

# UNDERSTAND AND COMBAT DISEASES





GRAND  
CHALLENGE

# CITIZEN HEALTH AND WELLBEING

MISSION

## UNDERSTAND AND COMBAT DISEASES

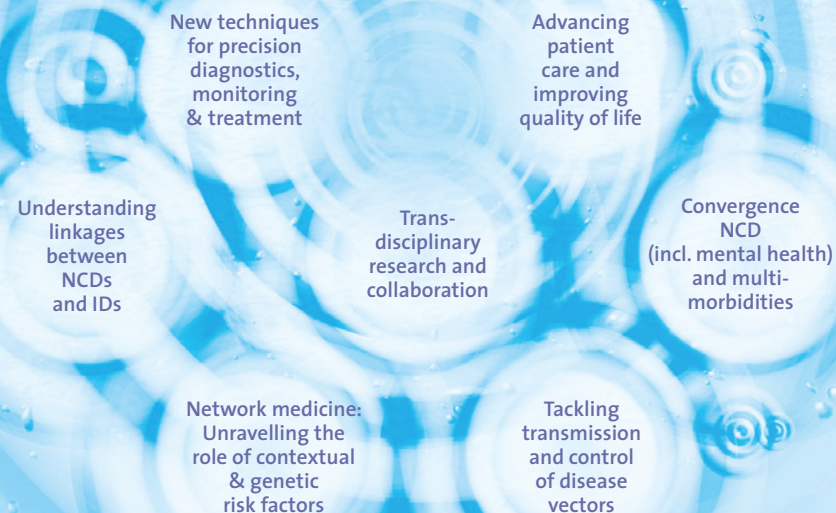
Integrated understanding of disease mechanisms to improve health, from prediction and prevention to detection and treatment

AREAS OF  
INTEREST &  
CROSS-SECTOR

Medical & Public Health Sector   Social Sector Legal & Ethics   Pharmaceutical Sector   Service Sectors

Tech Sector   Consumer Goods   Food Sector   Behavioral   Regulatory

R&I  
PROJECTS



## 1 Bold, inspirational with wide societal relevance

Reducing the impact of non-communicable diseases (NCD) and infectious diseases (ID) is considered one of the major challenges for sustainable health in the 21<sup>st</sup> century. At present, NCDs – which encompass most forms of cancer, diabetes, cardiovascular disease, osteoarthritis, chronic respiratory conditions, (rare) genetic and neurological diseases, as well as mental health conditions – are the leading cause of death worldwide with about 41 million mortalities every year<sup>1</sup>. Nearly 80% of NCD deaths occur in low- and middle-income countries<sup>2</sup>, but the impact of NCDs on Europeans is equally alarming: together, the five major NCDs (diabetes, cardiovascular disease, cancer, chronic respiratory diseases and mental disorders) account for an estimated 86% of premature deaths and 77% of the disease burden in the European Region<sup>3,4,5</sup>. Most individuals aged 45 years and older will develop a NCD during their remaining lifetime; indeed, many will develop multiple NCDs (multi-morbidities)<sup>6</sup>.

In addition to the most common NCDs, there are about 6000 rare diseases, that, collectively, affect around 30 million European Union citizens. These diseases are often chronic and life-threatening<sup>7</sup> and can be associated with considerable health care costs<sup>8</sup>.

Worldwide, infectious diseases (IDs) cause at least 5 million deaths/year<sup>9</sup>. Most occur in low-income countries where pneumonia, HIV/AIDS, tuberculosis, and malaria are still prevalent. The incidence of IDs in high- and middle-income countries has fallen dramatically over the last century. However, recent outbreaks of emerging and re-emerging diseases worldwide, such as severe acute respiratory syndrome (SARS), measles, avian and pandemic influenza, and zika virus, demonstrate the continuous challenge and urgency of controlling IDs. Based on future temperature projections across the world researchers<sup>10</sup> mapped where the mosquitoes that transmit diseases like dengue and Zika might travel if climate change continues unchecked. Based on their worst-case scenario projections, the researchers believe as many as a billion people could be newly exposed to these illnesses within the century, especially in major urban centers in Europe, the United States and China<sup>11</sup>.

<sup>1</sup> <https://apps.who.int/iris/bitstream/handle/10665/272596/9789241565585-eng.pdf?ua=1>

<sup>2</sup> [https://www.who.int/nmh/publications/ncd\\_report\\_full\\_en.pdf](https://www.who.int/nmh/publications/ncd_report_full_en.pdf)

<sup>3</sup> WHO. 2017. Fact sheets on sustainable development goals: health targets. Non-communicable Diseases.

<sup>4</sup> <http://www.euro.who.int/en/health-topics/noncommunicable-diseases/noncommunicable-diseases/fact-sheet-on-sdgs-noncommunicable-diseases-sdg-target-3>

<sup>5</sup> WHO. 2016 Action Plan for the Prevention and Control of Non-communicable Diseases in the WHO European Region. <http://www.euro.who.int/en/health-topics/non-communicable-diseases/pages/policy/publications/action-plan-for-the-prevention-and-control-of-noncommunicable-diseases-in-the-who-european-region-20162025>

<sup>6</sup> Licher S., Heshmatollah A., van der Willik K.D., Stricker B.H.C., Ruiter R., de Roos E.W., Lahoussel E.W., Koudstaal P.J., Hofman A., Fani L., Brusselle G.G.O., Bos, D., Arshi B., Kavousi M., Leening M.J.G., Ikram M.K., Ifram M.A. 2019. Lifetime risk and multimorbidity of noncommunicable diseases and disease-free life expectancy in the general population: A population-based cohort study. PLOS Med 16(2): e1002741. <https://doi.org/10.1371/journal.pmed.1002741>

<sup>7</sup> Licher S., Heshmatollah A., van der Willik K.D., Stricker B.H.C., Ruiter R., de Roos E.W., Lahoussel E.W., Koudstaal P.J., Hofman A., Fani L., Brusselle G.G.O., Bos, D., Arshi B., Kavousi M., Leening M.J.G., Ikram M.K., Ifram M.A. 2019. Lifetime risk and multimorbidity of noncommunicable diseases and disease-free life expectancy in the general population: A population-based cohort study. PLOS Med 16(2): e1002741. <https://doi.org/10.1371/journal.pmed.1002741>

<sup>8</sup> <https://www.eurordis.org/about-rare-diseases>

<sup>9</sup> [http://oecdobserver.org/news/fullstory.php/aid/3337/Rare\\_diseases:\\_A\\_hidden\\_priority.html](http://oecdobserver.org/news/fullstory.php/aid/3337/Rare_diseases:_A_hidden_priority.html)

<sup>10</sup> Numbers calculated based on WHO statistics report 2017 to illustrate – sum of TB, malaria, HIV, hepatitis, influenza

<sup>11</sup> <https://journals.plos.org/plosntds/article?id=10.1371/journal.pntd.0007213>

<sup>12</sup> <https://www.npr.org/sections/goatsandsoda/2019/03/28/707604928/chart-where-disease-carrying-mosquitoes-will-go-in-the-future?t=1554978641825>





Both NCDs and IDs can have risk factors of either environmental or intrinsic (genetic) origin, and these can interact to strengthen each other. The development of NCDs is associated with a cluster of common risk factors, including ageing, alcohol and tobacco use, unhealthy diet, physical inactivity, metabolic risk factors (e.g. elevated blood pressure, obesity or hyperglycemia), and environmental factors, such as urbanization, air pollution, and chemical exposure (e.g. endocrine disruptors, asbestos, chromium VI). Major risk factors for the development of IDs include ongoing (unplanned) urbanization, population growth, increased international travel and migration, animal husbandry and intensive farming practices, socio-economic circumstances and environmental pollution and climate change. Additionally, low vaccination rate is becoming an important risk factor for the (re)emergence of some IDs. This (re) emergence of IDs is exacerbated by an increase in antimicrobial resistance (AMR) and health-care associated infections (HAI).

In addition to these environmental and genetic risk factors, NCDs and IDs may cluster with each other as well. In 2012, 15.4% of cancer cases worldwide had an infectious origin<sup>12</sup>. Individuals infected with the human papillomavirus (HPV), *Helicobacter pylori*, and Hepatitis B and C viruses have an increased risk of developing cervical cancer, gastric cancer and liver cancer, respectively. In addition, patients suffering from (multiple) NCDs are generally more susceptible to infections. For example, diabetes has been shown to increase the severity of emerging, endemic diseases such as tuberculosis and malaria, and interferes with tuberculosis treatment, threatening infection control<sup>13,14,15,16</sup>. Yet despite this clustering, prevention and management research almost always focusses exclusively on a single disease.

In order to combat diseases and create better health for everyone, it is crucial to deepen our understanding of the main causes, risk factors and mechanisms underlying NCDs and IDs, and where they overlap. This information is crucial to develop prevention and treatment strategies tailored to the individual patient (precision medicine) in order to provide optimal care with minimal side effects at reasonable costs.

## 2 A clear direction: targeted, measurable and time-bound

The Hub mission is to integrate understanding of disease mechanisms into health care to improve health and well-being for all: from prediction and prevention to detection and treatment at reasonable costs and in a patient-oriented manner. This will ensure healthy lives and promote well-being through the entire life course.

By 2030, we intend to contribute to the United Nations Sustainable Development Goal aiming at reducing premature mortality rates due to NCDs by 1/3 (baseline 2015)<sup>17</sup> as well as reducing the burden of NCDs, improving quality of life and advancing mental health. For IDs, the 2030 target is to reduce the number of infected individuals and deaths caused by AIDS, neglected tropical diseases, tuberculosis and malaria, as well as to develop effective interventions to combat IDs, including hepatitis, water-borne diseases (e.g. norovirus), influenza, yellow fever, mumps, measles, and zika virus).

## 3 Ambitious but realistic research & innovation actions

Achieving these mission targets will require trans-disciplinary collaboration and synergy of fundamental and translational research. Novel insights regarding individual environmental and genetic factors and their interaction will provide the holistic understanding needed to advance prevention and treatment of IDs and NCDs. Drivers of (re)emergence, spread and transmission of infectious diseases must be unraveled. Additionally, ensuring healthy lives and promoting well-being of all individuals will demand innovative approaches, novel vaccines and medicines, and technological tools for early detection of diseases. Designing more efficient disease interventions and prevention strategies will be of utmost importance, to ensure the best outcomes for the patient, at the lowest costs and in a patient-oriented manner.

Continued commitment to basic science will advance our understanding of these diseases, launching novel practical and clinical interventions using value-based healthcare approaches to reduce the impact of these diseases on patients and society.

12 Plummer M, de Martel C, Vignat J, Ferlay J, Bray F, Franceschi S. Global burden of cancers attributable to infections in 2012: a synthetic analysis. *Lancet Glob Health* 2016; 4: e609-16

13 Van Crevel R, van de Vijver S, Moore DAJ. The global diabetes epidemic: what does it mean for infectious diseases in tropical countries? *Lancet Diabetes Endocrinol.* 2016

14 Danquah I, Bedu-Addo G, Mockenhaupt FP. Type 2 diabetes mellitus and increased risk for malaria infection. *Emerg Infect Dis.* 2010;16:1601-4

15 The Lancet Diabetes Endocrinology. Diabetes and tuberculosis—a wake-up call. *Lancet Diabetes Endocrinol.* 2014;2:677

16 Riza AL, Pearson F, Ugarte-Gil C, Alisjahbana B, van de Vijver S, Panduru NM, et al. Clinical management of concurrent diabetes and tuberculosis and the implications for patient services. *Lancet Diabetes Endocrinol.* 2014;2:740-53

17 <https://www.un.org/sustainabledevelopment/development-agenda/>





Recent advances in artificial intelligence (AI), including machine learning and big data analysis, have opened new horizons in the detection and/or management of diseases and enable the development of new theories, innovative strategies and tools for diagnosis and/or intervention. For instance the integration of various omics technologies (in the X-omic project) has the potential to further our understanding of the mechanisms underlying NCDs, which can ultimately result in an earlier diagnosis and an earlier and more accurate intervention.

Mining and analysis of real world data collected from different sectors and disciplines will identify novel diagnostic biomarkers, profiles, and leads for prevention strategies and/or treatment interventions that may not have been discovered in standard clinical trial settings. Indeed, the study of metabolism at the global or “-omics” level is a rapidly growing field that has the potential to have a profound impact upon medical practice.

An approach which integrates genetic, metabolic, clinical, social and environmental networks is needed to identify and understand the origins of NCDs and IDs. Further identification of intrinsic and extrinsic risk factors that are relevant for NCDs and/or IDs will also be crucial and provide novel insights that will lead to the development of vaccines and medicines, better diagnostics, and innovative, safe, and effective interventions to prevent, detect, diagnose, treat, and ultimately eradicate these diseases.

In addition, we will need to educate citizens and health care professionals and increase general public awareness on prevention measures and on optimal treatment interventions tailored to the individual patient (precision medicine).

## 4 Towards convergence innovation through cross-disciplinary, cross-sector and cross-actor research

To achieve a significant decline in the number of (severely) affected individuals and reduce the impact of NCDs and IDs on individuals and society, novel transdisciplinary strategies are needed. Erasmus MC will invest in the development of a common framework for defining and improving our understanding of multi-morbidities, in order to develop evidence-based strategies for multi-morbidities in health care systems.

Strong cross-disciplinary and cross-sectoral collaborations are crucial for understanding and managing public health risks at this interface and improving global health. To fully cover the complexity of this problem, we need to maintain and advance our position as a top research institute and hospital in key medical areas, such as cancer research and treatment, as well as built bridges between different research fields, including e.g. virology, immunology, public health, nano-/micro-biology, psychiatry, oncology, epidemiology and technology.

Innovative insights regarding medical technology must be leveraged with comprehensive understanding of how diseases function within the human body to launch new strategies for medical research. For example, novel imaging technologies enable early, accurate diagnosis, which in turn enables localized treatment using minimally-invasive techniques, avoiding the side-effects which are associated with the more traditional systemic and/or invasive treatments.

There is a need for trans- and interdisciplinary research and convergence to understand diseases and their interlinkages, leading to new forms of prediction, prevention and precision therapeutics. Cardiovascular disease (CVD) and cancer are the two leading causes of death worldwide. Although commonly thought of as two separate disease entities, CVD and cancer possess various similarities and possible interactions, including a number of similar risk factors (e.g. obesity, diabetes), suggesting a shared biology for which there is emerging evidence.<sup>18</sup>

Understanding the possible link between immune system activation and depression might help explain what many observational studies have reported: depression is more common in patients with type 2 diabetes, rheumatoid arthritis, and coronary artery disease — all of which involve chronic inflammation — than it is in people in the general population.<sup>19</sup>

Several studies have reported an association between osteoarthritis (OA) and cardiovascular disease (CVD). This might indicate that OA and CVDs share risk factors or pathophysiological processes. On the other hand, it might also indicate that OA directly or indirectly causes CVDs or, reversely, that CVDs cause or worsen OA. Understanding the exact nature of how AS and OA are linked might lead to new biomarkers and common treatments for these diseases in subgroups of patients<sup>20</sup>

As mentioned above, approximately 15.4 % of worldwide cancers are attributable to viral infections. Unraveling the infectious cause has led to interventions that may reduce the risk of developing certain tumors. These include preventive vaccines against HBV and HPV, HPV-based testing for cervical cancer screening, anti-virals for the treatment of chronic HBV and HCV infection, and screening the blood supply for the presence of HBV and HCV. Additional research to identify other oncogenic viruses in human cancer may lead to further understanding the etiology and pathogenesis and offer opportunities to develop novel methods for therapeutic and prophylactic intervention.<sup>21</sup>

18 <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4800750/>  
19 [https://www.health.harvard.edu/newsletter\\_article/infection-inflammation-and-mental-illness](https://www.health.harvard.edu/newsletter_article/infection-inflammation-and-mental-illness)  
20 <https://www.sciencedirect.com/science/article/pii/S1521694218300433>  
21 <https://www.ncbi.nlm.nih.gov/pubmed/24008290>



Engagement of the scientific and clinical community at all levels is required in order for the European population to benefit from novel insights and discoveries, to be translated into new digital or technological tools for prevention, diagnosis and prognosis, and into new treatment modalities. Additionally, collaborative involvement of all sectors, including health, ICT, education, agriculture, transport, and finance, is required to reduce the risks that are associated with IDs and NCDs and to promote the development of prevention or treatment interventions to prevent and control these diseases.

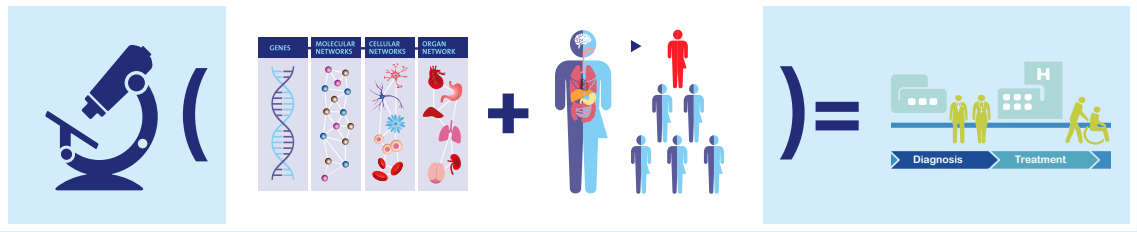
Human well-being and better care of individuals should be ensured through prevention of risks and mitigation of potential and/or existing health hazards originating from socioeconomic status, lifestyle, the human-animal-environment interface, and/or interactions between mental & physical health. This requires an interprofessional cooperation of, amongst others medical, clinical laboratory and social scientists, health insurance companies, health care professionals, veterinarians, industry, international bodies, charities and other non-profit organizations, patients, citizens, and (local) governments to develop appropriate and personalized interventions.

**5 Promote multiple, bottom-up solutions**

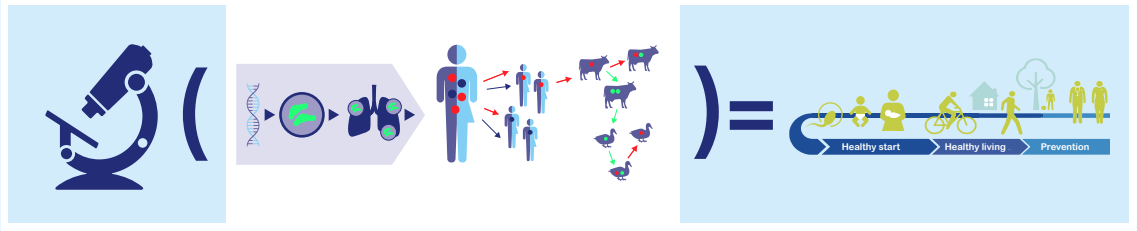
Given the vast number of factors influencing a person's health status during the entire life course, a large number of different actions are needed. From very fundamental projects resulting in new knowledge or development of new tests and diagnostics, to personalized and evidence-based lifestyle interventions, to highly-innovative grassroots projects which aim at developing new technologies in co-creation with centers of expertise, patients and stakeholders, to the development of new public health policies, and more.

To reduce the number of diseased persons and the number of premature mortalities caused by NCDs and IDs, multiple factors need to be considered simultaneously, as each of these factors have their own specific role and yet also influence response to other factors. This system approach generating holistic knowledge will ultimately lead to efficient prevention of NCDs and IDs, and the development of innovative interventions for patients and society. This will promote human well-being and health, leading to improved health for all.

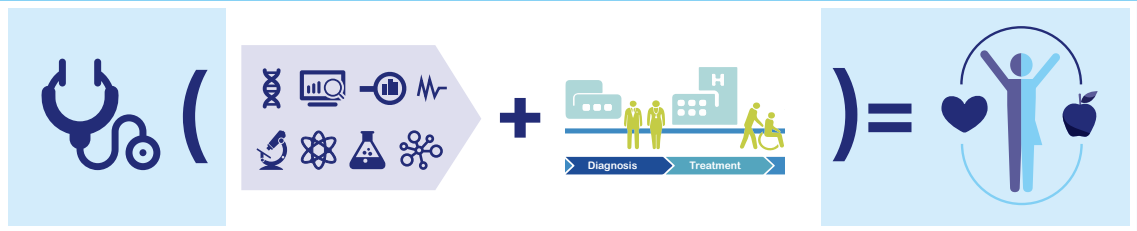
**UNDERSTAND AND COMBAT DISEASES RESEARCH FUNDING LINES:**



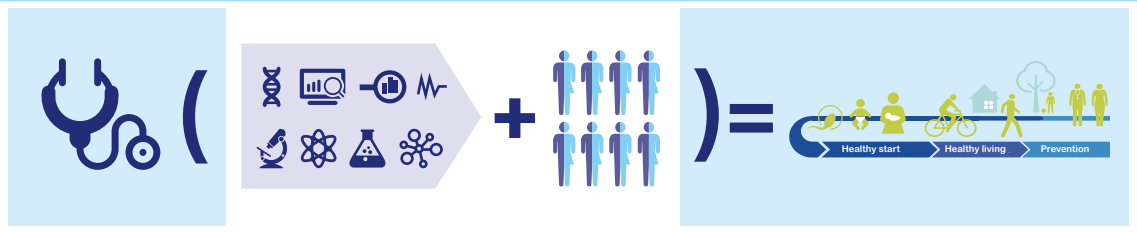
Understand & Unravel Non-Communicable Diseases (incl. Rare Diseases)



Understand & Unravel Infectious Diseases



Novel technologies for early diagnosis, precision treatment and advanced therapeutic approaches



Early detection tools for optimal prevention



# THE IMPACT WE WANT TO MAKE: 'A HEALTHY LIFE COURSE FOR ALL!'

Erasmus Medical Centre wants to enable health and a healthy life course for all!

We are using transdisciplinary approaches to develop strategies for prediction, prevention, and precision medicine that can be employed to solve current as well as emerging health challenges. It is how we impact the lives of healthy citizens and patients through our networks and collaborations.

We are an academic hospital with the DNA of Rotterdam, an academic hospital that walks the talk.

