilization by first responders after Paris attacks. Occup Med (Lond). 2022 Feb 22;72(2):81-90. doi: 10.1093/occmed/kqab150.

Prigent O, Porcherie M, Ridde V, Cambon L. Evaluation of a knowledge translation strategy to improve policymaking and practices in health promotion and disease prevention setting in French regions: TC-REG, a realist study. BMJ Open. 2021 Sep 30;11(9):e045936. doi: 10.1136/bmjopen-2020-045936. PMID: 34593485; PMCID: PMC8487168.

STATISTICS IN SYSTEMS BIOLOGY AND TRANSLATIONAL MEDICINE

BPH RESEARCH TEAM SISTM

Pr. Rodolphe Thiebaut

MD, PhD, SISTM Director

Rodolphe Thiebaut is a medical doctor specialised in Public Health. He holds a PhD in Biostatistics from Bordeaux University. He started his research career at the Institut National de Santé et de la Recherche Médicale (INSERM) as a research scientist between 2002 and 2009 and as research director between 2010 and 2013. He was a research fellow in the Immunobiology Division of the Institute of Child Health (London, UK) in 2007. He is now Professor in Public Health / Biostatistics at the University of Bordeaux. He leads a research group (SISTM-Statistics in Systems Biology and Translational Medicine) devoted to the modelling and analysis of high-dimensional data mainly applied to immunology through the French Vaccine Research Institute (https://vaccine-research-institute.fr/en/). This group, which is embedded in the INSERM U1219 Research Centre (https://www.bordeaux-population-health.center/), has been recognised as an INRIA project team since January 2015 (https://www.inria.fr/fr/sistm). He is in charge of the medical information department of the Bordeaux University Hospital. He is also the Director of the Graduate School of Digital Public Health, coordinator of the Master of Public Health Data Science at ISPED (Institut de Santé Publique d'Epidémiologie et de Dévelopement).

The two main objectives of the SISTM team are: i) to accelerate the development of vaccines by analyzing all the information available in early clinical trials and optimizing new trials ii) to develop new data science approaches to analyze and model big/ omics data.

The team is organised around three axes sharing a common objective. It is embarked in a double challenge of developing methods to deal with high dimensional data with low sample sizes and a main application for accelerating vaccine development.

In Axis 1, the relevant information is extracted from big data. This information is used to estimate mechanistic model parameters in Axis 2. Mechanistic models can then be used for simulating the optimal vaccine strategies to be evaluated in the next clinical trials. All this work is done in collaboration (Axis 3) with our partners from the Vaccine Research Institute, EUCLID/ANRS-MIE CMG platform and the Bordeaux Hospital.

Axis 1 High Dimensional Statistical Learning

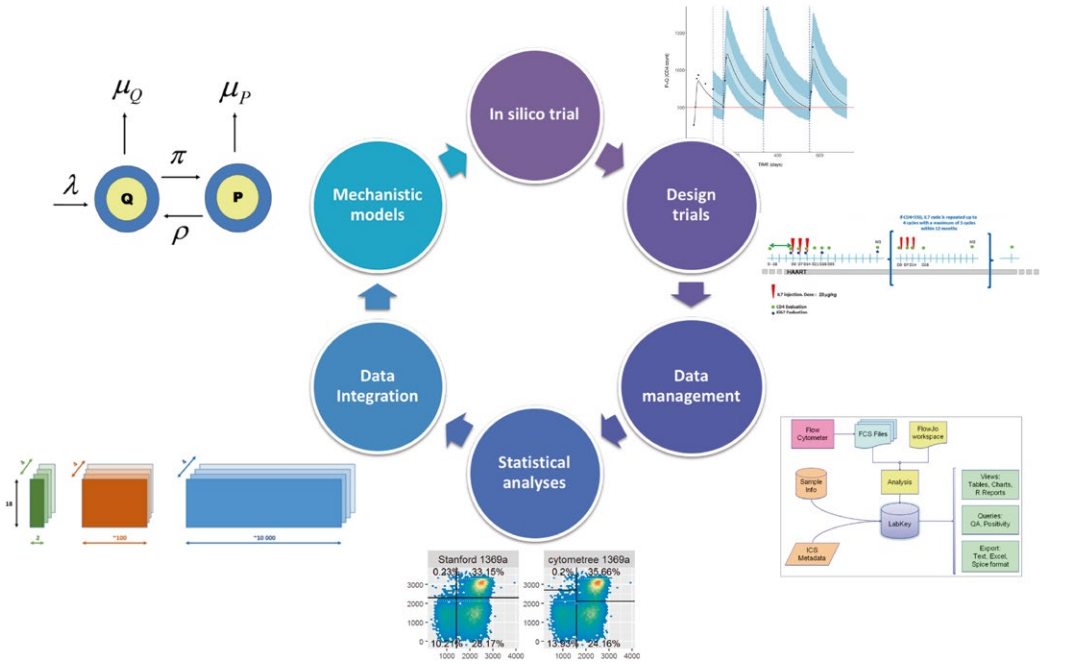
- To develop and apply methods to discover complex relationships between high dimensional data (multiblock analysis for data integration)
- To reduce data redundancy by 1) high dimensional reduction 2) deconvolution
- To visualize high dimensional data through statistically sound approaches
- To infer cell populations abundance through gene expression data by deconvolution

Axis 2 Mechanistic learning

- To infer ordinary differential equations (ODE) systems parameters by using high dimensional data
- To compare and implement control strategies through various approaches belonging to statistical control, stochastic control, reinforcement learning

Axis 3 Translational vaccinology

- To accelerate vaccine development using in silico trials
- To accelerate vaccine development using new adaptive designs
- To accelerate vaccine development through in depth analysis of data generated in early clinical trials



2021 Key publications

. Alexandre M, Prague M, Thiébaut R. Between-group comparison of area under the curve in clinical trials with censored follow-up: Application to HIV therapeutic vaccines. Statistical Methods in Medical Research. 2021;30:2130-2147.

. Capitaine L, Genuer R, Thiébaut R. Random forests for high-dimensional longitudinal data. Statistical Methods in Medical Research. 2021;30:166-184.

. Colas C, Hejblum B, Rouillon, S, Thiébaut R, Oudeyer P-Y, Moulin-Frier C, Prague M. EpidemiOptim: A Toolbox for the Optimization of Control Policies in Epidemiological Models. Journal of Artificial Intelligence Research. 2021;71: 579-519.

. Prague, M., & Lavielle, M. SAMBA: a Novel Method for Fast Automatic Model Building in Nonlinear Mixed-Effects Models. CPT: Pharmacometrics and Systems Pharmacology. 2021.

. Zhang HG, Hejblum BP, Weber GM, Palmer NP, Churchill SE, Szolovits P, Murphy SN, Liao KP, Kohane IS, Cai T. ATLAS: an automated association test using probabilistically linked health records with application to genetic studies. Journal of the American Medical Informatics Association. 2021;28:2582-2592.

. Lévy Y, Wiedemann A, Hejblum BP, Durand M, Lefebvre C, Surénaud M, Lacabaratz C, Perreau M, Foucat E, Déchenaud M, Tisserand P, Blengio F, Hivert B, Gauthier M, Cervantes-Gonzalez M, Bachelet D, Laouénan C, Bouadma L, Timsit JF, Yazdanpanah Y, Pantaleo G, Hocini H, Thiébaut R; French COVID cohort study group. CD177, a specific marker of neutrophil activation, is associated with coronavirus disease 2019 severity and death. iScience. 2021;24:102711.

. Lévy Y, Lacabaratz C, Lhomme E, Wiedemann A, Bauduin C, Fenwick C, Foucat E, Surenaud M, Guillaumat L, Boilet V, Rieux V, Richert L, Pantaleo G, Lelièvre JD, Thiébaut R; VRI02 ANRS 149 Study Group. A randomized placebo-controlled efficacy study of a prime boost therapeutic vaccination strategy in HIV-1 infected individuals: VRI02 ANRS 149 LIGHT Phase II trial. Journal of Virology. 2021; 95:e02165-20.

. Barry H, Mutua G, Kibuuka H, Anywaine Z, Sirima SB, Meda N, Anzala O, Eholie S, Bétard C, Richert L, Lacabaratz C, McElrath MJ, De Rosa S, Cohen KW, Shukarev G, Robinson C, Gaddah A, Heerwegh D, Bockstal V, Luhn K, Leyssen M, Douoguih M, Thiébaut R; EBL2002 Study group. Safety and immunogenicity of 2-dose heterologous Ad26.ZEBOV, MVA-BN-Filo Ebola vaccination in healthy and HIV-infected adults: A randomised, placebo-controlled Phase II clinical trial in Africa. PLoS Medicine. 2021;18:e1003813.

. Pollard AJ, Launay O, Lelievre JD, Lacabaratz C, Grande S, Goldstein N, Robinson C, Gaddah A, Bockstal V, Wiedemann A, Leyssen M, Luhn K, Richert L, Bétard C, Gibani MM, Clutterbuck EA, Snape MD, Levy Y, Douoguih M, Thiébaut R, on behalf of the EBOVAC2 EBL2001 study group. Safety and immunogenicity of a two-dose heterologous Ad26.ZE-BOV and MVA-BN-Filo Ebola vaccine regimen in adults in Europe (EBOVAC2): a randomised, observer-blind, participant-blind, placebo-controlled, phase 2 trial. Lancet Infectious Diseases. 2021;21:493-506.

. Loubet P, Wittkop L, Tartour E, Parfait B, Barrou B, Blay JY, Hourmant M, Lachâtre M, Laplaud DA, Laville M, Laviolle B, Lelievre JD, Morel J, Nguyen S, Spano JP, Terrier B, Thiebaut A, Viallard JF, Vrtovsnik F, de Lamballerie X, Launay O. A French cohort for assessing COVID-19 vaccine responses in specific populations. Nat Med. 2021;27:1319-1321.

2021 RESEARCH HIGHLIGHTS

2021 RESEARCH HIGHLIGHTS

ACTIVE

From the 29th of November to the 1st of December, Hélène Amieva co-organised a 3-day meeting in Paris where speakers from Canada, Belgium, Switzerland and France presented person-centred approaches of management of patients (children, young and older adults) suffering from various cognitive disorders.

On the 23rd & the 24th of September, Hélène Sauzéon co-organised the 2021 CREATE workshop. CREATE (Centre for Research and Education on Aging and Technology Enhancement) is a 20-year-old collaborative centre across prominent American Universities dedicated to ensure that older adults can successfully use technology. The major objective of this workshop was to learn from the CREATE experience and discuss opportunities for French research in the technology and aging field.

AHEAD

Pfizer

Coordination of the Pfizer BioNTech COVID-19 national pharmacovigilance safety monitoring: since January 2021, 19 national safety reports have been elaborated in collaboration with the French Network of Pharmacovigilance Centres and the French Agence Nationale de Sécurité du Médicament, published on a weekly basis from January to May before the frequency was lowered to a monthly and now a quarterly basis.

Monitoring of Health during the 2020 lockdown: development of an AI Transformer-based tool elaborated from the analysis of emergency calls. This approach showed that calls for flulike symptoms started to increase 3 weeks before lockdown and peaked 3 days before. They were strongly correlated with daily emergency room admissions, with a 14-day delay.

International project (AUF/ UBx) PATIENT-COVID19: provision of the AI tools for pre-diagnosis, contact tracing, awareness raising and fight against disinformation in Africa (http://www.patient-covid19.org/)

BIOSTATISTICS

De Courson H, Ferrer L, Barbieri A, Tully PJ, Woodward M, Chalmers J, Tzourio C, Leffondré K. Impact of Model Choice When Studying the Relationship Between Blood Pressure Variability and Risk of Stroke Recurrence. Hypertension. 2021;78(5):1520-1526. https://doi.org/10.1161/HYPERTENSIONAHA.120.16807

This work demonstrates that studying the association between blood pressure variability and cardiovascular events raises important methodological challenges that lead to inconsistent results when inappropriate methods are applied. This motivated a project funded by the French National Agency for Research (ANR) in 2021 on the development of joint models for studying the impact of the variability of markers on the risk of events.

Dinart D, Bellera C, and Rondeau V. Sample size estimation for cancer randomized trials in the presence of heterogeneous populations. Biometrics, 2021; https://doi.org/10.1111/biom.13527

A key issue when designing clinical trials is the estimation of the number of subjects required. Assuming for multicentre trials or biomarker-stratified designs that the effect size between treatment arms is the same among the whole study population might be inappropriate and sample size estimates might be biased. This article proposes a new approach to calculate sample size for clustered or stratified survival data.

Rouanet A, Avila-Rieger J, Dugravot A, Lespinasse J, Stuckwisch R, Merrick R, Anderson A, Long L, Helmer C, Jacqmin-Gadda H, Dufouil C, Judd S, Manly J, Sabia S, Gross A, Proust-Lima C. How selection over time contributes to the inconsistency of the association between sex/gender and cognitive decline across cognitive aging cohorts. Am J Epidemiol 2021; https://doi.org/10.1093/aje/kwab227

Performed within the framework of the International Initiative MELODEM, this work highlights the critical role of differential selection by dropout and death on the inconsistent results about the association between sex/gender and cognitive decline. In 8 studies, we compared the population-averaged and subject-specific estimands targeted by marginal models and mixed or joint models respectively, and we recommend focusing on subject-specific estimands in the living population for assessing sex/gender differences.

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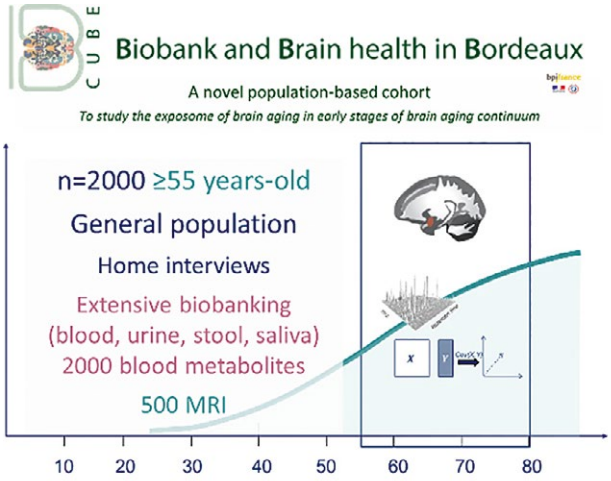
Biometrics JOURNAL OF THE INTERNATIONAL BIOMETRIC SOCIETY

MELODEM
MEthods for LOngitudinal studies in DEMentia

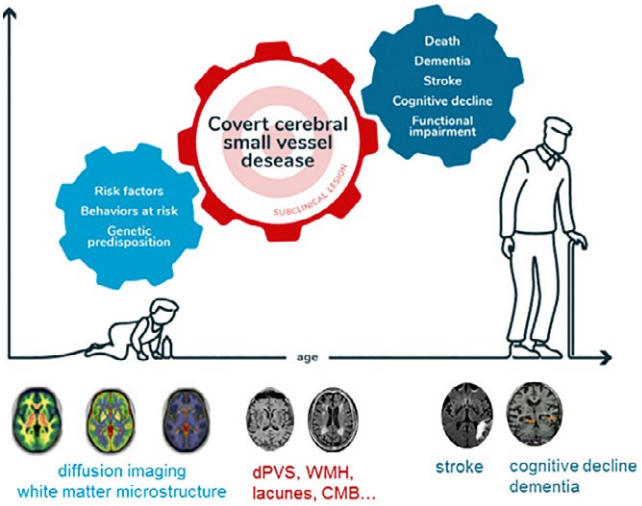
ELEANOR

A new cohort for exposomics and deep phenotyping of brain aging at early stages

The team has secured funding and is initiating building of a novel epidemiological research platform for the study of the determinants and natural history of cerebral ageing in the general population, through molecular epidemiology and deep phenotyping: the B cube (Biobank and Brain health in Bordeaux) cohort study (PI C. Samieri). By including young seniors from 50 to 55 years-old, this population-based cohort will help investigate the premises of dementia before extensive neurodegeneration.
https://cohorte-b-cube.fr/
https://www.youtube.com/watch?v=h1MxgXK7tUk

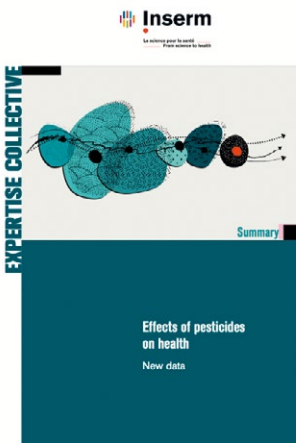


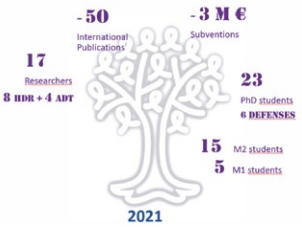
Deciphering the genetic underpinnings of covert cerebral small vessel disease (cSVD)
The team coordinated collaborative efforts leading to the identification of 18 novel genetic risk loci for white matter hyperintensity volume (WMH), the most common MRI-feature of cSVD (Saruguru premraj, Nat Commun Dec 2020). They found that WMH risk variants were associated with altered brain white matter integrity in young healthy adults, providing insight into the lifetime impact of SVD genetic risk. Using genetic instruments, they also provided evidence for a causal association of WMH with stroke and Alzheimer-type dementia, and of increasing blood pressure with larger WMH, particularly in persons without clinical hypertension. At the most significant WMH risk locus, the team also demonstrated combined evidence from tissue-specific gene expression data and profiling of human loss of function allele carriers for an inverse relation between TRIM47 expression in brain and blood vessels and cSVD. In collaboration with Inserm U1034 (Prof. Couffinhal), functional evaluation of TRIM47 by small interfering RNAs mediated knockdown in human brain endothelial cells showed increased endothelial permeability, a major hallmark of cSVD pathology, making TRIM47 an important candidate for future translational work (Mishra, Brain in press). This work was supported by ERC-H2020 N° 640643 and ANR-18-RHUS-0002 (https://rhu-shiva.com/)



EPICENE

The EPICENE team contributed to the drafting and dissemination of the collective INSERM expertise on Pesticides and Health in June 2021, a crucial report that describes the state of knowledge through a critical analysis of the international literature. Over 5,300 documents were analysed by a multidisciplinary group of experts, including two members of EPICENE.
In 2021, the European SPRINT project started in 11 European countries and in Argentina. The Bordeaux case study, conducted by the EPICENE team, enabled the collection of environmental and biological data from conventional wine growers and organic farmers in Gironde. Biological data was also collected from consumers not living in wine-growing areas, and samples from residents of wine-growing areas will be collected in 2022
In 2021, the 3,000th participant (6,000 expected) was included in the REALYSA cohort, a real-life study of patients with lymphoma recruited from hematology departments throughout France.
In December 2021, the compensation of occupational disease for prostate cancer linked to pesticides was created. The expertise provided by the EPICENE team has largely contributed to the implementation for this social support of people exposed to pesticides who develop prostate cancer following occupational exposure. Research on pesticide exposures and data from the AGRICAN cohort were important to this decision.
In 2021, we launched the Geo K Phyto project, funded in the ECOPHYTO-2 plan. It aims to set up an epidemiological surveillance system for adult cancers in relation with environmental exposures to pesticides of people living near agricultural areas – assess ment of individual exposures and health effects. This project is the result of a strong collaboration with the National Geographic Institute (IGN).
In 2021, the 17 researchers of EPICENE supervised 23 PhD students (6 defences during the year), 15 Master 2 students and 5 Master 1 students. About 50 articles were published in international scientific journals in the field of environmental and occupational health. Around 3 million euros worth of grants were obtained from various funders.





HEALTHY

Reasearch focus on mental health and COVID: studies CONFINS (students and young adults) and SAPRIS (school-aged children) led to the publication of 6 articles on youth mental health, their COVID representation and vaccinal acceptability. During the first two lockdowns, the prevalence of anxiety, depression and suicidal ideations were higher in students than in non-students.

Development of numeric Escape Room "EscapeCovid" for mental health of students during the COVID era.

Development of a research axis on perinatal inflammation biomarkers and youth mental health.

Pediatric tuberculosis: the preliminary results of the TB-Speed Pneumonia study, the first large-scale diagnostic trial on the detection of tuberculosis in children under 5 years of age with severe pneumonia, were presented at the 52nd World Union Conference on Lung Health, held virtually in October 2021. The results in terms of impact, diagnosis, and acceptability showed the importance of molecular screening in this group of vulnerable children. They were also shared with the Pediatric Guidelines Development Group convened by WHO in June 2021. They will be included in the Operational Handbook to be published by WHO in early 2022.

Emerging Infectious Diseases: results from the LASCOPE cohort studying Lassa Fever, a viral hemorrhagic fever in Nigeria, have been published in the Lancet Global Health journal. The LASCOPE research platform, set up in partnership with the NGO Alima (Alliance for International Medical Action, Senegal) and the Nigerian health authorities, has contributed to creating favourable conditions for setting up the first randomised therapeutic trial on Lassa fever (phase II trial SAFARI in the conduct of which IDLIC/GHiGS is involved). The data from the LASCOPE cohort is currently fueling reflection on the design of future phase III efficacy trials on Lassa Fever.

THE 52ND UNION WORLD CONFERENCE ON LUNG HEALTH

Covid-19 in Africa and France: The IDLIC/GHiGS team coordinated the Coverage-France and Coverage multisite randomised clinical trials, which aim to assess the effectiveness of treatments to prevent clinical worsening in COVID-19 patients with mild or moderate infection and at high risk of clinical deterioration (in France, those aged ≥ 50 years; in Africa, those aged ≥ 40 years or those suffering from obesity, hypertension or diabetes). Coverage-Africa (ANRS|MIE COV33, ANTICOV platform funded by Unitaid) recruited over 300 patients in Burkina Faso and Guinea, within the largest study of outpatient COVID-19 patients in Africa. Beyond therapeutic efficacy, the two trials will provide data on the acceptability and feasibility of early/home treatment of COVID-19, and shed light on the community and healthcare system challenges of clinical research performed on an outpatient basis.

Interdisciplinary research for development in Africa: in 2021, the IDLIC/GHiGS team obtained the Grand Programme de Recherche label for the IPORA program (Interdisciplinary Policy-Oriented Research on Africa), in partnership with the LAM (Les Afriques in the World)
/ Sciences Po Bordeaux and the Bordeaux School of Economics (formerly GREThA), as well as the Universities of Addis Ababa, Abidjan and Rabat. The objective of IPORA is to bring together researchers from a wide range of disciplines and from different countries, using complementary approaches, in order to develop interdisciplinary research and training, with a view to improving knowledge on major changes in African societies, and to disseminate the results of research to decision-makers and the general public.

THE LANCET
Global Health

Grand Programme de Recherche
IPORA | Interdisciplinary Policy-Oriented Research on Africa
université de BORDEAUX

LEHA

We developed a comprehensive prediction model for advanced AMD by applying a machine learning approach (Ajana S et al. Ophthalmology 2021). This model was implemented in a digital platform (www.macutest. net), allowing for a personalised prediction of AMD risk. S Ajana won the i-PhD innovation contest organised by BPI-France for his Retinet project, aiming at the development and commercialisation of this prediction platform.
In continuation of our work regarding the associations of exposure to herpes virus in Alzheimer's disease (Linard M et al. Transl Psychiatry 2021), we launched the VIRALZ project (PI. C Helmer) combining: 1/ an approach targeting specific viruses based on pathophysiological hypo theses: Herpes simplex virus 1 and Human Herpes virus.
6 for Alzheimer and other dementia; and 2/ an agnostic approach for the detection of other potential viruses involved in neurodegenerative diseases, using new technology allowing detecting the exposure to more than 200 viral species with 1,000 different strains.
We launched the EXPOLUX project (PIs A Cougnard-Gregoire & C Delcourt), which aims at quantifying the impact of occupational exposure to sunlight on skin and eye health (http://www.fondation.univ-bordeaux.fr/projet/soleil-et-sante-au-travail). This project is based on data from the nationwide Constances study (www. constances.fr).

MACUTEST

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SISTM

The results on the safety and efficacy of the Ebola vaccine strategy based on Ad26.ZEBOV and MVA-BN-Filo generated in the EBOVAC2 consortium have contributed to the market authorisation delivered by the FDA on 27th Feb 2021.
Setting of the ANRS COVPOPART cohort (https://www.covireivac.fr/vous-allez-etre-vaccine-contre-la-covid-19-faites-progresser-les-connaissances-en-participant-a-la-cohorte-anrs-cov-popart/) (Linda Wittkop)

eboVAC2

COVIREIVAC


École doctoral
Sociétés,
politique,
santé pu

PHD THESES DEFENDED

PHD THESES DEFENDED

CABE SÉVERINE
Prevention in the perinatal period-associated factors and consequences for maternal mental health
Pharmacology, option Pharmacoepidemiology, Pharmacovigilance
Direction by SUTTLER-DALLAY Anne-Laure

CASSOUDESALLE HÉLÈNE
Effects on microstructure and cerebral and cognitive functioning of repetitive minor cranial trauma in the practice of football and search for means of protection: studies by multimodal neuroimaging, electrophysiology and biomechanics.
Cognitive sciences Ergonomics option
Cognitive sciences option
Direction by DEHAIL Patrick

CHALOUNI MATHIEU
Sustained virological response to direct-acting antiviral therapy and HCV-related disease progression in terms of mortality, hepatic morbidity and extra-hepatic co-morbidities, in hiv and hcv co-infected patients.
Public health
Epidemiology option
Direction by WITTKOP Linda

GAUTHIER MARINE
Methods for bulk and single-cell RNA-seq data analysis for vaccine research
Public health Biostatistics option
Direction by THIEBAUT Rodolphe and HEJBLUM Boris

GUILLOT JORDAN
Chronic polypharmacy: description and risk
Pharmacology, option Pharmacoepidemiology, Pharmacovigilance
Direction by BEZIN Julien

KOUAME MENAN GÉRARD
Impact of viral B infection on severe morbidity in adults infected with early-stage HIV in Abidjan, study nested in the Temprano trial ANRS 12 136
Public health
Epidemiology option
Direction by DANEL Christine

KOUMAMBA AIMÉ PATRICE
Implementation of an information system for management, statistics and health monitoring in Gabon Public health
Information Technology and Health option
Direction by DIALLO Gayo

LAHOUD ODETTE
Relationship between food profiles and asthma and allergic diseases in children: French and Lebanese studies.
Public health
Epidemiology option
Direction by RAHERISON Chantal

LHOSPITAL OLIVIER
Development of construction conditions and preservation of occupational health for hospital staff Cognitive sciences Ergonomics option
Direction by GARRIGOU Alain

LINARD DE GUERTECHIN MORGANE
Herpes Simplex virus type 1: a potential target for the prevention of Alzheimer's disease
Public health
Epidemiology option
Direction by HELMER Catherine

MACALLI MELISSA
Suicidal behavior among students: analysis and modeling of risk in the i-Share cohort
Public health
Epidemiology option
Direction by TZOURIO Christophe

MANANGAMA DUKI GUYGUY
Maternal occupational exposure to nanoscale particles and child development
Public health
Epidemiology option
Direction by DELVA Fleur

MOUKOUMBI LIPENGUET GAETAN
Medico-economic evaluation of the hospital information system of the University Hospital Centers of Gabon Public health Biostatistics option
Direction by WITTWER Jérôme

N'TAKPE JEAN BAPTISTE
When Not to Start Antiretroviral Treatment Immediately in Sub-Saharan Africa
Public health
Epidemiology option
Direction by MOH DESMORYS Raoul

PEREZ DELPHINE
Addressing factors associated with poor prognosis in HIV-infected adults on antiretroviral therapy in sub-Saharan Africa
Public health
Epidemiology option
Direction by ANGLARET Xavier

PREZELIN MATHILDE
Metabolic Abnormalities and Chronic Kidney Disease Progression
Public health
Epidemiology option
Direction by LEFFONDRE Karen

ROJAS CASTRO MADELYN
Accidents of everyday life in France. Study of risk factors for domestic accidents within the MAVIE cohort Public health Epidemiology option
Direction by LAGARDE Emmanuel

SPINI ANDREA
Use of healthcare databases for the evaluation of effectivenest of drugs used in pa Pharmacology, option

THOMAS ALINE
Nutrition, santé et plasticité du cerveau à des âges clés : approche épidémiologique Public health Epidemiology option Direction by SAMIERI Cécilia

VILLA ANTOINE
Occupational exposure to anticancer drugs: from the assessment
Public health
Epidemiology option
Direction by CANAL RAFFIN Mireille
Pharmacoepidemiology, Pharmacovigilance
Direction by SALVO Francesco

ZAMUDIO-RODRIGUEZ
Alfonso
Successful aging: epidemiological approach in the general elderly population and evaluation of a digital home assistance platform (DomAssist) aimed at promoting home care for frail elderly people.
Public health
Epidemiology option
Direction by PERES Karine

SOCIETAL IMPACTS

SOCIETAL IMPACTS

The BPH is strongly committed to contributing to the United Nations' Sustainable Development Goals and to improving population health both locally and globally, embracing a comprehensive precision and global health approach targeting major health challenges, with a special focus on brain, vascular and infectious diseases, as well as cancer.

All the research conducted at the BPH contributes to addressing sustainable development goals, mostly SDG3 (good health) and SDG4 (quality education), but also SDG10 (reduced inequalities), and SDG11 (sustainable cities & communities). The BPH is also involved in the partnership recently established between UBx and the Ban Ki-moon centre for global citizens, a quasi-international organization chaired by former UN SG Ban Ki-Moon to support the implementation of SDGs, with the participation of 6 BKM scholars in the recent summer school organized by the IDLIC team on COVID19 in Africa.

BPH researchers are also acutely aware of sustainable development goals at large, including the climate emergency and environmental impacts. In fact, many researchers within the BPH are engaged in climate action (SDG13): the BPH is an active member of the "Action Climat Environnement" (ACE) group launched at UBx (www. ace-ub.fr) and meeting on a monthly basis to coordinate the actions implemented in the different research units and to develop common concerted actions. The objective of ACE is to: (1) perform an inventory of the impact of research activities on climate change (business travel, use of digital technologies, waste management); (2) carry out awareness-raising actions; (3) initiate concrete actions to save energy and water and optimize waste recycling.

Finally, despite a less prominent tradition in public health compared to other disciplines, BPH researchers are increasingly involved in innovation and technological transfer activities. Over the past 5 years, BPH researchers have produced >15 patents invention disclosures. They obtained 15 Cifre fellowships (joint academic-industry fellowships) and have established 25 industrial and R&D contracts, both with SMEs and large multinational pharmaceutical companies, particularly in the context of vaccine trials. Three start-ups have emerged from BPH teams: Synapse, UT4H, Tricky.

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