

# Netherlands Heart Institute

## Research Review 2016–2020

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**Floor Meijer**  
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# Preface

Cardiovascular diseases are major contributors to global suffering and mortality. Innovative research, education and capacity building are key in combatting the global epidemic of heart disease and stroke. The Netherlands is a key player in cardiovascular science and education and the Netherlands Heart Institute aspires to be a driving force and advocate of this position. It is therefore a pleasure to provide the written account of the research review of the Netherlands Heart Institute, covering the period 2016 to 2020, as carried out by an international committee of experts. The evaluation was based on a written self-assessment, several ancillary documents, and a two-day hybrid site visit with interviews with the board, staff members, patient representatives and several other stakeholders. The discussions during the site visit were lively, open and enlightening and the committee wishes to compliment the Netherlands Heart Institute for their openness and impeccable preparations.

In this document you will find our observations, evaluation and recommendations. Fifty years after its inception the Institute still plays, and may increasingly play, a major role in the Dutch and international cardiovascular landscape. However, the Institute has gone through some rough times, due to the organizational separation from its former mother institute, the Netherlands Academy of Arts and Sciences. Now, the moment is right to revisit some of its guiding principles and organizational and operational solutions. We thank the Netherlands Heart Institute for giving us the pleasure of learning about the details of their strategy and organization and hope our views will help to shape the Institute for a successful next phase.

**Diederick E. Grobbee, MD, PhD, FESC**  
Chair of the evaluation committee

18 February 2022

## List of abbreviations

CONCOR	CON genital COR vitia National registry and DNA-bank of adultswith congenital heart disease
DZHK	Deutsches Zentrum für Herz-Kreislauf-Forschung E.V
DCVA	Dutch CardioVascular Alliance
DHF	Dutch Heart Foundation
EU	European Union
FAIR	Findable (F), Interoperable (I), Accessible (A) and Reusable (R)
ICI(N)	Interuniversitair Cardiovasculair Instituut Nederland (predecessor NLHI)
ISAB	International Science and Advisory Board
KNAW	Royal Netherlands Academy of Arts and Sciences
NLHI	Netherlands Heart Institute
NWO	Dutch Research Council
PLN	Phospholamban
RACE	RAte Control Versus Electrical Cardioversion for Persistent Atrial Fibrillation
SEP	Strategy Evaluation Protocol
VVAO	<i>Vereniging van Aangesloten Organisaties</i> (United Coupled Organisations)
WCN	<i>Werkgroep Cardiologische Centra Nederland</i>

# I. Introduction

In 2021, the board of the Netherlands Heart Institute (NLHI) commissioned a research review of the 2016-2020 period as part of NLHI's quality assurance cycle. The year 2016 was chosen as the starting point for the review, since in this year NLHI became independent from the Royal Netherlands Academy of Arts and Sciences (*Koninklijke Akademie van Wetenschappen*, KNAW). Because NLHI wished to have the review completed in its fiftieth anniversary year 2022, the evaluation period was set at five years instead of the regular six years. NLHI appointed an international committee of independent experts to assess the quality of research conducted by Netherlands Heart Institute as well as to offer recommendations in order to improve the quality of research and the strategy of Netherlands Heart Institute. Additionally, the review of NLHI's quality and societal relevance contributes to fulfilling the duty of accountability towards government and society. The board of the institute may use the outcomes of the research evaluation for quality assurance purposes and institutional strategy development.

## Composition of the committee

The review committee consisted of:

- Prof. Diederick E. Grobbee (chair), Professor of Clinical Epidemiology at the University Medical Center Utrecht, the Netherlands;
- Prof. Raffaele De Caterina, Professor of Cardiology at the University of Pisa, and Director, University Cardiology Division, at Pisa University Hospital, Italy;
- Dr. Despina Sanoudou, Associate Professor of Pharmacogenomics, Director of the Clinical Genomics and Pharmacogenomics Unit, Medical School, National and Kapodistrian University of Athens, Greece;
- Prof. Peter Sinnaeve, Professor of Cardiology at UZ Leuven, Belgium;
- Prof. Karin Sipido, Professor of Experimental Cardiology at KU Leuven, Belgium;
- Prof. Uwe Zeymer, Professor of Cardiology at Klinikum Ludwigshafen, Germany.

Dr Floor Meijer was appointed independent secretary to the committee. Appendix 1 includes a short curriculum vitae of each of the committee members.

To ensure a transparent and unbiased assessment process, all members of the committee signed a statement of impartiality and confidentiality. During the first committee meeting on the evening prior to the site visit, existing professional relationships between committee members and research units under assessment were discussed. The committee concluded that there was no risk in terms of bias or undue influence.

## Assessment criteria

The Strategy Evaluation Protocol 2021-2027 ('SEP') was the starting point for the committee's review. This protocol describes the aims and methods used to assess publicly funded research in the Netherlands. It was drawn up and adopted by the Association of Universities in the Netherlands (VSNU), the Dutch Research Council (NWO), and the Royal Netherlands Academy of Arts and Sciences (KNAW).

SEP identifies three main assessment criteria: (1) research quality, (2) relevance to society and (3) viability. Furthermore, SEP asks committees to take four specific aspects into account when assessing the three central criteria. These are: (1) Open Science, (2) PhD Policy and Training, (3) Academic Culture and (4) Human Resources Policy.

The committee notes that the Strategy Evaluation Protocol is intended as a flexible

instrument that stands in the service of a productive conversation. This is exactly how the committee has sought to use SEP during the interviews with NLHI representatives and in this report. It notes that the requirements set by SEP are not fully in line with NLHI's current practice or needs. The institute does not necessarily have strategies and policies for every aspect highlighted by SEP. Where applicable, this is indicated in the report.



In addition to the guidelines and criteria suggested by the Strategy Evaluation Protocol, the committee considered the Terms of Reference issued by the NLHI Board. In this document, the committee was requested to offer its conclusions and recommendations on the SEP criteria and aspects as well as its findings on the added value of the Netherlands Heart Institute as (1) a cooperation of academic departments of Cardiology for the Dutch cardiovascular community and (2) as a platform for young talents.

### Documentation

Prior to the site visit, the committee received the self-evaluation report of NLHI, including the information and appendices required by

the Strategy Evaluation Protocol. The following additional documents were provided:

- Standard Evaluation Protocol 2021-2027;
- Terms of Reference for the research review;
- Netherlands Code of Conduct for Research Integrity (2018);
- Overview of staff fte's (2016-2020);
- NLHI Meerjarenbegroting 2021-2025;
- Concise benchmark analysis.

### Working method

Leading up to the site visit, the committee members were asked to study the documentation. In a kick-off meeting on the evening preceding the site visit, the committee discussed its preliminary findings. Additionally, it considered procedural matters and agreed upon a working method.

The site visit took place at NLHI in Utrecht on 21 October 2021. During the site visit, the committee met with representatives of NLHI, including the management, established and upcoming researchers, and stakeholders. The site visit was concluded with a meeting in which the committee discussed its findings and conclusions, followed by a final meeting with the NLHI Board, its managing director and project managers. The schedule for the site visit is included in appendix 2.

After the site visit, the secretary drafted a first version of the committee report, which she circulated to the committee for an internal revision round. Subsequently, the committee presented its draft report to NLHI for factual corrections and comments. After considering NLHI's feedback, the committee completed the report. The final report was presented to the Board of NLHI.

## II. Assessment

### Strategy and targets

#### *Introduction*

The Netherlands Heart Institute (NLHI) is a cooperation of the cardiology departments of all seven university medical centers in the Netherlands, intended to act as an accelerator for excellent cardiovascular research on national and international level. It was founded in 1972 by the prominent Dutch cardiologist Dirk Durrer as the Interuniversity Cardiology Institute (ICI), with the purpose of sharing knowledge and resources in the Netherlands, thus making better use of available funds. The institute was later renamed Interuniversity Cardiology Institute of the Netherlands (ICIN). In the 1993-2016 period it functioned as an institute of KNAW (KNAW-ICIN), operating as a subsidiary organ with coordinating tasks for externally funded studies connected with the departments of cardiology. Ultimately, KNAW decided that ICIN should once again be an independent foundation, responsible for raising its own funding after an initial five-year grace period. In 2016, the newly independent research institute changed its name to Netherlands Heart Institute. Currently, NLHI manages a project office that initiates and supports multi-center (inter)national academic studies covering a range of cardiovascular topics. Furthermore, the institute is a driving force behind national registries and national strategic research initiatives such as the recently established Dutch CardioVascular Alliance (DCVA, 2018).

#### *Vision, mission and strategic goals*

Recognizing that cardiovascular disease puts an increasing burden on society, NLHI's mission is to develop excellent new strategies for prevention, diagnosis and cure of cardiovascular disease by promoting research cooperation between the cardiology departments of all university medical centers in the Netherlands. This cooperation entails basic science, clinical research and public

private partnerships. The committee found that this well-defined mission is translated into two overarching strategic goals. First, NLHI aims to optimize cooperation between the academic cardiology departments and basic research groups that together build (multidisciplinary) research programmes from bench to bedside and improve patient care. Second, NLHI aims to coach talented researchers to the top of the cardiovascular field. NLHI has developed a number of corresponding strategies to achieve these goals.

The committee appreciates that NLHI's mission of fostering research cooperation across departmental borders is highly topical. Over the past decades, there has been a decisive shift away from individual-led research and towards inter-university collaborations. This is reflected by the subsidy climate that favors consortia of mutually reinforcing partners. As rightfully pointed out in NLHI's self-evaluation report, cooperation and networking are in the DNA of the institute. In its long history, NLHI has essentially functioned as a consortium *avant la lettre*. Nonetheless, the committee felt that NLHI's unique selling proposition deserved further elaboration in the documentation. During the site visit, the Board described NLHI as the glue that holds academic collaboration in place. By having a neutral partner organizing research and providing logistic support at the center of academic cardiology, some of the intrinsic competitiveness between the academical medical centers apparently melts away, ultimately benefiting all parties involved. The committee recognizes this central role of NLHI in facilitating and supporting the collaboration of cardiology clinics across the Netherlands that would have otherwise been challenging to initiate and/or short-lived. The committee encourages NLHI to capitalize on this strength in a future strategic plan.

A concise benchmark analysis that NLHI prepared at the request of the committee stresses mainly that there are no comparable

institutes to NLHI, with the possible exception of Deutsches Zentrum für Herz-Kreislauf-Forschung E.V. (DZHK), which is nevertheless distinct as it is not bringing together all national centers. While there may be lack of benchmarking institutes in the field of cardiology, the committee is of the opinion that this framework is perhaps a bit limiting. The committee encourages the institute to also look for inspiration outside of the field of cardiology, as the purpose of a benchmark analysis is not just to find institutes that are fully comparable/compatible, but also to broadly identify best practices in order to learn from them. In the same vein, the committee would have liked to see a somewhat more inclusive view on cardiovascular disease, acknowledging that other disciplines than cardiology could also contribute towards NLHI's mission. The committee suggests that contributing to the promotion of cardiovascular health in parallel to the fight towards reducing the burden of disease could have an even greater long-term impact. Finally, the committee sees opportunities in including top-quality non-academic centers and/or the WCN (*Werkgroep Cardiologische centra Nederland*) in NLHI, as there currently appears to be somewhat of a disconnect between academic centers and non-academic hospitals.

#### *Organization*

As the committee understood it, the daily management of NLHI is in the hands of a two-member board, consisting of representatives of the Dutch academic cardiology departments. The board is supported by the managing director and overseen by the supervisory board, which currently consists of three members with a legal/economic background. Board members are proposed and appointed by the VVAO (*Vereniging van Aangesloten Organisaties*), which consists of the collected heads of the cardiology departments. The VVAO was said to take an active role, advising both the board and the supervisory board. Additionally, NLHI comprises a scientific council whose members

– both clinicians and basic scientists – are selected for their expertise in cardiovascular research by the department heads. A brief experiment with opening up this council to an audience beyond the Dutch cardiology departments was considered unsuccessful as it diluted the focus. Currently, membership is once again limited to three representatives per department (department head plus two deputies). Finally, the International Science and Advisory Board (ISAB) acts as NLHI's scientific consciousness. It meets once a year to advise the board on the international context of cardiovascular research, rank internal proposals for NLHI cooperation grants and discuss the outcomes of research reviews.

The committee notes that the organizational structure of NLHI seems quite complex and to some extent non-transparent. The organogram in the self-evaluation report shows a beehive-like structure of boards, centers and other bodies. From the written documentation it was not immediately evident which purpose different parts of the organization serve within the larger whole and which interactions take place between the different levels and at which frequency. A seemingly haphazard collection of Dutch and English names and acronyms further adds to the confusion. The committee concludes that all of the above reflects organic growth, responding to needs that were felt at a particular time. It does not necessarily constitute the most effective and efficient organization. The time might now be right to rethink and (especially) simplify/clarify the whole organization, starting with the naming but perhaps also including the overarching structure.

#### *Research infrastructure*

Providing infrastructure at a central, project-transcending level is a key element in NLHI's strategy for optimizing cooperation and talent development. Amongst the facilities (co-) initiated and maintained by the institute are the cardiac tissue repository (*Hartenbank*), the

CONCOR registration of congenital cardiovascular abnormalities and the Durrer center which supports cardiovascular biobanks.

The committee notes that the quality of the infrastructure as offered by CONCOR, Durrer Center and *Hartenbank* is beyond dispute. These are valuable infrastructures with international and long-term impact. Nonetheless, it would have been helpful if NLHI had offered more details on the size and reach of these facilities (number of samples, number of users, projects and publications based on them etc.). The organization of the infrastructure seems complex to the committee. To the outsider it is, for instance, not immediately evident why CONCOR is separate from the Durrer Center. From the interviews, the committee learned that historical factors have largely determined the current structure, which raises the question whether some restructuring could result in a leaner organization. And again, the committee noted the heterogeneity in the nomenclature, which led to the conclusion that NLHI should consider a better branding of its constituent parts.

An important new player in the organization of cardiovascular research is the Dutch CardioVascular Alliance (DCVA). This alliance was co-founded in 2018 by NLHI and the Netherlands Heart Foundation as the overarching structure under which the associated parties will develop (what was termed) a 'delta plan' for cardiovascular diseases. The nature of this larger structure and NLHI's role within it were initially unclear to the committee (as this may indeed be to the outside world in general), but over the course of the site visit, it came to see the establishment of DCVA as a logical step. The board explained that the intention is for DCVA to act as a broker, lobbying society and government to secure more funding for cardiovascular research. For the time being DCVA is still *in statu nascendi*. The future intention, however, is for NLHI to assume an

active role within DCVA as the point of contact for academic cardiology, connecting academic partners with each other, with non-academic cardiology departments, with privately owned companies and with subsidiary bodies.

Project support is another major part of NLHI's reason for being. Under the umbrella of NLHI, academic centers can join international consortia as one party. The institute aims to maintain a high quality, highly versatile, time efficient, and cost-effective project coordination office specialized in consortium management. Services include support in writing and managing grants and contracts. On top of that, NLHI offers the possibility of centrally appointing temporary research staff such as PhD candidates and postdocs working across different academic centers. In 2020, NLHI employed a total of 53 academic staff, 6 technicians/nurses and 12 research support staff, who work at the academic centers. All of them are on fixed-term contracts related to research projects and fellowships. NLHI also has a limited number of support staff on site. This includes three project managers who manage NLHI's portfolio of over 100 projects and more than 200 bigger and smaller grants.

The committee established that interviewed researchers are highly pleased with the quality of facilities and level of project support offered by NLHI. They mentioned that the central infrastructure helps them navigate the complicated logistics of multi-center projects. The support staff was characterized as knowledgeable and efficient. While NLHI's project management team is small and to some extent in competition with the services of local support offices, all of which are rapidly evolving in capacity and expertise, NLHI has the distinct advantage of occupying neutral ground amongst the academic medical centers.

Another potential role NLHI could explore is whether it might facilitate central access to the

unique facilities that are present at the individual academic medical centers, thereby strengthening and extending ongoing collaborations, while offering more research opportunities to all its members (and especially early career investigators).

#### *Academic culture*

A SEP-aspect that was difficult for the committee to assess is that of the openness, (social) safety and inclusivity of the research environment, or, in short, NLHI's academic culture. Rather than an actual workplace with associated measures to ensure openness, safety and inclusivity, NLHI offers its researchers a structure of periodic meetings and events.

As mentioned in the self-evaluation report, promoting cooperation by organizing scientific meetings aimed at networking and knowledge exchange is an explicit part of NLHI's strategy. A tangible extension of this strategy is the Holland Heart House, which houses several research organizations in the cardiovascular field, including NLHI, the Dutch Association for Cardiology, the National Cardiovascular Data Registry, the Cardiovascular Education Institute and DCVA. Centrally located in Utrecht, the Holland Heart House offers meeting spaces that facilitate interaction and knowledge exchange.

The committee established that meetings at several different levels are part of the regular calendar of events. The heads of the cardiology departments meet three or four times a year in the closed sessions of the *Seniorenberaad*. Additionally, there are monthly thematic scientific sessions where principal investigators discuss a wide variety of topics and thematic working group meetings where leading researchers aim to elevate topics in emerging fields to the next level by exchanging information, building networks and writing grant proposals. Finally, the Translational Cardiovascular Research Meeting is an annual meeting at a conference venue in Utrecht (300+ attendees from the

Netherlands). Organized since 2017, this meeting provides a broad platform and networking opportunity for cardiovascular researchers.

Interviewed junior and senior researchers made it clear that they value NHLI as a network for exchanging ideas, establishing new collaborations and gaining inspiration. Senior researchers got to know the Heart House as a place where monthly meetings, frequented by department heads and other high-ranking researchers, but also their PhD candidates, brought about new initiatives and projects. This exchange was experienced as highly beneficial for careers in cardiovascular science. However, in recent years – even before the Covid-19 pandemic – the frequency of such gatherings was said to have diminished. The committee supports the suggestion made by senior researchers to revive these frequent meetings.

NLHI has not implemented specific strategies or targets with respect to promoting a diverse and inclusive environment. As part of the institute's house rules, diversity was said to be considered when installing boards, committees, and when opening calls and judging proposals. The house rules also provide guidance on appropriate interactions between staff. The committee concludes that NLHI demonstrates awareness of the need for diversity and equality, although it would be desirable to indicate what effect this has had on the composition of boards and other bodies. In the opinion of the committee, the lack of diversity is a concern for the whole discipline of cardiology. Representation of women and minorities in leadership is low and there is an urgent need for more diverse role models and mentors for junior staff. The committee sees a role for NLHI in initiating a discussion amongst its academic partners on promoting diversity, including but not limited to gender equality.

NLHI follows the standards for scientific integrity as laid down in the Code of Conduct

for Research Integrity (2018), focusing on three subthemes: (1) assessment of output and performance, (2) data sharing and management according to the FAIR principles and (3) Open Science. With respect to the latter, some promising initiatives were developed. NLHI found that it takes quite a lot of time before rapidly evolving policies are embraced by scientists and therefore decided to kickstart a conversation on open science amongst the academic cardiology departments, aimed at implementing a shared policy. Furthermore, NLHI has established biobanks and patient registries that are open to providing invaluable material and clinical information to scientists nationally and internationally. The committee was informed that NLHI regularly receives requests for sharing data and that such requests are almost always granted. Whether these requests are centrally curated by the NLHI or locally by individual academic centers was not entirely clear to the committee. A further initiative towards Open Science is that NLHI actively endorses preregistration of animal research so as to improve transparency and reduce the risk of reporting bias in case of preclinical studies. The institute is one of the initiators and supporters of the preregistration platform [www.preclinicaltrials.eu/](http://www.preclinicaltrials.eu/). A future goal is to earmark 5% of grant budgets for open science (e.g., open access publication, FAIR data management).

Currently, NLHI does not employ a confidential counselor for its employees. The committee applauds NLHI's decision to remedy this in the near future.

#### *HR policies*

HR policies at NLHI are mainly aimed at talent management and career development. As previously mentioned, stimulating young research talent and coaching it to the top of the discipline is an explicit strategic goal of NLHI. The institute acknowledges that pursuing a career in science may pose challenges on both a professional and a personal level and hopes to mitigate such

challenges for its young research staff. While PhD candidates and postdocs involved in NLHI projects are appointed at NLHI, they work in the laboratories and clinics of NLHI's partners. Together with these partners, NLHI organizes meetings and programmes aimed at improving research and competitive skills such as grant writing. The success of this approach was emphasized in the interviews: senior staff indicated that not just their own careers but also the careers of their former trainees had taken off because of the support of NLHI. Past PhDs and postdocs developed into successful PI's leading the next generation of collaborative research projects. Interviewed junior staff were similarly appreciative of the benefits of being associated to NLHI, specifically praising the support offered on grant writing, the exchange of ideas within the institute, and the opportunities to participate in exchange programmes abroad.

During the site visit, a number of structural initiatives were presented to the committee, including the career development network Young@Heart, which was established in 2012 and is now part of the 'talent pillar' of DCVA. Young@Heart organizes semi-annual events focused on soft skills and networking, and issues calls for research grants for young scientists. For more established researchers, a leadership programme was developed as part of DCVA. Within its fellowship programme, NLHI annually offers two to four postdocs the chance to work abroad for up to a year. Finally, NLHI together with NVVC organizes the Einthoven dissertation prize, an annual contest for the best cardiovascular thesis in the Netherlands.

Junior staff were clearly enthusiastic about these initiatives. Some interviewees were themselves alumni of the fellowship programme, which they considered a good opportunity for personal and professional development, even if the stipend was described as on the low side for destinations such as the US. According to junior staff, the

fellowship programme is known and well-regarded in the cardiovascular field. A suggestion made by junior talent that the committee fully supports is to introduce a mentoring programme that pairs junior researchers with established researchers. An existing initiative by Young@Heart was found to be more similar to a “buddy” than a mentoring system, as it lacked senior role models. In the committee’s opinion, the system should aim to continuously support young researchers and tie them to the NLHI throughout their career.

Building on a comment by young researchers that there is hardly any opportunity for research within the established medical specialty training, the committee suggests that NLHI could play a role in lobbying its partners for dedicated research time. The committee underlines that NLHI is in an ideal position to shape a common view and policy on research in medical specialty training. This would strengthen the profile of the physician-scientist, make it more attractive and potentiate the translational dialogue and team science. This aim could be supported through funding incentives.

#### *PhD policies and training*

The committee found that NLHI does not have specific policies regarding the training and supervision of its PhD candidates. Rather, the academic cardiology departments where these PhDs are embedded provide the framework for supervision and instruction. In the committee’s opinion, this is a necessary consequence of the way in which PhD arrangements are set up. Avoiding duplication of efforts and saving valuable resources is a good strategy on the part of NLHI. By liaising with well-established initiatives such as Young@Heart, NLHI succeeds in providing its PhDs (and postdocs) all the benefits of a rich career development network.

## **Quality**

### *Research agenda*

The research programmes of NLHI are executed within a number of themes that are deemed important areas of cardiovascular research, taking into account new developments and clinical and societal demands. The current themes are:

- Arrhythmias
- Cardiogenetics
- Congenital Heart Disease
- Heart-Organ axis
- Heart Failure
- Ischemic Heart Disease

The committee established that there is no central strategy in terms of the topics that NLHI covers. Rather, the choice of topics is influenced by external research agenda’s, subsidy calls and the principal investigators who collaborate with NLHI. Interviewees said that research projects develop organically, in a bottom-up fashion, giving the institute the flexibility to respond to new developments. Typically, ideas for new projects are brought to NLHI by researchers from the individual departments and subsequently ranked by the ISAB. As NLHI is aware, the downside to this organic approach is that there is currently no way of ensuring that NLHI has a broad coverage of all major cardiovascular topics. The committee, for instance, noted that NLHI has limited presence in the fast-growing field of cardio-oncology, as well as in fields such as hypertension, atherosclerosis and lipidology. The committee sees clear benefits of developing a strategic research agenda at NLHI level, perhaps accompanied by a renewed thematic organizational structure. This could lead to a more carefully considered and broader range of topics, preferably including the prevention of cardiovascular disease, which is increasingly recognized in national and international agendas as deserving priority. The committee was informed that the board of NLHI will evaluate a proposal for such organizational change in the coming year. The committee also sees opportunities in terms of adopting a more

deliberate trans/multi/interdisciplinary approach, which would be in tune with the changing funding landscape.

#### *Output*

While NLHI does not have a specific publication strategy, bibliometric indicators suggest that the volume and quality of its output is impressive. Over the reporting period, researchers working on NLHI projects achieved a combined output of 29 PhD defenses and 1101 publications (in Web of Science) with an average citation score of 19.97, which is higher than that of all individual cardiology departments except the UMCG in Groningen. This high citation impact gives the impression that collaboration within NLHI enhances the quality of research, highlighting that the institute is successful in its goal of fostering excellent research. The committee established that a very large number of publications focused on the selected themes of NLHI offered valuable new knowledge to the international scientific community. The visibility of NLHI publications might be improved. While its publications in WoS are earmarked as having been funded by NLHI, the committee found that a PubMed search does not yield many results. It therefore encourages NLHI to seek appropriate acknowledgement/recognition for its contribution to these projects.

#### *Collaboration*

As mentioned, NLHI's research is typically the product of collaboration. The institute is involved in competitive international research grants and large clinical trials (such as the RACE studies, HEBE Trial and Biomarc Study) and in the past five years the institute has supported several large consortia funded by Dutch and international programmes such as DCVA, DHF, Leducq, DHF-BHF-DZHK, Horizon 2020. In the committee's opinion, this reflects that NLHI is building a strong international reputation. A good example of combining local, national and international level collaborations is the PLN research programme, which has brought together

multiple expert clinical and basic research teams from across the Netherlands and the world, and at the same time, it has built a bridge of direct and effective communication with the PLN patient community (cf. Societal Relevance). On a local level, small seeding grants put NLHI on the map as the central body in the Dutch cardiovascular field and the driving force behind new ideas and possibilities. This role was boosted by the 2020 decision to reinstate the 'Cooperation Call' to revive the attention for new cooperative ideas and to attract researchers interested in cooperation.

In the interviews, senior researchers confirmed that NLHI is a highly useful instrument for getting collaboration going, as it provides a central point of contact for all local partners and helps to surpass mutual competition. Consortia were said to provide well-defined common goals and to increase mobility between partners, with researchers visiting each other's labs and gaining insight into the range of initiatives taking place across the Netherlands. In many cases, results from consortia have opened up possibilities for additional funding to continue their work in a follow-up consortium. The committee notes that the accounts given by younger staff put considerably less emphasis on NLHI being a driver for staff moving between and collaborating across departments within the Netherlands. While this observation may be coincidental, the committee encourages the institute to more strongly leverage its network position within the Netherlands to enhance introduction of ECI to work done at internationally leading departments in the Netherlands.

#### **Relevance**

NLHI does not have a direct approach to making an impact on society. Rather, it aims to achieve a significant impact through the promotion of pioneering cardiovascular research, and its translation to clinical practice. The committee established that this

has produced some very good outcomes in terms of clinical impact. The most impressive examples of NLHI's research making an impact on society, are the collaborative projects resulting in the establishment of clinical guidelines, and the programmes that involve close cooperation with patient organizations and communities. A particularly striking illustration is the PLN programme, which was created in collaboration with the PLN foundation. After raising initial funding, the PLN Foundation involved NLHI in building a research proposal around their combined network of research groups which resulted in a \$6M grant for the transatlantic Leducq network CURE-PLaN, involving six dedicated PLN research groups from the US and Europe and €3,6M from ZonMW to investigate the potential use of prime editing to further develop a cure. Future plans are to find funds for the next steps in (clinical) research, start companies when needed to protect IP and turn scientific results into new strategies for diagnosis and cure. Ultimately, a Phase I clinical trial will be started as soon as a suited strategy for curing PLN has been selected. As indicated by this example, NLHI has the will and know-how to co-design research with patient groups – its major societal stakeholders. In the committee's opinion, the close interaction with the PLN Foundation is setting an example for how clinicians, patients and basic scientists should work together to fight disease. Efforts are under way to liaise with more patient organizations along this same model, which is impressive. The committee feels that if NLHI wishes to have a broader societal impact, it has an advantageous strategic position in the Dutch cardiology arena as well as the network, to achieve this.

The committee notes that the documentation provided limited information on established and potential collaborations with industry, although affiliated researchers signaled this as a good opportunity for NLHI or (perhaps more suitably) the DCVA.

The committee established that patents and spin-offs are not (yet) a regular outcome of research done under the banner of NLHI. Recently, under the umbrella of DCVA, the FIRST investment fund for early-stage ventures was realized. Creating central expertise on patent findings, IP, start-ups and spin-offs was identified as an important opportunity for NLHI. The committee was pleased to see that NLHI considers to establish a dedicated office to offer these services to its members and beyond. However, the viability of such an office needs to be assessed in view of in-house solutions at the academic departments or their institutions.

Interaction with policy makers and advocacy is another area in which steps could be taken. With cardiovascular disease putting increasing strain on society, there is an obvious need for informing the public and lobbying the government for funding. This might be more in line with the mission of the new DCVA than with that of NLHI, whose activities lie in promoting academic research. Nevertheless, because of its representative network of clinical cardiology, NLHI has a unique position for providing credible and trustworthy information to public and funders.

With respect to making its research accessible to different publics around the world, NLHI has pushed for a joint policy of publishing in open access journals. Improving its PR activities is on NLHI's wish list for the coming period. The committee agreed with the NLHI approach to promote open data for sharing and re-use where possible but taking into account the sensitive nature of patient data and guidance by the GDPR.

### **Viability**

Considering NLHI's important contribution to nurturing young talents, establishing valuable infrastructures and establishing and promoting collaboration, the committee positively assesses the institute's viability. The high quality of NLHI's collaborative research and

the considerable societal impact made by establishing clinical guidelines ensure that the almost fifty-year old institute has enduring importance in the cardiovascular field. Nonetheless, there are some imminent challenges that the institute will have to deal with, as well as some opportunities that should be seized to promote future vitality. Most of these challenges and opportunities lie in the area of funding.

### *Funding*

The committee is well aware that NLHI went through a turbulent period after being forcibly separated from the KNAW. The institute had come to rely on the KNAW for bearing fifty percent of the costs of NLHI's permanent research infrastructure and support team, with the joint cardiology departments contributing the other fifty percent and providing laboratories and patient cohorts in kind. Disconnecting from the KNAW in 2016 caused quite a bit of financial insecurity, especially for the post 2021 period, when Academy funding stops altogether. For its future basic funding, NLHI will be reliant on the cardiology departments, which in their turn are threatened by budget cuts. For now, basic funding and thus NLHI's immediate future is secure. The committee was pleased to note that the departments have committed to renewing their contribution for a five-year funding period. Continuous support by the foundation 'Friends of Cardiology' enables NLHI to continue its talent programmes (fellowships and Young@Heart). Now that KNAW funding will stop, NLHI has aimed to increase income from grants, which is why the institute has invested in expanding its project support services. Additionally, NLHI has been discovering opportunities to utilize funding roadmaps to support research. In this respect, the institute is clearly on the right track: the amount of new grants added to the portfolio jumped from €5M in 2019-2020 to €13.5M in 2021, which is an impressive accomplishment. As was explained in the interviews, the considerable increase in grant funding was the result of actively stepping up acquisition

efforts in the past five years. The committee encourages NLHI to maintain this momentum by specifically targeting EU/international consortium grants in the coming period. The committee is firmly of the opinion that big opportunities in terms of competitive funding are to be found at the international rather than the national level. The institute, meanwhile, has not yet fully tapped into the potential of this funding stream, and large grants will surely help to underscore its position as a major player in cardiovascular research. Securing EU/international funding will also help to keep the Dutch cardiology departments on board. The academic medical centers are more likely to continue to contribute to the upkeep of infrastructure if they see a return in terms of enhanced participation in international/European calls. By further developing its model of representing the whole of Dutch cardiology within international consortia, NLHI has a good chance of success for multiple reasons. These include that an "umbrella" organization such as NLHI is administratively more versatile and efficient, can respond faster to grant opportunities that arise, is more attractive as one (rather than multiple) partner in large international consortia, and when considered as one partner offers a rare wealth of expertise/ infrastructures/patient cohorts/track record.

In the committee's opinion, all of this will require a clear business plan that considers different funding streams, and a proactive attitude, as international competition for grants will likely only increase in coming years. A business plan was not included in the documentation and the overview of projected funding that was provided to the committee seemed optimistic on the expected grant income. A contingency plan to face fixed costs and/or strategy for alternative funding should be considered.

While fundraising efforts have clearly paid off, the committee is under the impression that the split from the Academy and the subsequent

need to become self-supporting have claimed much of the attention of the Board, perhaps causing other issues to take the backseat for a while. Now that acute financial danger has been averted, the committee believes that the institute should turn its attention to simplifying its organizational structure and developing a solid strategic plan for the coming period, as detailed in the 'Strategy'-section of this report.

## **Conclusion and recommendations**

Almost fifty years ago, NLHI was funded as a means to stimulate cooperation and exchange between the academic cardiology departments, granting central access to patient populations for clinical studies and preventing duplication of scientific research. In today's context of a rising cardiovascular disease burden and the emergence of a consortia-oriented funding climate, the committee is convinced that NLHI still has a major role to play in promoting the collaboration of academic cardiology departments across the Netherlands.

The institute had two main goals over the past five years: fostering excellent research and coaching talented young researchers. The committee concludes that both goals have been successfully served. Identifying specific themes to focus on, enabled coordinated actions and joined forces towards high need and high impact cardiovascular research areas. The number of publications in leading journals is indicative of the high quality of research. NLHI is evidently building a strong reputation, as reflected by its involvement in competitive international research grants and large clinical trials. Strong teams have been formed over time, which has led to highly competitive funding being attracted (e.g. European Commission, Leducq Foundation). Since the success of the PLN research programme, NLHI is increasingly approached by patient organizations and there are promising signs that patient driven research will be expanded towards other cardiovascular diseases. Moreover, the institute supported

the cardiovascular field with numerous thematic (working group) meetings and the annual Translational Cardiovascular Research Meeting. The approach to talent development seems equally fruitful. NLHI has a well-regarded scholarship programme in place and also supports career development by initiatives such as Young@Heart. The output of the young scientists recruited is of high scientific quality and several of them are now replacing retiring faculty in leading scientific positions.

To encourage NLHI to maintain, and perhaps even further increase, the high quality of its research and services in the next reporting period, the committee offers the following recommendations:

- *Further develop the institute's USP.* NLHI would be served by further elaboration of its strengths in strategic plans. Performing a comprehensive benchmark analysis could contribute towards this.
- *Revisit the organizational structure.* The committee encourages NLHI to reconsider its structure and make it leaner. A new organization should reduce fragmentation or at least bring under one roof similar activities (biobanking, data registers) to streamline operations and simultaneously make the structures (and their names) more transparent to outside visitors.
- *Promote MD/PhD training and translational teams.* The committee believes that NLHI could lead the discussion on how to facilitate discover/bench research within the medical specialty training programme, as well as facilitate non-medical/PhD researchers exchange in clinical research programmes. As the platform of all academic cardiology centers, NLHI is in a unique position to push for change.

- *Develop a research agenda and publication strategy.* The committee encourages NLHI to lay down what the research priorities are and why: 'bottom-up' building on the excellence and capacities of the academic centers as well as aligning with a changing national and international research agenda. This implies a regular internal review and input from the ISAB.
- *Enhance NLHI's visibility.* This, in the committee's opinion, could be done by seeking appropriate recognition for the institute's contribution to (sponsored or organized) research publications. A mandatory affiliation link to the NLHI should be considered.
- *Assume an active role within DCVA.* Because of observed parallels in leadership, projects and mission, it is currently not so clear where NLHI ends and DCVA begins. The committee feels that NLHI's efforts within the umbrella structure should be aimed at synergy rather than duplication.
- *Expand societal relevance beyond patient participation.* The committee encourages NLHI to be more pro-active in societal interaction in order to achieve societal impact. This includes expanding on the example of the patient participation in the PLN project, as well as public information and awareness. It is also advised to incorporate societal aims in the strategic agenda.
- *Push for EU funding.* The committee is convinced that setting up a research agenda that considers the strategic funding priorities in EU programmes will allow NLHI to tap deeper into international collaborative funding, where the institute has a strong competitive advantage and delivers value to its members.
- *Professionalize budget management.* The NLHI is advised to develop a more in-depth business plan. This plan should distinguish funding through project-related services (fees that are by nature variable), from a steady income from the membership contributions and align fixed and variable costs to projected income. NLHI could identify the structural benefits of NLHI (biobank, training) to the potential investors stakeholders (NWO, KNAW, hospitals) to enhance funding for this part of its activities.

# Appendices

# 1. CVs of committee members

**Diederick (Rick) Grobbee (chair)** is Professor of Clinical Epidemiology at the Julius Center for Health Sciences and Primary Care ([www.juliuscenter.nl](http://www.juliuscenter.nl)), University Medical Center Utrecht ([www.umcutrecht.nl](http://www.umcutrecht.nl)), the Netherlands, and Distinguished University Professor International Health Sciences and Global Health, at Utrecht University. He has been a (principal) investigator in many large-scale epidemiologic studies and randomized trials of interventions for the prevention and treatment of cardiovascular diseases. Topics include hypertension, diabetes, risk factors in children and youngsters, coronary heart disease, women's health, cardiovascular aging, heart failure and non-invasive vascular imaging. Apart from his interest in cardiovascular disease he has worked on the theoretical principles and methods of diagnostic and prognostic research. More recently he initiated a global platform for educational exchange in health sciences ([www.elevatehealth.eu](http://www.elevatehealth.eu)). In 2011 he started a unit for research on Global Health, a summary of activities is given at <http://tinyurl.com/p9q7ud8>. He acts as Chief Scientific Officer and statutory director at Julius Clinical Ltd. an Academic Contract Research Organization established in 2008 as a spin-off of the University Medical Center Utrecht ([www.juliusclinical.com](http://www.juliusclinical.com)), currently running projects in over 40 countries. Rick was listed in the top 100 global most influential biomedical researchers (*Eur J Clin Invest.* 2013 Dec;43(12):1339-65). He serves on the board of the European Society of Cardiology and chairs its Global Affairs Committee; is a fellow of the Royal Dutch Academy of Sciences; and currently acts as the Editor-in-Chief of *Global Heart* (<https://globalheartjournal.com/>) the

official Journal of the World Heart Federation of which he serves on the board. He supervised over 150 PhD fellows and published more than 1700 scientific papers, chapters and books. Number of international citations (Web of Science) 111.755. Hirsch:  $h = 160$ . In 2017 he was knighted by the Dutch King (*Knight in the Order of the Dutch Lion*).

**Raffaele De Caterina** is Professor of Cardiology and Director of the Postgraduate School of Cardiology at the University of Pisa; and Director, University Cardiology Division, at Pisa University Hospital. He is also Scientific Advisor for the "G. Monasterio" Foundation, Pisa, and of the Fondazione VillaSerena per la Ricerca, Città Sant'Angelo, Pescara, Italy. He has been Vice-President of the European Society of Cardiology (2008-2010) and President (2009-2013) of the International Society on Nutrigenetics/Nutrigenomics. He is Executive Editor of the *European Heart Journal*, Associate Editor of the *Journal of the American College of Cardiology*, and Past-Editor-in-Chief of *Vascular Pharmacology*. He is author of >600 peer-reviewed manuscripts. Major research interests: Cardiovascular Pharmacology, Atrial Fibrillation, Coronary Artery Disease, Cardiovascular Thrombosis, Nutrigenetics and Nutrigenomics.

**Despina Sanoudou** is Associate Professor in Pharmacogenomics at the Medical School of the National and Kapodistrian University of Athens, Head of the Clinical Genomics and Pharmacogenomics Unit at the 4th Department of Internal Medicine, and collaborating Faculty at the Biomedical Research Foundation of the Academy of Athens. Her research work focuses on deciphering pathogenetic mechanisms in cardiovascular disease and the development of precision medicine therapeutic approaches. She has

participated in tens of competitive research projects funded from international or national organizations. She has over 100 publications in scientific journals and books, an H-index of 41, and over 400 oral and written presentations at international meetings. She serves on the evaluation committees of 20 international and national funding organizations, as Associate Editor in the *Metabolism* journal, in the editorial board and reviewer teams of 50 other international scientific journals. She has established and directed multiple continuing education, graduate, undergraduate and high school training programmes, and given multiple career development lectures internationally (in Europe, Asia and the USA, including for Karger and Springer Nature publishers). Dr Sanoudou has received multiple awards for her contribution to science and education including the Greek L'Oreal-UNESCO award, the European Society of Human Genetics, the American Society of Human Genetics, and more.

**Peter Sinnaeve** graduated summa cum laude from the University of Leuven, Belgium, in 1994, and was trained as a cardiologist at the same institution. He subsequently obtained a PhD degree in Medical Sciences, after doctoral research in cardiovascular gene therapy. In 2002-2003, he was a post-doctoral fellow at the Duke Clinical Research Institute in the USA as recipient of a Fullbright scholarship. Dr Sinnaeve then joined the staff at the University Hospitals Leuven, Belgium. He is currently professor at the University of Leuven. His clinical expertise lies in acute cardiac care, interventional cardiology, pericardiology, as well as cardiac rehabilitation, while his current research focuses on antithrombotic & secondary prevention therapies and the genomics of acute coronary syndromes. He is active in a variety of national and international boards and is involved in several clinical trials in cardiovascular

disease. To date, Dr Sinnaeve has (co)authored 195 peer-reviewed papers and 26 book chapters.

**Karin Sipido** is Professor of Medicine and Head of Experimental Cardiology at the Department of Cardiovascular Sciences at KU Leuven. Her research field is rhythm disturbances and heart failure, identifying cellular and molecular mechanisms, in a translational perspective. Her research is internationally recognized, she holds several editorial positions and is an elected member of the Academia Europaea. She is a member of the Ethics Committee Research UZ/KU Leuven. She is a member of the Board of Trustees of the national Fund for Scientific Research Flanders ([www.fwo.be](http://www.fwo.be)). She takes an active interest in research policy, serving in various positions at KU Leuven, at European and international level. She was member of board of the European Society of Cardiology, and led the Council for Basic Cardiovascular Sciences. She was a founding board member and President of the BioMed Alliance in Europe (<https://www.biomedeuropa.org/>). From 2015-2020 she chaired the European Commission's Scientific Panel for Health (SPH), a science-led expert group based on the provisions of Horizon2020, tasked with helping to achieve better health and wellbeing for all, identifying long-term trends and strategic priorities. She is a member of Scientific Advisory Board of ORE, the European Commission's Open Research Platform.

**Uwe Zeymer** is Head of Interventional Cardiology at the Heart Center Ludwigshafen, Department of Cardiology, Germany. He is Vice-Director of the Institut für Herzinfarktforschung Ludwigshafen. He has been board certified in internal medicine, cardiology, interventional cardiology and intensive care medicine. After his graduation from Medical School at the Universities of

Munich and Marburg in 1985, Dr Zeymer gained experience as a resident, fellow and attendee in the Department of Cardiology, Municipal Hospital, Kassel, and as a clinical research fellow in the Department of Cardiology, Cedars-Sinai Medical Center, Los Angeles, USA. He is full Professor of Medicine at the University of Göttingen. Dr. Zeymer is or has chaired or been a member of the Steering Committee numerous trials in patients with acute coronary syndromes, antithrombotic therapies and anticoagulants. In addition he has been chair or member of the Steering committee of several international registries in interventional cardiology, treatment of hypertension, anticoagulation for atrial fibrillation and acute coronary

syndromes. Dr. Zeymer has authored and co-authored over 500 scientific papers on cardiovascular disease in journals such as the New England Journal of Medicine, Lancet, JAMA, European Heart Journal, Circulation and Journal of the American College of Cardiology. Dr. Zeymer has been the Chair of the Scientific Committee of the Acute Cardiovascular Care Association of the ESC, the Chair of the Working Group of Thrombosis of the German Cardiac Society and the Chair of the Working for Quality Insurance and Registries of the German Cardiac Society. He was President of the annual Autumn Meeting of the German Cardiac Society 2013. He is currently chairing the ongoing STEMI-Registry of the EORP of the ESC.

## 2. Schedule for the site visit

21 October 2021

Timeschedule	Activity	Location, Attendants
17:00 – 18:15	Meeting Assessment Committee	Holland Heart House
	Prepare for the interviews on October 22 <sup>nd</sup> . Discuss preliminary findings, working method and distribution of labour	Committee + secretary
18:30	Departure to restaurant	
19:00	Dinner	Utrecht City center
		MT NLHI Committee + secretary

22 October 2021

Timeschedule	Activity	Location, Attendants
9:00 – 9:45	Management	Holland Heart House
	Introduction with Management team NLHI	NLHI board, Managing director Chair self-evaluation committee
9:45 – 10:45	Senior staff	
	presentation #1 – Race program – Pro. I.C. van Gelder presentation #2 – IHZ and HF programs – Prof. H. Boersma presentation #3 – xxx 10-minute pitches	Management team NLHI Sr. staff members
10:45– 11:30	Mini-meeting Assessment Committee	
	<i>Wrap-up and prepare for next presentations</i>	
11:30 – 12:30	Early Career Investigators	
	presentation #1 – Renee Maas (UMCU) presentation #2 – Fleur Tjong (AUMC) presentation #3 – Wouter Meijers (UMCG) 10-minute pitches	Early Career Investigators
12:30 – 13:15	Lunch	
13:15 – 13:45	Talent program	
	Young @ Heart 10-minute pitch Talent program/ fellowships Q&A	Board Y@H Early Career Investigators
13:45 – 14:15	Mini-meeting Assessment Committee	
	<i>Wrap-up and prepare for next presentations</i>	
14:15 – 14:45	Infrastructure Q&A	
	<u>Durrer Center</u> <u>Hartenbank</u> <u>Concor Registry</u>	Coordinator <u>Durrer</u> Chair <u>Concor</u> Leader <u>Hartenbank</u> MT NLHI
14:45 – 15:15	Mini-meeting Assessment Committee	
	<i>Wrap-up and prepare for next presentation</i>	
15:15 – 15:45	Stakeholders Q&A	
	<i>10-minute pitch PLN program</i>	Representative PLN foundation Representative DCVA MT NLHI
15:45 – 16:45	Meeting Assessment Committee	
	<i>Discuss outcomes and define conclusions and advice for NLHI. Input for Secretary to prepare draft Assessment report.</i>	
16:45 – 17:00	Feedback session with Management team NLHI	
	<i>Committee chair presents findings and conclusions</i>	MT NLHI