Research assessment

Leiden University Medical Center

2018

Preface

The evaluation committee owes thanks to the Board of the LUMC and all the Programme Directors for the excellent preparation of the documents for the review. The committee experienced the meetings with the delegations of the programmes and profiles as extremely useful and appreciated the open nature of the discussions. The overall quality, societal relevance and viability of most of the programmes was very good with some excellent scores and some good scores. The Graduate school has made a good start but needs to be further professionalised. The arrangements for research integrity are state of the art, whereas the mechanisms to increase diversity and internationalisation should be further professionalised and more integrated into the organisation of human resources. With respect to the planned transition of the seven profiles to ten themes, the committee concluded that generally the profiles are felt to have been helpful to support interdisciplinary research and to enable the establishment and support of infrastructure. Further steps in this direction would be welcomed by the organisation. However, when these steps are taken, the committee feels that the 59 research programmes should be disbanded and a proper balance between the department chairs as the human resource managers, the division leadership as the organisers of the clinical and research infrastructure and the leadership of the themes as the research content managers should be developed.

Finally, the support of Marielle Kroon as the omnipresent facilitator and the two secretaries of the committee, Annemarie Venemans and Meg van Bogaert, made a difficult job feasible and pleasant.

Sibrand Poppema
Chair

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1. Introduction

1.1 The Netherlands System of Quality Assessment of Research

The Executive Board of the Leiden University Medical Center (LUMC) invited an international committee to review its scientific research. This quality assessment is part of the six-year cycle of evaluation of research in all Dutch universities and University Medical Centers (UMC's). It is guided by the Standard Evaluation Protocol (SEP) of the Royal Academy of Sciences and Arts of the Netherlands (KNAW), the Netherlands Organisation for Scientific Research (NWO) and the Dutch Association of Universities (VSNU). The aims of the evaluation are:

- to assess the quality of the research output of LUMC research programmes;
- to assess the position of and focus of LUMC research according to national and international standards of quality, societal impact and viability;
- to reflect on the prospects of the research, with recommendations on strategies for the future.

In addition, according to the SEP, the assessment considers three further aspects: the Graduate school, research integrity and diversity. The LUMC has recently drawn up a new strategic plan describing an organisational change in the structure of the research organisation: a transition from seven research profiles to ten themes. The LUMC has therefore asked the committee to pay special attention to the way the seven research profiles can be further developed to the ten identified themes. It also asked the committee to provide recommendations to increase the added value of the new themes to support the LUMC organisation towards its strategic targets.

This report describes findings, conclusions and recommendations of this external research assessment of the LUMC. Each research programme is reviewed in relation to programmes and institutes worldwide in similar disciplines and on similar topics. Consequently, the research programmes within the LUMC working on different research topics are not compared to each other. This might lead to differences in argumentation of a certain score, for example when it comes to critical mass and size of a research programme, or amount of external funding obtained.

1.2 Organisation of the review

The Executive Board of the LUMC invited one core committee and four expert committees to assess the research programmes conducted in the four divisions of the LUMC. The four specific expert committees received a self-evaluation report of the division they were assigned to and visited the LUMC between May 23th and May 30th, 2018. Additionally, the core committee interviewed the Executive Board, Division leaders, researchers of the seven medical research profiles, management and PhD students of the Graduate school and

researchers involved in integrity and diversity policy to provide a qualitative assessment of the LUMC in relation to its strategic targets.

Prior to the interviews, each research programme was assigned to two expert committee members as reviewers, who independently formulated a preliminary assessment. The final assessments were made by the entire specific committee accompanied by the core committee members, based on the documentation provided by the LUMC, the key publications and the interviews with the researchers of the research programmes. After the interviews on the research programmes of each division the committee discussed its findings and the scores. The drafts for this assessment report were finalised through email exchanges. The final version was presented to the LUMC for comments concerning factual inaccuracies.

1.3 The review committee

Members of the review committee were:

Core committee:

- Professor Sibrandes Poppema (chair), University of Groningen;
- Professor Jan Goffin, KU Leuven (Belgium);
- Professor Ernst Hafen, ETH Zürich (Switzerland).

Committee division 1:

- Professor George Hamilton, University College London (UK);
- Professor Freddy Hamdy, University of Oxford (UK);
- Professor Gordon Drummond, University of Edinburgh (UK).

Committee division 2:

- Professor Brian Walker, Newcastle University (UK);
- Professor Jérôme Bertherat, Cochin Hospital Paris (France);
- Professor Roderic Pettigrew, Texas A&M University (USA);
- Professor Katja Simon, Kennedy Institute of Rheumatology, University of Oxford (UK);
- Professor George Hamilton, University College London (UK).

Committee division 3:

- Professor Jes Olesen, University of Copenhagen (Denmark);
- Professor Simon Herrington, University of Edinburgh (UK);
- Professor Bernard Sabbe, University of Antwerp (Belgium);
- Professor Jan de Maeseneer, Ghent University (Belgium);
- Professor Colin Morley, University of Cambridge, (UK).

Committee division 4:

- Professor Marcel van den Brink, Memorial Sloan Kettering Cancer Center, NY (US);
- Professor Anton Berns, Netherlands Cancer Institute, Amsterdam;
- Professor Rick Maizels, University of Glasgow (UK);
- Professor Diana Kuh, University College London (UK).

All members of the committee signed a declaration and disclosure form to safeguard that the panel members judge without bias, personal preference or personal interest, and that the judgment is made without undue influence from LUMC or stakeholders. Any existing professional relationships between committee members and programmes under review were reported. The committee concluded that there was no risk in terms of bias or undue influence.

2. Assessment of the scientific research of the LUMC

2.1 Mission, goals and research strategy of the LUMC

Findings

The LUMC has as its mission that as an innovator, it aims to improve healthcare and people's health. The LUMC will achieve this mission by providing patients with optimised, state-of-the-art healthcare based on pioneering research and innovative teaching, in cooperation with its partners within and outside its region. The ambition of the LUMC is to become one of Europe's top ten University Medical Centres affiliated with a research-intensive university.

The research at LUMC is organised in departmental research lines, or research programmes. The heads of the departments are fully responsible for the research within their department. Many of the forty departments have one research programme, some have two or more (up to four) research programmes. The size of the research programmes differs strongly, the committee had to review research programmes with less than one research fte up to research programmes with close to twenty research fte's.

In 2012, the Executive Board established seven medical research profiles to combine research efforts in broad biomedical domains and bring answers not found when working in a stand-alone fashion. There are four biomedical research profiles and three generic research profiles. A biomedical research profile aims at a specific biomedical theme, while a generic profile has a generic approach and aims for example at the development of an approach of a certain research area, not related to a specific biomedical theme. Every research programme within the LUMC relates to one biomedical research profile and with at most two generic research profiles.

At the beginning of 2018, the LUMC presented a new strategic plan: 'Getting better by breaking new ground'. This strategic plan outlines LUMC's vision on further developing its research organisation. The focus will be on three priorities for society: cancer, regenerative medicine and population health. Based on the demand from society and the reputation that LUMC aspires to, it has therefore been decided that the research profiles will be further developed into ten thematic areas that address the questions raised by society and LUMC's three priorities as much as possible. In addition, there will be three fundamentals for innovation: 1) Biomedical imaging, 2) Data Science, Bio-Informatics & Research Methodology and 3) Technological Focus Areas, Facilities & Clinical Research Support. The ten themes and three fundamentals will further link the focus areas in patient care and research.

Considerations

The committee applauds the initiative of the medical research profiles implemented in 2012. During the site visit the committee noted that most researchers believe in the added value of these profiles and support this research strategy. Researchers mentioned that the profiles

gave them the opportunity to bring their research to a next level in terms of research collaborations and shared investments.

The committee concluded that the current structure of research programmes and medical research profiles has worked well with regards to coordination of research and research facilities. The initiation of the medical profiles resulted in a better investment strategy and more cross-fertilisation of research projects. The committee noted that the new strategic plan is another step forward to reorganise the research organisation of the LUMC. It applauds the alignment between patient care and research in the new plan. However, according to the committee, several managerial decisions must be made with the introduction of this new structure in themes.

First, the committee believes that the introduction of ten themes and three fundamentals for innovation in addition to 59 research programmes will further increase the complexity of the research organisation. It therefore recommends including all research of the LUMC only in research themes and not in research programmes anymore. It suggests to, for example, appoint or attract a research coordinator in each department who coordinates the organisation of research, personnel and equipment of the department over the themes.

Second, the committee suggests strong leadership of the themes, in terms of prominent professors with overview. These leaders should closely interact with department heads and research coordinators. In addition, more central governance and strategic steering is desirable to effectively align theme development and research priority decisions.

Third, the committee urges the board to balance the power of departments and themes. Currently, medical profiles have limited funding at their own disposal since resources are linked primarily to the departments. This compromises the freedom to operate in terms of planning and implementing new initiatives and limits the development of the profiles. With the introduction of the themes, the committee advises to change this funding model to create a direct link between funding and scientific leadership, research excellence or research strategy. The committee recommends the board to make sure that the relevance of the three new so-called 'fundamentals for innovation', 1) biomedical imaging, 2) data science, bio-informatics & research methodology and 3) technological focus areas, facilities & clinical research support, will not be reduced to providing excellent service to research activities inside the thematic areas, but that PI's from the three 'fundamentals for innovation,' will be allowed and even encouraged to go ahead with their own strong independent research as well.

2.2 Career planning

Findings

The LUMC is focussing on recognising talent at an early stage in order to conduct research at the highest level and obtaining external grants. The LUMC Graduate School is established to encourage young talent.

Strategic talent management is the joint responsibility of each department, the division and the Executive Board. From the self-evaluation report it becomes clear that LUMC considers scouting talent internally and externally an important step. Subsequently, ensuring that a talented scientist can work in the right position, followed by making clear arrangements about the desired career. For this the LUMC will work on a tenure track policy over the next few years.

Considerations

The committee noticed that, like many other Dutch universities, the LUMC has a high number of PhD students in relation to the number of postdocs. The incentive of a promotion-bonus for PhD students has led to a very low number of postdocs across Dutch universities. The committee considers that improving the balance between PhD students and postdoc researchers will not only boost the quality of the research, it will also fill the pipeline for talented researchers.

By not having formally introduced the tenure track system, the LUMC seems to be lagging compared with other Dutch Medical Faculties. The committee believes the LUMC risks losing very talented young scientists, who might find a more secure future elsewhere. The fact that some departments decided to organise a tenure track system themselves should clearly not be ambitioned and might even be a risk factor because differences between departments on this aspect could lead to lawsuits. The committee strongly recommends introducing an institutional policy on tenure track sooner rather than later. This will add to the transparency and clarity on hiring policy and will result in increased attractiveness of the LUMC to young, talented researchers. Those who left the LUMC and the Netherlands to do an international postdoc, will be tempted to return if there is a perspective of becoming full professor in time.

2.3 Support at LUMC level

Findings

The LUMC has implemented the decision making at the level of the departments. The human resources of individual scientists below professor level at the LUMC are the responsibility of the departments and thus department heads. In addition, the larger departments in general have the critical mass to not only do high quality research but also have the financial freedom to hire specific expertise that is required to do the research.

Considerations

The committee concludes that on the one hand decision-making at departmental level makes clear where responsibilities lie, but at the same time it potentially makes it more difficult to have strategic appointments that involve more than one department.

In addition, the committee noticed that specifically the smaller programmes/departments were struggling with several organisational issues:

1. Clinical trial unit (CTU)

The LUMC does not have a central clinical trial unit. Larger programmes were able to deal with this by setting up their own trial unit and hiring the required expertise within the programme. Smaller groups tried to join the larger departments, but this was not always successful. The LUMC should consider dealing with this issue, although the committee understands that larger departments do not necessarily want to join a general CTU. The committee therefore recommends a central CTU where larger departments have their own CTU officer whose employment is shared by the CTU and the department. This person would know the specifics of clinical trials in the discipline of the department. Smaller departments can share this function.

2. Technology Transfer Office

Some of the smaller research programmes indicated that despite the existence of a Technology Transfer Office (TTO, see also 2.5 on societal relevance), it is difficult to get the right support with respect to the valorisation of the research outcomes. Like the clinical trial unit, larger research programmes manage better as they can hire specialised support themselves. The committee suggests that the LUMC considers institutionalising thematically specialised TTO officers.

3. Bio-informatics support

The committee noticed that the perspective of the departments with respect to usefulness of the Bio-informatics support was varying strongly. Several departments were very happy with the support and considered the department of Bio-informatics to be very accessible. Other - often larger – departments were able to hire their own experts on specific topics, for example a postdoc. Initially the committee had some minor concerns on this, as the postdoc that was hired might be at risk of becoming isolated from his or her own field of expertise. However, on multiple occasions, the committee was reassured that the hired expert in one way or another was embedded in the Bio-informatics department. Finally, several departments stated that it was difficult to connect to the department of Bio-informatics and find the required expertise. The LUMC is recommended to look for a solution for these groups, for them to also make use of the high-quality Bio-informatics department, or appointment of themes specific bio-informatics officers.

2.4 Facilities and infrastructure

Findings

In the self-evaluation report it is stated that a future-proof infrastructure is essential for research and innovation. During the site visit, the topic was regularly discussed and there

seems to be satisfaction on the developments on research equipment in the recent years. A topic of discussion remains the organisation of the equipment and the physical location of the different laboratories. Some research labs already have merged and have been renovated successfully. Others will have to follow in the upcoming period. Several research programmes that collaborate are physically not connected in their labs, or offices. In many interviews it was stated that collaboration would be facilitated if the offices or laboratories would be next to each other.

Considerations

Overall, the committee has a very positive impression with respect to the facilities and equipment at the LUMC. A point of attention is the maintenance and replacement of research equipment. It is relatively easy to get external funding to acquire new, state of the art equipment. However, external funding to replace or maintain this equipment is much more difficult to get. The Executive Board of the LUMC should consider an internal funding scheme. The committee recommends the relocation of offices and laboratories in such a way that people who work together are also physically located near each other. The committee realises that relocation of laboratories is more easily said than done and recommends starting to share offices.

2.5 Societal relevance

Findings

All research programmes are individually scored on their societal relevance and impact. The committee did make some general observations that surpass the programme level and even the departmental level.

LUMC supports the valorisation of promising innovations often in public-private partnerships with existing or new companies. Luris, the Technology Transfer Office (TTO) of Leiden University and LUMC, connects academics to the market and society at large, to make the most of their scientific knowledge. The LUMC is putting focus on not only doing high quality research, but also on translating the outcomes to the clinic.

Considerations

The committee is positive about the fact that the LUMC and the University of Leiden have set up Luris, of which 50% works for the LUMC. However, the smaller departments seem to struggle with the expertise that is needed on issues related to TTO. Larger groups decided to set up their own support, since the required specific expertise could not be gotten from Luris.

The LUMC is putting focus on not only doing high quality research, but also on translating the outcomes to the clinic. This translational research could very well be the unique selling point of the LUMC. Bringing together basic researchers and clinicians was mentioned

throughout the site visit by both clinicians and more fundamental researchers. The committee emphasises the importance of including patients/citizens in the research. Not merely by using them as test objects and collecting information from them, but by actively involving them in the generation of research data. With that rapid raise in the quality and in the reduction in cost of smartphone and other mobile sensors this patient/citizen participation will be gaining importance rapidly in the upcoming years. According to the committee the LUMC is in the perfect position to, in a trustful manner, make healthy citizens and patients' partners in their research. The documented willingness of citizens to contribute their data for scientific research combined with their role as maximal data aggregators offers new ways of systematic patient reported outcomes (PRO) research via smartphone apps and the transformation of Leiden's established patient cohorts into cohorts in which citizens/patients continuously contribute real world personal data, including nutritional and socio-economic data.

2.6 Research integrity

Findings

To promote and maintain an ethical research environment, LUMC works with rules and conditions imposed by Good Research Practice. Part of this involves the training of young researchers, but also organising regular meetings for all researchers to discuss integrity.

With effect from 1 January 2018 the Leiden University Committee for Academic Integrity and the Committee for Scientific Integrity at the LUMC have been merged into a single committee. Leiden University and LUMC each have appointed a Confidential Advisor and installed a Committee Scientific Integrity with new regulations and a dual chairmanship. The Confidential Advisor is the first to contact for questions or complaints about Research, e.g. conflicts about authorship. During the site visit, it became clear that in addition to the Confidential Advisor a technician and PhD student are appointed as trust persons.

Open Access and the FAIR (findable, accessible, interoperable and reusable) data principles are important in the LUMC strategy.

Considerations

The committee is pleased with the processes in place for ensuring research integrity. In its opinion, the LUMC is aware of the ethical dimensions of science. The committee applauds the merger of the integrity committee of University of Leiden and LUMC. It is also very positive about the appointment of trust persons that lower the barrier for PhD students and technicians to make mention of issues they encounter.

Although the LUMC is well ahead in its approach to research integrity and good research practice, the committee believes it might be even more an integral part of the culture of the LUMC. For instance, the committee noted that some policies and tools are still in the

implementation phase, such as the introduction of electronic lab journals, co-authorship agreements, and data management access.

2.7 Diversity and internationalisation

Findings

In addition to the diversity policy as described in the self-evaluation report, the committee interviewed representatives of two committees. The first committee, Vitaal, is a network for female academics and is intended to improve the position and opportunities for all (female) academic personnel at LUMC. In this network the focus lies on skills training and many activities are organised. Furthermore, the committee provides solicited and unsolicited advice to the Executive Board of the LUMC. The second committee focuses on enhancing internationalisation at the LUMC. Predominant focus lies on the educational programmes, but also on international collaborations. The present committee on internationalisation only recently started. The percentage of international professors was 5.5 % in 2016. The number of female professors is slightly increasing, from approximately 19% in 2012 to 22% in 2016. The aim of the LUMC is to have 24% female professors appointed by 2019.

Considerations

The committee was impressed by the enthusiasm and approach of the representatives of the two committees. It did notice, however, that the embedding of the committees in the organisation of the LUMC could be improved. The committee recommends involving HR and prioritise institutionalisation of the committees. Currently, a lot is depending on voluntary activities by those involved. For example, the committee Vitaal supported several initiatives on external funding, while these could and should be supported by institutional money. By formalising and embedding these committees with the Human Resources department, the Executive Board of the LUMC will get them closer to the organisation, which will subsequently improve their impact. The committee believes continued attention to and formal embedding of diversity issues is necessary. Although the LUMC seems to reach its own goals, the number of female professors is, like in many other universities, too low. LUMC should consider increasing the percentage of newly appointed female professors. At the same time the LUMC should make efforts to substantially increase the number of professors from abroad. The start-up of a central tenure track system might be a first step.

2.8 Recommendations

The committee recommends:

- to reduce the complexity of the research organisation of the LUMC by including all research only in research themes and not in research programmes;

- to increase the power of the themes by changing the funding model, strong leadership and more central steering;
- to introduce a tenure track system;
- to give all themes access to a central clinical trial unit, bio-informatics support and Technology Transfer Office (TTO);
- to provide internal funding to replace or maintain equipment;
- to actively involve citizens in the generation of research data;
- to implement a comprehensive strategy covering multiple aspects of integrity, including electronic lab journals, co-authorship, transparency and data management and access;
- to increase the percentage of newly appointed female professors and professors from abroad.

3. LUMC Graduate school

Findings

The LUMC has one Graduate School, of which the Dean is the Director. An independent Graduate School Committee with representatives from the Medical Research Profiles, the Master Curricula and the PhD student population advises the Dean on matters concerning PhD education. At LUMC, PhD students are appointed to a department and linked to one of the Research Programmes.

The LUMC offers PhD students education that typically consists of specific (specialist) courses and lecture cycles and Summer School-like activities. PhD students are also offered a series of Generic Biomedical Courses and Transferable Skills training courses. There are three mandatory courses for all PhD students:

- PhD introductory meeting;
- Basic Methods and Reasoning in Biostatistics;
- eBROK course (basis regulations in the organisation of clinical research).

The LUMC recruits candidates for a vacant position via open application and by way of a selection committee. Talent scouting in the (international) research and educational networks plays a prominent role in identifying talented PhD students.

Each PhD student is required to have at least two thesis advisers of which one must be a full professor. In addition, all PhD students must have a Guidance Committee of at least two senior researchers not directly involved in the PhD research. This Guidance Committee meets once a year with the PhD student to discuss research progress, education and supervision. The committee considered the self-evaluation report and interviewed the Dean accompanied by coordinators of the PhD programme and the chair of the LUMC Association for PhD candidates (LAP). The Chair of the Graduate School Committee was, unfortunately, unavailable at short notice. The committee also interviewed a group of four PhD candidates including the chair of the LAP.

Considerations

Overall the panel recognised the central role of PhD training at LUMC. The clear majority of students receive good training in strong research groups, and the LUMC Association for PhD candidates (LAP) is an asset and is proactively involved in responding to candidates' needs (e.g. for career or personal advice). Finally, the employability of PhD graduates is extremely high.

The committee identified some specific concerns:

- inconsistencies between the perspectives of the PhD candidates (specifically international) and the senior leadership team regarding the clarity of supervisory arrangements (co-supervisors could not always be identified by candidates) and the

role of the Guidance Committee (attendance and even conduct of the required meetings appears to be sporadic);
- the limited diversity of candidates recruited through local rather than international advertising, e.g. with ca. 80% candidates Dutch;
- the apparently limited scope for 'student-centric' PhD project design and selection, with many if not most candidates following 'off the shelf' projects;
- the lack of a career guidance centre at an institutional level, that assists PhD students, who have questions about their careers, and that advices them about labour market topics and opportunities, both academic and non-academic, both national and international
- the high proportion (ca. 30%) of students taking longer than five years to graduate;
- the high proportion (ca. 20%) of supervisors with responsibility for more than eight students simultaneously;

One of the reasons for the high proportion of PhD-students who need more than five years, as well as for the high number of students to be supervised by one individual professor might be the fact that most of the medical school graduates who have the ambition to be selected for a clinical residency programme must start with a fulltime research project, that takes three to four years prior to starting their residency. A number of these MD PhD students finish their PhD during the clinical years that follow the research project years. This situation is not without risk from a few perspectives: first, some future clinical specialists might not be genuinely interested in performing (basic) research, which might jeopardise the quality of the research that is performed. Consequently, not necessarily the best candidates (from a research point of view) are selected for the PhD projects. At the same time, some potentially excellent future clinicians might be discouraged by the long duration of the full research time before they go into clinical training and therefore might not enter a residency programme at all. Eventually one must consider that clinical specialists will have reached the age of about 35, before they start practising independently, which is old from an international perspective;

In the context of the overall review of research at LUMC the committee noted:

- that PhD candidates are the responsibility of individual departments, with apparent variation in practice (including, for example, permission for candidates to participate in training courses);
- that it was unclear how many students benefit from co-supervision across departments;
- the high numbers of PhD candidates relative to academic and postdoctoral research staff, despite the leadership ambition to grow postdoctoral training opportunities;
- the questionable reliability of data generated from the (recently implemented) LUMC information management system for each of the research programmes (with research directors questioning the data).

It is recommended that:

- the PhD candidate cohort be considered as a strategic agent for change at LUMC, and as part of a more visible and coordinated career development plan at LUMC which extends beyond doctoral training;
- teaching and courses on how to become a good lecturer in a time when medical training is undergoing a digital transformation should be strengthened;
- LUMC considers developing thematic PhD programmes which span disciplines and departments and involve PhD candidates proactively in project design and supervisor selection;
- proactive and recurring anonymised surveys be conducted of student satisfaction as well as understanding and execution of supervisory and Guidance Committee roles by students and academics, followed by action to address deficiencies in process;
- targets are set for PhD completion times, with clear incentives for supervisors and candidates to achieve these and a systematic approach to overcoming disincentives to completion (e.g. competing demands of clinical service delivery);
- (international) recruitment be modernised to exploit social and other media and attract a more diverse community of PhD candidates;
- efforts should be reinforced to address the under-representation of post-doctoral training opportunities at LUMC, e.g. by encouraging principle investigators to request external funding for such posts.

4. Assessment of the research programmes - Division 1

4.1 Anaesthesiology/Intensive care

Department:	Anaesthesiology/Intensive care
Research programme:	10101
Scientific staff (2016):	7.7 fte
Quality:	2
Societal relevance:	2
Viability:	2

Brief description of the research programme:

The programme's aim is to improve acute and perioperative care outcomes in patients with often complex conditions, and improve outcome in patients with chronic pain, particularly after trauma and those with neuropathy. The programme is the result of a merger between anaesthesia and intensive care in 2016 and with experimental pain research in 2017, following comments in the previous review and interim review. It has three elements:

1. Translational pain research: experimental studies, in animals and humans;
2. Perioperative care: optimizing outcome, using a variety of clinical studies;
3. Intensive care: optimizing outcome.

Within the LUMC, cohesion is strong. The principal investigators of all studies form a joint research committee, and PIs and postdocs supervise research units.

Research quality:

All the elements in the programme are of clear relevance, although the first two are more likely to yield early and clear results. Large scale data collection, for example of pain phenotypes, may prove valuable. Progress of the previous core research review has been very good, internationally recognised in pharmacokinetic/pharmacodynamic modelling and the development of valuable tools to assess drug properties. Innovative studies of profound muscle relaxation have had substantial impact and should be continued to assess long term clinical outcomes. The use of advanced statistical modelling and modern methods of statistical analysis such as decision trees is a substantial strength.

Smart telemedicine monitors promise a future valuable research stream. Novel aspects of neuropathic pain investigation are using confocal imaging of the corneal nerves, which provides a promising technique with scientific and therapeutic value.

Clinical research is strong, with several mechanistic and outcome studies in progress, and an increasing number of clinical trials. Teaching links with other specialties may help sustain collaboration. Intensive care research is less active, addressing the effects of appropriate

oxygen therapy, and collaborative large-scale outcome studies. There are few recent publications. Future research aims, particularly improving teamwork, are promising, with societal advantages. Generally, the publication record and external funding of the department is very good.

Relevance to society:

The social relevance of almost all the research is substantial: long-term pain is an important contributor to morbidity, and the research interests of the department directly address several elements of this problem. The public importance of excessive opioid prescription with addiction and overdose is probably under-recognised. This is being addressed, with many media impacts, but would require a more co-ordinated and systematic approach to be fully effective. Likewise, better management of both acute postoperative and chronic pain may well respond to the large-scale analysis and modelling being done: this too would require systematic promotion. Research on appropriate levels of oxygen therapy during intensive care has been used for national and international guidelines. Development of better methods of pain relief, with less side effects, is clearly of direct social benefit. In addition, better understanding of the factors that affect outcome and reduce complications is likely to improve satisfaction and well-being, if translated into widespread practice.

Viability:

The use of personnel in the programme is excellent, with retention of trained staff in key research management positions. Several promising elements of research are open, and there is the potential for commercial development in some of these although large scale evaluation studies would be required. Careful planning of succession for some positions will be needed to be certain that progress is maintained in the successful fields. Not all the current research avenues may prove fruitful, and careful monitoring of progress may be needed to avoid wasted effort. Setting progress goals would guide future resource allocation, particularly the primary workforce which is PhD students.

Conclusion and recommendations:

The programme has made clear progress since the last review. It has an effective organisation and seems well integrated. Sustaining the interest of clinical colleagues in research would be an important element, and a more strategic approach to societal impact would be advantageous. Better linkage of clinical data collection systems appears to be needed.

4.2 Surgical Oncology

Department:	Surgery
Research programme:	10202
Scientific staff (2016):	10.9 fte

Quality:	2
Societal relevance:	2
Viability:	2

Brief description of the research programme:

The aim of the research programme is to improve diagnosis and treatment of cancer focussing on 1) technological innovation in surgical intervention, 2) personalised medicine, and 3) clinical trials and outcome research. The research aims to better individualised health care for patients by technical innovations, improved evidence-based medicine through clinical trials and improved risk prediction. The multidisciplinary research programme strengthens the research pipeline from basic research to high-end patient care.

Research quality:

The activities of the Surgical Oncology programme are very well described, although more detail would have been helpful, but understandably this was restricted by space in the self-evaluation report. Of the three themes outlined, the stellar and world-leading component is undoubtedly the image-guided surgery programme. This demonstrates a very strong multidisciplinary team and multicentre efforts with good industry links and investment to move the boundaries of precision surgery and develop exciting and evolving new technologies with promising impact. The next strongest component is the formation and exploitation of a large biobank of stored material from patients. While this had been performed *ad hoc* in the past, LUMC has now created a new organised institutional structure, which the specialty is using. A team of scientists provides the basic and translational research component. This complements well the other strengths of the department, and tangible examples of added value were given to the panel. The clinical trial portfolio is strong, with many PIs from the Leiden department. Metrics suggest that the scientific staff have a very good research income track record, almost four-fold the amount received from direct funding. Out of the nine selected publications by the group, six are stellar, and three are very good. There are strong synergies between Surgery and Urology, and it is a pity that the departments are separated structurally.

Relevance to society:

The research programme demonstrated very good societal value for their work, which closes the loop well between bench and bedside. There is strong engagement with media and the

public, and all themes are highly relevant to society in general. A greater formalised engagement with patients, and formal patient support groups would be very useful and helpful in developing surgical oncology research strategy and needs further development. The major advances in achieving 'precision surgery' will be transformational to society and health care providers.

Viability:

The training and development of trainees and mentoring of young talented surgeons to become 'surgeon scientists' is excellent and is likely to foster surgical academic careers in the future. The team and Head of department must be congratulated for their approach. The committee was particularly impressed by their efforts in providing protected research time and an excellent, supportive and multidisciplinary research environment. It is a great pity that the synergies between Surgery and Urology are not exploited fully, because of organisational structures, which need to be explored further. The external funding track record is very good. Bigger, more ambitious sustainable research programmes are achievable, to be led from LUMC, particularly from International sources like NIH and the European Commission.

Conclusion and recommendations:

- The Surgical Oncology programme presented a cohesive, strong research programme, which has developed over the years into very good collaborative and multidisciplinary efforts. Members of the team who attended the interview responded well to the queries and provided additional helpful information;
- The research quality is very good overall, with a stellar component in the image-guided surgery work, which has tremendous future for transformational changes in precision surgery, and the creation of health and wealth for society;
- There is a robust basic and translational research component, creating a very good environment for surgeon scientists, but there needs to be stronger cohesion between the programmes with medium to longer-term vision about taking ideas from conception and discovery, through to development, first-in-man and evaluation in large phase III comprehensive clinical trials;
- The committee also recommends further discussion regarding a possible merge between Surgical Oncology and Urology to strengthen both specialties, synergise talent and expertise, bringing together a larger critical mass of surgical academics;
- The synergy between surgical oncology and cancer research strategy at LUMC, which was not clear at the time of the interview nor in the documents submitted but raised as a threat - needs to be developed as a more cohesive and visionary long-term programme.

4.3 Transplant Surgery

Department:	Surgery
Research Programme:	10203
Scientific Staff (2016):	0.7 fte
Quality:	3
Societal relevance:	2
Viability:	2

Brief description of the research programme:

The aim of the programme is to optimise the ability to assess, improve and/or repair organs prior to transplantation, and to develop novel immunotherapeutic interventions to improve outcomes. The research has traditionally centred on elucidating the molecular and metabolic pathways of ischemia/reperfusion injury in transplantation and using registry databases. The recently established Transplant Centre and the Organ Preservation and Regeneration Room allowed the programme to initiate the development of new innovative research themes.

Research Quality:

The LUMC Transplant Centre was only recently established in 2017 with the appointment of a new leader. It is therefore not possible to assess research quality based on one year's follow up and comparison with previous reviews is not realistic. Throughout the interview the programme leader responded cordially and realistically to the various questions and most importantly encouraged contribution from his attending colleagues where required. With the new appointments come established and future proposals for national and international collaborations within the research theme of transplant surgery. Regarding the research strategy of the Transplant Centre, three items of focus were detailed, namely ex-vivo machine perfusion research, ischaemic/ reperfusion research, and transplant outcomes. The specific clinical research areas relate to transplantation in kidneys in which 100 are performed a year, liver and pancreas both approximately 30 a year. In addition, there are islet cell transplants. Many major Transplant Centres have an ex-vivo perfusion programme but here there is necessary focus into improving the function of ex-vivo supported organs and in reduction of ischaemia re-perfusion once transplanted.

Regarding ischaemia re-perfusion, this PI has been incorporated from Vascular Surgery because of his expertise in ischaemia re-perfusion injury and the role of metabolism. Regarding Transplant Outcomes there is a focus on the predictors of outcomes after liver transplantation, risk factors in pancreas transplantation, assessment of donor and recipient risk factors in liver transplantation in addition to other outcome measurements. There appears to be satisfactory focus on these research areas with appropriate diversification of

several interested members of the Transplant Centre. There is a total of ten fte's devoted to transplant care in total. This is with dedicating one day a week to non-clinical time which can be used for research. All the surgeons within the Transplant Centre will have an academic interest either clinical research or in education and accreditation programmes for clinical training and transplantation. During the interview it was clear that this new Transplant Centre is well led with focus to the future consolidation the LUMC Transplant Centre as a major international entity.

Relevance to Society:

Outcomes from the research focus on ex-vivo perfusion and ischaemia re-perfusion injury have the significant potential societal impact of increasing the number of donor organs available for transplantation. This new group are engaging with the Dutch Transplant Foundation and Eurotransplant focused on organ donation and allocation.

Viability:

The members of the centre feel well supported by the LUMC, particularly with the allocation of more clinical and research personnel and support for collaboration with other departments. There has been an historical increase in funding as documented in 2016 before the new centre was set up. Regarding current and future funding, during 2017 two new grants, including one on kidney perfusion have been awarded. There is also a significant application under review to add significant income from the Benefit Fund. There is clarity of vision and focus evident with the new leadership, new blood since establishment of the Centre in 2017. Overall, the viability appears to be very good although after only one year it is impossible to be more objective.

Conclusion and Recommendations:

- This is a very promising reorganised research programme which is actively engaged after only one year of existence in all relevant areas of its growth and consolidation. LUMC should continue to strongly support the development of the Transplant Centre;
- The Centre should continue to develop and build on its collaborations nationally and internationally particularly based on the strong links with Canada and Oxford;
- The incorporation of ischaemia re-perfusion into the Transplant Centre seems logical. It is however a potentially uncomfortable arrangement in that the PI is working within two departments in similar but differing research programmes. It is recommended more clarity and focus on his future role in transplantation;
- The volume of renal and pancreas transplants is acceptable for a major Transplant Centre; however, 30 liver transplants a year is low by international comparisons. Collaborations with other Dutch centres for liver transplantation, perhaps with centralisation, should be explored as a strategy to increase the number of transplants performed and should be a major focus of this new centre, not only in terms of clinical

outcomes as such, but also from the perspective of relevance of clinical research in the field;

- At this early stage of the Transplant Centre collaborative research strategies with Nephrology, Hepatology and Diabetology should be explored and defined.

4.4 Orthopaedics, Trauma Surgery and Rehabilitation

Department:	Orthopaedics and Surgery
Research programme:	10404
Scientific staff (2016):	10.1 fte
Quality:	3
Societal relevance:	3
Viability:	3

Brief description of the research programme:

This joint programme distinguishes two research themes, *Prognostic Clinical Modelling* and *Optimising Clinical Outcome.* Some of the topics the research programme addresses are unsatisfactory and varying clinical outcomes and complications after intervention of knee or hip arthroplasty, hip, ankle or wrist fractures. By aiming at the better selection of patients for specific management strategies the programme contributes to the concept of Value Based Health Care. LUMC has been appointed as level-1 regional Trauma Centre and as such is charged with the provision of complex trauma care. Although the biomedical research theme *Cancer Pathogenesis and Therapy* focuses mainly on basic research, clinical evaluation of the patients adds to this profile.

Research quality:

This is a recently merged programme with the three components of Orthopaedics, Trauma and Rehabilitation. The merge was executed on the recommendation of a previous review to strengthen the themes. Although each of the components had specific strengths, the cohesion between them was lacking and needed further development towards a forward-looking focused strategy and improved vision. It was difficult for the committee to understand, for instance, the place of Cancer Pathogenesis and Therapy in the programme, and the cross-fertilisation with the rest of the work. There is a rich bone sarcoma programme, but it was insufficiently highlighted, and its integration with Orthopaedics was not clear. The team is to be congratulated for having been nominated as one of four orthopaedic oncology centres in the Netherlands, but while it was specified that a pre-requisite for nomination was clinical outcome related scientific research, it was difficult to get tangible examples of achievements or future projects. The integration of the Stroke and Brain Injury research was convincing and good as well as the general direction of Rehabilitation research. There was an intriguing association with haematological research, albeit associated with orthopaedic interventions. The 3-D printing programme has enormous potential, but the strategy was not clear. The publication metrics, based on the eleven selected publications demonstrate 1 stellar output on thromboprophylaxis and lower leg trauma after knee arthroscopy, but the rest were of low to moderate impact, with one

strong review and an important publication on guidelines. The department otherwise produces many papers every year. External funding is good.

Relevance to society:

All the programmes are relevant to societal and unmet needs for patients and their families. Tangible examples of impact were given such as the thromboprophylaxis paper which changed practice, a specialised 'App' for professionals and patients to assist with the complexity of treatment combinations, and the management of ankle injuries. The 3-D printing programme will be particularly powerful when fully implemented.

Viability:

The programme relies heavily on connecting with other departments and multidisciplinary involvement, which is good, but surgeons do not seem to be embedded in suitable research environments. The three themes host a very large number of PhD students, but the mechanisms of supervision were not clear. It was mentioned that many of the PhD students are being supervised by clinical surgical staff in collaboration with investigators from other departments. There is a major concern about the provision of the right environment for surgeons who have academic ambitions. Strong emphasis appears to be on clinical training rather than research for academically talented trainees, and this is unlikely to be successful in producing strong leaders in the department. The responses about the clear challenges of training in surgery and academia and how to address them were disappointing, particularly regarding protected time to undertake research. The interview would have benefitted from a broader input from the members of the team. There appears to be a lack of focus, and insufficient vision and credible strategy for the next 5-10 years, and this needs further development.

Conclusion and recommendations:

- The overall activity of the merged programmes is good, but there is considerable untapped potential, and a distinct lack of focus in orthopaedics;
- The themes are not joined up and lack coherence. There is little vision and strategy is not clear, particularly for hard-core orthopaedics research. It was therefore difficult to extract a 'story' and to give a research 'label' to the programme;
- A major concern is the lack of a defined strategy to develop surgeon scientists and academics, and provision of a suitable environment for talented trainees to thrive does not appear to be optimised;
- The clinical workload for sarcoma is very high, with unparalleled opportunities to conduct world-leading research, but it was not felt that this was exploited optimally;
- There appears to be plenty of talent in the three components of the programme, and the panel recommends that the department take a time of reflection to shape the strategy, focus on strengths, and decide how to provide a rich training environment for talented surgical trainees.

5. Assessment of the research programmes - Division 2

5.1 Metabolic health: pathophysiological trajectories and therapy

Department:	Internal Medicine/Endocrinology
Research programme:	20102
Scientific staff (2016):	7.8 fte
Quality:	2
Societal relevance:	2
Viability:	2

Brief description of the research programme:

The research programme is concentrated around the pathophysiology, prevention and treatment of metabolic disease, including regenerative strategies. The programme is presented as three themes: 1) regulation of energy metabolism, 2) beta-cell regeneration, and 3) bone and mineral research.

At the interview, the programme identified their major strengths as: stress steroids & metabolism; islet differentiation to alpha cells; brown adipose tissue activation; and sclerostin and Impact microindentation (IMI) in metabolic bone disease.

Research quality:

The research quality of this programme is a somewhat mixed picture. Publications, markers of esteem, and h-indices of investigators all point to the bone & mineral theme as an established and highly productive group, albeit with recently refreshed faculty. In the Metabolism theme, the brown adipose work stands out as having attracted substantial attention and there are interesting pockets of interest around lipoproteins and glucocorticoid signalling. The islet cell transplantation work appears to have a lower profile.

The programme is strongly represented in collaborative networks, notably in European Rare Disease Networks. The top papers are in excellent journals and address important topics, although leadership by LUMC investigators is not always apparent.

Relevance to society:

The research programme is well represented in clinical guidelines nationally. There are some excellent public engagement activities including a patient website. The significance of the impact indentation test in bone disease is not explained. Research on glucocorticoid receptor modulation has thus far been investigator-initiated but will be partly industry-initiated. There is impressive industrial engagement with multiple partners, but the number of inventions that have been reduced to practice is more difficult to identify. There are no licenced patents although it is unclear to the committee if patents have been filed.

Viability:

The programme is modest in scale, with 22 researchers, 7 support staff and on average 25 PhD students. Around 100 papers per annum is a reasonable output from a group of this size. Funding is reasonable. According to the committee, the forward strategy in the self-evaluation report was largely descriptive and project-based. It does not identify specific actions or priorities.

Conclusion and recommendations:

This programme seems to get along well as equals, sharing an enthusiasm for endocrinology but lacking strategic direction or leadership to ensure that the whole is greater than the sum of the parts. The committee recommends that:

- the programme identifies more overtly the major scientific strengths for which it is internationally leading, and distinguishes these from participation in collaborative networks;
- a more explicit forward strategy is developed that encompasses interactions across the programme themes and beyond Endocrinology, is focused on major strengths, and will drive a more ambitious future funding strategy;
- this may justify a new more focused research programme to be developed, for instance on body weight regulation, on which to grow a capacity-building strategy to refresh the faculty in future.

5.2 Nephrology

Department:	Internal Medicine/Nephrology
Research programme:	20603
Scientific staff (2016):	12.9 fte
Quality:	2
Societal relevance:	2
Viability:	2

Brief description of the research programme:

The scientific research of the research programme 'Nephrology' is concentrated around the pathophysiology and treatment of renal disorders, renal replacement therapy, transplantation in diabetes and regenerative strategies. Research in the division is multidisciplinary and covers clinical, translational and basic areas with the aim to improve patient care.

Research quality:

This is a good research programme resulting from the previous merge of two programmes. This results in a very diverse research build on eight different main subjects with kidney transplantation as a common theme. Despite the apparent important number of sub-themes for the size of the programme there is a good interaction between the various researchers allowing to obtain significant results in most of the projects. The clinical and translational research is good. Basic research is improved by the re-organisation of the Einthoven Laboratory. Overall, this research is quite original and competitive at the international level. Significant results were obtained for each axis resulting in a good publication list with some articles in high impact factors journals.

Relevance to society:

The results of studies performed in various axes by the programme had significant impact on patient management. The research programme is involved in national guidelines and one international very focussed consensus. This is already quite satisfactory, but it lacks some international leading role. Educational tools for students and physicians as well as patients on line monitoring have been developed. Involvement in various national communication and media activities for patients and the lay public is good.

Viability:

The level of funding is excellent. It would probably further benefit from application to consortium international competitive funding (i.e. H2020 or others EU biomedical research funding). The current restructuring of the Einthoven laboratory is highly beneficial to basic

and translational research projects of the programme, especially in tissue regenerative researches.

Merging of the previous programmes has been achieved but would probably still need some efforts to reach a more focussed and/or synergistic organisation of the various axes among all the programme members. One option would be to reduce the numbers of subjects or to merge some of them using the same approaches or using common tools and methodology.

Conclusion and recommendations:

The overall research programme is of very good quality, with significant results for the advance of medical science and impact on patients' management. Funding is very good. The productivity is also good, but the numerous parallel axes of research is a potential limiting factor to reach the international highest level that the programme would have the potential to do.

5.3 Pathophysiology, epidemiology and therapy of ageing

Department:	Internal Medicine/Gerontology and Geriatrics
Research programme:	20801
Scientific staff (2016):	6.1 fte
Quality:	2
Societal relevance:	1
Viability:	2

Brief description of the research programme:

The main aim of the research programme is to develop evidence-based medicine for older patients by unravelling the pathophysiology and therapy of the ageing process and its associated diseases. The focus is on studies in older people in the whole spectrum from healthy to diseased in four research topics: evidence-based medicine of older patients, metabolic health, the heart-brain connection, and thyroid hormone function.

Research quality:

The research programme is of very good quality and has been very productive, especially in consideration of the rather limited size of the team and of the evolution of its staff. Considering the limited size of the programme the role of PhD students and to some lesser extent post-docs is very important and they are apparently managed in a quite efficient way. The research programme is of high quality at the international level and members of the team participate in and coordinate some very good international projects or consortia. The publication list is excellent in terms of number of articles and impact factor. However, one should note that the CWTS analysis suggests that the impact in the specific field of geriatrics and gerontology, that represent most of the team's publications, is surprisingly not above the average.

Relevance to society:

The results of the research clearly have impact on clinical practice. It should be noted that the results of the recent TRUST study had a lot of media coverage and a clear impact on management of a frequent clinical situation in the aging general population. The research programme is active in guidelines production and health care policy development for aging. There is a very good activity for professional as well as patient education. The research programme is also involved in large projects in the field of aging with companies like Philips or biotechs.

Viability:

Funding is good and increasing in the report period. The research programme works in strong interaction at the international level, resulting also in consortium support from high level international grants (i.e. FP7 or H2020). On the long term the strategy described will probably be very productive. However, at present the programme size is rather limited. Furthermore, as explained by the investigators there is a need for renewal with the development of new cohorts to address new questions and this will be challenging. The long-term evolution of the planned research is well explained, and the programme expects an initial phase of low productivity. This is acceptable and very well justified by the investigators both in the written report and during the interview, but nevertheless this represents a challenge for the viability of the planned research.

Conclusion and recommendations:

This research programme is of very good international quality and reflects a very well organised team with a very efficient management of students. Considering the programme's size, it will be very important to either develop even more synergistic collaborations with local or distant collaborative programmes, or to recruit new members to develop the various axis of research described in the programme. Increasing the number of investigators by attracting young specialists in Geriatrics is challenging but should be an important goal to initially maintain and latter progress from the very good level of research developed in the recent years.

5.4 Thrombosis and Hemostasis

Department:	Internal Medicine/Thrombosis and Hemostasis
Research programme:	21101
Scientific staff (2016):	6.9 fte
Quality:	1
Societal relevance:	2
Viability:	1

Brief description of the research programme:

The research programme Thrombosis and Hemostasis focuses on the fundamental mechanistic understanding, diagnosis, treatment, and prevention of blood coagulation disorders, such as bleeding or thrombosis. Research themes are: a) Prevention, diagnosis, and treatment of thrombosis, b) Pathophysiology and etiology of thrombosis and c) Pathophysiology and treatment of bleeding.

Research quality:

The section of Thrombosis and Hemostasis clearly develops a very innovative and successful programme of research with international high-quality level. This research involves fruitful collaborations with other LUMC teams, especially the Clinical Epidemiology programme, that are highly beneficial for the institution and also with national and international collaborations. It covers various aspects addressing key issues in bleeding disorders on one side and thrombosis on the other side. More recently research activities with a very high potential in the field of cancer and thrombosis have been developed. There is an excellent interaction between pre-clinical research, clinical research and clinical care, although basic research could be more developed.

Relevance to society:

The research conducted has significant impact in decision making for prevention or cure of bleeding disorders or thrombosis. The research programme is very active in international and national guidelines production and education of health care professionals, albeit a little less active for patients or family and lay public although this is one of the future objectives. The knowledge resulting from the research offers new prediction models for thrombosis as well as perspectives of new treatments for bleeding disorders. With future studies more precise identification of situation at risk of thrombosis requiring to be targeted for prevention will be possible. For bleeding disorders, the development of new therapies, especially new proteins, should have major impacts but still need to be confirmed.

Viability:

The overall strategy is very well designed and planned, and the team has the ambition to grow. Funding is excellent and has expanded during the reporting period. The balance between bleeding disorders and thrombosis in term of team members, approaches and perspective is what one could expect.

Conclusion and recommendations:

This is an excellent programme, with high quality research oriented along two strong axes with clinical relevance and a rather good equilibrium between clinical, translational and basic research. The research programme has many local, national and international collaborations and currently good funding. However, efforts could be made to attract more post-doc and consortium funding from international academic (especially European grants) sources that would be expected for a programme of this quality. This would help to fulfil the reasonable ambition of the programme to grow and maximise their impact on health care and society.

5.5 Cardiology, Cardiothoracic Surgery, Vascular Surgery

Department:	Cardiology
Research Programme:	20303
Scientific Staff (2016):	17.2 fte
Quality:	2
Societal relevance:	2
Viability:	3

Brief description of the research programme:

The research programme is responsible for the generation of new insights into the complex cardiovascular diseases enabling the development and implementation of new diagnostic and therapeutic modalities to further improve modern clinical care in a sustainable manner. Themes of the research programme are:

- Arrhythmias;
- Atherosclerosis, aneurysmatic diseases, and genetics;
- Congenital heart disease;
- Valvular disease;
- Ventricular dysfunction and heart failure.

Research Quality:

In response to previous reviews Vascular Surgery has recently been incorporated into the organisation of the Cardiovascular Center Leiden (CCL). The stated purpose of this reorganisation is to deliver synergies across the various research groups within the cardiovascular domain and to strengthen vascular surgery. The CCL is clearly an important clinical and research entity within the LUMC with an overarching scientific committee constituted of the leads of the various research groups. The committee had some difficulty distinguishing the priorities of the department in the delivery of best clinical practice from its priorities in primary research. As in many large groups there are areas of mixed research excellence and success but focus on the research themes with the greatest potential has been resolved. However, from review of the self-evaluation report and interview responses, a pragmatic strategy for communication, cross fertilisation and development of synergies across the many constituent research groups is not clear. Indeed, the impression is one of lingering ‘silos’ of research with yet insufficient integration. The appointment of a teaching professor with responsibility for coordination and integration of the different teaching programmes, and of a scientist to oversee data management and data-to-source analysis, are good steps in the right direction. Vascular Surgery is represented in this structure by two professorial leads, clinical and basic research, primarily focused on aortic disease and atherogenesis. A significant omission from this research strategy is of Peripheral Vascular

Disease encompassing diabetes and its complications, specifically the diabetic foot – which are epidemic in the world. The research components exist within CCL (ischaemia, cellular pathobiology, reperfusion etc) but are not obviously integrated or highlighted within the vascular domain. Regarding staff, approximately half of the 45 staff members are involved in scientific work but the drive to academically involve as many clinicians as possible is encouraging. The fact that each member of staff had sufficient time to engage in research, supervision and teaching was also reassuring. This is particularly important given the very high number of PhD students – 75 – who have yet to complete and need supervision, even given the pre-clinical structure of the PhD programme at the LUMC. The bibliometric review confirms a high and consistent output of publications with distinction in the fields of electrophysiology and cardiac arrhythmia.

Relevance to Society:

The research programme scored high on societal relevance with all projects focused on early translation to improve clinical outcomes and evidence of engagement with providers and patients. There are several projects with potential for major societal impact, highlighting the bio-ICD project, and the Project 1317 aiming to reduce the need for patients to attend the outpatient clinic using telemonitoring.

Viability:

There is conflicting evidence regarding the funding of the research programme. The 2016 data documents a total decrease in funding - both internal and external - of €2.4millon. During the interview there was some surprise expressed at this data and an opinion given by the CCL chair that financially the Centre was stable. The issue of funding mandates urgent review, in particular how comprehensively LUMC plans to support infrastructure investment. Overall, this is a large successful clinical and scientific programme with areas of international excellence – viability should be assured but cannot be assumed. The issue of size of the research programme in comparison to international competitors is addressed with the proposal to develop the Cardiovascular Centre Southwest Network to incorporate the hospitals and population of Southwest Holland. This appears to be at the proposal stage but represents a real opportunity which should be rapidly implemented in the LUMC and CCL strategy going forward.

Conclusion and Recommendations:

The committee makes the following recommendations:

- A research strategy which is distinct from a clinical excellence strategy would be helpful in exploiting the leading discovery science opportunities, such as gene therapies for arrhythmias, that exist at the LUMC;
- There is clear intent to further integrate within the separate domains of the Centre – a clearer strategy for better integration, cross fertilisation and development of synergies needs to be defined and clarified. Infrastructure is also important with institutional

commitment to increased co-location of both research and clinical facilities across the disciplines an imperative. This in turn will be most important in realisation of the Cardiovascular Centre Southwest Network;

- A realistic strategy to maintain and increase funding both internal and external is required;
- In common with several other LUMC themes, a strategy to staff CCL with clinical scientists and academics thus attracting the best cardiovascular specialists of the future, needs further analysis and implementation (facilities, job planning, support etc);
- The discipline of vascular and cardiovascular interventional radiology has largely throughout the world been subsumed into Endovascular Surgery, potentially making the relationship with Radiology less important and the need to support and train vascular and cardiothoracic surgeons in this specialty imperative. With a very strong Radiology department, LUMC may or may not follow this trend. Across Vascular and Cardiothoracic Surgery and Radiology a defined leadership and management structure specific to endovascular surgery will consolidate the already significant potential for CCL in this area. Reference is made to a proposed LUMC facility to accommodate all the required catheter labs, hybrid theatres and supporting infrastructure. Implementation of these strategies is a priority to compete internationally with the many international centres currently realising such integrated facilities;
- Despite passing reference, there is a lack of strategic planning regarding the huge importance of interaction with Engineers within the domains of device development, biomaterials, fusion imaging and artificial intelligence to give a few examples. Development of a focused strategy of broad collaboration and integration with Engineering is strongly recommended and an opportunity that CCL cannot afford to underestimate.

5.6 Pathogenesis and treatment of chronic lung diseases

Department:	Pulmonology
Research programme:	20403
Scientific staff (2016):	3.3 fte
Quality:	3
Societal relevance:	3
Viability:	3

Brief description of the research programme:

The aim of the research programme is to improve patient care and treatment of patients with chronic lung diseases through a better understanding of the pathogenesis. The programme encompasses epithelial toxic injury and immune regulation in these diseases, in which both underlying mechanisms as well as targeted therapeutic interventions are explored, using e.g. biologicals such as monoclonal antibodies. At interview the programme identified Alpha 1 Antitrypsin deficiency and the availability of an epithelial cell model for disease modelling.

Research quality:

Contributions are spread across a wide range of topics (COPD, asthma, AATD, microbiome, MSC therapy). Not all the 'top' papers are in leading journals although citation statistics are strong. From the paperwork, the activities are clear, but the discoveries and their impact are not. Overall, the outputs suggest that the group is making incremental contributions on a wide range of topics rather than leading any major high impact programmes.

Relevance to society:

There is some evidence of contribution to guidelines, but on a national scale. There is also evidence of undertaking several clinical trials, but probably not of a scale to change international clinical practice. There is modest commercial engagement (one AATD project).

Viability:

This is a small programme with just seven staff members who are sustaining approximately fifteen PhD students and around Euro 1M in funding. There is evidence of an attempt to refocus on priorities (regenerative medicine, new recruitment in cancer), but these are large topics and high risk, starting from a low baseline. As written, the strategy risks compounding the diversity and lack of focus of the programme.

Conclusion and recommendations:

There is obvious enthusiasm for clinical research but a significant increase in critical mass and strategic focus would be required to generate a world-leading programme of work.

5.7 Cellular mechanisms in basic and clinical gastroenterology and hepatology

Department:	Gastroenterology and Hepatology
Research programme:	20501
Scientific staff (2016):	3.7 fte
Quality:	2
Societal relevance:	3
Viability:	3

Brief description of the research programme:

The research programme with currently five PIs focuses on the functional and clinical impact of mesenchymal stem cells therapy, intra- and intercellular factors like Hedgehog signalling, the BMP pathway, glucocorticoid signalling, the lectin-complement pathway and matrix metalloproteinases on several diseases, namely chronic inflammation, carcinogenesis, liver disease and liver transplantation.

Research quality:

While the written self-evaluation report did not make the main contributions to the field of Gastroenterology and Hepatology very clear, during the interview four examples were listed of those discoveries judged to be of highest impact:

- The work on TGFβ signalling via endoglin in colon cancer cells. This is based on a well-cited paper and the programme received a 500K grant from the Dutch Cancer Society and another smaller grant from Stichting Fonds Oncologie Holland (125K). The plan is to exploit this work further by targeting endoglin in phase II and II trials;
- The work on Crohn's disease using mesenchymal stem cells. This is work done with the immunohematology department. Cells can be obtained from bone marrow to circumvent patenting issues for adipocyte derived mesenchymal cells. This seems to be one of many LUMC departments that have started working on applying/trialling MSC therapy for diverse diseases. It was not entirely clear what this work was precisely based on and whether this group has a clear competitive advantage over other international groups applying regenerative medicine in this area;
- Developing novel biomarkers for liver failure;
- The work on the development of new tracer consisting of an intravenously administered fluorescent peptide targeted against c-Met for the detection of colorectal polyps (published in Nature Medicine with Hardwick as last author). The implementation into the clinic had seemingly progressed slowly, but some recent progress was reported.

The programme is also an expert and part of the European Renal Network on alpha-1-antitrypsin deficiency (AATD) and NAFLD. Nevertheless, from both the self-evaluation report and the interview, it is difficult for the committee to judge how the grouping of PIs work together in synergy to make the whole greater than the sum of their parts.

Relevance to society:

Very little information was given as to how the programme has disseminated their research or engaged with the public. Some contributions to guidelines are mentioned, but it is not clear whether the PIs have taken an active and/or leading role in these guidelines.

Viability:

The research programme is part of or has led consortia including EU-FP7 and H2020 on non-alcoholic fatty liver disease (as a partner) and Radical 2 study (as leading PI). The research programme is working on a Horizon 2020 application with Amsterdam and Edinburgh.

About personal fellowships and project funding: the programme has managed to obtain some funding from the Dutch government, charities and industry, which were not reflected in the automatically generated numbers. The committee cannot sufficiently judge from the documentation how much this represents per PI per year. However, it has the impression that more recently in 2016 and 2017, this group of relatively young PIs has made progress on this front.

Conclusion and recommendations:

The committee discussed the diverse range of topics that are being addressed by this programme. Even though some of these might be linked more than initially obvious to the committee (e.g. mechanisms in colorectal cancer are very similar to pancreatic cancer), for such a small group of PIs, the committee recommends applying more focus in the next six years. A clear strategy for the future needs to become apparent that draws together the strengths of this talented and energetic group of PIs and enables more collaborative working within the department. Appointment of a director of research would be beneficial to deliver this strategy.

5.8 Pathophysiology and treatment of rheumatic diseases

Department:	Rheumatology
Research programme:	20701
Scientific staff (2016):	7.7 fte
Quality:	2
Societal relevance:	2
Viability:	2

Brief description of the research programme:

The overall aim of the research programme is to integrate patient care and research to increase understanding of rheumatic diseases and thereby improving patient care. It focusses on recent onset inflammatory arthritis (the early arthritis cohort and arthralgia cohorts), recent onset spondyloarthritis (SpA) (the SPACE-cohort) as well as hand osteoarthritis (HOSTAS cohort).

Research quality

The research programme has made some interesting contribution to the field of RA:

- discovery of novel anti-carbamylated antibodies, a new class of anti-modified protein antibodies that may be helpful in diagnosis and disease prediction. The discovery of these antibodies also provides a better animal model for the disease;
- they are currently interested in glycosylation state of RA antibodies;
- they have developed a technique to isolate ACPA specific B-cells.

In the field of osteoarthritis (OA), the programme has an interest in the role of inflammation with a special focus on fatty acids and lipid mediators. It is commendable that an OA cohort was started as early as 1999, when it was perhaps not as clear as it is now that OA would be a costly disease to our ageing society. The department has been named a Centre of excellence by the European arthritis organisation EULAR. Lastly, they have become a referral centre for rare autoimmune diseases such as scleroderma and SLE. It was noted that this programme has a good number of female PIs. They also have very many PhD students, which seems like a heavy training load for a relatively small group of PI's. The research programme has a good publication record in specialised journals. The programme has chosen to mainly publish in specialised journals on arthritis and rheumatism and has also chosen to represent these in the lists of their most important scientific and societal publications. However, during the site visit it has been clarified that they also have a significant number of articles in prominent journals with a more generalised readership.

Relevance to society:

The research themes are very societally relevant, with large impacts at the national and international level. Examples are:

- Patent on anti-carbamylated antibodies;
- Re-evaluated efficacy of early arthritis recognition clinic, better outcome compared to regularly referred patients;
- New diagnostic tools, ten-year follow-up study after treatment;
- Clinical trials benchmark for content and methodology.

The research programme is also heavily involved in EULAR guidelines

Viability:

Going forward, the research programme proposes to cure and /or prevent disease. For this, early cohorts will be expanded to study early disease processes and treat early. For OA the inflammation process will be the focus. The expertise on autoantibodies will be expanded to scleroderma and SLE. For SLE, imaging will help to understand a group of patients with neuro-psychiatric complaints. In scleroderma sequencing of actives versus non-active skin cells will be pursued (with a company). For the main diseases dedicated groups have been formed which consist of at least one medical specialist, an epidemiological/outcome expert and translational/ basic researcher. Active talent management has led to the recruitment of a new PI to the immune-haematology department. The programme is endowed with a healthy sustained grant income.

Conclusion and recommendations:

Overall the strategy is clear and focused. One concern is that the scientific approaches are sound but on the conservative side with little technological innovation (as far as recorded in the self-evaluation report). The committee recommends improving the vision, in order not to be left behind by innovation. This may also lead to higher impact publications.

5.9 Neuro Imaging Research

Department:	Radiology
Research programme:	20901
Scientific staff (2016):	12.4 fte
Quality:	1
Societal relevance:	1
Viability:	2

Brief description of the research programme:

This research programme studies specific diseases of the central nervous system using state-of-the-art imaging technology, with an emphasis on MRI. A unifying theme of the research is the assessment of vascular based neurological disorders with techniques explicitly designed for this purpose. Within the department of Radiology, there are investigations with researchers from the Cardiovascular Imaging Research Group to pursue understanding the interactions between the heart and systemic vasculature, and the brain; the so-called heart-brain axis. Both groups have a technology development orientation, which allows for a broader impact with a moderate group size.

Research quality:

The committee notes that the overall quality of the research done to date is excellent for a programme of moderate size. Group size is referenced in assessing quality since critical mass becomes a concern with smaller groups in the field of Radiology. The overall importance of the programme's work is highlighted by several awards and grants of note (ERC; Simon Steven Meester award). One key member of the research programme is internationally recognised as an expert in MRI RF technology, important for designing methods and hardware modifications that help capture the inherent signal-to-noise advantages of ultra-high field (7 T) that can be countered by concomitant RF penetration and homogeneity challenges with increasing field strength. The citation index is high though this is not reflected in all the listed most important papers. This list does contain one multicentre study that is very highly cited, contributing to a bit of an index skew. Another paper includes a contribution to a major paper that defined the value of clot removal in acute occlusive/ischemic stroke (by far the highest cited paper). A minor concern is the relatively wide range and sheer number of different neurological problems and challenges being studied, particularly given the modest group size. The programme lists approximately twelve such different topics under study. Given that each should require a team effort, focus on a smaller number might be advised. This concern was addressed by the research programme in indicating that vascular/small vessel disease is a unifying theme. Though overall effective, the programme might be even more impactful if they were to focus and restrain the number of different pursuits.

Relevance to society:

The research programme continued to do excellent in societal relevance. Members of the programme have contributed to several useful reviews and guidelines on how best to conduct neuroimaging studies for evaluation of small vessel disease and brain perfusion using advanced MRI techniques. Clinical studies have led to important findings in common migraine headaches, and in Duchenne's dystrophy found to also affect the brain as well as the muscles. The technical developments have helped the broader research community in analysing neuro images, and in the non-invasive assessment of cerebral perfusion. The hardware pads for improving high field / 7T MRI are also used internationally. Of note, the programme has developed both hardware and software that is being used by other international groups. Their high dielectric pads are used (by others) to improve the performance of ultra-high field MRI by helping to mitigate magnetic field inhomogeneities, and their technique for arterial spin labelling to assess cerebral perfusion has been commercialised by Philips.

Viability:

The research programme is well funded from both internal and external sources. Still there has been a decline in staff. There is an articulated concern with an increasing clinical workload, a global trend in Radiology. Going forward, more focus on key/major problems might help address this concern. Also, of some note is the relative delay in acquiring PET/CT which is now 1.5 decades old. One committee member was similarly concerned that no PET-MR, found in several world class neuro imaging programmes, was in the plans - though another member noted the substantial cost and financial challenge this brings. Finally, improved synergy might be helpful going forward utilizing more of the strengths of the cardiovascular imaging programme. The cited specific study area of the heart-brain axis, also of interest to others in the Medicine department, would seem to offer a practical vehicle for closer investigative relationships within Radiology.

Conclusion and recommendations:

Overall this is a very strong neuroimaging research programme relative to its modest size, particularly in development of MR technology. This has included both useful hardware innovations (Webb), analytical software (data processing group), and large multi-group based optimal use guidelines for advanced techniques. The work has been of benefit to the patient community and the broader neuro-imaging research community. The programme is effective but going forward could improve through enhanced intradepartmental synergies and use of funds to explore integrated studies, e.g., multi-organ systems such as cardiovascular-neurovascular which are also of value to other LUMC departments. In this effort, consideration might also be given to a more balanced distribution of direct funds related to group size and productivity. This would further support department symbiosis scientifically, which is even more important for moderate sized groups with high demands on limited resources.

5.10 Cardiovascular aspects of Radiology

Department:	Radiology
Research programme:	20902
Scientific staff (2016):	11.3 fte
Quality:	1
Societal relevance:	1
Viability:	1

Brief description of the research programme:

This research programme studies congenital and acquired cardiovascular diseases using state-of-the-art imaging technology, including MRI, CT, ultrasound and nuclear medicine. They develop techniques for quantitative assessments and for integrated multi-organ evaluation for detection of systemic/metabolic changes that lead to cardiovascular disease.

Research quality:

This is a well-established research programme that has excelled in using state-of-the-art technologies to address practical challenges in cardiovascular medicine. The programme has a long track-record and history of being successful in this domain, excelling in developing analytical tools and the evaluation of the clinical utility of cardiovascular radiology imaging techniques. A more recent area of leadership has been in the early assessment of atherosclerosis as a multi-organ metabolic-based disease. This provides opportunities for the early detection due to metabolic changes (e.g. in the liver) before downstream end-organ damage is consequential.

The publication history is very good and though the citation index is well above average it is not perhaps as high as the international standing of the research programme. This is related to the nature of CV imaging research that is technology based and thus published in more technical imaging journals with less broad distribution and readership. The journals in which most of their top contributions have published, however, are among the top in the field of Radiology and medical imaging. In comparison to similar sized international groups in this field, their work is world-class.

Relevance to society:

This research programme has made substantial contributions to the cardiac patient community and to the CV imaging research community. Value is noted for the individualised characterization and management of congenital and paediatric cardiovascular abnormalities through clinical studies and tool development, the direct quantitative MR assessment and evaluation of coronary artery heart disease, and their global leadership in establishing the evaluation of metabolic changes (starting with the liver) as early indicators which may lead

to acute cardiovascular syndrome events. Work which is planned for the assessment of the heart-brain interplay will further advance the more systemic approach to the pre-symptomatic detection and assessment of cardiovascular disease, still the western world's leading killer. The early tools the programme has developed for the quantitative assessment of cardiac and vascular images has steadfastly continued with progressive development of analytical features (3D + motion+ blood flow quantification in 3D). These tools have been commercialised and are broadly distributed internationally. Advances being pursued through Artificial intelligence (AI) are well reasoned and should help automate, streamline and improve cost-effectiveness of these analytical techniques, particularly for the comprehensive but time-labour intensive assessment of 4D (3D+time) cardiovascular MR images. This programme's history of contributions of value to the patient and research communities is strong, particularly for a group of this modest size. However, the leadership's articulated vision for inculcating AI through computer science experts, a more holistic approach to understanding and the early detection of atherosclerotic/cardiovascular disease, and the development of MR image guided interventional procedures for improved minimally invasive treatments is also encouraging that the high societal value of the programme's work will continue.

Viability:

The research programme is well organised and cohesive with both effective new and retained immediate past leadership. The transitional support and mentorship of the new leadership by the prior leadership and scientists is evident. This, in conjunction with their well-conceived plans, is a strong indicator of continued viability for this programme. There is a well-articulated set of goals for the future with a practical number of key developmental areas on which to focus. This includes more integrated and collaborative projects to improve image guided treatment of atrial fibrillation with real-time temperature monitoring, developing and harnessing the emerging power of AI, and further development of assessing metabolic changes that foretell heart disease through a collaboration with metabolism assessment experts (using MR spectroscopy) at Oxford. In addition, the programme will focus on the development of a hybrid MR-X-ray interventional lab with Cardiology, and the rapidly emerging use of machine learning in collaboration with Computer Sciences, as well as partnerships to pursue the systemic nature of CV disease. Their external research funding has increased over the last two years as a sign of significant relevance and quality of research. This will help sustain the programme.

Conclusion and recommendations:

This is a well-established research programme with a long-standing history of excellence in cardiovascular (CV) clinical imaging research and the application thereof. This tradition is continuing under new leadership supported by the prior generation of leaders. The work is impactful in the areas of congenital heart disease characterization, the quantitative assessment of coronary heart disease with global leadership in the evaluation of systemic

metabolic precursors, and in the progressive development of analytical tools that are commercialised. The future focus on developing an interventional CV lab with cardiology is planned and is encouraged, as is the further development of techniques for assessing more systemic changes that are actionable diagnostic features of multi-organ disease (metabolic syndrome; heart –brain axis), and the integration of AI into advanced image acquisition and analysis techniques. Suggested is departmental attention to the apparent uneven distribution of direct (departmental) support funds, which appears -based on the tabulated data- to be disproportionately low.

5.11 Imaging- and therapeutic targets in neoplastic and musculoskeletal inflammatory disease

Department:	Radiology
Research programme:	20903
Scientific staff (2016):	11.7 fte
Quality:	2
Societal relevance:	2
Viability:	3

Brief description of the research programme:

This research programme aims to image cancer and inflammatory diseases with the use of multi-parametric state-of-the-art imaging, including MR. Main ongoing research themes are a better understanding of disease pathophysiology, image guided therapies and effectiveness assessment, improving imaging based cost effectiveness of medicine, developing criteria with US and MR to allow early diagnosis of inflammatory diseases such as RA and SPA, defining phenotypes related to progression of these inflammatory diseases and impact of therapy including TNF-block, quantitative MRI to monitor disease and developing advanced data post-processing to improved diagnostic value using MR, CT, Nuclear, Optical and hybrid methods.

Research quality:

The research programme is relatively new and has been organised along the stated cancer and musculoskeletal disease themes, but also as a collection of a wide range of individual research activities that did not fit within the other two Radiology department programmes. As such, the range of activities is rather broad, reporting work that extends from tracer development to uveal melanoma, to Duchenne and Becker muscular dystrophy, to optical image analysis, to proton bean therapy and minimally invasive and surgical image guided analysis, to mass spectrometry to the various other directions listed in the programme description. Given the loose relationship among these, it appears to be a research programme that would benefit from more focus. Overall the quality of the work, particularly that done on technology development, appears to be very good based on the awards and grants received by group members, although there is membership overlap with the other research programmes. The list of the most important papers is less impressive than would be expected, with half having less than 10 citations. This was explained by the research programme as having been chosen to show the range of research pursuits in combination with some being recent and one being in press. Indeed, the overall citation index is good.

Relevance to society:

The problems being addressed are quite relevant to society. Musculoskeletal and inflammatory joint diseases as well as improved detection, assessment and targeted removal of neoplastic lesions are indeed major/global healthcare challenges. Advances have been made in using low dose CT and MRI for the assessment of inflammatory/degenerative spine disease and rheumatoid arthritis, and MRI in Duchenne's muscular dystrophy. In image guidance for oncology diagnostics/therapeutics, acquisition and data analysis methods have been developed to help co-register and fuse images, analyse data in large studies and provide quantitative assessment of disease progression. The PET-CT was installed in the last year, with new staff so the impact of contributions from their nascent Nuclear programme is still to come. The research programme indicates they have developed products with industrial partners and list multiple such companies inclusive of GE, Intuitive Surgical and Quest Medical but exactly what products have been developed are not well described and thus difficult to discern. One example, however, was given in the interview with the programme. The high level of external research funding is noted and would appear to be supportive of some significant industrial engagement.

Viability:

There is concern for the viability of this research programme given the rather large and broad array of project pursuits for a modest sized group. At present the work has some very good elements, but the projects are loosely coordinated. In addition, a new group and recent equipment in Nuclear Medicine is being integrated into the programme. This could have substantial future impact in assessing oncology and inflammatory diseases. This research programme might benefit most from more streamlined investigative targets and focus that follows the programme's strengths and major clinical opportunities. The strength of the programme and the entire department appears to be in technology development inclusive of image analysis and quantitative assessments. Integration of these strengths across well-chosen disease targeted projects may be beneficial and contribute to greater viability going forward.

Conclusion and recommendations:

This research programme is very good in some areas such as technology advances and the development of image analysis methods for the assessment of neoplastic and some inflammatory diseases. However, it describes a very wide range of loosely correlated research activities and thus could benefit from more cohesion and focus on major topics of substantial interest and need. A reorganisation of departmental research with a more integrated approach that may, for example, focus on (1) continued technology innovations for the assessment of multi-organ or systemic disease with a unifying physiologic process, as well as (2) some key targeted disorders, might benefit the department as a whole. The department leadership has also suggested integration of existing programmes given the common theme of technology development that appears to be a departmental core

strength and the apparent overlap of some personnel. This might also present an opportunity to address the current uneven distribution of direct departmental funds among the current programmes which - based on the information presented - has an unclear basis when all three current programmes are considered.

5.12 Clinical Epidemiology

Department:	Clinical Epidemiology
Research programme:	21001
Scientific staff (2016):	6.3 fte
Quality:	1
Societal relevance:	1
Viability:	1

Brief description of the research programme:

Clinical epidemiology consists of the application of general epidemiologic principles in clinical research. This research programme focuses on the general population to understand disease development and prevent disease, and on patients to improve treatment and understand disease mechanisms. Diseases in which the department is structurally active include haemostasis and thrombosis, obesity-related disease, chronic kidney disease, osteoarthritis and transfusion medicine.

Research quality:

The research developed is clearly of very high quality with a demanding methodology resulting from excellent expertise of the members. The self-evaluation report clearly and precisely describes the research goals and achievements. The research is of high recognition internationally. This is the result of expertise and experience in the methodology of observational research and interventional trials. The high quality and added value of the cohorts that the programme contributed in developing from the start also contributes substantially to their international recognition. The research programme is indeed involved from the initial design phase in many projects and there the expertise of the programme's staff is of major importance. In this way it allows the programme from the methodological point of view to control the elements that are key to the high quality of their studies, both for cohort studies or clinical trials. Due to strong interactions with various clinical departments and laboratories, meaningful questions are addressed resulting in significant and innovative knowledge in various fields of medicine. By doing so the research in clinical epidemiology is also beneficial to various research programmes of the LUMC.

Relevance to society:

The research programme has a clear vision on the relevant questions addressed in its research projects and this is implemented from the initial design of the studies. The research clearly has impact on medical practice as evidenced by meta-analysis used for international guidelines, patients reported outcome monitoring and algorithms for treatment adaptation.

Viability:

This is a programme of eight principal investigators supervising an increasing number of students, that seem to be mentored efficiently and thereby contributing substantially to the development of the various projects. The strategy to interact with various programmes of the LUMC is very efficient. This also compensates for potential funding difficulties for which the programme has a proactive attitude. This will be further developed with the development of the Centre of Quantitative Medicine to be founded with the department of medical statistics.

Conclusion and recommendations:

This is clearly a high quality and successful research programme with a clear strategy, very strong interactions within the LUMC and international collaborations. The programme has significant contributions to the advancement of medical science with societal relevance. The Clinical Epidemiology programme is clearly excellent in all aspects reviewed by the committee. The programme should maintain its major efforts to sustain good funding and to balance and organise its activities to preserve the high level of science, continue to give methodological advice to the LUMC community and contribute to the current development of big data in medical research.

6. Assessment of the research programmes - Division 3

6.1 Innovation in gynaecological surgery & oncology

Department:	Gynaecology
Research programme:	30101
Scientific staff (2016):	1.9 fte
Quality:	3
Societal relevance:	3
Viability:	3

Brief description of the research programme:

The research programme aims to bridge the results of basic and translational research, new surgical techniques & technologies and to evaluate and improve quality of life after treatment for gynaecological (cancer) diseases into daily practice.

Research quality:

The research of this programme focuses on the holistic approach towards diseases of the female genital track. The research programme is small, and the focus of the research is not always very clear to the committee: there is work on robotics, on therapeutic vaccines, on treatment of vulvar cancer, etc. Since 2011, there is a clear dip in the citation numbers, reflected in the MNCS (from 1.71 to 1.17). The research programme is looking for collaboration with Erasmus University. However, this collaboration is both seen as an opportunity and a threat, this needs clarification. As there is no programme leader at the time of the site visit (the programme is looking for a professor with an oncology-profile but was not yet successful in finding the person with the appropriate profile), which means that credits for PhD graduations sometimes go to other departments.

Relevance to society:

There is a start of patient involvement in research proposals. In IVF-studies, there was use of an app. However, societal relevance seems limited.

Viability:

The future of this programme depends on the formulation of a clear focus, finding the appropriate partnerships, but the main issue is to find the needed leadership.

Conclusion and recommendations:

The future of this research programme is not clear. Focus and leadership are needed. There is little evidence that indicates a successful future. Linking with strong oncology programmes is of utmost importance.

6.2 Research into foetal development and medicine

Department:	Obstetrics
Research programme:	30201
Scientific staff (2016):	1.9 fte
Quality:	3
Societal relevance:	3
Viability:	3

Brief description of the research programme:

The research programme aims to provide the best care for pregnant women, aiming for happy mothers and healthy babies. The programme focuses on three themes: foetal medicine, maternal health and reproductive immunology. The research programme is embedded and organised in the department of Obstetrics. This programme has four different research lines:

- Foetal medicine
- Foetal cardiac diagnoses
- Maternal health
- Reproductive immunology

Research quality:

The quality of most of the research is good. The foetal cardiac work is very good, particularly the large number of patients investigated, the database and teaching. There are many large research units in the world also doing foetal cardiac diagnoses, so it is difficult for this research line to compete at the highest level because of its small size.

The foetal therapy is doing well in twin to twin transfusion therapy research. Although good clinical work is obviously being done there is little other innovative research. Hopefully the treatment of open spina bifida will prove successful. Maternal health has good epidemiological data, which has provided new insights into the associations and possible causes of some serious maternal morbidities. However, now this is not being translated into studies to see if they can be modified. The immunology of maternal-foetal interaction is exciting and hopefully the findings will lead to a better understanding of miscarriages and how they can be prevented. It will be interesting if they can investigate the influence of the fathers on recurrent miscarriages and related topics.

The committee noted that staff numbers seem to have risen but external funding has reduced over the last years. The committee could not see a specific financial strategy. In addition, the programme needs more publications of innovative research in higher impact journals.

Relevance to society:

There is evidence of the relevance of the research to society in the foetal therapy research line of this research programme such as organising an international research consortium leading to a new treatment strategy in Twin-Transfusion-Syndrome. The research programme has also developed a foetal therapy simulator model and a training course has been developed. However, the impact involvement in other areas (maternal health and reproductive immunology) is less influential.

Viability:

The committee believes members of this research programme are individually doing well. However, the programme is too isolated. It aims to integrate three themes, but it is not clear how this will be achieved. According to the committee the vision for the future is not clear.

Conclusion and recommendations:

The committee concludes that this programme does promising research but needs a clear vision to stay viable. The committee believes more staff will be needed to expand their collaborations and follow-up work. The research programme also needs professional support from a clinical trials unit to start large randomised controlled intervention trials. The programme might consider integration of their immunology research with immunology and transplantation research of other programmes.

6.3 Dermatology-oncology

Department:	Dermatology
Research programme:	30401
Scientific staff (2016):	2.5 fte
Quality:	2
Societal relevance:	2
Viability:	2

Brief description of the research programme:

The research programme focusses on three topics: 1) cutaneous lymphoma 2) (familial) melanoma; and 3) keratinocyte carcinoma, particularly in organ-transplant recipients. Central themes within the research programme are characterization of clinically relevant patient subgroups, identification of (epi)genetic alterations and interaction of tumour cells with the immune system.

Research quality:

There is synergy between the three themes, particularly in relation to laboratory techniques and clinical infrastructure. This synergy has been fostered by more formal interaction between the different groups, overlap in assays between themes and the development of functional platforms. There is also greater interaction and synergy with haematology, particularly in the cutaneous lymphoma theme and in relation to clinical trials.

Overall research quality is high, with very good papers in high impact journals. Bibliometric indices are very good and output volume is around 35 papers per annum, despite the fall in staff numbers since 2014. The research programme has demonstrated international leadership in cutaneous lymphoma and melanoma, and has a good presence in keratinocyte neoplasia, particularly in in vitro models.

Relevance to society:

Societal impact policy was not clearly stated within the self-evaluation report, with little evidence of specific targeting, but the group has good involvement in, and impact on, international guidelines, particularly in cutaneous lymphoma. There is a melanoma platform with patients, technicians, doctors and others.

Viability:

There is a clear plan, focused around the three themes. However, the financial aspects are not clear. The programme appears to be contracting, with a reduction in fte number from 5.6 in 2014 to 2.5 in 2016. However, a research line has been discontinued as a result, and the programme considered present funding to be sufficient. Nevertheless, it is trying to

expand and is applying for grants, particularly from the Dutch Cancer Society. The programme reflected that funding was now more in the form of personal grants, so they are looking for young people who want to apply for grants.

The programme highlighted a problem with support for clinical trials, an issue that they have addressed by increasing their collaboration with haematology.

Conclusion and recommendations:

This research programme has produced very high-quality research. The programme has contracted but the group has responded strategically by focusing their efforts on three related research areas. The issue with clinical trials appears to be significant and review of institutional support in this area would be warranted.

6.4 Disorders of the head and neck

Department:	Otorhinolaryngology
Research programme:	30501
Scientific staff (2016):	3.5 fte
Quality:	2
Societal relevance:	2
Viability:	2

Brief description of the research programme:

The research programme focuses on (neuro-)otology (disorders of the inner ear, i.e., the cochlea and vestibular organ), specifically auditory implants (CIs and ABIs, electrical prostheses for the deaf) and vestibular disorders, with a focus on Meniere's disease. There are three main research tracks, the first being more technical, the second more biological, and the third one focussing on evaluation of care.

Research quality:

This programme has mainly built-up high-quality research on auditory implants, i.e. cochlear implant (CI). In this domain its research is integrated in the second largest Dutch clinical programme on auditory prostheses for the deaf and severely hard of hearing and achieved an internationally high ranking in terms of scientific output. The number of papers is rather limited but shows very good MNSC scores (1.44). Multicentred studies and new collaborations could be beneficial for further development. The research is increasingly integrating the more biological-translational and technical aspects of this domain (including longstanding collaboration with several groups of the TU Delft): computer modelling, CT scan protocols, eCAP recording chips, speech production tests. This CI-related research seems not strongly connected with the Leiden Centre For Translational Neuroscience. The funding is largely external and depending on one commercial partner. Overall, this research programme developed well, became more focused, coherent and integrated, encompassing biological and technical aspects, besides evaluation of care. Multicentred studies and new collaborations could be beneficial for its further development. With the recent arrival of the new chair of the department, research will be expanded also to vestibular pathology, especially Meniere's disease, but this project seems to be in an initial stage and needs further elaboration.

Relevance to society:

The research in CI has a clear societal input (e.g. paediatric C.I., speech production tests, etc.), but this is a limited niche in otorhinolaryngology. The new work on Meniere's disease is already integrated in a Meniere platform, in which also patients are involved and can ask research questions. This research programme opens larger possibilities for societal benefits.

Viability:

The research of this programme has become more targeted and integrated in the evaluation period. The combination of clinical, fundamental and technical aspects remains challenging. The research staff is limited, seems to be enthusiastic and well collaborating, with low ratio staff to externally funded researchers and clinically active PhD's.

Conclusion and recommendations:

This programme has shown a positive evolution during the past years, performing at an international level regarding the CI research, and developing a more coherent, focused and collaborative project. These efforts must be increased and continued in the prospective of expanding the research to the vestibular field. Searching for new collaborations and participation in multicentred trails, and for possibilities to broaden the staff, can support further positive development.

6.5 Scientific Assessment and Innovation in Neurosurgical Treatment Strategies (SAINTS Leiden & The Hague)

Department:	Neurosurgery
Research programme:	30601
Scientific staff (2016):	1.3 fte
Quality:	1
Societal relevance:	2
Viability:	2

Brief description of the research programme:

The objective of the research programme is to clinically improve the outcome of peripheral nerve surgery, as well as in in degenerative, traumatic and oncological disorders of the spine. Traumatic brain injury and skull base pathology are rather new areas of interest. The pre-clinical objective is to improve nerve regeneration with gene therapy and find new solutions for the treatment of neuropathic pain related to trauma.

Research quality:

The quality of this programme's scientific work is very high at an international level. There are several publications in journals of the highest impact such as New England Journal of Medicine and Lancet Neurology. The biggest strength has been in organising multicentre randomised clinical trials of neurosurgical treatment. This was internationally a neglected area and it seems very likely that the programme can continue this work at the international front line.

Internationally the treatment of traumatic brain injury (TBI) has not improved very much over the last 30 years, so the programme´s efforts are much needed. The TBI work will be done in collaboration with The Hague which, although this is a reasonable development, is also a bit hazardous because it will be more time demanding. The Hague (HMC) and Leiden (LUMC), however, are constructing one department of neurosurgery, including research and education besides clinical work. The skull base group of this programme was started a couple of years ago and seems to be doing very well. There is strong national collaboration including a national quality database and collaboration inside the LUMC. Thus, the multidisciplinary aspect is in focus. Multicentre trials of treatments can only be done for relatively common tumours, mainly pituitary tumours and they are already in planning. The nerve surgery group of this programme has consistently been at the top international level. New developments using Gene Therapy and other advanced methods to improve results point forward.

Relevance to society:

The programme is involved with patient organisations and has considerable focus on patient reported outcomes. An app for patients with pituitary tumour has been developed and awaits security clearance.

Viability:

In general, the viability of research in this programme is very good. There are strategic plans and the programme is not threatened by forthcoming retirement. There are vigorous experts in charge of all subgroups within the programme.

Time is a problem for neurosurgical research because all leaders have a heavy commitment to clinical work not least to operations. More direct funding and external funding is needed to relieve some of the leaders of part of their clinical burden. It should also be considered that post docs could release more time and energy in the leader group. It is laudable that the programme stopped collaboration with industry because of a perceived undue influence. Fortunately, the programme will consider opening new collaborations with associated funding if a form of collaboration can be developed that does not compromise research integrity and independence.

Conclusion and recommendations:

The committee concluded that this research programme is very strong. The committee commented, however, that the spine group of this programme should try to preserve its international reputation by elaborating on complementary specific and visionary plans. For brain trauma, greater focus on European consortia and EU funding should be considered since randomised trials need volume and must be transnational. The committee also recommends a stronger collaboration with the highly advanced MR function at the LUMC.

6.6 Paroxysmal Cerebral Disorders (PaCD)

Department:	Neurology
Research programme:	30702
Scientific staff (2016):	3.2 fte
Quality:	1
Societal relevance:	1
Viability:	1

Brief description of the research programme:

The research programme aims to study the clinical features, diagnosis, epidemiology, socio-economic impact, structural and functional cerebral consequences, pathophysiology, and treatment of highly disabling and mechanistically-related brain disorders that primarily are characterised by recurring attacks of disabling acute transient cerebral dysfunction.

Research quality:

This programme performs at the highest international level with several publications in high impact journals and a MNCS over 3. It is extremely difficult to give advice about what could be done better. The core line of research is migraine. It is pointed out that a clinical trials unit is missing at LUMC and that this has limited the number of clinical trial that the group can do. Nevertheless, the programme has completed a very large randomised, double blind trial of treatment with botulinum toxin. The programme has collected material of spinal fluid and blood from 200 migraine patients and 100 healthy volunteers, something that other programmes have considered impossible. It is extremely important that the group obtains collaboration and support from advanced chemistry to do metabolomics and proteomics on these incredibly valuable samples. Likewise, the collaboration with the Motor Disorders programme at the LUMC is very important. It has already yielded impressive results, but much more is waiting if the programme can get enough time on the 7T scanner.

The low hanging fruits in the genetics of migraine have already been harvested but it is important to continue the work on migraine genetics. The programme has a leading position within the International Genetics Consortium which needs to be maintained. In addition, direct collaboration with leading groups with large well characterised cohorts about whole exome and whole genome sequencing is likely to be productive soon. The programme has shown great proficiency in generating genetically modified mouse models of migraine. If variants with high relative risk of migraine can be identified, the programme is well positioned to turn this into yet another mouse model, perhaps with even more important than the ones presently available. A spin-off group on rare monogenic forms of stroke focuses on amyloid angiopathy, CADASIL, RVCL-S and migraine with aura. It has developed rapidly and has produced very interesting publications in international journals with middle

to high impact. The syncope group is another interesting newly started group. The problem with this research field is the funding. Therefore, the programme must be prepared to spend a lot of effort to get the sufficient funding and not to be discouraged by several negative outcomes of grant applications. The synergism with the migraine group is obvious and should be in focus also in the future.

Relevance to society:

This programme focuses on very common disorders affecting a large part of the population. It has been active with patient organisations, has developed an IT programme for patients who are willing to join research and it has produced an app for patient reported outcomes that is just awaiting security clearance.

Viability:

Considering the incredible track record of this programme, there is no reason to doubt that it can continue at the highest international level. If one tries hard to look for problems the following could be mentioned: The whole programme is led by relatively few people who have relatively little research time. They have amply proven that they can do it by hard work and intelligent leadership, but one wonders how sustainable it is to run such a top international group with so little formal research time in case of unforeseen retirement or illness. In relation to this, the committee wondered if it is possible to supervise over 30 PhD students sufficiently well.

Conclusion and recommendations:

In conclusion, this is a programme that has performed at the highest international level and with certainly will continue at this level. It is recommended that leaders should have more time for research. Other than that, it is just recommended to continue as planned.

6.7 Neurological Motor Disorders

Department:	Neurology
Research programme:	30703
Scientific staff (2016):	7.7 fte
Quality:	1
Societal relevance:	1
Viability:	1

Brief description of the research programme:

The research programme focuses on diseases related to two complementary levels of the motor system. The aim of the programme is to conduct innovative research on clinical profiling, disease course, quality of life, clinical and radiological biomarkers, pathophysiology and development of new treatments.

Research quality:

The quality of research in this programme is generally very high and for several lines it is at the top international level. It is a, however, a rather heterogeneous group where it is difficult to see that the common name has a real meaning. Particularly it is difficult to see the relatedness of peripheral and central motor disorders. The programme leader did, however, point to several synergies, mostly in relation to the investigational techniques. So, it is recommended to continue without disbanding any of the lines of research.

Duchenne muscular dystrophy (DMD) continues to be the flag ship although the exciting study of exon skipping unexpectedly was negative. The experience is now being used in studies of Huntington's Disease (HD) and CADASIL, which are also badly in need of effective therapy. Other therapies are now being studied in DMD. Of interest is the demonstration of MR abnormalities in the brain and the possibility to study this in a genetically modified mouse model. The unique material of patients with Myasthenia Gravis (MG) is being further expanded and refined and used in multinational studies. The search for biomarkers that are suitable as surrogate markers for therapeutic response is important both for DMD and MG because it will increase strengthen clinical trials and shorten them as seen in other diseases. This will make it possible to screen more potential treatments. In DMD patient reported outcomes are not relevant until a treatment has a proven effect and it should not consume energy at this stage. The possibility to study muscle diseases on a chip with cells derived from patients is tantalizing and should be pursued vigorously. The committee notices with satisfaction that a special grant has been obtained for this research. The group on HD harbours a unique collection of patients as a centre of excellence in The Netherlands. This group is also at the high international level. Antisense oligonucleotide and exome skipping are exciting new potential treatments in a disease where no disease modifying treatment

exists. Also, the organ on a chip project and the development of MR biomarkers as surrogate markers in clinical trials are very important research topics.

Parkinson's disease is a more difficult field because of fierce competition in this relatively common disease. Furthermore, it is a relatively new research field at LUMC. It does seem, however, that it has been added with success and has reached a competitive national but not yet a top international level. It seems important to continue, partly because the NMD needs research into a more common disease and partly because there are synergistic opportunities in relation to some of the basic techniques mentioned above especially the TIM laboratory.

Relevance to society:

The programme has been very active with patient organisations. It focusses on patient reported outcomes and it produces informative articles in lay journals and other public media.

Viability:

This programme has produced at a high international level for many years and there is no sign of weakening. Likelihood is, therefore, that it will continue at a high international level. Four leaders are due to retire in the foreseeable future. The committee is pleased to note that the leadership has already taken measures for succession.

Conclusion and recommendations:

This programme is a conglomerate with some techniques linking the different lines of research. Several research lines are at a top international level. The committee recommends increasing synergy between research lines. Also, efforts to let younger colleagues assume leader responsibility should be increased.

6.8 Ophthalmic research

Department:	Opthalmology
Research programme:	30801
Scientific staff (2016):	6.2 fte
Quality:	3
Societal relevance:	3
Viability:	2

Brief description of the research programme:

The research programme focusses on four clinically-relevant areas: ocular oncology, retinal diseases, paediatric ophthalmology and cornea and refractive surgery. Clinical and translational research is disease initiated, and involves improving diagnoses, prognosis, treatment and individualised eye care.

Research quality:

The main topic of this programme is ocular oncology, especially ocular melanoma, in which the programme is an international expertise centre and the national reference centre. The programme combines clinical (local irradiation, imaging) and translational (molecular pathways; immunology research). Also, in retinal diseases (e.g. central serous chorioretinopathy and age-related macular degeneration) the programme is investigating genotype-phenotype relationships, and the participated at over fifteen clinical trials on drugs for improving visual function; their new focus is on regenerative therapies. In paediatric ophthalmology, the focus on abnormal angiogenesis, e.g. in Retinopathy of Prematurity (ROP) by developing imaging (camera) and oximetry is interesting. It definitively needs collaborations with other centres to constitute sufficiently large patient groups.

Ocular oncology remains the major topic of this programme. The integration of the Eye lab in the lab of clinical oncology seems already fruitful and promising. New possibilities for genetic research and future clinical gene therapy are in development. A major problem consists of poor data collection and there is need for improvement of data registration, patient follow-up systems and detailed outcome analysis. Overall, the research of this programme still seems too broad and too little focused, regarding the size of the programme. The scientific output is average regarding the bibliometric output. The staff has profoundly changed: young ophthalmologists with keen interest in research joined the staff and two new professors were appointed. The number of PhD’s highly increased. Funding remains a main problem: externally supported staff decreased, and more external sources for funding (EU-industry) must be sought.

Relevance to society:

The societal relevance of the research work of this group is limited. A fast one-day track for uveal melanoma patients was developed, and the department puts efforts in patient information. The programme invests highly in optimizing patient care.

Viability:

Overall the programme has achieved a more stable and viable position. The scope remains too broad and efforts must be maintained to achieve more collaboration and cohesion. The position and the future of the cornea and refractive surgery research line remains uncertain. A decision must be made concerning the future of this research (limiting or stopping?). In regard of the expansion of the programme, funding seems to become a more urgent problem.

Conclusion and recommendations:

The size of this programme is expanding with enlargement of staff and increasing number of PhD's. This stresses the urge for clearly defining the scope of the research and putting efforts in the major strengths (oncology, retinal diseases and ROP), and in more efficient data collection. Also, a clear funding strategy is needed.

6.9 Immunopathology of vascular and renal diseases and of organ and cell transplantation

Department:	Pathology
Research programme:	30901
Scientific staff (2016):	1.3 fte
Quality:	2
Societal relevance:	2
Viability:	2

Brief description of the research programme:

This research programme aims to elucidate the underlying mechanisms of defective vascular and epithelial repair. The diseases the programme studies concern: diabetic nephropathy, lupus nephritis, ANCA-associated vasculitis, polycystic kidney disease, IgA nephropathy, focal segmental glomerulosclerosis, preeclampsia, and renal allograft rejection. In addition to the investigative approach, the group is also interested in molecular testing, with the increasing recognition that a significant proportion of renal diseases have a genetic component.

Research quality:

The output volume of this programme is relatively low (around 15 papers per annum) but is of high quality with excellent citations and other bibliometric indicators. The programme is stable in terms of fte number but has a high PhD student number per supervising staff member. The programme has temporarily stopped applying for external grants as they already have sufficient funding to support their current activity.

The programme interacts with the other research programme in pathology (30902) and they hold weekly joint lunches. However, there are clear differences in focus between the two programmes. There are also difficulties in linking data to tissue samples because of regulatory pressures.

Relevance to society:

The programme has active collaborations and discussions with patient organisations, relating not only on to use of data but also to the interests of patients. However, the output of the programme is largely academic and further consideration of how this research could interface with patients would be appropriate. It is acknowledged, however, that pathologists do not regularly interact directly with patients, so this might be best achieved indirectly, via the treating clinicians.

Viability:

The plans are wide-ranging but are, in general, focused on endothelial cell dysfunction in a range of renal and vascular diseases. This focus is logical but does lead to a breadth in terms of disease processes that may be difficult to sustain at the highest level. Although the programme is currently recruiting for a postdoctoral researcher, the low fte number is a concern for viability as the programme's future is dependent on a small number of individuals.

Conclusion and recommendations:

This is a high-quality research programme with international reach. The programme is stable but the low staff numbers present a risk for future viability and development. The interaction with the other research programme in pathology is good but more formal linkage to other cognate research programmes, including those involving immunology and immunopathology, may help to improve sustainability. Formalisation of the processes by which data are linked to tissue would also help to sustain the already high-quality output.

6.10 Molecular tumour pathology - and tumour genetics

Department:	Pathology
Research programme:	30902
Scientific staff (2016):	4.2 fte
Quality:	1
Societal relevance:	2
Viability:	1

Brief description of the research programme:

The research programme aims to deliver personalised medicine for the treatment of bone and soft tissue tumours, female cancers, breast cancer, colorectal cancer and endocrine tumours. The whole pipeline from bench to bedside is covered with special focus on cancer genetics, immunotherapy and molecular therapeutics.

Research quality:

This is an internationally-recognised and influential research programme. The interests cover a range of tumour types, but the research is integrated by common mechanisms and investigative techniques. The research outputs are excellent, with very good bibliometric indices. The programme has made significant contributions across the range of tumour types being studied and produces around 75 papers per annum. Following the 2015 mid-term review, two previous programmes were merged to form the current programme; this has been highly successful and, together with cohesion with other components of the LUMC, provides significant strength.

The tumour types were chosen based on the LUMC top centres and the expertise of the pathologists. Genomics is a very competitive field, but the group is competing very effectively and is increasing its profile internationally, for example in gynaecological cancers, where the work on endometrial carcinoma is world-leading.

Relevance to society:

The programme contributes significantly to the development of guidelines and useful tools for the profession, particularly in relation to hereditary cancers, clinical testing and clinical trials. Members of the programme commented that involving patients in their grant applications had been a useful process.

Viability:

The programme has expanded since 2014, with a rise in fte's from 2.9 in 2014 to 4.2 in 2016. The PI's in the programme are excellent and recruitment of younger faculty members has been highly successful. The strategy for the future is excellent, with appropriate recognition

that clinical workload and legislative frameworks that have an impact on research present threats.

Conclusion and recommendations:

This is an excellent and highly productive research programme. The challenge for the future will be to sustain the upward trajectory, particularly in the face of the constant developments in genomics and other molecular technologies. The programme clearly recognises this issue and gave confidence that they can cope with the challenges.

6.11 Stress-related psychiatric disorders across the life span

Department:	Psychiatry
Research programme:	31001
Scientific staff (2016):	5 fte
Quality:	1
Societal relevance:	2
Viability:	1

Brief description of the research programme:

The research programme aims to better understand the onset, course and chronicity of stress-related psychiatric disorders across the life span and to translate our findings into personalised treatment and prevention for our patients and their families.

Research quality:

This research programme is a strong and coherent programme, targeting mood, anxiety and stress-related disorders during the life span (children/adolescents, adults, elderly), combining clinical, neurobiological, psychological and social determinants. The previously separate research programmes of the department of Psychiatry and the department of Adolescent and Child Psychiatry have merged into a single programme. This new programme builds on the collaboration of the eight chairs in adjoining fields of psychiatry.

A major strength of this programme is longitudinal cohorts with extensive clinical, psychometric and increasingly neurobiological data. This transdiagnostic and multidisciplinary life span approach allows the deepening of the projects into neurobiological determinants of these disorders, early detection and prevention, the role of trauma, and more symptom and dimension - driven personalised medicine. The work of this programme fits well in current trends in psychiatry research, i.e. the combining of large cohort data with deep phenotyping. The scientific outcome of this programme is very high, in quantity and in quality, regarding the bibliometric analysis. The number of PhD's has increased to more than 30. A minor threat is the limited size of the research staff and limited capacity to respond to new developments, i.e. in primary care and at the population level. The funding is stable, and the programme does not intend to grow.

Relevance to society:

The research of this programme has important societal relevance: symptom network analysis, dimensional and life span approaches, output concerning directly the clinical care (ROM-data). Products (instruments-guidelines) have direct clinical relevance. However, the societal translation of the research to all stakeholders and its impact could be improved; and a clear strategy for this is lacking.

Viability:

The viability has clearly increased. The programme is coherent and future-oriented, the researchers demonstrate a clear and adequate strategy. The cohesion and collaboration within this programme seem strong and well established. Changing contextual factors in Dutch mental health care and psychiatry could influence future developments (i.e. the decentralisation of adolescent and child psychiatric care). The age structure of the senior staff will necessitate rejuvenation.

Conclusion and recommendations:

This research programme is a strong and coherent programme, directed to future developments in psychiatry. The programme has an impressive scientific output. However, the age structure of the senior staff will necessitate rejuvenation and more attention must be given to the improvement of societal translation of the research findings and their implications.

6.12 Geriatrics in primary care

Department:	Public Health and Primary Care
Research programme:	31201
Scientific staff (2016):	5.5 fte
Quality:	1
Societal relevance:	2
Viability:	1

Brief description of the research programme:

The aim of the research programme is to improve health, functioning and quality of life for all older persons outside the hospital by building on scientific knowledge and evidence for (the organisation of) medical care. Improvement of health, quality of life and daily functioning of older people are the main aims of the research, with perspectives and needs of older people as a guide.

Research quality:

This is a world leading programme in the field of research on the elderly, especially focusing on chronic conditions, comparable at least with leading programmes internationally. There is a strong focus on care organisation. The output is excellent, and the programme has now clearly chosen a transition towards organisation of primary care for all the persons, geriatric rehabilitation, using a goal-oriented approach, with emphasis on 'functional status'. In the output there is important 'additional' work e.g. on the management of sub-clinical hypothyroidism and clinical infections, a very relevant topic. One of the strong points of the programmes is a comprehensive approach, looking at quality of life and palliative care. The programme is very successful in the application for important funding.

Relevance to society:

The research of the programme is relevant, as it deals with the important challenge of multi-morbidity. In addition, there are contacts with population- and patient-groups. Patients are more and more actively involved in the research, and progress is ongoing. There is also an 'elderly board', advising about new projects.

Viability:

The perspectives for this programme are very positive and there are clear indicators that they will strengthen their position as a leading research programme in the field of chronic care for the elderly, multi-morbidity and goal-orientated care.

Conclusion and recommendations:

The committee concludes that this is an excellent programme with very good output. The capacity to deliver is high in this programme. The future therefore looks very promising.

6.13 Prevention, population health and disease management

Department:	Public Health and Primary Care
Research programme:	31202
Scientific staff (2016):	6.3 fte
Quality:	2
Societal relevance:	1
Viability:	2

Brief description of the research programme:

The main objectives of the research programme are 1) Developing pro-active approaches to identify and reach individuals/groups with an increased risk of chronic disease or adverse health conditions; 2) Developing and evaluating indicated prevention and disease management programmes; and 3) Developing strategies for and evaluating the implementation of (cost)effective structured care programmes.

Research quality:

This research programme is in a clear transition phase, from traditional research on chronic obstructive pulmonary disease, development of questionnaires in relation to certain chronic conditions, research on asthma, evolving towards a population health approach. However, the programme is looking for an appropriate framework to address the research on population health as comprehensive as possible. The group is actually exploring the 'syndemics-approach, combining information on multi-morbidity with contextual information. The programme will certainly come up with new ideas and strategies in relation to the study of population health in the future, after a critical analysis of the actual trends in research in this field. It chose for an interdisciplinary methodology, which is worthwhile. A strong point is that the programme has contacts with a lot of practices in the field of primary care, also in the new The Hague-campus. In the new field of e-health, the team addresses new and challenging research questions.

Relevance to society:

The work this programme is doing, is highly relevant to society, and the research is completely embedded in the local primary care structures, involving all the relevant stakeholders: care providers, policy makers, local authorities, population representatives, etc.

Viability:

This programme has the potential to become a very important player in the research field of population health, starting from a primary care orientation. It will be important that

connections with the programme ‘geriatrics in primary care’ (31201) will develop the important link between comprehensive care provision on the one hand and population health approach on the other hand. The strength of the programme is that a lot of staff members are embedded and active in the local community in primary care. However, nowadays, there is no clear vision yet on the way to go. Definition of a clear focus is of utmost importance and conditional to further successful developments. There is an important challenge for the leadership to make this happen, as this process needs a clear direction.

Conclusion and recommendations:

This programme has the potential to become a very strong research group in the interesting field of population health, from a primary care perspective, provided the leadership will be able to help the programme to focus. Moreover, new developments such as e-health and the active promotion of citizen science are promising in terms of future research.

6.14 Transplantation and immunomodulation

Department:	Paediatrics
Research programme:	31301
Scientific staff (2016):	3.9 fte
Quality:	1
Societal relevance:	2
Viability:	1

Brief description of the research programme:

The aim of the research programme is research projects is to identify molecular mechanisms of disease and to develop novel therapeutic and/or preventive strategies to modulate these immune-mediated diseases leading to improvement of health care and quality of life of paediatric patients. This programme has research into four projects:

- Allogenic stem cell transplants for non-malignant diseases (SCT)
- Coeliac disease (CD)
- Juvenile idiopathic arthritis (JIA)
- Langerhans cell histiocytosis (LCH).

Research quality:

According to the committee, the groups within this programme have all contributed internationally to the knowledge and treatment of the conditions. They are actively publishing in relevant journals and very well cited. All the senior staff have (high) international recognition. The research of this programme is very innovative with new ideas and techniques to improve the understanding and treatment of these serious conditions. The SCT team has a longstanding international reputation for their clinical and laboratory research programme. They are coordinating or participating in several EU funded groups and have a unique and competitive multidisciplinary research team. The coeliac disease team has strong LUMC centred international collaborations and robust research projects including coordination of/participation in EU funded consortia. The JIA team has longstanding expertise and innovative clinical research programs focused on treatment of children with autoimmune diseases. Strong collaboration with Rheumatology department and Centre for Human Drug Research. Leading position in the Medical Delta alliance with Erasmus MC, and in addition strong collaboration with paediatric rheumatology in AMC/Amsterdam.

Relevance to society:

The committee noted that a relevant impact is provided. The research programme has good contact with relevant patient groups. The programme is targeting important diseases that

can be difficult to manage. Even if the programme is only partially successful, this will be very good for patients with these diseases.

Viability:

The committee believes the programme has a good future strategy. It is very well organised and has good plans for future work. The programme has obvious strengths. The only possible threat is the retirement of two professors in 2020. The committee expects that they will be successfully replaced for the work to continue. The committee is confident that this research programme will continue to be successful.

Conclusion and recommendations:

The committee is convinced that the programme is internationally highly visible and well on its way to be an influential leader in transplantation and immunomodulation research. Researchers in this programme should continue to be well supported for them to progress. If possible, it would be good to increase their time for research and possibly number of staff members. As the programme is running big trials it should be ensured that it has professional support from a clinical trials team.

6.15 Development

Department:	Paediatrics
Research programme:	31303
Scientific staff (2016):	2.4 fte
Quality:	2
Societal relevance:	2
Viability:	2

Brief description of the research programme:

The research programme studies the development and regenerative capacity of the lung, cardiovascular system and skeleton from a basic science setting to clinical practice with a special focus on early (intrauterine) life events and their effects on future development of disease. This programme has five different research lines:

- Neonatal transition / resuscitation
- Cardiovascular imaging
- Arrhythmias
- Genetics of growth
- Neurodevelopmental outcomes after foetal surgery

Research quality:

After the midterm review of 2015 this programme was centred around five themes and other themes were discontinued. More joined research and important collaborations were realised in several projects. The committee applauds this reorganisation. The quantitative data provided in the self-evaluation report give a good picture of the research activities of the programme and of the productivity of its researchers during the reference period. The programme has a very good record of publications in appropriate journals. According to the committee, there is an increasing impact in all five research lines. In addition, the principle investigators all have high reputations in their fields.

Relevance to society:

The committee noted that a relevant societal impact is provided. Although there is some variation across research lines, it became clear that the published papers create changes in treatments like delayed cord clamping and more effective resuscitation of all babies at birth. The close collaboration between neonatologists and foetal therapists has led to a substantial improvement in the management and outcome of twin to twin transfusion syndrome and will lead to the improvement in other foetal therapies. The novel cardiac imaging of children with congenital heart disease and ability to make 3D models of affected hearts will improve the outcome for these children.

Professionals, patients and patient groups both in the Netherlands and internationally recognise the leading role of the Leiden-Amsterdam collaboration in improving the management of foetal arrhythmias. The work into the genetics of rare growth disorders is now providing the Netherlands with a referral centre to improve the medical understanding and care of these children.

Viability:

The committee believes there is no reason to believe that this group of researchers and projects will not build on their successes in the upcoming period. All research lines have good future perspectives. The research plans are at the leading edge and have the potential to be very informative and have a good impact on the effected children and their futures. Possible threats are the limited number of (permanent) staff to achieve these plans and limited funding in several lines, especially genetics of growth.

Conclusions and recommendations

This research programme is very successful and has good future perspectives. The committee has two recommendations:

- Expert support is needed to ensure the clinical trials are professionally prepared, planned and managed. This does not imply that they are doing badly but running clinical trials requires an expertise that will result in excellent studies.
- Good follow-up is vital to all foetal and neonatal research endeavours. Facilitating this should be a priority.

7. Assessment of the research programmes - Division 4

7.1 Analysis and support of clinical decision making

Department:	Biomedical Data Sciences/Medical Decision Making
Research programme:	10801
Scientific staff (2016):	6.8 fte
Quality:	3
Societal relevance:	3
Viability:	2

Brief description of the research programme:

The programme aims at improving quality of care and outcomes of care, by improving decision-making and care processes, and by developing and evaluating methods for quality of care research. The research themes are a) Modelling, b) Patient-level decision-making, and c) Processes and outcomes of care.

This programme recently moved to the department of Biomedical Sciences with a newly appointed chair. In the future the research programme will be part of the Leiden Centre for Quantitative Methods, in collaboration with the department of Clinical Epidemiology and Statistical Modelling Group. All research fits within the medical research profile Innovation in Health Strategy and Quality of Care.

Research quality:

The committee assessed the research quality as good. The reliable indicators of care quality this programme develops in collaboration with statisticians, are of interest to external researchers in this field. Getting these methodologies to the clinic to improve quality of care is seen as a high priority. Some of the publications are in high impact journals, including JAMA, BMJ paper on shared decision making and JCO. This impressed the committee which recognised it was harder to achieve such publications in this field compared with fundamental science. However, bibliometrics have been falling in more recent years. This programme gets many relatively small amounts of funding (often linked to studentships) and the total earning capacity appears rather low in 2016. The programme does not just wait for the clinicians to drive the research but works closely with them to identify new research areas. The committee thought there might be more scope to integrate biological information and self-reported patient outcomes across the programme with a focus on personalised medicine. The committee felt a more careful analysis of weaknesses of the programme in the self-evaluation report would have been helpful.

Relevance to society:

This type of research by itself has considerable societal relevance, but some concerns exist about how well it was executed. The research programme is undertaking good research but is still in an early stage of translating the outcomes to societal impact. The committee considers that active participation of citizens in research can be done more strongly. Creating citizen scientists is a relevant goal for this programme.

Viability:

The committee believed the new department head will be able to take advantage of the research programme's clinical and methodological strengths and there will be benefits for this group in joining the department of Biomedical Science in terms of greater interactions, critical mass and expertise in getting grants. The vision and plan for a Centre for Quantitative Methods would also benefit this programme and make it more visible and attractive to master students and potential PhD students. There are opportunities for greater integration of multidisciplinary approaches with the more biologically oriented research programmes. The field of clinical decision making, and self-reported outcomes is a growth area in which this programme should be able to build an even higher profile with their nice ideas for the future and by thinking slightly more outside traditional boundaries.

Conclusion and recommendations:

The committee recommends that the vision/plan for a Centre for Quantitative Methods be supported by LUMC and that this programme would sit well in this new centre.

7.2 Precision Haematology

Department:	Haematology
Research programme:	40103
Scientific staff (2016):	5.7 fte
Quality:	2
Societal relevance:	2
Viability:	3

Brief description of the research programme:

The natural behaviour of haematological diseases and their responses to targeted therapeutic interventions are governed by recurrent and individual pathogenic drivers. In treating patients with stem cell transplantation inherited and adaptive immune mechanisms of the host and of the stem cell donor play decisive roles for success and outcome of the therapy. The programme aims to:

- Exploit advanced molecular profiling for mechanistic understanding of molecular and immunological pathogenic factors to individually optimize therapeutic interventions;
- Unravel mechanisms of haematopoiesis- and malignancy-directed immune reactivity;
- Develop novel diagnostic and bench-to-bedside therapeutic strategies based on this new knowledge.

Stem cell transplantation remains a cornerstone for the treatment of haematological malignancies with its own specific advantages such as graft-versus-leukaemia response and disadvantages such as graft-versus-host disease. The repertoire of treatment options has been significantly enlarged in recent years. This has resulted from the capacity to acquire detailed knowledge of the molecular aberrations underlying these diseases as well as more treatment options based on an increasing number of targeted drugs and immunomodulatory strategies for intervention. The programme can now capitalise on their long-term experience in this field and explores strategies based on manipulating T-cells and their recognition of tumour-specific antigens, pathogens, minor histocompatibility antigens, or lineage-specific antigens.

Research quality:

The committee was impressed by the scope of the translational research of the programme, although their prominent position in immunology of haematological diseases is not quite reflected in the publication record. In this regard the programme could be more ambitious. The research portfolio of the department is quite broad and with the rapid expansion of this field it will require discipline to maintain sufficient focus, especially for a modestly sized research department. At the same time the committee acknowledges that this concern is mitigated by the many interactions investigators have with other LUMC groups involved in

immunological research and immunotherapy. T-cell receptor focused interventions are an evident emphasis of the department and offer excellent future perspectives. However, with one of the driving PI's taking a leading position in the Dutch Cancer Society the programme will lose a critical driver of its research portfolio even though he will remain associated part-time with the department. The discussion of the committee with programme representatives during the site visit raised some concerns as the committee got the impression that the management of the research programme is at too large a distance from the actual research.

Relevance to society:

The research programme has a prominent translational research line and conducts several innovative clinical trials in which it teams up with other partners in Europe. The area of research of the programme is booming and holds ample promise for innovative and more effective treatments for haematological diseases. The strong immunological angle is an evident strength.

Viability:

The committee has rated the viability as good. The background for this relatively modest rating is because one of the leading PIs will have less of an imprint on the research programme in the years to come. Although part of the supervision of projects will be transferred to capable younger colleagues and the leadership proposes a 'succession plan' with training on the job, the committee was not convinced that this will suffice. It also has concerns that the programme leader, with a more clinically oriented background, will have difficulty to fill the gap in shaping the research portfolio in the years to come. This research should include more basic focus to underpin the translational activities. Given the fast developments in the field the committee believes that the programme should try to recruit a full-time internationally renowned researcher with interest in translation to oversee the research of the programme. Separate from the above, there is the issue of securing access to a sufficient number of patients to conduct the studies as there is quite some competition for patients with other academic centres.

Conclusion and recommendations:

Overall the research programme is of very good quality. Given the fast developments in the field of immunology and the expertise present, the programme is in a good position to meet the challenges that lay ahead provided that an adequate replacement is found for the position currently occupied by the PI who is taking a position elsewhere. Given these uncertainties and the notion that the committee was not quite convinced by the way the programme plans to deal with this loss, the committee could not rate viability as being very good.

7.3 Tumour immunology

Department:	Immunohematology and Blood Transfusion
Research programme:	40202
Scientific staff (2016):	4.3 fte
Quality:	3
Societal relevance:	2
Viability:	3

Brief description of the research programme:

The research programme aims to gain insight in the interaction between the immune system and tumours and to exploit this knowledge for the development of immune intervention strategies against cancer. A major focus is the clinical application of concepts conceived through work in animal models. There is furthermore focus on tumour TLR ligand conjugated and improved peptide-based vaccine, targeting human papillomavirus (HPV) positive anogenital neoplasia and oropharyngeal cancers.

Research quality:

The research in this programme represents important strands in tumour immunology-neoantigen and viral peptide vaccines and TLR adjuvanticity. The output is largely collaborative work in which the programme's own contributions were not so clear to the committee. Only four out of ten of the listed key publications are senior authored within the programme and five out of ten publications have the former programme leader as first or last author. The tumour vaccine trials are well funded and innovative. Also, the work on developing Cytof analysis was outstanding and the collaboration with several groups at the LUMC has been very productive.

The academic reputation is good, but little evidence is presented of reaching the highest level yet. The scale of the programme's research results is also good, although most results appear to be the result of joint projects led by others. The forward-looking strategy could be more oriented towards the era of checkpoint immunotherapy and how to complement and/or supplement that. Immunotherapy is booming, and the programme is focussing on funding for new types of vaccines.

Relevance to society:

The relevance to society of the research is very good. The programme has direct involvement in bringing findings and products through to clinical trials (phase I clinical studies at the LUMC).

Viability:

The viability of the research programme is good. Tumour immunology is changing rapidly, and the future strategies of the research programme need to accommodate the latest developments. According to the committee, the opportunities section of the SWOT did lack some vision or breadth and no real analysis of the weaknesses was found. With 4.3 research fte this is not the smallest research programme at the LUMC, but the committee is wondering if in the field of tumour immunology this research programme might be too small. The question is if they have sufficient critical mass.

Conclusion and recommendations:

It is unclear to the committee why one of the PI's moved to oncology and why this group did stay at the Immunohematology and Blood Transfusion department. The committee considers that it might be better to reunite these two groups again into one research programme. The publication record is still dominated by the programme leader who has left, this is a concern to the committee in terms of future perspective.

In 2014, the department had organised an external site visit. That committee recommended to recruit young faculty to strengthen the programme. The position of one associate professor is secured, and another PI was recruited as young faculty together with the Medical Oncology department. Several senior members in the department have departed or retired (or will soon), so strong support for the two new recruits as well as additional recruitment is highly recommended.

7.4 Transplantation and autoimmunity

Department:	Immunohematology and Blood Transfusion
Research programme:	40203
Scientific staff (2016):	8.3 fte
Quality:	1
Societal relevance:	1
Viability:	2

Brief description of the research programme:

This research programme aims to prevent and modulate unwanted immune responses after organ and stem cell transplantation. For this the molecular mechanisms that lead to the unwanted immune reactions are defined with the goal to use the knowledge for the development of preventive and curative protocols.

Research quality:

The Transplantation and autoimmunity programme of the Immunohematology and Blood Transfusion is an outstanding, large and well-funded research programme with a long and rich history, especially in HLA and transplantation immunology. It has an outstanding publication record (Immunity, Nat Med, PNAS) in all areas and the research programme can be considered as one of the international leading groups in the field. The PI has been able to develop a core facility for Cytof while continuing his own research.

Relevance to society:

This research programme remains very important for transplantation immunology, including the national reference lab, the transplant reference lab and the connection with the European bone marrow and solid organ transplant programmes, which originated at IHB. There is also a clear connection with translational science, and the research is embedded in the haematology department for its clinical work.

Viability:

With respect to the mucosal immunology work, the funding for celiac disease research remains problematic and the PI has decided to switch to IBD research. After one PI having departed and another retiring, this research programme needs to recruit and regroup. The appointments of two new PI's, one with focus on tolerance during pregnancy and the other on complement and antibodies represent very good first steps towards this goal. In solid organ transplantation, more investigators are relying on immune suppression instead of HLA matching of allografts.

Conclusion and recommendations:

This is a large and well-funded programme, but with the retirement and departure of several senior faculty members this is a good time to reassess what the focus of this programme should be. For example, should these three areas (mucosal immunology (celiac), transplantation immunology and autoimmunity (especially T1D) be continued in one programme? Each one is outstanding, but is there an advantage of being together in one programme. The two new recruits bring excellent new research lines that are well aligned with transplantation immunology.

7.5 Stem cell biology/Regenerative medicine (including blood transfusion)

Department:	Immunohematology and Blood Transfusion
Research programme:	40204
Scientific staff (2016):	5.3 fte

Quality:	2
Societal relevance:	2
Viability:	2

Brief description of the research programme:

One of the major aims of this research programme is to develop effective stem cell expansion programmes applicable in clinical protocols. This also forms the basis for the development of a hematopoietic stem cell-based gene therapy programme. The three research themes in this programme are regenerative medicine, immune monitoring, and immune deficiency gene therapy.

Research quality:

This is a strategically important research programme at the interface of stem cell biology and immunology of regenerative medicine. The programme has considerable contribution to the body of scientific knowledge. The programme leader has a strong academic reputation as evidenced by a recent review with 450 citations in four years. The research programme is very well connected and has an impressive network. Peer-reviewed publications are very good, but not at the same level as the clinical translation funding and organisation of networks. For example, review articles are listed. Also, the primary data publications are quite niche rather than ground breaking.

Relevance to society:

The research programme leads large European trials regarding mesenchymal stromal cells. This is impressive and future relevance to society is expected.

Viability:

The research programme has an exceptional funding record, specifically the programme leader. The most important issue in the upcoming period will be the replacement of the programme leader. During the site visit this was not yet clear, the future of the programme will strongly depend on the new programme leader and his/her vision for the programme. The lack of GMP grade production facilities at the LUMC for viral batch production at non-pharma prices impairs the development of clinical trials. The focus on developing immune monitoring will support others as an (outstanding) core facility and do basic research at the same time. This research is focused on technology development and standardisation.

The committee concludes that the opportunities in the SWOT analysis are predominantly are organisational and internal, not scientific and outward-looking.

Conclusion and recommendations:

The most important issue for this programme will be the succession of the programme leader. The programme has furthermore established a high quality and well-integrated immune monitoring facility, which interacts with twelve departments. Finally, the programme is close to opening clinical trials regarding gene therapy for immune deficiency, but the progress is impaired by lack of vector production facility at the LUMC and overall high cost of his programme.

7.6 Immunogenetics and cellular immunology of bacterial infectious diseases

Department:	Infectious Diseases
Research programme:	40302
Scientific staff (2016):	6.9 fte
Quality:	2
Societal relevance:	2
Viability:	2

Brief description of the research programme:

The mission of the research programme is to develop, evaluate and apply novel strategies and agents for the prevention, diagnosis and treatment of patients with infectious diseases, and through patient-related and population- based approaches. The research programme encompasses several interrelated research themes.

Research quality:

The research programme is very wide in scope, with focus on TB, leprosy, malaria and antibiotic resistance, together with components such as immune deficiency, co-infections, fungal pathogens etc. The programme is well-connected to relevant patient cohorts and has biobanked a significant array of samples for their work. Current development of new molecular vaccines for TB is of high potential importance for global health, and the combination of research into the major mycobacterial pathogens in one unit is another strategic strength. The research programme has a clear vision of its mission at the interface of fundamental research with translational applications into vaccine development, modern point-of-care diagnostics and therapeutics. There is clearly the critical mass and breadth of expertise to achieve major advances in this area.

Research into mycobacteria is world leading, although in this as with other components such as antimicrobial peptides and antibiotic stewardship, there is a predominance of diagnostic/biomarker focus that is yielding important translational outcomes. In parallel, expanding future work into underlying mechanistic pathways may lead to innovative interventions for treatment and prevention of infection. Publications are generally very good with some highly-cited papers in the ‘top 10’. With only first authors given in the publication list it was not clear which papers originated in, and were led by, members of the unit, but if all are this is a very creditable output.

Relevance to society:

The research is very relevant as it seeks to treat and prevent some of the most pressing infectious disease pathogens worldwide; hence the programme’s work is of primary importance to human health and wellbeing. Both the vaccine work and the development of

antimicrobial peptides are very promising, and it may be important to consider protecting these IP rights for commercialisation. The external visibility of the research programme is felt to be ripe for improvement, for example through upgrading the website.

Viability:

This is a robust research programme with strong leadership; nevertheless, some longer-term planning needs to be developed, particularly over the structure and coherence of the programme. At present, the forward planning (Opportunities/Actions) outlined are shorter-term, more incremental or concern internal organisation. A better vision of the future strategy and integration of the programme would be desirable, to consider whether each of the components (e.g. immune deficiency) are in their best place for the future, and whether future actions should aim to create a broader balance in the programme's portfolio as a future leader in molecular vaccine research and analysis of host immune responses to bacterial pathogens. Cross-departmental interactions through the Centre of Infectious Diseases represent a very positive step in this direction.

Conclusion and recommendations:

The research programme is across the board doing very good work, with the specific mentioning of some world leading work in mycobacterial research. It will be important to progress strategic planning of the coherence of the programme's portfolio, recruitment to future leadership positions, and integration within the Centre for Infectious Diseases to maintain this lead.

7.7 Experimental cancer immunology and therapy

Department:	Medical Oncology
Research programme:	40401
Scientific staff (2016):	6.1 fte
Quality:	2
Societal relevance:	2
Viability:	2

Brief description of the research programme:

The aim of the research programme is to implement immunotherapy as treatment modality for patients with solid tumours. It specifically focuses on the exploration of key factors involved in host-tumour interactions as they might determine the successes and failures in the control of cancer by the immune system. Several types of fundamental, translational and clinical studies are performed with emphasis on Human Papilloma Virus-induced cancers, Ovarian cancer, Melanoma and Pancreatic cancer. The immunotherapy of cancer is one of the three major themes within the medical research profile area Cancer Pathogenesis and Therapy. Collaborations exist with many other departments inside and outside of the LUMC and the programme aims to further strengthen these. In the highly competitive field of immunotherapy focus is on tumour-specific antigens. These include neo-antigens, T-cell epitopes associated with impaired peptide processing (TEIPP), and NK-like receptors expressed by T cells. Furthermore, vaccination strategies including the use of synthetic long peptides (SLPs) are explored together with other treatment modalities such as immunomodulation, chemotherapy, and radiotherapy to enhance the efficacy and specificity of immune responses. Manipulation of the tumour microenvironment, e.g. using oncolytic viruses or myeloid cells to convert non- or low-immunogenic ‘cold tumours’ into ‘hot tumours’ is another focus of the programme while steering away from ‘me-too’ research on the checkpoint blocking antibodies directed against CTLA4, PD1 and PDL1.

Research quality:

The committee rates the research quality of the programme as very good. Some of the work is published in top journals although overall their publication record in the immunological and oncological disciplines is average. The work on TEIPP represents an interesting niche area. To a lesser extent this also applies to the work on NK receptors on T-cells. The work on Synthetic long Peptides (SLPs) remains one of the research lines conducted by the department of Medical Oncology. With vaccination gaining a new impulse in conjunction with immunomodulation using checkpoint inhibitors the programme is in an excellent position to explore selective combination therapies of chemo, radiation, targeted drugs, vaccination, and immunomodulation, especially when they can tie into the expertise present in other departments. Given the modest size of the research endeavour, focus is of critical

importance. However, despite the relatively small size of the department and the limited LUMC funding it has been very successful in securing outside funding and establishing collaborations with pharma.

Relevance to society:

Relevance to society was rated by the committee as very good. The work on TEIPP holds promise for future clinical application whereas also the work on SLP vaccination in combination with other treatment modalities, such as chemotherapy, are worth further exploring clinically. Members of the research programme have identified a 4-parameter immune signature that can predict whether alpha-interferon conditioned stage 4 melanoma patients will exhibit long-term survival following transfusion with in vitro expanded melanoma-specific T cells. The work on HLA-E expression on tumour cells that can interact with NKG2a on T cells indicates that this interaction likely has a negative impact on T cell mediated tumour rejection and therefore patients expressing HLA-E will likely poorly respond to immunotherapy. These findings can have significant consequences for how to treat patients.

Viability:

The viability is rated as very good. The programme has defined several niche areas which they should be able to further develop. The relatively small size of the research programme remains a concern as it easily jeopardises access to the required expertise and skills. Bioinformatic support is a case in point. Given the wide immunological expertise present within the LUMC it is critical that closer interactions and collaborations with other departments are being realised. Better coordination of similar but dispersed activities (e.g. oncology research, immune-monitoring, bioinformatics) is needed. Whether one should aim for creating larger units or by establishing a cross-sectional centre will depend on several factors the committee cannot oversee.

Conclusion and recommendations:

The committee scored the programme overall as very good. Several appealing research lines put the department in an excellent position to make significant contributions to the field in the years to come. It remains important, however, to focus the research especially given the small size of the department. The committee advises to explore how the oncological and immunotherapeutic research can be further enhanced by creating larger organisational entities with the aim to secure access to the necessary expertise and enhance opportunities for interactions between investigators.

7.8 Biological, physical and clinical aspects of cancer treatment with ionizing radiation

Department:	Radiotherapy
Research programme:	40402
Scientific staff (2016):	3.0 fte
Quality:	2
Societal relevance:	2
Viability:	3

Brief description of the research programme:

The research programme is involved in clinical and translational research, aimed at improving cancer treatments and the quality-of-life of patients. The focus is primarily on initiating and coordinating large national and international clinical trials, especially on rectal and endometrial cancer, and on translational research and quality-of-life studies within the scope of these trials. The research budget is relatively modest with external support slightly exceeding the support provided by the LUMC. Members of the programme have leadership positions in international organisations and networks such as ESTRO. Although the research lines in radiobiology or physics are modest in size at LUMC, they are actively involved in further advancing MR-guided radiotherapy and implementing proton therapy. For the latter, the programme is participating in the Holland Proton Therapy Centre (HPTC) together with the TU-Delft and Erasmus MC. With the recruitment of two PI's the programme contributes the necessary expertise to serve as a valuable member of HPTC. With proton therapy coming on line very soon some additional funding is likely becoming available through HPTC that can further enhance the research capabilities of the Radiotherapy department.

Research quality:

The committee rates the quality as very good. The output is of high quality and the focus on coordinating well-designed large clinical trials has given members of the programme ample recognition and visibility in the field. The quality-of-life studies are a valuable complement to the interventional studies. The programme has limited research lines in radiobiology and physics and this is a potential weakness. However, without additional resources they would spread themselves too thin to initiate such research. The participation in HPTC might provide additional funding for new initiatives but it is unlikely that this will result in long-term support for the research in the department. Therefore, teaming-up with other members of HPTC, and serving as the coordinator of trials and conducting associated quality-of-life research seems a sensible strategy for the programme also in the coming years.

Relevance to society:

The committee rated this aspect of the programme as very good. Evidently, the research executed in the Radiotherapy department is highly relevant for society. The research has a

very strong clinical focus. The type of clinical trials coordinated by the programme can have substantial consequences for how patients will be treated in the future. In this regard, also the QoL studies are an asset and a very valuable add-on to the clinical trials. In this role, the programme can make important contributions to the objective evaluation of proton therapy to treat those cancers for which the dispute about the added value of proton therapy over existing therapeutic methods using LINACs is still ongoing (effectiveness, side effects, and costs).

Viability:

The committee rated the viability of the programme as good. If the programme can maintain its prominent role as initiator and coordinator of clinical trials and perform the associated QoL assessments its future will be likely secure. However, it should be able to fulfil this role then also in the HPTC consortium. As a relatively small programme with almost no research lines in radiobiology and physics it is dependent on collaborations with other centres and runs the risk to become marginalised when such collaborations wither. Much will depend on how the HPTC will function and permit the programme to take a leading role in coordinating the larger trials and QoL studies within the HPTC context. The committee expects that funding through HPTC might provide temporary support for new research initiatives but deems it unlikely that these will be long-lasting.

Conclusion and recommendations:

The research of the programme is of high quality and rated overall as very good by the committee. However, the relatively small size and the narrow scope of the research makes it vulnerable. Therefore, building a radiobiology research line would be wise assuming suitable individuals (and budget) can be found. Further strengthening alliances with groups within and outside the LUMC is advised as it might enable the programme to take advantage of research and expertise largely lacking in the department, as well as create opportunities for (jointly) applying for additional funding (e.g. European sources). This will make the research programme also more attractive for young investigators.

7.9 Individualised pharmacotherapy in oncology

Department:	Medical Oncology
Research programme:	40403
Scientific staff (2016):	2.4 fte
Quality:	2
Societal relevance:	2
Viability:	2

Brief description of the research programme:

The aim of the programme is to develop personalised anticancer therapy for patients with solid tumours and to improve outcome and quality of life of patients through development and implementation of predictive biomarkers. The programme includes clinical drug development using pharmacokinetics and pharmacogenomics, research in age groups, health outcomes research and research on solid tumours for which the programme has unique expertise such as sarcomas, thyroid tumours, upper GI tract tumours, female cancer and uveal melanoma and for which the LUMC also serves as reference centre. There is a very active clinical trial programme with strong European-wide involvement (e.g. EORTC and EUROSARC). The research programme also conducts research on the effectiveness of treatment and quality-of-life aspects as a function of patient's age. Pharmacogenetic research including GWAS studies aim to optimize drug exposure and limit side effects (such as implementation studies for DPYD polymorphisms). The participation in the DRUP drug-repurposing trial fits in the overall strategy of the programme to concentrate on innovative research.

Research quality:

The committee rates the quality of the research of the programme as very good. The bibliographic scores are high. The expertise built over the years in a number of relatively rare cancer types with the concomitant collection of tumour samples puts the programme in a unique position and should enable it to retain and further build its leading position regarding these cancers. Similarly, its pharmacogenetics focus can only gain in importance. The increasing emphasis on exploring the effectiveness of cancer treatment and QoL studies as function of age (consolidated by the appointment of a chair of Geriatric Oncology) is appealing and constitutes another highly relevant and under-researched area in which the programme now has a solid and unique position on which it can further build.

Relevance to society:

The committee rated the relevance for society as very good. The programme has unique expertise in various rare cancers for which they serve as a national reference centre and it is also internationally renowned for its expertise in these cancers. The pharmacogenetic

research on DPYD conducted together with other groups has led to general acceptance of the DPYD genotyping guideline in The Netherlands. The development of the online PREDICT tool to estimate the 5-year overall survival of older patients with breast cancer is another evident example.

Viability:

The committee rates the viability as very good. It has several very strong research lines with Geriatric Oncology as one that is quite unique and with great potential especially if prospective trials can be organised to validate trends found in epidemiological studies based on existing cancer registries. To bring the substantial potential to full fruition, the research programme members need more protected research time. In view of the substantial clinical demands this can only be realised by either reducing the clinical load or by increasing the number of LUMC-funded clinical positions. The programme is very successful in securing outside funding (more than twice the core funding). Infrastructural provisions need attention (room space for staff, The clinical research unit).

Conclusion and recommendations:

The research programme has the potential to become a world leader in several of the research areas they focus on. Geriatric oncology does hold this promise. This also applies - although to a slightly lesser extent - to the other main research lines, provided members of the research programme can be given more protected research time. This will also enable them to increase their international visibility.

The committee recommends to thoroughly assess the specific needs of the research programmes involved in oncology research at LUMC and determine how the various bottlenecks that are brought to its attention and that recurrently include i) the number of allocated FTE, ii) assigned budget, iii) department structure and location, and iv) specific support facilities (e.g. clinical research unit), can be tackled.

7.10 Personalised therapeutics

Department:	Clinical Pharmacy and Toxicology
Research programme:	40501
Scientific staff (2016):	1.5 fte
Quality:	2
Societal relevance:	2
Viability:	2

Brief description of the research programme:

The aim of this research programme is to optimise drug treatment of the patient by personalizing the dose and drug selection based on a better understanding of the genetic variation that is causal for the variability in drug response. Models are developed that include both genetic and non-genetic markers that can be readily implemented in daily clinical practice.

Research quality:

The scientific quality of this programme is very good. The research group is enthusiastic and convincing. The scientific staff is small (1.5 research fte directly funded in 2016) and while there were five PI's at the time of the site visit, most have a predominantly clinical appointment which limits time for research. Through the very good external funding the programme manages to supervise many PhDs. Almost all staff hold a PhD which is unusual in a hospital pharmacy. Gene-drug interactions began to be investigated in 2005 with now 94 interactions being identified. The Horizon2020 programme on *ubiquitous pharmacogenomics* which started in 2016 is impressive, building and extending existing international collaborations. It involves comparing standardised measures of adverse drug reactions on around 7000 patients (already have 3000) across many studies. The results should be published in high impact journals. Overall the publications and bibliometric analyses and earnings capacity are very good.

Relevance to society:

Societal relevance was assessed as very good and includes pharmacogenomics guidelines. The committee was particularly impressed with the digital pass that was developed. The programme has an important role to play in the education and training of pharmacists and clinicians in pharmacogenomics, in collaboration with interested patients. The new master's programme is clearly an asset for training and capacity building.

Viability:

The future looks bright for this young and enthusiastic team; viability was rated as very good by the committee. There appeared to be good anticipation on expected changes in the field and the research programme has built up from a low critical mass through their ability to raise their profile through EU funding. As the junior PIs become more experienced there will be a need to keep the momentum going that has clearly been established with recent grants.

Conclusion and recommendations:

This is a very good programme for quality, relevance and viability. The committee recommends that the LUMC considers increasing the small level of direct funding that will help to maintain momentum in the upcoming years. At the previous review it was recommended that this programme merged with another programme. However, the PIs did not carry this forward, but instead set up the Leiden Personalised Therapeutics Centre involving all relevant programmes. There may be a need for a wider merger in the coming years and this Centre could help maintain access to state of the art facilities that this programme requires.

7.11 Molecular basis of virus replication, viral pathogenesis and antiviral strategies

Department:	Medical Microbiology
Research programme:	40601
Scientific staff (2016):	8.6 fte
Quality:	2
Societal relevance:	2
Viability:	2

Brief description of the research programme:

The research programme aims to develop strategies to identify, prevent, or treat infection, by the use of vaccines and antiviral drugs. The programme further includes studies on persistent DNA virus infections, aiming to identify triggers and markers of viral reactivation and unravel pathogenesis in the immunocompromised host, enabling early detection and prevention of symptomatic disease.

Research quality:

The research programme combines very good activity across a range of viruses with emphasis on positive strand RNA viruses including Zika, Yellow Fever, and coronaviruses (MERS, SARS). The programme thus covers both opportunistic infections (e.g. CMV) and the emerging pathogens for which the programme has been able to respond very quickly to new challenges. All the investigators are experienced and held in high esteem, and the research programme has formulated broad aims from basic molecular biology and evolution to new vaccines, while also developing screening and diagnostic tools. The research is inherently collaborative with some major international consortia publishing highly-cited papers on fast-moving research topics; investigators of the programme play important roles in some of the steering committees and as first and last authors, however, in other cases the leadership of these consortia (and first/senior authorships) appears to be from collaborating scientists rather than from within the programme.

The research programme has produced very good work on emerging viral genomics, viral replication, enzymology, and inhibitors of viral function, with extremely promising outcomes. In addition, the interaction with innate immune effectors has been described in a very productive project. Other than this, there is relatively little emphasis on host immune factors which could generate many new lines of hypothesis-driven research in the viral systems studied by the research programme.

Relevance to society:

The research programme has a very good level of societal relevance, working on infections of intense public interest and importance. They have also been active translationally with their products leading to industrial agreements and patents.

Viability:

The programme's strategy is presented in quite general terms - with this broad brush it is not so clear what the specific goals are over the next 5-10 years. In addition, the forward plans are focussed more in terms of the programme's positioning rather than new scientific opportunities. Two of the major developments are likely to be around *Big Data* and in innate immunity. For the former better articulation of the plans for the unique biobanked patient cohorts would be beneficial. For the latter there is relatively little consideration now, but there is an opportunity for stronger integration of the viral biology and host innate response studies.

Conclusion and recommendations:

The research programme's very considerable strengths have produced consistent and very good research; difficult as that may be, a better assessment of the programme's own contributions to large scale collaborations would help define where leadership can be established, particularly as valuable biobanks are being assembled. There is opportunity for including a greater element of host biology in terms of host innate immunity and viral immune evasion. In addition, the programme's own concerns about rejuvenating their staff are shared by the committee and should be an important part of its plans.

7.12 Molecular basis of bacterial pathogenesis, virulence factors and antibiotic resistance

Department:	Medical Microbiology
Research programme:	40602
Scientific staff (2016):	3.8 fte
Quality:	2
Societal relevance:	2
Viability:	3

Brief description of the research programme:

Early diagnosis and a better understanding of the virulence characteristics of Gram-Positive Clostridium difficile and resistant Gram-Negative bacteria should result in the development of more appropriate therapeutic interventions. In addition, prevention of spread of these bacteria is important in hospital infection control.

Research quality:

The programme produces very good research in a range of bacteriological projects with a primary focus on Clostridium difficile. Within this remit there are several key components: surveillance of C. difficile with modernised typing, including genomics and proteomics; involvement in pioneering faecal transplant therapy; epidemiological evaluation with respect to zoonotic transmission, and studies on molecular components of C. difficile. The surveillance component, which is more descriptive, is the dominant one. Although the research programme is entitled 'Molecular basis of bacterial pathogenesis, virulence factors and antibiotic resistance', the work in progress is more circumscribed.

The publications cited are largely specialist papers covering a good range from molecular biology, virulence and epidemiology, with one landmark publication on faecal-microbial therapy (FMT). However, the latter was a broadly collaborative study led from another institution. It is not clear whether involvement in FMT continues and if so, what are the research questions which are being driven from within the programme. There are additional technological strengths, including involvement with the National Donor Faeces Bank and the Microbiome Platform. These have great potential but need better definition of how they will be mobilised to address objectives within the research programme.

Relevance to society:

There is very good societal relevance because of the previously intractable problem of nosocomial C. difficile infection and the new therapies now being applied successfully. In addition, the spotlight on zoonotic infections is extremely important for public health in rural areas.

Viability:

An important point is that the programme leader has made many prominent and excellent contributions but is nearing retirement and the succession of departmental leadership needs to be resolved if the quality of the work is to be maintained. In addition to the retirement of the programme leader, there is a key weakness in the existing portfolio being over-concentrated on C. difficile research, so that forward planning should seek to broaden the remit of the research programme, as well as defining a clearer internal research agenda.

Conclusion and recommendations:

The work of the research programme over the evaluation period was very good, specifically with the focus on C. difficile. The main question for the committee is the future of the research programme after the upcoming retirement of the programme leader. Forward planning should be getting priority and broadening the remit of the research programme could be considered.

7.13 Chemical Immunology

Department:	Cell and Chemical Biology/Chemical Immunology
Research programme:	40801
Scientific staff (2016):	10 fte
Quality:	1
Societal relevance:	1
Viability:	1

Brief description of the research programme:

The primary aim of the research programme is to integrate chemistry and cell biology, with focus on several different enzyme classes that are relevant in oncology, immunology and cell differentiation and more generally in cell biology. The second aim is identifying and improving drugs active in a series of diseases, in particular in oncology.

Research quality:

The quality and scientific relevance of the Chemical Immunology programme are outstanding in both basic science and in translational activities. Programme members received multiple ERC awards and participate in multiple international scientific bodies, reflect an excellent international reputation for both PIs. The research programme displays an outstanding funding and publication record.

Relevance to society:

The relevance to society is excellent. Examples of this excellence include the relaunching of the aclarubicin drug, the link between enteritis and the work on colon cancer risk. Furthermore, the academic pharma programme has the potential to generate new drugs.

Viability:

The viability and prospect of the research programme naturally depend on the success of the planned restructuring. However, leadership, structure and talent are clearly in place and the committee is convinced of a bright future for this research programme.

Conclusion and recommendations:

This research programme will merge with four other research programmes into a new Molecular Cell Biology (MCB) programme. The future programme leader is an outstanding, well-published and well-funded scientist with a clear vision for this new programme. One of his goals for this new research programme is on academic pharma. This encompasses the complete programme from drug discovery to a drug ready for clinical trials. The new programme will leave the five current research programmes intact and will foster interaction

through a) sharing space, b) sharing technology, c) joint literature and work discussions, and d) sending publications from faculty members to the whole department. The future programme leader is considering new recruits, who work on TLRs, sterile inflammation and protein chemistry. The committee agrees with the future programme leader that a tenure-track programme at the LUMC would help with recruitment and retainment of talented scientists.

7.14 Functional Genomics of Muscle, Nerve and Brain Disorders

Department:	Human Genetics
Research programme:	50104
Scientific staff (2016):	15.5 fte
Quality:	1
Societal relevance:	2
Viability:	1

Brief description of the research programme:

The common focus of this research programme is to elucidate genetic, genomic and epigenetic modifiers in neuromuscular, neurogenetic, myodegenerative and neurodegenerative disorders. The mission is to elucidate molecular changes in the disease with the perspectives to develop new, reliable and feasible techniques for accurate clinical diagnostics; to refine prognostic precision; to study normal and abnormal gene products by reverse genetics and functional genomics; and to generate and use cellular and animal model systems to understand disease pathology, for therapy development and biomarker discovery, and ultimately to improve prevention

Research quality:

This is an excellent programme using a multidisciplinary approach with a strong focus on genetics to elucidate molecular mechanisms of neurological and musculoskeletal diseases. A top publication describes genetic factors involved in Migraine and FSHD. In addition, the programme leads the first clinical trial using exon skipping in DMD. Generating mouse models of different human diseases enables them to study mechanisms, identify molecular markers and possible therapeutic interventions. Highly original is also their approach to learn from rare monogenic diseases for more complex diseases. Case in point here is the OPMD mouse model for muscle aging in general. The human genetic groups are a hub for the interaction with different clinical departments. The vitality and effectiveness of these interactions is reflected in the many joint high impact publications and the fact that the same results are cited in many different programmes. Organisationally the programme has, like all research programmes in the Human Genetics department, outsourced routine DNA sequencing tasks for LUMC to the spin-off company GenomeScan thus being able to focus their own research more on technology development and research associated genomics services. The close interaction with the data science centre is another advantage. The interaction between clinical and human genetics have been identified by regular meetings at the level of the department chairs and researchers.

Relevance to society:

Excellent science is the first premise for a relevance to society. Building on this the programme is making significant contribution to society in several ways. Even though their first exon skipping clinical trial for DMD had to be stopped, it was the foundation for further similar trials and even more importantly has generated a lot of valuable insights on how to improve and reduce complexity of clinical trials. Based on the disease mouse models the programme also possesses many industry collaborations thereby ensuring funding and that their research output is valorised. So far there have been little initiatives to involve patients and citizens more directly in research (e.g. by contributing mobile health or genome data). But the interaction with patients/citizens is primarily through the clinical departments involved in the programme.

Viability:

The viability of the programme is excellent. The challenges coming from the rapid technological advances in omics- techniques and computational biology are recognised and measures have been taken (e.g. outsourcing routine work to companies, association with excellent data science groups and proteomics and metabolomics facilities). Their asset is the world leading science with the access to stable well characterized patient populations and cohorts. The high level of trust between patients and the LUMC in general will serve as a basis for an increased involvement of patients and citizens as citizen scientist.

Conclusion and recommendations:

The committee is very positive about this research programme that shows excellent research quality and a bright future. The movement from research profiles to themes in which patient care and research are better aligned and to make Genetics a separate scheme is a stimulant for this research programme. This will result in a further improvement of the interaction between Clinical and Human Genetics.

7.15 Genome Instability and Cancer

Department:	Human Genetics
Research programme:	50105
Scientific staff (2016):	21.2 fte
Quality:	2
Societal relevance:	2
Viability:	2

Brief description of the research programme:

The research programme has defined six main aims:

- To obtain mechanistic understanding of genome surveillance mechanisms;
- To elucidate how such mechanisms, act to prevent pathologies;
- To improve diagnosis of pathologies caused by impaired genome surveillance mechanisms;
- To identify biomarkers of susceptibility to DNA damage to improve personalised cancer therapy;
- To exploit opportunities for prevention and personalised treatment of cancer, with a focus on hereditary and sporadic colorectal, breast and ovarian cancer and head/neck paragangliomas;
- To unveil roles of DNA damage and antibody effector pathways in inflammation.

Research quality:

This is a very good research programme involving a large group of scientists. In the field of DNA repair and genome stability the programme is internationally competitive. One of the key achievements is the establishment of in vitro and in vivo tests to determine the functional significance of DNA variants in BRCA genes and other DNA repair genes. These are important tests for a personalised treatment of patients. Their strength is the combination of human genetics and different model organisms for functional validation of the DNA repair mechanisms.

Relevance to society:

The research programme established a spin-off company (Toxys), and several patents which generate licensing fees. The programme was also involved in developing clinical guidelines for risk on breast cancer. Since the research programme interacts with patients only indirectly - via the clinical departments - a more active engagement with patients and citizens is difficult. By engaging with patient organisations and collaborations with clinical departments the research programme is clearly making an effort.

Viability:

The programme leader has a clear vision for the future of the research programme. The expertise in genome stability and DNA repair will be important for the new proton facility, new personalised diagnosis and treatment together with clinical departments and in the collaboration within national and international consortia (e.g. Global Alliance for Genomics and Health).

Conclusion and recommendations:

Altogether this is a very good programme and an essential pillar in the human genetics' programmes. The research programme will benefit from the organisation of Genetics as a unique research and care theme combined with the concomitant fusion of the now separate research programmes. A major issue of this programme and for many other research programmes is the insufficient support from the TTO office. Especially when moving together with other programmes into the Genetics Theme it may be beneficial to employ a (part-time) technology officer with a strong background in genetics to act as liaison officer between TTO and the genetics teams.

7.16 Molecular Technology and Informatics for Personalised Medicine and Health

Department:	Human Genetics
Research programme:	50106
Scientific staff (2016):	13.3 fte
Quality:	2
Societal relevance:	1
Viability:	2

Brief description of the research programme:

The research programme in Molecular Technology and Informatics for Personalised Medicine and Health aims to better understand genotype-phenotype relationships in humans and in disease models, and to predict predisposition to and progression of disease by means of bio-M.I.S. (molecular, informatic and semantic) approaches. There is increasing opportunity for data-driven research.

Research quality:

The programme develops and provides internationally competitive services in next generation sequencing, sequence analysis and data infrastructure for LUMC and the international community. The department has installed 'data-stewards' to define what data will be needed and how to collect and manage these from the start of a research project. The programme is the initiator of the FAIR data principles providing internationally accepted guidelines how medical data should be made available for research. They also play an important role in developing and validating tests for forensic DNA science in which the Netherlands are one of the leading countries in Europe.

The programme provides important bioinformatics services to many other programmes. A recent departure of the leader of the bioinformatics research programme offers the opportunity to rethink how to combine service and research in the best possible way.

Relevance to society:

Indirectly, the standardisation and internationalisation of data sharing principles is of pivotal societal importance. Only interoperable, accessible data will make data sharing across institutions and countries possible and will permit precision medicine to become a reality. The research programme has also been a pioneer in promoting the FAIR use of patient data recorded via smartphones. With the concept of the Personal Health Train that presents a model how data analysis in the future will consist of sending the algorithms and not the data around and leaving the consent to data access with the individual patient/citizen as the rightful data owner.

In a more colloquial sense, their creation of expressions such as ‘reuseless data’, ‘data visiting rather than data sharing’ and the ‘SWOT analysis of one’s own genome’ helps to define understandable language also for the interested public.

Viability:

The importance of this programme as a hub for technological development (NGS sequencing), data aggregation and analysis will increase. The programme can build on its internationally competitive basis. Further strengthening the ties with the computer science department of Leiden University will be important. Similarly, the further building and maintenance of a top bioinformatics group that provides services and conducts research is critically important for the entire LUMC.

Conclusion and recommendations:

An internationally competitive programme that will, like all the other genomics programmes, benefit from a unification in the Genetics Theme and a collaboration with the data analytics groups. The challenge will be to keep up with the rapid technological advances in the omics data generation and data analysis using artificial intelligence techniques.

7.17 Functional Genomics of Systemic Disorders

Department:	Human Genetics
Research programme:	50107
Scientific staff (2016):	4.5 fte
Quality:	2
Societal relevance:	2
Viability:	3

Brief description of the research programme:

The common focus of this research programme is to apply functional *in vitro, in vivo* as well as genome wide studies to uncover and resolve the mechanisms underlying systemic disorders such as metabolic syndrome, type 2 diabetes, cardiovascular disease and kidney failure. This multidisciplinary programme aims at understanding and translating the insights gained into mechanisms and pathophysiology of these complex multifactorial diseases.

Research quality:

The research programme has a very good track record in monogenetic kidney diseases (PKD) in which they have led international consortia and established unique mouse models. Unique mouse models have also been established in different FcR knock-out mice. Making use of their expertise in lipid genetics and kidney research the programme is analysing complex diseases such as diabetes and rheumatoid arthritis. In type 2 diabetes they have identified novel genetic risk factors. The goal is to combine the knowledge in metabolomics to identify individualised disease matrices between genes and metabolites in the hope to identify the targets relevant for the individual patient. Since complex diseases such as type 2 diabetes and obesity also depend to a large extent on socioeconomic factors which cannot be modelled by the systems biological approach alone, it is appropriate that the programme also collaborates in the prospective Doetinchem cohort. Although this is a highly competitive field, a competitive advantage for this research programme is the availability of established patient cohorts which provide longitudinal data on the development of the disease.

Relevance to society:

The most relevant contributions to society come from the PKD programme. The PI is leading several international consortia with SMEs and pharmaceutical companies ensuring the translation of basic research results into pharmaceutical products. The unique mouse models generated by this group can also be used as a first step towards the identification of new drug targets.

Viability:

While the PKD programme continues to be excellent and clearly forms the flagship project for this programme in the future, the systems approach to metabolic diseases will see more international competition and need to formulate a strategy to deal with this, beyond the noted joint appointment with the Department of Internal Medicine/Endocrinology.

Conclusion and recommendations:

It was unclear to the committee how competitive a metabolic disease programme is that focuses largely on metabolic flux not considering other socioeconomic factors. Furthermore, flux analysis is highly complicated in bacterial cells: to extend this to an entire human organism will have many complications that should not be underestimated. Making use of the established patient cohorts is a strong asset for this programme, particularly when eHealth tools and the active participation of cohort members as citizen scientists is adopted rapidly. The Fc*γ*R programme is excellent but bears little connection to the other programmes. In general, this programme will benefit from the integration of research profiles into themes for research and care. In this scenario, the groups within the existing programme can arrange in a way in which societal impact will be improved.

7.18 Molecular cardiovascular developmental biology

Department:	Anatomy and Embryology
Research programme:	50201
Scientific staff (2016):	9.5 fte
Quality:	1
Societal relevance:	1
Viability:	2

Brief description of the research programme:

This programme aims to define molecular and biomechanical mechanisms that 1) are used by progenitors to form cellular components of the heart and vasculature, 2) support cardiovascular cell maturation to fully functional phenotypes and 3) cause deregulation in cardiac and vascular disease.

Research quality:

This is an excellent, internationally respected and leading research programme with high quality publications, citations, awards and international grants. The programme leader is very impressive as head of the programme and the earnings capacity has been high. The contribution in making multicellular 'mini-hearts' is cutting edge and there is innovative development of these models (e.g. introducing flow, inflammatory components etc.). The programme studies both normal and abnormal development, looking for the first stages of disease. In patients these signs may not manifest for many years. In cells, earlier detection is possible. An ambition is to join different organs to investigate interactions between organs and to study late onset disease. There are good links with the bioinformatics department, although not always clear who to go to for advice. For one of the research areas there is a bridging appointment with the sequencing facility in bioinformatics which works very well. The programme does a lot of teaching which is seen positively by the group members and supported by teaching staff.

Relevance to society:

Showing how relevant their research is to society, particularly stem cell research, is given priority by this programme and the outreach activities are impressive. When the topic is embryonic issues, then the programme leader still initiates the activities, but other topics are now shared with other members of the group (e.g. PhD students who do Tedex). The programme understands the benefits of technological advances that allow patients to collect their own data. Specific groups are obliging in donating tissue and cells and patient involvement is taken seriously. They are not medics themselves, so the programme does this via clinical departments. The programme was ahead of the curve in setting up the pluriomics spin out company to supply high quality cells. This was initially not strongly supported by the

LUMC, but now it has proven successful and the climate has changed; LUMC has made an investment and uses this company as an exemplar.

Viability:

There are two related concerns for the future. The first is that the forward thinking appeared incremental, and opportunities identified were rather internal; these do not match the high profile of the papers and output. The committee would have expected more visionary aims, although the participation in the Organs on a chip gravitational programme that was awarded in 2017 to a consortium of Dutch investigators is a favourable development. The second concern is that the impressive head of the programme will be stepping down in the next five years (although the LUMC has given permission to continue another couple of years). Succession planning is only just beginning, and plans must be developed and there is optimism that a suitable candidate will be found. However, this raises the question whether the excellent science will be maintained in the longer term. The programme leader recognises the need to develop her team and members of staff other than the leader increasingly sit on committees and gain experience; several junior staff are close to tenure and tenure track stage and support from the LUMC would be appreciated; but permanent appointments are in teaching and take up a large part of the budget.

Conclusion and recommendations:

To maintain and further develop this excellent group and their exciting research, the committee agrees with the programme leader's recommendation that the LUMC should reward personal fellowships by funding new tenure positions. The programme is open to becoming part of a larger entity and made some suggestions of the logical partners.

7.19 Circadian clocks in health and disease

Department:	Cell and Chemical Biology/Molecular Cell Biology
Research programme:	50303
Scientific staff (2016):	7.7 fte
Quality:	2
Societal relevance:	2
Viability:	2

Brief description of the research programme:

The aim of the research programme Circadian clocks in health and disease is to understand the physiological bases of circadian rhythms and sleep, and their influence on diseases, such as depression, metabolic syndrome and aging. The aim is furthermore to implement the consequences of the findings in clinical settings and society.

Research quality:

The research programme focusses on control of the diurnal cycle by the suprachiasmatic nuclei (SCN) in an evolutionarily ancient part of the brain, looking at afferent signals from retina (light being the primary timekeeping stimulus) with important links to ageing, metabolism and immune dysfunction, and effects on chemotherapy in cancer. There is expertise in cellular analysis of circadian clock. bioinformatics and complexity theory. The programme offers high quality integration of fundamental research with medical needs. The research quality is very good.

It was noted by the committee that many of the publications in interdisciplinary journals demonstrate wider interest and significance in the programme's work. In addition, there are excellent markers of esteem e.g. visiting professorship at Oxford as well as an important Award to the programme leader. The research programme is embarking in several new directions, both fundamental and translational. Elegant new cellular tools are being employed which together with opportunities for small molecule manipulation of the clock, give a very promising picture. The link to chronobiology of the immune system would be one that can be strengthened, although this may require better description of the downstream signals from the clock.

Relevance to society:

The clinical significance of chronobiology is well established and the relevance to society therefore very good. Application to burgeoning problems such as depression and cancer are undoubtedly important although the degree to which these diseases will respond to chronobiological therapies is not yet clear.

Viability:

The research programme works in a niche which is very important and is making very good contributions; the forward look towards new opportunities is quite short-term and logistical and a longer-term vision would help establish leadership in the field. The staff complement is strong which should allow for the programme not to be overly dependent on the programme leader.

Conclusion and recommendations:

The committee observed a very good research programme with a unique insight and capability that is likely to make major contributions in the future. The programme might want to better define how they plan to link chronobiology to the functioning of the immune system. Such research line would provide a unique opportunity for interaction with other prominent programmes within the LUMC.

7.20 Microscopic imaging and technology

Department:	Cell and Chemical Biology/Molecular Cell Biology
Research programme:	50304
Scientific staff (2016):	7.8 fte
Quality:	2
Societal relevance:	2
Viability:	2

Brief description of the research programme:

The aim of the programme is to develop and/or adapt microscopic imaging methods, instrumentation and fluorescent labelling technologies to study the molecular composition of tissues, cells and sub-cellular compartments. The programme involves both light and electron microscopy and supports projects within the realm of both cell and structural biology. The programme serves as a Technical Focus Area (TFA) providing extensive service to both the preclinical and clinical departments. They offer a broad spectrum of state-of-the-art microscopic and EM platforms. One of the PI's is scientific director of the Netherlands Centre for Electron Nanoscopy, a national facility for cryo electron microscopy.

The 'customers' of the facility have a defined point of contact with every microscopy project being discussed upfront to facilitate swift execution and getting the most out of it. The programme then also assesses the possibilities to attach own research questions to the study, e.g. around microscopic technology or methodology development. The research lines concentrate on cell-cell communication (using intravital imaging) and virus replication (largely EM-based techniques). This enables them to independently explore and introduce new microscopic techniques. The programme also works closely with manufacturers of microscopes. This enables early access to new equipment (often with a significant discount). The Department is investing in new technologies, such as correlative light – electron microscopy (CLEM) for which a new scientist is hired.

Research quality:

The committee rates the quality of the research as very good. It is undoubtedly a challenge for members of the research programme to identify interesting own research questions when serving the LUMC scientific community. However, the programme has been very successful in doing this, thereby adding substantial value to these studies. The committee was impressed by the organisational setup and enthusiasm of the staff to advance microscopic techniques as well as storing and handling of the data. New microscopic techniques such as CLEM are a case in point. The committee was particularly impressed by the exploratory research using DNA nanotemplates to organise protein lattices to optimize activation of the complement system. For this highly original idea an ERC grant was recently

received. This is an illustration how the programme with its many service tasks manages to conduct original and very good, internationally highly regarded research.

Relevance to society:

The committee rates the relevance to society as very good. The programme evidently contributes to many LUMC projects that receive a high rating for societal relevance and the contributions by the research programme have been very often indispensable for the high scores of these 'serviced' groups. But advancing new microscopic techniques is likely even of more value in the long-term as progress in science is so critically dependent on advances in technology. In addition, the programme has taken educational initiatives for the broader public (the 2D image viewer and the Cell Zoomer).

Viability:

The committee has rated the viability as very good. It is evident that the research programme provides unique and high-quality services for the research conducted within the LUMC. The way in which they provide this service enables them to keep these facilities state-of-the-art. Furthermore, their own research is aimed at new microscopic techniques that give investigators within the LUMC an edge in their projects. CLEM exemplifies this. Obviously, maintaining microscopy state-of-the-art requires a substantial budget for new equipment. Although the programme has been creative in finding external support through joint applications with other groups, this remains an Achilles heel of the programme in view of its extensive service task and the fact that infrastructure is difficult to finance from competitive funding sources. This also holds for recruiting and retaining expert personnel. Therefore, substantial continuous support from the LUMC will be necessary not only to cover personnel costs but also to continuously update the instrumentation.

Conclusion and recommendations:

The committee rates the research programme overall as very good. The committee was pleased to see how the staff of the programme manages to combine excellent service with very competitive research on microscopic technologies. Some of the research projects initiated from within the programme stand out and are truly excellent. It will be important to assure that the staff of the programme will not become overwhelmed by service requests and retain sufficient research time to invest in technology development. This must be accompanied with LUMC providing an adequate budget for highly skilled personnel and for keeping the wide range of instruments up-to-date. State-of-the-art equipment is indispensable for both the service function and technology/instrumentation development.

7.21 Cancer Signalling networks and Molecular Therapeutics

Department:	Cell and Chemical Biology/Molecular Cell Biology
Research programme:	50305
Scientific staff (2016):	13.1 fte
Quality:	1
Societal relevance:	2
Viability:	2

Brief description of the research programme:

The programme aims to understand how intra- and inter-cellular interactions control tissue homeostasis, how these processes become corrupted in cancer and how this information can be translated into therapeutic interventions. Research in the programme includes the identification of novel regulators of the TGFβ and Notch signalling pathways. The programme also explores the role of post-translational modifications in signal transduction, cell cycle progression, and the DNA damage response. The work nicely illustrates how basic research can lead to new inroads for treating cancer.

To enable the translation of this basic knowledge to clinical application - a point raised in previous evaluation round - the research programme has established closer interactions with (pre)clinical research programmes of the LUMC and organised regular meetings. This has resulted in the initiation of several translational research projects, such as p53 reactivation for uveal melanoma, and identification and functional characterisation of genetic alterations associated with sarcomagenesis. Work to be conducted in the coming years will focus on further identifying the mechanisms of action of these targets and on drug development. Academic drug development expertise is available in the LUMC. To limit the development of drug resistance and reduce the toxicity of drugs the programme should focus on downstream targets of derailed signalling pathways. It will also explore combinatorial targeting of cancer cells and their surrounding stroma.

Research quality:

The committee rates the quality of the research in the department as excellent. This is evident from the impressive publication record and from its international reputation and the capacity to secure highly competitive grants even though this is increasingly difficult for more basic research projects. The translational research initiated by the research programme is very promising and illustrates that translational research heavily depends on the insights acquired in basic research projects, in this specific case how signals via TGFβ and Notch are routed in cells. The anticipated teaming up with members of the department of Chemical Biology can further boost this translational work.

Relevance to society:

The committee rates the relevance for society at large as very good. By definition, identifying the direct societal benefits of more basic research programmes is difficult. The effects are often indirect and can take a long time before they materialise. This also transpires from the translational research initiatives in this programme: they have become possible through basic research performed over many years. However, it is important to point out that basic research scientists fulfil a critical role in a clinical environment as they are more than other professionals trained to keep questioning the validity of scientific observations and interpretations, or the scientific basis of treatments. In this way they importantly contribute to the critical thinking within an organisation. This is not only essential for the education of a next generation of professionals, but also critical for the optimal functioning of an academic institution.

Viability:

The research programme has an interesting portfolio for the years to come, a capable and stable staff, and the proposed close engagement with the department of Chemical Immunology and clinical departments can further strengthen their translational research. However, also the 'blue sky' research needs to be fostered. External funding for the basic research programme is a concern in view of the demand of funding agents on 'translation' and 'valorisation'. This might be an issue for PIs that have not yet acquired international prominence. This is an aspect that needs close surveillance.

Conclusion and recommendations:

The quality of the research is rated as excellent by the committee. Altogether it is a solid programme in place with promising perspectives for clinical application. The interactions established within the LUMC should enable the programme to successfully translate the findings of their basic research. Close collaboration with the relatively new department of Chemical Biology is appealing as their activities are highly complementary. Together with the Chemical Biology department they are a jewel in the crown.

7.22 Therapeutic cell differentiation

Department:	Cell and Chemical Biology/Molecular Cell Biology
Research programme:	50306
Scientific staff (2016):	8.0 fte
Quality:	3
Societal relevance:	2
Viability:	3

Brief description of the research programme:

The research programme aims at understanding the molecular mechanisms that govern differentiation of normal and genetically corrected stem cells. The mechanistic insights are used for developing new approaches for the treatment of acquired and inherited diseases. The toolbox by the programme has been used extensively within the LUMC and the programme is intensifying efforts to seek employ of the tools in clinical projects. The focus on developing technology for personalised therapeutics connects the programme to many research profiles and departments within the LUMC. The group operates the LUMC Viral-Vector Facility, which provides many research groups with research-grade lentiviruses, reoviruses and adenoviruses.

Research quality:

The research programme works in an exciting area with enormous potential. The research is primarily technology-driven and through collaborations focuses on key questions in cardiology, type 1 diabetes, primary immunodeficiency, muscular dystrophy and neurology; new topics now include haemoglobinopathies and oncolytic viruses for cancer. A major role for the programme is to provides key tools and facilities for these collaborations.

The questions and problems being addressed are extremely important, and it will be important for the group to demonstrate their intellectual leadership of collaborative work in an environment where publications are often senior authored by other groups. Where research aims are led externally this can lead to a lack of internal coherence with staff members pursuing projects which are not well related to each other.

On the other hand, the benefits of the collaborative emphasis with external partners have been a good publication record, and significant contributions to many important projects. In addition, younger staff have gained good funding, and have good connectivity with other groups.

Relevance to society:

There is very good engagement on a wide range of issues of clinical importance as stated above, although most projects appear still to be more developmental than ready for the clinic.

Viability:

For the future, the research programme will be applying very powerful approaches to highly relevant problems, but the question arises whether it is the Therapeutic cell differentiation programme that will be driving the initiatives and receiving public recognition for it. In some of the areas, such as extracellular vesicles, it is not clear that the research programme will be competitive.

Conclusion and recommendations:

To avoid fragmentation, more co-ordination of the research strands towards a coherent programme would be very desirable. The forward looking of the research programme is more focussed on technology acquisition, networking and positioning relative to other programmes. Rather the programme should consider focussing more on defining the best scientific portfolio for the future, to create more intellectual coherence which is presently lacking.

7.23 Host-parasite interaction

Department:	Infectious Diseases/Parasitology
Research programme:	50401
Scientific staff (2016):	12.4 fte
Quality:	1
Societal relevance:	2
Viability:	1

Brief description of the research programme:

The research programme focuses on understanding host-parasite interactions at the molecular, cellular and population level and the knowledge gained is being applied to achieve the two missions of the department of Parasitology developing effective vaccines against parasitic diseases and to identifying parasite-derived immune modulatory molecules to control hyper-inflammatory diseases.

Research quality:

This is an interdisciplinary research programme with an exciting agenda for both tropical diseases and 'first world' disorders of inflammation and metabolism. The programme offers advanced analytical and transgenic technologies, a strong commitment to endemic countries, and new initiatives for controlled human infection trials – in this they are unique and a world leader.

Current research initiatives are innovative, bold and high risk but promise major advances; collaborations are in place in key areas, and the technology platform is very strong. Work in a genetically attenuated malaria vaccine strain is one excellent example, and others include the search for parasite-derived immune modulatory molecules and exploring the infection-metabolism link; all appear to be very fertile areas for research. Some weaker areas include facilities for experimental mouse work, and access to bioinformatic expertise, leading into the era of big data. Retention of key technical staff is essential to maintain the parasite life cycles in the laboratory.

The senior PIs are very highly regarded and younger staff members are also successful in both publication and grant funding including 3 VENI grants and 1 VIDI grant. Publications have been in high-profile and interdisciplinary journals, demonstrating widespread interest in the work, and represent all members of the unit.

Relevance to society:

There is very good relevance to a raft of societal issues including the parasitic diseases themselves and the potential for new therapies for inflammatory diseases of affluent countries; however, these are at a relatively early stage and have not advanced as far as

seen in other areas of infectious disease. It was also noted that there is excellent targeting of endemic country populations for health education and public engagement in measures to prevent or treat parasite infections, as well as very strong account of other media interactions.

Viability:

The programme is in a very strong strategic position in areas of growing priority, with a clear organisational structure and purpose. There are clear longer-term objectives, and although quite generic, these map closely to latest achievements and expertise of staff and are far-sighted rather than incremental. A further notable point is the recruitment of excellent and enthusiastic younger scientists leading novel research initiatives, and the overall doubling of external funding from 2014 to 2016. Together with the excellent orchestration and coherence of the research programme, the future viability of the groups appears outstanding.

Conclusion and recommendations:

The programme is managing an admirable combination of novel high-risk research, strong publications and strong career development of the younger staff members. Concerns expressed in the self-evaluation report about bioinformatics/big data support appear to be well founded, and if addressed would synergise with the new opportunities afforded by the research programme.

7.24 Proteomics

Department:	Centre for Proteomics and Metabolomics
Research programme:	50402
Scientific staff (2016):	15.5 fte
Quality:	2
Societal relevance:	2
Viability:	1

Brief description of the research programme:

The Centre for Proteomics and Metabolomics is a Technology Focus Area of the LUMC. The Centre aims to develop and implement cutting-edge proteomics and metabolomics methodology and technology for analysing disease-associated molecular mechanisms and fingerprints within all research focus areas of the LUMC to promote innovation within biomedical research and public health. The research is focussed on the elucidation of molecular mechanisms of diseases and disease -associated molecular signatures using MS and related techniques.

Research quality:

This centre undertakes very good science, from providing a service to the hospital and face to face consultations with clinical scientists from other research programmes - who wish to carry out proteomics and metabolomics - right through to being at the forefront of developments in this highly technically challenging and fast-growing field and collaborating with clinical and biological scientists on innovative joint projects. For example, there are close collaborations with Clinical Chemistry and Molecular Epidemiology which work well. There are also strong international collaborations (e.g. with Scripps and LMU Munich). All proteomics questions come to this centre, there are no other groups at LUMC with same level of expertise. These days there is a strong focus on lipidomics, in addition to mass spectrometry.

The programme wishes to expand the NMR metabolomics platform to investigate flux analysis. Bridging personnel with various clinical and basic groups is encouraged and there are funding schemes within the LUMC for this. The group has various EU grants and very good earnings capacity. There are three centres of this type in the Netherlands, the LUMC centre distinguishes itself with high quality expertise, equipment and funding, and strong links with clinical research groups. The centre's research includes longitudinal measurements of proteomics and metabolomics which allow the investigation of individual change and comparisons across individuals and labs. An example is the lipidomics platform they are setting up with a strong focus on reproducibility and comparison across labs and

countries. Having established analytical accuracy, the intention is to move forward into preclinical research.

Relevance to society:

The research programme has very good contacts with industry (predominantly through the Leiden BioScience Park) which gives them access to state-of-the-art technology, allowing confidence in renewing and replacing equipment over time as part of a continuous development.

Viability:

Prospects look excellent, given the programme's contacts and collaborations with academic science and industry. The research programme is involved in both innovative science and providing a high-quality service. The recently appointed programme leader came across as dynamic with a clear future direction. The future of the programme looks very bright.

Conclusion and recommendations:

The committee was impressed by the interview and found the programme leader dynamic and the group interactive, supportive and enthusiastic and embedded in the scientific questions. The LUMC should continue to support this centre well and fund bridging positions that link this group to LUMC clinical and biological research programmes to foster its contribution to clinical translation and personalised medicine.

7.25 Development and application of statistical models for medical scientific research

Department:	Biomedical Data Sciences
Research programme:	50601
Scientific staff (2016):	14.4 fte
Quality:	2
Societal relevance:	2
Viability:	1

Brief description of the research programme:

The goal of this research programme is the development and application of statistical models and designs in a broad spectrum of medical research. The main involvements are design, analysis and reporting of experimental as well as observational medical studies aimed at understanding the biological processes and obtaining prognostic models relevant for patient care and therapy. Traditionally there is a close cooperation with nearly all clinical groups. The new programme leader took over as head of the programme in 2017 which is the largest Dutch biostatistical group in an academic hospital.

Research quality:

This research programme develops and applies statistical models and designs for a wide range of experimental and observational medical research to understand biological processes and predictive models. Therefore, they cover a very broad spectrum of methodological topics. The main areas – clinical prediction, causal inference, multiple testing and survival analysis are well represented and strong, and a new appointment has brought in infectious disease modelling. The programme works in a technologically and methodologically challenging area that is changing fast as the size, and complexity of medical data increases rapidly.

The model of concentrating many staff in one research programme, not scattered and isolated within other groups is appropriate. The programme combines its different roles very well. As such it makes the science better - from providing a statistical service, to establishing the FAIR data system, to working in scientific collaboration with basic scientists, clinicians and epidemiologists and putting together joint grants. Joint bridging appointments with the biological and clinical groups should be encouraged. There are the classic difficulties in funding statistical methodology but given the essential skills and services they provide to LUMC colleagues a formula should be found to secure funding for this group to work on new statistical methodologies.

Relevance to society:

The research programme is highly relevant to society because the skills of this programme make the science of the entire LUMC better. The relevant software provided by the programme to accompany their methods development is popular and benefits many scientists being open source.

Viability:

The committee was impressed with the programme's leadership and sees a bright future for this research programme. Furthermore, the committee expects the programme to keep its leading edge and develop more international collaborations.

Conclusion and recommendations:

The committee supported the programme leader's vision and plan to bring relevant groups together into a Leiden Centre for Quantitative Methods.

7.26 Molecular Epidemiology

Department:	Biomedical Data Sciences
Research programme:	50602
Scientific staff (2016):	7.5 fte
Quality:	1
Societal relevance:	2
Viability:	1

Brief description of the research programme

The mission of this programme is to exploit multi-layered molecular data in clinical and population studies to discover biological pathways and biomarker profiles that mark or explain variance in ageing processes. The programme investigates the rate of ageing, the increasing susceptibility to osteoarthritis with age, factors that promote healthy ageing and longevity, and the role of epigenetic mechanisms. The common focus is metabolic health and disease.

Research quality

As well as very strong collaborations with other LUMC programmes, this research programme has been very successful in developing national and international collaborations, involved in running big European projects and building strong research connections (e.g. with Max Planck). Two PI's are already internationally well renowned for their highly original and relevant population research, combining epidemiological methods with strong biological insights; a third PI in this research programme has a bright future having received a VICI grant. The programme leader is PI of the internationally known Leiden Longevity Study.

The research programme has publications in high ranking journals with high and increasing bibliometrics. Some minor concern on the panel about rather sweeping generic statements in their self-evaluation report existed prior to the interview, but the programme members answered the committee's questions very well, providing evidence and detail about their accomplishments in terms of recent research (from metabolic age scores to the identification of subgroups with different metabolic responses in intervention study). In their epigenetic research, genotypes and phenotypes were linked many years ago, they then stepped back to understand what is really going on at genome level which has strengthened later research on phenotypes, applying causal interference methods.

Relevance to society

In terms of the use of Artificial Intelligence (AI) and new technologies, the research programme is aware of the benefits of engaging participants in research and of continuous reporting. The group has collaborations with LIACS on these kinds of data and may use

watches in collaboration with Philips. They are gearing up for their use, have developed appropriate processes for informed consent, and will apply for research money. Working in larger consortia, public-private partnerships have been and will continue to be developed.

Viability

There was a clear strategy for future direction and funding that builds on the multidisciplinary research platforms the programme has established. This should keep the earnings capacity high. This programme is well placed to benefit from WHO Decade of Healthy Ageing. In terms of where the science is going, metabolomics in ageing was seen to have a bright future, both specific markers and generic pictures are interesting. They will also integrate more with other 'omics (e.g. proteomics, exomics). More longitudinal repeated phenotypic data will be required in established cohorts with more than 20 years of prospective data, and there are plans to collect new samples (e.g. stool samples for microbiome studies).

Conclusion and recommendations

The programme members gave an impressive interview, showed determination, and gave very good answers. It is an unusual research programme, combining several strengths, and both scientific quality and viability were rated as excellent. The research programme has a bright future.

7.27 Genetics of disease, diagnosis and treatment

Department:	Clinical Genetics
Research programme:	50801
Scientific staff (2016):	1.8 fte
Quality:	2
Societal relevance:	2
Viability:	1

Brief description of the research programme:

The goals of this research programme are to identify the genetic causes of disease, understand the pathogenic mechanisms, define phenotypic disease spectra and identify disease modifiers. The programme is expecting to identify therapeutic targets and develop therapeutic strategies and prevention for the genetic disease areas with the scope of the programme. The main aim is that patients will ultimately benefit from the results of the research efforts of the programme.

Research quality:

The high-quality research is focused on genetics of neurodegenerative diseases (CADASIL, Notch 3) and hemoglobinopathies. The research programme has a very good publication record. There have been some struggles in the earlier years of the evaluation period, which is reflected in the numbers provided in the self-evaluation report, but the new leadership has immediately resulted in improved funding and expansion of the research effort.

Relevance to society:

The relevance to society is very good. An impressive example is their population screening programme in the city of Volendam. On the other hand, not being part of clinical genetics makes it more difficult for the research programme to translate research findings. There are plans for population screening, but these plans need further development.

Viability:

The research programme is one year under the current leadership and will focus on neurologic diseases, especially those related to neurodegeneration. First results of new leadership are already visible in the success in grant applications. Funding in the last two years has increased, which has resulted in the recruitment of five PhD students and three postdocs.

This programme has only two full time researchers and a very modest funding portfolio. In 2012 it was recommended to merge this programme with other genetics programmes. According to the current programme leader this would be feasible on the research side, but

more difficult for the clinical diagnostics to merge. The infrastructure for this programme is excellent and includes, for example, two bio-informaticians for NGS data analysis.

Conclusion and recommendations:

In 2012 it was suggested to integrate research line 50801 (Genetics of disease, diagnosis and treatment) with 50803 (Genomics, population genetics and bioinformatics). This has happened, and under the current leadership the programme has undergone substantial improvements and growth. The work on neurodegenerative disorders, especially CADASIL, should be considered outstanding.

7.28 Hereditary cancer genetics

Department:	Clinical Genetics
Research programme:	50802
Scientific staff (2016):	1.0 fte
Quality:	3
Societal relevance:	2
Viability:	3

Brief description of the research programme:

The research programme studies predisposition of inherited cancer from bench to bedside. Clinical and psychological consequences of identifying predisposing genes are studied with the aim of formulating evidence-based guidelines and recommendations for clinical and laboratory practice. The focus is on familial breast and ovarian cancer, familial colorectal cancer, polyposis, melanoma and endocrine tumours.

Research quality:

The areas of special interest of this research programme are focussed patient cohorts including the largest PMS2 (Lynch syndrome) cohort of 250 families and database of 105 children with thyroid cancer and a large cohort of families with hereditary breast and/or ovarian cancer. How cancer risk in these patients is modulated by interaction with germline variants is of specific interest and with their large cohorts of specific patient groups (such as Lynch) this is an interesting research line.

The core research funding is rather modest. As to be expected, the external funding of the research programme is in the same range. The programme's listed publications were slightly disappointing, although their bibliometrics for the field appear quite good. The programme is very small in research fte and many of the staff members are spending most of their time in clinical work. To make major steps in the quality of the work, the programme would need a new, stimulating PI with considerable research time.

Relevance to society:

The diagnostic work is highly relevant, but the research in genetics is modest. The research programme is well connected to the clinical work, which is a major advantage with respect to the societal relevance.

Viability:

Time dedicated for research is limited to 0.2 fte per PI on average due to competition with other (higher prioritised) medical academic tasks: teaching and patient care. Given the small size of the programme, this provides very limited capacity to develop new appealing

research lines in this fast-expanding omics era. The programme would seem particularly well positioned to further explore the interactions between strong predisposing lesions with germline variants, but the question is whether the limited research capacity of the research programme will enable it to play a significant role in this field.

Conclusion and recommendations:

In general, this programme is mostly focused on clinical diagnostics and has a modest research effort. The research could benefit from more collaborations with basic scientists to focus on functional genomics.

Although no merger with any other research line was recommended in the previous review, close collaborations with other programmes and departments are in place. The committee considers these collaborations valuable. Especially since the programme leader of one of the other programmes has already shown to have impressive necessary vision and leadership qualities. Moreover, clinical genetics is an exciting and rapidly moving field, which is worthy of strong leadership and institutional support.

Appendices

Appendix 1 Programme site visit

Division 3

Monday 21 May
17:00 Briefing, followed by diner Villa Beukenhof
Tuesday 22 May
8:30 - 9:30 **Core Committee meets Executive Board** *Prof Willy Spaan (chair), Prof Pancras Hogendoorn (dean)*
Welcome members: prof. Olesen, prof. Sabbe, prof. de Maeseneer, prof. Herrington, prof. Morley
9:45 - 10:15 preparation site visits **Division 3** by committee
Neurology 10:15 - 10:40 Research programme **30702** *Prof Jan Verschuuren (HoD), Prof Michel Ferrari, Mrs Dr. Gisela Terwindt, Mrs Dr Marieke Wermer, Dr Roland Thijs* 10:40 - 11:05 Research programme **30703** *Prof Jan Verschuuren (HoD), Prof Bob van Hilten, Dr Erik Niks, Dr Martijn Tannemaat, Dr. Han Marinus*
Obstetrics 11:05 - 11:35 Research programme **30201** *Prof Jan van Lith (HoD), Prof Dick Oepkes, Dr Monique Haak, Dr Marie-Louise van der Hoorn, Caroline Zwiers (PhD Student)*
BREAK 10'
Dermatology 11:45 - 12:15 Research programme **30401** *Prof Maarten Vermeer (HoD), Dr Kees Tensen, Coby Out (technician), Suzan van Santen (PhD Student), Dr Abdoel el Ghalbzouri*
12:15 - 13:15 Discussion Division 3 programmes (committee)
LUNCH 13:15 – 14:00
Otorhinolaryngology 14:00 - 14:30 Research programme **30501** *Prof. Peter Paul Van Benthem (HoD), Prof. Johan Frijns, dr. Jeroen Briaire, dr. Margriet Huisman, drs. Monique de Jong*
Ophthalmology 14:30 - 15:00 Research programme **30801** *Prof Gré Luijten (HoD), prof Nicolien Schalij-Delfos, Dr Jan Willem Beenakker*
Gynaecology 15:00 - 15:30 Research programme **30101** *Prof Frank Willem Jansen (HoD), Dr Mariette Poelgeest, Dr Cor de Kroon, Dr Monique ter Kuile*
BREAK 15'
15:45 - 17:00 Discussion Division 3 programmes (committee)
18:00 Dinner DIV 3 Committee, Faculty Club

Wednesday 23 May
Neurosurgery 8:30 - 9:00 Research programme **30601** *Prof Wilco Peul (HoD), Dr Carmen Vleggeert, Prof Martijn Malessy, Dr Wouter van Furth, Dr Marike Broekman*
Pathology 9:00 - 9:25 Research programme **30901** *Prof. Vincent Smit (HoD), Prof. Jan Anthonie Bruijn, Dr. Ingeborg Bajema, Dr. Hans Baelde* 9:25 - 9:50 Research programme **30902** *Prof. Vincent Smit (HoD), Prof. Judith Bovée, Dr. Noel de Miranda, Dr. Tjalling Bosse, Dr. Jan van Wezel*
BREAK 15'
Psychiatry 10:05 - 10:35 Research programme **31001** *Prof Bert van Hemert (HoD), Prof Roos van der Mast, geriatric psychiatry, Prof dr Robert Vermeiren, child and youth psychiatry, Prof dr Nic van der Wee, biological psychiatry, drs S. Bauduin, PhD student*
Public Health and Primary Care 10:35 - 11:00 Research programme **31201** *Prof Mattijs Numans (HoD), prof Jacobijn Gussekloo, prof Wilco Achterberg, Dr Jeanette Blom, Drs Maartje Klapwijk (PhD student)* 11:00 - 11:25 Research programme **31202** *Prof Mattijs Numans (HoD), prof Niels Chavannes, Dr Matty Crone, Prof Ria Reis, Dr David van Bodegom*
BREAK 10'
11:35 - 12:15 discussion Division 3 programmes (committee)
LUNCH 12:15 – 13:15
Pediatrics 13:15 - 13:40 Research programme **31301** *Prof Edmond Rings (HoD), Dr Arjan Lankester, Dr Marco Schilham, Rebecca ten Cate, Dr Luisa Mearin* 13:40 - 14:05 Research programme **31303** *Prof Edmond Rings (HoD), Dr Arno Roest , Prof Enrico Lopriore, Dr Arjan Te Pas, Dr Christiaan de Bruin*
BREAK 10'
14:15 - 15:30 Concluding discussion Division 3 programmes (committee)
15:45 – 16:15 Excursion 'Technology in Motion Laboratory'

Division 4

Core Committee & prof. Van den Brink, prof. Maizels, prof. Kuh, prof. Berns

Wednesday 23 May

16:45 taxi transport from the hotel to restaurant

17:00 Briefing, followed by diner, Engelbertha Hoeve

Thursday 24 May

Human Genetics

8:30 - 8:55 Research programme **50104**

Prof Silvère van der Maarel (HoD), Prof Annemieke Aartsma Rus, Prof Arn van den Maagdenberg, Dr Willeke van Roon-Mom, Dr Louise van der Weerd

8:55 - 9:20 Research programme **50105**

Prof Silvère van der Maarel (HoD), Prof Marcel Tijsterman, *prof Haico Van Attikum, Dr Martijn Luijsterburg, Dr Niels de Wind*

9:20 - 9:45 Research programme **50106**

Prof Silvère van der Maarel (HoD), Prof Peter de Knijff, Prof Barend Mons, Prof Johan den Dunnen, Dr Lucia Clemens Daxinger, Dr Susan Kloet

9:45 - 10:10 Research programme **50107**

Prof Silvère van der Maarel (HoD), Dr Peter Hohenstein, Prof Dorien Peters, Prof Ko Willems van Dijk

BREAK 15'

Clinical Genetics

10:25 - 10:50 Research programme **50801**

Prof Christi van Asperen (HoD), Prof Frank Baas, Dr Saskia Lesnik Oberstein, Dr Gijs Santen, Dr Marian Weterman

10:50 - 11:15 Research programme **50802**

Prof Christi van Asperen (HoD), Dr Frederik Hes, Dr Maartje Nielsen, Dr Nienke van der Stoep, Prof Arend Tibben

Radiotherapy

11:15 - 11:45 Research programme **40402**

Prof Carien Creutzberg (replaces the HoD), Prof Uulke van der Heide, Prof Marco van Vulpen, Dr Femke Peters

BREAK 10'

11:55 - 13:15 discussion Division 4 programmes (committee)

LUNCH 13:15 – 14:00

Medical Oncology

14:00 - 14:25 Research programme **40401**

Prof Hans Gelderblom (HoD), Prof Sjoerd van der Burg, Dr Ellen Kapiteijn, Dr Judith Kroep, Dr Els Verdegaal

14:25 - 14:50 Research programme **40403**

Prof Hans Gelderblom (HoD), Dr Marije Slingerland, Dr Ellen Kapiteijn, Dr Judith Kroep, Prof Johanneke Portielje

Clinical Pharmacy and Toxicology

14:50 - 15:20 Research programme **40501**

Prof Henk Jan Guchelaar (HoD), Dr Jesse Swen, Dr Dirk Jan Moes, Dr Anton Terwisscha van Scheltinga, Dr Yahya Anvar

BREAK 15'

Biomedical Data Sciences

15:35 - 16:00 Research programme **50601**

prof Ewout Steyerberg (HoD), prof Jelle Goeman, Dr Hein Putter, Prof Saskia le Cessie, Dr Jacco Wallinga

16:00 - 16:25 Research programme **50602**

Prof Ewout Steyerberg (HoD), prof Eline Slagboom, Dr Elske van den Akker, prof Ingrid Meulenbelt, dr Bas Heijmans

16:25 - 16:50 Research programme **10801**

Prof Ewout Steyerberg (HoD), prof Anne Stiggelbout, dr Perla Marang- Van de Meheen, Dr Jaap Sont

Center for Proteomics and Metabolomics

16:50 - 17:20 Research programme **50402**

Prof Manfred Wuhrer (HoD), Dr Martin Giera, Dr Paul Hensbergen, Guinevere Kammeijer (PhD candidate), Dr Elena Dominguez Vega

BREAK 10'

17:30 - 18:15 discussion Division 4 programmes (committee)

18:15 taxi transport from LUMC

18:30 Dinner Division 4 Committee, Faculty Club

Friday 25 May 2018

Anatomy and Embryology

8:30 - 9:00 Research programme **50201**

Prof Christine Mummery (HoD), Prof Marco de Ruiter, Dr Valeria Orlova, Dr Susana Chuva de Sousa Lopes, Dr Richard Davis

Immunohematology and Blood Transfusion

9:00 - 9:25 Research programme **40202**

Prof Wim Fibbe (HoD), prof Ferry Ossendorp, Dr Ramon Arens, Marieke Herbert-Fransen, prof Frits Koning

9:25 - 9:50 Research programme **40203**

Prof Wim Fibbe, Prof Frits Koning, Dr Sebastiaan Heidt, Dr Leendert Trouw, prof Jaap Jan Zwaginga

9:50 - 10:15 Research programme **40204**

Prof Wim Fibbe (HoD), Prof Frank Staal, Prof Jacques van Dongen, Dr Liesbeth Oosten, prof Frits Koning

BREAK 15'

Infectious diseases, Parasitology, Medical microbiology

10:30 - 10:55 Research programme **40302**

Prof Leo Visser (HoD), Prof Tom Ottenhoff, Prof Annemiek Geluk, Dr. Peter Nibbering, Dr Simone Joosten en Dr. Mark de Boer

10:55 - 11:20 Research programme **50401**

Prof Maria Yazdanbakhsh (HoD), Prof Ron Hokke, Dr Shahid Khan, Dr Meta Roestenberg and Dr Hermelijn Smits

11:20 - 11:45 Research programme **40601**

Prof Louis Kroes (HoD), Prof Eric Snijder, Prof Sasha Gorbalenya, Dr Marjolein Kikkert,

Dr Mariet Feltkamp 11:45 - 12:10 Research programme **40602** *Prof. Louis Kroes (HoD), Prof. Eric Snijder, Prof. Ed Kuijper, Dr.Wiep Klaas Smits, Dr. Jeroen Corver*
12:10 - 13:00 discussion Division 4 programmes (committee)
LUNCH 13:00 – 13:30
Hematology 13:30 - 14:00 Research programme **40103** *prof Hendrik Veelken (HoD), Prof Fred Falkenburg, Dr Mirjam Heemskerk, Dr Marieke Griffioen*
Cell & Chemical Biology 14:00 - 14:25 Research programme **50303** *Prof. Sjaak Neefjes (HoD), Prof. Joke Meijer, Dr. Jos Rohling, Dr. Claudia Coomans, Dr. Stephan Michel* 14:25 - 14:50 Research programme **50304** *Prof. Sjaak Neefjes (HoD), Prof. Bram Koster, Dr. Thom Sharp, Dr. Roman Koning, Dr. Lennard Voortman* 14:50 - 15:15 Research programme **50305** *Prof. Sjaak Neefjes (HoD), Prof. Peter ten Dijke, Dr. Alfred Vertegaal, Dr. Karoly Szuhai, Dr. Laila Ritsma*
BREAK 15'
15:30 - 15:55 Research programme **50306** *Prof. Sjaak Neefjes (HoD), Prof. Rob Hoeben, Dr. Arnaud Zaldumbide, Dr. Manuel Goncalves, Prof. Marie-José Goumans* 15:55 - 16:20 Research programme **40801** *Prof. Sjaak Neefjes (HoD), Prof. Dr. Huib Ovaa, Dr. lana Berlin, Dr. Monique Mulder, Dr. Paul Geurink*
16:20 - 18:00 Concluding discussion Division 4 programmes (committee)

Division 1

Core Committee & prof. Hamdy, prof. Hamilton, prof. Drummond

Sunday 27 May
17:45 taxi transport from the hotel to restaurant **18:00** Diner**:** Villa Beukenhof,
Monday 28 May
8:30 - 9:15 Core committee meets Executive Board
BREAK 10' and *welcome members Division 1 prof. Hamdy, prof. Hamilton, prof. Drummond*
9:30 -10:30 Briefing Committee Division 1
Orthopedics, Trauma and Rehabilitation Medicine 10:40 - 11:10 Research programme **10404** *Prof Rob Nelissen (HoD Orthopedics), Prof Rob Tollenaar (HoD Surgery) Dr Monique Termaat, prof Peter Dijkstra, Prof Thea Vliet Vlieland, Suzan Dijkink (PhD student), Banne Nemet (PhD student)*
Surgery 11:10 - 11:35 Research programme **10202** *Prof Rob Tollenaar (HoD), Dr (Wilma) Mesker, Dr Gerrit-Jan Liefers, Dr Alexander Vahrmeijer, Dr Gabri van der Pluijm, Dr Petra Voorham-van der Zalm* 11:35 - 12:00 Research programme **10203** *Prof Rob Tollenaar (HoD), Prof Ian Alwayn, Dr Jan Lindeman, Dr Volkert Huurman, Dr Dries Braat*
BREAK 10'

15:30 - 17:00 Core committee meets three Medical research profiles 15:30 - 16:00 **Cancer Pathogenesis and Therapy** *Prof Peter Devilee, Prof Hendrik Veelken, Prof Peter ten Dijke, Prof Sjoerd van den Burg* 16:00 - 16:30 **Translational Neuroscience** *Prof Michel Ferrari, Prof Silvère Van der Maarel Prof Van der Wee, Dr Mark Kruit, Dr Willeke van Roon* 16:30 - 17:00 **Immunity, Infection and Tolerance** *Prof Maria Yazdanbakhsh, Prof Eric Snijder, Prof Tom Huizinga, Dr Meta Roestenberg, Prof Rene Toes*
17:00 - 17:30 Discussion Medical research profiles (core committee)
Anesthesiology 12:10 - 12:40 Research programme **10101** *Prof Leon Aarts (HoD), Prof Albert Dahan, Prof Evert de Jonge, Marieke Niesters, Dr Monique van Velzen*
LUNCH 12:40 – 13:45
13:45 - 14:45 Concluding discussion Division 1 programmes (committee)
15:00 – 16:00 Excursion Smart Surgery

Division 2

Core Committee & prof. Hamilton, prof. Walker, prof. Bertherat, prof. Pettigrew, prof. Simon

Tuesday 29 May *Conversation room H1-14, Building 1*
8:30 - 9:00 Committee meets to prepare site visit
Heart diseases/Pulmonology 9:00 - 9:30 Research programme **20403** *Prof Piet Postmus (HoD), Prof Pieter Hiemstra, Dr Jan Stolk* 9:30 - 10:00 Research programme **20303** *Prof Martin Schalij (HoD), Prof Paul Quax, Prof Robert Klautz, Dr Jerry Braun, Prof Wouter Jukema, prof Katja Zeppenfeld, Dr Daniel Pijnappels*
BREAK 15'
Clinical Epidemiology/Thrombosis and Hemostasis 10:15 - 10:45 Research programme **21001** *Prof Frits Rosendaal, Prof Friedo Dekker, Prof Suzanne Cannegieter, Dr Renee de Mutsert* 10:45 - 11:15 Research programme **21101** *Prof Ton Rabelink (HoD), Prof Henri Versteeg, Prof Jeroen Eikenboom, Dr Martine Bos, Dr Erik Klok, prof Olaf Dekkers*
Gerontology 11:15 - 11:45 Research programme **20801** *Prof Ton Rabelink (HoD), Prof Gerard Jan Blauw, Dr Diana van Heemst, Dr Simon Mooijaart, Dr Stella Trompet, prof Olaf Dekkers*
11:45 - 12:30 discussion Division 2 programmes (committee)
LUNCH 12: 30 - 13: 30
Endocrinology 13:30 - 14:00 Research programme **20102**

Prof Ton Rabelink (HoD), Prof Alberto Pereira, Prof Patrick Rensen, Prof Eelco de Koning, Dr Natasha Appelman, prof Olaf Dekkers
Nephrology 14:00 - 14:30 Research programme **20603** *Prof Ton Rabelink (HoD), Prof Anton Jan van Zonneveld, Prof Cees van Kooten, Dr Joris Rotmans, Dr Onno Teng, prof Olaf Dekkers*
Gastroenterology and Hepatology 14:30 - 15:00 Research programme **20501** *Dr Roeland Veenendaal (HoD), Dr Luuk Hawinkels, Dr Minneke Coenraad, Dr Andrea van der Meulen, Prof James Hardwick, Prof Bart van Hoek*
BREAK 15'
15:15 - 16:30 discussion Division 2 programmes (committee)
16:45 – 17:45 Excursion 'Einthovenlaboratory'
17:45 taxi transport from the hotel to restaurant **18:00** Dinner**:** Faculty Club,
Wednesday 30 May
Radiology 8:30 - 8:55 Research programme **20903** *Prof Mark van Buchem (HoD), Prof Hans Bloem, Prof Boudewijn Lelieveldt, Dr Eric Kaijzel, Prof Lioe-Fee de Geus, Dr Mark Burgmans* 8:55 - 9:20 Research programme **20901** *Prof Mark van Buchem (HoD), Prof Thijs van Osch, Dr Louise van der Weerd, Ahmed Mahfouz Dr Marianne van Walderveen* 9:20 - 9:45 Research programme **20902** *Prof Mark van Buchem (HoD), Prof Hildo Lamb, Prof Albert de Roos, Dr Rob van der Geest, Ilona Dekkers*
BREAK 15'
Rheumatology 10:00 - 10:30 Research programme **20701** *Prof Tom Huizinga (HoD), Prof Margreet Kloppenburg, Prof Annette van der Helm, drs Theresa Kissel and Dr Uli Scherer*
10:30 - 12:30 Concluding discussion Division 2 (committee)
LUNCH 12:30 – 13:3
Graduate school (*Core committee and Prof. Brian Walker*) 13:30 – 14:10 **Management GS** *Prof Pancras Hogendoorn (dean), Yvonne Mees ten Oever (policy advisor), Drs Pauline de Graaf (office manager Graduate School), Drs Ir Jacqueline Ton (director Directorate of Research), Fleur Meijer (LUMC Association for PhD candidates)* 14:15 – 15:00 **PhD students** *Fleur Meijer (LUMC Association for PhD candidates, Heart Diseases), Karin Simons (LUMC Association for PhD candidates, Surgery), Tine van de Donk (*Anesthesiology*), Dong Yu (Otorhinolaryngology*)
BREAK 15'

15:15 - 16:00 **Integrity policy**
Prof Frits Rosendaal (co-chair Leiden University committee Scientific integrity), prof Frits Koning (Confidential Advisor), Prof Frans Helmerhorst (chair committee Good Research practice)

BREAK 10'

16:10 - 16:45 **Diversity policy**
Prof Jacobijn Gussekloo (chair Vitaal), Prof Maria Yazdanbakhsh (LUMC committee internationalisation)

17:00 - 17:45 concluding discussion (core committee)

17:45 *taxi transport from the hotel to restaurant*
18:00 Dinner**:** De Moerbei,

General

Thursday 31 May

Core committee meets four Medical research profiles
9:00 - 9:30 **Vascular and Regenerative Medicine**
Prof Wim Fibbe, Prof Ton Rabelink, Prof Christine Mummery, Prof Douwe Atsma
9:30 - 10:00 **Biomedical Imaging**
Prof Boudewijn Lelieveldt, Dr Itamar Ronen, Dr Louise van der Weerd, Dr Laila Ritsma, Dr Lennard Voortman

BREAK 15

10:15 - 10:45 **Innovation in Health Strategy and Quality of Care**
Prof Anne Stiggelbout, Prof Mattijs Numans, Prof Anske van der Bom, Prof Wilco Peul, Rishi Khusial, MD-PhD student
10:45 - 11:15 **Ageing**
Prof Gerard Jan Blauw, Prof Jacobijn Gussekloo, Dr Gerrit-Jan Liefers, Dr Marian Beekman, Max van der Sijp (PhD student)
11:15 -12:30 discussion Medical research profiles (core committee)

LUNCH 12:30 – 13:30

13:30 - 14:15 **Meeting with chairmen divisions**
Prof Leon Aarts (DIV1), Prof Ton Rabelink (DIV2), Prof Bert van Hemert (DIV3), Prof Wim Fibbe (DIV4)

14:15 Foto moment

14:20 - 15:30 **Meeting with Executive Board**
Prof Willy Spaan (chair), Prof Pancras Hogendoorn (dean)

15:30 - 17:00 **Wrap up core committee**

17:00 - 18:00 DRINKS FOR EVERYONE INVOLVED (Venue 't Paleijhs)

Appendix 2 Explanation of the SEP scores

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