SIMCor

In-Silico testing and validation of Cardiovascular IMplantable devices

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Lead beneficiary	Lynkeus (LYN)
Author(s)	Anna Rizzo (LYN)
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Executive summary

The data management plan represents a comprehensive analysis of the nature of data to be handled, generation, collection, de-identification and other processing, data flow and usage in the context of the project research activity and beyond, accessibility, interoperability, FAIR, long-term storage and backup. The deliverable also includes security measures adopted to prevent unauthorised access to personal data in the virtual research environment, and procedures for the inclusion of data and other resources in the European Open Science Cloud.

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Acronyms

Acronym	Full name
AI	Artificial intelligence
AU	Authorised users only
AVD	Aortic valve disease
CT	Computed tomography
DPO	Data Protection Officer
EOSC	European Open Science Cloud
EQ	Assessment and quantification of healthcare, industrial and socioeconomic impacts
FAIR	Findability, accessibility, interoperability, and reusability
GPU	Graphics processing unit
HF	Heart failure
IAM	Identity access management
MDR	Metadata repository
MRI	Magnetic resonance imaging
OA	Open access
PAPS	Pulmonary artery pressure sensor
PI	Principal investigator
SOP	Standard operating procedures
TAVI	Transcatheter aortic valve implantation
VC	Generation and validation of virtual cohorts
VD	Virtual device implantation and device effect simulation
VRE	Virtual research environment
UR	Availability upon registration

Introduction

SIMCor aims to establish a computational platform for in-silico development, validation and regulatory approval of cardiovascular implantable devices as an open resource for collaborative R&D for cardiovascular device manufacturers, medical authorities and regulatory bodies.

To do so, SIMCor will develop and validate in-silico technologies for realistic device implantation and effect simulation under patient-specific conditions, with clinical focus on two specific use cases: *transcatheter aortic valve implantation* (TAVI) procedures for non-invasive treatment of *aortic valve disease* (AVD), and a *pulmonary artery pressure sensor* (PAPS) device for the measurement of pulmonary artery blood pressures for *heart failure* (HF) patients. The platform will be designed for: a) generation and validation of virtual animal and human patient cohorts for in-silico trials, and b) virtual implantation and evaluation of device effects.

This activity is mostly based on the secondary analysis of retrospective data sources, including (1) clinical routine data and (2) clinical trial studies on AVD and HF patients, and (3) preclinical studies on TAVI, and the conduction of two prospective preclinical studies on PAPS. These data resources will be further integrated with additional synthetic geometries and functional variants to be generated through *artificial intelligence* (AI) models, and with the virtual cohorts to be developed in the project. This data, after being de-identified at local level for privacy-preservation where relevant, and processed for anatomic and functional modelling purposes, will be shared by data providers into the project *virtual research environment* (VRE) and made available for modelling activities.

Data will be made *findable, accessible, interoperable, and reusable* (FAIR) and, together with virtual cohorts, simulation models, methodologies and *standard operating procedures* (SOPs) will be made available for other possible users in the context of the *European Open Science Cloud* (EOSC).

The following paragraphs will discuss all these aspects in detail, including data sources description and collection purposes, data flow and processing, data storage and interoperability, platform security, accessibility and inclusion in the EOSC.

Data sources

SIMCor will leverage a wide range of retrospective clinical and preclinical data sources from consortium clinical centres (CHA, UCL), academic and industrial partners (BIO, TUG), network registries (*ECRIN metadata repository*, ECRIN-MDR), or publicly available as open data, coming from hospital clinical routine care or previous research actions (EU H2020, EU 7FP, German Federal Ministry of Education and Research), plus a new prospective preclinical study to be conducted in the course of the project, for the PAPS device developed by BIO. These data resources will be further integrated with additional synthetic geometries and functional variants to be generated through AI models at UCL and CHA, in the context of WP5, and with virtual cohorts of AVD and HF patients and animal models, as part of WP7. Datasets will be utilised for conducting different types of activities: *(1) generation of synthetic anatomical and functional variants* (WP5); (2) *generation and validation of virtual cohorts* (VC), as part of WP7; (3) *virtual device implantation and device effect simulation* (VD); *(4)* A*ssessment and quantification of healthcare, industrial and socioeconomic impacts* (EQ).
A schematic overview of SIMCor data sources is reported in *Table 1*, while full description of datasets is included in the *Appendix*.

Type	Source	N	Dataset[1]	Usage[2]
(A) CLINICAL ROUTINE DATA from hospital repositories (2014–2023)	CHA, UCL	250	Group R1: AVD, undergoing TAVI	VC
		250	Group R2: HF, requiring PAPS	VC
(B) SYNTHETIC CLINICAL DATA to be generated in SIMCor[3]	UCL, CHA	1,000	Synthetic additional AVD patient geometries and boundary conditions	VD
		1,000	Synthetic additional HF patient geometries and boundary conditions	VD
(C) CLINICAL TRIAL DATA from consortium's previous research, network registries and open data	CHA, UCL	60	SMART (NCT03172338)	VD
		120	EurValve (NCT04068740)	VD
		120	Cardioproof (NCT02591940)	VD
		1,200	ArtiCardio	VD
	BIO	86	BIOVALVE (NCT002249000)[4]	VD
	Open data	550	CHAMPION (NCT00531661)[4]	VD
	ECRIN-MDR	-	To be identified	EQ
(D) PROSPECTIVE ANIMAL STUDY to be conducted in SIMCor	CHA, BIO	10	Prospective acute pig study for PAPS	VC
		10	Prospective chronic pig study for PAPS	VC
(E) PRECLINICAL DATA from consortium's previous research	CHA, BIO	10	Acute and chronic pig and sheep data for TAVI	VC
		30	SCATh[4]	VD
		6	Chronic sheep study for PAPS[5]	VC
(F) HUMAN AND ANIMAL TISSUE SAMPLES for mechanical tests	TUG, BIO, CHA	30	Human tissue (N=10), sheep tissue (N=10), porcine tissue (N=10)[5,6]	VD

Table 1: SIMCor data sources, including retrospective clinical and preclinical data (A, C, E, light blue), synthetic clinical data (B, grey), a new prospective animal study for PAPS (D, orange), and human and animal tissue samples (F, green) as collected/generated in WP5. This data will be further integrated by the virtual animal and human patient cohorts to be developed in the course of the project as part of WP7.

[1] Dataset brief description or project name (clinical trial number) for data from previous studies. For human data, the clinical focus is either *aortic valve disease* (AVD) or *heart failure* (HF), while preclinical studies are performed on healthy animal models (pigs).
[2] Usage purposes. VC: virtual cohort generation and validation. VD: virtual device implantation and effect simulation. EQ: assessment and quantification of healthcare, industrial and socioeconomic impacts.
[3] This dataset is still to be produced, so it is not described in the *Appendix.*
[4] These datasets, still included for completeness and in alignment with previous deliverables (i.e., D5.1, D5.2, D1.9), the Grant Agreement and original proposal, will eventually not be used for project activity, and therefore they are not described in the *Appendix*.
[5] These datasets were recently added, so were not included in data tables of previous deliverables (i.e., D5.1, D5.2, D1.9).
[6] Human tissue is obtained by BIO from the University of Rostock; sheep tissue: CHA; porcine tissue: butcher Marcher (TUG).

Data flow

In SIMCor, the data flow and processing are highly facilitated by the competence of its clinical partners (CHA, UCL) in both clinical cardiology and cardiac modelling, including identification of descriptive parameters, requirement identification and documentation templates for the modelling activity.
The collection/generation of data in SIMCor is carried out within the clinical centre and shared in local repositories. Here, data processing activities take place, including:

- **De-identification (i.e., pseudonymisation) of clinical records**, with removal of identifiers (e.g., full name) and quasi-identifiers (i.e., other sensitive information, e.g., address, able to identify the data subject).
- **Segmentation and extraction of geometries and anatomical and functional parameters of the heart, heart valves and large vessels from anonymised CT and MRI DICOM images**, so to extract the modelling-relevant information without sharing real patient images (e.g., geometry, diameters, lengths, volume flow rates).
- **Post-processing and statistical analysis**, including identification and quantification of descriptive parameters (e.g., distributions, ranges, variances, covariances, correlations) for clinical data, definition of boundary conditions for geometries and dynamics (i.e., haemodynamics and movements) for subject-specific simulations, and their uncertainty and sensitivity analysis.

All these activities are carried out at local level, so that only numerical distributions are shared outside the hospital databases. The resulting **library of models** will contain **anatomical information** (i.e., geometric representations of heart chambers, heart valves, large vessels); **functional information** (i.e., parametric representation of haemodynamics and ventricular function) and **material properties** (i.e., distribution of strains, compliance/distensibility with regard to the anatomy).

The library of models is going to be shared within the **temporary cloud repository (VRE Drive)**, developed at the end of M3 by the UTBV team to allow the sharing of data between data providers and modelling partners (BIO, IIB, PHI, TUE, TUG), as well as the execution of some modelling activities and virtual cohort generation activities, even though most of them will be carried out in the local environments of the relevant partners.

Once the **VRE** of the project is available, data resources, templates, SOPs and models will be moved there, to allow the complete development, testing, refinement and validation pipeline. A schematic representation of the SIMCor data workflow is provided below.

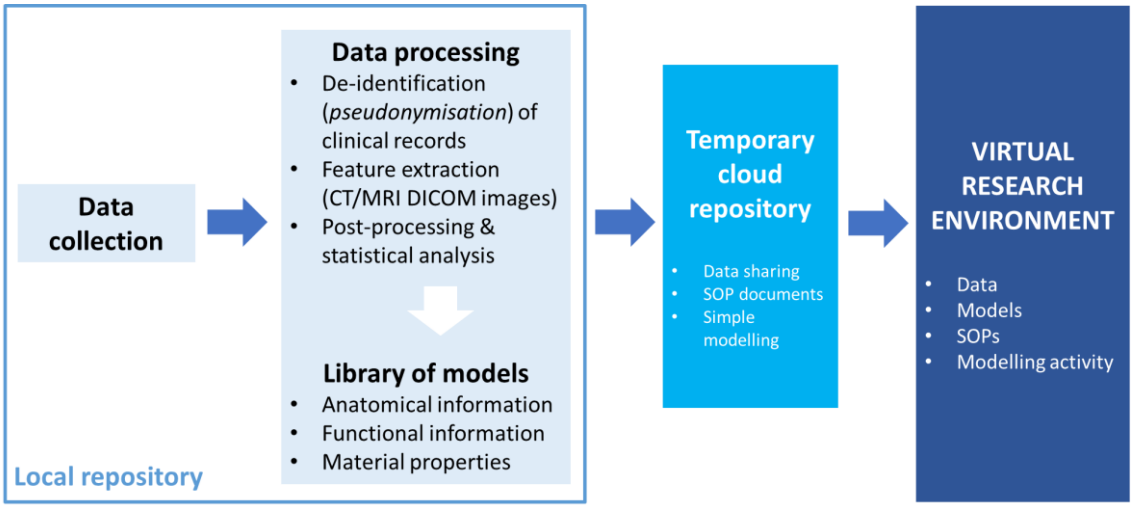

Figure 1: Data collection, processing and storage flow concerning clinical records and images collected at consortium clinical centres (CHA, UCL).

Data collection

Clinical data

Clinical routine data

Retrospective collection of clinical routine data is carried out by consortium clinical partners (CHA, UCL) with the involvement of their respective university hospitals (Charité – Universitätsmedizin Berlin, Great Ormond Street Hospital, Barts Heart Centre), as described in *D5.1 - Protocol for clinical data collection (UCL, M3)*. This data includes retrospective datasets of adult and paediatric patients treated at CHA or UCL clinical centres over the period 2014-2023.

- **Group R1**: routinely collected retrospective datasets of AVD patients who underwent (or will undergo) TAVI procedure at CHA or UCL clinical centres over the period 2014-2023. Since AVD is rare in children and TAVI is hardly indicated in paediatric patients, the TAVI population only includes adult patients (i.e., >16 year).
    - **Exclusion criteria**: patients aged ≤16 years, patients who have objected to their data being used for secondary research purposes.
    - **Variables**: demographic information, pre-procedural imaging assessment of the left ventricular outflow tract and aortic root through *computed tomography* (CT), ultrasound images and *magnetic resonance imaging* (MRI), peri-procedural data from fluoroscopy images, and invasive pressure measurements, and 1-year follow-up outcomes (i.e., ultrasound images, record of events).
- **Group R2:** routinely collected retrospective datasets of patients with left HF and indication for a PAPS over the period 2014–2023 at CHA. As many paediatric patients with congenital heart defects also suffer from severe HF and would benefit from PAPS, the cohort also includes paediatric patients (i.e., 6-18 year).
    - **Exclusion criteria:** patients aged ≤5 years, patients who have objected to their data being used for research purposes.
    - **Variables**: demographic information, pre-procedural MRI and ultrasound imaging assessment of the left and right ventricular outflow tract, pulmonary arteries, left and right atria, ventricle, ventricular outflow tract and great arteries (pulmonary artery and aorta). Quantitative blood flow information in the pulmonary artery will be provided by velocity-encoded cine MRI.

Synthetic clinical data

Synthetic clinical data consists of a series of geometric and functional variants (i.e., anatomical models and boundary conditions) of AVD and HF patients, generated by UCL and CHA to integrate available clinically derived patient features with further variants, less represented in the clinical cohort, to study their evolution over time.

For synthetic data generation, partners will utilize an AI-based (i.e., CycleGAN / InfoGAN) approach combining feature extraction and generation steps. Patient-specific anatomical models and functional data are transformed to a latent space (i.e., a compressed representation that directly contains relevant features), and then new models are generated by random sampling from the latent space, allowing to explore the physiological envelope and variation over time, up to the creation of 1,000 synthetic records for aortic valve stenosis and 1,000 for heart failure population.

Clinical trial data

Retrospective clinical trial data will be gathered from consortium partners' repositories (CHA, UCL, BIO), project databases or network repositories (ECRIN-MDR registry). For these datasets, informed consent procedures have been carried out at the time of the original study and include consent for secondary usage of research data.

Preclinical data

Retrospective preclinical data

Retrospective preclinical data, includes data sources already available for TAVI from previous research projects conducted by BIO, that will be gathered from relevant consortium partners' repositories or project databases.

Prospective preclinical data

For PAPS, a device still under development, the consortium has envisaged the conduction of a new prospective study including acute and chronic tests on healthy pigs for preliminary investigation of short- and long-term effects of PAPS implantation. A detailed description of the animal study protocol, including justification for animal use, tested properties, sample size and statistical methods is included in *D5.2 - Protocol for prospective animal study (CHA, M3)*.

Data processing

De-identification procedures

Clinical routine data

De-identification (i.e., pseudonymisation) of clinical routine data collected during clinical care will be performed at local hospital repositories (Charité – Universitätsmedizin Berlin, Great Ormond Street Hospital, Barts Heart Centre) by clinical personnel, prior to sharing data with research units at CHA and UCL, that receive it in de-identified form. De-identification procedures are carried out following hospital guidelines, under the responsibility of the respective *Data Protection Officers* (DPOs). These procedures consist of the removal of *identifiers* (i.e., names and surnames) and *quasi-identifiers* (i.e., parameters to be potentially used for re-identification of subjects), including:

- *patient's birthdate*
- *patient's address*
- *patient's telephone number*
- *referring physician*
- *patient's age* (will be grouped)

This processing mostly affects the information stored in DICOM tags. Here, a list of DICOM tags to be overwritten must be defined for each clinical center and imaging protocol, as different protocols usually include different levels of information in the metadata. Overwriting of the DICOM tags can be performed directly upon export of the image data from the clinical archive systems. Remaining DICOM tags can be removed using various tools (e.g., MATLAB). As only information regarding the patient-specific anatomy and haemodynamics is required, no burnt in information (e.g., patient name in the pixel image information) is to be expected. However, quality control of imaging sequences for burnt-in information is performed. If sequences with burnt in information are found, they are either deleted, if not relevant for reconstruction of the patient-specific anatomy, or cropped/overwritten to remove the identifying information if the images are required for the scope of the project.

As only information derived from this image data, as for example tabular data, surface geometries, flow profiles, will be shared, there is no risk of transfer of relevant information from the DICOM tags towards the derived data.

Clinical trial data

For what concerns other clinical data sources (i.e., clinical trials and other research projects) partners will provide these in de-identified form as processed by hospitals and research coordinators at the time of collection.

Data processing for anatomy and function

Clinical data

When shared with local research teams (CHA, UCL) data will be processed for anatomical and functional modelling, in the context of WP6. Particularly, this activity will consist of

- **Extraction of anatomical and functional information from image data for the generation of 3D anatomical model samples**: extraction of anatomical structures from clinical datasets to provide processing tools for the automatic extraction of volumetric and surface representations of the heart, heart valves and large vessels, according to a set of commonly defined standards, leveraging and integrating solutions for the semi-automatic segmentation of vascular structures, heart chambers and valves.
- **Determination of 4D and local properties**: determination of local properties (e.g., strain, wall thickness, motion, calcification) and functional parameters (e.g., ejection fraction, regurgitation) of heart, heart valves and large vessels will be determined through 3D segmentation and extended with 4D propagation and local intensity analysis, and the resulting 4D segmentations will be used to derive global functional parameters, and added to the sample description.
- **Determination of boundary conditions for subject-specific simulations (4D and local properties) and virtual cohort simulations**: boundary conditions for modelling of haemodynamics and biomechanics of valves and large vessels will be derived from preclinical or clinical data, and missing data will be derived from lower order models (lumped, 0D/1D) and subject-specific data for model validation; additional boundary conditions (e.g., geometries and flow profiles) will then be derived based on literature and mathematical models fitted for different sub-cohorts (i.e., age, gender, device and disease specific) as well as usable for automatisation of the modelling pipeline process.
- **Uncertainty and sensitivity analysis**: selection of device and disease specific parameters of interest and the respective physical model and modelling approach, including assumptions for translation of the real physical situation into the model including simplification. Separately, validation parameters will be defined.

Preclinical data

Prospective preclinical data will be taken for PAPS devices in a similar systematic as clinical data. Yet, within the project only with preclinical studies the direct interaction of implant and biologic environment is studied. The processing is applied as follows:

- **Extraction of anatomical and functional information from image data for the generation of 3D anatomical model samples**: extraction of anatomical structures with and without the sensor device.
- **Determination of 4D and local properties**: determination of local properties (e.g., strain, wall thickness, motion) and functional parameters (e.g., ejection fraction) of heart and pulmonary artery will be determined through 3D segmentation and extended with 4D propagation and local intensity analysis, and the resulting 4D segmentations will be used to derive global functional parameters, and added to the sample description.
- **Modelling and simulation validation**: retraction force tests are conducted in order to validate the simulations.

Data usage

Synthetic data generation

Synthetic data generation describes generation of all boundary conditions including anatomical and functional parameters, as for example inlet and outlet boundary conditions, that are required for simulation of virtual device implantation and device efficacy. Anatomical and physiological variabilities, coherent with patient cohort features, will be generated using an AI-based (i.e., CycleGAN/InfoGAN as well as statistical/parametric shape models) approach that combines feature extraction and generation steps, up to 1,000 synthetic records for aortic valve stenosis and 1,000 for heart failure population.

Patient-specific anatomical models and functional data extracted from clinical routine or literature data **(Group A)** are used for two aspects. First they are used as anatomical boundary conditions for patient-specific simulation of device implantation and device effect. Also, they are transformed to a latent space (i.e., a compressed representation that directly contains relevant features), and then new models are generated by random sampling from the latent space. Patient-specific anatomical models are subdivided into two groups: the major group of anatomies used to generate a statistical shape model and a small test cohort of at least 20 cases used to validate this shape model. The latent space consists of parameters describing a parametric shape model. Using random sampling distributions and considering correlations between all parameters or weights, virtual anatomies can be generated from this latent space description. Not all data required for generation of synthetic data can be derived from clinical data. The unavailable data, which however are required for numerical models, will either be acquired from literature or other available models. Synthetic shapes for the aortic valve stenosis population should describe anatomy of the left ventricular outflow tract, the aortic root with the aortic valve as well as the aorta. Synthetic shapes for heart failure population should describe the pulmonary artery including the main pulmonary artery (MPA), the right (RPA) and left (LPA) pulmonary arteries as second order vessel segments as well as third order vessel segments (side branches of the LPA and RPA).

Virtual cohort generation and validation

Virtual cohorts will be generated and validated for in-silico testing of TAVI and PAPS, including

1. a small but well characterized cohort of healthy pigs;
2. a representative AVD patient population (for TAVI testing);
3. a representative HF patient population (for PAPS testing).

The activity will encompass the following phases:

- **Definition of model output**: definition of the output of the simulation model to be used to generate the virtual patient population, including quantitative engineering metrics to be used as endpoints of clinical/preclinical trials, with a probability distribution that captures the population spread of the output within a real cohort:
  - paravalvular leakage (TAVI)
  - thrombosis (both TAVI and PAPS)
  - device migration and vessel perforation (PAPS).
- **Selection of model templates**: model templates will be selected for each of the clinical targets described for virtual device implantation, based on the required output of the simulation model, the predictive accuracy of the output metric, and the computational costs of the model.
- **Selection of data templates**: definition of type, source, format, distribution model and uncertainty/variability ranges of the data to be used, by the use of sensitivity analysis tools guiding the collection of the relevant data for the target use cases.
- **Generation of virtual patient population**: development of the virtual patient population generation system, based on the defined simulation model output and its range, the different models that comprise the combined simulation model and the input data that will be used to perform model simulations. Patient datasets will consist of a list of parameters combined with one or more scalar and vector functions defined on a single (time) axis or on internally defined 3D meshes, and one or more digital images of vessel geometries.
- **Three-level validation of virtual patient population**: validation of the final virtual patient and animal populations, based on three steps: (1) validation of the model-derived metrics on a patient-specific level; (2) self-validation, where the effect of TAVI intervention is simulated using AVD virtual cohort patients and compared with the effect of the interventions observed in real clinical trials; in the self-validation step, the available dataset will be divided in three independent subsets that are ordered randomly: 80% to develop the cohort, 10% to evaluate the effect simulations (validation set), 10% for the final cross-validation step (testing data). In the cross-validation, we will simulate the effect measure within a virtual cohort that had not been used for virtual cohort development but that consists of statistically similar patients (e.g., age, comorbidities), and we verify whether the effect measure is equivalent to the truly observed effect found in the real clinical trials.

Virtual device implantation

A standardized framework for the **virtual implantation of PAPS and TAVI on bench test environments, animal and patient cohorts** will be elaborated, based on device and tissue models, finite element and finite volume approaches as well as reduced order models. Particularly, the activity will be based on the following phases:

1. **Refinement of current TAVI and PAPS models**: proprietary and commercially available device models will be developed and refined. Definition of physical properties of device components including material, structural, geometrical and mechanical features will be derived based on imaging and scanning techniques (e.g., microcomputer tomography scanning), CAD software parameterization and experimental mechanical testing.
2. **Definition of simplified vessel models**: simplified constitutive vessel models will be elaborated to perform the implantation with reasonable computational effort. These models will describe the material behaviour of the vessel wall during the implantation of PAPS and TAVI, and will be used in combination with the virtual device models, with the numerical consideration of contact between the vessel wall and the device.
3. **Validation of simplified vessel models**: simplified vessel models will be validated with the use of ***experimental study data, from previous studies (Group E) and new experimental laboratory tests on animal and human tissue samples*** (i.e., biaxial tensile tests for mechanical properties; second-harmonic generation for structure of the vessel tissue).
4. **Development of fast device deployment simulation models**: computationally efficient, position-based dynamic models will be developed for simulation of device deployment in virtual cohorts, while attaining adequate accuracy with simplified parameterization of geometric anatomy and device representations. This approach will leverage 3D anatomical representations, 3D CAD device models, and assumptions on tissue elasticity derived from the local model parameters, as calculated in the generation of virtual cohorts. The approach will result in a deformed 3D geometry and computational domains for fluid dynamics analysis.
5. **Creation of 3D finite element implant simulation models**: fully detailed simulations of the deployment of PAPS and TAVI will be created leveraging anatomical data and refined device models. Model implementation will be carried out using the finite element approach. Besides simulation of device-vessel contact, we will generate dedicated computational discretizations respecting different modelled aspects, such as anisotropy or the layer structure of the vessel wall, depending on the complexity of the vessel wall model. Simulations will be parameterized by material properties of device and tissue, device angulations and anatomical data. The resulting deformed vessel geometries will be compared with the ones of the fast deployment models.
6. **Model simplification (order reduction)**: simplified models of device-wall interactions will be created based on finite models through the Response Surface technology, exploring through regression models the relationships between input parameters and response variables. A selected number of simulations, as defined by a design-of-experiment approach, will be used to find these relationships and provide approximated values of the output parameters in the analysed design space without performing further simulations with complete 3D, patient-specific models. Sensitivity analysis and identification of the most important model parameters will also be carried out, thus reducing the parameter space.
7. **Isogeometric analysis for high order description of device, vessel and device-vessel interaction**: advanced discretization and higher-order description of device, vessel and device-vessel interaction during deployment will be based on isogeometric and immersogeometric methods. In particular, it will enable automatic discretisation of complex geometries and high-fidelity results describing the device-wall interactions by means of

higher-order formulations. This will also result in a quicker whilst highly accurate generation of personalised models, making this approach applicable to large scale clinical applications.

Effect simulation modelling

A comprehensive simulation framework will be developed for the **modelling of device short- and long-term effects, particularly in regard to safety, efficacy and usability endpoints**, necessary to achieve device validation and regulatory approval. Particularly, the activity will be based on the following phases:

1. **Vessel model refinement**: based on the developed simplified vessel models describing the material behaviour of the vessel wall during the implantation of PAPS and TAVI, an enhanced vessel model will be developed to simulate device effects within the target vessel for the simulation of device-specific effects for PAPS and TAVI; this model will take into account mechanical behaviour of the vessel wall (collagen fibres, elastic fibres, vascular smooth muscle cells and the ground substance) by performing biaxial tensile tests and second-harmonic generation imaging.
2. **Generation of device-specific effect models**: device and vessel models will be combined with generic baseline models as well as subject-specific patient and animal vessel geometries (obtained from retrospective data processing and virtual cohort data) to obtain complex biomechanical and fluid dynamics models for assessing specific device effects (e.g., structural mechanics, haemodynamics). Particularly, the focus will be on device migration, perforation and thrombosis for PAPS, and thrombosis, paravalvular leakage and durability for TAVI.
3. **Low-fidelity model validation**: a first level of model validation will be achieved through bench and acute animal tests measuring engineering properties mentioned above. Particularly, for PAPS, device migration (through implantation of the device in mock vessels and measurement of axial retention force), device perforation (through mechanical testing of device properties and device-vessel interaction in elastic mock vessels and animal and human specimens), thrombosis (through particle image velocimetry experiments using 3D-printed mock vessels); for TAVI, thrombosis (through simplified in-silico benchmark experiments, particle image velocimetry, high-speed cinematography), paravalvular leakage (through hydrodynamic measurements), durability (in-vitro hydrodynamic measurements, high-speed cinematography). Also, in-silico methods for PAPS will be validated on ***acute preclinical study data*** **(Group D)** by assessing engineering properties (e.g., deformations) in regard to device migration (pull tests), device perforation (CT scans and X-Ray), thrombosis (MRT scans and ultrasound doppler imaging in various implant positions). Observations of the occurrence or non-occurrence of thrombosis during **chronic preclinical study data (group D)** will also be in use for the model validation.
4. **Device effect simulation for assessing mechanisms of device failure and design optimization**: models will be applied in an iterative process for simulating device effects concerning safety, efficacy and usability endpoints. Sensitivity analyses will be performed to identify the most critical design parameters and robustness analyses will be performed to assess device performance in the presence of inter-patient variations in the target population. In the first step, simulations will be performed with generic models based on selected parameters reflecting inter-patient variability. In a second step, results will be verified by simulations of a few patient-specific models. Properties for PAPS assessment with generic and patient-specific models will be device migration, device perforation and thrombosis. TAVI assessment will be based on generic models with defined distributions of selected parameters reflecting interpatient variability and subsequent verification by simulations of a small number of patient-specific models; design features for TAVI improvement will include thrombosis, paravalvular leakage and durability.
5. **High-fidelity validation of device simulations (chronic animal studies and virtual cohorts)**: after low-fidelity validation in bench and acute animal tests, optimized models will be validated through high-fidelity validation steps with chronic animal models and virtual

cohorts, where engineering properties will be translated into clinical endpoints. The validation methodology. In the case of PAPS, we will investigate occurrence of device migration (through fluoroscopy and CT images in chronic animal experiments), device perforation (through histological investigations), thrombosis (assessment of the extent of thrombus formation by histological investigation in chronic animal studies). For TAVI, we will make use of patient-specific models and virtual cohorts to validate in-silico results with measurements as obtained from ***retrospective clinical data conducted with a predecessor device (Group C)*** and in-silico trials using virtual patient cohorts. We will assess clinical endpoints only, particularly thrombosis (through hemodynamic findings, such as vortex structures, high shear regions, wall shear stress and washout behaviour, compared to clinical results based on previous clinical studies); paravalvular leakage (spatial distribution, as well as jet form of the leakage, will be correlated between in-silico and in vivo findings); durability (mechanical failure of the prosthesis such as stent or leaflet damage occurring in clinical practice will be compared with high-stress regions according to in-silico findings).

6. **Formulation of best practices for device approval**: complementing and replacing traditional verification and validation results with simulation results for providing evidence of safety, efficacy and usability will be discussed with the regulatory authorities on the example of a mock submission for PAPS. The aim of this activity is to increase the level of confidence regulatory bodies have in-silico results and provide device manufacturers with guidelines for the use of computer methods in approval processes.

Assessment and quantification of effects on healthcare, the industry and society

The **expected impact of the use of virtual cohorts and computer simulations on the "real world", i.e., on the innovation process, the medical devices industry and the healthcare system, will be assessed through qualitative and quantitative methods**. Particularly, we will carry out an assessment of expected effects of the integration of in-silico models, tools and procedures in traditional clinical trials, evaluating the beneficial impact of this integration on the whole value chain, from preclinical and clinical trials, manufacturing and use in the healthcare industry in terms of efficiency, safety and costs, including testing, validation, preparation of regulatory approvals and time-to-market for new medical devices. This activity will be based on the following phases:

1. **Development of an in-silico trial impact assessment framework**: we will develop a framework for estimating the impact of in-silico methods and technologies on clinical and preclinical trials, and in turn on patient safety, animal welfare and industry workflow, based on theoretical, literature-based assumptions and available statistical techniques (e.g., Bayesian approaches, multivariate techniques). A set of parameters will be analyzed and selected for evaluation in the second phase, including device-related endpoints (migration, perforation, thrombosis, perivascular leakage, durability) with impact on device designs and, secondarily, patient safety, and patient-related parameters (anatomies, patient features, clinical presentations), to identify study populations where the treatment effect is higher, allowing to recruit fewer patients and have a higher power trial design.
2. **Application of the in-silico trial impact assessment framework**: the theoretical framework will be applied to the two use cases (TAVI and PAPS) under study. The previously validated in-silico models will be applied to ***additional data from real-world clinical trials that have not been used in the development or validation of in-silico models*** - to assess the validity, applicability and practical value of hypothetical assessments and to quantify the identified parameters. In addition, ***studies related to PAPS and TAVI stored in trial repositories providing IPD for sharing will be identified within the ECRIN MDR (Group C)***. Based on the quantification of those parameters, their impact on past clinical trials in target areas will be quantified. Alternative trials designs, with same clinical endpoints or equivalent (digital) ones, will be evaluated and the resulting characteristics in terms of sample size, duration, incidence of adverse events will be assessed to then serve as inputs into the other tasks. Based on these indicators, we will analyse specific outcome variables to reduce the number of animals or humans involved in trials, including surrogate endpoints highly predictive of the desired outcome to further shorten trials duration and provide earlier estimates of efficacy. During this phase, the informative power of the selected number of parameters will also be assessed as a tool in the definition of the best design for a real clinical trial (e.g., parallel or sequential design or adaptive randomisation) with additional effects on the sample size. In addition, impact is to be expected from refining clinical trials through clearer, more detailed information on potential outcomes and greater explanatory power in interpreting any adverse effects that might emerge, as well as better understanding of how the tested medical device interacts with the individual patient anatomy and predicting long-term or rare effects that clinical trials are unlikely to reveal. The selection of study parameters will be guided by principles of generalizability, allowing the resulting framework to be adaptable in other clinical areas, including drug trials.
3. **Development of a conceptual framework for the analysis of socio-economic effects**: a second theoretical framework will be developed for the quantitative and qualitative evaluation of socioeconomic effects of in-silico technologies, considering cost-effectiveness from a societal perspective and the impact on the value-chain. The conceptual framework will be developed by enriching scoping reviews of the literature through interviews with relevant stakeholders including patients and their representatives, payers (i.e., health insurers,

national health systems), regulators, manufacturers, clinicians. The aim is to provide a landscape of possible effects that the use of in-silico trials can have on the industry, the medical devices market, the healthcare system and society.

4. **Assessment of the impact on the biomedical device industry and the market**: the theoretical framework will be applied to assess the effects of the use of in-silico testing solutions in terms of reduction in the number of animal tests, the number of patients in clinical trials and thus costs and development time, device redesign and optimisation etc.. These impacts will be analysed at the level of the single firm (on the development process, collaboration efforts with universities, notified bodies and regulators as well as customers and the environment) and the market as a whole (reduced costs mean reduced capital requirements, making it easier for smaller firms to succeed increases sales potential due to the easier inclusion of children, increased safety of products with reduction of liability issues, in turn affecting market competition and the availability and diversity of products).
5. **Assessment of the socio-economic impact**: the impact of virtual cohort technology on the healthcare system and wider society will be assessed by adopting the perspectives of patients, the healthcare system and society as a whole. Based on the conceptual framework, the mechanisms laid out there will be populated with ***real-world data where possible from the previous activities, the literature (i.e., the valuation of reduced animal testing, price elasticities and impact of virtual technologies on production costs), databases (e.g., reimbursement data, prices and quantities sold, unit costs) and interviews (e.g., valuations and quality of life increase of patients, cost dynamics of firms)***. For the assessment of the impact, different scenarios will be defined based on input from stakeholders. Scenarios will differ by the perspective used (patient, healthcare system, society) as well as the counterfactual (the situation of the real world without the use of virtual cohorts). For some scenarios, the benefits will be multidimensional, and the units of measurement will differ (e.g., valuation of reduction of animal trials and cost reductions in the industry). As some parameters are also uncertain (e.g., the reduction of necessary patients in a clinical trial), sensitivity analyses will be used to assess the range of possible impacts.

Data storage and security

VRE structure

The SIMCor VRE infrastructure will have a significant computational power to allow the execution of different algorithms (e.g., statistical shape models for the creation of geometries) or advanced physics-based simulation models. To improve the runtime of computationally demanding models, advanced state-of-the-art metamodeling (reduced-order) techniques will be integrated into the infrastructure. Since many of the above-mentioned tools are run on massively parallel processors (*graphics processing units*, GPUs) UTBV will employ the methodology for GPU instance orchestration on the UTBV private cloud (Figure 1).

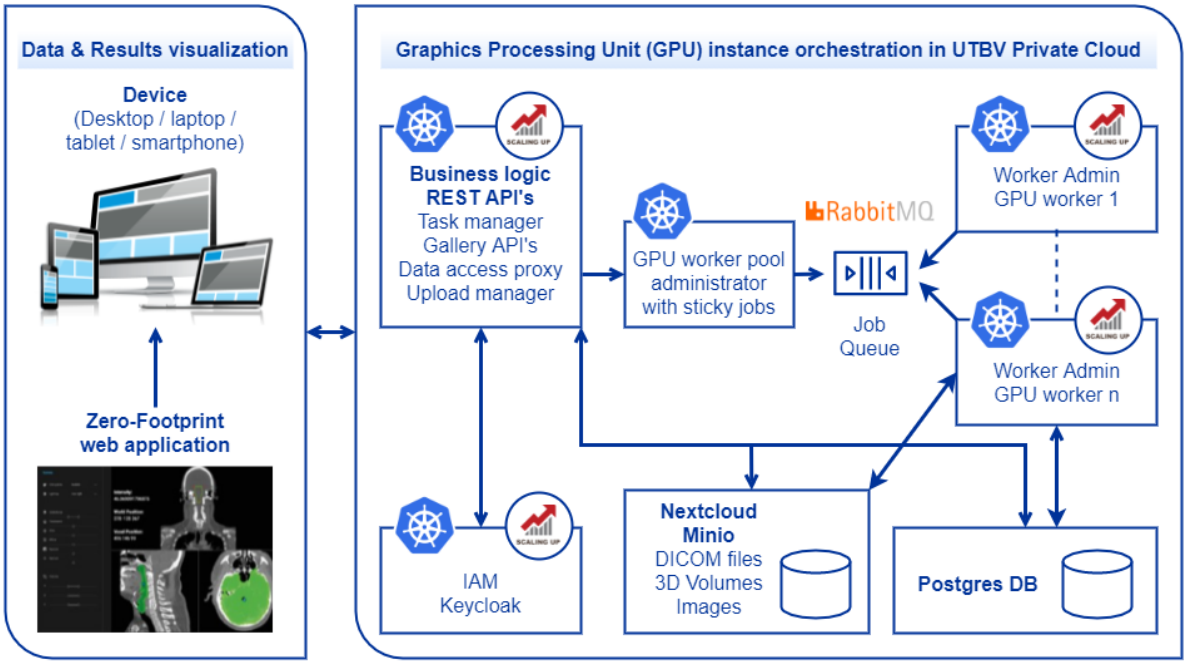

Figure 2: GPU instance orchestration in the UTBV private cloud solution for the SIMCor virtual research environment. Since many of the advanced analytics tools are run on massively parallel processors (graphics cards) a methodology for GPU instance orchestration in the UTBV private cloud solution will be employed. Data and results can be visualized using zero-footprint apps from different devices: desktop, laptop, tablet, smartphone.

Security measures

SIMCor needs to know the identity of entities that attempt actions on data, to categorize them by means of a roles system in order to systematize access control rules, to have a system that enforces those access rules, and a system for recording access to resources and various parts of the system at a reasonable and suitable granularity level (see 'Data accessibility' section).

To do that, SIMCor VRE will have an *Identity and Access Management* (IAM) system which will be defining and managing the roles and access privileges of individual network entities (users and devices) to SIMCor VRE applications and data assets. Users can include consortium partners or external partners; devices can include computers, smartphones or tablets. The core objective of the IAM systems is one digital identity per individual or item. Once the digital identity has been established, it must be maintained, modified and monitored throughout each user's or device's access lifecycle.

The integrity of SIMCor' s executables, configuration files and data (including models) must be protected at rest and in transit; only authorised entities (users, software components etc.) must be allowed to make changes and only in the ways allowed. For ensuring data protection in-transit, the

SIMCor VRE will use end-to-end SSL/TLS encrypted connections. The SIMCor VRE will store data on encrypted volumes to ensure data protection at rest. Also, the SIMCor VRE will provide data safety by using a RAID system for data storage.

FAIR and interoperability

In 2016, the *'FAIR Guiding Principles for scientific data management and stewardship'*[7] were published in Scientific Data. The authors intended to provide guidelines to improve the findability, accessibility, interoperability, and reuse of digital assets. The principles emphasize machine-actionability (i.e., the capacity of computational systems to find, access, interoperate, and reuse data with none or minimal human intervention) because humans increasingly rely on computational support to deal with data as a result of the increase in volume, complexity, and creation speed of data. The FAIR principles refer to three types of entities: data (or any digital object), metadata (information about that digital object), and infrastructure.[8]

Based on the European Commission's '*Guidelines on FAIR Data Management in Horizon 2020*'[9], the SIMCor consortium has agreed to define a common strategy for ensuring findability, accessibility, interoperability, and reusability of SIMCor digital assets based on the following steps.

1. **Making data findable, including provisions for metadata**. The first step in (re)using data is to find them. Metadata and data should be easy to find for both humans and computers. Machine-readable metadata are essential for automatic discovery of datasets and services.
   Leveraging the experience of ECRIN in the field, from M7 onwards all partners providing data, UTBV and ECRIN will carry out a series of monthly meetings, in the context of the *Data management and ethics working group* (DME-WG), to define project-related **metadata standards, persistent and unique identifiers (e.g., Digital Object Identifiers, DOIs), naming conventions, search keywords, versioning approach, metadata creation standards.**

2. **Making data openly accessible.** Similarly, based on the level of sensitivity, privacy-related risks (e.g., re-identification) and foreseen exploitation and *intellectual property rights* (IPRs) management strategies, the DME-WG will define, in due course, **which data sources (if any) will be made openly available, its rationale, methods or software tools (together with documentation and source code, if relevant) to access the data and other resources, where data, metadata documentation and code will be deposited, and how access will be provided for both open access and restricted access resources**.

3. **Making data interoperable.** In order to integrate the various SIMCor data sources and make them interoperate with applications or workflows for analysis, storage, and processing, the DME-WG will define **standard data vocabularies, based on commonly used ontologies.**

4. **Increase data re-use (through clarifying licences).** Contextually with the definition of open access for project data sources, the consortium will define (where relevant) **re-use licences, including re-use period (from/to), conditions for re-use and quality assurance processes**.

5. **Allocation of resources, roles and responsibilities.** Finally, the consortium will **estimate costs for making data FAIR and will define roles and responsibilities** of relevant partners in this process, together with costs and potential value of long term preservation.

[7] Wilkinson, M. D., Dumontier, M., Aalbersberg, I. J., Appleton, G., Axton, M., Baak, A., ... & Mons, B. (2016). The FAIR Guiding Principles for scientific data management and stewardship. Scientific data, 3(1), 1-9. Available at https://www.nature.com/articles/sdata201618

[8] Go FAIR. FAIR Principles. Available at: https://www.go-fair.org/fair-principles/

[9] European Commission. H2020 Programme. Guidelines on FAIR Data Management in Horizon 2020. Available at https://ec.europa.eu/research/participants/data/ref/h2020/grants_manual/hi/oa_pilot/h2020-hi-oa-data-mgt_en.pdf.

Data accessibility

Data access modalities

SIMCor will focus on integration, interoperability and exploitation of established infrastructures, data sources, models, tools and developed standards and methodology frameworks, in view of maximising the contribution to the research and industrial community while preserving intellectual property, following FAIR principles and EOSC initiative guidelines.

During the project timeframe, data will be accessible on the VRE for consortium partners only to carry out project research activity. After the end of the project, resources will be made available to the cardiovascular device community at large for R&D purposes, together with other project-generated resources such as virtual cohorts, device and vessel models, SOPs and implantation and device effect simulation models.

The consortium, however, will define differential access rights for system resources in relation to the exploitation and IPR management needs of developing partners, including:

1. ***Open access*** **(OA, i.e., publicly available with no registration)**
2. **Availability *upon registration* (UR)**
3. ***Authorised users*** **only (AU).**

Distinct user profiles and relevant web-based user interfaces will be created for each user group. External parties will be able to locally process (e.g., encrypt, anonymize, perturbate) their private data and send the transformed data to the cloud to be used as input for the algorithms.

Contribution to the European Open Science Cloud

The EOSC: a trusted digital platform for data and interoperable services

The *European Open Science Cloud* (EOSC), initiated by the European Commission in 2015, is an environment for hosting and processing research data to support EU science, as a trusted, virtual, federated environment that cuts across borders and scientific disciplines to store, share, process and re-use research digital objects (like publications, data, and software) following FAIR principles[10]. To do so, the EOSC brings together institutional, national and European stakeholders, initiatives and data infrastructures to develop an inclusive open science ecosystem in Europe, with the goal of bringing new insights and innovations, higher research productivity and improved reproducibility in science[11].

EOSC is part of the European Cloud Initiative — Building a competitive data and knowledge economy in Europe[12], which aims to provide European science, industry and public authorities with a world-class data infrastructure to store and manage data, high-speed connectivity to transport data, and powerful high-performance computers to process data. The Cloud Initiative aims to make it easier for researchers, businesses and public services to fully exploit the benefits of Big Data by making it possible to move, share and re-use data seamlessly across global markets and borders, and among institutions and research disciplines, in turn boosting Europe's competitiveness, especially for start-ups, SMEs and companies who can use data as a basis for R&D and innovation, and spur new industries.

[10] Wilkinson, M. D., Dumontier, M., Aalbersberg, I. J., Appleton, G., Axton, M., Baak, A., ... & Mons, B. (2016). The FAIR Guiding Principles for scientific data management and stewardship. Scientific data, 3(1), 1-9. Available at https://www.nature.com/articles/sdata201618

[11] European Commission. *European Open Science Cloud (EOSC)*. Available at https://ec.europa.eu/info/research-and-innovation/strategy/goals-research-and-innovation-policy/open-science/european-open-science-cloud-eosc_en

[12] European Commission. *The European Cloud Initiative.* Available at https://ec.europa.eu/digital-single-market/en/european-cloud-initiative.

EOSC timeline

The creation of the EOSC was proposed by the Commission to the Competitiveness Council in May 2015[13], with the aim to federate existing research data infrastructures in Europe and realise a web of FAIR data and related services for science, making research data interoperable and machine actionable following the FAIR guiding principles.
In the initial phase of development until 2020, the Commission invested around €320 million to start prototyping the EOSC through project calls in Horizon 2020.
In March 2018, the European Commission published the EOSC Implementation Roadmap detailing the main action lines of the first EOSC implementation phase until 2020.
A multi-layered, interim governance structure was established from November 2018 to steer and oversee the implementation of the EOSC from 2019-2020.
EU countries and countries associated with Horizon 2020, represented in the EOSC Governance Board, agreed unanimously to run the EOSC as a co-programmed European Partnership under Horizon Europe from 2021. The proposal for a candidate EOSC partnership was published in June following a process of co-creating its vision including strategic and operational objectives to be achieved by 2027.
In July 2020, an EOSC association was set up to provide a single voice for advocacy and represent the broader EOSC stakeholder community. This association aims to become operational by early 2021 and rapidly expand its membership.

EOSC Portal

The EOSC Portal is the universal access channel to EOSC services and resources. It already covers a wide range of disciplines including medical and health, natural sciences, physics, earth sciences, arts, humanities, agriculture, and engineering.

Through the portal, researchers and professionals can access open and seamless services, data, and other resources from a wide range of national, regional and institutional public research infrastructures across Europe. The portal facilitates interoperability of datasets and tools from different providers, and enables researchers to perform their work more quickly and disseminate their research results more widely.

The EOSC Portal[14] is the result of the progressive integration and consolidation of e-infrastructure projects, with the help of Horizon 2020 funding. It started as a collective effort from OpenAIRE, EOSC-hub, eInfraCentral and EOSCpilot projects building on the experience and technology of major pan-European e-infrastructures, universities and research infrastructures.

The EOSC Portal is currently being enhanced and maintained by the EOSC Enhance project in collaboration with the EOSC-hub and OpenAIRE projects, through the addition of further high-level functionalities and a wide range of scientific data and data analysis services. The overarching objective is to make the portal more inclusive, covering all phases of the research cycle and all scientific communities and widening its user base to the public and private sector[15].

SIMCor contribution to the EOSC

SIMCor has, among its goals, to *"Contribute to the EOSC with data, virtual cohorts, simulation models, methodologies, standards and guidelines"*. To accomplish this goal, SIMCor should become an EOSC provider. An EOSC Provider (i.e., an EOSC System User responsible for the provisioning of one or more

[13] COMMUNICATION FROM THE COMMISSION TO THE EUROPEAN PARLIAMENT, THE COUNCIL, THE EUROPEAN ECONOMIC AND SOCIAL COMMITTEE AND THE COMMITTEE OF THE REGIONS. *European Cloud Initiative - Building a competitive data and knowledge economy in Europe*. Available at https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:52016DC0178&from=EN

[14] EOSC Portal. Available at https://eosc-portal.eu/.

[15] European Commission. *European Open Science Cloud*. Available at https://digital-strategy.ec.europa.eu/en/policies/open-science-cloud

Resources to the EOSC) can be an organisation, a part of an organisation or a federation that manages and delivers Resources to End-Users. EOSC Providers can be: Resource Providers, Service Providers, Data (Source) Providers, Service Developers, Research Infrastructures, Distributed Research Infrastructures, Resource Aggregators, Thematic Clouds, Regional Clouds, etc.[16]

The 3 phases of the Onboarding Process are:

1. Provider registers him/herself into the EOSC Portal.
2. Provider onboards (and updates) the Provider information.
3. Provider onboards (and updates) the Resources offered by the Provider.

As soon as each phase is concluded (approved or rejected), the user is notified to proceed accordingly. If the three-phase onboarding process is successful, then the Provider is registered to the EOSC Portal and their Resources become publicly accessible[17].

At present, only services are being onboarded[18]. Particularly, resources must be specific services offered 'live' to customers, such as IT services, or a human service (e.g., training, consultancy). For the moment, it may not be a research product, such as a document, a dataset or a piece of software. For other research products, the rules and onboarding process are pending, and will hopefully be defined in the next period.

In the course of the project, the consortium will discuss and agree on **which resources, among real data, synthetic data, virtual cohorts, models and SOPs, are eligible to be made available through the EOSC, and under which conditions**. Meanwhile, the consortium will **make the necessary steps for the onboarding**, to possibly become an EOSC Provider by the end of the project.

[16] EOSC Provider Portal - Provider Profile. Available at https://eosc-portal.eu/providers-documentation/eosc-provider-portal-provider-profile.

[17] EOSC Provider Portal - Basic Guide. EOSC Portal Onboarding Process. Available at https://eosc-portal.eu/providers-documentation/eosc-provider-portal-basic-guide.

[18] EOSC Provider Portal - Inclusion Criteria. Available at https://eosc-portal.eu/providers-documentation/eosc-provider-portal-inclusion-criteria.

Appendix

Data sources

Data sources used in the project, as reported in *Table 1,* are described in detail in the tables below along with the following fields (please note that legal terms used are purely indicative and shall not be intended as strictly binding under a legal assessment perspective):

- **Dataset name**
- **Data Controller** *(partner providing/producing the data)*
- **Source** *(data directly collected from data subjects/patients, or made available by third parties)*
- **Type** *(pre/clinical, pro/retrospective)*
- **Activity from which the data derive** *(clinical routine data, clinical trial, preclinical study, etc.)*
- **Main purpose of data** *(clinical care, research, etc.)*
- **Data produced specifically for this project** *(Y/N)*
- **If not, PROJECT data were produced in/for** *(if relevant; grant name, acronym and number, funding institution, period)*
- **If not, CLINICAL TRIAL data were produced in/for** *(if relevant; clinical trial name and number, leading institution, period)*
- **Information notice / "informed consent"** *(Y/N; whether data were collected by providing data subjects/patients with an information notice aligned with the GDPR or with laws applicable before the GDPR)*
- **Legal basis for the collection of data** *(consent, or other purposes such as: contract execution, scientific research in the public interest, etc.)*
- **Beneficiary(ies)** *(centres utilising the data and institutions accessing the data)*
- **Specific activities to be performed with the data within SIMCor** *(project activity/ies involved, including WP and tasks)*
- **Clinical focus** *(TAVI, PAPS)*
- **Subjects** *(patients/animal species, healthy/disease, age, gender)*
- **Size** *(n° of records)*
- **Period of collection**
- **Variables**
- **Format(s)**
- **Type of exams** *(e.g., MRI, blood test, etc.)*
- **Pseudo/anonymisation procedures applied to the data** *(e.g., removal of identifiers and quasi-identifiers and which ones, other. Existing links/keys to original data. Encryption techniques and other security measures applied, etc.)*
- **Data flow description** *(e.g., hospital repository ---> temporal working environment ---> VRE)*
- **Level of re-identification risks foreseen within the project** *(high/medium/low)*

- **Access status after the end of the project (for inclusion in the EOSC):** *open access, upon subscription, restricted (for authorised users only).*

(A) CLINICAL ROUTINE DATA from hospital repositories (2014–2023)

Dataset name	WP5 – Human Data TAVI
Data Controller	CHA
Source	directly collected from patients
Type	retrospective
Activity from which the data derive	clinical routine data
Main purpose of data	data is routinely acquired for planning of the TAVI procedure
Data produced specifically for this project	N
If not, PROJECT data were produced in/for	N/A
If not, CLINICAL TRIAL data were produced in/for	N/A
Information notice / "informed consent"	Not required, due to retrospective nature of data
Legal basis for the collection of data	Scientific research in the public interest, German legislation (Berliner Landeskrankenhausgesetz)
Beneficiary(ies)	
Specific activities to be performed with the data within SIMCor	Data processing (WP6): segmentation of the patient-specific anatomy of left ventricle, aorta and aortic valve; measurement and/or collection of anatomical parameters (e.g., diameters CHA, UCL, TUE, BIO, IIB, PHI, UTBV, TUG, sizes, aortic valve area) and hemodynamic parameters (e.g., stroke volumes, volume flow curves, pressure gradients). Data use (WP7-9): virtual cohort generation, device implantation simulation and device effect simulation.
Clinical focus	TAVI
Subjects	adult patients (age > 18 years) with aortic stenosis, both genders
Size	approx. 250
Period of collection	2010 – 2020
Variables	For an exhaustive list of parameters and variables to be collected, we refer to deliverable 5.1
Format(s)	Image data: DICOM. Surface geometries: triangulated surface mesh formats, e.g. STL file format. All other data: either Excel or CSV tables.
Type of exams	Computer tomography; magnetic resonance imaging; cardiac catheterization; cuff pressure measurements; anamnesis / case history.
Pseudo/anonymisation procedures applied to the data	Pseudonymization by removal and/or omitting of all identifying information: name will be omitted, age will only be provided in categories
Data flow description	All data, except patient-specific image data, will be derived from clinical information systems (e.g., PACS, document archives) and will be directly submitted to the VRE. Image data won't be shared but will be processed (WP6) at CHA
Level of re-identification risks foreseen within the project	Low; image data won't be shared. Re-identification would still be difficult using the image data, as it does not contain any characteristics allowing easy recognition of the patient (e.g., face). Without image data, de-identification would only be possible by full access to the clinical information systems at CHA and even then, parameters must be gathered from different subsystems to allow cross-referencing.
Access status after the end of the project (for inclusion in the EOSC)	Most likely restricted, we'll try to get information whether unrestricted access can be realised without explicit opt-in-consent by the patients

Dataset name	R1_TAVI_London
Data Controller	UCL
Source	Data will be collected retrospectively from Barts Heart Centre at St Bartholomew's Hospital (Barts)
Type	Clinical retrospective
Activity from which the data derive	Clinical routine data
Main purpose of data	Clinical care
Data produced specifically for this project	N
If not, PROJECT data were produced in/for	N/A
If not, CLINICAL TRIAL data were produced in/for	N/A
Information notice / "informed consent"	Consent from patients is not obtained for several reasons; the data is collected for clinical reasons, the large number of patients involved, many patients are elderly, have died or cannot be contacted anymore and the registry already has a large number of patients on it, which makes obtaining retrospective consent very difficult. We will ensure that we comply with the National Data Opt Out for any data use after the compliance deadline (or after the Trust declare compliance if earlier) by using the NHS digital Message exchange for social care and health (MESH) opt out system, which will identify any patients that have opted out of having their data used. These patients will be removed from any research.
Legal basis for the collection of data	Scientific research
Beneficiary(ies)	CHA, UCL, TUE, BIO, IIB, PHI, UTBV, TUG
Specific activities to be performed with the data within SIMCor	Data processing (WP6): segmentation of the patient-specific anatomy of left ventricle, aorta and aortic valve; measurement and/or collection of anatomical parameters (e.g., diameters CHA, UCL, TUE, BIO, IIB, PHI, UTBV, TUG, sizes, aortic valve area) and hemodynamic parameters (e.g., stroke volumes, volume flow curves, pressure gradients). Data use (WP7-9): virtual cohort generation, device implantation simulation and device effect simulation.
Clinical focus	TAVI
Subjects	Patients aged >16 years, treated at Barts, that underwent (or will undergo) TAVI over the period 2014-2023, in accordance with the guidelines recommended by the European Society of Cardiology (ESC), disease (see demographic of D5.1)
Size	125
Period of collection	2014-2023
Variables	See D5.1
Format(s)	Tables of numerical and categorical values and 3D models as derived from medical images
Type of exams	Imaging assessment including CT, US
Pseudo/anonymisation procedures applied to the data	When data is used for research, the databases and clinical systems are used to extract the necessary data, the clinical care team will pseudonymise all data before being passed onto the research team. The only exception is when data is sought from NHS digital. In this case, a minimum dataset of identifiable data required will be constructed and submitted to NHS digital via established, secure and encrypted pathways.
Data flow description	Hospital repository ---> temporal working environment ---> VRE
Level of re-identification risks foreseen within the project	Low
Access status after the end of the project (for inclusion in the EOSC)	Restricted

Dataset name	WP5 –Human Data PAPS
Data Controller	**CHA**
Source	Directly collected from patients
Type	Retrospective
Activity from which the data derive	Clinical routine data
Main purpose of data	Clinical care
Data produced specifically for this project	no
If not, PROJECT data were produced in/for	Data is acquired for clinical routine (e.g., diagnosis and/or treatment planning)
If not, CLINICAL TRIAL data were produced in/for	N/A
Information notice / "informed consent"	Not required, due to retrospective nature of data
Legal basis for the collection of data	Scientific research in the public interest, German legislation (Berliner Landeskrankenhausgesetz)
Beneficiary(ies)	BIO, TUE, PHI, CHA
Specific activities to be performed with the data within SIMCor	Data processing (WP6): segmentation of geometries, measurement of hemodynamic and anatomic parameters): Processed data will be used throughout WP 7 to 9, for virtual cohort generation, device implantation simulation and device effect simulation.
Clinical focus	PAPS
Subjects	Adult and paediatric patients (age >= 6 years) with pulmonary hypertension and/or heart failure, both genders
Size	Approx. 250
Period of collection	2010 – 2020
Variables	For an exhaustive list of parameters and variables to be collected, we refer to deliverable 5.1
Format(s)	Image data: DICOM. Surface geometries: triangulated surface mesh formats, e.g., STL file format. All other data: either Excel or CSV tables
Type of exams	Computer tomography, magnetic resonance imaging, cardiac catheterization, cuff pressure measurements, anamnesis / case history.
Pseudo/anonymisation procedures applied to the data	Pseudonymization by removal and/or omitting of all identifying information: name will be omitted, age will only be provided in categories.
Data flow description	All data, except patient-specific image data, will be derived from clinical information systems (e.g., PACS, document archives) and will be directly submitted to the VRE. Image data won't be shared but will be processed (WP6) at CHA
Level of re-identification risks foreseen within the project	Low; image data won't be shared. Re-identification would still be difficult using the image data, as it does not contain any characteristics allowing easy recognition of the patient (e.g., face). Without image data, de-identification would only be possible by full access to the clinical information systems at CHA and even then, parameters must be gathered from different sub-systems to allow cross-referencing
Access status after the end of the project (for inclusion in the EOSC)	Most likely restricted, we'll try to get information whether unrestricted access can be realised without explicit opt-in-consent by the patients.

(C) CLINICAL TRIAL DATA from consortium's previous research, network registries and open data

Dataset name	WP5 – SMART
Data Controller	CHA
Source	directly collected from patients
Type	Retrospective
Activity from which the data derive	clinical routine data
Main purpose of data	data was routinely collected for diagnosis and/or treatment planning
Data produced specifically for this project	N
If not, PROJECT data were produced in/for	SMART. Funded by the German Federal Ministry for Education and Research
If not, CLINICAL TRIAL data were produced in/for	"SMART - Systems Medicine of Heart Failure", registered at www.clinicaltrials.goc under trial #: NCT03172338
Information notice / "informed consent"	Y (before GDPR)
Legal basis for the collection of data	consent and scientific research in the public interest, German legislation (Berliner Landeskrankenhausgesetz)
Beneficiary(ies)	CHA, UCL, TUE, BIO, IIB, PHI, UTB, TUG
Specific activities to be performed with the data within SIMCor	Data processing (WP6): segmentation of the patient-specific anatomy of left ventricle, aorta and aortic valve; measurement and/or collection of anatomical parameters (e.g., diameters, sizes, aortic valve area) and hemodynamic parameters (e.g., stroke volumes, volume flow curves, pressure gradients) Data usage: processed data will be used throughout WP 7 to 9, for virtual cohort generation, device implantation simulation and device effect simulation.
Clinical focus	TAVI
Subjects	Adult patients (age > 18 years) with aortic stenosis, both genders
Size	approx. 60
Period of collection	2015 – 2019
Variables	For an exhaustive list of parameters and variables to be collected, we refer to deliverable 5.1
Format(s)	image data: DICOM; surface geometries: triangulated surface mesh formats, e.g., STL file format; all other data: either Excel or CSV tables.
Type of exams	computer tomography; magnetic resonance imaging.
Pseudo/anonymisation procedures applied to the data	data is only available in already pseudonymized manner, as the project in which the data was acquired is already ended. No directly or indirectly identifying information (e.g., name, address, etc.) is available for this data set.
Data flow description	All data, except patient-specific image data, will be derived from clinical information systems (e.g. PACS, document archives) and will be directly submitted to the VRE. Iimage data won't be shared but will be processed (WP6) at CHA
Level of re-identification risks foreseen within the project	Low; image data won't be shared. Re-identification would still be difficult using the image data, as it does not contain any characteristics allowing easy recognition of the patient (e.g., face). Without image data, de-identification would only be possible by full access to the clinical information systems at CHA and even then, parameters must be gathered from different sub-systems to allow cross-referencing
Access status after the end of the project (for inclusion in the EOSC)	most likely restricted, we'll try to get information whether unrestricted access can be realised without explicit opt-in-consent by the patients.

Dataset name	WP5 – EurValve
Data Controller	CHA
Source	directly collected from patients
Type	Retrospective
Activity from which the data derive	clinical routine data
Main purpose of data	data was routinely collected for diagnosis and/or treatment planning
Data produced specifically for this project	N
If not, PROJECT data were produced in/for	EurValve. Funded by the European Commission under grant #689617
If not, CLINICAL TRIAL data were produced in/for	"Personalised Decision Support for Heart Valve Disease", registered at www.clinicaltrials.gov under trial #: NCT04068740
Information notice / "informed consent"	Y (before GDPR)
Legal basis for the collection of data	consent and scientific research in the public interest, German legislation (Berliner Landeskrankenhausgesetz)
Beneficiary(ies)	CHA, UCL, TUE, BIO, IIB, PHI, UTB, TUG
Specific activities to be performed with the data within SIMCor	Data processing (WP6): segmentation of the patient-specific anatomy of left ventricle, aorta and aortic valve; measurement and/or collection of anatomical parameters (e.g., diameters, sizes, aortic valve area) and hemodynamic parameters (e.g., stroke volumes, volume flow curves, pressure gradients) Data usage: processed data will be used throughout WP 7 to 9, for virtual cohort generation, device implantation simulation and device effect simulation.
Clinical focus	TAVI
Subjects	adult patients (age > 18 years) with aortic stenosis, both genders
Size	approx. 120
Period of collection	2016-2019
Variables	For an exhaustive list of parameters and variables to be collected, we refer to deliverable 5.1
Format(s)	Image data: DICOM. Surface geometries: triangulated surface mesh formats, e.g., STL file format. All other data: either Excel or CSV tables.
Type of exams	computer tomography, magnetic resonance imaging
Pseudo/anonymisation procedures applied to the data	data is only available in already pseudonymized manner, as the project in which the data was acquired is already ended. No directly or indirectly identifying information (e.g., name, address, etc.) is available for this data set.
Data flow description	All data, except patient-specific image data, will be derived from clinical information systems (e.g. PACS, document archives) and will be directly submitted to the VRE. Image data won't be shared but will be processed (WP6) at CHA
Level of re-identification risks foreseen within the project	Low; image data won't be shared. Re-identification would still be difficult using the image data, as it does not contain any characteristics allowing easy recognition of the patient (e.g., face). Without image data, de-identification would only be possible by full access to the clinical information systems at CHA and even then, parameters must be gathered from different sub-systems to allow cross-referencing
Access status after the end of the project (for inclusion in the EOSC)	most likely restricted, we'll try to get information whether unrestricted access can be realised without explicit opt-in-consent by the patients

Dataset name	WP5 – CARDIOPROOF
Data Controller	CHA
Source	directly collected from patients
Type	Retrospective
Activity from which the data derive	clinical routine data
Main purpose of data	data was routinely collected for diagnosis and/or treatment planning
Data produced specifically for this project	N
If not, PROJECT data were produced in/for	Cardioproof. Funded by the European Commission under grant #611232
If not, CLINICAL TRIAL data were produced in/for	"Proof of Concept of Model Based Cardiovascular Prediction", registered at www.clinicaltrials.goc under trial #:NCT02591940
Information notice / "informed consent"	Y (before GDPR)
Legal basis for the collection of data	consent and scientific research in the public interest, German legislation (Berliner Landeskrankenhausgesetz)
Beneficiary(ies)	CHA, UCL, TUE, BIO, IIB, PHI, UTB, TUG
Specific activities to be performed with the data within SIMCor	Data processing (WP6): segmentation of the patient-specific anatomy of left ventricle, aorta and aortic valve; measurement and/or collection of anatomical parameters (e.g., diameters, sizes, aortic valve area) and hemodynamic parameters (e.g., stroke volumes, volume flow curves, pressure gradients) Data usage: processed data will be used throughout WP 7 to 9, for virtual cohort generation, device implantation simulation and device effect simulation.
Clinical focus	TAVI
Subjects	adult patients (age > 18 years) with aortic stenosis, both genders
Size	approx. 120
Period of collection	2013-2016
Variables	For an exhaustive list of parameters and variables to be collected, we refer to deliverable 5.1
Format(s)	image data: DICOM; surface geometries: triangulated surface mesh formats, e.g., STL file format; all other data: either Excel or CSV tables.
Type of exams	computer tomography. magnetic resonance imaging
Pseudo/anonymisation procedures applied to the data	data is only available in already pseudonymized manner, as the project in which the data was acquired is already ended. No directly or indirectly identifying information (e.g., name, address, etc.) is available for this data set.
Data flow description	all data, except patient-specific image data, will be derived from clinical information systems (e.g., PACS, document archives) and will be directly submitted to the VRE. image data won't be shared but will be processed (WP6) at CHA
Level of re-identification risks foreseen within the project	Low; image data won't be shared. Re-identification would still be difficult using the image data, as it does not contain any characteristics allowing easy recognition of the patient (e.g., face). Without image data, de-identification would only be possible by full access to the clinical information systems at CHA and even then, parameters must be gathered from different sub-systems to allow cross-referencing
Access status after the end of the project (for inclusion in the EOSC)	most likely restricted, we'll try to get information whether unrestricted access can be realised without explicit opt-in-consent by the patients

Dataset name	WP5 – ArtiCardio
Data Controller	CHA
Source	purely synthetic data generated using statistical shape modelling
Type	n/a
Activity from which the data derive	n/a
Main purpose of data	data was generated for the purpose of training of machine learning algorithms
Data produced specifically for this project	N
If not, PROJECT data were produced in/for	Articardio. Funded by the German Federal Ministry for Education and Research under grant #13GW0208B
If not, CLINICAL TRIAL data were produced in/for	n/a
Information notice / "informed consent"	No, no actual patient data involved
Legal basis for the collection of data	GDPR does not apply, as the data does not contain any patient-specific or patient-related information but is purely synthetic in nature
Beneficiary(ies)	CHA, UCL, TUE, BIO, IIB, PHI, UTB, TUG
Specific activities to be performed with the data within SIMCor	Data will be used throughout WP 7 to 9, for virtual cohort generation, device implantation simulation and device effect simulation
Clinical focus	TAVI
Subjects	n/a
Size	approx. 1200
Period of collection	2017 – 2020
Variables	only geometric parameters described in Deliverable 5.1 as well as simple demographic parameters (e.g. age, weight). However, all parameters are generated using statistical shape models and random number generators
Format(s)	surface geometries: triangulated surface mesh formats, e.g., STL file format. all other data: either Excel or CSV tables
Type of exams	none
Pseudo/anonymisation procedures applied to the data	data does not contain any information on real subjects or patients
Data flow description	all data will be directly submitted to the VRE
Level of re-identification risks foreseen within the project	none
Access status after the end of the project (for inclusion in the EOSC)	Open access

Dataset name	TAVI and PAPS clinical trials are identified by the metadata repository (MDR) developed by ECRIN and partners. The MDR has access to metadata of around 600000 clinical studies and nearly 1 Million related data objects (e.g., study protocol, statistical analysis plan, CRF, individual participant data). Currently, it covers all WHO study registries and a selection of repositories storing clinical trial data. With a powerful search engine and filtering process the MDR is able to discover clinical studies from any medical field, where individual participant data are available. The metadata are retrieved and the access procedure to the data is presented (public, different types of managed access). Identification of relevant trials is performed with the MDR user portal using adequate search and filtering (http://51.210.99.18/). The parameters to be accessed are defined in the ECRIN metadata schema (Based upon the ECRIN metadata schema - version 5) (https://zenodo.org/record/4133889#.X_RoY9hKjcs). The MDR is explained in detail in a wiki (http://ecrin-mdr.online/index.php/The_ECRIN_Metadata_Schemas).
Data Controller	Usually the data controller is the principal investigator, who shares the data of a clinical trial via a repository. Neither ECRIN nor other SIMCor partners will have the role of data controller.
Source	Sources are datasets shared by the data controllers through a dedicated repository and identified via the ECRIN MDR. The MDR data sources are listed in the wiki: http://ecrin-mdr.online/index.php/MDR_Data_Sources.
Type	Prospective interventional trials, randomised trials
Activity from which the data derive	Clinical trials
Main purpose of data	research
Data produced specifically for this project	No
If not, PROJECT data were produced in/for	N/A
If not, CLINICAL TRIAL data were produced in/for	For individual trial sponsor/principal investigator.
Information notice / "informed consent"	This information is kept by the data object schema from the ECRIN MDR: E. Obiect Attributes and Descriptors. E.5 Associated consent
Legal basis for the collection of data	This information is kept by the data object schema from the ECRIN MDR: F. Object Location and Access details. F.2.Access type. F.3 Access details. F.5 Rights: Including the information above (informed consent).
Beneficiary(ies)	Beneficiaries from SIMCor.
Specific activities to be performed with the data within SIMCor	Mainly in WP10 Quantification of healthcare, industry and socioeconomic effects for carrying out the Tasks 10.1 and 10.2 (in-silico trial impact assessment framework development and application). The exact use of the data will be defined as the Tasks evolve and the deliverables are due.
Clinical focus	TAVI and PAPS
Subjects	Depends on the individual clinical trial selected.
Size	Depends on the individual clinical trial selected.
Period of collection	Depends on the individual clinical trial selected.
Variables	Depends on the individual clinical trial selected.
Format(s)	Depends on the individual clinical trial selected.
Type of exams	Depends on the individual clinical trial selected.
Pseudo/anonymisation procedures applied to the data	This information is kept by the data object schema from the ECRIN MDR: F. Object Attributes and Descriptors. E.4 De-identification level. E.6 Description E.7 EOSC category.
Data flow description	This has still to be decided as the project evolves. It depends mostly on the interaction between the VRE and the in-silico trial impact assessment framework.
Level of re-identification risks foreseen within the project	Has to be determined dependent on the trials selected.
Access status after the end of the project (for inclusion in the EOSC)	The use of the trial data is not restricted to the SIMCor project. The data access conditions for the trials are defined in the data sharing plans of the individual trials, which are usually not restricted to a specific project.

(D) PROSPECTIVE ANIMAL STUDY to be conducted in SIMCor

Dataset name	WP5 – Animal Data PAPS
Data Controller	BIO, CHA
Source	directly collected from animals
Type	prospective study
Activity from which the data derive	preclinical study
Main purpose of data	research
Data produced specifically for this project	Yes
If not, PROJECT data were produced in/for	n/a
If not, CLINICAL TRIAL data were produced in/for	n/a
Information notice / "informed consent"	n/a
Legal basis for the collection of data	n/a
Beneficiary(ies)	BIO, TUE, CHA, TUG
Specific activities to be performed with the data within SIMCor	Data Processing (WP6): segmentation of geometries, measurement of haemodynamic and anatomic parameters. Data usage: processed data will be used throughout WP 7 to 9, for virtual cohort generation, device implantation simulation and device effect simulation. Segmentation of the patient-specific anatomy of the pulmonary artery. Measurement and/or collection of anatomical parameters (e.g., diameters, sizes, aortic valve area) and hemodynamic parameters (e.g., stroke volumes, volume flow curves, pressure gradients). Additional activities for animal data: in-vivo pressure measurements using the PAPS and a catheter, for validation of pressure measurements; collection of tissue samples post euthanasia; CT acquisition before implantation, during the chronic trial and after euthanasia.
Clinical focus	PAPS
Subjects	pig and sheep
Size	20
Period of collection	2021 – 2023
Variables	For an exhaustive list of parameters and variables to be collected, we refer to deliverable 5.1
Format(s)	image data: DICOM. surface geometries: triangulated surface mesh formats, e.g., STL file format. all other data: either Excel or CSV tables
Type of exams	computer tomography. magnetic resonance imaging. cardiac catheterization. cuff pressure measurements. anamnesis / case history
Pseudo/anonymisation procedures applied to the data	n/a
Data flow description	all data, except patient-specific image data, will be derived from clinical information systems (e.g. PACS, document archives) and will be directly submitted to the VRE. image data won't be shared but will be processed (WP6) at CHA
Level of re-identification risks foreseen within the project	n/a
Access status after the end of the project (for inclusion in the EOSC)	most likely restricted, we'll try to get information whether unrestricted access can be realised

(E) PRECLINICAL DATA from consortium's previous research

Dataset name	Acute and chronic pig and sheep data for TAVI
Data Controller	CHA
Source	Data directly collected from subjects
Type	Preclinical, retrospective
Activity from which the data derive	Preclinical study
Main purpose of data	Research
Data produced specifically for this project	N
If not, PROJECT data were produced in/for	N/A; data originated from different animal experiments
If not, CLINICAL TRIAL data were produced in/for	N/A
Information notice / "informed consent"	N/A
Legal basis for the collection of data	State approval for animal trial
Beneficiary(ies)	CHA, IIB, PHI, UCL, TUE
Specific activities to be performed with the data within SIMCor	Image processing, segmentation, statistical analysis, model generation
Clinical focus	TAVI
Subjects	Sheep and pigs, healthy
Size	30 pigs, 15 sheep
Period of collection	2010-2020
Variables	None
Format(s)	DICOM, segmented parameters
Type of exams	CT, MRT
Pseudo/anonymisation procedures applied to the data	N/A
Data flow description	CT/MRT: hospital repository @ CHA → temporal working environment → VRE
Level of re-identification risks foreseen within the project	N/A
Access status after the end of the project (for inclusion in the EOSC)	restricted to partners for project work, no access after end of project

Dataset name	Previous chronic study for PAPS
Data Controller	BIO
Source	Data directly collected from subjects
Type	Preclinical, retrospective
Activity from which the data derive	Preclinical study
Main purpose of data	Research
Data produced specifically for this project	N
If not, PROJECT data were produced in/for	Grant name: Response FV16 institution: BMBF grant number: 03ZZ0926C, period: 2019-2021
If not, CLINICAL TRIAL data were produced in/for	N/A
Information notice / "informed consent"	N/A
Legal basis for the collection of data	State approval for animal trial
Beneficiary(ies)	CHA, TUG, TUB, IIB, BIO, UCL, TUE
Specific activities to be performed with the data within SIMCor	Image processing, segmentation, statistical analysis, model generation
Clinical focus	PAPS
Subjects	sheep, healthy
Size	6
Period of collection	6 months
Variables	none
Format(s)	DICOM, segmented parameters, ASCII, jpg
Type of exams	CT, MRT, PAPS data (pressure, temperature), catheter pressure data, histology cut images and reports
Pseudo/anonymisation procedures applied to the data	N/A
Data flow description	PAPS: BIO owned data base; catheter: BIO owned data base, CT: hospital repository @ CHA à temporal working environment à VRE
Level of re-identification risks foreseen within the project	N/A
Access status after the end of the project (for inclusion in the EOSC)	BIO-data: restricted to partners for project work, no access after end of project

(F) HUMAN AND ANIMAL TISSUE SAMPLES for mechanical tests

Dataset name	Mechanical tests and structural investigations on human tissue
Data Controller	Graz University of Technology (Institute of Biomechanics) - TUG
Source	University Medical Center Rostock (Institute of Anatomy)
Type	Human tissue
Activity from which the data derive	Organ donation
Main purpose of data	Obtaining the mechanical behaviour and the structural composition of the ascending aorta and pulmonary artery for the development of validated constitutive models
Data produced specifically for this project	Y
If not, PROJECT data were produced in/for	N/A
If not, CLINICAL TRIAL data were produced in/for	N/A
Information notice / "informed consent"	Y
Legal basis for the collection of data	Scientific research in the public interest
Beneficiary(ies)	Graz University of Technology (Institute of Biomechanics)
Specific activities to be performed with the data within SIMCor	Validation of the developed constitutive models (WP8, Task 3)
Clinical focus	TAVI, PAPS
Subjects	Human tissue, healthy, age group 60+ years, male and female
Size	10 human samples
Period of collection	June 1, 2021 – June 1, 2022
Variables	N/A
Format(s)	N/A
Type of exams	Biaxial extension tests, SHG (second harmonic generation) imaging
Pseudo/anonymisation procedures applied to the data	Removal of identifiers
Data flow description	Institute of Anatomy, University Medical Center Rostock → Laboratory of Graz University of Technology (Institute of Biomechanics) → post-processing of the experimental data → Validation of constitutive models
Level of re-identification risks foreseen within the project	Low
Access status after the end of the project (for inclusion in the EOSC)	Human tissue: Restricted (for authorised users only) Post-processed experimental data: Open access

Dataset name	Mechanical tests and structural investigations on animal tissue (sheep and porcine)
Data Controller	Graz University of Technology (Institute of Biomechanics) - TUG
Source	Sheep tissue: Charité; Porcine tissue: Butcher "Marcher" (Lagergasse 158. 8020 Graz)
Type	Animal tissue (sheep, porcine)
Activity from which the data derive	Sheep tissue: Animal trials; Porcine tissue: Slaughter
Main purpose of data	Obtaining the mechanical behaviour and the structural composition of the ascending aorta and pulmonary artery for the development of validated constitutive models
Data produced specifically for this project	Y
If not, PROJECT data were produced in/for	N/A
If not, CLINICAL TRIAL data were produced in/for	N/A
Information notice / "informed consent"	N/A
Legal basis for the collection of data	Scientific research in the public interest
Beneficiary(ies)	Graz University of Technology (Institute of Biomechanics)
Specific activities to be performed with the data within SIMCor	Validation of the developed constitutive models (WP8, Task 3)
Clinical focus	TAVI, PAPS
Subjects	Animal tissue (sheep, porcine), healthy, age group (porcine: none, sheep: none), male and female
Size	10 sheep samples, 10 porcine samples
Period of collection	June 1, 2021 – June 1, 2022
Variables	N/A
Format(s)	N/A
Type of exams	Biaxial extension tests, SHG (second harmonic generation) imaging
Pseudo/anonymisation procedures applied to the data	N/A
Data flow description	Charité/Butcher "Marcher" → Laboratory of Graz University of Technology (Institute of Biomechanics) → Post-processing of the experimental data → Validation of constitutive models
Level of re-identification risks foreseen within the project	Low
Access status after the end of the project (for inclusion in the EOSC)	Animal tissue: Restricted (for authorised users only) Post-processed experimental data: Open access