FWO DMP Template

Project supervisors (from application round 2018 onwards) and fellows (from application round 2020 onwards) will, upon being awarded their project or fellowship, be invited to develop their answers to the data management related questions into a DMP. The FWO expects a **completed DMP no later than 6 months after the official start date** of the project or fellowship. The DMP should not be submitted to FWO but to the research co-ordination office of the host institute; FWO may request the DMP in a random check.

At the end of the project, the **final version of the DMP** has to be added to the final report of the project; this should be submitted to FWO by the supervisor-spokesperson through FWO's e-portal. This DMP may of course have been updated since its first version. The DMP is an element in the final evaluation of the project by the relevant expert panel. Both the DMP submitted within the first 6 months after the start date and the final DMP may use this template.

1. General Information	
Name applicant	**Philip Moons (Department of Public Health and Primary Care)**
FWO Project Number & Title	G072022N Paving the way to precision medicine in childhood-onset diseases: A lifespan perspective on accelerated aging using the epigenetic clock
Affiliation	☒ KU Leuven ☐ Universiteit Antwerpen ☐ Universiteit Gent ☐ Universiteit Hasselt ☐ Vrije Universiteit Brussel ☐ Other:
2. Data description	
Will you generate/collect new data and/or make use of existing data?	☒ Generate new data ☒ Reuse existing data

Describe the origin, type and format of the data (per dataset) and its (estimated) volume

*If you **reuse** existing data, specify the **source** of these data.*
*Distinguish data **types** (the kind of content) from data **formats** (the technical format).*

The project consists of three studies, in which observational data and biomarkers are collected. The population under study are persons with congenital heart disease (CHD) and their mothers. Study 3 is nested in Study 2, as additional data are collected in a subgroup of patients included in Study 2.

STUDY 1: NEWBORNS WITH CHD

Aims: To (i) compare telomere length in newborns with or without CHD; and (ii) to assess pregnancy-related/clinical and mother-related (behavioral, psychological, social) predictors of telomere length in newborns with CHD.

Subjects: Consecutive newborns with CHD, who are diagnosed and/or treated in the University Hospitals of Leuven or Ghent University Hospital in their first week of life, are eligible for inclusion. Data on telomere length of healthy newborns will be retrieved from the ENVIRONAGE study, which includes data of more than 2000 newborns in Flanders *(T. Nawrot: University Hasselt)*.

Variables and measurements:

Biomarker: Telomere length will be determined on leukocyte DNA, using quantitative polymerase chain reaction (qPCR). Telomere length will be expressed as the ratio of telomere copy number to single-copy gene number (T/S ratio). Blood for this study will be drawn during routine venipuncture. The procedure is identical to the one used in ENVIRONAGE.

Predictors: The following variables are measured as predictors because they have been found to be of potential importance in previous research.

Factors	*Variables*	*Measurement/source*
Pregnancy-related/ Clinical	• Gestational age and weight • Type of heart defect on the newborn • Medical complications of pregnancy/ delivery • Neonatal complications	Medical patient records
	• Timing and nature of recognition of pregnancy • Weight changes • Blood pressure • Vitamin and medication intake • Symptoms of illnesses	Modified life history calendar methodology
	• Maternal leukocyte telomere length	qPCR

Behavioral	• Maternal smoking during pregnancy • Maternal alcohol consumption during pregnancy • Maternal physical activities during pregnancy	Modified life history calendar methodology
Psychological	• Maternal stress during pregnancy • Maternal anxiety and depression during pregnancy	
Social	• Educational status of mother • Family composition • Neighborhood income	

STUDY 2: (YOUNG) ADULTS WITH CHD

Aims: To (i) compare telomere length in age strata of (young) adults with or without CHD; (ii) to assess clinical, behavioral, psychological, and social predictors of telomere length in patients with CHD; and (iii) to explore the relationship with functional outcomes, such as frailty and cognition.

Subjects: An age-stratified random sample of (young) adults with CHD, followed-up at the University Hospitals of Leuven and Ghent University Hospital. Age strata for this study are: 18-24y; 25-34y; 35-44y; 45-54y; 55+. Data on healthy individuals will be retrieved from the blood donation service of the Belgian Red Cross-Flanders.

Variables and measurements:

Biomarker: Telomere length will be determined on leukocyte DNA of peripheral blood, using quantitative polymerase chain reaction (qPCR). Telomere length will be expressed as the ratio of telomere copy number to single-copy gene number (T/S ratio). The procedure is identical to study1.

Predictors: The following variables are measured as predictors.

Factors	*Variables*	*Measurement/source*
Clinical	• Type of heart defect • Past and current treatments • Arterial hypertension • Body Mass Index • Cumulative dose of low-ionizing radiation • Co-morbidities (Charlson comorbidity index)	Medical patient records
	• Retinal microvasculature	Retinal imaging

	Behavioral	• Smoking history • Alcohol consumption history • Fruit and vegetable consumption history • Physical activities history	Modified life history calendar methodology
	Psychological	• Anxiety and depression history • Loneliness history • Post-traumatic stress disorder history	
	Social	• Educational status history • Family composition history • Neighborhood income history	

Functional outcomes: The frailty phenotype and cognitive functioning are assessed as functional outcomes of aging. The frailty phenotype, operationalized by Fried, is the most commonly used approach for assessing frailty in patients with chronic disorders. Based on the presence or absence of 5 components (unintentional weight loss; exhaustion; low physical activity level; weakness assessed with handgrip dynamo-meter; slow walking speed operationalized by time to walk 5 meters) patients are categorized as: non-frail (i.e., score 0/5), pre-frail (i.e., score 1-2/5) or frail (i.e., score ≥3/5). Cognitive functioning is assessed using the Montréal Cognitive Assessment Screener (MOCA). The MOCA is a well-established instrument and its validity to be used in CHD has been demonstrated. The MOCA assesses visual–spatial skills; executive functions; short-term memory recall; attention, concentration, working memory; language; and orientation to time and place.

STUDY 3: EPIGENETIC CLOCK IN ADULTS WITH CHD

Aims: To (i) assess the biological age by measuring DNA methylation in mild, moderate and complex heart defects, with or without complications, and (ii) determine if the disparity between biological and chronological age is a function of anatomical complexity and functional status of the patients.

Subjects: At the University Hospitals of Leuven and Ghent University Hospital, patients with selected complex (Fontan operation; Systemic right ventricle), moderate (Tetralogy of Fallot; Coarctation of the aorta), and mild heart defects (isolated atrial septal defect; isolated ventricular septal defect) are eligible. For each type of heart defect, 10 patients with complications and 10 patients in good health are enrolled. The overall sample will comprise 120 patients, who will be part of study 2 as well.

Variables and measurements:

Biomarkers:

- Telomere length will be determined as part of study 2.
- As a measure of systemic chronic inflammation, soluble urokinase plasminogen activator receptor (suPAR) will be measured. suPAR reflects inflammation and immune activation and its blood concentration is positively correlated with established biomarkers of inflammation, but in contrast to many currently used markers of systemic inflammation, suPAR is minimally affected by acute changes and short-term influences. Therefore, it is a better marker of aging than other inflammation biomarkers.
- To triangulate the validity of suPAR in CHD, high sensitivity C-reactive protein (hsCRP) will be assessed as a more traditional marker of inflammation.
- The epigenetic clock based on DNA methylation will be determined.

Predictors: The clinical, behavioral, psychological and social predictors as measured for study 2 will be used for this study as well.

Summary of data to be collected

	Study 1	**Study 2/ *Study 3**
Observational data		
Medical Chart Review	X	X
Modified life history calendar methodology	X	X
Fried frailty phenotype		X
Montreal Cognitive Assessment Screener		X
Retinal imaging		X
Biomarkers		
Telomere length in persons with CHD	X	X
Maternal telomere length	X	
Telomere length in healthy controls	X	X
Soluble urokinase plasminogen activator receptor (suPAR)		*X
High sensitivity C-reactive protein (hsCRP)		*X
Epigenetic clock based on DNA methylation (DiffAge, GrimAge)		*X

	Observational data will be collected on paper, and will be pseudonomized. Afterwards, the data will be imputed in a secured online database using REDCap. For archiving purposes, the hard copies of the research documents will be stored in a locked room at the respective university hospitals. When data are extracted from REDCap for analysis, they will be stored on drives that are protected with multi-factor authentication (e.g. OneDrive for Business). We expect the total volume of each study not to exceed 1 GB. Blood for biomarkers will be stored in the biobanks of the respective University Hospitals. Assessment of telomere length will be done at the core lab for the project, located at the University of Hasselt, under supervision of Prof. T. Nawrot. The assessment of the epigenetic clock will be done at the center of medical genetics of the University Hospital of Ghent, under supervision of Prof. P. Coucke. Samples will be shipped to the respective labs in a pseudonomized way.

3. Ethical and legal issues	
Will you use personal data? If so, shortly describe the kind of personal data you will use AND add the reference to your file in your host institution's privacy register. *In case your host institution does not (yet) have a privacy register, a reference is not yet required of course; please add the reference once the privacy register is in place in your host institution.*	☒ Yes ☐ No If yes: - Privacy Registry Reference: - Short description of the kind of personal data that will be used: Since this project will collect personal data, approval from the Ethics Committee UZ/KU Leuven and UZ Ghent will be sought. The Committee of UZ/KUL Leuven will serve as central committee. Both the observational data as the biomarkers (see section above) are seen as sensitive data, and will be treated accordingly.

Are there any ethical issues concerning the creation and/or use of the data (e.g. experiments on humans or animals, dual use)? If so, add the reference to the formal approval by the relevant ethical review committee(s).	☒ Yes ☐ No If yes: - Reference to ethical committee approval: Since this project will collect personal data, approval from the Ethics Committee UZ/KU Leuven and UZ Ghent will be sought. The Committee of UZ/KUL Leuven will serve as central committee. Both the observational data as the biomarkers (see above) are seen as sensitive data, and will be treated accordingly. Ethical guidance as stipulated in the Declaration of Helsinki will be followed.
Does your work possibly result in research data with potential for tech transfer and valorisation? Will IP restrictions be claimed for the data you created? If so, for what data and which restrictions will be asserted?	☐ Yes ☒ No If yes, please comment:
Do existing 3rd party agreements restrict dissemination or exploitation of the data you (re)use? If so, to what data do they relate and what restrictions are in place?	☐ Yes ☒ No If yes, please comment:

4. Documentation and metadata	
What documentation will be provided to enable understanding and reuse of the data collected/generated in this project?	A codebook will be made, explaining the variables and their response categories. Further, a file with the patient identification and the study number will be stored separately, to which only the principal investigator and the data collection officers in the respective hospitals have access to.

Will a metadata standard be used? If so, describe in detail which standard will be used. If not, state in detail which metadata will be created to make the data easy/easier to find and reuse.	☐ Yes ☒ No If yes, please specify: The codebook will be made in REDCap, to ensure that the variables and responses are properly coded and accessible to all researchers that have to work with the data.

5. Data storage & backup during the FWO project	
Where will the data be stored?	The data will be stored on a REDCap server of the KU Leuven, and will be accessible for the participating researchers from UZ Leuven and UZ Gent.
How will the data be backed up?	The REDCap server of KU Leuven is automatically backed-up according the following scheme: Back-up of the webserver • Back-up every hour, of which the last 6 versions are saved • Daily back-up, of which the last 7 versions are saved • Weekly back-up, of which the last 6 versions are saved Back-up of the database • Every night, a cold dump of all database is made • Cold dumps are saved for 1 month
Is there currently sufficient storage & backup capacity during the project? If yes, specify concisely. If no or insufficient storage or backup capacities are available, then explain how this will be taken care of.	☒ Yes ☐ No If no, please specify:

What are the expected costs for data storage and backup during the project? How will these costs be covered? *Although FWO has no earmarked budget at its disposal to support correct research data management, FWO allows for part of* ***the allocated project budget*** *to be used to cover the cost incurred.*	The annual cost per database is 80 euro per year. Different databases will be made, to enter and manage the data from different sources (medical charts; observational data; biomarkers; …) for the different studies. The costs will be covered by the project budget.
Data security: how will you ensure that the data are securely stored and not accessed or modified by unauthorized persons?	Access to the databases is only granted to privileged researchers (Prof P. Moons, Prof. W. Budts, Prof J De Backer, Prof R Heying, Prof K De Groote, Dr. Muino Mosquera and the PhD students and lab technicians). Multi-factor authentication is used. A data sharing agreement will be made between KU Leuven and U Gent.

6. Data preservation after the end of the FWO project FWO expects that data generated during the project are retained for a period of minimally 5 years after the end of the project, in as far as legal and contractual agreements allow.	
Which data will be retained for the expected 5 year period after the end of the project? In case only a selection of the data can/will be preserved, clearly state the reasons for this (legal or contractual restrictions, physical preservation issues, ...).	All data will be preserved for a minimum of 10 years. If longitudinal follow-up studies are planned in the future, it will be possible to link future data with data collected in the present project.
Where will these data be archived (= stored for the long term)?	Digital data remain stored on the REDCap server of the KU Leuven. Hard copies will be stored in a locked room in the respective hospitals. Biological samples are stored at the biobank of the respective hospitals.

What are the expected costs for data preservation during these 5 years? How will the costs be covered? *Although FWO has no earmarked budget at its disposal to support correct research data management, FWO allows for part of* ***the allocated project budget*** *to be used to cover the cost incurred.*	The expected costs do not exceed 500 euro per year. This will be covered by the present project budget, and by the research funds of the principal investigator.

7. Data sharing and reuse	
Are there any factors restricting or preventing the sharing of (some of) the data (e.g. as defined in an agreement with a 3rd party, legal restrictions)?	☐ Yes ☒ No If yes, please specify:
Which data will be made available after the end of the project?	All data can be made available in a pseudonomized way to third parties upon reasonable request. A data sharing agreement will be made between the third party and the applicants/co-applicants of the present project.
Where/how will the data be made available for reuse?	☐ In an Open Access repository ☐ In a restricted access repository ☒ Upon request by mail ☐ Other (specify):
When will the data be made available?	Data can be made available to third parties after the end of the present project, the publication of the main articles, and the defences of the PhD students.
Who will be able to access the data and under what conditions?	If third parties want to use (part of) the data for secondary data analysis, benchmarking, or follow-up studies, they can submit a request to the principal investigator: Philip Moons. The appropriateness of the request will be evaluated by the co-applicants of the present proposal.

What are the expected costs for data sharing? How will these costs be covered? *Although FWO has no earmarked budget at its disposal to support correct research data management, FWO allows for part of **the allocated project budget** to be used to cover the cost incurred.*	This will depend on the nature of the request. For data retrieval and management, 100 euro/h will be charged. These costs for data sharing with third parties will be covered by the third party.

8. Responsibilities	
Who will be responsible for the data documentation & metadata?	Prof Philip Moons: principal investigator In collaboration with Prof W. Budts, Prof J De Backer, Prof R Heying, Prof K De Groote, Dr. L Muino Mosquera
Who will be responsible for data storage & back up during the project?	Prof Philip Moons: principal investigator In collaboration with Prof W. Budts, Prof J De Backer, Prof R Heying, Prof K De Groote, Dr. L Muino Mosquera
Who will be responsible for ensuring data preservation and sharing?	Prof Philip Moons: principal investigator In collaboration with Prof W. Budts, Prof J De Backer, Prof R Heying, Prof K De Groote, Dr. L Muino Mosquera
Who bears the end responsibility for updating & implementing this DMP? *Default response: The PI bears the overall responsibility for updating & implementing this DMP*	Prof Philip Moons: principal investigator In collaboration with Prof W. Budts, Prof J De Backer, Prof R Heying, Prof K De Groote, Dr. L Muino Mosquera