Preface

Dear colleague,

We are pleased to present to you the Health-RI business plan – an ambitious yet realistic plan to assemble all stakeholders and create a sustainable infrastructure that will facilitate world-class personalized medicine & health research in the Netherlands.

The Health-RI business plan has been developed over the past months based on input and discussions with a comprehensive series of stakeholders. The Health-RI conferences held in November 2015 and December 2016, as well as the Health-RI stakeholder meetings in May 2016, June 2017 and October 2017 proved highly productive in providing feedback, direction and commitment that have been crucial for developing this plan for building Health-RI.

To continue in that vein of transparency and inclusivity, this plan is made public and consists of a 15-page summary and the full business plan. We hope that as an important shareholder in the Dutch Life Sciences & Health community you will recognize the valuable benefits of the plan to your own organization, as well as to the wider life-science research community and Dutch society as a whole.

After the Health-RI conference on December 8, we will enter into a process to evolve from the current temporary governance to a permanent governance as described in the plan, including the financial structures. We look forward to meet with you soon to formalize the role of your organization within Health-RI and hope to receive your full commitment like we have had in the earlier stakeholder meetings: only together we can realize and operationalize this important initiative.

On behalf of the Health-RI steering committee,

Gerrit Meijer & Ronald Stolk

Co-chairs Health-RI

Health-RI steering committee:

Jaap Heringa, Alain van Gool, André Dekker, Peter Luijten, Ruben Kok, Ronald Stolk, Gerrit Meijer
Health-RI – laying the foundations for personalized health in the Netherlands

Good health is one of the most precious things in life. Without it, we are unable to reach our full potential and enjoy life to the full. So staying healthy as much of the time as possible, and if we do fall ill, returning quickly to good health, is important to us all. The prevalence of chronic disease means we are not there yet, but within the next twenty years we will be.

By the year 2040, medicine will be truly predictive, preventive, personalized and participatory – P4 Medicine. The health sector will primarily focus on keeping people healthy rather than treating the sick. Disease will be identified in its early stages, before radical intervention is required, and treatment will be based on our own unique characteristics – right down to our individual DNA. Care will move out of expensive hospital settings into lower cost community and home-based settings. Healthcare will be democratized and personalized, with individuals engaged and empowered to take an active role in looking after their health. Prescriptive healthcare systems will be replaced by learning healthcare systems that learn and improve the delivery of care with every patient treated. As a result, everyone will benefit – individual citizens from healthier lifestyles and disease prevention, healthcare systems and payers from reduced costs, and society from greater productivity and more efficient use of resources.

Will it happen in the Netherlands, and equally importantly, be driven by the Netherlands – a country that is already a world leader in life-science research? Not unless concerted action is taken now to realise a national infrastructure that brings together all stakeholders in the end-to-end process of bringing personalised medicine & health and a learning healthcare system to reality. The disturbing truth is that even in today’s world of seamless digital connectivity, research resources remain fragmented, vital data remains locked away in silos, and even when it is accessible, a lack of standardization limits its interoperability and re-use. It is therefore no surprise that the innovation gap between research results and healthcare practice remains alarmingly wide.

Health-RI will take the concerted action that is needed to bridge the innovation gap towards personalised medicine & health in the Netherlands. Health-RI will create a shared national infrastructure and a shared service center that unlocks the data and resources needed for world-class evidence-based health research along the full citizens journey from conception to the end of life. Equipped with the data and tools to develop a better understanding of the transitions between health and disease, algorithms to predict and detect these transitions in individuals, and personalized treatments to reverse them with little or no side effects, the Dutch health research community will be able to realize the personal and societal benefits of P4 Medicine for the good of the nation. The unlocking of data will also create the optimum environment for a learning healthcare system that continuously adapts to people’s needs, while the active participation of individual citizens in both the process and the agenda will make sure those needs are fully understood.
Creating a shared infrastructure fit for developing the predictive, preventive, personalized and participatory medicine of the future will require some creative thinking. Ethical, legal and societal issues, for example, will preclude the setting up of centralised and monopolised data repositories. Health-RI therefore embraces approaches that do not rely on centralised data, like the Dutch Techcentre for Life Sciences (DTL) ‘Personal Health Train’ initiative, which allows researchers to query distributed databases via a secure, authenticated network, only requiring data owners to make their data FAIR (Findable, Accessible, Interoperable and Reusable). Ownership and control of such data could ultimately be extended to individual citizens, so imagine a world in which you control your data and are free to donate it securely to whichever research groups you choose. It’s something that cancer patient Dirk Jan van der Pol is already exploring, see ‘It’s my data’ below.

Building on the current strength of public-private partnership research in the Netherlands, Health-RI will bring together the best of the country’s expertise and resources for open-science health research, make them accessible to researchers by means of connecting activities and shared services, and act as a collective voice for the sector both nationally and internationally. In doing so, it will lay a strong foundation for creating a democratized, value-based, learning healthcare system for the Netherlands that will empower its citizens to stay healthy and achieve their true health potential.

It’s my data

When Dirk Jan van der Pol* was diagnosed with thyroid cancer in 2003, the overwhelming emotion he experienced was one of powerlessness – a feeling that critical decisions in his life were being taken over by the healthcare system. After recovering from his thyroid removal operation, he decided not to let that happen again. He immediately started to collect as much of his personal medical data as he could find. Today he holds around 52 terabytes of that data, including his full genome sequence. Much of it he had to fight for.

Within a couple of years of the operation to remove his thyroid, Dirk Jan developed chronic obstructive pulmonary disease (COPD). His doctors put it down to coincidence, but somehow, he felt that it was linked to his cancer. Via patient forums and social media, he has since discovered around 200,000 other people around the world who have had a similar experience – thyroid problems followed within a few years by COPD. His background in healthcare and data science also enabled him to identify at least two genes in his genome that could possibly link the two problems. All circumstantial evidence, of course, but it has been sufficient to attract the attention of the research community to something that could be a real problem. If enough of the other 200,000 patients who Dirk identified were able to grant access to the type of personal data that he held via initiatives like the DTL’s Personal Health Train, answering the relevant research questions would be much simpler. It’s just one example of how the research infrastructure that Health-RI is committed to creating in the Netherlands could close the loop between patients, the research community, and new innovations in patient care.

* Among his other interests, Dirk Jan van der Pol is an ambassador for the Human Genome Foundation
Contents

Business plan content

Executive summary business plan 6

Business plan in detail

The need for Health-RI 23
— Trends and challenges in health research 25
— Failing to operationalize Health-RI 29

Health research environment 30
— Current Dutch health research environment 31
— Similar infrastructures abroad 39

Strategy of Health-RI 41
— Mission, ambition and strategy 42
— The Health-RI network and ecosystem 43
— Design principles 47

Health-RI value proposition 48
— Health-RI services and activities 49
— What does Health-RI offer the different stakeholders 53

Organizational structure 55
— Governance model and legal structure 56
— Operational model 58

Business plan content - continued

Financial structure 59
— Income sources 61
— Expenses categories 65
— Detailed financials 66

Bibliography 71

Definitions and abbreviations 74

Appendices

Ia. Overview of partnering, collaboration and convergence of initiatives till now 78
Ib. Actions performed by Health-RI until now 79
II. Explanation of meta-data levels 80
Executive summary business plan
Health-RI is the solution to today’s challenges in the health research environment

Challenges and issues in the health research environment

- **Fragmentation of infrastructures** due to limited willingness to share data/facilities, competition for funding and limited coordination of funding in the past
- Infrastructures, contributors and researchers operate in separate worlds. Integration and professionalization is needed
- The promise of personalized medicine & health is not delivered (the innovation gap)
- There is a lack of reproducibility of research outcomes (50% not usable)
- Researchers are rewarded for generating publications, not for translating science to society
- Return-on-investment of health research is insufficient
- With major investments, other countries* are already setting up similar infrastructures, giving their researchers better access to research facilities and to relevant data

Opportunities and solutions to these challenges

- Develop a **top-of-the-bill infrastructure** for health research in the Netherlands supported by a shared service center
- **Strong collaboration** between infrastructures, contributors, and all relevant stakeholders, including scientists, health professionals and citizens
- Acceleration of the development of a learning healthcare system
- Implement data stewardship based on **FAIR principles** (Findable, Accessible, Interoperable, Re-usable) and stimulate secure re-use of resources
- Change incentives to **reward researchers for sharing**
- **Efficient use** of available funds via coordination of an investment agenda
- Shared infrastructure to facilitate **access to data** under inclusive governance

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*Swiss SPHN (Switzerland), US Precision Medicine Initiative (USA), Genomics England (United Kingdom), Stratified Medicine Scotland (Scotland), Medizininformatik (Germany)
Executive summary

Health-RI will improve efficiency by connecting infrastructures in the Dutch health research field

**Size of the Dutch Health research environment in Euros**

- **Annual total funding** for health research is \( \sim \€ 500 \text{ million} \)\textsuperscript{S1,S2,S3}
- Around \( \€ 30 \text{ million} \) is marked directly for infrastructure
- With a **small part of the total budget**, Health-RI will improve efficiency by organizing the national infrastructure
- In addition to the health research budget yearly around \( \€ 100 \text{ million} \) is spent on registries of health(care) data\textsuperscript{S4}

**Selection of players in the Health-RI field (non-exhaustive)**

- **Main funders**
  - NWO
  - ZonMw
  - Government
  - Health funds
  - Others

- **Existing infrastructures**
  - TraIT
  - ELIXIR-NL
  - DTL
  - BBMRI.nl
  - SURF
  - Others

  In addition to the infrastructures mentioned, several smaller and bigger infrastructure functionalities exist. These are often locally based infrastructures that develop and maintain their facility individually, and these services are not shared amongst organizations.

- **Infrastructure users and contributors**
  - Healthcare providers (Hospitals, UMCs, …)
  - Knowledge institutes & universities
  - Healthtech industry
  - Drug, supplement and food industry

\*The \( \€ 500 \text{ million} \) is an estimation based on the budgets of funders in the health research environment\textsuperscript{S1,S2,S3}
Executive summary

Health-RI has defined its mission, ambition and strategy, demonstrating how Health-RI will create value for society

**Why are we in business?**
Creating value for society by facilitating all steps in the process of health research.
As a result, Health-RI will achieve major societal transformation, for:
- Researchers: enabling them to perform excellent cross-disciplinary and data-intensive research
- Funders: enabling them to obtain optimal return-on-investment
- Citizens: who will be more involved in high quality research, leading to faster implementation of personalized health
- Others (e.g. government, care providers, industry, health insurers, etc.): who will be part of a well organized network for health research and prevention

**Where do we want to be in 2023?**
We will have realized a state-of-the-art infrastructure for data, samples and images that will be key to facilitating excellent health research and sustainably bridging the health innovation gap.

**How do we get there?**
- By all stakeholders in the ecosystem working together at strategic, tactical and operational levels
- By functioning as a shared service center that provides a single platform for delivering an integrated suite of functionalities, assets and support to researchers, leading to compliance-by-design
- By delivering a balanced financial model with transparent and logical prioritization of resources that are made collectively available
- To this end, Health-RI will work with jointly determined standards, conditions and ‘rules of engagement’

**How are we going to achieve this?**
- Establish an effective and efficient organization
- Defragment infrastructures
- Cooperate with all stakeholders
- Adopt an integral funding system
- Make a long-term commitment
Connecting existing and new infrastructures is an essential step towards a national infrastructure

TraIT enables integration and querying of information across the four major domains of translational research: clinical, imaging, biobanking and experimental (omics)\[^{55}\]

ELIXIR-NL provides the FAIR-based interoperability platform for tools, data resources and cloud services. It develops and implements virtual research environments for data stewardship and distributed analytics\[^{56}\]

DTL has established a network of expert groups that offer their high-end technologies and the associated expertise and infrastructure to researchers who do not have access to such facilities at their home institute\[^{57}\]

BBMRI-NL makes biomaterials, images and data from (longitudinal) research retrievable, accessible and exchangeable for research on the prevention and treatment of diseases\[^{58}\]

The Parelsoer Institute offers researchers an infrastructure and standard procedures for the establishment, expansion and optimization of clinical biobanks for scientific research\[^{59}\]

Data4Lifescience (D4LS) is connecting the data infrastructure for biomedical research of the eight University Medical Centers\[^{510}\]
Health is one of the most important quality aspects along the entire timespan of our lives. Health-RI facilitates research that leads to innovations that allow us to stay healthy as much of the time as possible, and if we do fall ill, to regain health as much and as quickly as possible. With this live long scope, Health-RI interacts with the whole range of health related topics, like environment & health, healthy ageing, primary healthcare, prevention, food & health, mental health, healthy youth, personalized medicine, and others.

Increasingly, personal data are being collected that are relevant for the understanding of our personal health. Citizens collect more and more of their own data and a vast array of data is gathered in the health system. Having personal data on these health aspects available for research is crucial to reach this goal of better health outcomes. As a consequence, Health-RI interacts with health related initiatives and concepts like a learning healthcare system, value based healthcare, closing the innovation gap, big data, e-health, quantified self, and self management.

In a health sector that broadens at spectacular speed to allow inclusion of a wide variety of aspects that influence our personal health, from biology to socio-economic aspects, to how our food and lifestyle interact, there is a huge potential to better learn how we can self-manage our personal vitality, functioning and health. Health-RI will offer the platform that allows citizens and all other stakeholders in the health research domain to securely combine and interpret such variable data.

Health-RI thus supports a broad variety of disciplines and sources of information to allow for a democratic and accessible science and innovation environment in which citizens can participate extensively. The infrastructure offers stakeholders specialized in certain aspects or phase of our lifespan, from early conception to ageing, to build on each other’s expertise and information.

Health-RI thus strongly supports the health sector to offer high quality innovative services along the ‘citizen’s journey’, with great attention to prevention and early detection of health-threats, and with increased handles to treat disease at the personal level: personalized medicine and health.
Executive summary

Health-RI will build on existing infrastructures and attract new partners to establish the Dutch health research infrastructure.

Health-RI consolidates the activities of multiple Dutch ESFRI and e-infrastructure nodes by their landing into the Health-RI platform.

Health-RI is highlighted as the future Dutch research infrastructure for health research by other parties.

Highlighted Health-RI as a key player in various agenda programs.

Mentioned Health-RI as a necessary data infrastructure to achieve personalized medicine.

Listed Health-RI as a one of the “must have” large-scale research facilities.

Named Health-RI “an essential (data) infrastructure for health research and personalized medicine.”

Listed Health-RI next to personalized medicine initiatives abroad.

*Swiss SPHN (Switzerland), Precision Medicine Initiative (USA), Genomics England (United Kingdom), Medizininformatik (Germany)
Health-RI will offer functionalities to researchers by means of connecting activities and shared services. The Platform Health-RI will be the interface between the network and its users, the researchers.

- On an operational level, contributors are enabled to provide local functionalities via the platform, conveniently accessible to researchers through a one-stop-shop. Health-RI will operationalize this platform and provide support in the use of its functionalities. Furthermore, Health-RI will provide shared services to researchers and contributors directly at a level not offered by individual stakeholders (further explanation on next page).

- We distinguish two types of contributor: ‘data contributors’ offering data, samples, images etc. and ‘infrastructure contributors’ offering tools, facilities and services.

- In addition to the operational activities of Health-RI, Health-RI will act as a collective voice and perform activities on tactical and strategic level to achieve its ambition to transform the system and eliminate commonly experienced bottlenecks in the research process (further explanation on next page).
Health-RI will provide shared services and acts as the collective voice

**Provide shared services via the platform**

- Data
- Tools
- Facilities

**Act as a collective voice on the research infrastructure**

- On behalf of all stakeholders, Health-RI will represent the health research ecosystem on topics where a collective voice is needed to achieve changes that support the research process. This requires bringing the different stakeholders together. Stakeholders will be represented in the Health-RI governance.

- Health-RI will provide this collective voice on both tactical and strategic level. Examples of Health-RI activities include:
  - **Tactical:**
    - Drive and connect to the development of international data standards
  - **Strategic:**
    - Set a collective infrastructure financing agenda together with stakeholders and influence them to commit to the agenda
    - Align the Health-RI strategy with developments in healthcare infrastructures, for example, electronic patient files and MedMij, to create the possibility of connecting data that, for example, supports citizens to live a healthy life

Health-RI will provide shared services that contributors cannot provide individually, but that are nevertheless essential to connecting different resources (data, tools, services) to users, reusing data, and efficiently performing excellent cross-disciplinary and data-intensive research.

Some examples of Health-RI activities:

**Operational:**
- Operationalize a platform that provides an overview of all available content (data, samples, images, tools, facilities, etc.) and connect contributors and users to provide access
- Be the landing zone of Dutch health research infrastructure nodes such as BBMRI-NL, EATRIS-NL, and the health parts of ELIXIR-NL, NL-BioImaging and others
- Provide shared services directly to users (from existing initiatives BBMRI-NL, TraIT, ELIXIR-NL and EATRIS-NL)

**Tactical:**
- Provide education and training on common themes - e.g. FAIR* and ELSI**

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*FAIR: Findable, Accessible, Interoperable, Reusable
**ELSI: Ethical, Legal, Social, Impact*
The Health-RI infrastructure will grow over time along seven domains/themes

<table>
<thead>
<tr>
<th>Domain/Theme</th>
<th>The growth model of Health-RI: services provided and activities taking place within each domain / theme over time</th>
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<tbody>
<tr>
<td>Collections domain</td>
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<td>IT services domain</td>
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<td>Facilities domain</td>
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<tr>
<td>Theme 1 Research process management</td>
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<td>Theme 2 FAIR</td>
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<td>Theme 3 ELSI</td>
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<td>Theme 4 Strategy and relations</td>
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Connection of partners is not projected over time and overview of partners is not exhaustive

* FAIR level 1 is the current TraIT office suite level. ** Pilot FAIR level 2: https://www.dtls.nl/fair-data/personal-health-train/
Executive summary

Health-RI services and activities will lead to an infrastructure that facilitates the entire research process

Health-RI activities at different steps in the research process (non-exhaustive)

Services and activities provided

Research Process

Define research question

Experimental design

Access to data and samples

Data generation

Analysis

Translation and dissemination

Improvement of research / care

Operational level (platform services)

- FAIR data management training, education and support
- ELSI Service desk
- Legislation compliance tools
- Biobanking registry support center
- Central catalogue and request tool for data, samples and images
- Linked data-backbone
- Coupling between data sources
- Catalogue of facilities and expertise centers
- Interoperable data acquisition tools
- Interoperable analysis tools
- Federated analysis workspace
- Helpdesk IT-tools and services
- Linked data-backbone
- Coupling between data sources

Tactical level (connecting the network)

- FAIR data management guidelines
- Citizen’s / patient’s voice in the strategic committee
- Reuse of previous research
- Standardized ethical review procedures
- A network of ELSI experts offering ELSI support
- Compliance-by-design
- Connected registries and biobanks
- Single identification, authentication and authorization system
- Network of data experts
- Covenants for use of facilities by others
- Harmonize data acquisition protocols
- Interoperability standards
- Coordination of IT platforms
- Promotion of the use of FAIR services
- Connections to Open Science initiatives
- Participation in Health-deals
- Commitment of user associations

Strategic level (transforming the system)

- Increasing citizen participation
- Prioritizing of research questions by specialists and patients
- Promotion of the reuse of routine care data for research
- Promotion of omnibus legislation
- Promotion of the opening up of industry trial data
- Promotion of all data to be available in the public domain
- Coordination of investments in data infrastructures via the financing agenda, resulting in sustainable long-term funding
- Coordination of investments in IT tools, facilities and infrastructures via the financing agenda, resulting in sustainable long-term funding
- Coordination of investments in IT tools, facilities and infrastructures via the financing agenda, resulting in sustainable long-term funding
- Promotion of active data sharing and Open Science policy
- Promotion of the recognition of data as academic output
- Promotion of learning care system
- Promotion of public-private partnerships

The Health-RI platform will offer researchers solutions-on-demand for each step of the research process. By simultaneously operating on the tactical and strategic level, Health-RI will connect the needs of researchers and other stakeholders (funders, society, etc.) transforming the total health research system.
Health-RI has clear benefits for all stakeholders in the health and medicine research field

Health researchers and research organizations

Researchers will be enabled to perform excellent research via:
- Better access and easy use of IT tools and facilities
- User support (for tools, ELSI*, FAIR** issues, etc.)
- Better access to (high-quality) FAIR data through standardization and harmonization of data, tools and processes

Citizens and patients

Better healthcare quality and access to personalized health will be within reach for citizens and patients, because Health-RI:
- Offers the research scale needed to drive the understanding of personalized indicators of health and disease
- Connects stakeholders to accelerate translation of knowledge into (preventive) treatments
- Gives patients and citizens a voice to ensure that the infrastructure that is built addresses society’s concerns

Funders

Funders will obtain optimal return-on-investment, because Health-RI will:
- Enable and stimulate reuse, translation and dissemination of research data and outcomes
- Help to ensure the efficient use of available infrastructure funds by coordinating the financing agenda with all stakeholders involved
- Facilitate adoption of standards by researchers, leading to better reproducibility (and quality) of research and compliance-by-design

Government and society

The Netherlands will consolidate its leading role in the global healthcare field because Health-RI will:
- Act as a ‘launch pad’ for excellent health research
- Facilitate translation of research into practice
For the government and society, this will lead to increased return-on-investment, healthier citizens, and a significant increase in the economic contribution of the Dutch health research field

Private parties

Innovative companies will be able to accelerate development of of solutions in (personalized) medicine and health, because Health-RI will:
- Provide a platform to connect to research data and researchers
- Empower researchers to perform research that meets standards and regulations
Health insurers will be able to service their clients better, because Health-RI:
- Supports research targeting the development of personalized healthcare and improvement of healthcare quality

Contributors

Infrastructure contributors will become more effective organizations because Health-RI will:
- Increase the visibility of their offering and its use by researchers
- Commit to design a structural financing agenda for infrastructures
Data contributors will be able to generate more knowledge from their data because Health-RI will enable standardization and interoperability of content, thereby increasing its suitability for use by other researchers
The Health-RI governance is inclusive for all stakeholders

The governance structure of the Health-RI organization is efficient, effective and supported by its stakeholders

1. All stakeholders can join the general assembly, which is informed at least once a year by the managing board. All ten chambers of stakeholders will be present in the general assembly. Each chamber appoints their representative in the strategic committee.

2. The strategic committee will consist of designated representatives from each of the ten chambers. The strategic committee will set the strategic agenda and infrastructure agenda. Furthermore, they will advise on the five members that sit on the supervisory board.

3. The supervisory board will consist of four designated individuals chosen from the representatives of the chambers of citizens / patients, funders, users, medical research institutes and general research institutes. The supervisory board will supervise the managing board on the execution of the strategic and infrastructure financing agenda, and will appoint and discharge the members of the managing board.

4. The Health-RI organization will consist of the managing board and the operational teams. They will be responsible for the daily operations of Health-RI. The managing board will consist of a Chief Data Science, Chief Health & Medicine and a Chief Executive Officer. They will connect all disciplines within Health-RI to ensure effective execution. The structure of the operational teams will be flexible, because they have to execute a strategic agenda that will change over time.
Three income sources for the Health-RI organization ensure a sustainable and effective execution of the strategy

Income and expenses of the Health-RI organization

The Health-RI organization is expected to have an annual turnover (P&L) of around € 20-25 million in 2022.

We differentiate three income sources:

1. **Fee for service** is income generated by users paying for services offered on or via the platform.
2. **Direct funding** by the government, knowledge institutes or private parties like health funds. Sustainable income is needed for Health-RI to connect and represent stakeholders in the Health-RI ecosystem and to offer certain shared services.
3. **In-kind contribution** (FTE) from data contributors, e.g. contact points within each UMC and university to be able to deliver our services locally.

We differentiate three expenses categories:

4. **Direct services related expenses** that are connected to the offering of Health-RI services and the related activities.
5. **Indirect services related expenses** that are not directly related to the provided services and cover strategic and tactical activities.
6. **Other expenses** that include participation fees to connect with European hubs and unforeseen expenses.

S2. ZonMw, Jaarverslag ZonMw 2015, March 2016

S3. Rathenau instituut, Overzicht van Gezondheidsfondsen, hun budgetten voor onderzoek, in miljoen euro en het onderzoeksbudget als % van de totale lastenwebsites fondsen, https://www.rathenau.nl/nl/page/onderzoeksuitgaven-van-de-gezondheidsfondsen, retrieved on 5 October 2017


S13. KNAW, KNAW-agenda grootschalige onderzoeksfaciliteiten, 2016


### Definitions used in the business plan

<table>
<thead>
<tr>
<th>Term</th>
<th>Definition</th>
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<tbody>
<tr>
<td>Data contributor</td>
<td>Partner organizations that can provide researchers with data, samples or images for research. They provide this content via the platform</td>
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<tr>
<td>Health gap</td>
<td>The gap between the actual health of an individual and their health-potential</td>
</tr>
<tr>
<td>Health-RI ecosystem</td>
<td>All stakeholders in the field of medicine &amp; health research</td>
</tr>
<tr>
<td>Health-RI network</td>
<td>The community of partners that execute infrastructure tasks coordinated by Health-RI and funded from the collective Dutch health research infrastructure budget</td>
</tr>
<tr>
<td>Infrastructure contributor</td>
<td>Partner organizations that can provide researchers with expertise, tools and other services to perform research. They provide these services via the platform</td>
</tr>
<tr>
<td>Innovation gap</td>
<td>The current lack of translation of research results into healthcare practice</td>
</tr>
<tr>
<td>Learning healthcare system</td>
<td>A system in which science, informatics, incentives, and culture are aligned for continuous improvement and innovation, with best practices seamlessly embedded in the delivery process and new knowledge captured as an integral by-product of the delivery experience.</td>
</tr>
<tr>
<td>Personalized medicine &amp; health research</td>
<td>Research related to gaining a better understanding of human health and disease and to developing or improving the prevention of disease or the treatment of disease. This ranges from fundamental research to research into societal practice covering all phases of human life, and can be related to healthcare, drug development, technological advances, food and lifestyle research, social research, etc.</td>
</tr>
<tr>
<td>Partner</td>
<td>Organization connected to Health-RI, either via the Health-RI network or the Health-RI ecosystem</td>
</tr>
<tr>
<td>Research environment</td>
<td>The surrounding (involved parties, total euro’s, etc.) in which health research is performed</td>
</tr>
<tr>
<td>Users</td>
<td>Individual researchers, research groups and research organizations who make use of services on or via the platform</td>
</tr>
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</table>
The need for Health-RI
# Health-RI is the solution to today’s challenges in the health research environment

Starting Health-RI will solve challenges in the health research environment. On the next pages these challenges, issues, opportunities and solutions are shown in more detail.

## Challenges and issues in the health research environment

### Fragmentation of infrastructures
- Due to limited willingness to share data/facilities, competition for funding and limited coordination of funding in the past.
- Infrastructures, contributors and researchers operate in separate worlds. **Integration and professionalization is needed**.
- The promise of personalized medicine & health is **not delivered** (the **innovation gap**).
- There is a **lack of reproducibility of research outcomes** (50% not usable).
- Researchers are **rewarded for generating publications**, not for translating science to society.
- **Return-on-investment** of health research is **insufficient**.
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- Develop a **top-of-the-bill infrastructure** for health research in the Netherlands supported by a **shared service center**.
- **Strong collaboration** between infrastructures, contributors, and all relevant stakeholders, including scientists, health professionals and citizens.
- Acceleration of the development of a **learning healthcare system**.
- Implement data stewardship based on **FAIR principles** (Findable, Accessible, Interoperable, Re-used) and stimulate secure re-use of resources.
- Change incentives to **reward researchers for sharing**.
- **Efficient use** of available **funds** via coordination of an investment agenda.
- Shared infrastructure to facilitate **access to data** under inclusive governance.

*Swiss SPHN (Switzerland), US Personalized Medicine (USA), Genomics England (United Kingdom), Medizininformatik (Germany)
## Trends in health research define the need for Health-RI

### Challenges in the health research field

<table>
<thead>
<tr>
<th>Trend</th>
<th>Challenges</th>
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</thead>
</table>
| **Health, demographic changes and well-being** | * More focus needed on prevention and healthy aging  
* Bridge the gap between health and health-potential ("health gap")  
* Validate healthcare solutions in a population with comorbidity  
* Use patient-reported outcomes for decision making |
| **Technological developments** | * Gap between research and care*: lack of high-quality accessible data  
* Increased understanding of biological causes of disease  
* Handle larger and more detailed multi-source datasets  
* Consent procedures meeting legal obligations & patient expectations  
* Develop innovative solutions aiding patients & their care providers |
| **Increasing healthcare costs** | * Ecosystem needed for clinical validation and cost-effectiveness analysis of innovations  
* Precision diagnostics for precision treatment: early identification of failing treatments  
* Address funders and societal requests on return-on-investment  
* Make data FAIR (Findable, Accessible, Interoperable, Reusable)  
* Reply to societal demands for Open Science and Data  
* Address possible interference between open science standards, privacy law and regulations  
* Address profitability of 'Open' access science & data for all parties, including transformation of the academic reward system |
| **Open science** | * Growth in citizen generated data (e.g. from wearables)  
* Provide tools for shared decision making  
* Involve citizens in research agenda and priorities  
* Feedback: reporting of research results to participants |

### The 'Why' of Health-RI

Health-RI will serve as the rocket launcher for excellent cross-disciplinary and data-intensive research by providing a national health research infrastructure, ultimately promoting better healthcare and healthier aging.

- Defragmentation of data, samples, images, tools, expertise, regulations, research initiatives and funding is needed for the development of innovative solutions which contribute to translation of research results into healthcare practice ("innovation gap") and thereby to full utilization of each individual's health potential ("health gap")
- Interconnection of stakeholders to make full use of technological developments to close the innovation gap and to empower patients and citizens.
The need for Health-RI

The health research environment needs to improve to address the current challenges

The examples in the boxes illustrate the challenges in the current health research environment to perform excellent research and translate this into practice. Health-RI is seen as the solution to these challenges.

In a public consultation on science by the EU, 85% of individual scientists partially or totally agree with the statement that there exists a lack of integration in existing infrastructures.¹

Current funding structure contributes to the focus by researchers on their own projects, data and tools. Currently, incentives for individual researchers are mainly focused on generating publications, whereas it should be on actual contributions to society.²

Protocols, full study reports, and participant-level datasets are rarely available, and journal reports are available for only half of all studies and are plagued by selective reporting of methods and results. Furthermore, information provided in study protocols and reports varies in quality and is often incomplete. When full information about studies is inaccessible, billions of dollars in investment are wasted, bias is introduced, and research and care of patients are detrimentally affected.³

Freedman et al state that “half of published biomedical research cannot be reproduced because of a lack of agreed quality standards in reagents, analytics and data sharing”.⁴ Prinz et al revealed that in only 20-25% of the projects the relevant published data was completely in line with their in house findings.⁵

Whereas collaboration between researchers at Dutch universities and other organizations is of good quality, the collaboration with other stakeholders in the research field needs improvement. Knowledge is currently only shared through scientific articles, intellectual property and graduates.⁶

An absence of detailed written protocols and poor documentation of research is common. Several problems relate to the research workforce, including failure to involve experienced statisticians and methodologists, failure to train clinical researchers and laboratory scientists in research methods and design.⁷

It was recognized that the main challenge for transformation of data into knowledge to improve health at the individual and population level requires new analytical tools to discover novel relationships and patterns in a very heterogeneous data set. In turn, it was stressed that our ability to organize, integrate and transform health Big Data into better health outcomes depends on the ability to create a permissive and enabling ecosystem. Developing such an ecosystem in Europe relies on data sharing between multiple stakeholders, from public and private organizations involved in biomedical R&D to other disciplines (for example ICT, social sciences) that has to put citizens and patients at its center. Such an ambition requires development of an adequate framework to collect and interpret health-related data, as well as the right infrastructure, funding models, expertise and reward mechanisms to support data-driven science.⁸
Health-RI defragments the current range of infrastructure initiatives

There is fragmentation of infrastructures in the health research field due to:
- **Limited willingness** on the part of researchers to share data / facilities in the past;
- **Limited coordination** of funding of research infrastructures in the past;
- **Competition between organizations for funding** of research infrastructures;
- **One-to-one translation** of the European fragmented infrastructure situation to the Dutch situation, leading to;
- Fragmented, overlapping, and thus less effective offering of services to researchers and institutes.

Fragmentation impedes excellent health research due to:
- Inefficient (re)use of available data, tools and facilities by researchers;
- Lack of standards and guidance to ensure compliance-by-design, which are important conditions for translation of research into healthcare (and a learning healthcare system), together leading to;
- Inefficient use of available (infrastructure) funds for health research.

Before the Health-RI era, there was no independent organization to bring the different stakeholders together.

Health-RI provides a solution to the fragmentation by bringing together the stakeholders in the health research ecosystem in order to support researchers in the entire research process via a shared infrastructure services center.

* Appendix Ia and Ib give an overview of actions, collaboration and convergence that has lately took place between stakeholders*
Health is one of the most important quality aspects along the entire timespan of our lives. Health-RI facilitates research that leads to innovations that allow us to stay healthy as much of the time as possible, and if we do fall ill, to regain health as much and as quickly as possible. With this live long scope, Health-RI interacts with the whole range of health related topics, like environment & health, healthy ageing, primary healthcare, prevention, food & health, mental health, healthy youth, personalized medicine, and others.

Increasingly, personal data are being collected that are relevant for the understanding of our personal health. Citizens collect more and more of their own data and a vast array of data is gathered in the health system. Having personal data on these health aspects available for research is crucial to reach this goal of better health outcomes. As a consequence, Health-RI interacts with health related initiatives and concepts like a learning healthcare system, value based healthcare, closing the innovation gap, big data, e-health, quantified self, and self management.

In a health sector that broadens at spectacular speed to allow inclusion of a wide variety of aspects that influence our personal health, from biology to socio-economic aspects, to how our food and lifestyle interact, there is a huge potential to better learn how we can self-manage our personal vitality, functioning and health. Health-RI will offer the platform that allows citizens and all other stakeholders in the health research domain to securely combine and interpret such variable data.

Health-RI thus supports a broad variety of disciplines and sources of information to allow for a democratic and accessible science and innovation environment in which citizens can participate extensively. The infrastructure offers stakeholders specialized in certain aspects or phase of our lifespan, from early conception to ageing, to build on each other’s expertise and information.

Health-RI thus strongly supports the health sector to offer high quality innovative services along the ‘citizen’s journey’, with great attention to prevention and early detection of health-threats, and with increased handles to treat disease at the personal level: personalized medicine and health.
Failing to operationalize Health-RI will substantially damage Dutch health research

The Netherlands cannot afford to not execute Health-RI as this will lead to:

<table>
<thead>
<tr>
<th>Endangered leading position of the Netherlands in personalized medicine &amp; health research</th>
<th>Loss of interest of R&amp;D organizations and individual researchers</th>
<th>Persistent ineffective use of funds</th>
<th>Persistence of the innovation gap</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Competing countries are investing heavily in creating similar infrastructures*. With these infrastructures they will have more capabilities to perform excellent research due to better cooperation and better use of resources.</td>
<td>• If it loses its leading position in the field of personalized medicine &amp; health research, the Netherlands will be less attractive to (innovative) healthcare research industry players, research institutes, and research and development departments of pharmaceutical and MedTech companies.</td>
<td>• Researchers and research organizations cannot use their funds as efficiently as they possibly could without good access to, and interoperability of, data, tools and facilities, and the possibility to (re)use these resources.</td>
<td>• Crucial studies cannot be performed due to lack of (efficient) infrastructure.</td>
</tr>
<tr>
<td>• These developments threaten the Netherlands’ leading position in the field of health research, which could eventually result in less international funding of Dutch research.</td>
<td>• Individual researchers in the Netherlands will have less access to data and technology than their colleagues abroad, making it harder to perform excellent research. Because of this, the Dutch research community will be less attractive for high potential researchers from both the Netherlands as well as from abroad.</td>
<td>• If fragmentation persists, organizations offering infrastructure functionalities will continue to compete for funds. As this is a time-consuming activity, their time will not be used as efficiently as it possibly could. Furthermore, this is certain to cause redundancy in the infrastructures being developed.</td>
<td>• This may slow down the development of personalized health in the Netherlands, possibly resulting in slower delivery to society of the promise of providing personalized healthcare.</td>
</tr>
</tbody>
</table>

*Swiss SPHN (Switzerland), Precision Medicine Initiative (USA), Genomics England (United Kingdom), Medizininformatik (Germany)
There is a fragmented field of existing infrastructures acting in a €500 million* health research environment

In the €500 million Dutch health research environment we currently see fragmentation of the numerous infrastructure services providing organizations.

**Size of the Dutch health research environment in Euros**

- **Annual total funding** for health research is ~€500 million*[^9,^10,^11]
- Around €30 million is marked directly for infrastructure
- With a small part of the total budget, Health-RI will improve efficiency by organizing the national infrastructure
- In addition to the health research budget yearly around €100 million is spent on registries of (health)care data[^12]

**Selection of players in the Health-RI field (non-exhaustive)**

- **Main funders**
  - NWO
  - ZonMw
  - Government
  - Health funds
  - Others

- **Existing infrastructures**
  - TraIT
  - ELIXIR-NL
  - DTL
  - BBMRI.nl
  - Parelsnoer Institute
  - NFU Data4lifesciences
  - SURF
  - Others

- **Infrastructure users and contributors**
  - Healthcare providers
    (Hospitals, UMCs, ...)
  - Knowledge institutes
    & universities
  - HealthTech industry
  - Drug, supplement and food industry

[^9]: The €500 million is an estimation based on the budgets of funders in the health research environment[^9,^10,^11]
Of the total € 500 million* health research funding, around € 30 million is directly granted annually to research infrastructures

Current funders whose budgets are (partly) marked for infrastructure services

NWO funding budgets

The Netherlands Organization for Scientific Research (NWO) annually receives a budget from the ministry of education, culture and science (Ministerie van OCW) that it distributes.

Via the ‘NWO roadmap large scale infrastructure calls’ NWO grants budget to large scale research infrastructures in the life science field. Apart from this marked budget for research infrastructures, NWO provides grants to individual researchers and research projects.

ZonMw funding budgets

ZonMw’s aim is to promote the quality and innovation of health research in order to make healthcare better and keep it affordable. In the Netherlands, ZonMw has a central role in this area as a national funding organization. Their activities cover the entire spectrum from fundamental research to implementation of new treatments, disease prevention, and healthcare improvements.

Funding budgets from health funds

Individual health funds (of which most collaborate via the SGF) distribute large sums of funding (millions) for research in their health field every year. Funds are distributed on a project basis. Parts of these project budgets are used on infrastructure services.

Figures NWO

NWO has € 55 million available to invest annually in largescale research infrastructures in the field of life sciences.

NWO annually spends € 600 million on (individual) research projects, of which we estimate that about a third will be used for health research. A part of this budget could be used for research infrastructure projects, supporting health research.

Figures ZonMw

In 2015, ZonMw spent € 121 million on research grants, of which a large part will be used for health research. A part of this budget could be used for research infrastructure projects, supporting personalized medicine research.

Figures Health funds

Part of these funds are used for research infrastructure projects, supporting individual researchers in each health research field.

*The numbers are based on estimation based on the budgets of funders in the health research environment.
The demand for existing research infrastructure functionalities illustrates the need for a good research infrastructure to support research (1/3)

Current offer and use of infrastructure functionalities

TraIT services provided

TraIT enables integration and querying of information across the four major domains of translational research: clinical, imaging, biobanking and experimental (any-omics). Scientists within multi-site projects should be able to share and disseminate data and analyses from these domains in the TraIT translational research space. TraIT offers several IT tools and related user support. TraIT is a partner in BBMRI.nl.15

<table>
<thead>
<tr>
<th>Figures TraIT</th>
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</thead>
<tbody>
<tr>
<td>Suite of 15 tools (2017) including:</td>
</tr>
<tr>
<td>• OpenClinica</td>
</tr>
<tr>
<td>• XNAT</td>
</tr>
<tr>
<td>• Galaxy</td>
</tr>
<tr>
<td>420 studies supported in 201616</td>
</tr>
<tr>
<td>3383 unique users in 201717</td>
</tr>
</tbody>
</table>

BBMRI-NL services provided

BBMRI-NL makes biomaterials, images and data from (longitudinal) biobanks retrievable, accessible and exchangeable for research on the prevention and treatment of diseases. BBMRI-NL offers users a searchable database with information on all its associated biobanks (catalogue), pathology samples, associated pseudonimized data, omics & imaging data and analysis tools (biobanks), and ELSI support.18

<table>
<thead>
<tr>
<th>Figures BBMRI-NL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Provide an overview of over 200 biobanks &amp; collections (2017)19</td>
</tr>
<tr>
<td>Ca. 200 sample requests in 201620</td>
</tr>
</tbody>
</table>

“The breast cancer part of the IMPACT study involves 200 patients, each of them undergoing four PET scans during diagnosis and treatment in addition to their normal therapy, and each PET scan needs to be reviewed by different clinicians in different hospitals,” says Liesbeth de Vries. “In the past, we would have had to physically mail CD-ROMs containing the PET scan images to all those involved.

Now however, the process is much simpler. By creating appropriate links between OpenClinica and the National Bio-Medical Imaging Archive (NBIA) – the TraIT team created a system that allows the clinicians to directly download the PET scans from the patient’s OpenClinica case record.”

Professor Liesbeth de Vries and Dr. Frederike Bensch of UMCG21
The demand for existing research infrastructure functionalities illustrates the need for a good research infrastructure to support research (2/3)

Current offer and use of infrastructure functionalities

**DTL services provided**

The mission of DTL is to leverage and integrate state-of-the-art experimental measurement and data technologies across life science disciplines, and to underpin such efforts with targeted training activities. One of the services that DTL provides is an overview of the technology hotels. Technology hotels are expert groups that offer their high-end technologies and the associated expertise and infrastructure to researchers who do not have access to such facilities at their home institute.22

**ELIXIR-NL services provided**

ELIXIR-NL is the Dutch Node of the ESFRI landmark ELIXIR, bearing the tagline "Data for life Science". ELIXIR-NL is active in the ELIXIR Interoperability platform, developing standards for FAIR (Findable, Accessible, Interoperable, Reusable) data and data FAIRification tools. ELIXIR-NL has initiated building a national linked FAIR data infrastructure that will serve as the data backbone for Health-RI. One of its initiatives is the Personal Health Train (see next slide), which aims to increase the utilization of existing biomedical data for research into personalized health and prevention, and into value-based healthcare.24

**Figures DTL**

More than 120 technology hotels are listed on the DTL website in 201722

DTL works with more than 50 partner organizations (2017)22

DTL provides more than 40 courses & training (2017)23

*Periodically, we get a clinical data dump from IKNL for all new patients who have enrolled in the cohort, and upload it to tranSMART, from where de-identified data can be made available to participating research groups,* says Robert Coeberg van den Braak. *But the real beauty of the system is that those research groups can then upload their own results back to the database. For example, if someone generates next-generation sequencing data for a set of patients in the PLCRC cohort, they can upload that data to tranSMART so that it’s integrated into the database and available for the next set of researchers to use. So the database is constantly being enriched, not just in terms of the number of enrolled patients, but also in terms of accumulated knowledge.*

Geraldine Vink and Robert Coeberg van den Braak, Program Managers in the Prospective Dutch Colorectal Cancer Cohort25
The key concept in PHT is to bring research to the data rather than bringing data to the research. The PHT is designed to give controlled access to heterogeneous data sources, while ensuring maximum privacy protection and maximum engagement of individual patients and citizens. As a prerequisite, health data is made FAIR (Findable, Accessible, Interoperable and Reusable). Stations containing FAIR data (‘FAIRports’) may be controlled by individuals, (general) physicians, biobanks, hospitals and (public) data repositories.

The demand for existing research infrastructure functionalities illustrates the need for a good research infrastructure to support research (3/3)

Current offer and use of infrastructure functionalities

Parelsnoer Institute services provided

Parelsnoer Institute offers researchers an infrastructure and standard procedures for the establishment, expansion and optimization of clinical biobanks for scientific research. By collecting and storing clinical data, images and human biomaterial together in a uniform manner from carefully documented patients suffering the same illness, large cohorts are established (the so-called ‘Pearls’) that enable broader scientific research.26

Figures Parelsnoer Institute

Catalogue with cohorts from 18 focus diseases (Pearls)

Data4Lifesciences services provided

Data4Lifesciences (D4LS) is a shared data infrastructure for biomedical research. The program is coordinated by the Netherlands Federation of University Medical Centers (NFU), in conjunction with national programs such as TraIT, BBMRI-NL, PSI, DTL, AcZie, Mondriaan and SURF. Data4Lifesciences aims to set up an innovative research data infrastructure at, for, by and between the UMCs and their (national and foreign) partners.27

Figures D4LS

9 program lines, with

- Collection and harmonization of guidelines for data stewardship
- Harmonization of IT processes and architecture
- Access to data and sample collections
- Reuse of clinical data for research

Offers an Handbook for Adequate Natural Data Stewardship

In addition to the infrastructures mentioned, several smaller and bigger infrastructure functionalities are known. These are often locally based, for instance at UMCs or universities. They develop and maintain these functionalities individually and the functionalities are not shared with other researchers. Health-RI can play an important role in identifying these functionalities, gather them in a central platform and thereby reduce redundancy, resulting in defragmentation of the infrastructure field.
Healthcare providers & research institutes

- In the Dutch Academic Medical Centers (UMCs), other (topclinical, STZ) hospitals and in primary healthcare, researchers perform health research in all hospital departments, varying from fundamental to clinical research, partly using data coming from patients in the hospitals. Big challenges are the efficient sharing of data and knowledge and the translation from research results into care practice.

Royal Academy institutes

- The Royal Academy is responsible for three research institutes with a work field related to health research. All institutes perform excellent research and have a prominent place in the worldwide research field.38

Science faculties from Dutch universities

- Several universities in the Netherlands have researchers related to health at science faculties. These researchers have backgrounds in biomedical science, biology, bioinformatics, pharmaceutical science, health science, chemistry and life science. Examples of institutes with a focus on health research within these science faculties are the LACDR* and GUIDE**.

<table>
<thead>
<tr>
<th>Illustrative figures UMC and STZ hospitals</th>
<th>Illustrative figures Royal Academy institutes</th>
<th>Illustrative figures Science faculties</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong># of UMC</strong></td>
<td><strong># organizations</strong></td>
<td><strong>Universities with science faculties</strong></td>
</tr>
<tr>
<td>828</td>
<td>3 (2017)38</td>
<td>- Leiden</td>
</tr>
<tr>
<td>2629</td>
<td></td>
<td>- Utrecht</td>
</tr>
<tr>
<td><strong># of researchers UMC</strong></td>
<td></td>
<td>- Nijmegen</td>
</tr>
<tr>
<td>1615 (2015)30-37</td>
<td></td>
<td>- VU Amsterdam</td>
</tr>
<tr>
<td><strong>€ yearly received for research</strong></td>
<td></td>
<td>- Maastricht</td>
</tr>
<tr>
<td>&gt; € 384 M (2015)30,32-34,36</td>
<td></td>
<td>- UvA Amsterdam</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Wageningen</td>
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<td></td>
<td></td>
<td>- Groningen</td>
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<tr>
<td></td>
<td></td>
<td>- Delft</td>
</tr>
</tbody>
</table>

* Leiden Academic Center for Drug Research: is a centre of excellence for multidisciplinary research on drug discovery and development41
**Groningen University Institute for Drug Exploration: Its main asset is the integration of clinical, biomedical and pharmaceutical research, which promotes the education of researchers with a keen eye on the complete spectrum of biomedical research in a unique research and teaching environment: from bed to bench to drugs42
There are different types of research organizations that host a potentially large number of Health-RI platform users (2/2)

In the Netherlands, potential researchers that could make use of the platform come from:

**Other research institutes**

- Other research institutes like NKI, TNO and RIVM also harbor researchers performing research related to personalized medicine & health.
- The Netherlands Cancer Institute (NKI) accommodates approximately 650 scientists and scientific support personnel. The Antoni van Leeuwenhoek Hospital is the only dedicated cancer center in The Netherlands and maintains an important role as a national and international center of scientific and clinical expertise, development and training.\(^43\)
- TNO is an independent research organization. They believe in the joint creation of economic and social value, with one theme being ‘Healthy Living, for a fit, healthy and productive population’\(^44\)
- The Dutch National Institute for Public Health and the Environment (RIVM) conducts research and provides advice to assist the government in the task of keeping ourselves and our environment healthy.\(^45\)

**HealthTech industry and Drug, supplements and food development industry**

- In the private HealthTech Industry and Drug, supplements and food development sector, a considerable number of prominent organizations actively perform research within the Netherlands. Examples are Phillips Healthcare, DSM, numerous pharmaceutical product design / manufacturing companies and numerous medical biotechnology companies, e.g. in the Bioscience Park Leiden. The drug development sector is largely responsible for translating research into new drugs. Their data come from clinical trials and fundamental research. A big challenge for this sector is speeding up drug development by efficient use of resources and existing knowledge.

**Illustrative figures other research institutes**

<table>
<thead>
<tr>
<th>Institute</th>
<th>Figures</th>
</tr>
</thead>
<tbody>
<tr>
<td>NKI</td>
<td>566 researchers (2015)(^46)</td>
</tr>
<tr>
<td>TNO</td>
<td>2926 researchers (2015)(^47)</td>
</tr>
<tr>
<td>RIVM</td>
<td>1,500 staff members (2016)(^48)</td>
</tr>
</tbody>
</table>

**Illustrative figures private health research sector**

<table>
<thead>
<tr>
<th>Category</th>
<th>Figures</th>
</tr>
</thead>
<tbody>
<tr>
<td># organizations Drug development sector NL</td>
<td>ca. 420 (2016)(^48)</td>
</tr>
<tr>
<td>Medical biotechnology</td>
<td>(54%)</td>
</tr>
<tr>
<td>Pharmaceutical product industry</td>
<td>(38%)</td>
</tr>
<tr>
<td>Pharmaceutical base material industry</td>
<td>(7%)</td>
</tr>
<tr>
<td># clinical and observational trials Drug dev. sector NL</td>
<td>16,856(^48)</td>
</tr>
<tr>
<td>€ yearly spent on R&amp;D Drug dev. sector NL</td>
<td>€380 M(^48)</td>
</tr>
<tr>
<td># organizations in medical technology</td>
<td>199 (2015)(^49)</td>
</tr>
</tbody>
</table>
With major investments, other countries are already setting up similar infrastructures (1/2)

The following are examples of similar infrastructures in other countries. Health-RI needs to be operationalized now to strengthen the Dutch position in this field, in the meanwhile connecting to these international research infrastructure developments.

**Swiss SPHN (Switzerland)**
- The Swiss Personalized Health Network (SPHN) is a national initiative designed to promote the development of personalized medicine and personalized health in Switzerland.
- SPHN will lay the foundations that are needed to facilitate research projects in this area such as a system for a nationwide exchange of health-related data.
- Based on its Funding Principles and Funding Regulations, the Swiss Government has allocated a total of CHF 68 million (~ €59 million) to SPHN for the first period 2017-2020.

**Precision Medicine Initiative (United States of America)**
- The Precision Medicine Initiative (PMI) is a long-term research endeavor, involving the National Institutes of Health (NIH) and multiple other research centers, which aims to understand how a person’s genetics, environment, and lifestyle can help determine the best approach to prevent or treat disease.
- The NIH All of Us Research Program is a historic effort to gather data from one million or more people living in the United States to accelerate research and improve health. By taking into account individual differences in lifestyle, environment, and biology, researchers will uncover paths toward delivering precision medicine.
- In 2016 the USA government made a $215 million (~ €183 million) investment in PMI.

**Medizininformatik (Germany)**
- Medizininformatik is an infrastructure in which healthcare data and clinical and biomedical research data are connected and can be shared between healthcare providers and researchers. This enables researchers to perform better research, leading to better healthcare outcomes.
- With a €120 million investment, the German government supports high-end interdisciplinary consortia to develop ‘data integration centers’ at German Academic Medical Centers and partner organizations. These centers will show how data, information and knowledge for healthcare providers, and clinical and biomedical research can be connected.
The following are examples of similar infrastructures in other countries. Health-RI needs to be operationalized now to strengthen the Dutch position in this field, in the meanwhile connecting to these international research infrastructure developments.

<table>
<thead>
<tr>
<th>Stratified Medicine Scotland (Scotland)</th>
<th>FIMM (Finland)</th>
<th>Genomics England (United Kingdom)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Stratified Medicine Scotland’s (SMS) focus is on linking Scotland’s domain expertise, data assets and delivery capability to accelerate the adoption of Precision Medicine: new products and services for a global market, leading to:</strong></td>
<td><strong>The Institute for Molecular Medicine Finland (FIMM) is a research institute focusing on human genomics and personalized medicine. FIMM integrates molecular medicine research, Technology Centre and Biobanking Infrastructures “under one roof” and thereby promotes translational research and adoption of personalized medicine in health care.</strong></td>
<td><strong>Genomics England, with the consent of participants and the support of the public, is an infrastructure creating a lasting legacy for patients, the NHS and the UK economy, through the sequencing of 100,000 genomes. They aim to create an ethical and transparent program based on consent, enable new scientific discovery and medical insights, and kickstart the development of a UK genomics industry.</strong></td>
</tr>
<tr>
<td>• Better diagnostics and earlier intervention</td>
<td>• FIMM Technology Centre and Biobanking Infrastructures provide research services for local, national and international customers. The infrastructures operated by FIMM are networked with the ESFRI infrastructures BBMRI, EATRIS, ELIXIR and EU-Openscreen.</td>
<td>• A total of £311 million (~ €349 million) is invested in Genomics England, with money coming from private parties and the Government.</td>
</tr>
<tr>
<td>• Optimal treatment selection</td>
<td>• FIMM had a total income of € 20.5 million in 2016, coming from the University of Helsinki, grants and external services (ca. 20%).</td>
<td></td>
</tr>
<tr>
<td>• More effective medicine development</td>
<td>• SMS received an initial investment of £8 million (~ €9 million) in 2013 and further funding of £4 million (~ €4.5 million) in 2016.</td>
<td></td>
</tr>
</tbody>
</table>

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Strategy of Health-RI
Health-RI has defined its mission, ambition and strategy, demonstrating how Health-RI will create value for society

**Why are we in business?**

Creating value for society by facilitating all steps in the process of health research. As a result, Health-RI will achieve major societal transformation, for:

- **Researchers**: enabling them to perform excellent cross-disciplinary and data-intensive research
- **Funders**: enabling them to obtain optimal return-on-investment
- **Citizens**: who will be more involved in high quality research, leading to faster implementation of personalized health
- **Others** (e.g. government, care providers, industry, health insurers, etc): who will be part of a well organized network for health research and prevention

**Where do we want to be in 2023?**

We will have realized a state-of-the-art infrastructure for data, samples and images that will be key to facilitating excellent health research and sustainably bridging the health innovation gap.

**How do we get there?**

- By **all stakeholders** in the ecosystem working together at strategic, tactical and operational levels
- By functioning as a shared service center that provides a single platform for delivering an integrated suite of functionalities, assets and support to researchers, leading to compliance-by-design
- By delivering a balanced financial model with transparent and logical prioritization of resources that are made collectively available
- To this end, Health-RI will work with jointly determined standards, conditions and ‘rules of engagement’

**How are we going to achieve this?**

- Establish an effective and efficient organization
- **Defragment** infrastructures
- **Cooperate** with all stakeholders
- Adopt an integral funding system
- Make a long-term commitment
Health-RI will build on existing infrastructures and attract new partners to establish the Dutch national research infrastructure

Health-RI is launched from existing research infrastructures, being highlighted as the future Dutch infrastructure for health research

Health-RI consolidates the activities of multiple Dutch ESFRI and e-infrastructure nodes by their landing into the Health-RI platform

Health-RI is highlighted as the future Dutch research infrastructure for health research by other parties

Highlighted Health-RI as a key player in various agenda programs

Mentioned Health-RI as a necessary data infrastructure to achieve personalized medicine

Listed Health-RI as a one of the "must have large-scale research facilities"

Named Health-RI "an essential (data) infrastructure for health research and personalized medicine"

Listed Health-RI next to personalized medicine initiatives abroad

Further in this chapter you find a schematic overview of all stakeholders in the ecosystem. Appendix Ia and Ib give an overview of actions, convergence and collaboration already undertaken

*Swiss SPHN (Switzerland), US Personalized Medicine (United States of America), Genomics England (United Kingdom), Medizininformatik (Germany)
The Health-RI platform will function as the interface between the Health-RI network and researchers

Below a description of how Health-RI will offer functionalities to researchers

Health-RI will offer functionalities to researchers by means of connecting activities and shared services. The Platform Health-RI will be the interface between the network and its users, the researchers.

Within the Network Health-RI, Health-RI interconnects contributors that can provide researchers with expertise, data, tools and services to perform excellent cross-disciplinary and data-intensive research. We distinguish two types of contributor: ‘data contributors’ offering data, samples, images etc. and ‘infrastructure contributors’ offering tools, facilities and services. Health-RI engages the essential contributors in the network. All contributors have to follow certain rules of engagement (see further in this chapter).

The functionalities of the contributors in the network are offered to researchers via the Platform Health-RI. The platform is the interface between the Health-RI network and the researchers. Health-RI operationalizes this platform and provides support in the use of this platform. Furthermore, Health-RI provides shared services to researchers directly (see chapter ‘Health-RI value proposition’, first page).

Easy access to different functionalities via this platform simplifies the research process for the researcher, ultimately benefiting society and funders. In addition to the operational activities of Health-RI in the platform, Health-RI performs activities on tactical and strategic level to achieve its ambitions, explained on the next page.

* Data refers to data, samples and images
Below is a description of how the Health-RI Network interacts with organizations within the Health-RI ecosystem

**Interaction with all stakeholders in the Health-RI ecosystem is necessary to achieve the mission of Health-RI**

To achieve the value of health research for society, activities of different stakeholders in the Health-RI ecosystem (figure left) should be aligned. In addition to acting on the operational level (the platform), Health-RI therefore also acts at a tactical and strategic level to connect partners in the ecosystem and transform health research.

For example (not exhaustive), Health-RI:

- Brings network contributors together to cooperate, and thereby achieves efficient use of resources, creation of new services and alignment in applications for infrastructure funding;
- Cooperates with funders to create funding conditions that stimulate use of the platform by researchers, and to align funding of infrastructures;
- Cooperates with regulators to smoothen the regulatory process for researchers;
- Cooperates with patient foundations to increase the role of patients in defining and performing research;
- Connects with (international) partners to drive definition of standards for data sharing and facilitate implementation in the Netherlands.

The third page of chapter ‘Health-RI value proposition’ (page 51) shows more examples of specific services of Health-RI on operational ('Platform'), tactical ('Connect') and strategic ('Transform') level.
The following topics will be addressed in the rules of engagement

- **Accessibility to the network, e.g.:**
  - Network partners will not try to obtain exclusivity at the expense of other (potential) partners
  - Network partners will follow the infrastructure financing agenda
  - Network partners collaborate with Health-RI to reduce redundancy in infrastructures
  - Network partners comply to security requirements

- **Requirements regarding data and services offering, e.g.:**
  - Quality criteria apply for data, images and samples and infrastructures regarding FAIR, compliance to legislation, and ethical standards
  - The procedure to request access, and the conditions under which this access is granted, are openly available and applied in a transparent manner
  - Services offered via Health-RI are sustainable for a reasonably foreseeable horizon. Researchers should be able to rely on its existence during the lifetime of the project. Nevertheless, if a service has to be phased out, the service provider supports the migration to a reasonable alternative to its best possible capabilities

- **Financial agreements, e.g.:**
  - Network partners will contribute a part of their fee for service income to Health-RI, to support the maintenance of the Health-RI platform

**Formalization of cooperation in contracts**

The rules of engagement are an integral part of the contracts to be signed by each network partner.
To enable good functioning of the Health-RI platform it is essential to meet several conditions:

<table>
<thead>
<tr>
<th>Health-RI promotes FAIR data stewardship</th>
<th>Access to data*, tools and facilities is organized in the most effective way</th>
<th>Compliance-by-design with relevant regulations (including privacy)</th>
<th>The platform is well secured</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Health-RI promotes FAIR data stewardship to prevent monopolization of data by parties.</td>
<td>• <strong>Authentication</strong>: Users have to log in to the platform as a ‘trusted’ user, for example, via a log in from a known trusted organization.</td>
<td>• Standards for data contribution describe how data are to be offered in a safe and FAIR way via the platform, including the aspect of privacy and pseudonimization.</td>
<td>• Security measures are in place on relevant areas as described in the ISF framework.**</td>
</tr>
<tr>
<td>• Health-RI promotes open science and accessibility of data* for all parties.</td>
<td>• <strong>Authorization</strong>: Based on conditions of use, users have certain privileges to access data, tools and facilities. Further access depends on arrangements between contributor and user.</td>
<td>• There is support on the legal, ethical and societal issues concerning health research.</td>
<td>• Security measures are in place to protect the underlying infrastructure against cyber attacks (on people, process, technology layers).</td>
</tr>
<tr>
<td>• In principle, data* connected to the platform remain at the source.</td>
<td>• An audit trail will be made to track what has been done and who did it.</td>
<td>• Quality requirements for infrastructure contributors guarantee the quality of offered services.</td>
<td>• The organization is able to detect cyber-attacks on, or malfunctioning of, the infrastructure.</td>
</tr>
<tr>
<td>• Health-RI offers an overview of the content of the data* on the platform, not the data set itself. The overview is offered via metadata.</td>
<td></td>
<td></td>
<td>• The organization can effectively respond to cyber incidents (isolate, limit, recover).</td>
</tr>
</tbody>
</table>

* Data refers to data, samples and images

** The Standard of Good Practice for Information Security 2016 provides comprehensive controls and guidance on current and emerging information security topics enabling organizations to respond to the rapid pace at which threats, technology and risks evolve. [https://www.securityforum.org/tool/the-isf-standardrmation-security/](https://www.securityforum.org/tool/the-isf-standardrmation-security/)
Health-RI value proposition
Health-RI will provide shared services and act as the collective voice

Health-RI will operate as a connecting force to support the health research process

Provide shared services via the platform

Act as a collective voice on the research infrastructure

• Health-RI will provide shared services that contributors cannot provide individually, but that are nevertheless essential to connecting different resources (data, tools, services) to users, reusing data, and efficiently performing excellent cross-disciplinary and data-intensive research.

• Some examples of Health-RI activities:
  • Operational:
    • Operationalize a platform that provides an overview of all available content (data, samples, images, tools, facilities, etc.) and connect contributors and users to provide access;
    • Be the landing zone of Dutch health research infrastructure nodes such as BBMRI-NL, EATRIS-NL, and the health research parts of ELIXIR-NL, EuroBioImaging and others;
    • Provide shared services directly to users (from existing initiatives BBMRI-NL, TraIT, ELIXIR-NL and EATRIS-NL).
  • Tactical:
    • Provide education and training on common themes – e.g. like FAIR and ELSI.

• On behalf of all stakeholders, Health-RI will represent the health research infrastructure ecosystem on topics where a collective voice is needed to achieve changes that support the research process. This requires bringing the different stakeholders together. Stakeholders will be represented in the Health-RI governance.

• Health-RI will provide this collective voice on both tactical and strategic level. Examples of Health-RI activities include:
  • Tactical:
    • Drive and connect to the development of international data standards
  • Strategic:
    • Set a collective infrastructure financing agenda together with stakeholders and influence them to commit to the agenda
    • Align the Health-RI strategy with developments in healthcare infrastructures, for example, electronic patient files and MedMij, to create the possibility of connecting data that, for example, support citizens to live a healthy life.

*FAIR: Findable, Accessible, Interoperable, Reusable
**ELSI: Ethical, Legal, Social, Impact
The Health-RI infrastructure will grow over time along seven domains/themes

<table>
<thead>
<tr>
<th>Domain/Theme</th>
<th>The growth model of Health-RI: services provided and activities taking place within each domain / theme over time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Collections domain</td>
<td>- Offer an overview of collections on meta data level 1*&lt;br&gt; - Find and connect missing collections&lt;br&gt; - Find and connect appropriate IT tools for health research process steps not sufficiently covered&lt;br&gt; - Establish support nodes at organizations with high number of users&lt;br&gt; - Document and standardize PH&amp;H process chains&lt;br&gt; - Establishment of FAIR level 3 activities&lt;br&gt; - Define and pilot FAIR level 3 activities&lt;br&gt; - Implementation of standards in all data, tools and facilities (Reusable)&lt;br&gt; - Establish a mature professional research infrastructure life cycle management&lt;br&gt; - Develop a standardized method for pseudonimization (used in collections 5)&lt;br&gt; - Contribute to the development of a finance model for infrastructure development and maintenance</td>
</tr>
<tr>
<td>IT services domain</td>
<td>- Offer overview of available tools&lt;br&gt; - Connect facilities to Health-RI&lt;br&gt; - Offer overview of available facilities&lt;br&gt; - Build and maintain platform&lt;br&gt; - Offer support regarding the use of platform facilities&lt;br&gt; - Select standards for FAIR data and implement FAIR level 1**&lt;br&gt; - Provide education &amp; training on FAIR stewardship&lt;br&gt; - Offer help with ELSI issues via helpdesk&lt;br&gt; - Develop a template for standardized contracts between users and contributors&lt;br&gt; - 1st Personal health train (PHT) pilots***&lt;br&gt; - Migrate FAIR level 1 to level 2 (Findable and Accessible)&lt;br&gt; - Establish support nodes at organizations with high number of users&lt;br&gt; - Develop a standardized method for pseudonimization (used in collections 5)&lt;br&gt; - Contribute to the development of a finance model for infrastructure development and maintenance</td>
</tr>
<tr>
<td>Facilities domain</td>
<td>- Connect facilities to Health-RI&lt;br&gt; - Offer overview of available facilities&lt;br&gt; - Build and maintain platform&lt;br&gt; - Offer support regarding the use of platform facilities&lt;br&gt; - Select standards for FAIR data and implement FAIR level 1**&lt;br&gt; - Provide education &amp; training on FAIR stewardship&lt;br&gt; - Offer help with ELSI issues via helpdesk&lt;br&gt; - Develop a template for standardized contracts between users and contributors&lt;br&gt; - 1st Personal health train (PHT) pilots***&lt;br&gt; - Migrate FAIR level 1 to level 2 (Findable and Accessible)&lt;br&gt; - Establish support nodes at organizations with high number of users&lt;br&gt; - Develop a standardized method for pseudonimization (used in collections 5)&lt;br&gt; - Contribute to the development of a finance model for infrastructure development and maintenance</td>
</tr>
<tr>
<td>Operational (Platform)</td>
<td>- Continuous activity</td>
</tr>
<tr>
<td>Tactical (Connect)</td>
<td></td>
</tr>
<tr>
<td>Theme 1 Research process management</td>
<td>- Personal health train (PHT) pilots***&lt;br&gt; - Migrate FAIR level 1 to level 2 (Findable and Accessible)&lt;br&gt; - Develop a standardized method for pseudonimization (used in collections 5)&lt;br&gt; - Establish and provide researchers with proficient process management tools&lt;br&gt; - Support implementation of, and training in, process management tools</td>
</tr>
<tr>
<td>Theme 2 FAIR</td>
<td></td>
</tr>
<tr>
<td>Theme 3 ELSI</td>
<td></td>
</tr>
<tr>
<td>Strategic</td>
<td></td>
</tr>
<tr>
<td>Theme 4 Strategy and relations</td>
<td>- Connect partners needed to provide shared services (contributors)&lt;br&gt; - Ensure sustainable funding for infrastructures by designing and coordinating a common infrastructure financing agenda&lt;br&gt; - Contribute to the development of a reward model for FAIR stewardship in Health&lt;br&gt; - Contribute to the development of a finance model for infrastructure development and maintenance</td>
</tr>
</tbody>
</table>

Connection of partners is not projected over time and overview of partners is not exhaustive

* The four meta-data levels are explained in appendix II  ** FAIR level 1 is the current TraIT office suite level, *** Pilot FAIR level 2: https://www.dtls.nl/fair-data/personal-health-train/
Health-Ri services and activities will lead to an infrastructure that facilitates the entire research process.

Health-Ri activities at different steps in the research process (non-exhaustive)

**Operational level (platform services)**
- FAIR data management training, education and support
- ELSI Servicedesk
- Legislation compliance tools
- Biobanking registry support center
- Central catalogue and request tool for data, samples and images
- Linked data-backbone
- Coupling between data sources

**Tactical level (connecting the network)**
- FAIR data management guidelines
- Citizen’s / patient’s voice in the strategic committee
- Reuse of previous research
- Standardized ethical review procedures
- A network of ELSI experts offering ELSI support
- Compliance-by-design
- Connected registries and biobanks
- Single identification, authentication and authorization system
- Network of data experts
- Covenants for use of facilities by others
- Harmonize data acquisition protocols
- Interoperability standards
- Coordination of IT platforms
- Promotion of the use of FAIR services
- Connections to Open Science initiatives

**Strategic level (transforming the system)**
- Increasing citizen participation
- Prioritizing of research questions by specialists and patients
- Promotion of the reuse of routine care data for research
- Promotion of omnibus legislation
- Promotion of the opening up of industry trial data
- Promotion of all data to be available in the public domain
- Coordination of investments in data infrastructures via the financing agenda, resulting in sustainable long-term funding
- Coordination of investments in IT tools, facilities and infrastructures via the financing agenda, resulting in sustainable long-term funding
- Promotion of active data sharing and Open Science policy
- Promotion of the recognition of data as academic output

The Health-Ri platform will offer researchers solutions-on-demand for each step of the research process. By simultaneously operating on the tactical and strategic level, Health-Ri will connect the needs of researchers and other stakeholders (funders, society, etc.) transforming the total health research system.
One of Health-RI’s key activities as a collective voice is setting a widely adopted infrastructure financing agenda

Health-RI coordinates the design of an infrastructure financing agenda that is widely accepted as guidance for all investments in the health research infrastructure

Annually, around € 500 million* is spent on health research in the Netherlands. Funds are mainly provided by the government (including NWO and ZonMw) and private funders like health funds. To efficiently utilize these funds to perform excellent cross-disciplinary and data-intensive health research, it is crucial that researchers get support from research infrastructures. These infrastructures provide functionalities that help with obtaining data, samples, and images, analyzing the data and translating the results into practice.

Currently, most infrastructure contributors do not have a sustainable income. Their existence depends on funds from one of the funding rounds (calls), in which they compete with other infrastructure contributors. This competition prohibits efficient and effective building of the required infrastructure, defragmentation of infrastructures, and structural maintenance of the research infrastructure. In the end, this leads to ineffective use of the available funds for a health research infrastructure.

Health-RI wants to promote the effective use of infrastructure funds by setting a national health research infrastructure financing agenda. In this agenda, the allocation of infrastructure funds is based on the needs of the clinical and health researchers. Multiple stakeholders, such as funders, users and citizens / patients, determine the content of the financing agenda (see also chapter ‘Organizational structure’). The infrastructure financing agenda follows from the strategic agenda, in which the strategic topics are determined. To ensure that the financing agenda is effectively executed, Health-RI approaches funders to commit to the financing agenda, getting an effective use of funds for infrastructures in return.

*The € 500 million is an estimation based on the budgets of funders in the health research environment[9, 10, 11]
Health-RI has clear benefits for all stakeholders in the health research field (1/2)

Different stakeholders in the research field benefit from the Health-RI infrastructure

<table>
<thead>
<tr>
<th>Health researchers and research organizations</th>
<th>Citizens and patients</th>
<th>Funders</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Users are individual researchers, research groups and research organizations who make use of services on or via the platform</td>
<td>• Dutch society with its citizens and patients. They are the users of the common goal of the health research field: better healthcare.</td>
<td>• Funders are organizations that fund Health research and research infrastructures. Examples are NWO, ZonMw and health funds.</td>
</tr>
</tbody>
</table>

How they benefit from Health-RI

Researchers will be enabled to perform excellent research via:

• Better access and easy use of IT tools and facilities;
• User support (for tools, ELSI, FAIR issues, etc.);
• Better access to (high-quality) FAIR data through standardization and harmonization of data, tools and processes.

Furthermore, users benefit from the Health-RI efforts on the strategic level. E.g. omnibus legislation* will ease using data from existing cohorts.

How they benefit from Health-RI

Better healthcare quality and access to personalized health will be within reach for citizens and patients, because Health-RI:

• Offers the scale to perform research to drive the understanding of personalized indicators for health and disease;
• Connects stakeholders to accelerate translation of knowledge into (preventive) treatments.
• Gives patients and citizens a voice to ensure that the infrastructure that is built addresses society’s concerns.

How they benefit from Health-RI

Funders will obtain optimal return-on-investment, because Health-RI will:

• Enable and stimulate reuse, translation and dissemination of obtained research data and outcomes;
• Ensure efficient use of available infrastructure funds by coordinating the financing agenda with all stakeholders involved.
• Facilitate adoption of standards by researchers, leading to better reproducibility (and quality) of research and compliance-by-design.

*Legislation regarding Wet bescherming persoonsgegevens (including patient consent)
Health-RI has clear benefits for all stakeholders in the health research field (2/2)

Different stakeholders in the research field benefit from the Health-RI infrastructure

<table>
<thead>
<tr>
<th>Government and society</th>
<th>Contributors</th>
<th>Private parties</th>
</tr>
</thead>
<tbody>
<tr>
<td>• The prime responsibility or a good working healthcare system and research field rests with the government.</td>
<td>• Contributors are providers of infrastructure services via the platform. We distinguish data* contributors and infrastructure contributors</td>
<td>• Private parties can be healthcare insurers, pharmaceutical and healthtech companies, organizations in the field of sports and nutrition and other health(care)-related industry.</td>
</tr>
</tbody>
</table>

**How they benefit from Health-RI**

The Netherlands will consolidate its leading role in the healthcare field worldwide, because Health-RI will:

• Act as a ‘launch path’ for excellent health research;
• Facilitates translation of research into practice.

For the government and society, this leads to an increased return-on investment, healthier citizens and a significant increase in the economic contribution of the Dutch health research field.

**How they benefit from Health-RI**

Infrastructure contributors will become more effective organizations, because Health-RI will:

• Increase the visibility of their offer to and the use by researchers;
• Commit to design a structural financing agenda for infrastructures.

Data* contributors will be able to generate more knowledge from their data because Health-RI:

• Enables standardization, interoperability of content (FAIR data), thereby increasing its suitability for use by other researchers.

**How they benefit from Health-RI**

Innovative companies will be able to accelerate development of solutions for (personalized) health, prevention and medicine, because Health-RI will:

• Provide a platform to connect research data and researchers
• Empower researchers to perform research that meet standards and regulations.

Health insurers will be able to service their clients better, because Health-RI:

• Supports research targeting the development of personalized healthcare and improvement of healthcare quality

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* Data refers to data, samples and images
Organizational structure
The Health-RI governance is inclusive for all stakeholders (1/2)

The governance model ensures:
- Support for the strategy of Health-RI, by giving influence to all stakeholders
- Efficiency and effectiveness, through decision-making by a smaller group

Description of bodies, tasks and responsibilities

1. General assembly
   - Consists of:
     - Representatives of all organizations in the Health-RI ecosystem. Organizations are grouped in ten chambers, being:
       - Citizens / patients, funders, users, government & regulators, medical research institutes, general research institutes, industry, healthcare insurers, contributors (infrastructure and data contributors) and healthcare (hospitals, primary care, etc.)
       - Chambers form and regulate themselves
       - The exact composition of the chambers will be further discussed with the involved stakeholders in Q1/2 of 2018

2. Strategic committee
   - Consists of:
     - Designated representatives from each of the ten chambers.
   - Tasks and responsibilities
     - Every chamber appoints representatives for the strategic committee
     - In a yearly meeting with the general assembly, the year plan for the coming year and the progress of the last year is discussed

3. Supervisory board
   - 4 members: one designated representative from each of the following chambers: citizens / patients, funders, users and one from the research institutes
   - Tasks and responsibilities
     - Set the Health-RI strategic agenda
     - Set the infrastructure financing agenda
     - Advise on the four members to take place in the supervisory board
The governance model is set up in a way that it is efficient, effective and supported by stakeholders.

**Governance model**

1. **General assembly**
   - Chambers: Unlimited number of representatives
   - Designated representatives from each of the 10 chambers
   - General assembly consists of:
     - Citizens / patients
     - Funders
     - Users
     - Government & regulators
     - Medical Research Institutes
     - Health insurers
     - Contributors
     - Healthcare
     - General research institutes

2. **Strategic committee**
   - Limited number of representatives: Designated representatives from each of the 10 chambers

3. **Supervisory board**
   - 4 members: One designated representative from each of the following chambers: citizens / patients, funders, users, and one from the research institutes
   - Tasks and responsibilities:
     - Supervise the managing board on (financial) management
     - Supervise the managing board on execution of the strategic agenda and the infrastructure financing agenda
     - Appoint and discharge members of the managing board

4. **Managing board**
   - Consists of:
     - Three members:
       - Chief Data Science: Has a technical background
       - Chief Health & Medicine: Has a clinical research background
       - Chief Executive Officer: Has a business background
     - Is supported by finance, HR, marketing, and IT divisions
   - Tasks and responsibilities:
     - Translate the strategic agenda to an operational plan and supervise the execution by the operational teams
     - Influence stakeholders to follow the financial infrastructure agenda that has been set
     - Responsibility for the overall daily management

5. **Operational teams**
   - Consists of:
     - People with knowledge of different domains and themes mentioned in chapter ‘Health-RI value proposition’, based on the execution needs of the strategic agenda.
   - Tasks and responsibilities:
     - Daily execution of activities related to the strategic agenda

---

The Health-RI governance is inclusive for all stakeholders (2/2)

The Health-RI governance is inclusive for all stakeholders (2/2)
The operational organization is structured in a matrix of domains and themes

A matrix organization forms the basis of the operational organization

- The operational organization is a matrix organization consisting of three domains and four themes with representative team members. The structure of the operational teams will be flexible, because they have to execute a strategic agenda that will change over time.

- The three domains that are now envisaged are the ‘collections domain’, the ‘IT services domain’ and the ‘facilities domain’. Within their domain, team members ensure the availability of platform content and functionalities by connecting network partners. Furthermore, they ensure that the offer meets the latest standards and matches the needs of the users during the entire health research process. To realize this, all domains collaborate with their colleagues (specialists) dealing with the four main themes, being 1) research process management, 2) FAIR, 3) ELSI and 4) strategy and relations.

- Types of platform content and functionalities per domain:
  - Collections: data collections, sample collections, imaging collections
  - IT services: data backbones, analysis tools, etc.
  - Facilities: unique devices and medical services (e.g. mass spectrometry, high quality MRI, etc.)

- The second page of chapter ‘Health-RI value proposition’ provides an overview of the activities undertaken and services provided within each domain and theme.

- The managing board supervises the operational teams and is responsible for the overall (financial) management. The different chiefs will connect all disciplines within Health-RI to ensure effective execution. Furthermore they will connect to stakeholders (outreach) in the Health-RI network and ecosystem.
The Health-RI organization needs financing of around € 20-25 million yearly in 2022

This chapter describes the income sources, expenses categories and a P&L for the Health-RI organization

Required funding for the Health-RI organization in relation to total annual funding for health research

Annual total funding for health research (~ € 500 M*)

Health research infrastructure financing agenda applies

Infrastructure marked funds (~ € 30 M)

Health-RI organization direct funding from infrastructure marked funds

Health-RI organization fee for service and direct funds from 'non-infrastructure marked' funds

In addition to the health research budget, around €100 million is spent annually on registries of Healthcare data.¹²

Annually, around € 500 million* is spent on health research in the Netherlands. Support to researchers is provided by several infrastructure services. Around 10-15% of the total research expenditure is spent on these infrastructures. To ensure that all (relevant) infrastructures receive sustainable funding, Health-RI aims to allocate all ‘infrastructure marked’ funding (ca. 7.5%) to contributors according to the Health-RI infrastructure financing agenda (see chapter ‘Health-RI value proposition’, fourth page). The Health-RI organization needs a share of the infrastructure marked funds to deliver the shared services infrastructure (BBMRI-NL, EATRIS-NL, ELIXIR-NL, TraIT) and to be the landing zone for newly developed infrastructures that need structural embedding in the national infrastructure.

Because of the convergence of the Dutch nodes of multiple ESFRIs into the Health-RI organization, we expect that we can use the allocated budgets more efficiently, providing space for those services additional to the platform (e.g. the collective voice, see chapter ‘Health-RI value proposition’, first page).

The next pages provide more insight into the income and expenses of the Health-RI organization, including a detailed budget overview.

*The € 500 million is an estimation based on the budgets of funders in the health research environment⁹, ¹⁰, ¹¹
Overview of income flows for Health-RI: income from three types of sources

Below is an overview of the income and expenses flows and a clarification of the three types of income sources

Overview of financial flows, focus on income

Income is generated from three types of sources

1. Fee for service
   - Fee for service is income generated by users paying for services offered on or via the platform. For example, users pay for specific software tools or access to data. Around 25% of the structural Health-RI income should be generated by fee for services in 2022.

2. Direct funding
   - Direct funding are funds that are made available directly to Health-RI via the government, knowledge institutes or private funders like health funds. Sustainable income is needed for Health-RI to connect and represent stakeholders in the Health-RI ecosystem and to offer certain shared services. Around 55% of the structural Health-RI income should be generated by direct funding in 2022.

3. In-kind contribution
   - To be able to successfully perform its activities, it is essential that Health-RI receives in-kind contribution (people) from data contributors. This can, for example, be an employee at a UMC who is dedicated to support Health-RI users within the UMC and paid by the UMC. Around 20% of the structural Health-RI income should be generated via in-kind contributions in 2022.

On the next pages a more detailed explanation of the three income sources is shown.
Fee for service as a structural, sustainable income for Health-RI

Fee for service is dependent on the demand for services offered by or via Health-RI

The fee for service is generated by **users paying for services offered** on or via the platform. Users* either make use of a service offered by the Health-RI organization (e.g. ELSI support), or a service offered by a contributor (e.g. data) via Health-RI. In the first case, Health-RI will gain the amount paid by the user, in the latter case Health-RI receives commission, based on agreements with the contributor.

By building a fee for service system, a **structural and sustainable income flow** can be realized for Health-RI. Furthermore, a fee for service system stimulates the Health-RI platform to continually **respond to the demands of users**.

Fee for services for these types of services, however, are currently not very common in the health research field. Therefore, in addition to the possibility of paying for services in cash, Health-RI wants to make agreements with funders to provide users* with budget that they can use for Health-RI services, for example via a **voucher system**.

In a **voucher system**, part of the funding for research projects is reserved as vouchers that can be used at Health-RI for Health-RI services. With these vouchers, the user can buy services from or via Health-RI for the research project. The user cannot use this part of the budget for other purposes, unless the service requested is not available via Health-RI. Health-RI can budget a part of the budget for vouchers as expected income. The user is not obliged to use the vouchers. **This stimulates Health-RI to provide and connect services that really match users’ demands** and thereby continue this income flow. Furthermore it ensures that funds are used on high quality infrastructures provided via Health-RI, and users do not unnecessarily build their own infrastructures or collect data which are already available. Vouchers that are not used during a research project return to the funder after the ending of the project. **Support of and collaboration with funders is essential to create a voucher system.**

*Explanation of the example ‘Health-RI voucher’ system*

- **User** applies for funding of a research project
- **Funder** grants a €0.5 million budget
- 5% (€25K) of the budget is reserved for Health-RI vouchers
- **User** uses vouchers worth €20K to retrieve and analyze data via Health-RI. Remaining vouchers (€5K) are not used
- **Unused €5K remains at funder**
- **Funder pays Health-RI (including contributors) €20K**

*A user or users can either be an individual researcher, a research group or a research organization*
Direct funding enables Health-RI to offer shared services and operate as a collective voice

Direct funding is needed to enable the Health-RI organization to offer shared services and undertake activities benefitting all researchers

Direct funding

- Direct funding comes from funds made available to Health-RI via the government, knowledge institutes or private funders like Health funds directly. These funds are granted to Health-RI as they offer services and undertake activities that do not benefit one individual researcher in particular but support all researchers in health research. This support is essential to efficiently perform high quality research. Think of services and activities like providing an overview of all available data (catalogues) and activities that drive the movement to FAIR data.
- Direct funding can come directly from the government, from ‘infrastructure marked’ funds like the NWO roadmap large scale infrastructure calls, or from other funding opportunities.
- Because funders have influence on the strategic and infrastructure financing agendas (see chapter ‘Organizational structure’) they can influence how the Health-RI organization utilizes the received funds. The specific benefits for these funders are explained in the chapter ‘Health-RI value proposition’. For direct funding to become a source of structural income, it is important that direct funding is not (only) provided on a project basis, but that longer term agreements can be made with funders.
- Direct funding is also needed to cover start-up costs. Before Health-RI can generate income via the fee for service mechanism, the platform and its services must be up and running. This will require some initial investments. The detailed budget overviews provide more background and figures on the required investments.
In-kind contribution is requested to ensure commitment to Health-RI

In-kind contribution ensures commitment from data contributors offering services via Health-RI

In-kind contribution

- Health-RI expects an in-kind contribution from **contributors** (e.g. data contributors*, knowledge institutes) within the Network Health-RI. The in-kind contribution will mainly comprise **people that perform work for Health-RI**. These people are stationed at and paid by the contributors, but are dedicated to **Health-RI activities**. This in-kind contribution results in commitment from contributors to Health-RI. The size of the in-kind contribution can depend on the extent to which a contributor benefits from Health-RI.

- As an example: Parelsnoer Institute (an initiative from the UMCs) offers their data via the Health-RI platform. In return, one employee with a contract at UMCG works for Health-RI by helping users with retrieving the data, connecting Parelsnoer data to other data sources, etc.

**Explanation of in-kind contribution via an example**

* Partner organizations that can provide researchers with data, samples and images for research. They provide this content via the platform
Overview of expense flows of Health-RI: main part of expenses are related to the offering of services

Below is an overview of the income and expenses flows and a clarification of the three main expenses categories

Overview of financial flows, focus on expenses

There are three main expense categories

4 Direct services related expenses
• Direct services related expenses are expenses connected to the offering of Health-RI services and related activities. This, for example, includes the wages of the operational teams, IT costs for maintenance of the platform, travel and representation expenses. Costs that other organizations incur for in-kind contribution are included. These expenses are expected to be the gross part of total expenses.

5 Indirect services related expenses
• Indirect services related expenses are expenses that are not directly related to the provided services. They partly cover the strategic and tactical activities, and cover the organization’s administration on a day-to-day basis and the wages of the management board.

6 Other expenses
• Other expenses include participation fees and unforeseen expenses. Participation fees are paid to maintain the connection with the European hubs of BBMRI-NL, ELIXIR-NL and EATRIS-NL, after they have converged into the Health-RI organization. Around 5% of the total budget is reserved for other expenses.
Expenses grow due to convergence of existing and innovative organizations/initiatives into Health-RI

**Figures below give further insight on expenses – expenses are expected to grow due to convergence and innovation**

**Expenses**

- The largest part of the expenses is based on the costs of current activities of the initiatives that converge into Health-RI (see page 12 and 43) and the additional activities that Health-RI will perform (e.g. being the collective voice). The growth of these expenses (in grey) is mainly due to expected growth in the number of people that will be dedicated to Health-RI activities at the contributors in the Health-RI network (in-kind contribution).

- Total expenses will also grow due to convergence of existing and innovative organizations/initiatives into the Health-RI organization (in blue), for example current UMC infrastructures and registries.

- Start-up related expenses (in green) consist of expenses to operationalize the organization and a one-time investment in developing the portal and website. Operationalization of the organization will be a long term process, with higher investments at the start. Costs are made for legal assistance, organizing the governance, developing and managing the migration of existing organizations and shared services into the Health-RI organization, identifying blind spots, aligning stakeholders etc. A one-time investment in the portal and website is needed to develop a high-end interface between the infrastructures and users.
Financial structure

Health-RI organization: insight on expenses

Figures below give further insight on expenses – 80% to 90% of total expenses will be direct services related expenses

- Around 80% to 90% of total expenses are directly related to services or products provided by Health-RI (in blue).
- ‘Other expenses’ (in green) include the participation fees for the European hubs of BBMRI, ELIXIR and EATRIS, amounting to around € 0.8 million annually.

- In 2022, around 50% of the expenses will be related to new activities of Health-RI. On the one hand due to convergence of initiatives into Health-RI and to sustained innovation of Health-RI (23%). On the other hand due to growth of the capacity (people) to disseminate the Health-RI activities and train people throughout the Health network, for which people at contributors dedicated to Health-RI will also be needed (in kind contribution).
Health-RI organization: insight on income

Figures below give further insight on income – the fee for service income is expected to grow over time

Income

- Total income will have to grow over the years, following the growth in expenses.
- Income from the fee for service system is expected from 2019 onwards. Expected income is based on the costs of services directly applicable for users.
- We expect the fee for service to grow. In time, Health-RI aims to obtain 40% of its yearly income via fee for service (figure below). The growth is determined by three mechanisms:
  - Services must have reached a certain level of maturity to be able to ask for a fee for service. Over time, more services will reach this level of maturity.
  - To enable users to pay for the services, adoption of the fee for service system and its embedding in project grants conditions will be needed from funders.
  - Offered services should meet user demand. If not, no growth is expected.
- The in-kind income grows to over 20% of Health-RI income and is based on the in-kind contribution from organizations in the Health-RI network. As Health-RI deploys more activities, more local support will be needed.
Health-RI organization: insight on income

**Figures below give further insight on income – on the short term additional direct funding will be needed**

<table>
<thead>
<tr>
<th>Year</th>
<th>Direct funding to be obtained</th>
<th>Direct funding already obtained</th>
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</thead>
<tbody>
<tr>
<td>2018</td>
<td>€ 9.468</td>
<td>€ 15.8 million</td>
</tr>
<tr>
<td>2019</td>
<td>€ 10.274</td>
<td>€ 16.3 million</td>
</tr>
<tr>
<td>2020</td>
<td>€ 10.844</td>
<td>€ 14.6 million</td>
</tr>
<tr>
<td>2021</td>
<td>€ 10.456</td>
<td>€ 14.2 million</td>
</tr>
<tr>
<td>2022</td>
<td>€ 9.961</td>
<td>€ 13.7 million</td>
</tr>
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</table>

**Income**
- Apart from the fee for service income, direct funding will be needed (see page ‘direct funding’)
- A part of the total direct funding needed is already obtained through grants for activities of existing organizations that will converge into Health-RI. However, in addition, until at least 2022, yearly around € 10 million direct funding needs to be obtained from either the government (government-led funders) or private funders.
**Health-RI-organization: profit and loss statement**

**Clarification of the profit and loss statement**

- The profit and loss statement (P&L) discussed is the P&L of the Health-RI organization. It gives an overview of income and expenses of the Health-RI organization and is the basis for the figures on the previous pages. Given the not-for-profit position of Health-RI, ‘Unforeseen expenses’ is used to balance the income and expenses.

**Expenses**

- Expenses are largely based on current costs of activities undertaken by organizations converging into Health-RI – i.e. BBMRI-NL, TraIT, ELIXIR-NL and EATRIS-NL. Assumptions are made about the expenses for activities that are currently not performed by these organizations, but are performed by Health-RI.

**Income**

- Current funding of the organizations converging into Health-RI are included in the direct funding.
- Because the required income follows expenses, income is based on assumptions about potential fee for services for direct services, expected in-kind contribution, and required additional direct funding. Long-term agreements with funders should contribute to a structural funding of Health-RI.
- We expect income from fee for services to rise over the years as Health-RI develops and offers more and improved services. Fee for service income is both income in the form of cash as well as in the form of a voucher system (see detailed explanation on the fee for service).
- One-time funding to cover start up costs in 2018 is needed to operationalize Health-RI.

---

<table>
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<th>Health-RI - Profit and loss statement</th>
<th>EUR '000</th>
<th>EUR '000</th>
<th>EUR '000</th>
<th>EUR '000</th>
<th>EUR '000</th>
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<tr>
<td></td>
<td>2018</td>
<td>2019</td>
<td>2020</td>
<td>2021</td>
<td>2022</td>
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<td><strong>Net income</strong></td>
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Definitions and abbreviations
## Definitions used in the business plan

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<tr>
<th>Term</th>
<th>Definition</th>
<th>Term</th>
<th>Definition</th>
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<tbody>
<tr>
<td>Compliance-by-design</td>
<td>A process of developing a (software) system that facilitates a research process in such a way that its ability to meet specific compliance requirements is ascertained</td>
<td>Infrastructure contributor</td>
<td>Partner organizations that can provide researchers with expertise, tools and other services to perform research. They provide these services via the platform</td>
</tr>
<tr>
<td>Data contributor</td>
<td>Partner organizations that can provide researchers with data, samples and images for research. They provide this content via the platform</td>
<td>Innovation gap</td>
<td>The current lack of translation of research results into healthcare practice</td>
</tr>
<tr>
<td>Direct service related expenses</td>
<td>Expenses made in relation to activities leading to a (shared) service or product for users</td>
<td>Learning healthcare system</td>
<td>A system in which science, informatics, incentives, and culture are aligned for continuous improvement and innovation, with best practices seamlessly embedded in the delivery process and new knowledge captured as an integral by-product of the delivery experience.</td>
</tr>
<tr>
<td>Health gap</td>
<td>The gap between the actual health of an individual and their health-potential</td>
<td>Personalized medicine &amp; health research</td>
<td>Research related to gaining a better understanding of human health and disease and to developing or improving the prevention of disease or the treatment of disease. This ranges from fundamental research to research into societal practice covering all phases of human life, and can be related to healthcare, drug development, technological advances, food and lifestyle research, social research, etc.</td>
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<tr>
<td>Health-RI ecosystem</td>
<td>All stakeholders in the field of medicine &amp; health research</td>
<td>Partner</td>
<td>Organization connected to Health-RI, either via the Health-RI network or the Health-RI ecosystem</td>
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<td>Definition</td>
<td>Abbreviation</td>
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<td>---------------------------</td>
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<td>--------------</td>
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<td>Research environment</td>
<td>The surrounding (involved parties, total euro’s, etc.) in which health research is performed</td>
<td>Health-RI</td>
<td>Health Research Infrastructure</td>
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<td>User</td>
<td>Individual researchers, research groups and research organizations who make use of services on or via the platform</td>
<td>KWF</td>
<td>Dutch Cancer Society</td>
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<td>Abbreviation</td>
<td>Full name</td>
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<td>Biobanking and BioMolecular resources Research Infrastructure, the Dutch node</td>
<td>NFW</td>
<td>Netherlands Federation of University Medical Centres</td>
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<tr>
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<td>Center for Translational Molecular Medicine</td>
<td>NWO</td>
<td>Nederlandse organisatie voor Wetenschappelijk Onderzoek</td>
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<td>Dutch Techcentre for Life Science</td>
<td>PHT</td>
<td>Personal Health Train</td>
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<td>European Advanced Translational Research Infrastructure in Medicine, the Dutch node</td>
<td>TraIT</td>
<td>Translational Research IT project</td>
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<td>ESFRI</td>
<td>European Strategy Forum on Research Infrastructures,</td>
<td>ZonMw</td>
<td>The Netherlands organisation for Health Research and Development</td>
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<tr>
<td>FAIR</td>
<td>Findable, Accessible, Interoperable, Reusable</td>
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Appendices
European and national developments \((e.g.\) in funding) created the wish for a national health research infrastructure.

Over time, individual national infrastructure initiatives and organizations started partnering, collaborating and converging. This created the wish for a national health research infrastructure (Health-RI).

**Health-RI**

- "NWO cluster"
- BBRMI cluster, ELIXIR-NL collaborate in NWO call with X-omics and MRI & cognition
- Partnering of TraIT, BBMRI-NL 2.0 and NFU PSI
- DTL
- ELIXIR-NL
- NFU PSI
- NFU D4LS
- 8 Dutch UMCs partner

**Partnering of**

- TraIT to Health-RI
- Development towards Health-RI
- Program within Lygature
- Convergence
- Lygature
- CTMM
- TI Pharma
- NWO Roadmap Large Scale Infrastructures
- FES funding
- KWF funding
- NFU funding

**Over time, individual national infrastructure initiatives and organizations started partnering, collaborating and converging. This created the wish for a national health research infrastructure**

**European focus on research infrastructures through ESFRI activated development of national infrastructures**

**ESFRI roadmap 2018**

**EuroBioImagin**

**BBMRI EATRIS ELIXIR**

**2007**

**2017**
Considerable actions have been performed in preparation to become the leading Dutch infrastructure

Appendix Ib: actions performed by Health-RI until now

Considerable actions have been performed in preparation to become the leading Dutch infrastructure

Created endorsement of > 70 stakeholders in the field

Development of business plan with stakeholders


Actions

Several infrastructure initiatives* decided to have a joint annual meeting for Dutch infrastructures facilitating health research

Health-RI vision document is pitched at Royal Academy

Stakeholder meeting 2016: Announced steps for concretization of Health-RI

Temporary Health-RI governance established, starting 2017

Funding of €2.25 million for TraIT2Health-RI transition

Facilitated the collaboration of BBMRI-cluster, Elixir-NL and X-omics on the NWO call for large-scale research infrastructure 2017-2018

Start Health-RI

Website with animation video about Health-RI**

Stakeholder meeting May 2017: Input of stakeholders on proposition and business model

Stakeholder meeting October 2017 Presentation of business plan to stakeholders

Represent stakeholders in Health deals agreements

Activities to create stakeholder endorsement for Health-RI

Activities to operationalize Health-RI and first activities aligned with the strategy of Health-RI

* BBMRI, ELIXIR & EATRIS, together with DTL, TraIT and parts of EuroBioimaging. ** Health-RI to arrive at a single connecting national research infrastructure*, https://www.health-ri.org/
Explanation of the meta-data levels

**Meta-data can be arranged in four levels based on the Dublin Core Metadata Initiative (DCMI)**

**Level 1: Shared term definitions**
This level corresponds to using the natural language definitions of the Dublin Core terms.
- The use of the term URIs is not a requirement - terms may be referenced in any way.
- Conformance with the specified domains and ranges of the terms is not a requirement.
- Conformance with the DCMI Abstract Model is not a requirement.

**Level 2: Formal semantic interoperability**
This level corresponds to implicit or explicit use of the RDF semantics underlying DCMI terms. Thus, any usage of the terms needs to be precise in its conformance with the RDF model and the domains and ranges of terms.
- While the specification/application need not explicitly encode data using URIs, it must be possible to infer the term URIs.
- Conformance with the specified domains and ranges of the terms is a requirement.
- Conformance with the sub-property semantics of the used properties.
- Conformance with the DCMI Abstract Model is not a requirement.

**Level 3: Description Set syntactic interoperability**
This level corresponds to explicit use of the DCMI Abstract Model in the metadata.
- The metadata must be structured using the DCMI Abstract Model notions of Descriptions and Description Sets.
- The Statements in a Description must use the structure defined by the DCMI Abstract Model.

**Level 4: Description Set Profile interoperability**
The specification "Description Set Profiles: A constraint language for Dublin Core Application Profiles" [DC-DSP] provides an information model and XML expression of structural constraints on a Description Set. An application such as the Scholarly Works (Eprints) Application Profile can be said to be "Description-Set-Profile-interoperable" if it provides formal constraints on a Description Set that are compatible with those in the Description Set Profile specification.

A related specification, Singapore Framework for Dublin Core Application Profiles [DCAP], outlines a package of documentation elements needed in order to present a metadata application for maximum interoperability and reusability - elements such as Functional Requirements, a Domain Model, and a Description Set Profile covering the complete metadata set.