# Top Sector HTSM
# Healthcare roadmap 2018

## Contents

# 1. Societal challenges and economic relevance

## 1.1 Societal challenges addressed in this roadmap

The healthcare roadmap for Top Sector HTSM focuses on the technological and industrial innovation addressing primarily the Health and Care societal challenge (ref. *Maatschappelijk Uitdaging -MU- Gezondheid en zorg),* and will take into account and contribute to Secure Society (ref. *MU veilige samenleving)* and inclusive society (ref. *MU Inclusieve Samenleving*).

Top Sector Life Sciences and Health (LSH) is primarily in charge for addressing the Health and Care societal challenge and coordinates the contributions from other sectors and roadmaps, including the present HTSM Healthcare roadmap to increasingly combine expertise and efforts. LSH described healthcare major challenges and trends in the Health and Care Knowledge and Innovation Agenda 2018-2021[1].

Health and healthcare systems will face a huge challenge in providing the same level of services, in an appropriate, efficient and cost-effective way, to a rapidly growing and aging population.

Global healthcare expenditure is currently estimated a USD7.6 trillion and its growth will continue greater than the GDP, reaching double the rate in some countries. By 2030, world population will increase by 1.3 billion, the middle class by 3 billion. Due to ageing, the world's population aged 65+ is projected to increase by 436 million people and urban population by 1.5 billion requiring increased access to healthcare facilities and service.

The Netherlands will also face those challenges. Already today healthcare spending in NL ranks among the highest among OECD countries with 10.5% of the GDP and USD 5.4k per capita[2] and it is projected to increase (See Figure 1). Life expectancy is growing at an higher rate as the number of healthy years[3], resulting in a higher incidence of diseases. In 2040, it is estimated that 4.7 million people will be older than 65, against 2.9 million today (+62%).

It is also expected that there will be a shortage of health-care personnel; in healthcare many processes and treatments are difficult or not possible to automate, making it hard to increase the productivity per employee.

[1] https://www.health-holland.com/public/downloads/kia-kic/knowledge-and-innovation-agenda-2018-2021.pdf

[2] OECD Health Data 2017 http://www.oecd.org/els/health-systems/health-data.htm

[3] http://ec.europa.eu/eurostat/statistics-explained/index.php/Healthy_life_years_statistics

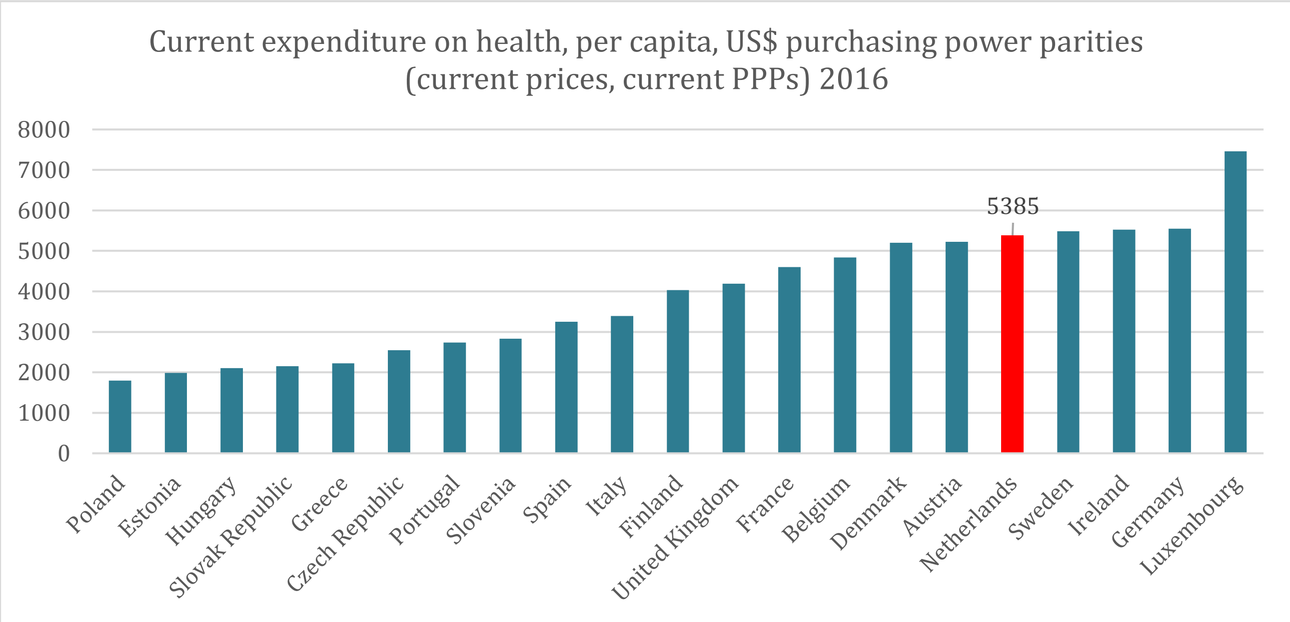


*Figure 1: Netherlands 2016 total healthcare spending in EU28 US dollars/capita [Source OECD database]*

Given the previous arguments of the ageing society and the fact that an increasing part of GDP will be spent on healthcare, it is evident that health and healthcare must be differently organized to further increase the quality level and enable further improvements in performance.

The process for the delivery of quality care – and the patient that receives it – have also changed dramatically in recent years. Increasingly, hospitals are challenged to adapt traditional in-patient models to ones that can be delivered amongst numerous providers, outside the hospital setting, and in various ways across the care continuum.

At the same time, patients are no longer passive recipients of medical treatment but active and discerning consumers of health services. They want and need to take more control over their own health and over where they receive care (participatory health). Provider reimbursements are becoming value-based and performance ratings are inextricably linked to patient outcomes. These factors are changing the very definition of patient-centric care as the significance of the patient experience intensifies and oversight of the patient journey becomes critical.

Value-based healthcare is commonly regarded a part of the solution for this immense problem because it aims to achieve the highest quality outcome for the patient relative to the cost of achieving those outcomes.

During a person’s lifetime, much progress can be achieved in developing means of healthier living, prevention and early diagnosis of potential diseases, and improved treatment and monitoring if that person becomes ill. All these healthcare domains are seen as a continuum in the life of a person (see Figure2). This overview is aligned with the three basic health-related elements of society mentioned by Top Sector LSH: Prevention, Cure and Care.

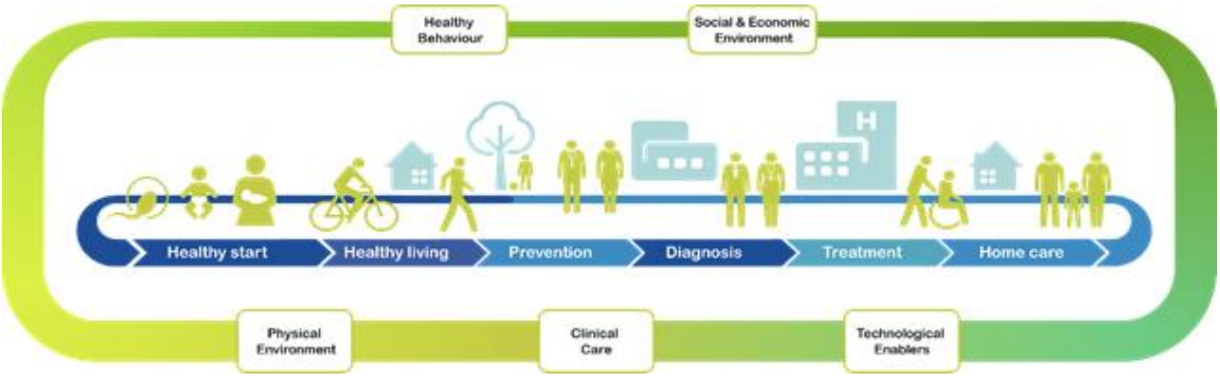

*Figure 2: Continuum of Health*

Improvement of the quality and sustainability of healthcare through digitization will drive efficiency in health, social, and informal care delivery, enable value-based healthcare systems and improve patient and citizen involvement in their personal health and care.

Digitalization is a crucial development that will have a tremendous impact in achieving sustainability of health care systems in the future by enabling:

- **Quality and efficiency of care**: optimizing (currently silo-ed) building blocks of healthcare, enabling health systems to deliver value-based healthcare with better outcomes at lower cost.
- **Personalizing health (care)**: convergence of professional healthcare and consumer health, enabled by wearable electronic devices, data and digitization, leading to increased self-management and individualized treatment paths.

Innovative technologies in healthcare are integrated into devices that treat patients with acute or chronic diseases, and which affect vital prognoses or alter drastically the functioning and quality of life of numerous citizens/people . Tremendous progress is expected in research and technology fields such as image-guided interventions, smart catheters, genomics and other -omics, personalized medicine, phenotyping, exposome bio-sensing, regenerative medicine, robotics, energy harvesting and low-power electronics for communicating securely and extending processing and memory capacities. Moreover they hold promise for completely new approaches based on artificial intelligence, deep learning and the understanding of psychobiological mechanisms at the origins of diseases that will radically change the way people with and without diseases are diagnosed and prognosed, treated and followed-up.
The way health is preserved and healthcare is provided is changing substantially, as medical diagnoses and interventions in the future are no longer confined to hospitals, clinics or medical offices, but are occurring anywhere in people's life, especially in their living contexts as school, home, sports and labour. These examples are supporting the trend of decentralized healthcare. Personal Digital Twins, ambulatory care, "point-of-care" and "home care" are terms that will gain significance in the future.

Digitization of healthcare will increase the amount of personal and sensitive data being recorded, analyzed and shared. As the risk for improper data use and fraud is high, adequate devices or systems are needed for ensuring security for managing personal data across any transaction related to Health and Care which are complying with existing and future regulations.

The consequence of patients being followed with nomadic health-status sensing is that data communication and exchange will have to be integrated into current open Internet-based platforms, so that the safety aspects of the overall monitoring system become crucial. Errors in such systems should not lead to catastrophic or damaging decisions and actions in the treatment. Elements of failure safety testing like in the aviation and aerospace industry should be adopted, black-box and hierarchical testing and system design become increasingly important. This also holds for all systems where computer-based control takes place, like in robotics. Subsystem failure should not lead to patients being injured or damaged in any kind. Subsystems -even from different providers- should be evaluated and tested independently and as a complete system. This implies that regulation should allow more testing possibilities and evaluation with patients, yet under controlled circumstances and the governance of manufacturers of medical equipment should be addressed. These elements will create challenges related to the Secure Society.

Aging population and an increase of chronic diseases will put pressure not only on the sustainability of the healthcare systems, but will also cause an increasing need for assistance for example for elderly people or people unable to participate in society (like school, work, leisure, etc.).
Technical innovations for prevention and health(care) have the potential to contribute to the inclusive society challenge by improving the interdependence of an aging population or by reintegrating people in the work market with solutions improving patient engagement and self empowerment.

## 1.2 World-wide market for this roadmap, now and in 2025

The HTSM Healthcare roadmap will affect different global markets that can be segmented in different ways.
As a market, healthcare including health & wellness represents up to 25% of the EU economy (when measured in terms of employment, expenditure and added value), making it the largest industry.
Looking at expenditure in Europe an average of 10% of gross domestic product (GDP) is spent on healthcare, of which major part (75.5%) goes to patient care, 17% on pharmaceutical and other medical non durables and 7.5% goes to medical technology which is the most relevant for the HTSM roadmap.
The global medical technology market, including devices used for pharmaceutical purpose, is expected to grow at 5.0 % p.a. (i.e. CAGR) from $363.8 billion to $513.5 billion between 2013-2020.[4]
The European medical technology market is estimated at roughly €100 billion. Based upon manufacturer prices the European medical technology market* is estimated to comprise approximately 30% of the world market. It is the second largest medical technology market after the US (~40%). Expenditure on medical technology per capita in Europe is at around EUR 197 (weighted average). The European medical technology market has been growing on average by 4.6% per annum over the past 8 years. EvaluateMedTech consensus forecasts that the Medtech world market will achieve sales of $529.8 bn in 2022, growing by 5.2% per year (CAGR) between 2015 and 2022. In vitro diagnostics (IVD) will be the largest device area in 2022, with sales forecast to reach $70.8 bn. Cardiology takes the second spot, with annual sales increasing to $62.3 bn in 2022. Neurology is forecast to be the fastest-growing device area, with a CAGR of 7.6% between 2015 and 2022.

[4] World Industry Outlook Healthcare and pharmaceuticals, The Economist Intelligence Unit, May 2014

Looking at the different medical applications the markets can be further specified.
The worldwide diagnostic imaging market is expected to reach $36.4 bn by 2021, at a CAGR of 6.6% from 2016 to 2021[5]. Geographically, North America holds the largest share of the market according to 2016 data, followed by Europe. However, the Asia-Pacific market is expected to register the highest CAGR during the forecast period. Factors such as increasing incidence of chronic diseases, rising awareness of the benefits of early disease diagnosis, development of new healthcare facilities, growing medical tourism in APAC countries, and increasing government initiatives for the modernization of healthcare infrastructure are driving the growth of the market in the Asia-Pacific region.
The global Interventional Radiology market is anticipated to reach $22.9 bn by 2024, registering a CAGR of 5.8% over the period between 2016 and 2024. This market covers the complete spectrum of medical imaging systems (MRI, CT, X-ray and US) used in various IR applications including angiography, balloon angioplasty, embolization, biopsy, vertebroplasty, kyphoplasty, and RF ablation. End-users are hospitals, catheterization labs, and ambulatory surgical centers. The main driving factor for the increased demand of IR is the higher incidence of chronic diseases and obesity, resulting from lifestyle changes such as sedentary lifestyle, busy lifestyle, and unhealthy habits such as smoking and poor diet[6].
Rising costs and expected shortages of healthcare staffing ask for new solutions and technical tools. These are provided by for example minimally invasive procedures, facilitated by expanding applications in hybrid operating rooms that combine operating room equipment with advanced imaging systems. The market for Hybrid OR Fixed C-Arms was estimated to be €240M globally in 2016. Structural heart and peripheral vascular procedure growth of 9.5% p.a. (2016-23), is expected to drive market growth for Hybrid ORs by more than 5%.
The market for surgical navigation systems comprises navigation platforms as well as navigation applications. Until 2023, this market will expand continuously at a CAGR of about 5%. In 2014, the market was valued at approximately $175M. Moderate growth will occur in this space over the forecast period, driven by increasing surgeon awareness of the clinical benefits of surgical navigation and a growing potential patient base; this will be fueled by the aging population as well as increasing demand for minimally invasive surgery. The installed base of surgical navigation systems is expected to grow over the forecast period given technological improvements and increased physician education. Increasing procedure volumes, rising demand for minimally invasive surgery and growing awareness of the clinical benefits of surgical navigation will support surgical navigation system sales throughout the forecast period. By 2023, the US surgical navigation system market will thus reach a value of approximately $260M.
The global medical robotics market is expected to reach $20.56 bn by 2022, from $6.36 bn in 2016 at a CAGR of 21.6% during the forecast period[7]. The US medical robotics market size was $3 bn in 2016 and is expected to grow towards $7 bn in 2022. Key factors driving the demand for medical robots market include[8]:

- Rapidly growing demand for precise and efficient minimally invasive surgeries

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5 Markets and markets – Diagnostic Imaging Market, February 2017

6 http://www.diagnosticimaging.com/interventional-radiology/growth-interventional-radiology?GUID=5FA29331-23EC-4569-B9BD-E66D8136D007&XGUID=&rememberme=1&ts=23092016
7 Grand View Research - Medical Robotic Systems Market Size & Share, Industry Report, 2022
8 PR Newswire Global 20 Billion dollar Medical Robotics Market to 2022

- Growth in the volume of these surgeries, as a consequence of growing disease prevalence levels
- Improvement in healthcare infrastructure and the introduction of advanced medical equipment are expected to facilitate further implementation of robotic systems in developed countries.

Another way to look at the impact of the HTSM roadmap is to look at the potential of digital technologies in Health. The market for digital health is gaining remarkable momentum across the world, thanks to the surge in the prevalence of people with diabetes and various other chronic diseases. With the increasing number of government initiatives and the rising uptake of information technology in the area of medical and healthcare, the market is anticipated to witness significant growth over the next few years. In 2016, the global digital health market was at $179.6 bn. According to Transparency Market Research (TMR), the opportunity in this market is anticipated to rise at a CAGR of 13.40% between 2017 and 2025 and increase to $536.6 bn by the end of 2025.

The global market for mobile digital health is assessed based on the product, component, end user, and the geography. Based on the product, the market is classified into wearable devices and healthcare information systems. An example of the former is the use of smart medical patches that measure vital signs for continuous (remote) on-body diagnostics. Healthcare information systems leads the global market due to the significant rise in the adoption of technological advanced products, such as telehealth, EHR/EMR, and population health management. Further, the healthcare information segment is bifurcated into clinical solutions and non-clinical solutions. Clinical decision support system (CDSS), EHR/EMR, computerized physician order entry (CPOE), telehealth, mHealth, and population health management are the key segments of clinical solutions. Of these, the market for mHealth is anticipated to propel at a significantly high growth rate on account of the rising penetration of smartphones across the world and the augmenting levels of awareness regarding health and fitness among people across the world.

The global healthcare IT market is estimated to reach $280.25 bn by 2021 with 15.9 percent growth, with the majority of the demand for healthcare IT solutions driven by the growing need to reduce healthcare costs while adhering to ongoing regulatory requirements. Healthcare IT is linked to information and workflow management, but also to e.g. clinical decision support as well as home health applications. In most high growth markets, the major European companies have an important presence[9].

Based on the component, the market is categorized into software, hardware, and services. The demand for digital health services is expected to remain high over the forthcoming years. Based on the end user, the market has been categorized into B2B and B2C. The B2B segment has emerged as the key contributor to this market over the last few years. Providers, employers, payers, and pharmaceutical companies are the main components of the B2B segment, whereas the B2C segment includes patients and caregivers[10].

According to the new market research report "Artificial Intelligence in Healthcare Market by Offering (Hardware, Software and Services), Technology (Deep Learning, Querying Method, NLP, and Context Aware Processing), Application, End-User Industry, and Geography - Global Forecast to 2022", AI

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[9] Healthcare IT Market by Product (EHR, RIS, PACS, VNA, CPOE, HIE, Telehealth, Healthcare Analytics, Population Health Management, Supply Chain Management, CRM, Fraud Management, Claims Management) End User (Provider, Payer) - Global Forecast to 2021, marketsandmarkets.com Publishing Date: March 2017

[10] https://www.transparencymarketresearch.com/digital-health-market.html

related healthcare is expected to grow from $667.1M in 2016 to $7,989M by 2022, at a CAGR of 52.68% during the forecast period. The growing usage of big data in the healthcare industry, anticipated ability of AI to improve patient outcomes, imbalance between health workforce and patients, reducing the healthcare costs, growing importance on personalized medicine, cross-industry partnerships, and significant increase in venture capital investments are expected to drive the AI in healthcare market.

Global Home Healthcare Market (Diagnostics and Monitoring Devices, Therapeutic Home Healthcare Devices, Mobility Assist Devices and Medical Supplies).

According to the report, global home healthcare market was valued at $228.90 bn in 2015 and is expected to generate revenue of $391.41 bn by 2021, growing at a CAGR of 9.40% between 2016 and 2021[11]. The global home healthcare market is mainly driven by an increasingly geriatric population, rising healthcare costs and technological advancements in healthcare devices. With increasing health awareness among people, growing numbers of people diagnosed with chronic diseases such as diabetes, cardiac disorders and respiratory diseases, the demand for `mobile healthcare is expected to grow in the near future. The population of geriatric people is growing rapidly across the world, a population that is more vulnerable to non-communicable diseases such as diabetes. This, in turn, is expected to fuel the growth of the home healthcare market. However, changing reimbursement policies and limited insurance coverage may pose a challenge to the home healthcare market growth in the near future. Rapid decentralized job growth, especially in home healthcare services, is expected to open alluring avenues for the market to grow over the next few years.

The global regenerative medicine market is expected to reach USD 38.70 Billion by 2021 from USD 13.41 Billion in 2016 at a CAGR of 23.6%[12]. The market is broadly classified into types, therapy, application and regions. Based on types, the market is segmented into cell-based products and acellular products. The cell-based products is expected to dominate the global market in 2016. Based on therapy, the market is segmented into cell therapy, gene therapy, tissue engineering, and immunotherapy. Immunotherapy is the fastest growing segment in the global market, during the forecast period.

## 1.3 Competitive position of the NL ecosystem (market and know-how)

In the markets described above, the Dutch industry has a global strength, while for all application areas, the combined knowledge base of players in the HTSM ecosystem is of world class. Areas with anticipated high growth and where the Netherlands has a strong competitive position are related to advances in more comprehensive non-invasive diagnostics (MR, CT, Ultrasound, Optical), and more precise and less invasive image-guided intervention and treatment, personalized medicine, Regenerative Medicine and robotics, healthcare informatics, Clinical Decision Support Systems (CDSS) and decentralized healthcare, bridging hospital, point-of-care and home. Personalized medicine requires companion diagnostics for which new technological advancements and opportunities are expected with further development of lab-on-chip and organ-on-chip concepts; also in this area the Netherlands will have a big opportunity.

[11] https://www.zionmarketresearch.com/report/home-healthcare-market

[12] https://www.marketsandmarkets.com/Market-Reports/regenerative-medicine-market-65442579.html

# 2. Applications and technologies

## 2.1 Applications

### Healthy living and prevention

**Vital functioning of citizens**

People's lifestyle (sedentary lifestyle, stress, unhealthy diet, smoking and drinking habits) is another factor entailing more chronic diseases and their physical, mental and social functioning consequences. Applications and services to change and maintain a healthy lifestyle are important means to reduce the risks for chronic diseases and play a key role in the area of prevention. We believe that monitoring lifestyle, coaching and behavioral change applications and services are important tools in this respect. Technology can help to keep people at home (or visit a nearby 1st line or primary support) instead of going to costly institutions such that they and the society both benefit.

Wellness is related to cognitive functioning. Significant influence can be made by integrating mental training techniques in people's lives, with modern techniques (e.g. serious gaming, web-based training). Furthermore, improving the health and wellbeing of citizens through the use of light-based and ultrasound treatments will provide a non-invasive therapeutic route for skin diseases, pain relief, sleep and mental disorders, and more.

Novel sensor technology at home or in wearable devices, communicating through smart phones embedded in an ICT infrastructure, bring together personal data and information about the subject's environment. Artificial Intelligence (AI) and deep learning techniques provide the user with individualized predictions, personalized decision making and feedback to improve a healthy lifestyle. Thereby, Data science enables a shift towards individual and personal treatment and advice. Importantly, the quality, robustness and relevance of the data generated by these wearables as well as the health advice generated by AI techniques based on these measured parameters must be appropriately verified.

Access to own data and comparison to peer data will result in patient empowerment, i.e. the patient is well aware of all diagnostic and treatment options, and the physician's task shifts to the guidance of the patient through these options.

**Population health**

Population health is a term used to describe a comprehensive approach to care that relies on segmenting a cohort of patients into separate groups, analyzing their care needs, and then implementing targeted interventions to those deemed most at risk.

Population health plays a pivotal role in chronic disease management to prevent avoidable progression of the disease, exacerbations, hospital (re)admissions, and to drive cost-efficiency by providing evidence-based insights to proactively manage and treat patients across the continuum of care (hospital, post-acute, ambulatory, community and home care).

To enable population health management, several fundamental technical challenges with respect to a digital platform need to be addressed, namely:

1) ensure that underlying infrastructure is capable of capturing and storing data acquired from sensor devices that are used for patient monitoring, e.g., health watches, activity trackers, blood pressure meters, glucose meters, etc.;

2) ensure that health management applications, both patient-facing and clinician facing can work seamlessly on the same platform;
3) ensure that the user experience is seamless across applications and clinicians. Via a single interface, clinical users can view all of their patients that are in the population health program; and
4) ensure that diversified program requirements related to clinical or self-care management are adequately addressed.
5) ensure that the data acquired from sensor devices is accurate, robust and relevant.

The increasing use of artificial intelligence (AI) to analyze large patient data sets promises to change the face of population health management in a way that will be far reaching across the industry and a game changer to the way physicians monitor and care for their patients.

AI's ability to raise the level of evidence-based medicine can help primary care physicians make better decisions in several areas. These include the ability to determine appropriate treatments for their patients and to how best to monitor their care during and after hospitalization, to improving efficiency and productivity in care team workflows and finding better ways to reduce overall costs associated with patient care.

Supercomputers that compare and analyze large groups of patients' clinical data, diagnostic images and claims data, are capable of identifying subtle patterns and changes in health and wellness that can foreshadow the start of an illness, monitor the effectiveness of drug treatments and identify patients' health risks[13].

## Diagnostics

Diagnostics applications and underlying technologies required could be categorized in the following sets:

**Person -specific modelling**

Patient-specific data is essential in contributing to quality of care, including:

- Biological data / genetic profiling
- Non-healthcare and social domain modeling
- Functional data from electrophysiological, optical, force and motion recordings to compare with image data, both recent and stored images
- Data from multi-array EMG electrodes, high-density EEG for EEG source localization and advanced ECG recordings can provide a profound insight in the control function of the central nervous system
- Motion and forces, statically and dynamic, of the human body provides rapid insight in functioning and control properties of the CNS, muscles and tissues
- Molecular data on patients and their response to specific treatments, as well as genetic information.
- Clinical Decision Support Systems (CDSS) for in-hospital and at home, pre- and post-operative treatment and guidance, support for continuative patient care.

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[13] http://medicaleconomics.modernmedicine.com/medical-economics/news/artificial-intelligence-play-key-role-population-health

- In combination with the previous points: patient co-responsibility and his surrounding care experts, techniques for and learning of acceptance of new technology

This process will raise the abstraction level of the information, leading to biomedical (risk) models of the patient's condition and providing the basis for patient-specific treatment planning, based on the anticipated response to therapy.

**Patient-specific monitoring**

Although a known area, specific innovations are emerging like

- Unobtrusive cardiovascular status monitoring, early warning systems to predict patient deterioration, unobtrusive sleep monitoring.
- (Neuro)monitoring with fundamental markers like heart rate, accelerometry, EMG or long-term EEG with limited channels. This area enables and is subject to fast product innovation.

**Medical imaging and signal processing**

- Image acquisition, with goals to
  - increase image resolution combined with a decrease in radiation
  - have real-time availability of images
  - increase sensitivity and specificity
  - provide quantitative information
  - work towards combination of imaging techniques
- Image processing, with goals to
  - develop user-friendly visualization techniques and new robust quantitative computer vision algorithms
  - develop, implement and validate quantitative imaging "biomarkers" that objectively assess presence and stage of disease, or response to treatment
  - combine diagnosis and treatment (theranostics), i.e. for image-guided interventions.
- Hybrid imaging for
  - correlative imaging techniques or near-simultaneous hybrid imaging with different modalities are needed for validation of diagnostics and treatment

**New Modalities for diagnostics**

Introducing new diagnostic methods in healthcare is only possible after thorough investigations. This leads to the following fields of research and innovation for the next years:

- Linking imaging and diagnostic modalities to genetic and molecular profiles understanding the interplay between structure and function on a cellular level (radio genomics) or proteomics as another example of molecular level investigations.
- Develop analytical techniques to advance (digital) pathology and histology, i.e. improving molecular specificity
  - Spectroscopy, NMR-based cyclotrons, optical and soft X-ray microscopy and (cryo) electron microscopy

    - (Diffuse) optical and photo-acoustic imaging, including combined image processing to yield spatially-resolved quantitative functional information, such as OCT (Optical Coherence Tomography) and SFDI (spatial frequency domain imaging).
- Obtaining sufficient throughput and sensitivity to acquire statistically significant results and combining various methods (imaging modalities) into integrated systems (e.g. SPECT/CT, SPECT/PET/CT&MRI, PET/MRI, EEG/fMRI, US/PA, US/Optical, OCT/Immunofluorescence ) and EM/LM.
    - Small optical imaging devices placed on slender long devices that can be navigated intuitively into the patient's body in a minimally invasive way.
    - Accurate navigation and steering of these devices is an important step to merge the data with macroscopic imaging, so that the "whole picture" is available for planning interventions.
    - Small implantable or wearable devices placed on flexible substrates that can sense health parameters and can be placed anywhere in or on the body.
- Exposome data

**Usage of Big Data and Artificial Intelligence**

Diagnostic applications benefiting from Big Data and Artificial intelligence technologies include amongst others:

- Cancer pathways diagnostics
- Cloud-based radiomics
- Predictive maintenance and services
- AI driven acquisition and diagnosis across imaging modalities
- Integrated cancer diagnostics for improving outcomes
- Clinical Decision Support Systems (CDSS), explanatory CDSS, clinically funded/inspired support exploiting large data sets

The ethical issues of big data usage and the privacy issues of the individual patient and citizen and their safeguarding in the adoption process of new technology, shared by all involved stakeholders need to be addressed.

## Interventions and therapy

Personalized medicine is a medical model emphasizing in general the customization of healthcare, with all decisions and practices being tailored to individual patients in whatever ways possible. Recently, this has mainly involved the systematic use of genetic or other information about an individual patient to select or optimize that patient's preventative and therapeutic care. This development will be a paradigm shift in the pharmaceutical industry from 'blockbuster' drugs developed by big pharma multinationals towards development of patient groups targeted drugs by high-tech biotech (SME) companies, spinning off from research at universities and institutes.

Minimally invasive techniques have the potential to improve patient comfort and to reduce hospital costs.

Further developments are foreseen in, amongst others, the following fields:

- Improve navigation/robotic guidance solutions

    - miniaturization and integration of intervention devices
    - technology for smart endovascular devices
- use of artificial intelligence and Virtual reality
- Endovascular therapy, e.g. cardiac Pressure-Volume loop and interventional oncology
- Use of patient data and artificial intelligence to personalize treatment planning and execution
- Radiation ablative therapy
- Workflow optimization using tracking devices and machine learning
- Use of robotics and navigation (in-body micro) devices
- Electroceuticals
- (Image guided ) Robotic (Oncology) surgery and therapy
- Use of wearables for continuous monitoring and therapy
- Regenerative Medicine

### Home and community care (0-line and 1st-line)

The lesser availability of health caregivers forces towards a situation with more home care and an increased role of family and friends in the care of patients. Monitoring of patients will be done on a regular basis requiring novel sensor technology and user interfaces, enabling (also elderly) patients to do the necessary tests at home, and send the data to the hospital. Even for more complex measurements, mobile laboratory can be established, visiting the patients at home. Patient management will be partially automated, setting alarms for adverse findings requiring the physician's attention.

It is the task of primary care professionals to refer ill patients to the right specialist when needed. The general practitioner (GP) acts as a gatekeeper for secondary care. The discrimination between healthy and ill individuals is not always obvious, however. More precise referrals can be achieved by improving the diagnostic tools at hand in primary care. However, often the diagnostic tools used by specialists are far too costly and difficult to operate for primary care use. Point-of-care diagnostic devices require the combination of high quality performance, affordable costs, small size and ease of use.

## 2.2 Enabling technologies

To realize the above-mentioned applications, we should focus on innovations and technologies that have the potential to become game changers in the health industry.

Healthcare is an application domain that will benefit from the different Key Enabling Technologies (KETs). The most important KETs expected to advance the HTSM Healthcare are listed below.

For extended state-of–the-art and expected developments for Photonics, high tech materials, Nanotechnology, Components and circuit and Embedded systems, we refer to the specific HTSM Roadmaps covering these fields.

**Photonics**

Medical devices including medical therapeutic systems and systems for in vivo and in vitro diagnostics. Major products include endoscopes, therapeutic laser systems, medical imaging systems, oximeters, CR systems, ToF-PET and PET-MRI, (targeted) fluorescence diagnostics systems, coherent detection, optical coherence tomography systems, fundus camera's, SPECT, Raman (CARS) based diagnostic systems, Photo Acoustic imaging technologies. All systems comprise a combination of photonic components (lasers, detectors), micro-electronica, mechanics and software[14].

**High-tech Materials**

Innovative (Nano)materials have the potential to be a disruptive technology for example in the field of prosthetics and artificial tissue creation. (Nanomaterials / carbon nanotubes / graphene)

**Nanotechnology, Components and circuit and Embedded systems**

These technology roadmaps have the potential to deliver potential disruptive innovations in topics of

- micro and nano electronics
- Integrated photonics
- Robotics
- Nanodevices
- biochips and biosensors
- Organs on a chip
- Low power low energy systems
- Special computing devices
- CMUT (capacitive ultrasonic transducers)

Micro and nano technology can contribute to all kind of (implantable) bio-devices for diagnosis or treatment of different pathologies that partly benefit from the use of active materials as actuators and sensors. Such active or "intelligent" materials are capable of responding in a controlled way to different external physical or chemical stimuli by changing some of their properties. These materials can be used to design and develop sensors, actuators and multifunctional systems with a large number of applications for developing medical devices.

The paradigm shift toward personalized medicine (see “Interventions and Therapy” in 2.1) suits very well the economic and technical potentials of lab-on-a-chip and organ on a chip technologies to provide dedicated instruments for patient screening and monitoring (companion diagnostics) and for ‘flow chemistry’ equipment for the flexible development and production of drugs. This development will be founded on the collaboration between biotech and micro/nanotechnology based companies, with an essential role for the innovative SMEs.

In the Netherlands many micro/nano and biotech SMEs, backed by world-renowned research groups at universities/institutes, have emerged since the last 10-15 years and these can play a leading role on a global level providing that a structural collaboration between the two disciplines can be realised. This need fits perfectly in the common opinion, especially advocated by the EU in its R&D Framework Programme strategies, that the ‘convergence’ of synergetic technologies, of which micro/nano and bio technologies are an excellent example, combined with a key role of high-tech SMEs, should allow for a sustainable leading role of Europe in certain areas.

[14] https://www.hollandhightech.nl/nationaal/innovatie/roadmaps/photonics/

**Data Analysis and ICT**

Big Data technologies will open new opportunities and enable breakthroughs related to healthcare data analytics addressing different perspectives:
(i) descriptive to answer what happened,
(ii) diagnostic to answer the reason why it happened,
(iii) predictive to understand what will happen and
(iv) prescriptive to detect how we can make it happen.

The main technological breakthrough in ICT are expected in the following topics

- Big Data- data Analytics
- Artificial intelligence and machine learning
- Cloud Technologies / computing
- Encryption technology / block chain/ digital security
- Internet of things / Cyber physical systems
- Platform technologies
- Augmented reality

# 3. Priorities and implementation

## 3.1 Selected priority areas for implementation

Addressing the applications and technological challenges from the previous sections, the following topics are selected as priorities based upon the strengths of the Dutch ecosystem of industrial players, research institutes and users. In particular imaging is an internationally renowned Dutch strength.
The following list of priority areas for implementation if fully aligned with the recently issued Electronics Components and Systems (ECS) Strategic Research Agenda[15].

### Healthy living and prevention

- Improved biomedical models of the health situation of healthcare customers, taking heterogeneous, longitudinal (image) data, context and population information into account
- Use large heterogeneous data sets from many sources to obtain precise information
- Longitudinal monitoring and data analysis of many patients, leading to precise alarms only when needed, e.g. by applying AI techniques
- Wearables or minimally invasive implants, Internet of Things, simple analysers for home use; reliable data collection and analysis – focus on input data quality assessment (we need to know whether we evaluate useful data or noise and artefacts); standardisation of calibration, process interoperability.
- Devices or systems for utilising/extracting/sharing new knowledge in the most informative and efficient manner (e.g. vitality data, molecular profiling, biotechnology, diagnostics, ICT tools) in the most appropriate personalised setting (e.g. healthcare system, at home)
- Devices or systems for protecting and enforcing individual health-related information: ownership and secure storage of health data, data sharing with healthcare providers, and rendering real time anonymity for wider data analytics. Devices or systems improving security for executing transactions in healthcare and wellbeing, like blockchains to improve health or personal records exchanges and interact with stakeholders
- Devices or systems for integration of health and prevention ICT solutions in national health systems. Also techniques and approaches for behavioral change of citizens and patients.
- Point of care systems, wearables or minimally invasive implants, including new sensor systems for easier and more efficient measurement of physiological parameters, incl. posture, sitting position, physical activity, dynamics of walking, perfusion, oxygen saturation, etc.

### Diagnosis and therapy

- Create and apply biomedical models for AI based automation, visualization and decision support, to get precise, quantified information of the person's health condition. This needs large amounts of images and other sensor data at many levels: from molecular imaging up to whole body imaging

[15] https://aeneas-office.org/publication/download/electronic-components-systems-ecs-strategic-research-agenda-sra.pdf

- Ensure low-latency analysis and reasoning involving 2D, 3D and 4D images, and prompt delivery of precise results, also in situations with partial and imperfect data
- Development of point of care diagnostic devices requiring the combination of high quality performance, affordable costs, small size and ease of use.
- Predictable and repeatable outcome of diagnostic imaging and sensing including providing quantitative information. Current diagnostic imaging is often of a qualitative nature, meaning that comparison over time or with other patient cases is impossible.
- Development of smart catheters used in (image guided) treatment and specialized operating theatres (e.g. Cathlabs, Bronchoscopy and G.I. suites)
- Development of active or passive implantable medical devices for diagnosis (e.g. biosensors) and for treatment of disorders currently not treated or treated by lifelong pharmacy (e.g. stimulators for spinal cord disorders, depression, obesity, hypertension)
- Development of surgical robots
- Development of novel regenerative medicine solutions
- New diagnostic modalities enabling the measurement of new biomarkers for diagnostic and therapeutic purposes
- Solutions improving accuracy in radiation therapy
- Solutions enabling or improving a more effective personalized treatment
- Diagnostic imaging equipment with sufficient accuracy for active/passive implantable medical devices placement, preventing trial-and-error approach.
- Transform large healthcare systems to optimize hospital workflow, automatically optimize diagnostic imaging and tracking of therapy results, enable preventive maintenance and generation of requirements and test cases for new generations of systems
- Apply generic standards (e.g. industry 4.0) to diagnostic and therapy systems and use of big data principles to reduce cost of ownership
- Less harmful and less expensive imaging and sensing modalities at several levels: from molecular imaging up to whole body imaging, in the prevention, diagnosis, therapy and monitoring phases, both in primary and secondary care.
- Robotics to improve treatments either in the operating room, minimal invasively inside the body, at general practitioners or at home.
- Real-time location services with badges that can track patients, staff and medical devices, Environmental monitoring — for example, checking hand hygiene compliance. Mobile apps will replace traditional physician visits.
- Smart, robust, secure and easy to use devices or systems (wearable or implantable and autonomous) for detection, diagnostic, therapy, through big data, artificial intelligence, machine learning, deep learning person-centred.
- Energy efficiency for medical wearables/implants: Improvement of energy consumption and battery life at device levels. Ability to deliver connected devices (wearable/implants) that are self sustainable from an energy point of view for the full duration of a medical treatment (weeks, months or years).
- Upgradability of medical wearables/implants: A wearable/implant must be able to adapt to several configurations in the function of the evolution of a disease and improvements in its treatment. The upgrade/downgrade must not imply obsolescence of the wearable/implant. Therefore, a supporting wearable infrastructure should support the possibility of running

virtual devices that complement the processing power and storage embedded in wearables/ implants
- High resolution minimally invasive in vivo molecular diagnostics

### Home and community care

- EHR (Electronic Health Record) involving patient health models supporting precise communication between different caregivers
- EHR involving health models that exactly describe the outcome health values for the patients, both short and long term
- Humanoid robots applying interpreted human body language and emotion in care delivery
- Devices or systems using biomedical models for better diagnostics, therapy and feedback to the patient for several chronic diseases e.g. musculoskeletal system and simulation of activity of muscle groups, joints, etc.
- Devices or systems using predictive models and/or sophisticated sensing to anticipate the appearance of co-morbidities because of the evolution of chronic diseases
- Multi-modal data fusion devices or systems: the generation of enormous amounts of data from different sources (e.g. vital signs from mobile apps, home monitoring, real-time sensors, imaging, genomic data, pharmaceutical data, and behavioral markers) brings valuable information to improve clinical decisions and to reveal entirely new approaches to treating diseases. But the fusion of multi-modal data poses several technical challenges related to modelling, data mining, interoperability, data share keeping privacy
- Devices or systems data with low-latency analysis performed with deterministic algorithms or deep learning that are able to deal with known levels of trust (both high and low) for precise presentation of the results to medical professionals and non-professionals
- Devices or systems based on cognitive computers providing support to professionals or non-professionals for healthcare or wellbeing

## 3.2 Implementation of this roadmap in public-private partnerships and ecosystems

The Health and Care Knowledge and Innovation Agenda presents an overview of relevant Public-Private partnerships [16]. Below we present additional collaborations relevant for the Healthcare roadmap .Fundamental research on healthcare is an essential area for NWO, covered by various programs and projects. It is of critical importance to keep a solid NWO contribution in the coming years. ZonMW and TTW will start a multidisciplinary collaboration in the field of medical technology, with emphasis on development of novel medical devices, and on clinical implementation. Eight IMDI Centers of Research Excellence (CoRE) have been established in 2012, with focus on image acquisition and processing, minimal invasive surgery and neurorehabilitation, home care and assistive devices. In 2018 the IMDI 2.0 program will be started for which also other consortia may apply.
At NWO domain TTW several public-private ''Perspectief'' programs and OTP projects on healthcare technology are currently running, with a total of about € 12M of grant money and € 4M in cash and in kind company contributions (2014 - 2018). Regarding the HTSM 2017 call, conducted by NWO domain TTW, 3 proposals have been granted that fit in the healthcare roadmap, with a total of about €2M of

[16] https://www.health-holland.com/public/downloads/kia-kic/kennis-en-innovatiecontract-2018-2019.pdf

grant money and almost € 1M in cash and in kind company contributions. In the Top Sector LSH the first IMDI call (2012) conducted by ZonMw has been kicked off with 8 IMDI CoREs running (total project costs: € 12M; contribution ZonMw: € 5M, contribution private parties: € 4M).The second IMDI LSH call in 2014 resulted in 13 projects which will start in the spring of 2015 (total project costs: € 13.3M €, ZonMw: € 6.3M private parties € 4.7M.
TNO's activities are well aligned with the HTSM healthcare roadmap with a focus on the development of photonics-based diagnostic devices for applications along the healthcare continuum, from compact, flexible and wearable sensors for (home) monitoring and personalized treatment applications to quantitative retinal imaging technology for the non-invasive detection of ophthalmic and systemic diseases through the eye.
Another important national PPP is NanoNextNL, with incorporates a critical nanomedicine program. Various companies and technical universities are participating in this, focusing e.g. on nanofluids for lab-on-a-chip, molecular imaging and integrated microsystems for biosensing.

In the past four years, another notable public-private partnership emerged from the cooperation between Philips, TU Eindhoven, MMC, Kempenhaeghe and CZH hospitals in the Eindhoven region. The Impuls-1 and 2 programs that were initiated by the TU/e in 2013 and 2014, have resulted in a joint research group of about 75 PhDs in the region fully funded within the strategic partnership. This health research group concentrates on perinatology, cardiology and sleep combined with various data science related technologies. Besides the PhDs all partners deliver a substantial in-kind contribution of fixed staff employees. Their mission is to improve value based healthcare by creating and expanding an ecosystem that enables fast track to high-tech health innovation.

In 2014 the Top Sector Creative Industry involved the Topsector LSH in creating a platform called ''Create Health''. It operates through the Creative Industry's TKI CLICKNL. In its program, mainly focusing on patient-centred design, several opportunities for HTSM Healthcare are mentioned.

It goes without saying that this HTSM Healthcare roadmap has clear links with other HTSM roadmaps, notably Components & Circuits, Embedded Systems, High Tech Materials, ICT, Mechatronics/Manufacturing, Nanotechnology and Photonics.

## 3.3 Linkage with other innovation instruments (e.g., public purchasing and risk investment)

Large companies increasingly rely on small firms and start-up companies to perform certain initial development work. The added value provided by those smaller companies are their pronounced innovativeness and short development cycle times. New medical devices are more and more developed by smaller firms. In the Netherlands these smaller firms often have no financial means and/or credit possibilities required to perform such R&D activities. As a result, they rely on (regional) investment funds for more risky technology developments and benefit a lot from innovative purchasing to receive an initial income. Examples here are the medical robotic start-ups from the TU/e. We expect that this roadmap will provide these (SME) companies additional supportive material in their request for funding. And in return for those funds we expect that at some point in time they themselves can be in a position to contract knowledge institutes for joint projects.

The ‘Take-off’ programme (NWO domain TTW ) aims to stimulate the implementation of novel (medical) devices by industrial partners. It aims to bridge the funding gap between the research phase and the market. Take-off feasibility studies provide grants to researchers with a maximum of € 40.000 to investigate commercial application of innovative knowledge available in knowledge institutes, and to start commercial activities. Take-off early phase financing provides a loan to start-up companies of researchers or entrepreneurs based on knowledge innovations of the knowledge institutes. The minimal loan is € 50.000 and the maximum is € 250.000. Early 2015, the first projects were granted, including several that fit in this Healthcare roadmap. The NWO domain TTW Demonstrator program (max. € 150.000 per project) is aimed at the marketing of technology. This is achieved by building a commercial demonstrator of a technology, developed by a knowledge institute, which shows all the unique selling points. Parallel to that commercial activities are carried out, ultimately resulting in the sale and transfer of the technology to a third party, i.e. a company.

## 3.4 Collaboration in and leverage with European and multi-national policies and programs

Internationally, the Healthcare domain of HTSM is embedded in a strong innovation network. The excellent Dutch knowledge base - both at company and knowledge institute level - plays a vital role in this context.[17] In order for companies and knowledge institutes to remain world class, continuation of international cooperation is crucial. Our position within international cooperation schemes should thus be safeguarded. Most prominent international public funding R&D schemes include EU’s Horizon 2020 program and the Joint Technology Initiatives (JTIs), such as ECSEL, and the Eureka programs ITEA3 and PENTA.
The HTSM Healthcare roadmap is well tuned to the priorities of the H2020 program, in particular the innovation pillars on Industrial Leadership (LEIT) and Societal Challenges (SC), as well as the European Institutes of Innovation and Technology (EIT) on Digital Technologies (EIT Digital), and Health (EIT Health).

The Eureka programs ITEA3 (software intensive systems and services) and PENTA (micro- and nanoelectronics) are most relevant to HTSM and enjoy prominent Dutch participation. Furthermore, the Joint Undertaking (JU) ECSEL has been running for some years now, in which Dutch HTSM actors participate significantly. The Dutch healthcare ecosystem attaches great value to the collaboration that is established through these programs, with a wide range of innovative projects creating both a knowledge and economic multiplier effect. It is vital that this network, as well as access to it, is further enhanced for all parties, including SMEs.

Therefore, the HTSM Healthcare community once more calls upon the Dutch government to further bolster the Dutch commitment for international R&D in the framework of the EUREKA and JU programs. A commitment over the years is needed in order to strengthen the international connection and ensure the proper level of additional funding (i.e. co-funding in case of the JU programs from Europe).

[17] Also see the letter of the NFU (Nederlandse Federatie van Universitair Medische Centra) to the EC Commissioner for Research, Science and Innovation dated Jan 26, 2015. This letter explains how Dutch UMCs and their partners contribute to the EC priorities on sustainable health and delivering health at a reasonable cost. Reference is made to several HTSM Healthcare areas, like enabling technologies.

In addition, Dutch knowledge institutes play a key role in defining Euro-BioImaging (EBI), a large-scale research infrastructure project part of the European Strategy Forum on Research Infrastructures (ESFRI) Roadmap. EBI's aim is to provide access to a complete range of state-of-the art imaging technologies for scientists in Europe, partnering with industry to realize this objective.

Other well-known European programs with participation from HTSM Healthcare players are Ambient Assistant Living[18] and the European Partnership for Active and Healthy Ageing[19] .

[18] AAL, see http://www.aal-europe.eu/

[19] EIP-AHA, see http://ec.europa.eu/research/innovation-union/index_en.cfm?section=active-healthy-ageing

## 4. Partners and process

The table below presents an overview of the HTSM Healthcare ecosystem including partners from Academia, Institutes, foundations and Industry.

| | |
|---|---|
| **Academia** | TU/e, TUD, UTwente, VU/VUMC, UvA/AMC, UU/UMCU, RUL/LUMC, EUR/ErasmusMC, RUN/RUNMC, RUG/UMCG, UM/MUMC |
| **Institutes** | TNO, Holst Centre, imec-NL NWO/FOM, NKI, Astron |
| **Health foundations** | KWF, Dutch Diabetes Foundation, Alzheimer Nederland, Parkinson Vereniging, Hersenstichting, Hartstichting, Nierstichting, Nationaal Epilepsie Fonds |
| **Industry** | Personal Space Technologies, Sopheon, Technolution, Sioux, Frencken, CCM, MI-Partners, Zorggemak, Prodrive, Medis, Pie Medical, Microflown, Logicacmg, C2V, NXP, FEI, Lionix, Maquette Netherlands, Medison, Orthoproof, Demcon, Mecon, Bruco, Baat Medical, Micronit, Noldus Information Technology, Optel, Bronkhorst High-Tech, Medspray, Wwinn-group, MMS International, Hemics, ICMCC, Magnamedics, Collectotec, U-Needle, Nano4Imaging, MediCorporate, Chematronics, Inviso, Stamhuis Lineair, Exactdynamics, Honeywell, Miscea, De Koningh Medical Systems, Vither Hyperthermia, Lavoisier, Biosenz, Scalene Medical, Alliance Medical, Canon Europa, D.O.R.C. International, Enraf-Nonius, Esaote Europe, Finapres Medical Systems, GE Healthcare, Getinge, GymnaUniphy, Lamboo Specials Sales, Macawi, Medtronic Bakken Research Center, NeoKidney, NightBalance, Novymed Int., Nucletron, Oldelft Benelux, Philips, RS TechMedic, Simed Int., Smit Mobile Equipment, Technomed Europe, The Surgical Company Int., VDL Groep, Reden, Quantib, Novioscan, Sorama, Sound Intelligence. |

The extensive industrial network with a lot of SMEs (more than 85% listed is SME) is very vibrant and every year more organizations are joining.

This HTSM roadmap reflects the enormous potential of technologies for the future for healthcare and the related societal challenge. In any case, an increased potential for substantial social national impact and economic revenues (from internal market and export) is expected by achieving further synergy between this technology roadmap and the vision and ambitions of the Top Sectors, Key Technologies and NWA-routes working on the Social Challenge Health (*MU G&Z*). The various parties are convinced that further mutual coordination will bring added value. In the coming months, the LSH Top Sector, leading the *MU G&Z* on request of the Dutch Cabinet, and HTSM leaders, will then further consult with each other and with the most important stakeholders. To this end, various workshops will be organized in the first half of 2018 in order to finally agree on a joint realization of these social and economic opportunities by further elaborating the common vision.

This roadmap 2018 -2021 has been developed under the guidance the of the Roadmap core team consisting of Peter de With (TU/e), Frans van der Helm (TUD), Piet Lommerse (NWO domain TTW), Arjen Amelink (TNO) and Ton Flaman (Philips).

## 5. Investments [20]

| **Roadmap** | **2017** | **2018** | **2019** | **2020** | **2021** |
|---|---|---|---|---|---|
| Industry | 100 | 105 | 110 | 115 | 120 |
| TNO | 4.0* | 4.0* | 4.0* | 4.0* | 4.0* |
| NLR | - | - | - | - | - |
| NWO | 32.0 | 32.0 | 32.0 | 32.0 | 32.0 |
| Universities | 45 | 45 | 45 | 45 | 45 |
| Departments and regions (excluding TKI) | 8.1 | 8.1 | 8.1 | 8.1 | 8.1 |
| **Grand total** | **189.1** | **194.1** | **199.1** | **204.1** | **209.1** |

| **European programs within roadmap** | **2017** | **2018** | **2019** | **2020** | **2021** |
|---|---|---|---|---|---|
| Industry | 60 | 60 | 60 | 60 | 60 |
| TNO | 0.4 | 0.4 | 0.4 | 0.4 | 0.4 |
| NLR | - | - | - | - | - |
| NWO | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 |
| Universities | 11 | 11 | 11 | 11 | 11 |
| EZ co-financing of European programs | 20 | 20 | 20 | 20 | 20 |
| European Commission co-financing | 20 | 20 | 20 | 20 | 20 |

* TNO is involved in many of the Topsectoren and accompanying roadmaps that also address the challenges and issues that are addressed in this roadmap. Investments of TNO in the topics that are presented in this roadmap HTSM Healthcare 2018 roadmap are depicted in the table above. Part of the investment is also entered in other roadmaps. Taken the synergy with other roadmaps and accompanying investment allocations into account, the investment leads to €1.2 M in 2015 and €1.0 M p.a. in 2016-2019.

[20] R&D in public-private partnership, including contract research; all figures in million euro cash flow per year (cash plus in-kind contribution)