EuroHeart

European Unified Registries for Heart Care Evaluation and Randomised Trials

EuroHeart Consolidation

Phase Planning

European Unified Registries on Heart care Evaluation and Randomised Trials

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Executive Summary

EuroHeart is an ESC initiative that started with a Pilot Phase from July 2019 to the end of June 2022. The initiative will continue into the next phase named the Consolidation phase up to the end of December 2024.

The aim of EuroHeart is to create a network of National/Regional Quality Registries for quality development in common cardiovascular diseases areas (ACS-PCI, Heart failure, Atrial fibrillation, and Aortic valve disease – TAVI) using continuous collection of agreed standardised data variables and direct online feedback to users on processes of care and outcomes. As part of the project, EuroHeart has developed an optional Registry IT Platform that may be licensed by the participating National Registries. Based on this collaborative international infrastructure, EuroHeart supports the improvement of the quality and equity of cardiovascular care and provides an infrastructure for collaborative outcome research such as registry-based randomised clinical trials and safety surveillance of novel drugs and devices in Europe.

The results of the pilot phase July 2019 – June 2022 can be summarised as follows:

1. The EuroHeart optional Registry IT Platform has been developed. A demo version of the Registry IT Platform is available for consultation on the EuroHeart website.
2. Presently, nine countries are part of the collaboration: Estonia and Romania have implemented the Registry IT Platform. Lithuania has also opted for the Registry IT Platform, but the project has been put on hold due to lack of local resources that were dispatched towards urgent tasks related to their geopolitical situation. Six countries are collaborating by using the common dataset. These are Hungary, Portugal, Denmark, Sweden, Iceland and one non-European country Singapore.
3. The EuroHeart Data standards have been developed for four disease domains: ACS-PCI, Heart Failure, Atrial fibrillation, TAVI and are published as scientific manuscripts.
4. Patient registration started during Q3-Q4 2021 in 194 centres. Two countries that have implemented the EuroHeart IT-platform.
5. Collaboration has been established with nine industry partners and one research foundation which has certified funding for the EuroHeart Pilot Phase.

Consolidation phase 2022 – 2024:

The EuroHeart project is transitioning into a 2-year Consolidation phase up to the end of December 2024. In this project phase, **the focus will be on expanding the network of countries and developing a stable long-term organisation enabling the execution of specific research projects**. By the end of the Consolidation phase, the EuroHeart network is expected to consist of 15 countries, which should constitute a sufficiently large network and be technically and organisationally prepared to start the first registry-based clinical trial (R-RCT) or drug/device surveillance project.

The specific goals of the Consolidation phase are planned to be:

1. Continue supporting ongoing and novel quality registries in the current network of nine countries.
2. Expand the EuroHeart collaboration to at least six additional countries.
3. Provide statistical analyses/reports on processes of care and outcomes in the network.
4. Develop data standards for cardiovascular outcomes.
5. Technical implementation of outcome and follow-up variables in existing domains.
6. Initiate an international framework to support EuroHeart R-RCTs or safety surveillance of novel drugs and devices.
7. Develop a stable, sustainable long-term governance for EuroHeart.

1. EuroHeart Mission

The mission of EuroHeart is to develop and maintain an international collaboration that provides general availability to systems with continuous online registration of high quality and harmonised patient data at entry and over time, with real-time information supporting continuous improvement of care and outcomes in patients with common cardiovascular diseases. EuroHeart will also provide an international infrastructure for cost-effective safety surveillance of new drugs and devices and registry-based randomised clinical trials in a general patient population across multiple geographies.

2. Introduction

EuroHeart aims to create a network of National/Regional Quality Registries in common cardiovascular disease areas that share the same data variables and data definitions. The EuroHeart programme will support the improvement of quality of care at the national and local level through continuous and structured collection of data, direct feedback to users on processes of care and outcomes, and national and international collaboration on the common goals. The EuroHeart collaboration also provides an optional Registry IT Platform supporting the registration and the opportunities to conduct outcome research and collaboration on drug/device surveillance studies and registry-based randomised clinical trials (R-RCTs).[1]

The participating national registries own their data and will be fully responsible for their registry infrastructure, IT systems, databases, and statistical analyses of patient level data. The EuroHeart collaboration on these observational data will only be at the level of aggregated data and compiled according to pre-defined statistical analyses. The aggregated results may then be transferred from the National Centres to the **EuroHeart Data Science Center** and used for meta-analyses and tabular or graphical comparisons of patient and disease characteristics, processes of care and outcomes between different countries, regions and other pre-defined subpopulations in countries participating in EuroHeart.

[1] For more details on the rationale of EuroHeart visit the *EuroHeart Pilot Phase Project Description* available on www.escardio.org/research/euroheart

If a participating country agrees to engage in specific research projects for device-drug monitoring or R-RCTs, these projects will be run under the same regulations as conventional clinical trials, where the recording of pre-specified data will be based on patient informed consent and applicable approvals by Ethical Committees and Legal Authorities.

The EuroHeart Pilot phase started in July 2019 and ended in June 2022. The planned milestones and deliverables were achieved (see page 3).

The project was assessed by external Auditors, and their evaluation was presented to the ESC Management Group in Q2 2022. In 2023, EuroHeart will deliver the first official annual report for 2022 data, including a high-level summary of the quality of care in ACS-PCI in the EuroHeart Network.

The EuroHeart programme is transitioning to a 2-year Consolidation phase from 5 October 2022 to 31 December 2024. The main objectives of the Consolidation phase are to expand the network to be sufficiently large and technically capable to perform the first R-RCT) or safety surveillance project. For the Consolidation phase, the activities will be managed within the same governance and organisational structure as during the Pilot phase, as outlined in **Figure 1**. During the Consolidation phase, EuroHeart and ESC will develop a new organisational structure for the planned long-term governance of the organisation. From January 2025, EuroHeart is expected to become a financially self-sustained and stable organisation within the ESC.

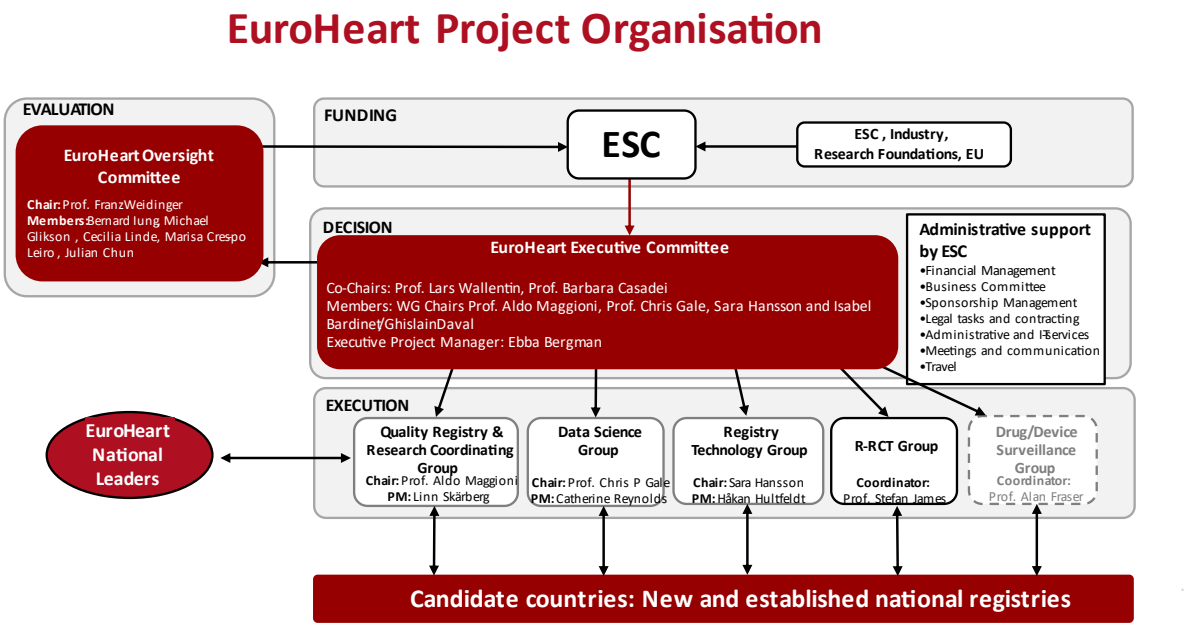

Figure 1. Project governance and organisational structure

3. Pilot Phase – Deliverables and Achievements

The main deliverables from the Pilot phase were to:

1. Create an international network of ESC countries interested in joining the EuroHeart collaboration.

2. Create a network of industrial, research foundation and public authority partners interested in collaboration with and supporting/sponsoring EuroHeart.
3. Develop and receive the international endorsement of the data variables/definitions and quality indicators for four clinical disease domains (ACS-PCI, HF-CRT, AF-Ablation, AS-TAVI).
4. Develop the EuroHeart Registry web-based Registry IT Platform for data entry/import, online reporting, and export to local/national data repositories.
5. Implement the EuroHeart Common Dataset and Registry IT Platform in two to three countries/regions.
6. Implement the EuroHeart Common Dataset in one to three countries/regions with existing registries.

During the Pilot phase, EuroHeart has achieved the following:

1. Developed the EuroHeart mission and vision and established an organisational structure for the Pilot phase.
2. Secured funding for the Pilot phase through sponsoring from industry partners and a research foundation.
3. Developed the EuroHeart website, a demo video, online demo registries and produced regular newsletters.
4. Started a dialogue with over 20 European countries on the roadmap for joining EuroHeart.
5. Participated in discussions on the development of the EU Health Data Space and interacted with EMA concerning recommendations for registry-based clinical trials.
6. Developed the EuroHeart Registry IT Platform that includes modules for data entry, data transfer, data export and automatic quality control and functionality for online statistical reports on quality indicators and production statistics.
7. Established the process for developing harmonised variables to assess quality of care.
8. Designed and locked the data variables, associated clinical data definitions and quality indicators for four clinical domains (ACS-PCI, heart failure, atrial fibrillation and transcatheter aortic valve implantation).
9. Published or submitted manuscripts describing the methodology and the datasets for ACS-PCI (EHJ 2022) and Heart failure (EHJ 2022), AFIB and TAVI.
10. Contracted and started the implementation of the common ACS-PCI and HF datasets and the registry IT-platform in three countries (Estonia, Romania, Lithuania - on hold).
11. Contracted and started on the implementation of the common ACS-PCI datasets in three countries with existing registry IT-platforms (Hungary, Portugal, Denmark).
12. Agreed on the implementation of the ACS-PCI datasets in two countries that already have a EuroHeart-compatible Registry IT-platform (Sweden and Iceland).
13. Agreed with the National Heart Centre in Singapore on the implementation of the ACS-PCI datasets in one centre as a first step in a collaboration on the development of National/Regional Registries for cardiovascular diseases in Singapore.
14. Finalised the implementation of the EuroHeart Registry IT platform in two countries and the common dataset for ACS-PCI in six countries in accordance with agreements with the included European countries and the first centre in Singapore.

15. Started registrations in Q4 2021 and by Q1-Q2 2022 194 and 113 centres registering data on ACS and PCI patients, respectively. Two countries have implemented the EuroHeart IT-platform.
16. Discussed the implementation of EuroHeart registers and common datasets in the other disease domains in the initial eight countries and, if feasible, in Singapore.
17. Discussed the implementation of the EuroHeart Registry IT platform and/or the common datasets in other candidate countries for implementation in the next phase.
18. Planned the first data extraction (2021 data) to test the flow of data. Deliver the first annual EuroHeart report for internal use only by Q1 2023.

4. Consolidation phase

The main objectives of the EuroHeart Consolidation phase are to expand the EuroHeart Network in order to create a broader basis for quality development and outcome research and to provide a sufficiently large network that is technically and organisationally prepared to start the first registry-based randomised trials or the first safety surveillance projects (**Figures 2** and **3**).

The goals of the Consolidation phase are to:

1. Continue supporting ongoing and novel quality registries in the current network of nine countries.
2. Expand the EuroHeart collaboration to at least six additional countries.
3. Provide statistical analyses/reports on processes of care and outcomes in the network.
4. Develop data standards for cardiovascular outcomes.
5. Technical implementation of outcome variables in existing domains.
6. Initiate an international framework to support EuroHeart R-RCTs or safety surveillance of novel drugs and devices.
7. Develop a stable, sustainable long-term governance for EuroHeart.

General aims of direct continuation in the Consolidation phase:

1. Maintain viable development in key areas.
2. Keep the momentum as a leader in areas of quality improvement, data science and R-RCT.
3. Maintain credibility with all external and internal stakeholders.
4. Maintain key competences in EuroHeart leadership and organisation.
5. Encourage high expectations and maintain positive engagement of all involved.
6. Foster sponsor opportunities, interest in new sponsorship and research contracts.
7. Maintain interest of countries, existing registries, and other partners.
8. Maintain the interest of health authorities, research foundations and regulatory agencies.

4.1 Expansion and Development of the EuroHeart Network

As of now the EuroHeart network involves nine countries: Estonia, Romania, and Lithuania (planned) using the optional Registry IT Platform; Hungary, Portugal, Denmark, and Singapore implementing the common ACS-PCI dataset in their local registries; and Sweden and Iceland implementing the common

data sets a EuroHeart compatible Registry IT Platform[2] (**Figure 2**). For the consolidation phase discussions are ongoing with other candidate countries presented in **Figure 2**.

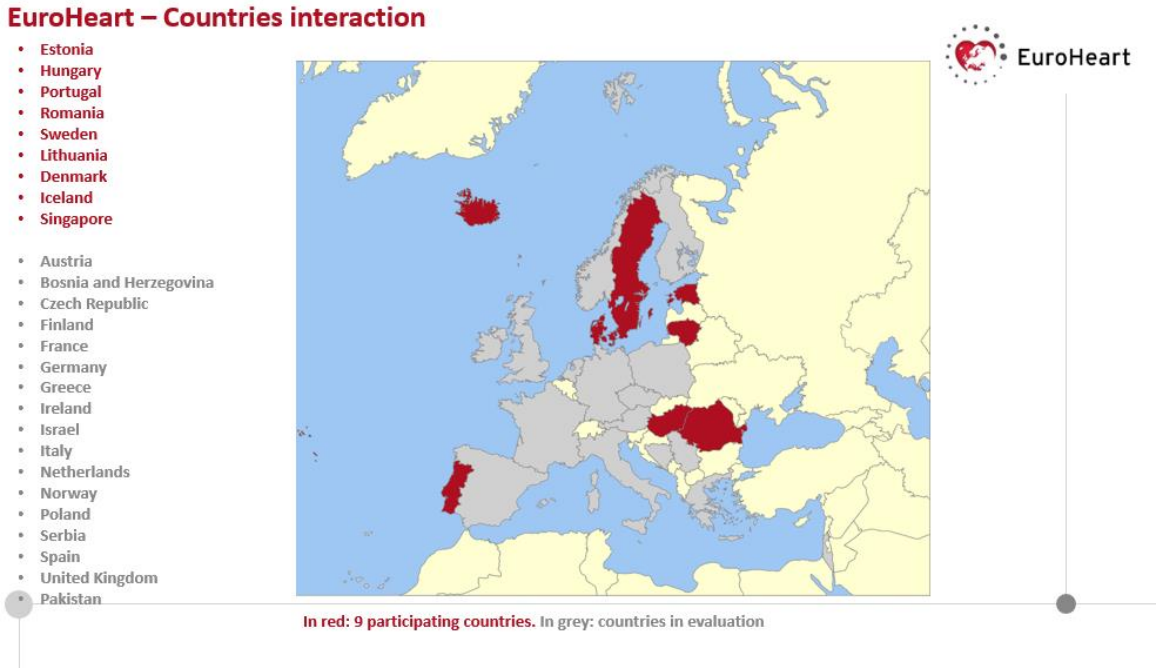

Figure 2. EuroHeart map as of June 2022 *(Countries in red are members of the EuroHeart collaboration; countries in grey have an ongoing dialogue on opportunities to participate).*

Building National Quality Registries is a long-term commitment that evolves over time in a stepwise process. Currently, the term **EuroHeart Country/Region** is defined as a country, but it can also be a region or a large network of hospitals or healthcare organisations within a large country pursuing a registry based on the EuroHeart common dataset in at least one of the four disease domains. Still, the registries' long-term goal is to obtain a complete National/Regional coverage in all four EuroHeart disease domains. In the Consolidation phase, EuroHeart will continue to expand the network aiming to include a range of countries/regions with different income levels, from large to small, and Western to Eastern, Northern to Southern European countries/regions. The process - from the initial contact with the president of the National Cardiac Society or national champions to joining EuroHeart - is a lengthy process that involves gaining local engagement not only at the medical, research and technical community but also engagement and preferably commitment from government and authorities. During the Pilot phase, eight European countries and one non-European country joined the network.

[2] UK, Sweden and Iceland are referred to as founding countries as their Registry IT-platforms were precursors to EuroHeart's and can therefore more easily be integrated with the EuroHeart Registry IT platform.

Based on the ongoing dialogue, there will be several countries/regions ready to commit when the project enters the Consolidation phase. It is estimated that EuroHeart will be able to expand to at least 15 countries adopting the EuroHeart common data standards, at least five countries would join by implementing the Registry IT platform and 10 countries would join using their own registry technology systems. All 15 countries would be partially harmonized to at least one common dataset by the end of the 2-year Consolidation phase. This would render a network of at least 14 European countries/regions and at least one non-European country/region by the end of Q4 2024, which is considered of sufficient size to start the first R-RCT (**Figure 2**).

4.2 Specific deliverables in the Consolidation phase

EuroHeart countries:

1. Continue to build the EuroHeart Network by communicating[3] with ESC National Cardiac Society (57 countries) and remain open to other countries wishing to join the project.
2. Support participating countries/regions with their continued implementation of registries for all established EuroHeart disease domains.
3. Expand the EuroHeart collaboration with at least six additional countries:
    1. Implement and establish at least one EuroHeart common dataset and Registry IT platform in **two** additional countries/regions.
    2. Implement and establish at least one EuroHeart common dataset in already established national registries in **four** additional countries/regions.

Common dataset – development, management, and analysis:

1. Continue updating variables for EuroHeart Disease Domains i.e., ACS-PCI, HF, AFib and TAVI.
2. Support countries in the consistent implementation of the data standards.
3. Develop statistical analysis plans for all active registries.
4. Develop data variables and definitions for cardiovascular outcomes.
5. Identify suitable pre-existing ESC quality indicators to be adapted and incorporated into a set of EuroHeart quality indicators for Cardiovascular Outcomes.
6. Develop processes for exporting aggregated data for central analysis.
7. Produce two annual reports on processes and quality of care in the EuroHeart Network.
8. Submit two EuroHeart manuscripts.

Individual research project for R-RCT, drug/device surveillance and outcome research:

1. Initiate an international framework to support EuroHeart R-RCTs or safety surveillance of novel drugs and devices.
2. Establish a network of academic service providers to support the research projects.

[3] Means of communications are regular newsletters, project website, information movie, individual and general meetings, and ESC general channels of communication.

3. Prepare the first EuroHeart R-RCT or research study.

Times schedule of the Consolidation phase:

The timing of the different activities is illustrated in **Figure 3**.

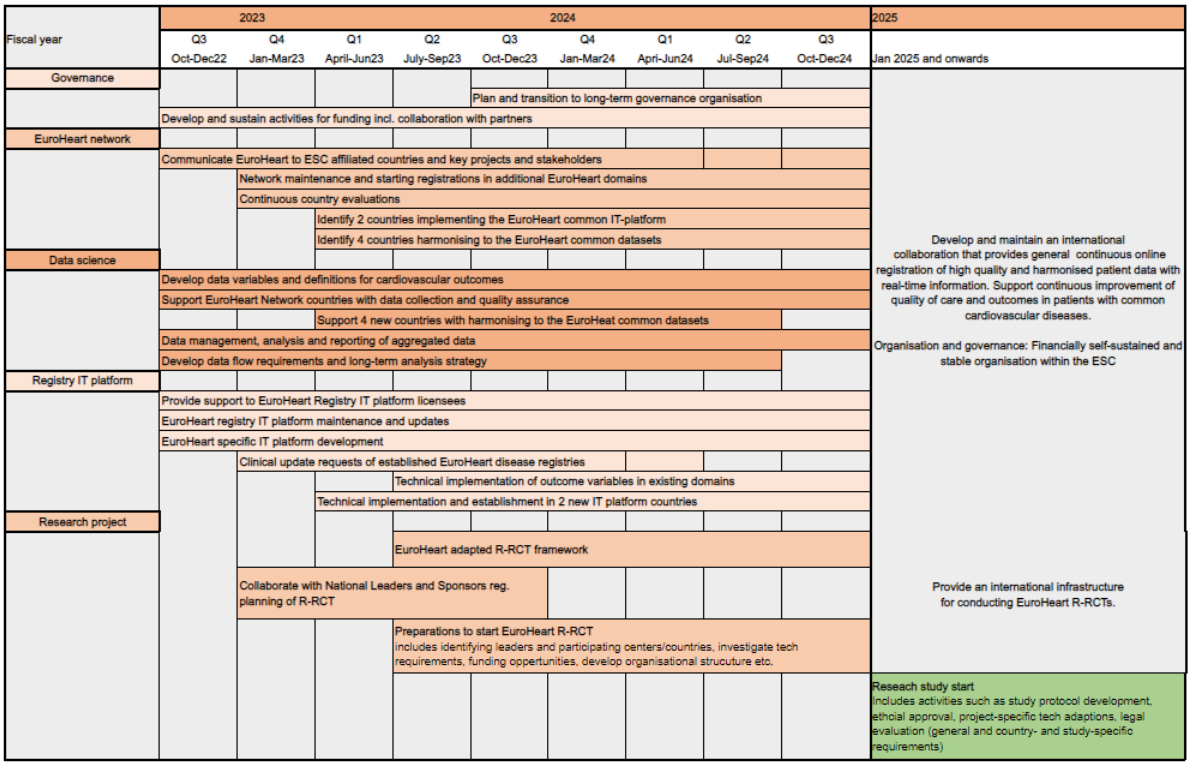

Figure 3. GANTT chart EuroHeart Consolidation Phase

Aimed project metrics in the Consolidation Phase:

1. Number of countries will be 15.
2. Number of EuroHeart Annual Reports will be 2.
3. Numbers of patients recorded per quarter in different registries and countries/regions will be continuously reported.
4. Number of countries/regions and sites actively recruiting and following patients per disease domain will be reported per quarter.

4.3 EuroHeart organisation

The working assumption is that a new organisation will be prepared and set up during the Consolidation phase to support the long-term EuroHeart activity. In the meanwhile, EuroHeart will continue with the current governance and organisational structure (**Figure 1**).

Organisational deliverables:

1. Develop and establish a long-term organisational and governance structure of EuroHeart.
2. Further develop and sustain activities for funding, including grant applications and collaborations with research foundations, public organisations, and industrial partners.
3. Engage with key projects and stakeholders in EU, e.g., in the European Health Data Space, DARWIN EMA, BigData@Heart, Core-MD, European CR Database, EU4Health, Horizons Europe etc.

5. EuroHeart Project – At a glance

Central Organisation
EuroHeart is the collaboration of national quality registries providing continuous data collection of standardised and/or harmonised variables in common cardiovascular diseases, including therapy, interventions, and devices. EuroHeart is an ESC initiated project executed by the *EuroHeart Executive Committee* and overseen by the *EuroHeart Oversight Committee*. The central organisation is under development from the pilot phase (**Figure 1**) to a stable long-term phase that will be determined by the end of the Consolidation phase.

National Organisation
Each country/region is fully autonomous and controls their own data, their registry infrastructure, their IT-systems, and all national/regional activities. A *Letter of Intent* agreeing on the terms of collaboration is signed upon joining EuroHeart. The only commitment made is to annually provide aggregated data for the annual *EuroHeart report on Quality of Care*.
All other engagements will be separate research project activities such as investigator-driven research studies, drug/device surveillance projects or registry-based randomised trials. These research projects will have separate agreements regulating the level and terms of collaboration, degree of data sharing, financial aspects etc. Participation in prospective research projects, such as R-RCT and drug/device projects, will require individual informed consent, as in any clinical trial.

Data variables and definitions
The core of EuroHeart is the common data, data definitions and quality indicators. All registries participating in EuroHeart are required to use the mandatory EuroHeart datasets. The number of *mandatory EuroHeart data variables* are set at a minimum to avoid adding to the clinical burden; however, there are additional *optional EuroHeart variables* available for registries that wish to enrich their dataset with pre-defined variables.
Specific research projects may result in additional temporary data variables, e.g., guidelines adherence, R-RTCs.
EuroHeart countries that lack the ability to pool long-term follow-up data from electronic health records or administrative databases may collect such information using historical methods and templating from the EuroHeart Outcomes Domain.
During the Consolidation phase, EuroHeart will develop the Cardiovascular Outcomes variables that will be integrated with the 4 existing registries.

Infrastructure – Data Collection
The EuroHeart Registry IT platform start-kit is licensable to countries/regions wanting to build quality registries with continuous and structured collection of data, direct feedback to users on processes of care and outcomes.

During 9-12 months, the Registry Technology Group train and support the national/regional registry centres to implement and set up their own national registries and infrastructures adjusted to their national settings. Once the registry centres are up and running, they are free to continue developing new registries within any disease area on the platform.	Established registries can remain on their existing platforms and collaborate by applying the common datasets. EuroHeart strive to continue improving means of collaboration across different platforms and provide technical solutions that minimise the clinical burden of registry participation.

Infrastructure – Data Management & Analysis At a central level, EuroHeart will only manage aggregated data provided by the registries upon request from EuroHeart. The data will be used to produce annual EuroHeart reports on quality of care. To ensure high data quality, EuroHeart will also centrally support participating registries with improving data quality.	Specific research projects may involve the transfer of individual patient data and these collaborations will be managed by separate agreements and project plans. EuroHeart will develop services to enable statistical analysis, research, R-RCTS and drug/surveillance projects.

For more information, visit the EuroHeart website on https://www.escardio.org/Research/euroheart.