EuroHeart

European Unified Registries for Heart Care Evaluation and Randomised Trials

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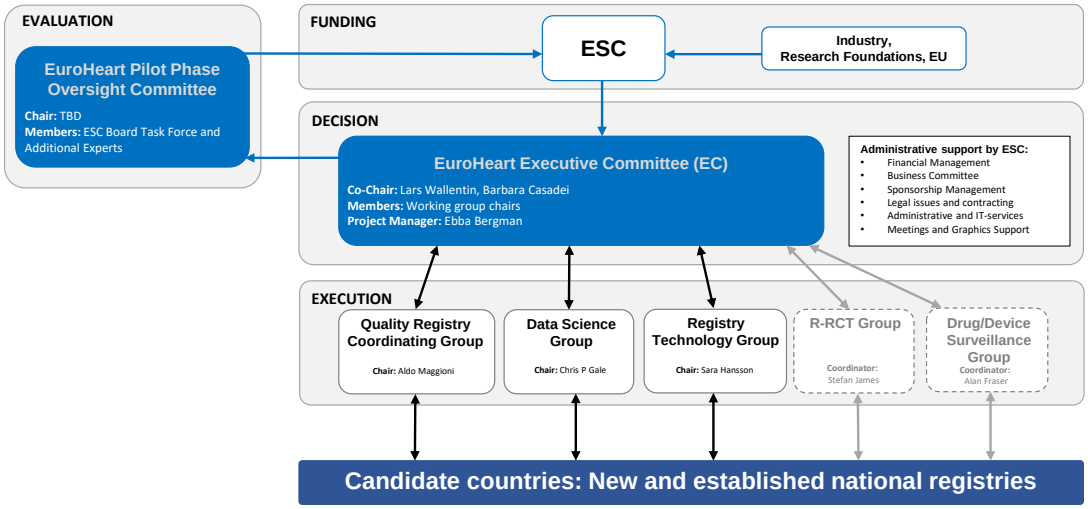
Executive Summary

The mission of EuroHeart is to develop and maintain an international collaboration that provides common definitions of quality of care indicators and the availability of an IT infrastructure for continuous online registration of high quality and harmonised patient data, with real-time feedback supporting continuous improvement of care and outcomes in patients with common cardiovascular diseases. EuroHeart will also provide an international infrastructure facilitating cost-effective safety surveillance of new drugs and devices and registry-based randomised controlled trials (R-RCT).

The EuroHeart programme is planned as a collaboration between National Registries providing continuous data collection of standardised and/or harmonised variables in common cardiovascular diseases, including therapy, interventions, and devices. Within this structure, the participating National Registries will be fully responsible for their own registry infrastructure, their IT-systems, their databases, and collaborative reports based on aggregated data without any transfer of individual data outside the country. In collaborative prospective research projects, such as R-RCT and drug/device monitoring, participation will be based on individual informed consent allowing the transfer of individual data to a common Data Science Centre for statistical analyses and reporting.

The EuroHeart programme will start with a Pilot Phase 2020-2021, organised as outlined below.



In the pilot phase, the **EuroHeart Executive Committee** will lead, plan and coordinate the pilot phase and prepare and propose an organisation for the long-term phase. The **EuroHeart Quality Registry Coordinating Group** will inform and investigate countries on their interest and feasibility to participate and invite 2-4 countries to the pilot phase. The **EuroHeart Data Science Group** will develop standardised data sets and quality indicators for the prioritised conditions ACS-PCI, heart failure, valve disease, and atrial fibrillation and also plan for a common EuroHeart Data Science Center. Simultaneously, the **EuroHeart Registry Technology Group** will develop the optional EuroHeart Registry IT-platform for continuous monitoring of quality of care, R-RCT, and surveillance of new devices and drugs and support its implementation in 2-4 pilot countries.

Why EuroHeart?

The EuroHeart programme has been initiated by the ESC. It is based on a collaboration between National Registries driven by or in collaboration with NCSs. The aim of National Registries is to continuously monitor quality of care at the national and local level as a necessary pre-requisite to improve it effectively. Thus, the programme is predominantly designed for the benefit of patients, citizens and the planning of health care investments.

The National Registries participating in EuroHeart are expected to be based on the continuous recording of and feedback on individual patients with regard to their characteristics, treatments and outcomes. The Swedish (SWEDEHEART) and the UK (NICOR) registries have already established that continuous patient registries improve quality of care and patient outcomes.(1) These systems also engender a culture of transparency and accountability, and empower professionals with evidence to underpin requests for appropriate investment in health care. The EuroHeart programme will therefore offer participating countries a licensable EuroHeart Registry IT-platform for facilitating the set-up of this type of system in the individual countries.

National Registries will be responsible for their data collection and own their data. The EuroHeart programme will harmonise data collection across ESC countries, develop common quality of care indicators, and provide a platform for both national and international benchmarking.

EuroHeart's further added value
Over the last decade, there has been a rapid increase in the development and use of implantable devices for cardiovascular diseases. The new European Regulation on Medical Devices mandates post-marketing surveillance for safety and efficacy and there is also an increasing regulatory demand for post-marketing surveillance of new pharmaceutical agents. Continuous patient-registries, such as SWEDEHEART, have already been shown to be ideally suited for independent surveillance of new drugs and devices, thereby improving patient safety and outcomes and reducing health care costs.(1)

The increasing complexity and costs of randomised clinical trials (RCT) has led to a reduction both in the development of new treatments for cardiovascular diseases and in the robust assessment of the efficacy and safety of interventions that are nevertheless routinely employed in clinical practice. Over the last years, the SWEDEHEART group has demonstrated that registry-based randomised clinical trials (R-RCT) are a very cost-effective technology that is able to provide evidence on the efficacy and safety of new and old treatments.(1)

Reference:
1. Wallentin L, Gale CP, Maggioni A, Bardinet I, Casadei B. EuroHeart: European Unified Registries On Heart Care Evaluation and Randomized Trials. Eur Heart J. 2019 Sep 1;40(33):2745-2749

The EuroHeart Mission

The mission of EuroHeart is to develop and maintain an international collaboration that provides common definitions of quality of care indicators and the availability of an IT infrastructure for continuous online registration of high quality and harmonised patient data, with real-time feedback 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 controlled trials in a general patient population across multiple geographies.

The EuroHeart Programme

The EuroHeart programme is planned as a collaboration between National Registries providing continuous data collection of standardised and/or harmonised variables in common cardiovascular diseases, including therapy, interventions, and devices. Within this structure, the participating National Registries will be autonomous and fully responsible for their own registry infrastructure, their IT-systems, their databases, and all national activities.

The National Registry data will be collected and used for the purpose of quality development in the local health care system. No individual registry data are planned to be transferred outside the country. Thus, for most countries, a signed informed consent is not required for the standard data collection. EuroHeart reports on standards of care in different countries will be based on analyses of aggregated data sets originating from synchronised performance of identical analyses in the individual countries.
However, participation in prospective research projects, such as R-RCT and drug/device monitoring, will require individual informed consent, as in any clinical study. In these cases, selected anonymised individual study data will, at predefined intervals, be transferred to a central Data Science Centre for statistical analyses.

Finally, in case anonymised retrospective registry cohorts may be included in epidemiological analyses and reporting, there will be a need to obtain ethical and regulatory approval for merging of different databases and transfer of the anonymised data set to a central repository.

EuroHeart can offer a common optional registry IT-platform that would provide immediate online feedback to users and allow them to continuously monitor and improve quality of care and provide the foundation for high-quality observational research. The EuroHeart Registry IT-platform will also substantially facilitate participation in international randomised research and post-marketing surveillance of new devices and drugs, in case the country is willing to participate.

The EuroHeart programme has the potential to include a large number of ESC member countries stepwise. Countries can either join EuroHeart by implementing the proposed registry IT-platform or by aligning existing national or local systems to record the mandatory EuroHeart data variables and adopt the same quality of care indicators. When implemented in several ESC member countries, EuroHeart will have the potential to continuously contribute to improve the standards of cardiovascular care, monitor the safety of new devices and medications, and provide an important collaborative infrastructure for observational research and cost-effective investigator- or industry-initiated R-RCTs.

The EuroHeart Pilot Phase

The development of the EuroHeart programme will start with a Pilot Phase. During the Pilot Phase the organisation will be led by an **Executive Committee** consisting of two chairs and the chairpersons of the three main working groups as outlined in **Figure 1**. The Executive Committee will plan, coordinate, lead, oversee and follow-up all activities in accordance with the current project plan.

The work by the Executive Committee and working groups will be coordinated by project managers. The Executive Committee will convene regularly (the frequency will depend on the project status) by video conference. Through the ESC and European Heart House (EHH), the EuroHeart organisation will have access to administrative services, financial management and legal advice. Sponsorship management and external contracts will be organised by a Business Committee and a project manager at the EHH.

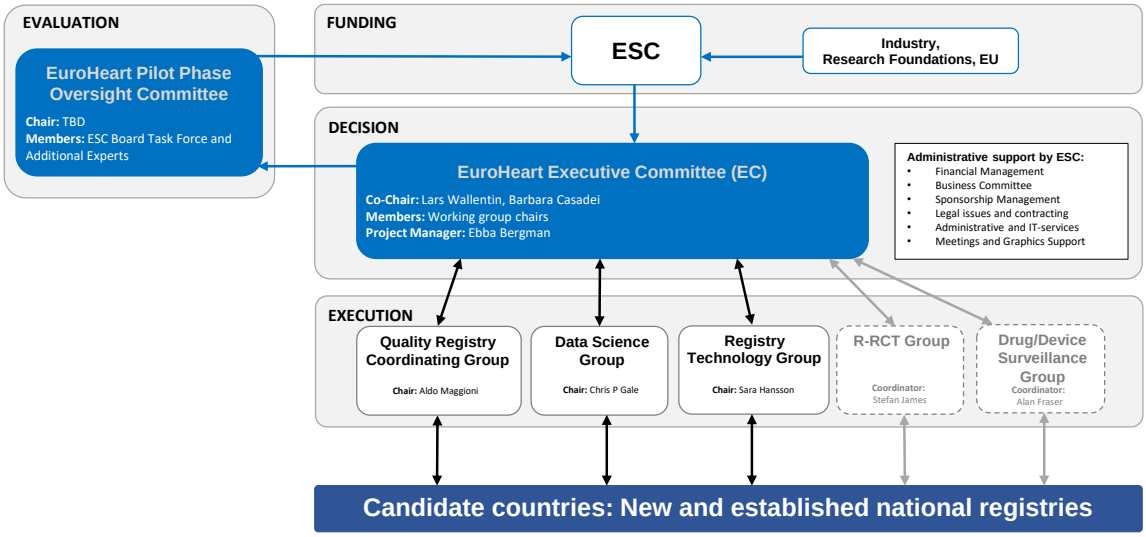


Figure 1. Organisational chart of the EuroHeart Pilot Phase

Funding of the costs for the personnel and the organisational and technology infrastructure in the Pilot Phase will be sought from ESC, device and pharmaceutical industry, and national research

foundations. After this initial investment, the plan is that EuroHeart will be mainly self-sustained through a combination of sources, including research grants and fees for services from research foundations, scientific societies, health care and regulatory authorities, pharmaceutical and device industry at international and national levels.

The performance of the EuroHeart programme in the Pilot Phase will be overseen by the **EuroHeart Pilot Phase Oversight Committee**. If the Pilot Phase is successful, the EuroHeart programme will continue under the auspices of ESC. Details of the long-term organisation will be described in a separate document.

Structure and Development of the EuroHeart Pilot Phase

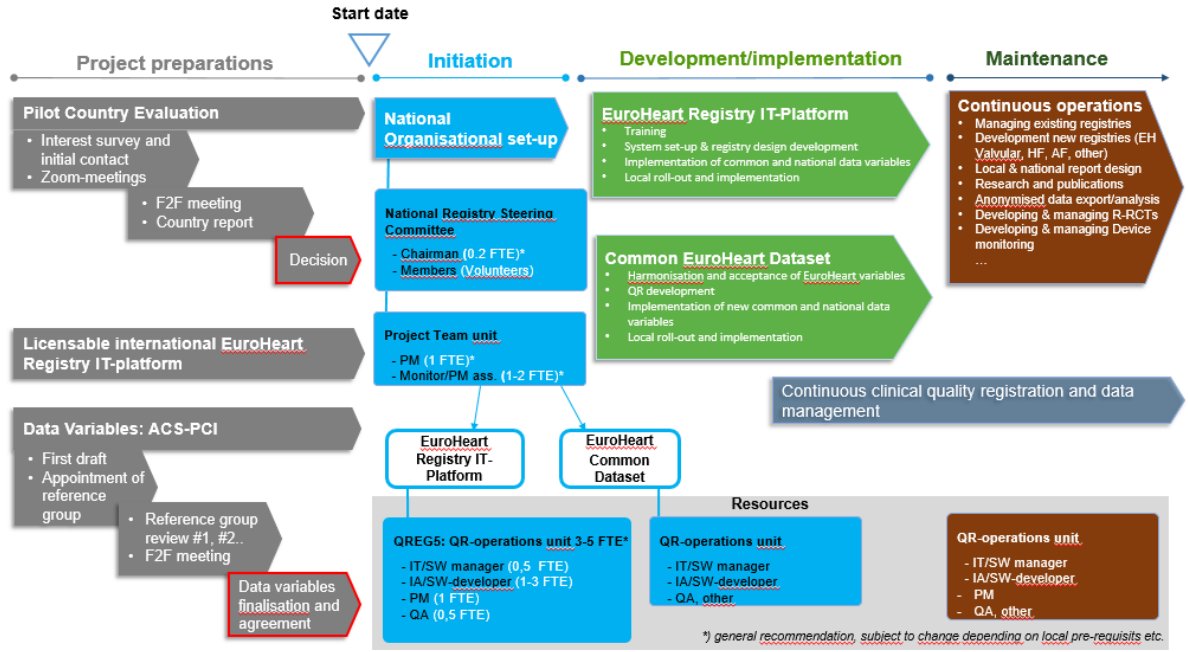


Figure 2. Overview of key project steps of the Pilot Phase

The EuroHeart Pilot Phase involves several parallel and sequential processes (**Figure 2**):

1. The **EuroHeart Quality Registry Coordinating Group** will, in collaboration with National Cardiac Societies, investigate the interest of countries and regions to participate in the EuroHeart Pilot Phase, assess feasibility, and establish a coordinated organisation for the development of the EuroHeart programme.
2. In parallel, the **EuroHeart Data Science Group** will develop standardised data sets and quality indicators for common cardiovascular conditions, aiming to harmonise data collection across the participating countries and allowing meaningful comparisons and benchmarking.
3. In parallel, the **EuroHeart Registry Technology Group** will update the well-validated SWEDEHEART Registry IT-platform for use and transfer to participating countries, under a license agreement with both the Uppsala Clinical Research Center (UCR), Sweden and EuroHeart. During the Pilot Phase of two years 2020-2021, the updated platform (EuroHeart Registry IT-platform) will be implemented and evaluated in 2 - 4 countries, after which it may be rolled out to other participating countries. The costs for adjusting and tailoring the

platform to the EuroHeart programme and make it internationally licensable is included in the project.

4. Subsequently, EuroHeart would also develop a **EuroHeart Data Science Centre** to coordinate the statistical analyses and present the combined aggregate results on quality of care from all participating countries. The Data Science Centre would also be able to manage the databases and statistical analyses of projects for drug and device monitoring and registry-based randomised clinical trials performed as part of the EuroHeart programme.

Quality Registry Coordinating Group

The Quality Registry Coordinating Group will be chaired by a medical and registry expert and supported by a project manager. In the Pilot Phase, the group's primary responsibility is to establish and maintain collaborations with National Registries. In the long-term perspective, the group will be responsible for maintaining the international collaboration and for initiating and coordinating proposals for further development/expansion of the system, projects, trials, etc.

During the Pilot Phase the group will, together with the chairs of the Executive Committee, communicate with and evaluate interested countries/regions with regards to their eligibility as pilot countries. These activities started in July 2019 and there is currently a list of 19 candidate countries/regions, all of which will be evaluated (**Figure 3**).

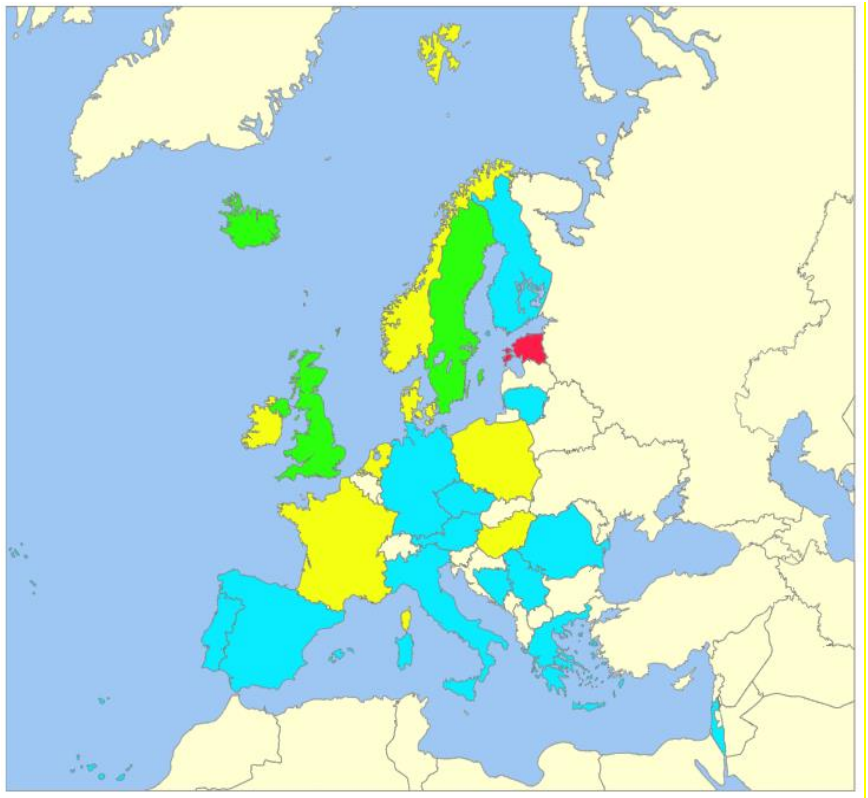


Figure 3. Potential EuroHeart countries for the pilot phase (Red = pilot countries; Blue = pilot phase candidate countries; Green = countries currently using a national version of the SwedeHeart Registry IT-platform; Yellow = countries known to have national quality registries using local registry platforms)

The Quality Registry Coordinating Group will select 2 - 4 pilot countries for implementing the new international EuroHeart Registry IT-platform during the Pilot Phase. After selecting the pilot countries, the group will continue to discuss the EuroHeart collaboration with other countries, including those with already established National Registries (see **Figure 3**). These countries may collaborate with EuroHeart by adopting the EuroHeart data variables within their existing registries on their current IT-platforms. This will enable them to participate in quality of care assessments and outcome research. However, the involvement in device and drug surveillance projects and R-RCTs would be substantially facilitated by switching to the EuroHeart Registry IT-platform, which might be preferred also by some of these countries.

Data Science Group

The Data Science Group will be chaired by a medical and epidemiology expert supported by a project manager. The group will include two junior medical experts working on reviewing and proposing data definitions and data sets. In collaboration with the involved registries and experts from the ESC Associations, their initial task is to develop an international agreement on standardised and harmonised variables for four common cardiovascular disease areas – ACS-PCI, heart failure, valve disease, and atrial fibrillation. The proposed concept is to base the collaborations on a minimal compulsory dataset for continuous use by all participating countries/regions and to provide availability to optional expansion modules potentially only implemented for limited time periods for specific projects, e.g. guideline adherence, drug-device monitoring and R-RCT (see **Figure 4**).

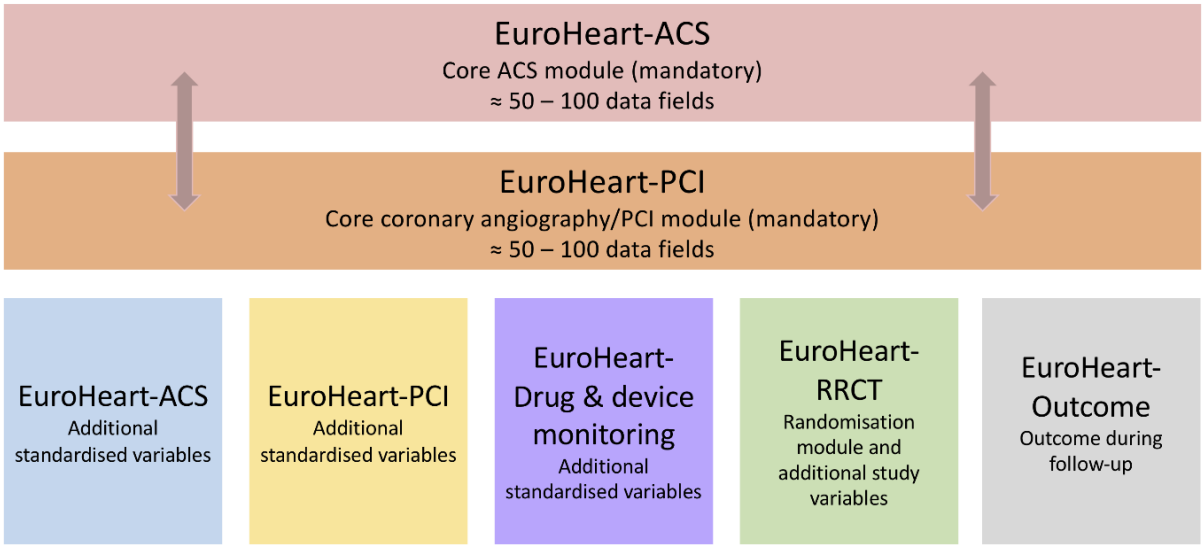


Figure 4. The module-based data structure of the harmonised EuroHeart data variables

The Data Science Group will also provide a catalogue of standardised additional variables per condition for optional use as decided by each country to expand their national/local dataset and adjust to national/local requirements. The additional modules may be electronically provided from the EuroHeart IT Centre to the National Centres, e.g. for monitoring of specific devices or performance of specific R-RCT. The specific variables for drugs and devices surveillance (e.g. serial numbers, implantation data) and R-RCT need to be agreed and developed for each project separately.

Key for quality of care assessment is the availability of long-term follow-up data (ie, at least 1 year). Outcome data may be obtained by merging with other national/regional registries or by obtaining individual patient follow-up data and completing the EuroHeart Outcome module (**Figure 4**). The availability and completeness of follow-up data will be used as a quality criterion to include national datasets in the analyses and reports.

The Data Science Group started its activities in September 2019 and is currently developing the datasets for EuroHeart ACS-PCI datasets based on the SWEDEHEART and MINAP/NICOR variables. In Q2 2020, these proposals will be reviewed by reference groups of representatives for candidate countries and established registries.

The EuroHeart Data Science Group will, over time, include the services of statisticians, statistical programmers, data managers, and IT-specialists to develop and coordinate collaborative and/or federated analyses and reports on the common datasets available in different countries. The Data Science Group will also be responsible for the development of a EuroHeart Data Science Centre that will manage the databases and statistical analyses of projects for drug and device monitoring and of registry-based randomised clinical trials performed as part of the EuroHeart programme.

Registry Technology Group

The EuroHeart Registry Technology Group is currently based in the Uppsala Clinical Research Center (UCR), which also will act as the EuroHeart IT-center for countries licensing the EuroHeart Registry IT-platform. UCR is a non-profit entity within Uppsala University and Uppsala University Hospital and the largest academic clinical research organisation in Sweden. UCR's mission is to improve human health in Sweden and worldwide.

The Chair of the Registry Technology Group is the head of the Quality Registry Section at UCR who is also a member of the EuroHeart Executive Committee. The project manager of the Registry Technology Group will also present and discuss the general and individual technical platform solutions and requirements with interested countries.

The development of the international EuroHeart Registry IT-platform is built upon the same infrastructure used for developing and supporting the SWEDEHEART Registries in Sweden and the NICOR Registries in the UK. UCR has 20 years' experience in developing and maintaining internet-based national quality registries and is currently responsible for the registry IT-platforms for more than 20 different registries within cardiology and several other disease areas in Sweden and internationally.

Over the last 15 years, the SWEDEHEART Registry IT-platform has also been used for safety and efficacy surveillance of cardiovascular devices. Finally, over the last 10 years, the registry IT-platform has been developed to support identification, randomisation and management of patients as part of registry-based randomised clinical trials.

The EuroHeart Registry IT-platform will be a start-kit for quality registry development and management organisations in pilot countries (or region in a country), which will enable a fast and reliable quality ensured implementation. This start-kit and a delivery and support organisation at UCR are currently being developed and set up to meet the expectations from the countries in the Pilot Phase. The Registry IT-platform will be licensed to the pilot countries/regions from UCR where one licence covers the use of the platform for development of cardiovascular registries in the respective country/region. The cost for the licensing of EuroHeart Registry IT-platform is the same regardless of the size of the country/region, the number of registering units, or recorded individuals. However, if a country had several different registry and IT-centres for different regions a licence fee for each IT-centre would be needed.

The registry IT-platform and know-how to run a quality registry organisation and develop national/regional quality registries will be delivered as described in **Figure 5**.

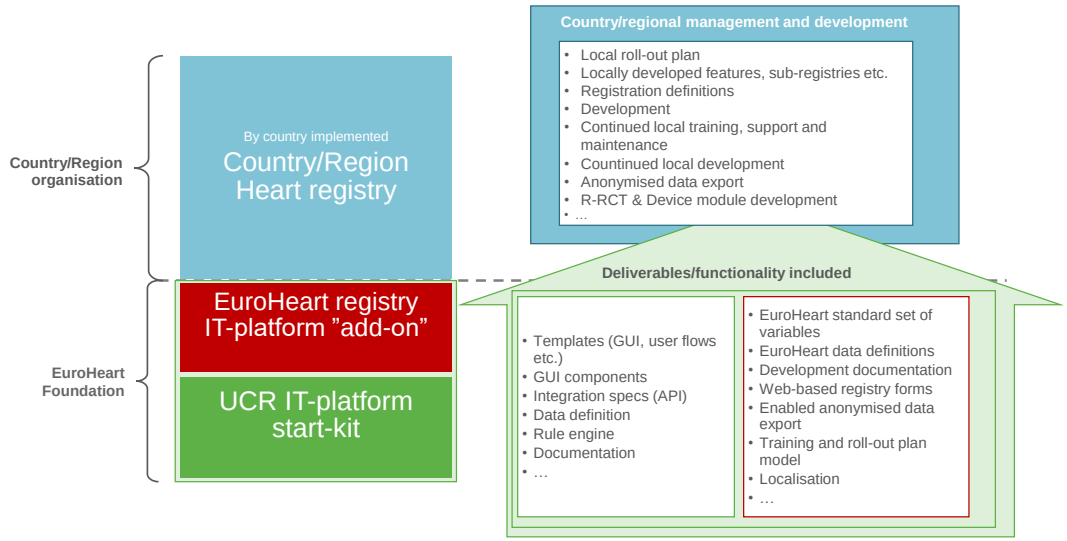


Figure 5. The delivery model of the national/regional EuroHeart Registry IT-platform

The schedule for transferring the EuroHeart Registry IT-platform technology and knowledge from the UCR-EuroHeart to the country IT-group is listed below and also illustrated in **Figure 6**.

The implementation of the Euroheart Registry IT-platform consists of the following main steps:
1 Start-up organisation: Project organisation set-up between UCR and national/regional quality registry (QR)-operation.
2 Training of national/regional QR-operation.
3 System set-up: System implementation and adjustments for local conditions (health care and registration process, report design, interaction with other national data sources (PID, death registry etc)) and roll-out (local training, user administration etc).
4 Start registration of patients and quality follow up.
5 Implementation delivery sign off.
6 Additional technical support, any other technical or specifically related know-how not covered in the initial stage and development/implementation.

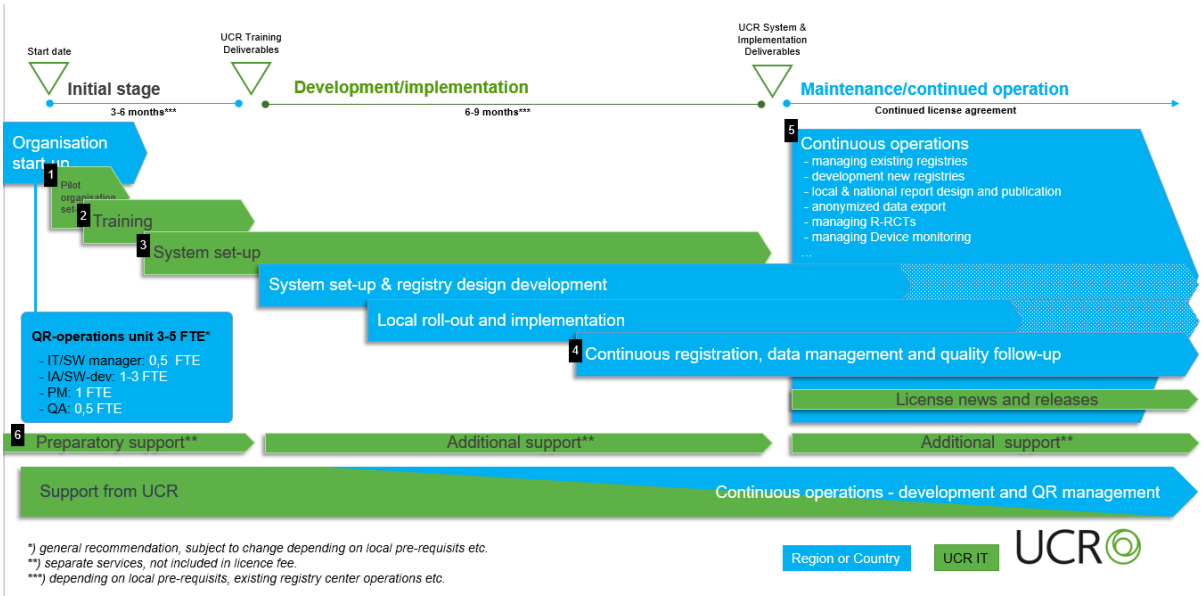


Figure 6. Process description and required resources for transfer of EuroHeart Registry IT-platform to participating countries

After the delivery and transfer of technology and competence to the national IT-group, the system will be supported by consultancy services and, as needed, electronic transfer of additional modules e.g. for drug/device monitoring or R-RCT.

R-RCT Group

The R-RCT Group will be led by a world-leading expert in this area. In the Pilot Phase of the EuroHeart Registry IT-platform, he/she will serve as an advisor and facilitate the later development of expansion modules for R-RCT that can be electronically transferred to the national/regional common IT-platforms. When the EuroHeart international network is established, the objectives of the group will be expanded to initiate, coordinate, and support the performance of R-RCTs, as proposed by investigators or other stakeholders, e.g. health care industry, ESC Guideline Committees, health care authorities, EMA/MHRA etc.

Drug/Device Surveillance Group

The Drug/Device Surveillance Group will be led by an investigator with a documented long-term interest and in-depth knowledge in this field. In the Pilot Phase of the EuroHeart Registry IT-platform, he/she will serve as an advisor for the drug/device monitoring expansion modules. These modules can then be electronically transferred to the national/regional EuroHeart Registry IT-platforms. When the EuroHeart international network is established, the objectives of the group will be expanded to initiate, coordinate and support projects on drugs and devices surveillance as proposed by investigators or other stakeholders e.g. health care industry, ESC Guideline Committees, health care authorities, EMA/MHRA etc.

National/Regional Groups

All participating national/regional registries will be independent and fully responsible for their own organisation, resources, personnel, technical system and infrastructure, databases, and national activities. The licensing of the EuroHeart Registry IT-platform will be based on a EuroHeart Pilot project contract with ESC and UCR and allow the country/region to develop registries in different areas of cardiovascular care. The use of the EuroHeart Registry IT-platform is optional and based on mutual advantages such as the utilisation of the common standardised variables and protocols; common interactive programmes and tools for online feedback on individuals and groups of patients; local, national and international audits; data transfer to external repositories for further analyses and merging with other datasets and statistical analyses; and participation in collaborative projects on drug and device surveillance and R-RCT.

All use of data in EuroHeart shall be certified to stay within the legal grounds for collection and statistical analyses of sensitive personal data at the national and international level and have approval from ethical committees when appropriate (see Chapter EuroHeart Programme, page 3-4).

The national/regional organisations need to be led by dedicated National Champions and involve a network of hospitals interested in developing and maintaining a quality registry infrastructure for continuous improvement of quality of care in the whole national/regional health care system.

The choice of countries for both the pilot project and its expansion will also be based on:

1. The presence of a strong commitment from National Cardiac Societies and national/regional/local health care authorities. A collaboration with the national health care authorities is also essential to enable linkage of the data with administrative data (prescriptions, hospitalisations, survival status etc).
2. The availability of resources to develop and maintain a national/regional IT-infrastructure, to manage and merge data from different sources for statistical analyses and reporting.
3. The availability of national/regional resources/finances to maintain a national/regional coordinator, monitors and hospital representatives.
4. The understanding of the legal grounds for collection and statistical analyses of sensitive personal data at a national and international level and approval by the national legislations and ethical committees.