UMC UTRECHT RESEARCH ASSESSMENT

RESEARCH ASSESSMENT ON THE SCIENTIFIC QUALITY OF THE RESEARCH PERFORMED BY UMC UTRECHT IN THE PERIOD 2013-2018

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CONTENTS

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REPORT ON THE RESEARCH REVIEW OF UMC UTRECHT

1. FOREWORD BY COMMITTEE CHAIR

The international committee that visited UMC Utrecht from October 30 to November 1 was pleased to encounter a very open atmosphere in the discussions with everyone involved, from members of the Board to PhD candidates. During the three days of the on-site evaluation, we had the opportunity to interact with highly motivated and skilled (bio)medical professionals. We concluded that UMC Utrecht has a number of unique assets, in particular its patient cohorts and the instruments to increase patient participation in setting the research agenda are impressive as well as the embedding at the Utrecht Science park, which fosters joint multidisciplinary research.

Our recommendations, which are based on ample discussions with both fundamental and clinical researchers, should be read as opportunities to further increase UMC Utrecht's societal and scientific impact.

Prof. R.A.W. van Lier, MD, chair.

2. THE REVIEW COMMITTEE AND THE PROCEDURES

2.1. Scope of the review

The review committee was asked to perform a review of research conducted by UMC Utrecht in the period 2013-2018. The resulting report consists of a general part and a specific evaluation of the six strategic research programs Brain, Cancer, Child Health, Circulatory Health, Infection & Immunity, Regenerative Medicine & Stem Cells.

In accordance with the Dutch Standard Evaluation Protocol 2015 – 2021 (SEP) for research reviews in the Netherlands, the committee was asked to assess the quality, the relevance to society and the viability of the scientific research in the research programs as well as the strategic targets and the extent to which the strategic research programs are equipped to achieve these targets. A qualitative review of the PhD program, research integrity and diversity formed part of the committee's assignment.

2.2. Composition of the committee

The composition of the committee was as follows:

- Prof. R.A.W. (René) van Lier MD [*chair*], professor of Experimental Immunology at the University of Amsterdam and member of the Executive Board of Sanquin Blood Supply Foundation and Research Director;
- Sir Prof. R. (Robin) MacGregor Murray [subcommittee Brain], professor of Psychiatric Research at the Institute of Psychiatry, King's College London (United Kingdom);
- Dr J. (Joost Verhaagen) [subcommittee Brain], head of the research group Neuroregeneration of the Netherlands Neuroscience Institute;
- Prof. D.A. (David) Jaffray, MD [subcommittee Cancer], professor of Radiation Physics with a joint appointment in imaging physics at MD Anderson Cancer Center, Houston, Texas (USA);
- Prof. G. (Gerald) de Haan [subcommittee Cancer], scientific director and group leader of the Laboratory of Ageing Biology and Stem Cells at the University Medical Center Groningen;
- Prof. M. (Marian) Knight [subcommittee Child Health], professor of Maternal and Child Population Health at the University of Oxford (United Kingdom);
- Prof. A.M.C. (Annemarie) van Rossum [subcommittee Child Health], professor of Paediatric Infectious Diseases and vice chair of the Department of Paediatrics at Erasmus University Medical Centre;
- Prof. M.J.A.P. (Mat) Daemen [subcommittee Circulatory Health], professor in Cardiovascular Pathology at University of Amsterdam/Amsterdam University Medical Centre;
- Prof. C. (Cecilia) Linde, MD [subcommittee Circulatory Health], professor at the Heart and Vascular Theme, Karolinska University Hospital in Stockholm (Sweden),
- Sir Prof. R.M. (Roy) Anderson [subcommittee Infection & Immunity], professor of Infectious Disease Epidemiology in the School of Public Health, Faculty of Medicine, Imperial College London (United Kingdom)
- Prof. T. (Ton) Schumacher [subcommittee Infection & Immunity], group leader of the Schumacher Group at the Netherlands Cancer Institute, Antoni van Leeuwenhoek Hospital

- Prof. U.(Ulrich) Martin, MD [subcommittee Regenerative Medicine & Stem Cell Research], professor in Cardiorespiratory Tissue Engineering, Head of the LEBAO, Hannover Medical School (Germany),
- Prof. A. (Anthony) Hollander [subcommittee Regenerative Medicine & Stem Cell Research], head of the Institute of Integrative Biology at the University of Liverpool (United Kingdom).

The committee was supported by Dr M. (Meg) Van Bogaert and Dr M. (Marijn) Hollestelle, who acted as secretary on behalf of QANU.

2.3. Independence

All members of the committee signed a statement of independence to guarantee an unbiased and independent assessment of the quality of research at UMC Utrecht. Personal or professional relationships between committee members and the research programs under review were reported and discussed at the start of the site visit amongst committee members. The committee concluded that no specific risk in terms of bias or undue influence existed and that all members were sufficiently independent.

2.4. Data provided to the committee

The committee received the self-evaluation report from the research programs under review, including all the information required by the SEP.

The committee also received the following documents:

- the Terms of Reference;
- the Dutch Standard Evaluation Protocol (SEP) 2015-2021;
- between five and ten key publications for every research theme within the six strategic programs.

2.5. Procedures followed by the committee

The committee used the criteria and categories of the Standard Evaluation Protocol 2015-2021 (SEP). For more information see Appendix 1. The site visit schedule contained plenary parts attended by the entire committee and program-specific parts, for which the committee was divided into fixed pairs of experts, or subpanels. Every strategic research program had several program-specific parts to present to the subcommittees, while providing ample time for questions. Before the first meeting, all committee members independently formulated a preliminary assessment of the strategic research programs under review based on the written information that was provided prior to the site visit.

The final review is based on both the documentation provided by UMCU and strategic research programs and the information gathered during the interviews with representatives of the research programs during the site visit. The site visit took place on October 30 and 31 and November 1 in Utrecht (see the schedule in Appendix 2).

Regarding the scores given, UMC Utrecht asked the committee to only score each strategic research program. Parts of the assessment also concern UMC Utrecht policy, however. This implies that along with the scores and advice regarding the six individual strategic research programs, the committee

provides separate findings and advice with a more general nature in a separate general chapter, preceding the assessments of the strategic research programs.

Before the interviews were held, the committee was briefed by QANU about research reviews according to the SEP. It also discussed the preliminary assessments and decided upon a number of comments and questions. It agreed upon procedural matters and aspects of the review. After the interviews, it discussed its findings and comments in order to allow the chair and each subcommittee to present their preliminary findings and to provide the secretary with arguments and substantiation to draft a first version of the review report.

The draft report was presented to UMC Utrecht for factual corrections and comments. In close consultation with the chair and other committee members, the comments were reviewed to draft the final report. The final report was presented to the Board of the University and to the management of UMC Utrecht and each of the research programs.

3. STRATEGY, LEADERSHIP AND VIABILITY OF UMC UTRECHT

3.1. Profile, strategy and management of the institute/Faculty

UMC Utrecht is a university medical centre generating, testing, sharing, and applying knowledge on health, illness, and health care for the benefit of patients and society. It was created in 2000 by merging the Academic Hospital Utrecht (founded in 1875), Wilhelmina Children's Hospital (founded in 1888) and the Medical Faculty of Utrecht University (founded in 1636). The merger of an academic hospital and the Medical Faculty into a new organisation with a single governance (University Medical Centre) is a typical Dutch development which started around 20 years ago and is internationally unique. UMC Utrecht is, thus, separate from but also closely intertwined with Utrecht University, for example in the development of strategic research programs and in the appointment of professors. Binding agreements about collaboration and responsibilities are defined in a formal cooperation agreement.

UMC Utrecht launched its "Connecting U" strategy in January 2015. This strategy elaborates on the previous strategic period "3.0" in which UMC Utrecht opted for a selected number of strategic research programs. Connecting U is all about connection: connection with patients, with general practitioners, with researchers, with each other, and with society. To achieve its ambitions, UMC Utrecht has formulated the following two strategic objectives:

- To increase its social impact with an emphasis on the strategic research programs;
- To strengthen the connection with patients and other stakeholders (including students, citizens and other healthcare providers).

Stakeholder involvement

UMC Utrecht aims to be in continuous dialogue with stakeholders to align itself with societal expectations. Stakeholders include patient organisations, hospitals, primary care organisations, municipal authorities, research institutes, research funders, and health insurers. Following the 'Connecting U' 2015-2020 strategy, which focuses on connection with patients and other stakeholders, several initiatives were undertaken by UMC Utrecht in terms of patient and public involvement. Structural strategic embedding started in December 2018 with the Patient and Public Involvement program. The mission of the Patient and Public Involvement program is to cooperate with patients and the public in a structural manner in care, education and research, to provide the care that supports meaningful life. It is articulated in the following goals:

- The experience of each patient will be the starting point of meaningful care.
- Patient and public involvement is part of the culture of UMC Utrecht. Healthcare professionals, teachers and researchers are facilitated to work in a way in which they profit from the expertise and experience of patients and the public.
- Care, education and research are shaped using a multi-expertise model of health and disease.
- Patient and public involvement is developed as an area for research. The methods for good and effective involvement are studied in UMC Utrecht.

The committee is pleased to see this emphasis on patient experience in UMC and the priority of patient involvement, since this leads to different choices in research focus, also addressing daily care, and to joint funding with patient organisations. As part of the UMC Utrecht strategic research program evaluation, UMC Utrecht asked a societal stakeholder committee to evaluate the societal value and patient involvement of the research performed in that period. The societal stakeholder committee has

based its findings and recommendations on two primary sources of information: the self-evaluation report written by the six strategic research programs of UMC Utrecht, and six presentations of best practices in which a researcher and patient or representative have collaborated successfully on a research project. The societal stakeholder committee met on two afternoons (October 2nd and October 16th, 2019) to discuss their findings and recommendations. During the site visit of the SEP committee, a representative of the societal stakeholder committee presented their findings. The societal research evaluation aimed to: map the efforts (policy and activities) regarding patient involvement and the societal value of research at UMC Utrecht; evaluate these activities regarding the process and the outcome; formulate recommendations for more and/or "better" societal value and patient involvement in future research.

The societal stakeholder committee evaluated both the societal impact itself and the efforts to achieve this impact. Its general findings are that the strategic research programs reflect little on the activities and their outcomes. An overarching policy and definition regarding patient involvement or societal impact are either lacking or are not being implemented by the strategic research programs. There are differences regarding the amount and quality of patient involvement and societal value activities between the research lines (both within and across strategic research programs), and the amount and quality of patient involvement taking place at UMC Utrecht seems partly dependent on external or contextual factors. Given these findings, the stakeholder committee made general recommendations:

- Define the intended societal value of the research, determine objectives and organize activities that contribute to these objectives;
- Determine and implement a policy on patient involvement regarding the aspects of representation, reimbursement, remuneration, support, communication and feedback;
- Encourage researchers to learn from each other within and across strategic research programs.

The stakeholder committee also made specific recommendations for each strategic research program (see the report of the societal stakeholder committee).

Management of the strategic research programs
UMC Utrecht is organised into ten divisions, mostly centred around healthcare:

- Imaging & Oncology;
- Neurosciences;
- Heart and Lungs;
- Woman and Baby;
- Anaesthesiology, Intensive Care and Emergency Medicine;
- Surgical Specialties;
- Julius Centre for Health Sciences and Primary Care;
- Paediatrics;
- Laboratories, Pharmacy & Biomedical Genetics;
- Internal Medicine and Dermatology.

The divisions are run by divisional management teams, consisting of two members, complemented by a ‘leadership team’, consisting of a manager of research and a manager of education, amongst others.

The two-person division management carries the integral responsibility for research, care and education, with a dedicated research manager being part of the broader 'leadership team'.

Since 2010 strategic research governance in UMC Utrecht has been assigned to six strategic research programs with a limited number of disease targets each. These six programs were developed and chosen through an extensive bottom-up process, building on past performance and critical mass but also on innovation, patient-centeredness and future perspectives. The research programs together with the divisions form a matrix structure, in which most divisions are involved in several (or even all) strategic research programs. In the diagram below, the dark grey tone indicates that the division is participating in the strategic program. The diagram shows just for illustrative purposes how strategic programs and divisions can interact. The light and dark grey areas don't reflect real or absent collaborations.

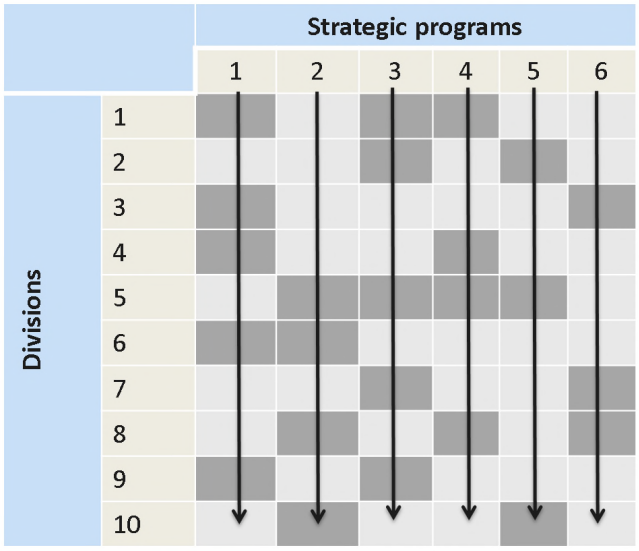

Figure 1: Schematic connection between divisions and strategic research programs.

Patient care is integrated in these programs, ensuring close collaboration between clinical and pre-clinical research. A multidisciplinary approach guarantees that patients benefit from the latest available expertise and innovative technological solutions. The research programs are in the lead regarding the research strategy, while divisions facilitate both research and healthcare. Hierarchical management of the strategic research program and funding remain the responsibility of the divisions.

For the period 2015-2020, the strategic research programs receive an annual budget of € 267,000 each for a chairperson, a program manager and other support. This includes a 'programming' budget for the organisation of program-specific tasks such as community building (e.g. interaction with clinicians and researchers, seminars with international speakers), outreach (e.g. development and organisation of patient-stakeholder interaction), and education (e.g. development and coordination of program-specific bachelor and master courses, education tools for patients).

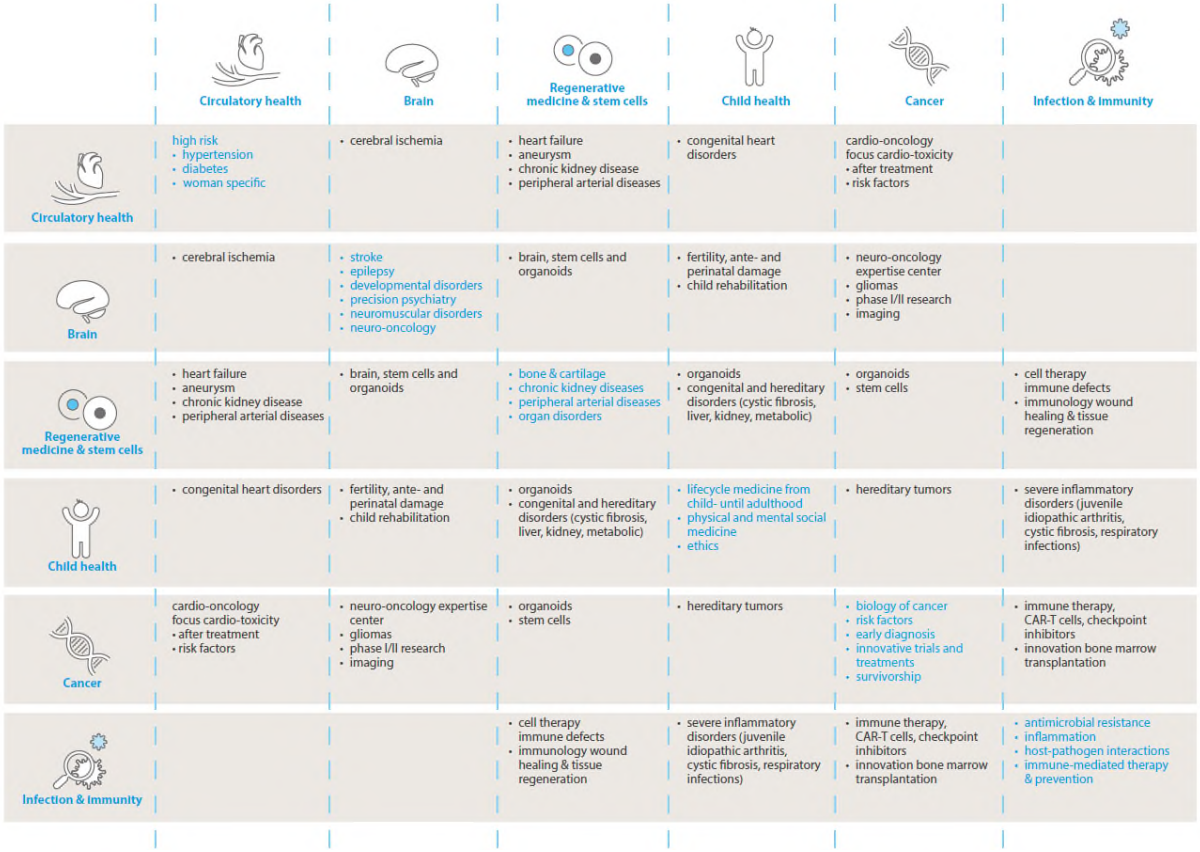

Figure 2: Research themes per strategic research program and collaboration between the six strategic research programs.

The committee noted that the atmosphere and attitudes of staff within the research programs are positive, and the management teams are generally well organised and clearly pay attention to staff wellbeing and career development, within the confines of the matrix organisational system. Program researchers for each individual program are mostly located within several divisions of UMC Utrecht.

The committee strongly supports the continuation of the strategic research program approach. In its opinion, the six programs have facilitated multidisciplinary research and patient care. It understands the choice for a matrix structure to combine the complex of care, research and teaching in the many areas involved. However, the committee also observed that governance is hampered by the complex matrix structure separating divisions from strategic research choices. Budgets – also for research – are held within the divisions, though strategic programs have the responsibility to deliver and execute research strategy. Without direct responsibility for the research budget, the strategic programs are clearly limited in their ability to deliver on the strategy. Differences in the amount of attention and prioritisation of research by division leadership likely exist. Reliance on the cooperation and decision-making of the division leadership hampers the viability of the strategic research programs, specifically when multiple divisions are participating in a strategic research program. The committee recommends giving the management teams of the strategic research programs greater control over the budget for research. There should be a better balance between the divisions and strategic research programs on decisions about research priorities, and definitely on appointments within the departments. The committee is of the opinion that the regulations and procedures concerning budgets for research should be clear, including key performance indicators (KPIs) and specific objectives regarding research

for the divisions. This will benefit the viability of all strategic research programs, specifically those that seem to be currently struggling with their budget for research.

Research funding

UMC Utrecht as a whole is annually financed by insurance companies (care/cure-related production), the Ministry of Education, Cultural Affairs and Science, the Ministry of Health, Welfare and Sports, Utrecht University and several other external funding organisations. The total UMC Utrecht budget for 2018 was € 1.193 billion, and the number of employees was 11,500. The UMC Utrecht research budget consists of two main sources. Governmental lump sum funding through different channels constitutes the so-called 'first money flow' of roughly € 50 million per year. UMC Utrecht also obtains competitive or external research funding from national and international research funders (NWO, ZonMW, KNAW, EU) and also from health charities and industry, which amounts to about € 102 million (2018). Specifically, the Top Sector Life Sciences and Health (LSH) has become an increasingly important research funder by supporting large public-private research programs such as Oncode and RegMedXB, and by providing direct funding of public-private projects. The annual amount of funding which is available for public-private projects for UMC Utrecht research projects has increased from just over € 600,000 in 2016 to € 1.45 million in 2017 to € 4.45 million in 2018.

Earning capacity is generally constant and satisfactory according to the committee. The importance of collaborative funding from the European Commission is increasing rapidly. On 1 January 2018 a start was made with centrally offering project management services for the coordination of European grant projects. Centrally appointed project managers are seconded to the relevant divisions as the responsibility for the research budget lies with the divisions at all times. UMC Utrecht is relatively stronger in obtaining collaborative and consortium grants than in obtaining personal grants. UMC Utrecht underperforms in obtaining individual grants compared to other UMC's. This is, for example, reflected in the very limited number of VIDI grants obtained between 2014 and 2018 and no VICI grants in 2016 for UMC Utrecht. For example, 69 VICI grants were awarded in 2016, but none were awarded to UMC Utrecht; and of 434 VIDI grants that were awarded in the period 2014-2018, only 7 (1.6%) were awarded to UMC Utrecht. At the moment, there is no dedicated, proactive support for national funding opportunities from UMC such as personal grants. The formalized support for national funding schemes is limited, and UMC Utrecht merely participates in the Utrecht University support programs for personal grants. Indeed, researchers reported to the committee that they do not experience support from the research support office for personal grants. The UMC Utrecht management acknowledged that their focal point lies on collaborative applications undertaken in consortia, but they agree that more attention must be paid to the support of personal grant applications. The committee is convinced that this has to be addressed, since this will add to the career development of young talented researchers. An increase of capacity for (pro-)active support and expertise regarding national funding schemes might increase the revenues from this source. It will be a challenge to find a balance between team effort and individual grants. During the conversations, the committee observed a willingness of UMC Utrecht management to address this issue. More collaboration between strategic research programs and divisions would be advisable with respect to the process of grant application. For instance, currently all strategic research programs make lists of funding opportunities. Merging these in a central newsletter could make this effort more efficient.

The support for public-private partnerships other than within the context of the Top Sector LSH is limited, primarily because the Knowledge Transfer Office of UMC Utrecht (Utrecht Holdings) plays a very limited role due to their strong focus on IP, IP licencing and start-up creation. Many other UMCs, which consider research collaboration as part of knowledge transfer, assume a more integral approach of knowledge transfer. Integrated research support (including TTO functions) is not present at UMCU level. The committee advises creating an easily accessible integrated central support office, including for personal grant advice and TTO functions.

Collaborations

UMC Utrecht has close ties with many faculties in research and teaching, specifically the Science Faculty and the Veterinary Faculty. In 'Utrecht Life Sciences' and in the Graduate School of Life Sciences, UMC Utrecht collaborates closely with those faculties. There are also many collaborations in the field of geosciences, law, economics and governance, and social and behavioural sciences. At the Utrecht Science Park, UMC Utrecht cooperates with the Hubrecht Institute, the University of Applied Sciences of Utrecht, the Princess Maxima Center for Pediatric Oncology, the National Institute for Public Health and the Environment (RIVM), and industrial partners located at Utrecht Science Park: Danone/Nutricia Research and Genmab. Within Utrecht Life Sciences (ULS) UMC Utrecht collaborates in an open innovation network, which unites authorities, business and knowledge institutions.

In 2011, Eindhoven University of Technology (TU/e), Utrecht University (UU) and UMC Utrecht started a strategic alliance. UMC Utrecht is working more closely with TU/e mainly on two themes: medical imaging and regenerative medicine including stem cells. Utrecht University, Wageningen University & Research, Eindhoven University of Technology and UMC Utrecht want to intensify cooperation in thematic areas. The institutes find complementary expertise in each other in scientific fields – for example, medicine, food, technology, social sciences – and will enter into cross-disciplinary cooperation.

UMC Utrecht researchers engage in a wide range of international collaborations. Current ones include University College London (UK), KU Leuven (Belgium), University of Toronto, Chinese University of Hong Kong (China). The committee is of the opinion that UMC Utrecht is ideally positioned on the Utrecht Science Park campus, in the national environment as well as globally. In talking to the representatives from UMC Utrecht involved in collaborations, the committee got the impression that an overarching strategy and plan concerning collaborations is lacking. It therefore recommends formulating specific goals and timelines concerning ongoing and new collaborations.

Human Resource Management

The committee is of the opinion that there is a need for a transparent and uniform tenure program and a mentor program to be able to retain and guide talents within UMC Utrecht. Some strategic research programs have some kind of talent program. The Circulatory Health strategic program for instance has a *Jacob Jongbloed* talent program, but it serves only 10-15 young talented researchers/ clinicians per cycle. Participants are mostly at the level postdoc/assistant professor. To scout talent in time and retain them at UMC Utrecht, an explicit scouting system should be set up. In general, more efforts concerning research talent across UMC Utrecht are needed. In the SWOT analysis in the self-evaluation report, UMC Utrecht has labelled the 'lack of a centralized talent policy and programs in UMC Utrecht and unclear career perspective for senior postdocs and assistant professors' as one of its

weaknesses. The committee agrees with this. A clear UMC Utrecht-wide career program should be developed which should outline the requirements that must be met in order to become assistant, associate or full professor. Currently, a portfolio is used for career assessment, including research, teaching, clinical work, innovation and impact, and leadership, development and collaboration. Although this is a good procedure, variability is still observed in policies and career development pathways across research programs and divisions. This is considered a threat to staff retention. For employees, it is unclear in what way the portfolio criteria are weighted. UMC Utrecht would benefit from clear criteria and indicators for career development, as this will have a positive impact on the retention of talented researchers. The committee observed that most of the research appointments are made by internal selection up through the system. A more open system of selection in competition with the international field would be beneficial for the selection and retention of talented researchers as well. The committee recommends that UMC Utrecht work on a transparent and uniform HR policy on talent, mentoring and tenure track. Talent management is a critical part of societal value.

An overall theme identified across all research programs is the challenge of developing clinical researchers without dedicated research time. UMCs in the Netherlands combine basic research with daily clinical practice. This is an opportunity, but also contains the threat that clinical work has to be undertaken instead of teaching and/or research. Clinical post-PhD scientists have a clinical job (with or without protected research time), in contrast to non-clinical post-PhD scientists. Some clinical academics are already spending 75% of their time on clinical care. The committee is convinced that it is highly challenging to maintain a high quality of research with such limited research time. There is little protected research time for clinical staff, and the committee is of the opinion that the societal impact could be accelerated more with dedicated research time. The importance of non-clinical scientists should be recognized and protected as well; the system of divisional research budgeting threatens the position of many non-clinical scientists and the overall viability of the research programs. Appointing dedicated clinical scientists is a major wish of the strategic research program chairs. There are already a number of clinical specialists with dedicated research time, but this is scattered among a large number of clinicians. Dedicated research time would help in prioritizing clinical needs versus fundamental research. The committee advises being careful with defining talent as a prerequisite for research time for clinical scientists. It recommends allotting dedicated and defined research time to selected clinicians with a specific research focus. It also recommends that UMC Utrecht ensure that it fully supports non-clinical researchers as well, as the combination of clinical and non-clinical scientists collaborating is essential for a UMC.

3.2. PhD program

Doctoral education within UMC Utrecht is organised by the Graduate School of Life Sciences (GSLS). The GSLS is an interfaculty school in which the faculties of Science and Veterinary Medicine of Utrecht University also participate. GSLS is probably one of the largest Graduate Schools in Europe, with up to 1750 registered PhD candidates. Many PhD candidates are employed on research grants obtained by one of UMC Utrecht principal investigators (PIs), who recruit and select the PhD candidates and also act as PhD supervisors. Clinical PhD candidates are often employed in a clinical capacity while pursuing their PhD. PhD candidates are admitted to the PhD program by the Board for the Conferral of Doctoral Degrees, and their program ends with approval of their thesis by the reading committee and its successful public defence.

Approximately 90% of the PhD candidates fit into one of the 14 thematic PhD programs of the GSLS. The programs provide activities such as an introduction to the program for new PhD candidates, thematic courses, seminars, masterclasses, symposia, PhD evenings and/or an annual retreat (PhD students only). The committee is pleased to see that PhD students are permitted to attend courses of other PhD programs, and even Master's programs, free of charge. There is a NFU-developed PhD competence model that PhDs can use to structure conversations with supervisors. A new assessment form based on this model is currently being piloted in the Neuroscience and cognition PhD track of GSLS and will be extended to all other PhD tracks. This is in line with the qualification portfolio the UMC Utrecht uses to assess assistant and associate professors up for promotion. There is an Utrecht qualification portfolio for PhD candidates' career assessment, including research, teaching, clinical work, innovation and impact, and leadership, development and collaboration, and UMC Utrecht wants to implement this for all promotion and career development. As already mentioned, it would be beneficial if clear criteria for promotion were to be implemented, along with a clear definition of the PI role and a description of responsibilities.

The PhD Council consists of representatives of the PhD programs and cares for the interests of PhD candidates, addresses program-overarching issues in the Board of Studies, and evaluates the PhD programs each year. It is represented on the Board of Studies by its chair. The MD-PhD sensor group is part of the PhD Council and represents the interests of medical PhDs. They organize events every 6 months.

The average number of candidates who finish their PhD within four years is 51%, about 17% finish within five years, and 6% drops out. An overview of the career paths of alumni is not available, and specific figures of the PhD program of the strategic research areas would also have been helpful for the committee.

In the different strategic research programs, the supervision and guidance of PhDs were considered to be well organised. Each PhD candidate has at least one supervisor and one co-supervisor. The latter is responsible for daily supervision. UMC Utrecht started a training scheme for young supervisors in 2018, aiming to create an atmosphere in which good supervision is a skill which can be learned. In addition, each PhD candidate has a Supervisory Committee ('aio-begeleidingscommissie'), consisting of one to two researchers not involved in the candidate's research project. Candidates have an annual assessment interview with their (co-)supervisor(s). In addition, they may meet with their Supervisory Committee, preferably once per year. In January 2019 a new online PhD registration tool, MyPhD, was launched, containing all relevant information on training, supervision and progression, which is accessible to the faculties and School.

The committee has some specific concerns that point to the need for complaints to be taken more seriously by managers, and feedback on actions taken (or not taken) communicated to the person making the complaint. There were discussions with PhD candidates about the lack of clarity on publication requirements, with the formal Utrecht University PhD regulations only globally describing that PhD research should be made public through scientific papers with some official documents indicating that no publications are required to be awarded a PhD while some supervisors specify that four first-author papers are absolutely required. The committee advises UMC Utrecht to provide consistent advice on this key aspect of the PhD experience and to make sure that all supervisors adhere

to these requirements. Finally, there were concerns that the monitoring of candidate progress by external advisors and the annual process for progression are not strictly adhered to. This is a serious issue for quality assurance, which seems to be related to Utrecht University governance rather than UMC Utrecht.

3.3. Research integrity

UMC Utrecht is a worldwide leader in the promotion of responsible research practices, and alternate evaluation of research practices to decrease perverse incentives in research, through the initiation of *Science in Transition* amongst other initiatives. It is a frontrunner in many aspects of developing a research culture that increases value and reduces waste. The committee agrees that less focus on quantity may be an asset, but this should not imply the translation of 'Fewer numbers, better science' to 'no numbers', as this would be equally detrimental to the scientific system. The absence of specific metrics in the self-evaluation report hampered the depth of probing done by the committee, making it difficult for the committee to assess the quality and difference between research lines within the strategic research programs on the basis of the qualitative information (also limited on some points).

UMC Utrecht has developed its own new Research Code that helps researchers to adhere to the Dutch Code of Conduct for Scientific Integrity. The code indicates what to do in case of dilemmas and misconduct or suspicion of misconduct and offers support to researchers to determine what good research practice implies. An implementation plan has been developed but not yet instigated. Attention to research integrity is also shown by the recent decision to make integrity training mandatory for all new PhD candidates. This integrity training could also be geared toward new postdocs and the more senior researchers. Journals require authors to describe their contribution to any publication; this could also be taken up within UMC Utrecht, according to the committee, to make clear who participated in what respect and to what extent.

The internal research culture is strong, and there is a commitment to data sharing. UMC Utrecht updated its Research Data Management in 2019, aiming to ensure that good scientific practice accords with the FAIR principles. A Data Management Plan template is offered to researchers along with guidance and examples of suitable IT infrastructure. Division data managers are available for advice and support. Regular follow-up of adherence to these policies is needed.

A general step the committee would recommend is concerted action on data science. Whilst there are good ICT facilities within the divisions, the approach to data science is fragmented between the research programs. The committee recommends a single data science strategy for all divisions of UMC Utrecht.

3.4. Diversity

UMC Utrecht has defined a policy and targets on Diversity and Inclusion for the period 2016-2020. As a basis for this policy, the following statement, aligned with the UU Diversity statement, applies: "Within UMC Utrecht, we work on an inclusive environment and culture, with employees that represent the society we live in. UMC Utrecht strives to be an organisation where patients, staff and students feel recognized. Factors like gender, origin, sexual orientation, religion, and physical or mental limitations should not stand in the way."

Gender diversity has been a specific goal for over ten years. UMC Utrecht joined the Charter Talent for the Top in 2009, aiming to have more female full professors and a good balance on leadership at all levels. Since then, the percentage of female professors has increased from 16% in 2010 to 28.6% on 31 December 2018 and is still increasing. In 2018 UMC Utrecht appointed 8 female professors and 7 male professors. The executive board consists of three women and one man.

The committee is pleased to see that the UMC Utrecht approach concerning gender diversity is bearing fruit. At the moment, little explicit attention seems to be paid across UMC Utrecht to other forms of diversity, although they are included in the UMC Utrecht diversity statement. There are no data on broader diversity as this is not permitted to be registered by Dutch legislation. UMC Utrecht is willing to pursue other diversity and inclusiveness targets and is currently investigating possibilities for registration and measurements concerning this. The committee hopes this will enable UMC Utrecht to set broader diversity goals (i.e. for cultural diversity) and will gladly see UMC Utrecht implementing these goals for the next period.

3.5 Recommendations

- Follow-up on the general points raised, as well as the specific recommendations for each of the strategic research programs made by the stakeholder committee.
- The mandate of the programs (strategy) and the divisions (execution) needs to be clear, to avoid ongoing negotiations around budgets and appointments; strategic choices need to be made by academic researchers. The committee recommends that the management team of the strategic research programs should be given greater control over the budget for research, and there should be a better balance between the divisions and research programs on the influence on decisions about research priorities and on appointments within departments. It is of the opinion that the regulations and procedures concerning the budget for research should be clear, including key performance indicators (KPIs) and specific objectives regarding research for the divisions. This will benefit the viability of all strategic research programs, specifically those that seem to be currently struggling with their budget for research.
- Ring-fence funds for research including seed money for new initiatives for program leaders.
- With respect to personal grants (VENI-VIDI-VICI and ERC), there appear to be possibilities to improve the success rates (based on the quality of the young scientists). Coordinate activities to help researchers submit competitive grants.
- Integrated research support (including TTO functions) is not present at the UMC Utrecht level. Create an accessible, integrated central support office.
- UMC Utrecht is ideally positioned on the Utrecht Science Park campus, in the national environment and globally. Formulate specific goals and timelines concerning ongoing and new collaborations.
- Formulate a uniform and structured UMC Utrecht policy on talent programs, tenure tracks and a mentoring system, and create clarity regarding career assessment.
- Time allotted for research by clinician scientists is not clearly defined, and a vision on the positions of non-MD scientists is unclear. Also, the PI role lacks a definition. Formulate UMC Utrecht policies on these issues, as attracting, developing, supporting and keeping personnel is needed to survive as an academic hospital.

- Considering the focus on Open Science with fewer metrics: Consult the staff and broaden the support base with respect to specifics and the impact the new science evaluation approach has on research areas and individual researchers.
- Across UMC Utrecht, there appear to be distributed pockets of ICT and data science. Create a coordinated approach across UMC Utrecht.

4. ASSESSMENT OF THE BRAIN STRATEGIC RESEARCH PROGRAM

4.1. Introduction

The Brain strategic research program is an internationally recognized research centre in clinical and experimental neuroscience. Its reputation is high. Its mission is to perform research on the development and function of the brain in health and disease and to apply the acquired knowledge in clinical care and education in interaction with relevant stakeholders, including patient organizations and the broader public. The overarching goal is to create value and lifelong impact for the patient. The Brain Center focuses on five disease areas: neuromuscular disorders, epilepsy, developmental disorders, psychotic disorders and stroke. Since January 2019 a sixth disease area is being developed: Neuro-oncology. In each of the disease areas, research is intertwined with patient care and patient participation. To facilitate patient-driven research, well-characterized and large patient cohorts have been established in each disease area. The disease areas share know-how, research approaches and techniques along horizontal lines. The research approaches include neurogenetics, brain connectivity and imaging, translational cell and animal models of disease, and testing new treatment options in clinical trials (within U-Trials). Three research facilities are part of the Brain Center - a facility for neurogenetics, the Mind facility, which includes organoids and induced pluripotent stem cells, and facilities for human brain imaging.

The UMC Utrecht Brain Center is managed effectively by an energetic leader and a management team. A number of initiatives indicate that the management of the Brain Center is in very good hands. These include an internal evaluation in 2017 (Bridging the Future), efforts to enhance collaborations between divisions that participate in the Brain Center, the internally funded fellowship program, the X-talks coupled to masterclasses, an annual research day, and the initiation of two new focus areas, neuro-oncology and precision psychiatry. Two advisory boards are in place, one for organisational/scientific issues and one for societal stakeholders. Interactions and collaborations between the divisions participating in the Brain Center and between the Brain Center and the other strategic research programs are productive and positive. The relationship between the Brain Center and the Division of Neuroscience is particularly crucial. The committee wants to emphasize that the Brain Center should be given greater influence over the control of the budget when it comes to implementing strategic decisions and appointments; all conversation partners during the site visit appeared to agree with the importance of this.

4.2. Research quality

The Brain Center performs excellent basic and clinical research. The committee is impressed with the outstanding level of collaboration between scientists and clinical academics and was presented with many, very good examples of clinical, patient-driven research. The quality of the research and excellent productivity are also reflected in the publication of outstanding papers in high-ranking basic science as well as clinical journals. Each of the six disease areas has a number of prominent world-leading scientists/clinicians in their field. The Brain Center appears to be well-funded by national and international (EU) grants. At the time of the site visit, seven ERC and four Vici grants had been granted. In contrast to some of the other programs, the Brain Center has the advantage of being largely accountable to one division, Neuroscience. Indeed, the Brain Center and the Director of the Division agree that the Brain Center should be given greater control over the budget and have greater influence on decisions about priorities and on appointments. Some of the associated departments are

unfortunately facing substantial cuts in their research budget, partly as a consequence of loss of present and anticipated income from the clinical services. One concern is the possibility of being asked to do even more clinical work - some clinical academics are already spending 75% of their time on clinical care. In the committee's view, it is difficult if not impossible to maintain a high quality of research with such limited time.

The committee met very able postdoctoral fellows and PhD candidates and got the impression that they were not only very productive but also felt that they and their work were valued by their supervisors. A fellowship program, funded in part by the divisions participating in the Brain Center, awards two fellowships per year to talented post-docs. Young researchers have been relatively successful in obtaining national (VENI, VIDI) and EU grants. Unfortunately, there appear to be very few assistant professor posts for young colleagues, and although the committee got the impression that the Brain Center recruits young scientists, an active talent-scouting program is not in place.

In its assessment of the research quality of the Brain Center, the committee evaluated the research quality of each of the five disease areas as follows:

Neuromuscular disorders: This theme benefits from the unique situation that nearly all ALS patients in the Netherlands are seen in UMCU. Important discoveries have been made in the genetics of the disorders with large-scale, international, co-operative studies. The team of researchers in neuromuscular disorders has carried out novel epidemiological research into environmental risk factors for ALS and led impressive international therapeutic trials. In an important step, the neuromuscular theme will participate in a Phase III gene therapy trial for spinal-muscular atrophy, and it leads the MinE project, which aims to sequence the whole genome of 15,000 ALS patients.

Epilepsy: The theme's ability to carry out high-quality research ranging from fundamental research into genetics right through to the important evaluation of new approaches to epilepsy surgery is impressive. The huge number of patients undergoing neurosurgery for epilepsy provides an excellent opportunity for translational research, which the team has enthusiastically taken up with excellent results. An epilepsy biobank has been established, and several international collaborations are funded by the EU.

Developmental disorders: Psychiatry, paediatric neurology and neonatology work together in this theme, which has numerous interactions with outside stakeholders, is a partner in many international consortia and has many collaborations with industry. The committee was presented with a project on research into the use of mesenchymal stem cells (MSCs) to treat neonatal brain injury caused by hypoxic-ischaemic insults. This project, which is a collaboration with the Stroke theme, has reached the stage of a clinical trial being approved by the medical ethics committee of UMCU. In this phase I study, infants with ischaemic brain injury will be treated with MSCs through their nostrils.

Stroke: The mission is to improve the diagnosis, treatment, and prognosis of stroke patients. This theme acts as an interdisciplinary unit with many internal and external collaborations. Stroke has developed several protocols to promote the rehabilitation of stroke patients. For instance, the B-stars protocol, which aims to promote arm recovery after stroke using repetitive transcranial magnetic

stimulation and the development of a virtual supermarket, which stroke patients can use to train and help recover their complex skills.

Psychotic disorders: Psychosis has been one of the strongest psychiatric research centres in the Netherlands over the period of assessment and has recently been enhanced by the appointment of one of the most distinguished psychiatric researchers in the Netherlands at the Division of Neuroscience. However, at present, it is in considerable disarray: the psychosis theme plans to transform itself into Precision Psychiatry but has not yet settled on its exact future strategy and academic leadership. Much effort, planning and investment are necessary to turn this transformation into a reality. To maximize the potential of Precision Psychiatry, a new integration will be necessary between clinical and epidemiological researchers on the one hand and animal and molecular researchers on the other. Although several leaders in the field of neuroimaging have left, the remaining expertise in this area should not be left to atrophy. A leadership strategy involving closer collaboration with the division of Cancer-Imaging needs to be developed. The committee recommends organizing brainstorm sessions to discuss the future research and leadership of Precision Psychiatry.

4.3. Relevance to society

All disease areas do research aimed at improving the situation of patients. The committee did see many great examples of the commitment of scientists and clinicians to (pre)clinical research that does or will eventually benefit patients and society. The Brain Center has built excellent collaborations with stakeholders, patient organisations and charities. The commitment to the training of students and young scientists is excellent. The Brain Center has paid appropriate attention to the new focus on "open science", i.e. "science in transition". However, the committee does feel that this new emphasis should be in tandem, rather than instead of, the traditional goal of achieving academic excellence. The Brain Center is realizing its ambition to have an impact on scientific discovery as well as on the life of patients, and the committee recommends that it continue with this dual strategy.

An important objective of each area is to translate fundamental research and clinical (patient-driven) questions into new treatment options. The Brain Center has taken the lead in paying appropriate attention to involving patients in research planning and execution, and patients have been taking the lead in certain new projects. For example, teenagers with cerebral palsy have built a website, which won a prize from the world cerebral palsy association. Patients have led research and publications on how to safely come off antidepressant drugs and antipsychotics. In the disease areas of neuromuscular diseases, epilepsy and stroke, several clinical trials have been conducted with significant patient involvement in their planning and execution.

4.4. Viability

The Brain Center has excellent viability at all levels, scientific, clinical and educational. Several important and strategically meaningful initiatives were taken that will create new opportunities for collaborations between scientists and academic clinicians, including the initiation of a new disease area (Neuro-oncology) and establishing a new focus on Precision Psychiatry. With its educational program, the Brain Center successfully fosters the training of young talent in clinical and experimental neuroscience. Its ambition to belong to the top neuroscience research centres in Europe has been realized for several of the disease areas. It is now crucial to take measures that guarantee the sustainability of this position. Budget cuts that impact the scientific activities of the Brain Center are a

threat and should be avoided. Investments should be made in a talent-scouting and development program to ensure the influx and improve the career opportunities of bright young scientists.

4.5. Conclusion

The Brain Center has a strong and vibrant research program within UMC Utrecht. It performs excellent fundamental, preclinical and clinical research with a noticeable relevance to patients and society. The committee believes that the new theme of neuro-oncology will be a valuable addition. The one aspect it has major concerns about is the current lack of direction of the Psychosis/Precision Psychiatry Theme.

4.6. PhD training

There is a large Master and PhD program in Neurosciences. There is good competition for the Master's program, which provides an excellent opportunity to select the best PhD candidates. Overall, the committee's impression is that the Brain Center has a very successful PhD program. Each disease area has delivered many PhDs over the evaluation period. Based on the information in the self-evaluation report, it is difficult to judge the effectiveness of supervision. The number of dropouts of PhD candidates was not provided. The PhD candidates were very positive about their experience, appeared to be very much involved in their projects, and were appreciative of the collaborative atmosphere in Neuroscience. Career advice is available but in spite of this, the vast majority of PhD candidates appear to leave academia after obtaining their PhD. It seemed unfortunate to the committee that the staff and PhD candidates believed that there was little that could be done about this.

4.7. Recommendations

1. The new area of Precision Psychiatry needs to be further developed by integration between clinical, epidemiological and fundamental neuroscientists with experience in neurophysiology and cellular and molecular biology and good animal models. The committee is convinced that this area has great potential but only when appropriately managed and supported.
2. Several of the themes address overlapping topics, but it is not clear to the committee the extent to which the Centre addresses them as a unity. For example, the Neurodevelopmental Disorders Theme researches child psychiatric conditions such as autism which are also a concern for Precision Psychiatry, and its work on cerebral ischaemia in the newborn has much in common with work in the Stroke Theme. Approaches worth considering to further integration across the Centre would be a) more joint appointments, b) an expansion of the number of seminars.
3. There appear to be some tensions between the "horizontal" Brain Center groups that provide expertise for the disease areas in fields such as imaging, genetics and epidemiology, and the extent to which the Brain Center groups should be integrated with the larger imaging, genetic, and epidemiology departments at UMC Utrecht. The committee recommends an internal evaluation to better align the support groups with activities within the Division of Neuroscience and UMC Utrecht.

The disparity between strategic decision-making by the leadership of the Brain Center and financial responsibility by the participating divisions is counterproductive. The committee therefore recommends that the management team of the Brain Center should be given greater control over the budget for research and should have greater influence on decisions about priorities and on appointments within departments. This is a more general conclusion, also taken up in chapter 3 (see also *3.5 Recommendations*).

4.8. Overview of the quantitative assessment of the research program

After having assessed the research quality, relevance to society and viability, and comparing them to the developments and standard in the field of basic and clinical neuroscience, the committee comes to the following quantitative assessments:

Research quality:	excellent
Relevance to society:	excellent
Viability:	excellent

5. ASSESSMENT OF THE CANCER STRATEGIC RESEARCH PROGRAM

5.1. Introduction

The leadership presented the four components of the innovation loop as their main strategic target with the mission to improve the outcome of cancer patients. These are linked to 11 tumour working groups. The site visit highlighted a focus on image-guided therapy, metabolic imaging, digital pathology, bioinformatics and organoid technology. The strategy towards impacting on patient outcomes by facilitating interactions among scientists from the various disciplines has proven to be fruitful and effective. Nevertheless, the program may benefit from better defined targets and objectives to be co-developed with the various stakeholders.

The overall organisation/organogram of the Cancer program appeared complicated on paper. However, the site visit clarified the intention to work within the governance, and the collaborative spirit among the researchers in the Cancer program is excellent. Fundamental scientists meet regularly with clinicians, and strong ties between the different disciplines have been forged. Nevertheless, there is a need for coordination within and across divisions. This should ensure that best practices, for example related to ICT and data management, are shared and not developed in parallel.

During the site visit the committee saw a research program which is very well led. The leadership is highly committed to developing a strong cancer program and is well respected by the team. Open and honest discussions among the PIs and the leadership are in place. Critical issues appear to be openly discussed, and there is consensus on how to best develop and deliver a strong Cancer program among the scientists and clinicians involved. The management needs strong executive support from UMC Utrecht Board to develop a cohesive UMC Utrecht cancer research strategy and succeed in its implementation. The four themes capture the full scope of an academic cancer program, and the presented innovation loop is very appropriate to deliver on its targets. The overall strategy would benefit from more specifically defined targets (i.e. needs more detail) and better coordination with UMCU's vision on research. The latter needs to be clearly communicated and illustrated in representation and action as a matter of priority.

5.2. Research quality

While no impact analysis on the research output was provided, nor a detailed overview of the output of research themes within Cancer, the research observed during the site visit, as far as this was within the reviewers' expertise, is of very high quality overall. Numerous original ideas and research approaches were observed, including organoid technology and MR-guided radiotherapy, which are world-leading. Research extended from fundamental science to strong evaluation of clinical technology (e.g. robotic surgery and MRL program). Organoid technology is a clear and distinctive asset at UMCU. MR-Linac technology is also very strong, with global leadership. Very substantial biobanking and cohort efforts are in place, with important coordinating roles being carried out by Utrecht scientists. The academic reputation of the scientists in this program is strong. Several fundamental scientists are members of the Oncode Institute, an independent institute dedicated to understanding cancer and translating research into practice more efficiently. Ample external research funding is secured, and high-profile papers are regularly published. There are several national and international initiatives being led by the UMC Utrecht faculty.

The quality of the research leads to real impact, and at multiple scales, from fundamental to systems, from biological to technical. The regional impact is considered to be strong. No quantitative productivity assessment was provided. The adoption of the Open Science paradigm without careful consideration of faculty motivation to replace traditional metrics is a concern and needs to be addressed at the executive level. No reward or sanctioning strategy for productivity aspects was encountered. Clinical resources are very good. Concerns were raised with respect to the lack of tenure-track policies. The research support office was reported as insufficient (with respect to grants, a tech office, and research support). The Translational Program, capitalizing on the organoid technology in concert with strong genomic approaches, can become a true goldmine for the UMCU Cancer program. This is a pretty unique set-up, difficult to copy for any institute. Strong features include genomic and proteomic technology and the presence of the PMC and Hubrecht (where significant cancer research takes place) on campus.

The overall evaluation of research quality of the Cancer strategic research program is very good, with several world-leading lines of research (MR-guided radiotherapy/organoid technology).

5.3. Relevance to society

The overall focus on societal relevance, including the impact on individual patient care and improvement of treatment options, is excellent. The contribution to health system changes through regional efforts and large-scale patient cohorts is evident. The focus on prevention and survivorship as a key part of the strategy demonstrates commitment to impact. This is realized, for example, through the DENSE trial. The committee did not encounter a real strategy regarding subpopulations. Many teams are developing valuable research products for society (e.g. radiotherapy and software systems, organoid technology, DNA sequencing Cyclomics).

The overall evaluation on relevance to society for the Cancer strategic research program is very good. Multiple efforts and measures are in place to ensure that this program contributes its relevance for society. The focus on discovery and conversion to commercial product or policy is quite robust.

5.4. Viability

Strategic planning: concerns relate to the coordination of the Cancer program with the broader UMC strategy. Research may be seen as a cost, not as an opportunity by the UMC Utrecht Board. A strong collaboration exists with PMC and Hubrecht, which is a great asset and seen as supporting long-term viability. Within the Cancer program there is a very good spirit of collaboration among researchers from different disciplines. Multiple, highly relevant research topics are addressed that should ensure the viability of the research portfolio. The strategy has flexibility but lacks intermediate milestones to measure success. The SWOT analysis and the discussions of the committee members with PIs in the program provided a good picture of strengths and weaknesses. Elements that were missing related to broader global trends in cancer research and how UMCU Cancer relates to them, and comparison with peers to identify opportunities and threats.

The research program has no dedicated research budget in place. Lack of transparency of the decision-making process within the divisions of how research money is allocated is a concern. The Cancer program consists of strong scientists, and the staff is highly engaged and collaborative. There is no

overall tenure-track program, and the requirements for career advancement are undefined and left to individual divisions.

The loss of two leaders in the imaging and radiotherapy domains is a major risk to the long-term stability of the imaging and radiation oncology components of the Cancer program and a concern for continued impact. A means of stabilizing the current leaders in alternative roles should be considered while recruitment of new leadership is pursued. There is a lack of any overarching technology and digital strategy in the UMCU plans – there may be opportunities to leverage existing senior talent to address this need.

The physical location of the program, adjacent to the PMC and the Hubrecht, opens incredibly strong opportunities for building a world-leading cancer program. Strong ties with regional partners are beneficial, but keeping the focus on further developing an academic cancer program, including the need to recruit and retain top-level scientists, will be important and require sufficient financial support. A major threat is the erosion of research capacity in the clinical setting (helping with trials, nurse support, imaging support).

5.5. Conclusion

The committee saw a vibrant and well-led cancer program, capitalizing on the exceptionally strong opportunities that exist in the Utrecht Science Park for collaborative cancer research. Strong interactions between fundamental scientists and physicians are in place. All conditions for a world-class cancer program are available, and it is of the utmost relevance to ensure that human capital (i.e. researchers and PhD candidates) is appropriately employed to develop the program further. This critically depends on enabling clinical doctors to develop and lead research projects, developing a uniform and transparent tenure program for junior staff, identifying key strategic projects and using core funding in these prioritized programs to retain and recruit new staff, and to foster and monitor PhD candidates.

5.6. PhD training

There are several strong cancer tracks in the graduate school. Community building in these tracks appeared to be excellent. The PhD program is very strong, and the connection with a MSc program on cancer biology is excellent. Candidates receive strong training in cancer research. PhD candidates appear to be well supervised. An independent supervision committee is in place. Guidance of PhD candidates regarding the job market and career prospects is in development. For proper career guidance it will be essential to assess where PhD candidates end up. The overall duration of a PhD project is between 4 and 5 years, which is in line with other programs. It is important to establish uniform guidelines on graduation criteria. While these criteria are probably set by the university, it will be important to ensure that supervisors adhere to them.

The Graduate Program appears to be strong. There are several clear PhD tracks, which have the potential to foster interactions among PhD candidates with complementary interests. Some tracks appear to be overlapping, and merging them could be considered. The Graduate School should be able to provide statistics on where graduates go after their degree to gain insight into how many jobs as postdocs, in academia or industry are available, and to monitor how many secured funding for themselves. This is important, if not essential, to assess the quality of the program.

There is no reason to believe that the PhD program is anything less than very good, but it remains difficult to confirm as no information was provided about where PhD candidates have ended up. Graduate schools should be able to provide these numbers.

5.7. Recommendations

1. The program may benefit from better defined targets and objectives: within the large field of oncology, what does the UMCU Cancer program want to focus on?
2. Best practices, for example related to ICT and data management, must be shared and not developed in parallel.
3. A reward or sanctioning strategy for productivity aspects may be useful. At very least, it should be clear to junior scientists what criteria will be used to evaluate their performance, particularly in the context of Open Science.
4. The graduate school should be able to monitor where former PhD graduates continued their career.

5.8. Overview of the quantitative assessment of the research program

After having assessed the research quality, relevance to society and viability, and comparing them to the developments and standard in the field of cancer research, the committee comes to the following quantitative assessments:

Research quality:	very good
Relevance to society:	very good
Viability:	very good

6. ASSESSMENT OF THE CHILD HEALTH STRATEGIC RESEARCH PROGRAM

6.1. Introduction

The Child Health program is an integrated framework for child-centred interdisciplinary research, aligning patients, clinicians, investigators and resources in order to fill gaps to improve the lives of children during childhood and thereafter. Within the program, the 'Cycle of Life' approach is strongly intertwined with the so-called 'Cycle of Innovation'. In the latter, interdisciplinary teams of patients, clinicians and investigators strive to develop and implement novel approaches for the treatment, (early) diagnosis, prognosis and monitoring of children with chronic diseases to fulfil unmet medical and psychosocial needs and improve the lives of these children and their relatives.

The Child Health program focuses on four research areas: Severe inflammatory disorders, Congenital & hereditary disorders, Antenatal & perinatal damage, Paediatrics and oncology. The research theme focuses on the healthy development of a child from pre-conception to adulthood in an interdisciplinary child-centred research community that aligns with the European Commission's philosophy of Responsible Research and Innovation to: 1) Improve paediatric disease outcomes within a lifespan context; 2) Cure congenital and hereditary diseases by unravelling their pathogenesis; by developing diagnostic and prognostic markers and tools; and by developing and implementing novel therapeutics and lifestyle interventions; and 3) Improve the resilience and quality of life for children and their relatives during childhood and thereafter. According to the committee the mission is clear, and the vision and aims are focussed on "Cycle of Life and Cycle of innovation". The ultimate goal to empower and engage children and their relatives to be fit for the future is a strong and meaningful, original, overarching aim, although the subcommittee's further comments about the inclusion of maternal health should be considered. The cycle of life and the cycle of innovation (the interdisciplinary approach) are evident and strongly implemented in all research lines. The physical versus mental theme is less pronounced in most research lines. Since the last review, new research areas have been added to the program. The congenital cardiac disease research line has led from fundamental science research to a clinical trial within the space of five years and a wider understanding of the importance of neuroprotection in cardiac interventions. The maternal and infertility research streams have also moved to the Child Health program; they link very well with the strategic focus on the 'cycle of life' and add valuable research and expertise to strengthen the overall program. There is, however, a slight incongruity now, and researchers in these streams could possibly feel excluded, due to the naming of the research program, which appears to focus entirely on child health.

Throughout the site visit the committee received the overall feedback that the Child Health program governance was strong and active. All researchers felt that this contributed to their ability to perform research, initiate collaborations, and have relevant and significant outputs. In 2014-2015 a major change in the governance was made that aimed to improve the societal impact and revenues for patients and align with the 'connecting U' strategy of UMC Utrecht. There was a new chairman and a new steering committee (the core team), and a process to rearrange the program was started. This rearrangement was done "bottom up" and resulted in a partially new core team in 2018. The governance, as noted in the general section of this report, is hampered by the complex matrix structure separating divisions from strategic research programs, with the latter having no direct responsibility for their research budget. The atmosphere and attitudes of staff within the program are overwhelmingly positive, and the management team is well organised and clearly pays attention to

staff wellbeing and career development, within the confines of the matrix organisational system. The program researchers are located within seven divisions of UMC Utrecht, although the majority are physically located within the Wilhelmina Children's Hospital. The management team copes well with the challenge of this wide divisional distribution.

The core leadership team is strong, and as a consequence there is a clear sense of identity amongst researchers within the Child Health program. The organisational matrix is quite complex, with heads of departments and divisions involved, core-team members, and individual PIs and investigators within four research areas that are divided into a number of research lines that are cross-linked by three strategic themes (cycle of life, physical and mental health, interdisciplinary). It is unclear whether there is strong leadership in each research line, and how leadership skills are nurtured. Junior investigators clearly value the leadership and mentorship of their PIs. Strategic targets are clear, such as focussing on becoming an international centre of excellence in targeted "rare disease" areas. The cycle of life focus is reflected in future plans and targets, for example, enhancing research in transitional care and adult survivors of childhood disorders. The complementary work in perinatal medicine and infertility ensures a strategic link to the 'connecting U' strategy through research that improves the care of the local population as well as national and international populations with rare diseases. The physical versus mental health theme needs further development.

6.2. Research quality

The four research areas within the Child Health program are all high performing in general. All four generate highly relevant publications and are successful in obtaining funding. They all show evidence of originality and innovation. Within the research areas, there is some variation between the research lines. Some are world leaders, while others could benefit from prioritization to fully realize their potential. The overall subcommittee score reflects the fact that not all research lines are world leading. Although the leadership team has implemented a number of strategies to identify and nurture talented researchers, there is an apparent conflict amongst some of the younger investigators, both clinical and non-clinical, as to whether they have achieved their desired aims. Fundamental scientists are essential to the delivery of high-quality research within the program, and division heads need to acknowledge that both are important. The model seen in Child Health of establishing pairs (clinical/non-clinical scientists) works very well and should be protected. A "fleet survey", first conducted two years ago, identified principal investigators and investigators within the program and facilitated a new series of PI/I meetings. Some felt this was beneficial in terms of recognition of success as a researcher, but others felt it was potentially demotivating for those with very little dedicated research time and/or part-time workers. This reflects the overall theme identified across all research programs of the challenge of developing clinical researchers without dedicated research time. The PI/I meetings were widely welcomed and should be maintained. All researchers reflected that their facilities were outstanding, with access to the equipment they need. The configuration of the research facilities facilitated the development and sustainability of collaborations (including interdisciplinary ones).

6.3. Relevance to society

All research lines presented outstanding evidence of societal impact. Some examples include:

- Antenatal and perinatal damage: trials undertaken as part of the NVOG trial network changed the clinical practice, allowing the transfer of care from a hospital to home model for women with specific pregnancy complications.
- Congenital cardiac disease: unique serial brain MRI data leading to increased attention to neuroprotection in the context of cardiac surgery, and subsequent clinical trials.
- Respiratory infections: investigation of maternal vaccination and subsequent infant response leading to a change in the infant immunization schedule.
- Cystic fibrosis: the use of organoids to enable personalized drug targeting as well as efficient clinical trials to allow the early introduction of new drugs.
- Neonatology: successful industry collaboration to develop a new EEG monitoring technique.

Although the committee did not meet with any parent/patient/stakeholder representatives during the site visit, there is ample evidence of the embedding of parent involvement within the program's research, including notable examples of parent-driven research, such as the JLA process undertaken with the juvenile inflammatory arthritis research team, and examples of the very close links with a patient organisation that has led to substantial research funding, as evidenced by the cystic fibrosis research line. There is additionally evidence of industry partnerships which have led directly to the development of new technologies, such as less invasive neonatal EEG monitoring. The societal impact is therefore very strong.

6.4. Viability

There is a long-standing and strong research environment with many research facilities within the Children's Hospital that is embedded in UMC Utrecht and university. Researchers have been very successful in sustaining research programs with external funding. However, clinician-scientists do not have dedicated research time, and the matrix structure with no protected research budget represents a major threat to the viability of the research program. A recent example of concern was a unilateral decision of one division to remove funding from several successful non-clinical scientists. This decision was not in line with the research program strategy. This will only be solved by a protected research budget.

Although the rare disease focus is a clear strength, it is important for the societal benefit that the research program should focus on the needs of the wider local population and not just the needs of children with uncommon conditions. In this instance, the local relevance is provided by the obstetric trials, which address moving care from hospital to home for women with pregnancy complications, enhancing efficiency of services, and addressing the preferences of women, for whom a home-based model is desirable. The committee examined the recommendations from the previous review, which highlighted the importance of strengthening public health research to address prevention and improve the health of the population. This does not appear to have been addressed, but the wider UMCU work on the exposome, focussed within the 'regional network for sustainable care', which is a priority for all UMCs, provides an opportunity to do this. There are additional opportunities for strengthening new work on paediatric oncology because of the newly co-located Princess Maxima Institute.

6.5. Conclusion

The Child Health program is clearly a strong and vibrant research program within UMC Utrecht. Although smaller than the other strategic programs in terms of the number of research FTE, the program has produced an impressive array of outputs, demonstrating ground-breaking research and innovation as well as notable societal benefit. The program has a very successful strategic focus within child health on rare disorders, leveraging the benefit of the UMC's position as the centre of excellence/reference centre for the medical care of these children within the Netherlands (and frequently across Europe and beyond) to drive robust and valuable research.

6.6. PhD training

The selection and recruitment of all PhD candidates are performed by the supervisor and co-supervisor. There are fourteen thematic PhD programs that provide introductions, thematic courses, seminars, etc. PhD candidates can participate free of charge. The programs are represented on the PhD council, and the program committees include PhD representatives. There is clear guidance for supervisors as well as for PhD candidates in terms of how the supervision should be organized and what the PhD program should look like. Courses and career events are organized. A benchmark for the success rate of the PhD programs is lacking, which hampers the interpretation of the numbers provided.

6.7. Recommendations

All of the research lines are strong, and the committee would not recommend disinvesting from any of the existing work. It has, nevertheless, a number of recommendations which would accelerate even more the research program's ability to execute ground-breaking research, develop patient involvement and drive societal impact.

1. Unity of the program could be strengthened by renaming the strategic theme to reflect the breadth of research, including care of women, children and families and not just child health.
2. Research on public health and prevention within maternal and child health needs to be strengthened, taking advantage of the wider UMCU work on the exposome. The strategic theme "physical vs mental health" is less evident amongst the research lines than the "cycle of life" and "cycle of innovation" themes. The Child Health program leadership team needs to decide whether this thematic focus will be retained, and if so, it should be better developed.
3. The hurdle to become a PI is viewed as very high within Child Health, and this is uneven across programs. Some feel penalised if they are not recognised as a PI. There are concerns about equality as this can potentially penalise part-time workers or those with only a small amount of protected research time. Criteria for recognition as a PI should be reviewed with this in mind.
4. Extending paediatric to adult care (already done in congenital heart disease, kidney) could be done in metabolic disorders with a more direct link to high-risk obstetrics, which would further enhance the cycle of life focus of the program.
5. There are some tensions between 'societal value' and the 'better care for the rare' focus. The balance between research on rare childhood diseases and improvements to wider clinical care, for example in obstetrics, should be maintained. The new U-trials infrastructure should be used to enhance the clinical trials within the Child Health program.

6.8. Overview of the quantitative assessment of the research program

After having assessed the research quality, relevance to society and viability, and comparing that to the developments and standard in the field of Child Health, the committee comes to the following quantitative assessments:

Research quality:	very good
Relevance to society:	excellent
Viability:	very good

7. ASSESSMENT OF THE CIRCULATORY HEALTH STRATEGIC RESEARCH PROGRAM

7.1. Introduction

The Circulatory Health strategic research program was launched in 2010 and was based on the existing portfolio of cardiovascular research of UMC Utrecht and on the existing infrastructure of the research departments involved. The mission is to reduce the burden of cardiovascular disease nationally and internationally. The main objectives of the Circulatory Health program are:

- Structure cardiovascular research more clearly within UMC Utrecht;
- Introduce a clear focus in this research;
- Stimulate collaboration between departments and divisions active in this field;
- Strengthen and extend cardiovascular research and become an internationally recognized cardiovascular centre;
- Provide state-of-the-art patient care and excellent cardiovascular education.

Based on recommendations by the previous committee, the program has focussed its research on the potentially most successful and competitive clusters, targeting four patient groups/research themes: heart failure, cerebral ischaemia, aneurysms and patients at higher risk for cardiovascular disease. Expertise areas defined for studying these patient groups include genetics, imaging, clinical epidemiology and global cardiovascular (CV) health/diversity.

There are clear strategies to support the mission to reduce the burden of cardiovascular disease nationally and internationally, which are improving the prediction, prognosis, prevention and treatment of cardiovascular diseases. A highly integrated cardiovascular research laboratory has still not been created. A greater focus on the potentially most successful research patient groups has been made: heart failure, cerebral ischaemia, aneurysms and high-risk patients supported by the expertise areas of genetics, imaging, epidemiology and global health. Research infrastructure (patient cohorts, databases, labs) has been merged, and the themes and expertise areas prioritized.

The management of the Circulatory Health strategic research program is good, even given the changes since the start of the program. The strategic program has a clear structure and strong leadership, and a program office with various skills to support operations is in place and is recognized by the researchers. The challenge is the interaction between the strategic and division leadership and the execution of innovative research projects. This is even more challenging if more than one division is involved. The cross-fertilization of best practices between the six strategic research programs seems to be a priority but turns out to be a challenge in practice. Incentives for such activities may spur initiatives.

7.2. Research quality

Circulatory Health is defined as one of the six strategic focus areas of UMC Utrecht, and new strategic patient groups and expertise areas have been identified for the next five years. The three patient groups are now atherosclerosis (encompassing aneurysms and cerebral ischaemia), heart failure and high-risk groups, such as premature vascular disease, and are supported by the expertise areas of genetics, imaging, clinical epidemiology, prevention and global health. Several personal grants (ERCs and VICIs) and a gravitation grant (Exposome, >€ 15 million) have been obtained.

Regarding the Biobank and patient cohorts, there are some clear assets such as the Utrecht Cardiovascular Cohort, a biobank which is being built up with the purpose to generate similar datasets, and bio-banking of all CV patients in Utrecht. It has three components: UCC-CVRM (enrichment in 2018 by primary care data and pharmaceutical key figures), UCC-SMART (includes additional measurements of 800 high-risk patients) and UCC-LRGP. The last will include imaging data, lifestyle information and cognitive function. A focus is on patients with atrial fibrillation, heart failure, AA and carotid stenosis. There is also the SMART cohort with data from 13,000 patients, which has been running for 22 years. The Heart Failure group consists of a strong group with international recognition and a research line that runs from fundamental science to therapy implementation. Future plans are to expand the early diagnosis of heart failure by machine learning linking primary care to secondary and tertiary care. HFpEF is a focus in the Queen of hearts consortia, RECONNECT and Chance. The research program has created ONCOR, a Cardio-Oncology registry. With respect to Data Science/U data, the committee is of the opinion that there are insufficient resources in mathematics, statistics and bioinformatics, and this needs to be centralized at the UMC Utrecht level. There is an established collaboration with the Innovative Medicines Initiative (IMI) consortium, a pan-European consortium, the ESC and European heart network. There is a circulatory health research table with quarterly meetings in the field of HF (plans for CVON, H2020, ERA CVD and more). Close collaboration with patient organisations is in place, such as PLN Foundation and Harteraad. There are also numerous international collaborations with funding from industry, the Netherlands and the EU. Both HFpEF and cardio-oncology are currently hot research topics with a great potential for the future, as well as an array of promising collaborative networks. The Heart Failure research program is outstanding and is clearly on the rise.

Since the last evaluation there has been a reprioritization of the focus areas, the number of PIs has decreased somewhat (-17), and a new unit of fundamental research was initiated after a suggestion from the previous review: Laboratory for Circulatory Health. This lab, in which preclinical and clinical researchers can work together, has been planned, but not yet inaugurated. Professors in fundamental science have been appointed and collaborative projects developed, in particular regarding heart failure with two professors from the Hubrecht Institute being employed 20% by UMC. Patient involvement is particularly related to the Phospholamban group (PLB), which is a strong driver.

Funding is substantial with € 10 million in 2018. The grant total seems to vary a bit year by year, and the amounts generated by personal grants could be improved. A large part of the funding is described as coming from external organisations, including industry, the EU and charitable organisations. Research coordinators who represent research themes are in place to support PIs in discussions on funding possibilities, infrastructure, etc. There is a Circulatory Health program committee to ensure that decisions and execution within the departments and divisions align with the research strategy.

The overall impression is that the research quality of this strategic research program is very good, but the committee did not have a complete overview of all publications per PI or patient groups to compare if they are all equally successful. The quality of parts of the Heart Failure and High-Risk research seems outstanding, but the unavailability of metrics of the specific themes precludes a detailed assessment. There are 71 PhD candidates in the focus area of cardiovascular disease. The PI supervisors are broadly distributed as follows: 38% is active in heart failure, 16% in cerebral aneurysms, 12% in cerebral ischemia and 9% in high-risk patients. The high-risk and prevention supervisors may come from the Julius Centre or elsewhere. Nonetheless, it is fair to say that Heart Failure has the

majority of PIs and is probably the program with the most hospital beds, procedures and outpatient visits, and hence the most staff, including students and cardiologists (qualified or in training). One project of the Cardio-Oncology initiative came from a PhD candidate recognizing a clinical need and a research opportunity from a case. It is a sign of visionary leadership that his initiative was encouraged and materialised, but more resources are needed to sustain it. Such readiness to develop new research ideas in a timely fashion is a key factor in competitive research today.

One key factor in successful research is to enrol the available patients in trials using the primary care hospital unit but preferentially also regionally. This seems to work well with the greater recruitment basis taking place in primary care than at UMC Utrecht, but figures cannot be given. The number of investigator-initiated clinical trials seems low. The recently launched U-trial initiative may change this. The focus is largely on cohorts, both regionally and internationally, with aspirations for potential registry-based randomised trials. Datamining and structured data ensure phenotyping.

7.3. Relevance to society

Measures to enhance the societal relevance have been applied since 2014 regarding the formulation of research questions. Attention is also paid to how the research fits with existing knowledge and how the findings will lead to the next step. The efforts are targeted at both global health, in particular in Ghana – Africa, and at primary and secondary prevention, including high-risk patients. Great examples are the evaluation of new catheters and fibre-optic real shape techniques, new apps for risk assessment and telemedicine for heart failure, risk scores for ARVD and sudden cardiac death, and new MRI technology. In addition, algorithms to reduce inappropriate ICD shocks are being developed with Medtronic. In some patient group areas, research questions are formulated and prioritized together with the patients. This could be applied to even more patient groups, and even earlier and broader involvements of patients would be welcome. The new high-risk outpatient clinics is an example in which trials with potential patient involvement can be created. Patient-initiated trials could also be considered.

7.4. Viability

The research program is very well equipped for the future, provided the existing structures can remain fruitful, and the research strategy developed in the Circulatory Health program is well aligned with its execution in the divisions and departments. The PhD program is excellent and vibrant. Patient involvement and education are very strong.

The changes made to the research strategy (described in the self-evaluation report) and fundamental research facilities must translate into academic excellence: it is too early to assess success, but the committee's impression is that such collaborations are already advanced and fruitful in the field of heart failure, e.g. for ARVD, hypertrophic cardiomyopathy and heart failure. The future (2020-2025) aims are to integrate cardiovascular care in regional networks and Utrecht, and to set up a strategic alliance to include acute care. There will be a greater focus on prevention (both primary and secondary). In particular, premature and progressive vascular disease will be targets as well as clinical epidemiology and women with cardiovascular diseases. The already available multidisciplinary cardiovascular outpatient clinic for high-risk patients shows that it is possible to achieve the integration of care and research. In this example which uses the SMART prediction of CV risk model together with patients, there is a potential for research with patient involvement.

The committee agrees with the SWOT analysis described in the self-evaluation report. Strengths are the excellent connections with GPs in the Utrecht area and international networks, strong cohorts, world-class research in end-stage HF and high-risk CV patients, and very strong imaging. The major weaknesses are that the program does not have seed money, and the organisation and budget do not align. Too many collaborative divisions weaken the decision-making and alignment of research strategy and execution. Better synergies with the top clinical hospitals in the region present an opportunity. Available CV high-risk cohorts provide great opportunities for society of very relevant, integrated, preventive care. A core facility for Data Science would enhance research, which is especially important since there is a focus on large cohorts. A major threat is the lack of dedicated research time for the clinicians and postdocs who are the future PIs. Also, too much of the regulatory work is the responsibility of clinically active researchers. The strategic program organised the Jacob Jongbloed Talent Society in 2014, 2016 and 2019 especially for young professionals. Looking into the future and with knowledge of the young PhD candidates postponing parenthood until the PhD is finalised, there is a need to analyse how to keep young collaborators at UMC Utrecht. The committee suggests considering facilitating research time for parents to keep them from going elsewhere (both men and women).

7.5. Conclusion

Overall, the program has strong resources and a structure which should grant a very successful research environment.

7.6. PhD training

The committee has been informed that a PhD candidate often has 2-3 additional tutors representing different aspects of their project. Some 75% is satisfied with their PIs. Overall, the PhD program appears excellent. PhD candidates are very positive about the quantity and quality of the program. There are confidentiality advisors for PhD candidates who are uneasy with aspects of their thesis work such as authorship. There is a workshop for career development in place. Senior postdocs and assistant professors have unclear promotion processes. The success rate is around 50% within the four-year time frame, and about 75% takes 1-2 more years. Drop-out numbers around 5%, but no figures were supplied for cardiovascular PhD programs.

7.7. Recommendations

1. With respect to Data Science/U data, the committee is of the opinion that there are insufficient resources in mathematics, statistics and bioinformatics, and this needs to be centralized at the UMC Utrecht level. A core facility for Data Science would enhance research, which is especially important since there is a focus on large cohorts.
2. The new high-risk outpatient clinics are an example in which trials with potential patient involvement can be created. Patient-initiated trials could also be considered.
3. In some patient group areas, research questions are formulated and prioritized together with patients. This could be applied to even more patient groups, and even earlier and broader involvement of patients would be welcome.
4. The research program should develop a clear career development plan for young researchers and consider giving dedicated research time to clinical researchers.

7.8. Overview of the quantitative assessment of the research program

After having assessed the research quality, relevance to society and viability, and comparing that to the developments and standard in the field of circulatory health, the committee comes to the following quantitative assessments:

Research quality:	very good
Relevance to society:	very good
Viability:	very good

8. ASSESSMENT OF THE INFECTION & IMMUNITY STRATEGIC RESEARCH PROGRAM

8.1. Introduction

The Infection and Immunity (I&I) strategic research program aims for a leading role nationally and internationally in obtaining and disseminating knowledge and innovations in the field of inflammatory and infectious diseases and immune-mediated therapy. The aim is to improve treatments for patients with difficult-to-manage infections, immune diseases or cancer. Researchers and physicians closely collaborate to deliver high-quality care and cutting-edge research, with close patient involvement where possible. The I&I program maintains its knowledge and expertise by training talented people to become the future generation of experts.

The strategic program aims to contribute to the understanding of how best to manage diseases with a large societal impact. It focuses on tertiary patient care and has excellent research facilities, with strong collaborative connections in the region and beyond. It makes great efforts to continuously respond to new developments and has an effective talent policy. To pursue this objective, I&I is organized into four connected research themes: 1) preventing antimicrobial resistance, 2) preventing inflammation, 3) elucidating host-pathogen interactions and 4) developing immune-mediated therapy and prevention. Each theme has distinct research lines, and clinicians, researchers and research groups are often active in several themes.

The strategic targets are very clear. They have great societal as well as biomedical importance and, more broadly, are of importance internationally. The four themes in the program have been well thought out. In the self-evaluation report, the mission was more clearly defined in some cases than the strategy to reach the proposed goals. The governance of the I&I strategic research program is very strong, and the leadership skills of the chair and vice-chair appear to be excellent. The one weakness in the current structure is the lack of financial control. The strategic program leadership lacks the means to translate their vision into specific actions. The committee recommends considering financial empowerment of the program leaders, giving them more power to allocate resources within the strategic research program. At present, this control lies with the division management.

8.2. Research quality

With the central direction of the content of the self-evaluation report, a detailed evaluation of the performance of each theme and research line could not be performed with great precision. However, the value of the antimicrobial resistance research is internationally prominent. In addition, the increased focus on immune oncology is starting to pay off, and the theme on preventing inflammation offers many opportunities with respect to translational research. The staff in the strategic program should be congratulated on the number of clinical studies performed over the research period and the genuine ambition to perform research with high societal importance. The committee concludes that the I&I strategic research program is vibrant.

All four research themes have produced important research over the past six years, with one of them (on antimicrobial resistance) having a higher visibility with regard to output. According to the committee, there are some key international figures amongst the research staff. The scarcity of

individual (career) awards over the review period does need attention. The committee met with skilled and motivated staff and a good atmosphere. Funding support appears more optimal for network grants than individual grants. The research facilities are good if not exceptional. Two highlights of the I&I research are the work on microbial resistance and the clinically highly relevant work on RSV. In addition, the increased attention paid to immune oncology offers substantial new opportunities. The mix between applied and more fundamental research creates a clear synergy. In the longer run it will be essential to maintain sufficient attention for fundamental research that has no direct clinical impact, but which has the potential to make a major contribution to the understanding of immunity and pathogen control in the longer run, according to the committee.

The income and publication output have been very good over the past six years. Many papers have high applied significance with good citation counts. The senior management of UMC Utrecht must ensure the continued support of fundamental biomedical research, even if its societal relevance is not clear at present. Like most research programs of UMC Utrecht, the I&I program lacks a well-defined mentoring and tenure-track system to advance the careers of talented junior staff. The committee recommends providing clarity on the required criteria to progress along the career path. The organisation would greatly benefit from a formalised system to appoint, support and evaluate clinician-scientists in the I&I area. Adequately protected research time for clinicians is an essential element of this.

Overall, the research quality is judged as very good, and some research lines are even considered to be excellent, but some variation exists between and within themes. Further improvement of the research quality may be achieved by the (re)structuring of talent recognition and retention schemes, the allocation of greater financial decision-making power to the management of the program, and the development of a formalized tenure-track and mentoring system.

8.3. Relevance to society

The staff in the program is dedicated and consists of a group of people who are genuinely interested in 'making a difference'. The I&I research program has some clear examples of measures to enhance societal relevance, such as the contribution of livestock to flows of antimicrobial resistance genes, the design and impact of vaccination programs and the various patient management practices. The committee considers them to be highlights of the I&I research program. The quality, scale and relevance of contributions are also very good; many of the themes and individual research lines target very important public health and patient management issues.

The I&I research program has been successful in generating new treatments in some of their research, such as a nasal delivery system for a biological treatment. Much of the work is generating a better understanding of what are the best policy options for key public health issues. The program has had a very significant impact, with some very clear examples of its research changing national health policies.

All of the topics are highly relevant to improving health in Europe and in some cases globally (e.g. antimicrobial resistance and the One Health theme where UMC staff are making a very substantial impact through their research). The committee does wish to emphasise a concomitant need to place adequate emphasis on fundamental research to support the applied activities.

8.4. Viability

The selection and organisation of the major themes look good to the committee. Ultimately, high-quality output depends on individuals and less so on the organisational structure. All key issues have been identified by the I&I program, except for the following:

1. With respect to immune-mediated therapies, there is a substantial effort with respect to spin-off creation, but the pharmaceutical industry relationships need to be enhanced to improve the viability of the small spin-off companies and the uptake of their technologies.
2. The need to have more control over finances and appointments to enhance the development of key young staff.

The themes and facilities within the I&I program are widely spatially distributed in UMC Utrecht. While this does not appear to be ideal, and may be resolved in the longer term, the output and atmosphere are excellent, with many examples of collaborations across groups.

A more clearly defined career development structure should be put in place to improve the attractiveness to high-quality researchers both within the Netherlands and internationally. The committee is of the opinion that some themes have very good international collaborations while others have less. In an international context the viability is very good on average, but there is variation between the themes. Nevertheless, all themes are viable and internationally active in producing very good-quality research with good income generation and publication output.

8.5. Conclusion

The research across the four research themes of I&I: (1) preventing antimicrobial resistance, (2) preventing inflammation, (3) elucidating host-pathogen interactions and (4) developing immune-mediated therapy and prevention, is of high quality overall but with some heterogeneity between the themes. Each theme has distinct research lines, and clinicians, researchers and research groups are often active in several themes, but the greatest international impact is probably theme one under the banner of 'One Health'. The strategic research program is well led and has good channels in place for consultation at all levels of staff appointments.

8.6. PhD training

The co-supervisor structure seems to be working well according to the interview with PhD candidates. In general, the committee is of the opinion that the strategic program is well organized, with appropriate consideration of requirements to develop a successful career inside and outside of academia. The range of taught courses appears to be excellent, but further thought regarding compulsory components would be desirable. Refining this component would be enhanced by a better understanding of the destinations of prior cohorts of PhD candidates. The small sample of PhD candidates interviewed seemed very happy with the arrangements for supervision and research activity.

8.7. Recommendations

Issues to address are:

1. More direct financial control is needed for the I&I strategic research program;
2. Greater thought needs to be given to how best to support clinician-scientists in order to give them clear guidelines on how much time should be spent on clinical duties and on research;

3. A strategic vision of the future technologies that need to be acquired and supported across the research theme needs to be developed to plan for future financial spending on equipment and facility needs;
4. International links within Europe are excellent, but more needs to be done to strengthen links to other continents.

8.8. Overview of the quantitative assessment of the research program

After having assessed the research quality, relevance to society and viability, and comparing that to the developments and standard in the field of Infection and Immunity, the committee comes to the following quantitative assessments:

Research quality:	very good
Relevance to society:	excellent
Viability:	very good

9. ASSESSMENT OF THE REGENERATIVE MEDICINE & STEM CELL RESEARCH STRATEGIC RESEARCH PROGRAM

9.1. Introduction

The Regenerative Medicine & Stem Cell (RM) strategic research theme of UMC Utrecht is also one within the campus-wide Utrecht Life Sciences, including the faculties of Medicine, Veterinary Medicine and Science. The three focus areas of the RM strategic research theme are centred around translational research and focus on three patient-oriented themes:

1) Musculoskeletal tissue regeneration;
2) Cardiovascular and renal regeneration: a) heart regeneration, b) kidney regeneration;
3) Stem cell-based interventions.

These are supported by a variety of technologies such as biofabrication, organoids, organ-on-chip, in vitro models, biomaterials, cell therapy, stem cell biology, single-cell analysis, imaging and ethics that are crucial to achieve the aims of the three themes, including modelling human diseases and developing new drugs using pluripotent stem cells and organoids.

In general, the committee is of the opinion that the research themes are well chosen based on international standing, existing strengths and clinical needs. In some areas the utilization of pluripotent stem cells and genome engineering approaches for application in stem cells should be fostered to generate cell culture models and facilitate novel strategies for organ repair.

The vision of the RM strategic research theme is to improve the understanding of stem cell biology and disease, to develop innovative technologies, and to translate the findings into novel regenerative therapies. The mission is:

1. To bring novel regenerative treatments for patients into standard clinical care.
2. To provide a centre of excellence for biomedical, technological and stem cell-based research.
3. To attract, train and educate the next generation of investigators and caregivers to develop and implement regenerative therapies.
4. To incorporate societal perspectives through active connections to patients (societies) and relevant stakeholders.
5. To actively foster national and international collaboration with academia, government and industry

The mission is ambitious, and the strategic research theme includes some very challenging projects. The RM strategic research theme is very well managed, with good leadership by experienced PIs, and clear attention is paid to the three focussed sub-themes and two platform technologies. Governance is limited only by the lack of funding aligned to the research program. Now that the RM research program has become well-established, the leaders are encouraged to develop a five- or ten-year strategy for building further on the quality of the research and creating societal impact. This could form the foundation for discussions with the divisions on funding needs.

9.2. Research quality

The committees' general impression of the entire RegMed Science research program is extremely positive. There is clear evidence of world-leading research in the organoid and musculoskeletal subthemes, with research in all areas being at least at the level of international recognition (very good). The strategic theme brings together 135 FTE of research time, which is thought to be the largest Regenerative Medicine grouping in the country. The move of this strategic theme into the Hubrecht Institute building has been very positive – it is a fantastic research environment which has stimulated some direct links between UMC Utrecht and Hubrecht researchers. The involved PIs have been very successful in raising additional external funds, often in collaboration with partners from other institutions in Utrecht. The RM strategic research program as a whole has a very large number of high-quality publications. Among the selected top papers for each of the three themes, the committee identified some very strong outputs.

The unique strength of the RM strategic research program theme is the existing well-developed platform technologies (organoids and biofabrication). The iPS platform is also developing well but is still too small to be internationally competitive. The committee recommends further investment in the iPS platform, to bring it into line with other two platforms. It also recommends that the theme leaders should consider defining exosome technology as a fourth platform. Finally, in its opinion, gene editing is crucial for a Regenerative Medicine centre and would add even further value to the organoid and iPS approaches. If not further developed at UMC Utrecht, strong collaborations should be established to enable efficient gene editing to be brought into the program.

9.3. Relevance to society

Regenerative medicine impacts on society generally take many years to achieve, so it is not surprising that there are not yet too many examples of an impact on society. However, there have been some significant and impressive outcomes of the research that are relevant to society. For example, the first IMPACT trial in 35 patients is very important, and it is a pity that the second trial has been delayed through lack of investment in the GMP facility for manufacturing the cell therapy product. Investments are urgently required with respect to the GMP facility for cell products, and the committee specifically recommends that the access fees for UMC Utrecht researchers using the GMP research facility should be reduced. Another prime example of societal relevance is the swelling assay, based on intestinal organoids, that is already used in many centres worldwide as a diagnostic tool for cystic fibrosis patients and to test new drugs and drug combinations.

There is a close connection to and interaction with various patient organisations, and PIs actively utilize different media to communicate with patients and the public. This impressive relation to patients even led to a new research project initiated by a patient organisation. The committee heard about the patenting process and the formation of a spin-out company for joint distraction technology, organoid technology and near to bedside biofabrication. These are all very interesting and important developments, though none has been easy to achieve. Some of the challenges include:

a) researchers experience only limited support for patent-writing and feel they have to write the patent document with minimal legal help;
b) a limitation by UMC Utrecht on the amount of equity inventors can hold in a company whilst employed at the Centre (limited to around 5%). This is out of line with many universities

worldwide and does not incentivise valorisation. As this limitation is only really necessary for clinical researchers running clinical trials to avoid conflicts of interest in patient care, the committee recommends that UMC Utrecht should enforce 5% equity limitation in spin-out companies only for clinical staff running clinical trials. Non-clinical research staff should be allowed a larger equity holding, where appropriate.

c) the decision by senior UMC managers to put all organoid IP into a not-for-profit company (HUB) with small royalty stream to the inventors and no funds recycling directly back into the research programs. Again, this does not incentivise valorisation.

9.4. Viability

The very strong research activity should mean there is a low risk with respect to sustainability. However, from the SWOT analysis and discussions with RM strategic research program managers, it is clear to the committee that sustainability is not completely ensured. Despite the strong commitment of the current staff to the research program, there is serious concern within the program about the loss of staff from the theme without any automatic possibility of their replacement. This is particularly true for non-clinical fundamental scientists, whose positions may not be seen as a priority in times of tight funding. The senior clinical researchers did inform the committee that they support the appointment of fundamental scientists to permanent posts as these positions are critical for linking the basic, fundamental science to the clinical research programs.

Another challenge for the research program is the complete lack of core technical staff funded by UMC Utrecht. This means that there is a constant risk of losing technical expertise when a grant comes to an end unless a salary can be found for the technician(s) on another grant. The lack of overhead funding for the strategic research program means there is no pool of money available to provide a bridging of salary between grants. The lack of effective funding for the GMP facility has delayed a key clinical trial and makes the planning of future clinical trial work difficult.

Notwithstanding this major threat, the current staff are fully committed to the strategic research program and therefore, despite the challenges outlined above, it is likely that Regenerative Medicine will continue to thrive, albeit under sub-optimal conditions.

9.5. Conclusion

The committee strongly recommends the continuation of the Regenerative Medicine & Stem Cell research program and encourages the theme leads to prepare a 5- to 10-year business case outlining a program built around 3 - 5 technical platforms (organoids; biofabrication; iPS; exosomes; gene editing), with consideration being given to the funding of new non-clinical research positions in each of these areas. The business case should be used to open out discussions with the relevant UMC divisions and senior leadership as well as to plan a strategy for achieving increased external grant funding. Finally, the committee would like to underline the clear need for flexible funds for the research program. The leaders of the research program (instead of the leaders of the divisions) should decide about the allocation of these funds within the program.

9.6. PhD training

There is a vibrant PhD community that has been broadened to include a larger number of overseas PhD candidates through participation in a large CoFunds EU program. The matched funding of

additional PhD candidates that is required by the CoFunds scheme has been provided by individual PIs raising funding elsewhere, rather than from core UMC funds. The PhD candidates are very positive about their experience, with no serious concerns expressed about supervision apart from some difficulties for those with clinical supervisors and arranging supervisory meetings with their sponsor. They are also very positive about the research environment in the Hubrecht Institute. There were some specific concerns on small matters which are reflected in the general committee findings, see chapter 3.

9.7. Recommendations

1. Further investment in the iPS platform, to bring it into line with the other two platforms. It also recommends that the theme leaders should consider defining exosome technology as a fourth platform;
2. UMC Utrecht should enforce 5% equity limitation in spin-out companies only for clinical staff running clinical trials and allow a larger equity holding to be allocated to non-clinical research staff, where appropriate.

9.8. Overview of the quantitative assessment of the research program

After having assessed the research quality, relevance to society and viability, and comparing that to the developments and standard in the field of regenerative medicine, the committee comes to the following quantitative assessments:

Research quality:	excellent
Relevance to society:	very good
Viability:	very good

APPENDICES

APPENDIX 1: THE SEP CRITERIA AND CATEGORIES

There are three criteria that have to be assessed:

- Research quality:
    - level of excellence in the international field;
    - quality and scientific relevance of research;
    - contribution to body of scientific knowledge;
    - academic reputation;
    - scale of the unit's research results (scientific publications, instruments and infrastructure developed and other contributions).

- Relevance to society:
    - quality, scale and relevance of contributions targeting specific economic, social or cultural target groups;
    - advisory reports for policy;
    - contributions to public debates.

The point is to assess contributions in areas that the research unit has itself designated as target areas.

- Viability:
    - the strategy that the research unit intends to pursue in the years ahead and the extent to which it is capable of meeting its targets in research and society during this period;
    - the governance and leadership skills of the research unit's management.

Category	Meaning	Research quality	Relevance to society	Viability
1	World leading/excellent	The unit has been shown to be one of the most influential research groups in the world in its particular field.	The unit makes an outstanding contribution to society	The unit is excellently equipped for the future
2	Very good	The unit conducts very good, internationally recognised research	The unit makes a very good contribution to society	The unit is very well equipped for the future
3	Good	The unit conducts good research	The unit makes a good contribution to society	The unit makes responsible strategic decisions and is therefore well equipped for the future
4	Unsatisfactory	The unit does not achieve satisfactory results in its field	The unit does not make a satisfactory contribution to society	The unit is not adequately equipped for the future

APPENDIX 2: PROGRAM OF THE SITE VISIT

Wednesday 30 October	Topic
8:30-9:00	Walk in with coffee/tea
9:00-9:30	Start with committee only: formulating todays goals and expectations
9:30-10:30	Welcome, introduction; research strategy & organisation
10:30-10:45	Short break
10:45-11:00	Research organisation and research support
11:00-11:30	UMC Utrecht perspective on research evaluation
11:30-12:00	Findings of societal stakeholder committee, presentation by chair
12:00-13:00	Grande lunch with panel, dean, research office, research programs
13:00-14:00	Parallel sessions: subpanels @ research programs
14:00-15:00	Parallel sessions: subpanels @ research programs
15:00-16:00	Parallel sessions: subpanels @ research programs
16:00-17:00	Parallel sessions: subpanels @ research programs
17:00-18:00	Private meeting panel & secretary: integrating todays findings
18:00-19:00	Private meeting panel & secretary: integrating todays findings
19:00-evening	Dinner of subpanel couples with research program management/representatives
19:00-evening	Dinner of dean with review panel chair and research office

Thursday 31 October	Topic
8:30-9:00	walk in and committee-only start
9:00-9:15	Welcome and overview of research collaborations
9:15-10:00	Gallery walk with five posters about research collaborations
10:00-11:00	Plenary discussion about research collaborations, with feedback from each presenter
11:00-11:15	short break
11:15-12:00	PhD programs and graduate school of life sciences
12:00-13:00	Parallel sessions: lunch @ research programs
13:00-14:00	Parallel sessions: subpanels @ research programs
14:00-15:00	Parallel sessions: subpanels @ research programs
15:00-16:00	Parallel sessions: subpanels @ research programs
16:00-17:00	Private meeting panel & secretary: integrating todays findings
17:00-18:00	Private meeting panel & secretary: integrating todays findings
18:00-19:00	Private meeting panel & secretary: integrating todays findings
19:00-evening	Walking dinner with panel, exec board, research programs, research office

Friday 1 November	Topic
8:30-9:00	Walk in and committee-only start
9:00-9:10	Welcome and brief introduction
9:15-10:00	Gallery walk with five posters about research support
10:00-10:45	Plenary discussion about research support, with feedback from each presenter
10:45-11:00	Short break
11:00-12:00	Final questions / informal feedback for dean and chairs of strategic research programs
12:00-13:00	Lunch break
13:00-14:00	Private meeting panel & secretary: preparing preliminary findings & presentation
14:00-15:00	Private meeting panel & secretary: preparing preliminary findings & presentation
15:00-16:00	Presentation of preliminary findings and reply executive board, for wide audience
16:00-17:00	Drinks

APPENDIX 3: QUANTITATIVE DATA

This section contains the quantitative data prescribed by the SEP. The strategic research programs each incorporated some supplementary data on publication output (Open Access) and EU funding information in the SEP self-evaluation report.

Research FTE and composition UMC Utrecht

	2018		2017		2016		2015		2014		2013	
	#	FTE	#	FTE	#	FTE	#	FTE	#	FTE	#	FTE
Scientific staff (1)	882	302	757	321	833	280	833	282	856	245	859	228
Post-docs (2)	340	163	331	198	525	279	562	283	391	133	417	138
PhD students (3)	962	552	662	410	403	256	463	275	855	384	870	375
Total research staff	**2183**	**1017**	**1750**	**929**	**1761**	**815**	**1858**	**840**	**2102**	**761**	**2146**	**740**
Other tenured staff	190	91	262	151	NA	NA	NA	NA	261	118	270	125
Total Staff	**2374**	**1108**	**2012**	**1081**	**1761**	**815**	**1858**	**840**	**2363**	**879**	**2416**	**866**

Note 1: Comparable with WOPI categories HGL, UHD and UD; tenured and non-tenured staff
Note 2: Comparable with WOPI category Onderzoeker
Note 3: Standard PhD (employed) and Contract PhDs (externally or internally funded but not employed)

Research FTE of Strategic Research Programs (2018)

Total UMC Utrecht (*)	Brain	Cancer	Child Health	Circulatory Health	I&I	RMSC	Other (**)
1108	**206**	**253**	**72**	**223**	**244**	**92**	**19**

*other staff included
**researchers outside strategic research programs

FUNDING

Brain	2018	2017	2016	2015	2014	2013
National grants (2)	2,645,472	€ 5,958,121	3,515,560	€ 5,353,261	€ 4,785,538	€ 6,248,458
External grants (3)	14,806,416	€ 9,693,711	5,226,790	€ 14,107,627	€ 18,288,026	€ 8,877,901
Contract research (4)	1,624,360	€ 1,863,042	862,107	€ 1,014,745	€ 943,207	€ 1,244,316
Total Funding	**€ 19,076,248**	**€ 17,514,874**	**€ 9,604,457**	**€ 20,475,633**	**€ 24,016,771**	**€ 16,370,675**

Cancer	2018	2017	2016	2015	2014	2013
National grants (2)	€ 5,648,771	€ 6,724,746	€ 9,572,216	€ 3,372,687	€ 4,455,670	€ 6,727,638
External grants (3)	€ 17,575,440	€ 14,711,525	€ 10,874,190	€ 14,460,948	€ 13,049,223	€ 14,998,057
Contract research (4)	€ 7,537,376	€ 1,110,919	€ 7,041,862	€ 2,150,060	€ 1,942,630	€ 2,984,618
Total Funding	**€ 30,761,587**	**€ 22,547,190**	**€ 27,488,268**	**€ 19,983,695**	**€ 19,447,523**	**€ 24,710,313**

Child health	2018	2017	2016	2015	2014	2013
National grants (2)	1,894,871	€ 3,529,020	2,168,355	€ 1,579,184	€ 1,031,585	€ 1,144,430
External grants (3)	4,599,053	€ 5,711,599	7,337,379	€ 2,268,385	€ 3,287,500	€ 3,808,356
Contract research (4)	1,627,640	€ 2,207,749	1,243,258	€ 969,618	€ 1,891,163	€ 624,306
Total Funding	**€ 8,121,564**	**€ 11,448,368**	**€ 10,748,992**	**€ 4,817,187**	**€ 6,210,248**	**€ 5,577,092**

Circulatory Health	2018	2017	2016	2015	2014	2013
National grants (2)	2,275,897	€ 4,168,455	2,920,090	€ 1,120,351	€ 1,743,250	€ 841,440
External grants (3)	4,762,502	€ 8,529,722	8,380,920	€ 3,953,706	€ 4,240,854	€ 6,281,845
Contract research (4)	2,997,926	€ 3,154,502	3,302,322	€ 3,407,703	€ 3,476,394	€ 2,408,798
Total Funding	**€ 10,036,326**	**€ 15,852,679**	**€ 14,603,332**	**€ 8,481,760**	**€ 9,460,498**	**€ 9,532,083**

Infection & Immunity	2018	2017	2016	2015	2014	2013
National grants (2)	€ 1,311,570	€ 3,814,841	€ 2,344,361	€ 3,842,218	€ 3,701,705	€ 3,562,295
External grants (3)	€ 17,481,309	€ 12,963,928	€ 6,500,119	€ 16,586,142	€ 11,688,963	€ 14,265,786
Contract research (4)	€ 3,921,197	€ 14,143,464	€ 5,426,932	€ 7,942,817	€ 3,773,936	€ 3,949,428
Total Funding	**€ 22,714,076**	**€ 30,922,233**	**€ 14,271,412**	**€ 28,371,177**	**€ 19,164,604**	**€ 21,777,509**

Regenerative Medicine & Stem Cells

	2018	2017	2016	2015	2014	2013
National grants (2)	1,186,422	€ 2,716,089	€ 1,036,860	€ 1,775,286	€ 2,197,318	€ 2,556,106
External grants (3)	€ 4,259,474	€ 3,383,714	€ 6,633,557	€ 5,070,750	€ 4,726,931	€ 3,714,171
Contract research (4)	€ 2,429,617	€ 1,364,728	€ 1,445,325	€ 2,206,997	€ 1,021,052	€ 2,075,567
Total Funding	**€ 7,875,513**	**€ 7,464,531**	**€ 9,115,742**	**€ 9,053,033**	**€ 7,945,301**	**€ 8,345,844**

Other Research

	2018	2017	2016	2015	2014	2013
National grants (2)	€ 378,704	€ 1,481,842	2,319,773	€ 19,438	€ 587,974	€ 411,547
External grants (3)	€ 2,743,316	€ 3,312,903	€ 2,197,330	€ 2,406,354	€ 820,307	€ 1,320,820
Contract research (4)	€ 283,326	€ 366,556	512,582	€ 193,066	€ 379,531	€ 383,830
Total Funding	**€ 3,405,346**	**€ 5,161,301**	**€ 5,029,685**	**€ 2,618,858**	**€ 1,787,812**	**€ 2,116,197**

Direct Funding (1) Block funding from government
National grants (2) Competitive grants from Dutch national research funders (e.g. NWO, ZonMw, KNAW)
External grants (3) Grants from external, not-for-profit parties (e.g. European Commission and health charities)
Contract research (4) Grants from industry

UMC Utrecht research funding by source

UMC Utrecht

	2018	2017	2016	2015	2014	2013
Direct Funding (1)	€ 51,400,000	€ 52,100,000	€ 56,300,000	€ 53,900,000	€ 53,900,000	€ 47,100,000
National grants (2)	€ 15,341,707	€ 28,393,113	€ 23,877,213	€ 17,062,423	€ 18,503,039	€ 21,491,913
External grants (3)	€ 66,227,511	€ 58,307,101	€ 47,150,283	€ 58,853,910	€ 56,101,803	€ 53,266,936
Contract research (4)	€ 20,421,442	€ 24,210,959	€ 19,834,387	€ 17,885,006	€ 13,427,912	€ 13,670,862
Total Funding	**€ 153,390,660**	**€ 163,011,173**	**€ 147,161,883**	**€ 147,701,339**	**€ 141,932,754**	**€ 135,529,711**

Direct Funding (1) Block funding from government
National grants (2) Competitive grants from Dutch national research funders (e.g. NWO, ZonMw, KNAW)
External grants (3) Grants from external, not-for-profit parties (e.g. European Commission and health charities)
Contract research (4) Grants from industry