

Research evaluation

EVALUATION REPORT OF THE UNIT
CRESS - Centre de recherche en épidémiologies
et statistiques de Sorbonne Paris Cité

UNDER THE SUPERVISION OF THE
FOLLOWING ESTABLISHMENTS AND
ORGANISMS:

Université Paris Cité - UP Cité

Conservatoire national des arts et métiers –
CNAM

Institut national de la santé et de la recherche
médicale - Inserm
Université Sorbonne Paris Nord

Institut national de recherche pour l'agriculture,
l'alimentation et l'environnement - Inrae

EVALUATION CAMPAIGN 2023-2024
GROUP D

Report published on April, 23 2024



In the name of the expert committee :

Cécile Delcourt, Chairwoman of the committee

For the Hcéres :

Stéphane Le Bouler, acting president

In application of articles R. 114-15 and R. 114-10 of the research code, the evaluation reports established by the expert committees are signed by the presidents of these committees and countersigned by the president of Hcéres.

To make the document easier to read, the names used in this report to designate functions, professions or responsibilities (expert, researcher, teacher-researcher, professor, lecturer, engineer, technician, director, doctoral student, etc.) are used in a generic sense and have a neutral value.

This report is the result of the unit's evaluation by the expert committee, the composition of which is specified below. The appreciations it contains are the expression of the independent and collegial deliberation of this committee. The numbers in this report are the certified exact data extracted from the deposited files by the supervising body on behalf of the unit.

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Experts:

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Mr Michel Vidal, UP Cité

CHARACTERISATION OF THE UNIT

- Name: Centre de recherche en épidémiologie et statistiques
- Acronym: CRESS
- Label and number: UMR 1153
- Composition of the executive team: Ravaud Philippe

SCIENTIFIC PANELS OF THE UNIT

SVE Sciences du vivant et environnement
SVE7 Prévention, diagnostic et traitement des maladies humaines

THEMES OF THE UNIT

The Center for Research in Epidemiology and Statistics (CRESS) is a large research center in epidemiology and statistics, initially created in 2014. It is currently constituted of nine teams and 381 members (180 researchers of whom 81 with an HDR, 122 engineers and technicians, of whom 46 are permanent and 79 PhD students). The center is organized in nine teams, covering perinatal and pediatric epidemiology (teams EPOPé, EARoH and EPICEA), nutritional epidemiology (EREN), age-related diseases (team EpiAgeing), rheumatic musculoskeletal diseases (ECAMO) and biostatistical and clinical research (teams METHODS and ECSTRRA).

For the next mandature, it is planned that the CRESS will be reorganized around five teams, representing about 303 members: Oppale (grouping EPOPé, EARoH and EPICEA), EREN, ECAMO, EpiAgeing and METHODS. The teams HERA and ECSTRRA plan to join other research units.

HISTORIC AND GEOGRAPHICAL LOCATION OF THE UNIT

CRESS was initially created in 2014, with five teams (about 260 members) and increased to nine teams over the two mandates (2 teams joined in 2015 and two others in 2019). The CRESS is a multi-site unit, with seven locations (hospitals Hôtel Dieu, Cochin-Port Royal, Paul Brousse, Tenon and Saint Louis, Faculty of Pharmacy of Université Paris Cité, and Université Sorbonne Paris Nord). For the next mandature, it should be regrouped in four locations (hospitals Hôtel Dieu, Cochin-Port Royal, Villemin, and Université Sorbonne Paris Nord), in particular thanks to the relocation of four of the current teams (EPOPé, EARoH, EPICEA and EpiAgeing) at Villemin. The move to Villemin was partially completed in 2023 (teams EPOPé and EpiAgeing) and is scheduled for completion in September 2024 for the other two teams.

RESEARCH ENVIRONMENT OF THE UNIT

The CRESS is supervised by four major institutions: Université Paris Cité, Université Sorbonne Paris Nord (USPN), Inserm, and INRAe (specifically in the department of Human Nutrition (AlimH)). Université Paris Cité was awarded the Initiative of Excellence (Idex) label in 2019 and CRESS plays a central role in various Idex project-related infrastructures, such as the School of Public Health and the Interdisciplinary Paris Public Health Institute.

CRESS is actively involved in several infrastructures funded by the Future Investments Program (PIA), including the RECONAI platform (Equipex 2011 and Cohorts 2019), the childhood cancer observation platform (CCOP/HOPE-EPI), @HôtelDieu (a public-private partnership dedicated to digital health and technology start-ups), and the Nutrition axis of the Labex "Milieu Intérieur."

Additionally, CRESS leads the University Hospital Federation (FHU) CHILD, participates in FHU PREMA, and heads the Women's Health Institute of the Health faculty of Université Paris Cité.

The center includes several researchers practicing various medical professions (pediatricians, obstetricians, midwives, nutritionists, orthopedists, rheumatologists, physiotherapists, neurologists, specialists in physical medicine and rehabilitation, geriatricians, general practitioners, etc.), who lead clinical departments and structures supporting clinical research mainly at the Assistance Publique - Hôpitaux de Paris (AP-HP). This strong collaboration with healthcare infrastructures ensures the relevance of the research conducted by CRESS and facilitates the translation of research findings into medical practice.

UNIT WORKFORCE: in physical persons at 31/12/2022

Catégories de personnel	Effectifs
Professeurs et assimilés	49
Maîtres de conférences et assimilés	26
Directeurs de recherche et assimilés	12
Chargés de recherche et assimilés	8
Personnels d'appui à la recherche	47
Personnels hospitaliers (PH et lgh)	41
Sous-total personnels permanents en activité	183
Enseignants-chercheurs et chercheurs non permanents et assimilés	34
Personnels d'appui non permanents	63
Post-doctorants	25
Doctorants	78
Sous-total personnels non permanents en activité	200
Total personnels	383

DISTRIBUTION OF THE UNIT'S PERMANENTS BY EMPLOYER: in physical persons at 31/12/2022. Non-tutorship employers are grouped under the heading "others".

Nom de l'employeur	EC	C	PAR
AUTRES	20	0	49
UNIVERSITÉ PARIS-CITÉ	45	0	5
Inserm	0	16	24
UNIVERSITÉ SORBONNE PARIS NORD	10	0	5
INRAE	0	4	6
CNAM	0	0	2
Total personnels	75	20	91

GLOBAL ASSESSMENT

The CRESS is an outstanding research center in epidemiology and statistics, federating a community of more than 300 researchers and research support staff. Its scientific productivity is exceptional, with about 3400 peer-reviewed articles (1500 as first, last or corresponding author), with 21 % in the top 10 % most cited articles and a normalized citation index of 3. The unit has demonstrated its impact on clinical practice and public health, by developing for instance new child growth curves and creating the nutritional front label 'Nutri-Score,' implemented in France and other European countries. Their research also shaped research practices by leading the development of reporting guidelines (STARD, CONSORT) requested by editors and the ICMJE. Open science principles and ethical research practices are implemented successfully.

The CRESS excels in organizing scientific events, participating in prestigious conferences, and holding editorial responsibilities. It is also actively engaged in expertise activities and serving in scientific councils of public institutions and agencies at the national (Parliament, Senate, Ministries, health authorities...) and international (European Parliament, US national academies, WHO...).

The capacity of CRESS researchers to raise funding is outstanding, with €67M obtained through 336 grants in 2017-2022, including 26% from European and US grants and 64% from national competitive funding (PIA, ANR, INCa...).

The unit is home to leading researchers who oversee world-class research infrastructures, including population-based cohorts of both children and adults, as well as innovative e-cohorts like Nutrinet santé and ComPaRe. Members also head large European platforms that harmonize data from international cohorts and population-based registries, totaling over 450,000 patients followed for several years.

The CRESS develops pioneering participative research, including patients and the public, evident in initiatives like Nutrinet Santé and the ComPaRe e-cohort, which collaborates with numerous patient associations. The unit recognizes the importance of patient perspectives, actively involving them in research processes, emphasizing patient-centered research, allowing patients to propose ideas, be involved in research processes, and define Core Outcome Sets.

The unit has a comprehensive strategy for attracting and developing talented researchers, resulting in the acquisition of more than 20 new university tenured researcher positions, four Inserm and three Inrae researchers (CRCN) and four promotions to Inserm directors of research (DR), eight to Professors with hospital duties (PUPH) and one to Professor. Moreover, two ERC consolidator grants were obtained, as well as several competitive positions for young researchers (1 post-doctoral Marie Skłodowska-Curie positions, four chair positions of excellence). Research support staff also benefit from this strategy, with fifteen new permanent positions and six promotions.

CRESS members actively disseminate their research to social, economic, and cultural actors through various channels (television and radio interviews, press releases, webinars, videos...) and national and international news outlets. Teams like EREN have an exceptional media engagement, contributing to high-impact national and international media outlets. The unit also encourages a culture of innovation and entrepreneurship, exemplified by the creation of SKEZI, a spin-off offering a technological platform derived from the ComPaRe e-cohort.

For the next mandate, two teams will be leaving (team ECSTRAA to the IHU THEMA and team HERA to UMR MERIT261 IRD-UPC) and three teams will be grouped (Épopé, Earoh and Epicea, to form Oppale). The five research teams and the SMART platform will be distributed on five sites, including the new Villemin site, for which the move of several teams is currently ongoing. While there will be a change of director (from Philippe Ravaud to Isabelle Boutron), the organization of the CRESS will globally be in continuity with the previous mandate. Some attention should be given by the direction of CRESS to the development of the smaller teams and thematic, which lead important and original research topics (in particular regarding pediatric cancers, rheumatic musculoskeletal diseases and age-related diseases), and assure their full participation to the animation of the center. Some attention should also be paid to a better integration of young researchers to the cross-team animation.

DETAILED EVALUATION OF THE UNIT

A - CONSIDERATION OF THE RECOMMENDATIONS IN THE PREVIOUS REPORT

Recommandations on scientific production

Most of the recommendations regarding scientific production have been taken into account and achieved during the period, in particular :

- A data sciences approach has been developed, by attracting researchers with specific skills, by participating to high level initiatives in the field, at the local and national levels and by initiating collaborations with excellent national teams from CNRS, ENS and Inria. They have also developed the interconnection of their own cohorts (in particular in the RECONAI platform), and at the European level, in particular by implementing the Data-Shield tool, which allows to overcome major regulatory and technical issues in the sharing of medical and personal data.
- European and international funding has been strengthened, representing 17 millions euros over the period (25 % of total funding), including highly competitive individual grants (two ERC, one Marie Skłodowska-Curie).
- Participative research including patients and public is well integrated in research activities of several teams.
- While activities targeting PhD students (speed meetings, annual seminar) have been implemented, PhD students still appear to have a deficit in the knowledge of the CRESS activities and express a lack collective discussions across teams.

Recommandations on unit's organization and life

- The unit life and organization has overall been improved, in particular through the creation of the SMART (Service Mutualisé d'Appui à la Recherche Transversal- Mutualized service to support research) platform, which

has provided very efficient support for human resources, administrative, regulatory and IT issues. This platform is highly appreciated by the researchers and research support staff.

- Internal and external communication at the level of the CRESS has been improved in particular by restructuring the dedicated website and setting up several steering committees (Club Data-Stat, communication, PhD students...), also favoring harmonization of methods and skills across teams.
- Collaborations and discussions across teams have been developed, and have been particularly successful among the teams in perinatal and pediatric research, leading to the planned merging of the three teams.
- A strategy has been implemented, in order to decrease the number of premises (from 7 to 4).

Recommendations on scientific strategy

A collective dynamic was implemented for the development of the scientific strategy, with the creation of steering committees, involving all types of personnel, and specific workshops.

B - EVALUATION AREAS

EVALUATION AREA 1: PROFILE, RESOURCES AND ORGANISATION OF THE UNIT

Assessment on the scientific objectives of the unit

CRESS aligns its strategy with its supervisory institutions, emphasizing clinical relevance, disruptive research, and major health perspectives. Actively contributing to Public Health research and training, the center engages in impactful, cutting-edge national and international projects. Committed to responsible and open science, CRESS aims to increase public health research within the universities, especially the Université Paris-Cité Idex project. The community-driven project ensures broad engagement, with evident success in societal impacts (for instance Nutriscore, child growth curves).

Assessment on the unit's resources

Between 2017 and 2022, CRESS secured €67M through 336 grants, including 26% from European and US grants and 64% from national competitive funding (PIA, ANR, INCa...). A strategic goal focused on AI (artificial intelligence) and data science expertise led to attracting talents and collaborations (Marie Skłodowska-Curie Fellow, Inserm chair professor). The reduction of the number of research sites will further facilitate internal collaborations and decrease management complexity, in particular in terms of IT infrastructure. Some of the premises (in particular in Hotel Dieu) would need modernization.

Assessment on the functioning of the unit

CRESS's human resources management adheres to directives from supervisory authorities, with the SMART platform facilitating recruitment and staff management, including proactive measures for gender equality, and staff training and career development (organization of workshops, personal support for career advancement). Safety is ensured through a Prevention Committee, training, and risk assessments, and a Pandemic Contingency Plan (PCA). IT security protocols are in place for managing sensitive data and complying with GDPR. Actions toward environmental sustainability are also organized.

1 / The unit has set itself relevant scientific objectives.

Strengths and possibilities linked to the context

CRESS is a research institution affiliated with Université Paris Cité, Université Sorbonne Paris Nord, Inserm and Inrae. Their strategy aligns with the strategic plans of these institutions, focusing on clinical practice, public health policy, disruptive research, global health approaches, and technological innovation. They actively contribute to research and training in public health, participate in national and international projects, and prioritize responsible, transparent, and reproducible research. Their ambition is to push the boundaries of knowledge

through collaboration, excellence, and innovation, leveraging diverse expertise within the CRESS community. They engage in participative research and innovative paradigms like precision population health. Additionally, they prioritize training the next generation of researchers and have achieved societal impacts, such as developing the Nutri-Score, which is endorsed by several countries. Their strategy reflects a commitment to societal impact and community engagement, evident through workshops and collaborative efforts within the CRESS community.

Weaknesses and risks linked to the context

While the scientific strategy is overall outstanding, some areas will need more attention from the direction of the CRESS:

- research on pediatric cancers needs to be secured and developed, as it is of major public health interest, by developing collaborations with other axes of the future OPPaLE team and by attracting new post-docs and permanent researchers, in particular in the context of the forthcoming retirement of the head of the Childhood Cancer Registry.
- Similarly, as the only french team specialized in epidemiology rheumatic and musculoskeletal diseases, the ECAMO team needs to be supported, in order to stabilize their number of researchers, in the context of several senior researchers at their end of their career. If possible, research in osteoarthritis, a major public health issue, would also need to be developed.
- Finally, regarding the EpiAgeing team, while the scientific production is outstanding, the size of the research group remains relatively small, although efforts to include clinicians have been performed successfully. In a context of major demographic and epidemiological transitions (number of elderly people at its maximum until 2050 in France and Europe, due to the baby boomers arriving into old age; slowing of the increase in life expectancy; decrease of age-specific incidence of dementia...), it appears crucial to gather more data on the French general elderly population, to describe and understand these ongoing changes.

2/ The unit has resources that are suited to its activity profile and research environment and mobilises them.

Strengths and possibilities linked to the context

Over the period 2017-2022, CRESS secured a total funding of €67M through 336 grants. The funding sources included international grants (26%), primarily from European programs and the NIH R01 programs, as well as competitive funding (64%) from government programs such as the Future Investments program, the National Agency of Research, and the National Cancer Institute. Additionally, 10% of funding came from other sources such as local authorities, associations, foundations, and industry. Recurrent endowment from institutions accounted for only 5% of total resources, with 10% allocated to CRESS functioning.

Some of the investment was directed towards attracting new expertise, particularly in artificial intelligence and data science, resulting in collaborations with institutions like CNRS, ENS and Inria.

During the mandate, collaborations between CRESS teams resulted in various projects and publications, including studies on food labels and dietary trajectories during pregnancy. Efforts were made to optimize scientific interactions and collaborations by consolidating premises and setting up the shared management unit SMART. Each premise has specific IT infrastructure tailored to its hosting institution, with creation of new infrastructure at the Villemin site to decrease the total number of premises and allow the grouping of several teams. Some efforts towards interoperability of the IT infrastructures are being performed.

Weaknesses and risks linked to the context

The CRESS capacity to raise funding is overall outstanding. It is understandable that some of the teams do not accept any industrial collaboration, in order to avoid potential conflicts of interest (true, or perceived by the general population and the society). However, CRESS teams could consider gathering more funding from foundations and associations (currently about 7% of the total funding), which might also contribute to further developing of participative research.

Some teams, in particular ECAMO, should also be encouraged to obtain more funding, in particular from competitive grant applications.

The premise in Hotel Dieu, although of historical value, would need modernization. In particular, some spaces in the central location (Hotel Dieu) should be dedicated to cross-team meetings and informal interactions, in order to favour cross-fertilization.

3/ The unit's practices comply with the rules and directives laid down by its supervisory bodies in terms of human resources management, safety,

environment, ethical protocols and protection of data and scientific heritage.

Strengths and possibilities linked to the context

CRESS adheres to human resources management principles guided by directives from supervisory authorities. The SMART platform, overseen by the General Secretary, supports staff recruitment, management, and compliance with administrative rules. To ensure parity and professional equality, CRESS has appointed volunteers dedicated to equity and gender equality, who disseminate information, organize awareness seminars, and implement unbiased recruitment strategies. Training and career development opportunities are provided to staff, including workshops organized by Inserm, Inrae, and universities, as well as events hosted by CRESS. The director ensures staff safety, supported by a prevention officer and reference agents. Data management complies with IT security and GDPR rules, with staff trained accordingly. Preventive actions are coordinated through a Prevention committee, addressing evolving needs such as those arising during the COVID-19 pandemic. Environmental risk assessment and sustainable development align with institutional strategies. A crisis management plan was implemented during the pandemic, facilitating remote work without compromising data security or continuity of research activities. The plan is regularly updated to address emerging risks.

Weaknesses and risks linked to the context

Young researchers expressed some lack of knowledge of the general administrative and regulatory rules (in particular foreign researchers). Efforts should be made for better integration procedures of young researchers. The direction of the CRESS expressed concern regarding work overload of the SMART platform, both due to major increase in administrative and regulatory procedures and to high turnover of the staff, due to short term contracts and low salary attractiveness (departure of 5 full-time equivalents in 2023). It is crucial to maintain the profiles of administrative assistants and technicians working with the teams of researchers, engineers and doctoral students.

EVALUATION AREA 2: ATTRACTIVENESS

Assessment on the attractiveness of the unit

The CRESS excels in organizing scientific events, participating in prestigious conferences, and holding editorial responsibilities. Its members actively engage in public institutions and international organizations, securing funding and awards for groundbreaking research. While providing strong support for junior researchers, there's room for improvement in integrating young researchers and enhancing cross-team collaborations. Despite this, the CRESS maintains exceptional scientific productivity and adheres to open science principles, contributing significantly to public health research.

- 1/ The unit has an attractive scientific reputation and is part of the European research area.*
- 2/ The unit is attractive because for the quality of its staff support policy.*
- 3/ The unit is attractive through its success in competitive calls for projects.*
- 4/ The unit is attractive for the quality of its major equipment and technical skills.*

Strengths and possibilities linked to the context for the four references above

The CRESS has a strong history of organizing diverse scientific events, including international conferences and workshops. Members of the unit are involved in scientific committees for prominent conferences and organizations, presenting their research at prestigious international conferences and institutions. They also have editorial responsibilities in internationally recognized medical journals, covering general medicine, epidemiology, methodology, statistics, and speciality medical areas.

The unit is actively engaged in expertise activities and serving in scientific councils of public institutions and agencies at the national (Parliament, Senate, Ministries, health authorities...) and international (European

Parliament, US national academies, WHO...). Members also contribute to international networks and committees, participating in research evaluation committees and reviewing of funding applications, at national and international levels. They are also actively involved in various academies, scientific institutions, and learned societies at national and international levels.

The unit's members have received prestigious awards and distinctions (Inserm Research Prize, « Grand Prix de la recherche médicale » of the Fondation de France, « Etoiles de l'Europe » trophy of the French Ministry of Higher Education, Research and Innovation...), with five researchers being recognized as Highly Cited Researchers. Early career researchers have also received awards like the L'Oréal Women for Science Young Talent Award, David Sackett Young Investigator Award, two Bettencourt-Schueller foundation awards, prizes in international congresses and PhD prizes.

The CRESS provides an excellent environment and supervision for junior researchers, supporting their career development through coaching policies and training programs, including speed meetings, seminars, and poster presentations. During the period, the unit has supervised about 200 PhD students and more than 300 Master students. The CRESS offers an extensive training catalog, and junior researchers have opportunities to present their work at scientific events.

The unit has a comprehensive strategy for attracting and developing talented researchers, resulting in the acquisition of more than 20 new university tenured researcher positions, four Inserm and three Inrae researchers (CRCN) and four promotions to Inserm directors of research (DR), eight to Professors with hospital duties (PUPH) and one Professor. Moreover, two ERC consolidator grants were obtained, as well as several competitive positions for young researchers (1 post-doctoral Marie Skłodowska-Curie positions, four chair positions of excellence). Research support staff also benefit from this strategy, with fifteen new permanent positions and six promotions.

The unit actively engages in collaboration and networking, in particular by hosting several renowned visiting researchers from European (Netherlands, Germany, Greece...) and non-European countries (Singapore, Brazil, USA), as well as nineteen visiting PhD students. It is committed to research integrity, transparency, and open science, leading a research axis on Research on Research and collaborating with the Inserm program LORIER. Various measures are implemented to promote transparent and responsible research, including training sessions and standardized procedures across teams. Starting in 2022, all CRESS scientific publications are posted in HAL, the French open repository.

The unit has outstanding track record in responding to international and European calls for projects, securing around 17 million euros during the mandate, in particular in the European research framework (ERC, Horizon 2020, Horizon-MSCA doctoral networks...), as well as from the USA (NIH) and the UK (MRC, Wellcome Trust). It actively participates in national projects funded by the PIA, raising approximately 13 million euros during the mandate. Notable achievements include the RE-CO-NAI platform, Cohorts programs, and the Childhood cancer observation platform (HOPE-EPI). The unit was also exceptionally successful in competitive national grants (ANR, PHRC, FUI, Inca...) totaling around 34 million euros. Finally, the unit has secured 4.5 million euros from non-profit foundations (Fondation pour la Recherche Médicale, Fondation de France, Fondation ARCFrance Alzheimer...). Overall, these diverse funding sources contribute significantly to the unit's groundbreaking research and scientific advancements.

The unit is home to leading researchers who oversee world-class research infrastructures, including population-based cohorts of both children and adults, as well as innovative e-cohorts like Nutrinet santé and ComPaRe. Members also head large European platforms that harmonize data from international cohorts and population-based registries, totaling over 450,000 patients followed for several years. These infrastructures collect diverse data, such as clinical, genetic, biological, radiological, social, and environmental information, often linked to the National Health Data System (SNDS). The unit also creates innovative infrastructures, such as an experimental online supermarket for interventional studies on consumer purchasing intentions. Most platforms are open to collaboration with researchers outside the CRESS, fostering numerous collaborations and publications. Specific research platforms developed by the unit include PROCESS, a technological "no-code" platform for setting up online surveys using citizen science methods, the COVID-NMA platform for real-time evidence mapping during the COVID-19 pandemic, and the TRUST platform aimed at transforming and upgrading the trustworthiness of clinical trials and epidemiology. Overall, these platforms are considered innovative models for public health and play a major structuring role in French and European research.

Weaknesses and risks linked to the context for the four references above

While CRESS activities are outstanding on all four criteria, the activities for the integration of young researchers (PhD students and post-doctoral researchers) could be improved. Indeed, the young researchers have expressed insufficient interactions at the level of the Unit, in particular regarding cross-team collaborations (some PhD students from smaller teams expressing a feeling of isolation). For instance, a club "young researchers" could be created, on the model of the club "data". A better description of the administrative and university environment would also be needed, in particular for foreign students.

EVALUATION AREA 3: SCIENTIFIC PRODUCTION

Assessment on the scientific production of the unit

The CRESS scientific productivity is exceptional, with about 3400 peer-reviewed articles (1500 as first, last or corresponding author), with 21 % in the top 10 % most cited articles. Notable achievements include developing influential tools like the 'Nutri-Score' label or the reporting guidelines (STARD, CONSORT) requested by editors and the ICMJE. Open science principles and ethical research practices are implemented successfully. Attention should be paid by the direction of the CRESS to the smaller teams, to further develop their scientific production.

- 1/ *The scientific production of the unit meets quality criteria.*
- 2/ *The unit's scientific production is proportionate to its research potential and properly shared out between its personnel.*
- 3/ *The scientific production of the unit complies with the principles of research integrity, ethics and open science. It complies with the directives applicable in this field.*

Strengths and possibilities linked to the context for the three references above

The unit scientific production is outstanding, with about 3400 original peer-reviewed articles (43% signed as first, last, or corresponding author), with 21% in the top 10 % most cited articles (and 162 in the Top 1% highly cited articles, of which 31 as first or last author, and 5 hot papers). The normalized citation index is about three times higher than the international average. The unit's output includes articles in the best international journals such as the New England Journal of Medicine, JAMA, BMJ, Lancet Public Health, and Nature Medicine.

The unit's global influence is evident through its commitment to international collaboration, with about 40% of its publications resulting from collaborations with international partners. This approach has enriched the unit's scientific output and solidified its reputation as a world-class research unit.

The unit emphasizes strong theoretical and methodological foundations in its scientific production, employing advanced statistical methods, innovative study designs, and state-of-the-art methodological approaches. Members lead various cohorts, platforms, and registries, providing high-quality data that has significantly contributed to understanding health determinants across different life stages.

The unit has demonstrated its impact on clinical practice and public health, by developing for instance new child growth curves and creating the nutritional front label 'Nutri-Score,' implemented in France and other European countries. Their research also shaped research practices by leading the development of reporting guidelines (STARD, CONSORT) requested by editors and the ICMJE.

The unit emphasizes a balanced scientific production in proportion to its research potential, prioritizing advancing knowledge over sheer volume of publications. It has robust initiatives and measures in place to uphold scientific integrity and rigorous research, including protocol registration, data management plans, and open access to research data and software. Ethical and regulatory compliance (including GDPR and regulations regarding human research) is ensured through the appointment of Ethics and Scientific Integrity referents. The unit follows guidelines from organizations such as NIH, EU, UK, and French regulations, actively participating in the Inserm LORIER program dedicated to ethical and responsible research. It also actively participates in collaborative efforts and national/international initiatives, highlighting its dedication to research quality and trustworthiness. Members receive regular training on this topic, and specific training is provided for young researchers.

A collaborative approach is valued within the unit, recognizing the contributions of all permanent research personnel, including full-time researchers, university-hospital clinicians, hospital clinicians PhD and post-doctoral researchers and research support staff. Various roles within the unit, such as publication in peer-reviewed journals, creation of tools, computer programs, and management of platforms, contribute to the overall scientific endeavor. Internal collaborations have led to outstanding projects, as seen in the development of the ComPare cohort with the support of EREN and Nutrinet Santé.

The unit embraces and promotes open science principles by publishing most of its research in open access. Since 2022, all publications are posted on HAL, and the unit complies with the FAIR principle. Protocols and

statistical analysis plans are made available, and data and metadata are accessible when possible, with access defined in each project. The unit contributes to the development of open-source software and engages in projects that promote open science and data sharing.

Weaknesses and risks linked to the context for the three references above

While the scientific output of the CRESS is exceptional, attention should be paid by the direction of the CRESS to the smaller teams and thematic (in particular pediatric cancers and rheumatoid and musculoskeletal diseases), in order to further develop their scientific production.

EVALUATION AREA 4: CONTRIBUTION OF RESEARCH ACTIVITIES TO SOCIETY

Assessment on the inclusion of the unit's research in society

The CRESS focuses on strategic non-academic partnerships, while avoiding conflicts of interest with certain industries. Patient involvement is central, enhancing research relevance and translation into practice. CRESS's expertise is sought after by governments, notably during COVID-19. They prioritize public health impact, offering tools like the Nutri-score freely. CRESS actively disseminates research and contributes to shaping health policies internationally. Cross-fertilization between teams should be encouraged, to increase skills in participative research in some of the teams.

- 1/ The unit stands out for the quality and the amount of its interactions with the non-academic world.*
- 2/ The unit develops products for the cultural, economic and social world.*
- 3/ The unit shares its knowledge with the general public and takes part in debates in society.*

Strengths and possibilities linked to the context for the three references above

The CRESS employs a strategic approach to partnerships in non-academic sectors, emphasizing diversity in research while avoiding conflicts of interest. This strategy is implemented at the team level, exemplified by certain teams avoiding partnerships with industries (e.g., EREN with the food industry, METHODS and ECSTRRA with the pharmaceutical industry) to preserve trust and research integrity.

Despite these constraints, specific partnerships with the economic sector have been formed, particularly in digital health, such as the @HôtelDieu project. The CRESS develops pioneering participative research, including patients and the public, evident in initiatives like Nutrinet Santé and the ComPaRe e-cohort, which collaborates with numerous patient associations. The Malin program, co-created with stakeholders, benefits disadvantaged families. The unit recognizes the importance of patient perspectives, actively involving them in research processes, emphasizing patient-centered research, allowing patients to propose ideas, be involved in research processes, and define Core Outcome Sets.

These partnerships enhance the relevance and novelty of CRESS research, facilitating the translation of results into clinical practice and public health policy. The unit is sought after by governmental entities for guidance, as seen during the COVID-19 pandemic, where members developed technologies for remote patient monitoring. The primary focus of the CRESS is advancing public health, by impacting clinical practice, public health decisions, and overall public well-being. Tools and products developed by the unit are often freely accessible and open access where possible. An example is the Nutri-score, contributing to healthier food choices with significant economic value through its impact on population health.

While hosting professionals and students funded by non-academic partners is limited, CRESS actively provides training for non-academic actors. This includes participating in training courses for healthcare professionals and offering specific methodological training.

The unit encourages a culture of innovation and entrepreneurship, exemplified by the creation of SKEZI, a spin-off offering a technological platform derived from the ComPaRe e-cohort. This platform simplifies the creation and implementation of e-cohorts and has been utilized in various public and private projects.

CRESS members actively disseminate their research to social, economic, and cultural actors through various channels, including webinars, press releases, videos, webcasts, podcasts, television and radio interviews, and national and international news outlets, engaging with students at various educational levels to raise awareness

about health misinformation and expose them to different roles within the field. Teams like EREN have an exceptional media engagement, contributing to high-impact national and international media outlets. The unit's expertise is recognized both nationally and internationally, leading to frequent contributions to the development of standards, procedures, and recommendations in various fields. CRESS researchers provide expertise to esteemed institutions such as the French and European Parliament, Ministry of Health, WHO-IARC, showcasing their impact on shaping health policies and practices. The dissemination efforts are targeted to benefit society, such as the integration of the French reference child growth chart into digital health records, impacting a significant number of healthcare professionals in France.

Weaknesses and risks linked to the context for the three references above

While some teams, in particular METHODS, EREN and EAROH are particularly excellent at developing participative research, other teams could benefit from cross-fertilization to enhance their skills and strategies in this important domain.

ANALYSIS OF THE UNIT'S TRAJECTORY

The CRESS is an interdisciplinary research center affiliated with Université Paris Cité, Université Sorbonne Paris Nord, Inserm, and Inrae. Initially comprising five teams with 260 members, it expanded over two mandates to nine research teams and a research support platform, with 381 members overall. The center focuses on diverse research areas, including perinatal and pediatric epidemiology, therapeutic evaluation methods, clinical epidemiology for musculoskeletal diseases, aging and neurodegenerative diseases epidemiology, and nutritional epidemiology. The CRESS is recognized for its international collaborations, large-scale cohorts, and commitment to research training. Notably, it will undergo restructuring for the next mandate, consolidating into five teams under new leadership.

The CRESS focuses on identifying determinants of population health from conception to aging. Its strategy includes: 1) Research Rooted in Clinical Practice: CRESS researchers, many of whom are healthcare practitioners, collaborate with "Assistance Publique des Hôpitaux de Paris", generating new hypotheses, ensuring research relevance, and facilitating translation into practice ; 2) Development of Robust Methods: CRESS employs innovative approaches, such as life course methodologies and machine learning, to understand health determinants and interactions, develop new research tools, and propose paradigm-shifting frameworks ; 3) Research Built on Societal Links: Pioneering citizen science, CRESS engages in co-constructing research questions and interventions, ensuring the relevance and quality of research questions and data ; 4) Partnership with Policymakers: CRESS collaborates with policymakers, informing national programs, contributing to maternal and child health monitoring, and participating in the development of clinical practice guidelines ; 5) Innovative Infrastructures: CRESS leads unique research infrastructures, including world-class cohorts and registries, gathering diverse data and fostering open science principles. These infrastructures are flexible and continually evolve to address new hypotheses and technological advancements.

For the next mandate, two teams will be leaving (team ECSTRAA to the IHU THEMA and team HERA to UMR MERIT261 IRD-UPC) and three teams will be grouped (Epopé, Earoh and Epicea, to form Oppale). The five research teams and the SMART platform will be distributed on five sites, including the new Villemin site, for which the move of several teams is currently ongoing. While there will be a change of director (from Philippe Ravaud to Isabelle Boutron), the organization of the CRESS will globally be in continuity with the previous mandate, with some new animation strategies (in particular by creating several steering committees to render the animation of the CRESS more participative).

RECOMMENDATIONS TO THE UNIT

Recommendations regarding the Evaluation Area 1: Profile, Resources and Organisation of the Unit

With the new structuration of the CRESS, the heterogeneity of team sizes will be high (some teams with more than 100 members, others with about 20). The direction of the CRESS should pay attention to the development of the smaller teams, and assure their full participation to the animation of the center. A better integration of young researchers to the cross-team animation is also desirable, for instance by the creation of a club "young" researchers, on the model of the club "data".

Regarding resources, CRESS teams could consider gathering more funding from foundations and associations (currently about 7% of the total funding), which might also contribute to further developing of participative research.

The direction of the CRESS should continue to strengthen and develop the SMART platform, the efficiency of which was highlighted by CRESS members. The dialogue with the research institutions regarding increasing administrative and regulatory complexity should also be further developed. Indeed, due to its size and reputation of excellence, the CRESS has the opportunity to discuss major improvements in the research procedures (in particular for medical research and IT security), which may benefit the whole national community.

The premise in Hotel Dieu, although of historical value, would need modernization. In particular, some spaces in the central location (Hotel Dieu) should be dedicated to cross-team meetings and informal interactions, in order to favour cross-fertilization.

Recommendations regarding the Evaluation Area 2: Attractiveness

While CRESS attractiveness is overall outstanding, some teams can still increase their attractiveness, in order to attract full-time researchers, creating an alliance of clinicians and full-time epidemiologists.

The activities for the integration of young researchers (PhD students and post-doctoral researchers) could also be improved. Indeed, the young researchers have expressed insufficient interactions at the level of the unit, in particular regarding cross-team collaborations (some PhD students from smaller teams expressing a feeling of isolation). For instance, a club "young researchers" could be created, on the model of the club "data". A better description of the administrative and university environment would also be needed, in particular for foreign students.

Recommendations regarding Evaluation Area 3: Scientific Production

While the scientific production and strategy is overall outstanding, some areas will need more attention from the direction of the CRESS:

- research on pediatric cancers needs to be secured and developed, as it is of major public health interest, by developing collaborations with other axes of the future OPPaLE team and by attracting new post-docs and permanent researchers, in particular in the context of the forthcoming retirement of the head of the Childhood Cancer Registry.
- Similarly, as the only French team specialized in epidemiology rheumatic and musculoskeletal diseases, the ECAMO team needs to be supported, in order to stabilize their number of researchers, in the context of several senior researchers at their end of their career. If possible, research in osteoarthritis, a major public health issue, would also need to be developed.
- Finally, regarding the EpiAgeing team, while the scientific production is outstanding, the size of the research group remains relatively small, although efforts to include clinicians have been performed successfully. In a context of major demographic and epidemiological transitions (number of elderly people at its maximum until 2050 in France and Europe, due to the baby boomers arriving into old age; slowing of the increase in life expectancy; decrease of age-specific incidence of dementia...), it appears crucial to gather more data on the french general elderly population, to describe and understand these ongoing changes.

Recommendations regarding Evaluation Area 4: Contribution of Research Activities to Society

While some teams, in particular METHODS, EREN and EAROH are particularly excellent at developing participative research, other teams could benefit from cross-fertilization to enhance their skills and strategies in this important domain.

TEAM-BY-TEAM OR THEME ASSESSMENT

Team 1: Epidémiologie Obstétricale Périnatale et pédiatrique EPOPé
 Name of the supervisor: Mr Pierre-Yves Ancel

THEMES OF THE TEAM

The research program of the EPOPé team is dedicated to obstetric, perinatal, and pediatric epidemiology. It aims at better understanding the mechanisms involved in the occurrence of adverse events in maternal, perinatal and child health, as well as their short- and long-term consequences, and at contributing to the definition and implementation of effective medical practices and health policies.

More specifically, the research theme covers prenatal and perinatal care in low-risk situations; severe maternal morbidity during pregnancy and its consequences for the child; prematurity and intrauterine growth restriction; risk factors and management of birth defects; risks and decision-making in pediatrics; inequalities in maternal, perinatal, and child health

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

During the contract and in line with its historical trajectory, EPOPé team's research has been fully aligned with the recommendations of the previous report.

New collaborations have been launched and are enriching the team's scientific production. Interventional approaches have now been adopted, such as the randomized cluster-controlled trial on medical decision-making in situations of extreme prematurity (PREMEX). The research axis timely opened on the impact of the CoViD on pregnancy (COROPREG cohort) shows the team's scientific responsiveness to dramatic challenges in public health.

At the international level, the team has strengthened its collaborations and its leadership: one example is the participation of the team as a co-leader in the European H2020 RECAP project, a platform dedicated to the monitoring of children born prematurely.

The project of merging the EPOPé, EAROH and EPICEA teams within CRESS is aligned with the recommendations of the previous report about the management and quality of working life of the team.

Scientific dissemination has been expanded through social media and two additional websites.

The team has launched multi-omics analyses in conjunction with the EAROH team and RECONAI platform. Several young researchers of the team are being trained in big data processing and artificial intelligence.

The EPOPé team maintains its international leadership through the STARD initiative for diagnostic test evaluation reporting and the EQUATOR network.

WORKFORCE OF THE TEAM: in physical persons at 31/12/2022

Catégories de personnel	Effectifs
Professeurs et assimilés	16
Maîtres de conférences et assimilés	7
Directeurs de recherche et assimilés	3
Chargés de recherche et assimilés	0
Personnels d'appui à la recherche	6
Personnels hospitaliers	11
Sous-total personnels permanents en activité	43
Enseignants-chercheurs et chercheurs non permanents et assimilés	7
Personnels d'appui non permanents	11
Post-doctorants	1
Doctorants	12
Sous-total personnels non permanents en activité	31
Total personnels	74

EVALUATION

Overall assessment of the team

The EPOPé team is active at an exceptional, international level in the area of obstetric, perinatal and pediatric epidemiology. It leads major national and international collaborations, thanks to its ability to obtain competitive funding and to bring together the most pertinent and outstanding clinical research teams. Its outstanding scientific output is characterized by publications at the highest level of general medicine and science journals. The prospect of merging with the unit's EAROH and EPICEA teams for the next contract should allow the team to further develop its performance.

Strengths and possibilities linked to the context

The EPOPé team's track record and attractiveness is clearly outstanding, in the field of epidemiology but also across the medical disciplines concerned at national, European, and international levels. This is the result of a long-standing, continued research program, particularly suited to clinical collaborations with perinatology, obstetrics and neonatology, with research axes that can have a major impact on current health challenges. It is also the result of the importance and quality of the structured observational and interventional medical databases (EPIPAGE2, PREMEX) coordinated by the team, and their open access. The team's responsiveness to epidemiological abrupt phenomena is illustrated by the results from the COROPREG cohort in the field of CoViD. Big data approaches have provided the best answers to problems such as the establishment of reference curves for children's growth, in connection with the FHU CHILD and the EAROH team, and their application in medical software, in children personal digital health records and health booklets. The development of such tools and of the associated technology were made possible thanks to the team's remarkable ability to obtain national and international funding (total k€ 19'438 over the 2017-2022 period). The expertise available within the team is high standard and particularly attractive due to its degree of openness to young researchers and clinicians, and to the various opportunities for collaboration.

The team's association with regional centers of excellence for women's and children's health, such as the FHU PREMA and CHILD, the Institute for Women's Health, the IHU InovAND project, the CIC P1419, but also the direct collaborations established with many perinatal university hospital centers, whose teams are involved in the collection and analysis of data, as well as scientific publications, continue to play an extremely important role of emulation.

In addition, EPOPé team is involved, including at levels of leadership, in different research networks and initiatives, such as the European RECAP platform dedicated to prematurity or collaborations with WHO and UNICEF, particularly in the area of stillbirths.

The quality of the EPOPé team's scientific production is high standard and reaches the level of international excellence: among the highly cited papers authored by team members, twelve are in the best general medical and scientific journals (NEJM, Lancet, BMJ, JAMA), with numerous publications in the best specialized medical journals. Various studies have had a general impact on medical practices, such as the care of premature infants (Pierrat BMJ 2017, 2018), the prevention of postpartum hemorrhage (Sentilhes NEJM 2018, 2021).

The contribution of team's research activities to society relies on the direct impact on medical practice of its research; on privileged links with public bodies and with patient associations/foundations; on effective dissemination of its main results in the media.

Weaknesses and risks linked to the context

The team's weaknesses are few and mainly related to the lack of full-time permanent researchers dedicated to research and a number of permanent staff limited to a few units. These difficulties can significantly limit its research capacities, given the importance and number of research axes that require direction and coordination, in particular with the various clinical collaborations. Developing a proactive plan to attract additional senior researchers from Inserm or internationally may help solving this issue.

Similarly, a chronic shortage of permanent research support professionals is reported, especially in stable positions of project managers, a weakness that needs further, decisive support from the supervising universities and national research supervisory organizations (Inserm and INRAE).

The safety and confidentiality of the patients' health data collected in the various cohorts, platforms and studies are ensured via heterogenous systems depending on study types, historical characteristics, multiple supervisory

institutions, open access. Despite the continuing efforts of the teams, the SMART service, CRESS and supervisory institutions, such heterogeneity may result in insufficient safety of data preservation.

Analysis of the team's trajectory

As part of the next contract 2025-2029, the team will merge with the current EAROH (Early life research on later health) and EPICEA (Epidemiology of childhood and adolescent cancers) teams, to form the OPPALE (Obstetric, Perinatal, Pediatric Life course Epidemiology) team.

This will provide the team with an added value in terms of coherence and synergies between the programs of the separate teams and will increase international visibility and attractiveness. The organizational chart will include approximately 55 seniors researchers and professors/lecturers (approximately 20 full-time equivalents), 10 post-doctoral fellows, approximately 40 researches support staff. The team will host approximately 20 PhD students and 20 master's students.

The research program announced in this context will be based on a life course approach of clinical epidemiology, from the peri-conceptual period to adulthood. The available platforms and prospective cohorts such as RECONAI, EDEN, RECAP; CCOP, COHOPER and BIOCAP for the epidemiology of childhood and adolescent cancers; RNHE, RNTSE, REMAPAR and OMIN registries, and randomized controlled trials, such as the important ECAIL prevention trial, will be integrated into OPPALE. The research strategy will be based on the complementarity and interdisciplinary coherence of six newly defined research axes (transmission of parental behaviors & medical practices; foetal and severe neonatal morbidity, child, and adolescent health; epidemiology of childhood cancer; social inequalities in health).

This trajectory appears particularly constructive. The links and collaborations already existing between the teams involved will facilitate the realization of this new stage of development.

RECOMMENDATIONS TO THE TEAM

The planning of the new OPPALE team makes sense and has the potential to take further the excellence of the research provided so far.

There is clearly a need for additional, permanent research support staff, given the life course profile of its research, independently on the external, temporary funding the team is able to obtain. Gaining further support from the supervisory bodies and external partnerships is critical for the long-term maintenance of data collection and data management of the different cohorts and platforms under the responsibility of the team.

Further growth of OPPALE may reside in the building and leading of large-scale international projects that have potential for a major impact in public and, eventually, in global health. This would imply increasing the capacity to raise international funding.

The development of population-based interventional studies would strengthen the impact of EPOPÉ's research. Such orientations could also increase the attractiveness of the team for external statutory researchers, while keeping the strong, remarkable characteristic of having a major number of academic clinicians included in the team at the national level.

The team's plan of developing further methodological tools in the fields of data science, massive data generated electronically by participants, multi-omics systems biology and artificial intelligence may support its future development, and enable the development of innovations that could be economically valued.

Team 2: Epidémiologie et statistiques cliniques, des voies respiratoires et de la réanimation

Name of the supervisor: Ms Sylvie Chevret

THEMES OF THE TEAM

The ECCSTRA team, based on the APHP hospital Saint-Louis in the heart of Paris, is a biostatistical team at the interface between more fundamental statistical research and applied clinical trials, which make use of these new methodologies. The applied topics are mostly in the field of hematology, closely linked with the AP-HP hospital Saint-Louis main domain of expertise. Two main axes have been developed: innovative (Bayesian) clinical trial designs and methods for inference in observational data.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

At the previous evaluation, the experts had suggested the expertise of the team should not be at the detriment of their own research, and proposed to develop industrial collaborations. The team took satisfying actions to deal with the recommendations: the team has been able to protect research time through international collaborations, students' supervisions and hiring of engineers. Due to its close relationship with the french health technology assessment agency, the team has defined a strategy to limit industrial partnerships.

WORKFORCE OF THE TEAM: in physical persons at 31/12/2022

Catégories de personnel	Effectifs
Professeurs et assimilés	10
Maîtres de conférences et assimilés	2
Directeurs de recherche et assimilés	0
Chargés de recherche et assimilés	0
Personnels d'appui à la recherche	2
Personnels hospitaliers	13
Sous-total personnels permanents en activité	27
Enseignants-chercheurs et chercheurs non permanents et assimilés	7
Personnels d'appui non permanents	6
Post-doctorants	0
Doctorants	10
Sous-total personnels non permanents en activité	23
Total personnels	50

EVALUATION

Overall assessment of the team

The multidisciplinary ECCSTRA team, is an (inter)national reference team for clinical biostatistics in hematology created in 2005 (joined CRESS in 2014) with a prominent scientific production. Its outstanding biostatistical research is fueled by real life clinical questions and includes applications, with a strong focus on hematology, but also bone-marrow transplants and intensive care. The two main biostatistical research axes are well defined: early/adaptive/Bayesian clinical trial designs and methods for observational data analysis; for both the team is internationally recognized.

Strengths and possibilities linked to the context

The scientific production of the ECCSTRA team is outstanding on the national and international level, with 698 peer-reviewed papers published in 2017-22, with about 1/3th of these as first, last or corresponding author and 150 in top 10% of citations of the field. Of note, 36 of these papers have students as first authors and 54 are biostatistical papers published in high-level journals in this field, which are difficult to publish in. It is worthwhile to mention ten PhD defenses on a biostatistics topic (Public Health) and ten Master 2 students. The portfolio of research projects is well balanced between a variety of biostatistical topics: early phase clinical trial designs, biomarker data exploration, external control inference, multistate models for Covid19 and adaptive designs. The team also has a large portfolio of publicly funded more applied clinical trials or studies (key funding by PHRC and other public calls). The team is extremely attractive for its academic reputation, illustrated by the number of invited talks, national and international scientific commissions, leadership in methodology in European networks, editorial duties (JAMA, J Hepatology); awards, students, and a very high number of grants funded at the national (PHRC, ANR, partner in three RHUs, a France 2030 program) and international level (H2020). There are several international collaborations with outstanding universities such as Columbia and Freiburg University. The research team is strongly involved in University teaching which has a positive effect on its significant reputation.

The ECCSTRA team has a very high impact on the socioeconomic environment because of its strong methodological implication in the health technology agency in France (HAS), which is a plus. The team strongly collaborates with clinicians in the clinical topics cited above and participates to the academic French clinical research of these topics through collaborative groups, and is in a good environment for accessing data for illustrating biostatistical method papers. Due to its closeness to the HAS, the team has chosen to limit its direct collaborations with pharma/biotech industry.

Weaknesses and risks linked to the context

The team lacks full-time Inserm researchers; in France, it is quite difficult to prepare talented biostatistical researchers for permanent Inserm positions (and potential future team leaders) with regards to the competition with industry.

The team is highly involved in university teaching and platform activities for the hospital, which could jeopardize the right balance between platform and "own" research.

Analysis of the team's trajectory

During the 2017-22 period, the team has had a remarkable scientific output. The team has been instrumental for the methodology of the health technology agency in France (HAS); a good number of young researchers have received awards for their research.

Note the ECCSTRA team is leaving CRESS and joining the IHU structure THEMA-2 European Leukemia Institute on the hospital Saint-Louis site.

RECOMMENDATIONS TO THE TEAM

The ECCSTRA team is encouraged to continue to its current strategy to protect sufficient time for its own biostatistical research topics.

The team has a solid scientific strategy and has the potential to train future researchers in important biostatistical topics.

The committee recommends further developing the Bayesian /adaptive clinical trials theme, and the methods for developing external control arms.

Team 3: Équipe de Recherche en Épidémiologie Nutritionnelle
 Name of the supervisor: Ms Mathilde Touvier

THEMES OF THE TEAM

The EREN team focuses on studying the associations between nutrition and health, analyzing underlying mechanisms and determinants influencing dietary intake. Its main objective is to provide evidence to national and international authorities, thereby contributing to the development of public health policies, for example the NutriScore as nutritional prevention tool. EREN's research covers various health outcomes related to nutrition, including non-communicable chronic diseases (such as cancer, diabetes), aging, mental health and environmental parameters. EREN adopts an interdisciplinary approach from mechanistic to participatory. Since 2009, EREN has coordinated the infrastructure of the NutriNet-Santé E-cohort, with regular measurements of various exposures, complemented by other cohorts.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

EREN achieved key milestones in response to the previous report, including securing European and international funding (e.g. an ERC Consolidator Grant on additives) and leading work packages in large-scale international projects such as a JPI HDHL Horizon Europe on physical activity sensors. Additionally, EREN established strong local collaborations with other research teams, including a project on students' diets and the PROSPECTIVE initiative for a sports complex. The team collaborated regularly with other CRESS teams. Thirdly, EREN improved its career management for scientists and technicians through regular meetings, seminars, and office equipment updates. Fourth, the team excelled in building its social media presence, gaining visibility for platforms like NACRe on nutrition and cancer, and maintaining consistent communication across various channels. Achievements, such as the Annual Public Health Chair from the Collège de France in 2022-2023, significantly contributed to this success.

Fifth, EREN provided access to NutriNet-Santé cohort data for collaborative projects and initiated efforts to pool data being assessed by other CRESS cohorts.

Sixth, the research in biostatistics expanded with the recruitment of two data scientists, strengthening the team's capabilities in this critical area. Finally, the team effectively managed methodological aspects related to food composition data, collaborating with partners like INRAE and ANSES to merge composition databases.

WORKFORCE OF THE TEAM: in physical persons at 31/12/2022

Catégories de personnel	Effectifs
Professeurs et assimilés	6
Maîtres de conférences et assimilés	8
Directeurs de recherche et assimilés	2
Chargés de recherche et assimilés	3
Personnels d'appui à la recherche	18
Personnels hospitaliers	0
Sous-total personnels permanents en activité	37
Enseignants-chercheurs et chercheurs non permanents et assimilés	7
Personnels d'appui non permanents	16
Post-doctorants	8
Doctorants	18
Sous-total personnels non permanents en activité	49
Total personnels	86

EVALUATION

Overall assessment of the team

EREN excels in nutritional epidemiology with a comprehensive approach. With 905 published articles, it demonstrates outstanding national and international research quality, recognized by distinctions like the Inserm Research 2019 award. Aligned with Inserm and Inrae strategies, EREN's impact is remarkable in the scientific community and civil society through strong presence at conferences and on social media. EREN's commitment is underscored by partnerships with renowned institutions and 55 grants emphasizing outstanding excellence in leadership and significant progress in the previous period.

Strengths and possibilities linked to the context

EREN presents several strengths and opportunities related to its context. Firstly, the team stands out for its focus on nutrition as major modifiable determinant of health. As the only team exclusively focused on nutritional epidemiology in France, EREN adopts an interdisciplinary approach spanning mechanistic to participatory methods. Since 2009, EREN manages the e-cohort NutriNet-Santé, placing it in a crucial role for the discipline in providing regular and up-to-date nutritional exposure data.

EREN is distinguished by its outstanding scientific output and communication efforts. Its research is published in renowned journals, such as in BMJ, JAMA Intern Med., Int J Epidemiol, Am J Clin Nutr, Nature Sustainability, Obesity Reviews. Overall, 50% were authored by a team member as the first, last, or corresponding author, among which 42% were among the top 10% of the most cited publications globally. A remarkable visibility has been also achieved by the strong presence at national and international conferences (175 oral presentations, 155 posters, and 302 invited conferences). EREN uses unique databases which are rich in data on pesticides, additives, and contaminants related to food processes which are crucial for understanding and assessing the current nutritional transition. The team has strengthened its collaborations and increased funding at the European and international level. During past evaluation period, EREN successfully secured 55 grants, totaling approximately 7.1 million euros (1 ERC Consolidator Grant project 2020-2025 on the important topic of the disease risk by food additives, five ANR projects, two InCa projects and involvement in various international projects, such as the Horizon Europe program "Genial" 2022-2027, the European project JPI Health Diet for Healthy Life "Wealth" 2022-2025, and the WCRF project "Biohealth" 2020-2024). The strategy for obtaining competitive research grants has also been successful for the use of the NutriNet-Santé biobank and recently launched stool sample collection.

Additionally, the team actively welcomed and supported 33 PhD students and 11 post-doctoral researchers, significantly contributing to the future of the discipline.

EREN's work aligns with the Inserm 2020–2025 Strategic Plan and the strategic priorities of INRAE 2030, particularly in the field of preventive nutrition for public and environmental health within the One Health concept. The development of tools for nutritional prevention, such as NutriScore, attests to the team's concrete impact on the society.

Furthermore, EREN's visibility within political institutions and participating in various working groups, enhance its influence and role in shaping public health and nutrition policies. In summary, EREN occupies a strategic and diversified position, capitalizing on its expertise to significantly contributing to the understanding of the links between nutrition, health, and the environment in France and beyond.

Weaknesses and risks linked to the context

EREN faces some risks that could impact its functioning and development in the future. Firstly, the limited number of permanent staff represents a vulnerability, posing challenges in terms of the continuity of research activities and team stability. Additionally, relying on internal resources to fund most non-permanent technicians creates financial dependence and may limit investment capacity in other priority areas.

The use of the biobank and more clinically oriented collections, heavily reliant on competitive calls for grant proposals, exposes the team to financial risks associated with the competitiveness of these calls. The dependence on administrative and technical staff activities further accentuates this risk, underlying the importance of SMART's support.

The team's comprehensive research objectives may pose a risk in terms of maintenance. Sustaining these aims while maintaining clear priorities and a distinct positioning within permanent research staff can become a strategic challenge, adding pressure to secure funding through grants, particular with regard to the future development of the NutriNetSanté cohort. Moreover, the ongoing effort to enhance expertise in data science must be sustained to ensure the high-quality use and innovative modelization of cohort data in the future.

Analysis of the team's trajectory

The EREN team, Inserm U557, was founded in 2006 under the leadership of Professor Serge Hercberg. It was one of the five founding teams of CRESS in 2014. The transition of leadership to Dr. Mathilde Touvier was initiated during the 2014-2018 mandate and officially confirmed in 2019. This period is marked by excellent leadership and the development of an ambitious scientific strategy.

The scientific strategy expanded to encompass diverse objectives, including the impact of nutrition on the environment (Bio NutriNet Santé), the study of health effects of ultra-processed foods, additives, sugar exposure, and the development and deployment of the NutriScore, adopted during this mandate in six European countries. Participatory research and mental health outcomes are also explored areas. Financially and in terms of human resources, the strategy was consolidated. The team secured 55 grants, totalling approximately 7.1 million euros. Among these, the ERC Consolidator Grant 2020-2025 and five projects funded by ANR illustrate the team's outstanding progress in academic research. Moreover, new collaborations were established with renowned institutions such as the IARC-WHO, Imperial College London, the University of Sao Paulo, or the Global Burden of Disease Network - University of Washington, USA.

EREN's scientific output, aligned with the strategies of Inserm and Inrae, is outstanding with 905 articles published in prestigious journals. Several articles have been developed together with other CRESS teams, like METHODS. EREN also excelled at national and international congresses. These achievements were acknowledged through distinctions such as Inserm Research Award 2019 (M. Touvier), the Bettencourt Foundation Impulse Prize 2021 (M. Touvier) and Young Researcher award 2020 (B. Srour), the Annual Public Health Chair of the Collège de France for the period 2022-2023 (M. Touvier), and individual recognitions including an Honoris causa degree for P. Galan, the title of Knight of the Order of Merit for C. Julia, and recognition as a "highly cited researcher" by Clarivate in 2022 for E. Kesse-Guyot and S. Hercberg.

The scientific strategy, articulated around six main axes (determinants of nutritional behaviors, psychopathological mechanisms, dietary exposures and physical activity, human health and planetary health, as well as public health policies and associated tools), demonstrates a profound understanding of current challenges related to food and public health research. EREN proposes comprehensive and complementary methodologies, including mechanistic approaches integrating metabolic biomarkers or those related to intestinal microbiota, as well as participatory interventional approaches.

The challenge lies in aligning this strategy with the maintenance and dynamization of collaborations, as well as securing competitive grants to strengthen permanent staff. It is essential to regularly reassess the team's organization to keep up with the dynamics and requirements of the field. This also includes the future evolution of the NutriNetSanté cohort as key research infrastructure.

RECOMMENDATIONS TO THE TEAM

- Prioritize and clarify elements of sustainable infrastructure and design for the future evolution of the NutriNet-Santé cohort.
 - Encourage the use of the NutriNet-Santé biobank, particularly for the discovery of biomarkers related to the consumption of ultra-processed foods; for integrated pooling projects involving biomarker, genetic, and self-reported information and/or early predictors of non-communicable diseases.
 - Continue studying the biological mechanisms underlying the association between additives and health, using experimental research conducted with partner teams.
 - Continue studying the determinants of healthy aging, mental health outcomes, and the axis on environmental health and sustainable food (BioNutriNetSanté).
 - Continue improving and innovating methodologies and tools for estimating dietary intake and physical activity, beyond databases.
 - Consider the use of new modelisation approaches for exposure data estimates and the integration of artificial intelligence (AI).
- Continue participatory research and real-life interventions with an emphasis on increased prevention effectiveness evaluation.

Communication/Scientific Outreach:

- Continue deploying a strategic communication approach to raise awareness of the NutriScore and other research outputs.

Organization within CRESS:

- Continue to strengthen the collaboration with other CRESS teams and local teams in Bobigny.

Team 4: Epidémiologie des maladies rhumatismales et musculo-squelettiques

Name of the supervisor: Mr Christian Roux

THEMES OF THE TEAM

The broader objectives of the ECAMO team are to identify risk factors for poor prognosis in rheumatic musculoskeletal diseases (RMDs), aiming to influence public health policies in this field.

The ECAMO is focussing on 3 RMDs in particular:

1. Osteoporosis
2. Inflammatory arthritides, in particular Spondyloarthritis
3. Rare RMD diseases, such systemic lupus erythematosus or rare bone conditions

The stated aims of the team are:

- To identify prognostic factors, including comorbidities affecting the long-term outcome of these conditions.
- To assess RMD outcomes, including patient reported outcomes (PROs) or radiographic joint damage/disease progression.
- To assess therapeutic strategies in RMDs, including a randomised studies of new therapeutic interventions

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The previous recommendations suggested to:

- (1) obtain research support from broader, non-academic sources
- (2) focus on a limited number of pathologies to avoid dispersion
- (3) increase the number of doctoral students and postdoctoral fellows
- (4) take advantage from the CRESS resources and new research technologies

Briefly, these recommendations were considered and partially achieved:

- (1) The group has obtained a limited number of academic grants (FOREUM, PRHC, ...), and has participated in some pharmaceutical-sponsored research
- (2) The ECAMO's research focus has overall remained fairly constant, with a focus on osteoporosis and spondylarthritides. The constancy of research themes is partly associated with the predominance of work by senior researchers in the team. Some new research directions should be underscored, stemming from the younger researchers.
- (3) Four PhD students have been supervised within the ECAMO team, which appears to be an increase from the previous five years period but remains not a large proportion compared to the number of ECAMO investigators. The PhD students are predominantly MD's (rheumatologists or orthopaedic surgeons), - and by contrast to other CRESS teams -, no non-MD public health specialists, epidemiologist or statisticians.
- (4) More scientific 'cross-fertilisation' has occurred in collaboration with other CRESS teams, such as the EpiAgeing or the Methods teams, which has led to original research papers.

WORKFORCE OF THE TEAM: in physical persons at 31/12/2022

Catégories de personnel	Effectifs
Professeurs et assimilés	7
Maîtres de conférences et assimilés	2
Directeurs de recherche et assimilés	0
Chargés de recherche et assimilés	0
Personnels d'appui à la recherche	0
Personnels hospitaliers	1
Sous-total personnels permanents en activité	10
Enseignants-chercheurs et chercheurs non permanents et assimilés	2
Personnels d'appui non permanents	0
Post-doctorants	0
Doctorants	3

Sous-total personnels non permanents en activité	5
Total personnels	15

EVALUATION

Overall assessment of the team

The ECAMO research group has an original clinically focussed research program in RMDs. Research has expanded by including new sources of data, such as new patient cohorts or nutritional data. The scientific output is excellent, considering that the ECAMO group employs no full-time researchers or dedicated support staff.

To maintain its level of excellence, the team must be vigilant in the following areas: a limited number of larger competitive research grants, a limited number of doctoral students and the need to replace several senior investigators during the next period.

Strengths and possibilities linked to the context

The ECAMO team consists in ~10 part time researchers (clinician-researchers, but no full-time researchers); three doctoral students and two master's students, including a number of internationally well recognized researchers. This team of researchers has produced an impressive number of scientific articles over the past five years, of which 183 were conducted by a member of the team as first, last, or corresponding author. Divided by the number of researchers, this represents ~3 research papers per investigator per year, considering only the projects where the ECAMO investigators played a major role. The scientific production is excellent given the absence of full-time researchers within the team, which has been acknowledged by the European League against Rheumatism (EULAR), which has labelled the ECAMO as one of the few centers of excellence in Europe. Furthermore, some of the research performed is truly innovative, such as for example the opportunistic screening for osteoporosis or the use of nutritional data as a risk factor for inflammatory rheumatic diseases.

The ECAMO team has taken a leading position in the coordination of several cohorts of patients with rheumatic diseases in France, which represents an important asset and a substantial time commitment. The ECAMO team are the only large research team specifically focussed on the epidemiology of rheumatic musculoskeletal diseases in France, which implies that young talented rheumatologist aiming for an academic career in this field, are likely to consider a doctoral program at ECAMO

Weaknesses and risks linked to the context

The ECAMO team has made a conscious decision not to hire methodological support staff, but to rely on the CRESS's METHODS team. While this makes sense given the geographical proximity to the METHODS team, it may also limit the capacity of the team to raise major national or international research funds and may contribute to the lack of attractiveness for full-time researchers, that has been pointed out by the team members themselves. Potentially the lack of larger competitive grants may also limit the ability to attract a larger number of young talented researchers, PhD students, post-docs or full-time researchers

Analysis of the team's trajectory

ECAMO does not expect new position openings and anticipates the same number of researchers for the next five years. Some of the senior principal investigators (PIs) will need to be replaced (retirement) over the next period. While a couple of younger postdocs researchers have joined the team, the departure of several senior PIs is likely to leave a void in the scientific output of the ECAMO team. However, the remaining younger members of the team are talented and are still benefitting from the expertise, the experience, the infrastructure and the network of these senior investigators, and we can see the newer generation progressively replacing the vacuum left by retiring investigators.

In terms of research focus, ECAMO proposes continuing on very similar grounds: (1) management of osteoporosis, (2) assessment of outcomes in inflammatory RMDs, and (3) epidemiology of rare RMDs. However, they propose using other sources of data, including e-cohorts, large administrative databases, and multi-center

registries. Some of these venues have not been outlined in detail yet and need to be considered aspirational, at this stage.

RECOMMENDATIONS TO THE TEAM

As the only research team in France focussed on the epidemiology of rheumatic and musculoskeletal diseases, the ECAMO team bears a responsibility for raising the next generation of academic researchers in this field. We would strongly encourage the ECAMO team to attempt to raise the number of master and doctoral students (physicians and not physicians) over the next period. International exchange of researchers with other European countries should also be encouraged, which will usually help developing a broader network and new opportunities. Attracting more non-MD researchers, including as epidemiologists and public health specialists should also be considered.

To increase its attractiveness, ECAMO should aim at obtaining more competitive research funding from major national and international funding agencies, which could allow to increase the number of researchers and doctoral students.

As a whole, the CRESS has a strong public health focus. The two most frequent RMDs, which represent a true public health concern, are osteoarthritis / arthrosis and osteoporosis. While the latter is well covered by the current research focus of the team, ECAMO's unique environment within the CRESS offers an exceptional opportunity to get involved in the field of osteoarthritis, which represents a major burden for the nation and colossal associated costs. This could be done by attracting younger researchers, with an interest in this field or in collaboration with the team EpiAgeing.

Team 5: Méthodes de l'évaluation thérapeutique des maladies chroniques
 Name of the supervisor: Ms Isabelle Boutron

THEMES OF THE TEAM

The team's scientific field of interest is the evaluation of treatments of chronic diseases. The team is divided into four subgroups, each led by a senior researcher, whose themes are the production of evidence, the synthesis of evidence, personalized medicine, and research on research. In addition, several cross-cutting themes are addressed: public participation in research, digital health development, a platform trial of Covid treatments and a living meta-analysis of Covid treatments that were set-up in response to the pandemic.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

Recommendations of the previous evaluation related to promoting the discipline in France, sharing leadership responsibilities within the team, and enhancing collaborations within CRESS. On all accounts the response is appropriate. National recognition is reflected by the invitation from Inserm to organize and lead the Lorier program on ethical research, and invitations to deliver keynote speeches at national conferences. Sharing responsibilities was accomplished via the appointment of four sub-group leaders. Within CRESS collaborations include the joint conduct of clinical trials of the Nutri-score, with the EREN group, and collaborations on meta-analyses with EPOPEE.

WORKFORCE OF THE TEAM: in physical persons at 31/12/2022

Catégories de personnel	Effectifs
Professeurs et assimilés	6
Maîtres de conférences et assimilés	2
Directeurs de recherche et assimilés	1
Chargés de recherche et assimilés	1
Personnels d'appui à la recherche	3
Personnels hospitaliers	4
Sous-total personnels permanents en activité	17
Enseignants-chercheurs et chercheurs non permanents et assimilés	3
Personnels d'appui non permanents	12
Post-doctorants	4
Doctorants	15
Sous-total personnels non permanents en activité	34
Total personnels	51

EVALUATION

Overall assessment of the team

METHODS is a well-established multi-disciplinary research team, endowed with an exceptional ability to produce top-shelf research, obtain competitive research funds, and attract and develop promising faculty members. Furthermore, the team makes outstanding contributions to training of the next generation of researchers and to the involvement of society in clinical research.

Strengths and possibilities linked to the context

The scientific production of the team is remarkable; >500 scientific articles were co-authored during the mandate, of which 189 in key authorship positions (first/last), and many in the most selective international journals (e.g. 31 papers in Lancet, JAMA, BMJ, Annals of Internal Medicine, JAMA Internal Medicine, Nature or PNAS).

The team has been very successful at attracting competitive funding (>8 million euros) from European funding schemes, ANR, APHP, etc.

Team members participate in leading international research infrastructures, including the Cochrane collaboration, the Equator network, and Prisma; they act as experts in bodies such as the US Strategic council for research excellence; they are active on editorial boards of scientific journals (Cochrane, PLoS). They maintain international collaborations in Europe and the USA (notably Columbia university).

The team has attracted young researchers who obtained personal competitive support (Inserm Junior professorship which was tenured as Inserm researcher in 2019, Marie Skłodowska-Curie fellowship, excellence chair in health from U Paris-Cité), and three researchers obtained a "Habilitation à diriger des recherches".

The team has developed projects to enhance the societal value of its work, such as an online cohort of patients with chronic diseases (ComPaRe) to obtain patient-centered assessments of treatment outcomes, and the development of "core outcome sets".

The team has made several online resources available to the research community (e.g., Process, to facilitate online surveys; NMAstudio to facilitate network meta-analysis).

Weaknesses and risks linked to the context

The team is highly dependent on competitive funding, which creates uncertainty in strategic planning, and forces the team to be reactive to funding opportunities.

The office space (site of Hôtel-Dieu) has great historic and symbolic value, but is in need of modernization.

Analysis of the team's trajectory

The team has maintained an outstanding level of activity over the mandate. The scientific production was at the highest level, with >500 papers. The team has attracted brilliant researchers who have obtained individual honors and awards, and who have diversified the research agenda. Public service developments and teaching activities have also been outstanding.

RECOMMENDATIONS TO THE TEAM

Overall, the scientific strategy is solid and should be maintained. The following areas deserve specific mention and should be treated as priorities: a) evaluation of innovative medical interventions, such as personalized medicine and digital health, b) critical assessment of current research practices, and development of interventions to increase the trustworthiness of clinical research (research on research), c) continued investment in methods and demonstration projects to better integrate the needs of society into research (citizen science), and d) translation of research results into clinical practice (e.g. meta-analysis, evidence ecosystem). Furthermore, METHODS should strengthen its role as a cementing force for other CRESS teams, through the provision of methodologic support, methodologic training and other activities.

Team 6: Recherche sur les déterminants précoces de la santé de l'enfant et de l'adulte

Name of the supervisor: Ms Marie-Aline Charles

THEMES OF THE TEAM

The EARly life Research on later Health (EAROH) team focuses its research on the period from preconception to the early years of the child, as a window of opportunity for later health in childhood and adulthood. This research aims to better understand the corresponding mechanisms, particularly at the biological and behavioural levels, and to ensure translation of the generated knowledge into preventive interventional trials in the population.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The recommendations of the previous report were clearly followed by the team during the course of this contract. In particular, new fields of research have been opened, including: the study of the medium- and long-term impact of some specific components of lifestyle in childhood (parents and infant nutrition, exposure to screens, sleep); taking into account the environmental dimension of food; and research on public health interventions. Collaborations within CRESS have been strengthened, specifically with the EPOPé and EPICEA teams, with which a merger is planned during the next contract, as well as with the EREN team. At the international level, EAROH is committed to the establishment of the EU Child Cohort Network. The team ensured open access to the data from the ELFE and EDEN cohorts. New methodological approaches have been adopted, for example: in the context of collaborative work on the establishment of new child growth curves in France, through an approach adapted to high-dimensional data; the ECAIL randomized controlled trial for the evaluation of a maternal and child health intervention program in situations of social vulnerability.

WORKFORCE OF THE TEAM: in physical persons at 31/12/2022

Catégories de personnel	Effectifs
Professeurs et assimilés	1
Maîtres de conférences et assimilés	0
Directeurs de recherche et assimilés	3
Chargés de recherche et assimilés	4
Personnels d'appui à la recherche	3
Personnels hospitaliers	0
Sous-total personnels permanents en activité	11
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	2
Post-doctorants	6
Doctorants	9
Sous-total personnels non permanents en activité	17
Total personnels	28

EVALUATION

Overall assessment of the team

EAROH team has developed a remarkable, excellent research with an international impact on the effect of early life environment on the later health of children and adults. The high value of their ever-enriched

infrastructures (e.g. EDEN and ELFE cohorts), ensured EAROH a regular, first-rate scientific production, and development of high-level collaborations at national and international levels. EAROH's growing attractiveness has enabled it to strengthen its work capacity.

Strengths and possibilities linked to the context

The construction of the EDEN and ELFE cohorts is increasingly proving to constitute the historical strength of the team. Opening up access to the data of both cohorts has confirmed their potential and opened new collaborations. In addition, the team has been able to combine the information provided by these cohorts with the use of cohorts of complementary characteristics, especially the Constances cohort, made up of a large population of adults. ELFE is integrated into the RECONAI platform as part of a collaboration with the EPOPé team, with the support of France cohorts. The launch of the EU Child Cohort Network project, of which the team is a stakeholder, further expands the potential of accessible, standardized data. The adoption of new methods by the team, such as the big data approach or the implementation of the ECAL interventional study broadens the team's expertise and capacity to reach the highest levels of scientific evidence.

The OPPALE entity, which will bring together the team with the EPOPé and EPICEA teams within the CRESS will provide additional synergies.

The attractiveness of the team is demonstrated by the increasing number of new researchers (8 since 2017), of PhD students (15 since 2017); the continuous development of Internal and external collaborations, national and international, often in a context of leadership. The members of the team are involved in leading positions in the DOHaD Societies. They are regularly invited as speakers at national and international congresses. Members are involved in the boards of national and international public organizations, such as the French Agency for Food, Environmental and Occupational Health & Safety (ANSES). They hold editorial positions with specialist journals of international scope. The team received several awards and recognitions during this contract.

The team's ability to obtain funding is excellent, both at the national level (4 ANR projects, and the major RECONAI project providing funding for the ELFE and EPIPAGE2 cohorts) and internationally (including 2 Horizon2020 projects as work package leaders). The team had the capacity to finance hosting contracts for 15 PhD students.

The scientific output of the EAROH team is excellent. 20% of the team's publications are among the top 10% of the most cited articles globally, often published in the best specialized journals, in the fields of infant nutrition, child behavior, and growth. A large proportion of these publications are the result of international collaborations based on cohorts set up or managed by the team.

The contributions of the team's research to society are particularly useful. The co-development of new child growth curves with EPOPé is valorised as an invention and, through the intermediary of Inserm Transfert and numerous distributors of medical software, to general practice by health professionals and to the general population through the « Mon Espace Santé » portal of the French government.

Weaknesses and risks linked to the context

The team aims to further increase its international visibility. It clearly has the capacity to do so, as the acquired expertise, the results obtained in activities structured in international networks or through specific collaborations, the platforms and databases directly available within the team, and the integration of randomized controlled trials into its tools, offer indeed a potential for international presence and distribution that is probably still incompletely exploited.

The main risks lie in: i) the relatively limited number of Research Supervisors in the team compared to the increasing number of research projects developed and coordination tasks. The establishment of the OPPALE team, planned with constant human resources, may not be sufficient to meet this challenge; ii) the current dispersion of the teams within the CRESS, as long as the regrouping of OPPALE on the Villemin site of the Faculty of medicine of Paris-Cité University is not acquired.

Analysis of the team's trajectory

As part of the next contract 2025-2029, the team will merge with the current EPOPé (Obstetric, Perinatal and Pediatric Epidemiology) and EPICEA (Epidemiology of childhood and adolescent cancers) teams, to form the OPPALE (Obstetric, Perinatal, Paediatric Life course Epidemiology) team, in the spirit of a CHILD department.

This will provide the team with the added value of coherence and synergies between the programs of the separate teams. The organizational chart will include approximately 55 university researchers and professors/lecturers (approximately 20 full-time equivalents), 10 post-doctoral fellows, approximately 40 research support staff; The team will host approximately 20 PhD students and 20 master's students.

The research program announced in this context will be based on life-course epidemiology approaches, extending from the peri-conceptual period to adulthood. The platforms and prospective cohorts of the various current teams such as RECONAI, EDEN, RECAP; CCOP, COHOPER and BIOCAP for the epidemiology of childhood and adolescent cancers; RNHE, RNTSE, REMAPAR and OMIN registries, and randomised controlled

trials, such as the ECAIL prevention trial, will be integrated. The research strategy will be based on the complementarity and interdisciplinary coherence of the different research axes defined (transmission of parental behaviours & medical practices; foetal and severe neonatal morbidity, child and adolescent health; epidemiology of childhood cancer; social inequalities in health).

The attractiveness of the team will remain strong and will probably even be strengthened, as the future paths of the structure are thus clearly defined. Governance will be facilitated by its participatory nature at a time when the planned end of the activity of two major team leaders in the coming years is looming.

This trajectory seems particularly constructive and is at least a partial response to the weak points identified by the constitutive teams of OPPaLE, particularly in terms of permanent staffing. Moreover, the links and collaborations already existing between the teams will facilitate this major project.

RECOMMENDATIONS TO THE TEAM

The planning of the new OPPaLE team makes sense and should be carried on. Attention should be paid to maintaining and increasing the coherence of the scientific themes within the team and to the development of joint research work within the new team.

The collaboration with the university hospital entities, which are already strongly committed to the current EPOPé team, will benefit from being developed with the EAROH and EPICEA current teams.

The attraction and continuous integration of new young researchers is also a priority.

It will be important to keep seeking support from the supervisory bodies or external support, to strengthen permanent research support staff and further reinforce data security.

The further growth of OPPaLE may reside in leading large-scale, national, and international projects that have potential for a major impact in public and eventually in global health. The development of population-based interventional studies, such as the ECAIL trial currently being implemented, will be an important added value, and help increasing the number of team publications in the best general science and medicine journals.

The team's plans of further developing methodological tools in the fields of data science, massive data generated electronically by participants, multi-omics systems biology and artificial intelligence are likely to support the future development of the team, and to enable the development of innovations that could be economically valued.

Team 7: Epidémiologie des cancers de l'enfant et des adolescents
 Name of the supervisor: Ms Jacqueline Clavel

THEMES OF THE TEAM

EPICEA team has developed research on aetiology of paediatric cancers (especially risk factors associated with maternal exposure during pregnancy, environmental exposure of parents and children, and genetic risks factors), and long-term consequences of treatment of paediatric cancers. These works rely on two major tools developed by EPICEA Team: 1) the National Childhood Cancer Registry (RNCE), which offers opportunities to conduct high-quality case-control studies enriched with DNA collections or environmental data collected using geographic information systems (GIS), and 2) the prospective Cohort of childhood cancer survivors (COHOPER), that is hosted on the Childhood Cancer Observation Platform (CCOP), an infrastructure created by EPICEA Team and supported by the French Government.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

In response to the recommendations of the previous report, EPICEA team has developed external collaborations in the domain of environmental exposure, both at national (ELIXIR team of Inserm U1085 IRSET Unit, US-ODR of INRAE) and international (Swiss Tropical and Public Health institute) level, resulting in ongoing works using GIS-based data on both agricultural activity and air pollution close to birth place.

Furthermore, collaborations with EPIPHARE are ongoing, exploring associations between medical consumption around pregnancy and cancer incidence in child using National System of Health Data (SNDS) database. Expertise on SNDS will be particularly important for the incoming exploitation of COHOPER study, whose linkage with SNDS obtained CNIL approval during the contract. The recruitment in a tenure position as Inserm CRCN of a researcher of EPICEA with a long post-doctoral international mobility will also ensure strong international collaborations on genetic risk factors of childhood cancer (PI of a 5-year CLIC consortium project).

The cross-team initiative called the "Child department" established during the past mandate led to the merger of EPOPé, EAROH and EPICEA teams in the OPPaLE new team, illustrating the development of collaborations within CRESS.

WORKFORCE OF THE TEAM: in physical persons at 31/12/2022

Catégories de personnel	Effectifs
Professeurs et assimilés	0
Maîtres de conférences et assimilés	0
Directeurs de recherche et assimilés	1
Chargés de recherche et assimilés	0
Personnels d'appui à la recherche	4
Personnels hospitaliers	9
Sous-total personnels permanents en activité	14
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	14
Post-doctorants	1
Doctorants	4
Sous-total personnels non permanents en activité	19
Total personnels	33

EVALUATION

Overall assessment of the team

EPICEA Team has a central position in the french national childhood cancer landscape, bolstered by its high-value ANR funded infrastructures. It has developed national collaborations in environmental epidemiology, and international collaborations on genetic risk factors within the CLIC consortium and CONCORD group. The team has a high-quality scientific production in specialty journals, but lacks of leadership position in the best international publications. The recruitment of Inserm CRCN in 2023, with strong international collaborations, demonstrates the attractiveness of the Team.

Strengths and possibilities linked to the context

Childhood cancer is a national public health priority that led to financial support. Apart from characterisation of the aetiology of these cancers, issues in survivors or those cancers who face sequelae and the long-term consequences of treatment are particularly relevant, and can lead to health promotion programs. The infrastructures developed by EPICEA teams, and its expertise give them a critical place in this scientific domain. The EPICEA team has been able to obtain substantial funding to maintain its research infrastructures (6.5 M€) under the ANR-PIA program, and to develop its research projects (2.6 M€) in response to national calls for projects. Several staff have been promoted (IR1, recruitment as CRCN, AI, ARC diploma) and three defended their HDR (the promoted IR1, one hospital practitioner, and the recruited CRCN). Scientific activities are adapted to take account of the geographical remoteness of some of the staff (organization of videoconferences, etc.). Team members are involved in several international working groups (EUROCARE with an elective mandate, PANCARE, ENCR, IARC and CLIC as PI in a starting program on genetic predisposition to childhood cancer), which enables them to be associated with international publications in high-level journals. The EPICEA team has succeeded in developing and enriching its databases, in a complex, demanding and evolving regulatory environment. The team's attractiveness to young researchers is attested by the fact that it welcomed sixteen masters, eleven PhDs and three post-docs during the previous term. Publication activity has been stable since 2017, with around twenty publications per year, of which around 25% are signed as first or last author. The development of the CCOP platform, and the COHOPER cohort, especially once SNDS linkage would be effective, should enable the development of original work and scientific collaborations.

Weaknesses and risks linked to the context

As for other cancer registries in France, ensuring regular funding for the National Childhood Cancer Registry is challenging, and time consuming, complicating staff recruitment. Due to the scarce number of cases and centralised care, collaborations with physicians involved in the care of children suffering from cancers in France, and international collaborations are fundamental.

Increasing regulatory constraints on access and sharing of healthcare data led to delays in the conduct of some research projects.

International collaborative publications account for a significant proportion of the team's scientific output, although not in leadership positions.

Analysis of the team's trajectory

The EPICEA team has been working on the descriptive and analytical epidemiology of pediatric cancers for over 20 years, and for the past ten years has been focusing on the fate of pediatric cancer survivors. It occupies a strategic position in this field, and manages databases that are essential for research and health monitoring, in particular the National Childhood Cancer Registry. It has also developed skills in the analysis of complementary data, in particular medico-administrative and geomatic data. The team anticipated the departure of the researchers who historically developed this theme, with three additional HDRs during the previous mandate, and effective recruitment in 2023 of a full-time researcher who came back in the EPICEA team after several years' international mobility in a prestigious team. The new organizational chart reflects the change in leadership of the theme. The gradual handover of scientific projects is underway.

In the new mandate, the EPICEA team will merge with the EPOPE and EARoH teams to become the OPPaLE team. This merger was initiated within the framework of a Child Department over the past few years. The new team has a coherent scope, integrating common methodologies (cohorts) and cross-disciplinary projects in mother-child or child-adolescent development.

The research strategy of Axis 5 (epidemiology of childhood and adolescent cancers) is broadly in line with continuity, with the exploitation of data from the GEOCAP program, and the start of exploitation of data from the COHOPER cohort, and includes the development of works on genetic predisposing factors to pediatric

cancer and gene-environment interactions as part of the CLIC consortium, and collaboration with the Institut Pasteur de Lille. The COHOPER cohort and work on the link between assisted reproductive techniques and pediatric cancer will provide links with the other OPPaLE team axes. Finally, research on survivorship could lead to development of interventional studies in health promotion.

RECOMMENDATIONS TO THE TEAM

The coherence of the future OPPaLE team seems natural, and the cross-disciplinary aspects are quite obvious. Grouping staff of EPICEA, EPOPE and EAROH in the same premises at Villemin site is important in order to favour inter-axis projects and mutualise methods and technical supports.

Attention should be paid to secure and support the research on childhood cancer, which may appear quite undersized compared to the OPPaLE team's other areas of focus, but is of major public health interest. Collaborations could be developed in the next mandate between the 5th axis of the OPPaLE team, which is dedicated to childhood cancer and largely corresponds to ex-EPICEA team, and the other four axes.

The Team is highly encouraged to attract new post-docs and researchers on tenured position. The forthcoming retirement of the head of Childhood Cancer Registry needs to be anticipated to ensure continuity in the participation of unit members in international research networks and consortia.

Team 8: Epidémiologie du vieillissement et des maladies neurodégénératives

Name of the supervisor: Ms Archana Singh-Manoux

THEMES OF THE TEAM

The team is specialized in the life course epidemiology of ageing, more specifically in the fields of Neurodegenerative Disease, and has more recently developed specific expertise in terms of biomarkers collected through cerebrospinal fluid as well as measures of physical activity using accelerometer data. Emerging points of research expertise are multimorbidity, frailty and disability.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

While the recommendation to interact with clinical research has been taken fully on board, the team feels it could do more in terms of stakeholder engagement with society given it allocated five points out 100 to research dissemination and five to valorisation.

The recommendation to involve clinicians and diversify recruitment has been fully implemented, recruiting a neurologist (Dumurgier), setting up a project with the memory centres as well as two further clinical recruitments (Schnitzler and Jacob) related to rehabilitation research and two postdocs (Machado-Fragua and Landré) who will seek tenure within Inserm /Inrae, as well as multiple incoming short-term researchers (Abell, Barbiellini Amidei, van Gennip).

In terms of scientific strategy and projects, there is a clear main research focus, ageing, but there also does seem to be some branching out which is understandable given the specialisation of the field: life course approaches/genetics and biomarkers in relation to Alzheimer's Disease and other Dementias, improvement of measurement of physical activity in later life and multimorbidity/frailty/disability. Diversity in types, size and sponsors of projects funds has been secured.

While a certain reliance on Whitehall remains, clear efforts have been made to broaden to other population cohort studies (SHARE, UK Biobank, CONSTANCES) as well as patient cohort studies. The recommendation to reinforce links with French teams has been followed (CONSTANCES, memory centres).

WORKFORCE OF THE TEAM: in physical persons at 31/12/2022

Catégories de personnel	Effectifs
Professeurs et assimilés	1
Maîtres de conférences et assimilés	1
Directeurs de recherche et assimilés	2
Chargés de recherche et assimilés	0
Personnels d'appui à la recherche	2
Personnels hospitaliers	0
Sous-total personnels permanents en activité	6
Enseignants-chercheurs et chercheurs non permanents et assimilés	1
Personnels d'appui non permanents	0
Post-doctorants	5
Doctorants	2
Sous-total personnels non permanents en activité	8
Total personnels	14

EVALUATION

Overall assessment of the team

The research group is outstanding and its internationally oriented research program, originally on life course epidemiology of neurodegenerative disease has expanded in depth, by including other types of data (proteomics and CSF biomarkers), and other sources of data (patient cohorts) and in width by expanding to innovative research on accelerometer measurement and most recently multimorbidity.

Weaknesses are few, and contained in the interdependencies of the research group on external data and services, and self-limitation to a more classical engagement with public and policy.

Strengths and possibilities linked to the context

The team is an outstanding internationally recognized innovative research powerhouse in the life course approach to ageing as well as biomarker and omics data to better predict the risk of Dementia and Alzheimer's Disease, as well as in the data crunching and synthesis needed to make use of accelerometer data collected to more accurately monitor physical activity in later life, which is showcased by securing funds at international (ERC, NIH) and national level (ANR, SOFMER, France Alzheimer, French Society of Diabetology), as well as securing very competitive national funds from the UK and US (Wellcome Trust, MRC, BHF, NIH R01, NIH RF1, NIH R56), next to an impressive research output in terms of quality and quantity given the modest team size (525 publications). The attraction of this team is highlighted by key positions as PI's or collaborators in key data sources for these topics (Whitehall II, UK Biobank, CONSTANCES, CSF biomarkers network), the attracting and hosting of international researchers (5 PhD students, 2 medical internships, 6 postdocs). The team has a large scientific impact and engages substantially in passing on their gained knowledge through teaching and training, as well as membership of multiple high-level committees, boards and councils (26 memberships).

While it has clear links to established and existing large scale cohort studies, above all others Whitehall II, that enable the fostering of research at the cutting edge of population research, clear steps have been taken to control of the data supply, by engaging multiple clinical researchers as well as seeking connection with hospital-based memory centres. This choice has been fruitful and opened up ways to test new research questions, bringing the innovations of Whitehall tested on the population to more defined patient cohorts. This illustrates a clear methodological emphasis on ensuring results are robust by triangulation, making use of the pooling of cohorts and separate replication of analyses in different data sources, such as the population cohorts in the G2aging HRS family of data, which include SHARE and ELSA, the UK Biobank cohort and CONSTANCES, and equally by setting up own networks around new types of data such as CSF biomarkers (EU CSF collaboration, Neuro-Thalys). In line with open science standards, the innovative work on accelerometer data is also shared and packages in R is provided to the research community.

While the third research arm on aspects of ageing such as multi-morbidity and disability currently has not yet developed to the same internationally leading level as the other topics, with the relatively recent recruitment of leading researchers with high potential (Schnitzler in 2021 and Jacob in 2022), there is a clear potential to grow in terms of defining what the precise research strength for this domain is, spelling out methodological points of attention, innovative data sources or biomarkers.

Weaknesses and risks linked to the context

The weaknesses of the team are few and it is evident in the self-assessment they have been already pre-empted in the current term to some extent, as they are clear points of attention.

The strong reliance on Whitehall II, while clearly being an asset as well as being counteracted with multiple other data sources, contains some potential weaknesses and risks for the team.

It renders making a translational link with both health policy and stakeholders more difficult, as it is a cohort study of Civil servants in the United Kingdom recruited in 1985. While key biological mechanisms might be relatively robust to this type of selection, the life course perspective proposed by the team also champions the role of context (here for example with possible quantitative and qualitative differences in the BMI, distribution of education, migration or the experience of economic crises). While there is nothing against publishing on data from another country, especially when done in a robust way with triangulation with other cohorts and data sources as the team clearly does, it makes impact work more difficult.

In the new constellation of CRESS, this team is one of the smaller teams, which could mean it is less well served by the overarching SMART admin team, or less involved in setting up relevant CRESS activities for PhD students, post-docs.

Analysis of the team's trajectory

The team is in clear expansion on multiple domains: its research focus areas, the type of data (accelerometer data, CSF biomarkers, proteomics) considered as well as the sources (patient cohorts, population cohorts), methodologic rigour as well as team size, thanks to very successful grant capture efforts, excellent integration in both national and international networks as well as the fostering of own talent and attracting external talent to the team. Building on a core expertise in terms of life course approaches to Alzheimer's disease and dementia, new subject areas were expertly added to the team's research portfolio in this team. Importantly, and in response to previous recommendations, a conscious decision to establish a clinical focus has led to new and highly innovative ways of combining insights from different data types and sources. This agility to change over time, in response to both feedback and opportunity structures is highly laudable and illustrates a dynamic leadership with an attitude that there is always room for improvement.

RECOMMENDATIONS TO THE TEAM

We recommend that the team continues its current growth trajectory, ideally by converting soft money posts in Inserm funded research posts or finding other ways to consolidate the profile of the younger team members.

Given the emergence of two very large teams in CRESS (OPPALE and METHODS), a closer integration may be considered between EPIAGEING and the more clinically focussed ECAMO team on related research interests in terms of ageing and musculoskeletal diseases, in line with their first collaboration experience through joint PHD candidate. This will be beneficial to assure equal support and attention in terms of topics inside CRESS.

We recommend the team continues to develop its collaborations with French teams in the field of ageing, and that it takes part in efforts to create data collection on ageing of the French population as this is a key issue to French health institutions.

Team 9: Evaluation des risques sanitaires liés à l'environnement
 Name of the supervisor: Ms Isabelle Momas

THEMES OF THE TEAM

The HERA team works in the field of environmental health. It specializes in the study of air pollution in general and in the occupational context. Its research methods are epidemiology, expology and toxicology, and its original results are based in particular on data from two Parisian cohorts, enabling it to produce new knowledge on allergic and respiratory diseases in the early stages of life.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The team has taken on board two of the recommendations made during the last visit:

1 - by developing more interactions with other teams in the Unit, in particular the EARoH and EREN teams.
 2 - by developing more interactions within the team between epidemiological and toxicological approaches, in particular on the study of pathologies linked to particulate pollutants present in the air, thanks to the use of Epitox, which is capable of studying the response of certain genes linked to inflammation.

3 - In recent years, the team has been unable to recruit any new permanent researchers, a weakness highlighted by the last visiting committee. However, its future integration into the MERIT unit will enable it to take on two IRD researchers.

WORKFORCE OF THE TEAM: in physical persons at 31/12/2022

Catégories de personnel	Effectifs
Professeurs et assimilés	2
Maîtres de conférences et assimilés	4
Directeurs de recherche et assimilés	0
Chargés de recherche et assimilés	0
Personnels d'appui à la recherche	1
Personnels hospitaliers	3
Sous-total personnels permanents en activité	10
Enseignants-chercheurs et chercheurs non permanents et assimilés	7
Personnels d'appui non permanents	1
Post-doctorants	0
Doctorants	5
Sous-total personnels non permanents en activité	13
Total personnels	23

EVALUATION

Overall assessment of the team

The main results have focused on the natural history of respiratory and allergic diseases during the first years of life, and their links with diet, road traffic pollution and exposure to fine particles. The scientific production was excellent, with over 150 scientific articles in peer-reviewed journals during the period under review. The team's national and international visibility, already assured by its membership of five European networks and the strong expert activity of several team members, could be further enhanced by new works not limited by the specificities of the Parisian population and environment, particularly in expology.

Strengths and possibilities linked to the context

The team's theme is one of Inserm's strategic priorities, and is part of various national plans on environmental and occupational health.

In this theme, the team has a strong reputation, particularly in its core expertise concerning the early stages of life.

The team's highly original cohorts have enabled it to achieve an excellent level of scientific production. It is now aiming to collect health events from teenagers still in the cohort. It also has a second cohort which has collected exposure and health data on 50 Parisian cab drivers. Some air pollution exposure modeling tools have been developed and shared between the two cohorts. The team's research is enriched by ongoing contact with clinicians, notably pediatricians at AP-HP.

The team is part of 5 European networks, two of which are funded by COST actions.

Several team members have a strong international activity, in addition to their expertise activity for numerous national authorities and agencies, and their involvement in learned societies

Several team members are involved in the production of recommendations, as well as in the sustained production of didactic articles for professionals (some fifty over the period).

The team's ability to obtain competitive national funding is high; more than ten grants were obtained over the period, including 4 ANR grants

Weaknesses and risks linked to the context

Despite the team's reputation, the number of temporary staff has remained low in recent years.

The scope of some of the team's results is limited by the specificities of the studied populations (mainly in Paris) and tools used. The team has not developed any major new projects that would enable it to contribute to the theme of environmental health outside the areas of expertise in which it is already recognized.

Analysis of the team's trajectory

The team's future integration within IRD's MERIT unit will enable it to integrate two full-time researchers into its workforce, and to benefit from the pooling of other personnel from IRD. This new perspective will also provide the team with a single location for its research and teaching activities

RECOMMENDATIONS TO THE TEAM

The team could seek to broaden the scope of its environmental health research beyond the areas of expertise for which it has already been recognized for many years.

The team could seek to produce knowledge useful to air pollution exposure assessment methods beyond its own cohorts.

The team's future integration into the MERIT unit represents an opportunity to develop its activities beyond their current scope, to investigate environmental health issues in developing countries, particularly in the field of chronic and allergic diseases

Team 10: Service Mutualisé d'Appui à la Recherche Transversale

Name of the supervisor: Ms Stéphanie Chardon

THEMES OF THE TEAM

The SMART platform was created during the last mandate, in order to face the increasing administrative and regulatory workload of the researchers. It manages the relations with the four institutions and the five main employers, in the context of a multi-site unit, with different administrative rules in each institution and site. Overall, it manages about seven million euros spending each year (currently 115 ongoing research contracts, with about 800 missions and more than 1000 purchase orders), as well as about 300 contractual employees (researchers and research support staff). It also helps researchers to face regulatory issues, which have become extremely complex (more than 100 ongoing projects, with 4 different promoters), manages IT infrastructures (again different from site to site) and premises.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

Not applicable

WORKFORCE OF THE TEAM: in physical persons at 31/12/2022

Catégories de personnel	Effectifs
Professeurs et assimilés	0
Maîtres de conférences et assimilés	0
Directeurs de recherche et assimilés	0
Chargés de recherche et assimilés	0
Personnels d'appui à la recherche	8
Sous-total personnels permanents en activité	8
Enseignants-chercheurs et chercheurs non permanents et assimilés	0
Personnels d'appui non permanents	1
Post-doctorants	0
Doctorants	0
Sous-total personnels non permanents en activité	1
Total personnels	9

EVALUATION

Overall assessment of the team

It is globally a very successful structure, benefiting from the outstanding personal engagement of its director, Stéphanie Chardon. Its activities are also extremely valued by the researchers and the research support staff, in terms of help for conducting research, but also of training and career development. We encourage strongly further strengthening and development of this structure within the CRESS, as a crucial help for the conduct of research, the development of careers and skills and the internal and external communication.

Strengths and possibilities linked to the context

Beyond the direct management of the administrative, human resources and regulatory issues, the SMART platform performs an institutional dialogue with the four institutions, regarding the strategy, management and request for resources (in particular premises, IT infrastructure and permanent positions). In particular, it has been leader in real estate project management and facility management, notably for the move to the Villemin site. It is also responsible for the internal and external communication, to increase the sense of belonging to the CRESS community, cross-fertilization between teams, and to increase visibility. Finally, it supports the staff (researchers and research support personnel) for their career development (promotions, competitive examinations), thereby enhancing their careers and skills.

Weaknesses and risks linked to the context

While researchers and research support staff expressed extremely positive views on the activities of SMART, young researchers were less aware of these activities, and of the general administrative and regulatory rules (in particular foreign researchers). Efforts should be made for a better integration of young researchers in the platform activities.

The direction of the CRESS expressed concern regarding work overload of the SMART platform, both due to major increase in administrative and regulatory procedures in the last years and to high turnover of the staff, due to short term contracts and low salary attractiveness (departure of 5 full-time equivalents in 2023). It is crucial to maintain the profiles of administrative assistants and technicians working with the teams of researchers, engineers and doctoral students. Replacing them with delocalized shared services would appear to be wholly unsuited to the tasks performed by these administrative staff at CRESS. Their activities go far beyond entering purchase orders or handling travel and request very specific skills and close relations with the researchers (in particular regarding regulatory issues).

Analysis of the team's trajectory

The SMART platform was created during the last mandate and has been very successfully in rendering itself a key infrastructure of the CRESS, allowing to tackle the major increase in complexity of administrative and regulatory procedures for research (in particular medical research regulations). For the next mandate, it is planned to further strengthen this platform, which we strongly encourage, around four axes: a financial pole, a human resources pole, a regulatory pole and an IT pole.

RECOMMENDATIONS TO THE TEAM

We recommend a further strengthening and development of the SMART platform, in particular by securing permanent positions, with attractive salaries and a better recognition by the institutions of their indispensable skills and work.

The dialogue with the research institutions regarding administrative and regulatory complexity, which has been underlined as a threat by most CRESS teams, should be further developed. Indeed, due to its size and reputation of excellence, the CRESS has the opportunity to discuss major improvements in the research procedures (in particular for medical research and IT security), which may benefit the whole national community.

Finally, we recommend an increased integration of young researchers in SMART activities (see above).

CONDUCT OF THE INTERVIEWS

Dates

Start: 11 janvier 2024 à 08h30

End: 12 janvier 2024 à 17h00

Interview conducted: on-site

INTERVIEW SCHEDULE

Jour 1 – 11 janvier 2024 sur site Hôtel-Dieu

- 8:30** **Accueil du Comité de visite HCERES par le Délégué scientifique**
(salle Marie Curie B1 3ème étage)
- 9:00** **Session plénière**
Présentation du Comité HCERES, son rôle et ses procédures
(amphithéâtre Dupuytren A1 rdc) Séance publique (tous les membres de l'unité)
- 9:10** **Présentation du CRESS** (40' présentation, 15' discussion) - **Philippe RAVAUD et Isabelle BOUTRON** *Séance publique (tous les membres de l'unité)*
- 10:05** **Equipe 3 - EREN** (20' présentation + 15' discussion) - **Mathilde TOUVIER**
Séance publique
- 10:40** Pause *(galerie)*
- 11:00** **Equipe 6 - EAROH** (15' présentation + 15' discussion) - **Marie-Aline CHARLES**
Séance publique
- 11:30** **Equipe 7 - EPICEA** (15' présentation + 15' discussion) - **Jacqueline CLAVEL**
Séance publique
- 12:00** **Equipe 1 – EPOPé /OPPaLE** (30' présentation + 15' discussion) - **Pierre-Yves ANCEL**
Séance publique
- 12:45** Lunch *(galerie)*
- 13:50** **Equipe 5 - METHODS** (20' présentation + 15' discussion) – **Isabelle BOUTRON**
Séance publique
- 14:25** **Equipe 4 - ECAMO** (20' présentation + 15' discussion) - **Karine BRIOT**
Séance publique
- 15:00** **Equipe 8 - EpiAgeing** (20' présentation + 15' discussion) - **Archana SINGH-MANOUX**
Séance publique
- 15:35** Coffee break *(galerie)*
- 15:50** **Equipe 2 - ECSTRRA** (20' présentation + 15' discussion) - **Sylvie CHEVRET**
Séance publique
- 16:25** **Equipe 9 - HERA** (20' présentation + 15' discussion) - **Isabelle MOMAS**
Séance publique
- 17:00-18:00** **Débriefing Comité HCERES - Membres du comité HCERES**
(salle Marie Curie B1 3ème étage) Réunion à huis clos

Jour 2 – 12 janvier 2024 sur site Hôtel-Dieu

9:00 Réunion Comité des Tutelles – Représentants des tutelles et Membres du comité HCERES
(salle Marie Curie B1 3^{ème} étage)

10:00 Trois réunions parallèles avec le personnel sans les Responsables du Centre, équipes et représentants de personnel

Discussions avec les personnels Ingénieurs, supports scientifiques et administratifs

(salle Marie Curie B1 3^{ème} étage)

Discussions avec les personnels chercheurs *(amphithéâtre Dupuytren A1 rdc)*

Discussions avec les doctorants et post-doctorants *(salle Cicely Saunders ou A2 salle de staff + de place)*

11:00 Coffee break *(galerie)*

11:20 Discussion avec le Directeur d'unité contrat en cours et futur contrat (30')
(salle Marie Curie B1 3^{ème} étage)

11:50 Deux réunions en parallèle entre le Comité HCERES et les Responsables d'équipe

Discussions with Team 1,6,7,2,9 : $5 \times 15' = 75'$ *(salle Marie Curie B1 3^{ème} étage)*

Discussions with Team 3,4,5,8 : $4 \times 15' = 60'$ *(salle Cicely Saunders B1 3^{ème} étage)*

13:05 Lunch *(6th floor)*

14:00 Réunion de clôture du Comité de visite en présence du Conseiller scientifique HCERES
(salle Marie Curie B1 3^{ème} étage) Réunion à huis clos

17:00 Fin de la visite

GENERAL OBSERVATIONS OF THE SUPERVISORS

Le Président

Paris, le 18 Avril 2024

HCERES
2 rue Albert Einstein
75013 Paris

Objet : Rapport d'évaluation de l'unité DER-PUR250024165 - CRESS - Centre de recherche en épidémiologies et statistiques de Sorbonne Paris Cité.

Madame, Monsieur,

L'université Paris Cité (UPCité) a pris connaissance du rapport d'évaluation de l'Unité de Recherche **CRESS - Centre de recherche en épidémiologies et statistiques de Sorbonne Paris Cité**. Ce rapport a été lu avec attention par la direction de l'unité (cf courriers joints), par le vice-doyen Recherche et le doyen de la Faculté de Santé d'UPCité, par la vice-présidente Recherche d'UPCité et par moi-même. L'ensemble des acteurs UPCité remercie le comité pour son travail d'évaluation.

Présidence

Référence

Pr/DGDRIVE/2023

Affaire suivie par
Christine Debydeal -
DGDRIVE

Adresse

85 boulevard St-Germain
75006 - Paris

www.u-paris.fr

Le Doyen de la Faculté de Santé et moi-même souhaitons souligner que le CRESS est un centre de recherche en épidémiologie et statistiques ayant pour tutelle l'université Paris Cité, l'INSERM, l'université Sorbonne Paris Nord, et l'INRAE. L'unité porte une recherche d'excellence dans son domaine et jouit d'une excellente réputation à l'international. Le CRESS se focalise sur la compréhension de facteurs déterminants pour la santé des populations aux différents âges de la vie afin de concevoir et d'évaluer des interventions permettant d'améliorer les pratiques cliniques et les politiques de santé publique, tout en développant des méthodes d'études innovantes. Sa contribution est majeure auprès des décideurs en matière de santé publique (e.g., NutriScore - courbe de croissance dans les carnets de santé - prévention de mort subite chez les nouveaux nés...). Avec le soutien fort et l'accompagnement constant de l'ensemble des tutelles, le CRESS se restructure au prochain mandat avec un changement de directeur, le départ de deux équipes et le regroupement sur un même lieu de certaines des équipes actuellement dispersés. Ces changements profonds permettront d'engager une nouvelle dynamique soutenue par les tutelles.

Je vous prie d'agréer, Madame, Monsieur, l'expression de ma considération distinguée.

Édouard Kaminski



Monsieur Eric Saint-Aman
Directeur du département d'évaluation de la
recherche
Hcéres
2, rue Albert Einstein
75013 PARIS

Villetaneuse, le 18 mars 2024

*Objet : Rapport d'évaluation DER-PUR250024165 - CRESS - Centre de recherche en
épidémiologies et statistiques de Sorbonne Paris Cité*

Cher Monsieur,

Nous faisons suite à votre courriel du 15 mars 2024 par lequel vous nous avez transmis le rapport d'évaluation du Centre de recherche en épidémiologies et statistiques de Sorbonne Paris Cité.

L'université Paris XIII – Sorbonne Paris Nord souhaite remercier au nom de l'ensemble des personnels de l'unité de recherche Madame Cécile Delcourt, Présidente du Comité, ainsi que les membres du Comité pour la qualité des échanges lors de la visite d'évaluation, ainsi que pour la qualité du rapport provisoire d'évaluation de l'Unité.

L'université Sorbonne Paris Nord remercie chaleureusement le Comité d'évaluation HCERES pour ses retours extrêmement positifs et constructifs. L'USPN est honorée d'être tutelle du CRESS et d'accueillir dans ses locaux l'équipe EREN dont elle abrite la banque réfrigérée du NutriNet-Santé. Nous partageons pleinement les avis formulés, tant sur les forces que sur les « menaces » (partagées d'ailleurs par de nombreuses équipes en France et lié au mode de financement de la recherche publique actuellement : personnels ITA sous contrat précaire alors que les missions, notamment de maintien de la cohorte NutriNet-Santé s'inscrivent sur le long terme ; budget de fonctionnement presque exclusivement basé sur les grants à décrocher dans le cadre d'appels à projets compétitifs avec très peu de financements récurrents accordé aux équipes, etc.).

Nous sommes également reconnaissants au Comité pour ses recommandations pour le prochain mandat. L'USPN continuera à soutenir le CRESS dont nous sommes si fiers d'être parmi les tutelles. Nous allons collectivement et avec enthousiasme travailler à leur mise en œuvre, pour continuer à faire progresser le domaine de l'épidémiologie et de la nutrition de santé publique et son impact sur la société, dont les nombreuses références qui lui sont faites dans l'espace public attestent et qui contribue largement au rayonnement de notre université.

Je vous prie de croire, Monsieur le Directeur, en mes sincères salutations.

Le Président de l'Université Sorbonne Paris Nord



Christophe Fouquère

UNIVERSITÉ SORBONNE PARIS NORD MEMBRE :

CAMPUS  **ASPC**
CONDORCET Alliance Sorbonne
PARIS - AUBERVILLIERS Paris Cité

@univ_spn / Université Sorbonne Paris Nord





CRESS – Observations de portée générale 28/03/2024

UNIT

La direction du CRESS tient à remercier le comité pour la qualité des échanges lors de la visite sur site et pour le rapport très complet transmis.

Nous sommes particulièrement heureux que le comité évalue très favorablement notre production scientifique considérée comme 'exceptionnelle', notre capacité à lever des fonds notamment dans le cadre de financement internationaux compétitifs, notre rayonnement national et international, notre attractivité avec l'arrivée jeunes talents (CPJ, Marie Curie fellowship), l'impact de notre recherche sur les politiques de santé et la santé publique, ainsi que l'originalité et l'efficacité de notre infrastructure SMART.

Nous avons pris bonne note des recommandations concernant les jeunes chercheurs. Nous espérons que les difficultés de certains d'entre eux pour développer des liens avec les autres équipes seront réduites par la limitation du nombre de sites qui devrait faciliter les échanges. Par ailleurs, nous allons généraliser certaines actions vis à vis de nos jeunes chercheurs, actions déjà existantes dans plusieurs équipes (ex : welcome book). Nous avons également initié une discussion autour de la constitution d'un club 'young researcher' et mis en place un accueil des nouveaux doctorants avec présentation de la direction et échange avec le parrain/marraine de la promotion.

Nous avons mal compris la recommandation plus générale faite à la direction du CRESS de « porter plus d'attention » aux petites équipes. La direction du CRESS porte une attention identique à toutes ses équipes et cherche à renforcer toutes ses équipes au premier rang desquelles les petites équipes. Il nous semble que le comité de visite surestime les capacités et marges de manœuvre, dans le système français, d'une direction de centre pour renforcer une équipe par des moyens humains supplémentaires (chercheurs ou personnels de support à la recherche). La direction du centre, en relations étroites avec les responsables d'équipes, ne peut qu'aider à identifier, attirer, former, mentorer et faire recruter de nouveaux talents ce qui bien sûr constitue un processus long, difficile et souvent aléatoire. Il est impossible pour la direction du CRESS d'ouvrir des postes de chercheur ou de chercheur hospitalo-universitaire dans une équipe. Il nous semble aussi important de souligner que toutes les « petites » équipes du CRESS (en particulier les équipes cancer pédiatrique et maladies musculo-squelettiques) ont vu leur personnel de recherche Inserm ou HU et/ou de support à la recherche renforcé au cours du dernier mandat (dans une période de réduction globale de postes). Ces renforts sont parfois perçus comme insuffisants au vu des besoins, mais ce n'est en aucun cas lié à une stratégie du CRESS valorisant les plus les grosses équipes.

Concernant le support apporté à l'équipe « cancer pédiatrique », nous tenons à souligner que la direction du CRESS a soutenu autant que faire se peut tout au long du mandat précédent toutes ses équipes en particulier l'équipe « cancer pédiatrique ». Nous apportons un soutien administratif, logistique, financier et stratégique. Cependant, notre champ d'action reste limité car nous n'avons, dans le système français, aucun moyen pour attribuer des postes de chercheurs à une équipe. Cette attention à l'équipe « cancer pédiatrique » mobilise au-delà du CRESS également très largement l'Université Paris Cité, la Faculté santé Paris Cité et l'UFR de médecine ainsi que l'institut thématique INSERM de santé publique. Pour le prochain mandat, cette équipe devient un axe de recherche au sein de l'équipe OPPaLE (responsable PY Ancel). En lien avec le responsable d'équipe, nous continuerons à travailler à la structuration de cet axe considéré comme crucial à la fois par l'Université Paris Cité et l'INSERM. Nous avons déjà commencé en créant une nouvelle plateforme de collaboration nommée

REACCT (*Real Life Assessment of Children Cancer Therapy (REACCT) Interdisciplinary Group*) qui n'a été évoqué que rapidement lors de la visite HCERES. Cette nouvelle plateforme impliquant l'axe cancer pédiatrique et l'équipe METHODS, a pour ambition de mettre en œuvre des essais émulsés nichés dans le registre cancer de l'enfant et dans la cohorte HOPE-EPI.

Enfin, les difficultés évoquées des petites équipes à participer aux activités du CRESS ne nous semblent pas liées à la taille des équipes. Toutes les activités du CRESS sont bien évidemment accessibles à tous et tous les membres du CRESS reçoivent les mêmes informations concernant les activités communes. Si des difficultés existent, elles sont le plus souvent liées à la multiplicité des sites et donc à la nécessité de se déplacer ou à des difficultés liées aux emplois de temps des personnels Hospitalo-Universitaires. Les «petites» équipes sont très impliquées dans la stratégie scientifique du CRESS et participent activement à tous les comités de pilotage (doctorants, émulation scientifique, science intègre, communication, etc).

Des réponses plus spécifiques sont apportées par certaines équipes à la suite de ces observations générales.

TEAM-BY-TEAM

Team 1: EPidémiologie Obstétricale Périnatale et pédiatrique EPOPé

Pas d'observation

Team 2: Epidémiologie et statistiques

Pas d'observation

Team 3: Équipe de Recherche en Épidémiologie Nutritionnelle

L'équipe EREN remercie chaleureusement le Comité d'évaluation HCERES pour ses retours extrêmement positifs et constructifs. Les enjeux liés à l'équipe ont été parfaitement compris. Nous partageons pleinement les avis formulés, tant sur les forces que sur les « menaces » (partagées d'ailleurs par de nombreuses équipes en France et lié au mode de financement de la recherche publique actuellement : personnels ITA sous contrat précaire alors que les missions, notamment de maintien de la cohorte NutriNet-Santé s'inscrivent sur le long terme ; budget de fonctionnement presque exclusivement basé sur les grants à décrocher dans le cadre d'appels à projets compétitifs avec très peu de financements récurrents accordé aux équipes, etc.). Nous sommes également reconnaissants au Comité pour ses recommandations pour le prochain mandat. Nous allons collectivement et avec enthousiasme travailler à leur mise en œuvre, pour continuer à faire progresser le domaine de la Nutrition de Santé Publique et son impact sur la société.

Team 4: Epidémiologie des maladies rhumatismales et musculo-squelettiques

We thank the committee for their positive comments. Enclosed are answers to elements highlighted by the HCERES committee that necessitate further information.

A. Limited number of doctoral students and the need to replace several senior investigators during the next period.

1. Human resources :

- While building the new project, we anticipated the retirement of 2 senior researchers : Pr Maxime Dougados at the end of 2024 and Pr Christian Roux in 2027 . During the last 2 years we have indeed anticipated these retirements through the career development of young colleagues. We strengthened the academic positions of team members: Dr Yann Nguyen (Internal Medicine) and Dr Olivier Fogel (Rheumatology) and we plan to recruit Dr PA Juge (Rheumatology). All of them are MD, PhD, 35 years old on average, having expertise in both epidemiology, and inflammatory joint disorders. A doctoral student (thesis in 2023) will become an MCU-PH at Paris-Cité University, and will then apply for a PUPH position at Paris-Cité University's Faculty of Medicine (Dr Baptiste Boukebous, Orthopedic Surgery). One of our researcher obtained her HDR in 2023 (Dr Anna Molto) and is applying for a PUPH position at Université Paris-Cité's Faculty of Medicine in 2025.

As these colleagues are currently, or will be located in other hospitals within our University, this increases the possibility of recruitment of Masters and PhD. With all these recruitments of young researchers, we plan to increase the number of master's degrees and theses.

2. Recruitment of « non-physicians » researchers

We are also raising the number of « non-physicians » involved in the team: with the boost of Alexandra Roren, previously post-Doc in ECAMO and now Professor in the Department of Rehabilitation Sciences, we are incorporating 2 post-doc : one post-doctoral researcher in

rehabilitation (physiotherapist) has just been recruited (Anthony Demont). He will be applying for a position as Maitre de Conférences in the Department of Rehabilitation Sciences at Université Paris-Cité. Another post-doc is currently being recruited, with an objective for an academic position in a Department of Rehabilitation Sciences (Amélie Kechikian).

Our strategy is therefore to increase the recruitment of experts with clinical research activity in osteoarticular diseases through the career development of young colleagues and the recruitment of research members in rehabilitation who are candidates for an academic position. We will also consider recruiting non-MD researchers, as public health specialists.

B. Limited number of larger competitive research grants and international exchanges

To increase its attractiveness, ECAMO team is involved in a number of international projects such as

- RheumaFacts which is a EULAR (European Alliance of Associations for Rheumatology) initiative dedicated to the collection of data about rheumatic and musculoskeletal diseases (RMDs).

- Participation as investigator part of a consortia submitting a EU Horizon Call on Tackling high-burden for patients, under-researched medical conditions with the STEPS (Addressing Unmet Needs in the Diagnosis and Treatment of Spondyloarthritis). The project has successfully passed the first phase.

- We are just beginning a collaboration with S. Cadarette's team from Toronto, through a Joint Research proposal from Université Paris Cité, and University of Toronto, with discussion for shared PhDs.

C. Analysis of the team's trajectory and choice of topics

We are reinforcing our expertise in Inflammatory and Immunological diseases on one hand, Bone diseases on the other hand, and so far we do not have the possibility to extend our expertise in osteoarthritis. However, the recruitment of researcher in rehabilitation will enable us to develop our theme around the care and follow-up of patients with spinal diseases (including low back pain).

D. Collaboration with other teams of CRESS

Our team is only 10 years-old and this is the determinant of its size. We have a research focus, which is not shared by the other teams of CRESS. Moreover being a small team will help the next Director to minimize human resource management. Equal support and attention in terms of topics inside CRESS have been carefully checked during a number of pre-project meetings, and the emergence of 2 large teams is not considered as a risk in the future for either EPIAGEING or ECAMO teams ; ECAMO will have closed collaborations with EPIAGEING as well as all other teams of CRESS : this has always been done since the beginning of the CRESS activity, driven by shared scientific questions.

Team 5: Méthodes de l'évaluation thérapeutique des maladies chroniques

Pas d'observation

Team 6: Recherche sur les déterminants précoces de la santé de l'enfant et de l'adulte

Pas d'observation

Team 7: Epidémiologie des cancers de l'enfant et des adolescents

Pas d'observation

Team 8: Epidémiologie du vieillissement et des maladies neurodégénératives

We thank the committee for their positive comments overall. In the section below, we respond to 4 elements highlighted by the HCERES committee that would benefit from some clarification.

1. Reliance on the Whitehall II study

The committee raised some concern about “interdependencies of the research group on external data”. We would like to clarify the fact that the ageing component of the Whitehall study is not external, it is our baby. We have secured funding from the NIH to allow Whitehall data collection in the UK with funding for the research staff coming to Paris. Singh-Manoux is one of two PIs of the study (the other being Prof Mika Kivimaki, based at UCL and Helsinki university). Sabia is the PI of the accelerometer project. This is an unusual arrangement but reflects modern science, and EpiAgeing’s history and origin.

We have turned Whitehall study into an internationally unique study due to repeat measures of clinical, behavioural, and social data over 40 years, and we share all the data we collect with the scientific community. Unfortunately, a similar resource does not exist in France and starting such a study is unreasonable; furthermore, the French CONSTANCES study with which we are involved will over time become an important resource to test our lifecourse hypotheses.

Please note that the committee recognized efforts we have been made to broaden our research to other population cohort studies (SHARE, UK Biobank), including in France (CONSTANCES) as well as patient cohort studies in memory centres (CMRR) in France.

Conclusion: Please note HCERES committee’s comments on this point below (verbatim text).

- *“The recommendation to involve clinicians and diversify recruitment has been fully implemented.”*
- *“Clear efforts have been made to broaden to other population cohort studies (SHARE, UK Biobank, CONSTANCES) as well as patient cohort studies.”*
- *“Diversity in types, size and sponsors of projects funds has been secured, ... securing very competitive funding.”*
- *“A conscious decision to establish a clinical focus has led to new and highly innovative ways of combining insights from different data types and sources. This agility to change over time, in response to both feedback and opportunity structures is highly laudable and illustrates a dynamic leadership.”*

2. Translational impact

The committee noted that the translational impact on health policy and stakeholders is likely to be affected as part of our work is on the Whitehall study. We feel that further aspects of our work need to be considered.

1. Our research on memory centre data is primarily on French individuals, so completely adapted to French health policy and other stakeholders.
2. As the team gets more established we have extended our collaborations to allow us to contribute to translational aspects with French data. We are part of the recent “Chaire Aging UP!” <https://agingup.u-paris.fr/> program with health economists, and we have ourselves been awarded a PPR Autonomic ANR grant, <https://ppr-autonomie.com/les-projets-finances/projet-models-of-autonomy/>, that will allow further work in this direction. We are also part of “Paris Public Health” that has “ageing” as one of its themes.
3. Although contextual factors (e.g., migration, experience of economic crises) are important, our expertise is in individual level social, behavioural, and biological risk factors of ageing outcomes. Thus, for BMI mentioned by the HCERES committee, the distribution of BMI might be different in France but associations (beta in the regression) with ageing outcomes (e.g. dementia) are mostly similar across developed countries. This is why it is possible to pool datasets in large research initiatives and findings from the Whitehall study appear to be similar to those from other cohorts in individual-patient data (IPD) studies or in replication studies (see our list of publications that reflects our effort for replication of findings).

4. We have chosen to influence important stakeholders at the highest international level, recognizing the trickledown effect to France. Some examples are World Alzheimer Report, National Institute on Aging (NIH) policy documents on ageing, Lancet Commission on dementia, SAPEA mechanism for EU policies, the World Health Organization's work on lifecourse approach to ageing.
5. Within France our approach has also been to play a role at ITMO Santé Publique, ITMO Neuroscience (part of expert panel), Santé Publique France (part of *conseil scientifique*), and FRM (shaping funding decisions in public health). The effect of this "soft" approach is evident in Santé Publique France's primary approach to ageing outcomes now becoming the lifecourse approach.
6. In a similar manner, no other team in France highlighted the term "lifecourse" in their research ten years ago, this has changed now with the emergence of several teams in France (including at CRESS) wanting to adopt this approach.

Conclusion: Please note HCERES committee's comments on this point below (verbatim text).

- *"The team has a large scientific impact and engages substantially in passing on their gained knowledge through teaching and training, as well as membership of multiple high-level committees, boards and councils (26 memberships)."*
- *"Excellent integration in both national and international networks as well as the fostering of own talent and attracting external talent to the team."*
- *"This illustrates a clear methodological emphasis on ensuring results are robust by triangulation, making use of the pooling of cohorts and separate replication of analyses in different data sources, such as the population cohorts in the G2aging HRS family of data, which include SHARE and ELSA, the UK Biobank cohort and CONSTANCES, and equally by setting up own networks around new types of data such as CSF biomarkers (EU CSF collaboration, Neuro-Thalys)."*

3. Data collection in France, collaborations with French teams

The committee highlighted the need to collaborate with French teams and "create data collection on ageing of the French population". In response to both these issues, we note the following:

1. We listed above two new major collaborative arrangements: "Chaire Aging UPI!" and PPR Autonomie. We also collaborate with Bordeaux Public Health centre, PARCC, projects involving data from French memory centers, etc.
2. Our view has always been to use the best data available to answer our research question rather than waste time, money, and effort collecting the team's "own" data if data already exist and are accessible.
3. We have put considerable effort in building the *Banque nationale Alzheimer* (BNA) that aims to collate data from all CM2R in France to allow research. Dumurgier and Singh-Manoux are part of the *conseil scientifique* that is in the process of making these data ready for research.
4. Another example is *DREES* that has nationally representative panel surveys (Handicap-Santé in 2007-2009, Care in 2014-2016, and Autonomie in 2021-2025). We wish to use these data, we have already published a paper using the first two surveys and our ANR PPR project will use data from all three surveys.
5. We played an important role in defining the cognitive test battery in the CONSTANCES study. Our findings led the CONSTANCES ageing battery to be administered starting age 45 rather than 55 as planned earlier. This will become a valuable source of data in the future.
6. Data collection at CM2R Ile-de-France Paris Nord on French patients is managed by Julien Dumurgier, who is a team member.
7. The final element of response is CIRCAME, our new cohort study on 1500 individuals funded by an ERC Consolidator award to Sabia. It uses a clever study design by adding measures of circadian rhythm and a standardized interview to routinely collected data at the memory clinics (dementia diagnosis, neuropsychological tests, MRI, CSF data when clinically indicated) at 2 Paris-based hospitals (Lariboisière-F. Widal and Bretonneau, CMRR). CIRCAME is a perfect demonstration of our approach, new data collection only when it addresses a research question that cannot be addressed with existing data.

Conclusion: Please note HCERES committee's comments on this point below (verbatim text).

- *"Clear efforts have been made to broaden to other population cohort studies (SHARE, UK Biobank, CONSTANCES) as well as patient cohort studies."*

- *“This illustrates a clear methodological emphasis on ensuring results are robust by triangulation, making use of the pooling of cohorts and separate replication of analyses in different data sources, such as the population cohorts in the G2aging HRS family of data, which include SHARE and ELSA, the UK Biobank cohort and CONSTANCES, and equally by setting up own networks around new types of data such as CSF biomarkers (EU CSF collaboration, Neuro-Thalys).”*

4. Size of team

In the new constellation of CRESS, EpiAgeing is indeed one of the smaller teams as noted by the committee. We do not see this to be a limitation because:

1. As noted by the HCERES committee, the small size of the team has not been a hindrance in producing excellent science.
2. The size of teams is determined primarily by its history. Some team were put together decades ago, with team leadership passed down to younger team members on retirement of the founder, and it is normal that they are much larger than us. One of the teams in the new CRESS mandate is the result of a merger between three teams created many years ago. The merger is due to a common research focus. In our case, no other team at CRESS works specifically on ageing or Alzheimer’s disease and related dementias.
3. The committee recommended we collaborate with ECAMO on common themes. We agree, as demonstrated by the completed joint supervision of a PhD student. We also note other possibilities of collaboration, with OPPALE on methodological insights into the lifecourse approach, with METHODS on multimorbidity (using COMPARE data), with EREN on the role of nutrition for ageing outcomes, etc.
4. We are actively involved in all overarching CRESS activities: preparation of researchers for the concours/grants (Sabia, Singh-Manoux), leadership role in Club data stat (Dugravot), mentoring of CRESS PhD students (Sabia), CRESS animation (van der Heide). Our size does not imply a smaller involvement in CRESS activities.
5. The SMART admin team ensures that it addresses the needs of all teams, irrespective of size. In our case, this has involved handling NIH funding, managing the sub-award to UCL for Whitehall data collection, managing ERC and other European grants for us. We also have a regular flow of international young researchers, whose stay with us has been expertly managed by SMART.
6. Our view is that there are multiple advantages to being a small team, these are: very little time of senior scientists is taken up by human resource management so that they can be more involved in the science (including data analyses), we have greater flexibility in shaping/adapting the research agenda in response to new findings at the international level, we can work in a truly collaborative manner with a flat structure that we find is key to “disruptive” science. There are a number of young promising researchers in the team and we hope that the team will grow a little over the next mandate. We are nevertheless keen to remain small, supple, and dynamic. The HCERES committee itself summed up our view perfectly, as shown below.

Conclusion: Please note HCERES committee’s comments on this point below (verbatim text).

- *“The recommendation to involve clinicians and diversify recruitment has been fully implemented.”*
- *“The research group is outstanding and its internationally oriented research program, originally on life course epidemiology of neurodegenerative disease has expanded in depth, by including other types of data (proteomics and CSF biomarkers), and other sources of data (patient cohorts) and in width by expanding to innovative research on accelerometer measurement and most recently multimorbidity.”*
- *“An impressive research output in terms of quality and quantity given the modest team size.”*
- *“The team is an outstanding internationally recognized innovative research powerhouse in the life course approach to ageing as well as biomarker and omics data.”*

Team 9 : Evaluation des risques sanitaires liés à l'environnement

We thank the committee for its comments. Separating the HERA results from its trajectory which is presented in the report of its future unit is detrimental to the overall picture of the HERA activities. Thus, a few points deserve to be clarified and precisions are given below.

THEMES OF THE TEAM

The HERA team works in the field of environmental health. It specializes in the study of air pollution in general and in the occupational context. Its research methods are epidemiology, expology and toxicology, and its original results are based in particular on data from two Parisian cohorts, enabling it to produce new knowledge on allergic and respiratory diseases in the early stages of life.

The HERA results are based on several Parisian cohorts and not only two:

- the population-based PARIS birth cohort;
- asthmatic cohorts: SAMP1 and 2, BIOMAS;
- and an occupational cohort of taxi drivers.

CONSIDERATION OF THE RECOMMENDATIONS OF THE PREVIOUS REPORT

The team has taken on board two of the recommendations made during the last visit:

- 1 - by developing more interactions with other teams in the Unit, in particular the EARoH and EREN teams.
- 2 - by developing more interactions within the team between epidemiological and toxicological approaches, in particular on the study of pathologies linked to particulate pollutants present in the air, thanks to the use of Epitox, which is capable of studying the response of certain genes linked to inflammation.
- 3 - In recent years, the team has been unable to recruit any new permanent researchers, a weakness highlighted by the last visiting committee. However, its future integration into the MERIT unit will enable it to take on two IRD researchers.

In recent years, the HERA team has not recruited permanent researchers but the team greatly strengthened by attracting two associate professors, and seven hospital AP-HP clinician researchers who have enriched and reinforced the different research areas of the team: one associate professor in environmental epidemiology, one associate professor in toxicology, three paediatric pulmonologists-allergologists, two medical biologists specialised in allergology, and two occupational physicians.

In the future, two IRD permanent researchers will join the HERA team on January 2025. Moreover, one epidemiologist physician studying the interactions between malaria and air pollution in collaboration with the HERA team will apply for a tenured researcher position at IRD.

EVALUATION

Overall assessment of the team

The main results have focused on the natural history of respiratory and allergic diseases during the first years of life, and their links with diet, road traffic pollution and exposure to fine particles. The scientific production was excellent, with over 150 scientific articles in peer-reviewed journals during the period under review.

The team's national and international visibility, already assured by its membership of five European networks and the strong expert activity of several team members, could be further enhanced by new works not limited by the specificities of the Parisian population and environment, particularly in expology.

The team has already ongoing new projects not limited to the Parisian population and environment.

They were presented in the trajectory report.

The AVISAN project, in partnership with Air France, aims to assess for the first time, the occurrence of accidental fume events in aircraft cabins from an airline company, and their health impact on the flight crew. This research will allow to document cabin air quality which is likely to impact aircrew as well as passengers' health.

Two other projects in collaboration with IRD deals with:

- the interactions between gestational malaria and air pollution (study enrolling pregnant women in Cotonou – Benin);
- an intervention study to assess the effects of air pollution episodes alerts via apps on asthma control in asthmatic teenagers in Cotonou (Benin).

Weaknesses and risks linked to the context

Despite the team's reputation, the number of temporary staff has remained low in recent years.

The HERA team hosted 4 postdoctoral fellows: 1 from Canada: Cristina Paunescu (2016-2018), 1 from France: Emeline Seurat (2017-2018), 2 from Lebanon: Margueritta Al Zallaoui (2019-2021), and Melissa Hachem (2020-2022). The team waited until the end of the health check-up at adolescence in the PARIS cohort to recruit new post-docs to analyse data (2 recruitments ongoing). A third post-doc is about to

be recruited in the UrbaSanté study, an interdisciplinary and collaborative work, involving both researchers and local stakeholders, to explore how urban interventions can modify various environmental exposures (built, social, and food environments; air quality; noise), health-related behaviours using a natural experiment approach.

The scope of some of the team's results is limited by the specificities of the studied populations (mainly in Paris) and tools used. The team has not developed any major new projects that would enable it to contribute to the theme of environmental health outside the areas of expertise in which it is already recognized.

The team has developed new projects on air pollution expology and epidemiology which are presented in the trajectory report (see above the AVISAN project, and new projects with IRD) or briefly evoked in the Hcéres evaluation report (see above the UrbaSanté project).

Furthermore, the in vitro research yields general results related to air pollution effects on various physiological barriers (cutaneous, ocular, and respiratory). These mechanistic results are general in scope and can be extrapolated anywhere in the world.

RECOMMENDATIONS TO THE TEAM

The team could seek to broaden the scope of its environmental health research beyond the areas of expertise for which it has already been recognized for many years.

The team could seek to produce knowledge useful to air pollution exposure assessment methods beyond its own cohorts.

The team's future integration into the MERIT unit represents an opportunity to develop its activities beyond their current scope, to investigate environmental health issues in developing countries, particularly in the field of chronic and allergic diseases.

Joining the MERIT unit, the HERA team will extend its activities to Southern countries, which are increasingly affected by an epidemiological transition towards non-communicable diseases often linked to environmental factors, especially respiratory and allergic diseases. Tools to assess air pollution exposure (measurements, modelling) and the Epitox tool will be shared between Southern and Northern countries, enabling unprecedented comparisons to be made, both in expology, in epidemiology and toxicology.

Monsieur Eric Saint-Aman
Directeur du département d'évaluation de la
recherche
Hcéres
2, rue Albert Einstein
75013 PARIS

Villetaneuse, le 18 mars 2024

*Objet : Rapport d'évaluation DER-PUR250024165 - CRESS - Centre de recherche en
épidémiologies et statistiques de Sorbonne Paris Cité*

Cher Monsieur,

Nous faisons suite à votre courriel du 15 mars 2024 par lequel vous nous avez transmis le rapport d'évaluation du Centre de recherche en épidémiologies et statistiques de Sorbonne Paris Cité.

L'université Paris XIII – Sorbonne Paris Nord souhaite remercier au nom de l'ensemble des personnels de l'unité de recherche Madame Cécile Delcourt, Présidente du Comité, ainsi que les membres du Comité pour la qualité des échanges lors de la visite d'évaluation, ainsi que pour la qualité du rapport provisoire d'évaluation de l'Unité.

L'université Sorbonne Paris Nord remercie chaleureusement le Comité d'évaluation HCERES pour ses retours extrêmement positifs et constructifs. L'USPN est honorée d'être tutelle du CRESS et d'accueillir dans ses locaux l'équipe EREN dont elle abrite la banque réfrigérée du NutriNet-Santé. Nous partageons pleinement les avis formulés, tant sur les forces que sur les « menaces » (partagées d'ailleurs par de nombreuses équipes en France et lié au mode de financement de la recherche publique actuellement : personnels ITA sous contrat précaire alors que les missions, notamment de maintien de la cohorte NutriNet-Santé s'inscrivent sur le long terme ; budget de fonctionnement presque exclusivement basé sur les grants à décrocher dans le cadre d'appels à projets compétitifs avec très peu de financements récurrents accordé aux équipes, etc.).

Nous sommes également reconnaissants au Comité pour ses recommandations pour le prochain mandat. L'USPN continuera à soutenir le CRESS dont nous sommes si fiers d'être parmi les tutelles. Nous allons collectivement et avec enthousiasme travailler à leur mise en œuvre, pour continuer à faire progresser le domaine de l'épidémiologie et de la nutrition de santé publique et son impact sur la société, dont les nombreuses références qui lui sont faites dans l'espace public attestent et qui contribue largement au rayonnement de notre université.

Je vous prie de croire, Monsieur le Directeur, en mes sincères salutations.

Le Président de l'Université Sorbonne Paris Nord



Christophe Fouquère

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