

AMC
RESEARCH
EVALUATION 2011

PREFACE 4

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PREFACE

Research is one of the core tasks of the Academic Medical Center (AMC) at the University of Amsterdam. Therefore, we seek to perform our research at the highest possible level and to strive for excellence in research at an international top echelon. This endeavour also encompasses excellent education and training of young researchers in our PhD program within the context of the AMC Graduate School.

As part of the quality control of our research programme, the AMC has performed a thorough evaluation of its research activities. This evaluation was directed by our Research Council and included an extensive self-assessment of our principle investigators (PIs), departments and divisions followed by a site visit in March 2011 by an International Evaluation Committee, consisting of world leaders in biomedical and health care research. The evaluation comprised the performance and the quality as well as the organization of the AMC research and the Graduate School.

The present report summarizes this evaluation. We are very proud that the International Evaluation Committee was impressed by both the quantity and quality of the research and considered the research at the Academic Medical Center "...to be at a very high level according to international standards and achieving the level of world leadership in various fields.". We also appreciate that the Committee in general agreed with the self-assessment of the PIs and the research themes. This underlines that the systematic approach as chosen by our Research Council is helpful in discriminating top-level research from areas that show a somewhat less impressive performance.

Significantly, the International Evaluation Committee generated important and very useful recommendations for further improvement of the research governance. The Committee stressed that research performance and research resources should be more strongly matched, i.e. that the AMC should look for methods that would more tightly link research budgets (both personnel and material) and research space to achievements of the various groups. In addition, the AMC should develop a system in which the careers of the top talented young researchers (e.g. post-docs and mid-career fellows) could be fostered in order to keep these researchers associated with the AMC in the long run. Lastly, the Committee pointed to the fact that some of the core research facilities should be better funded in the next years.

Importantly, these recommendations fully concur with the Strategic Goals of the AMC that have recently been established for the period 2011-2016. Hence, the Executive Board of the AMC recognizes and accepts these recommendations and proposes that it will start a series of initiatives to improve on these issues in the next months and years.

We are very grateful for the massive amount of work that has been done by our PIs, department heads and division chairmen, and in particular by the Research Council, to produce this impressive overview and assessment of the AMC research. In addition, we thank the International Evaluation Committee for its very constructive and positive appraisal of our research efforts and its clear recommendations regarding the research governance. On behalf of our Executive Board I may add that we are proud of the outcome of this research evaluation and we are especially pleased that the Committee has recognized both our strong ties and close links between basic and clinical research efforts, our ability to promote the translation of our research findings into innovative practice and policy, and the overall strong interest of our young students and researchers to make a career in biomedical research.

On behalf of the Executive Board,
Marcel Levi, MD PhD
*Dean of the Faculty of Medicine, University of Amsterdam and
Chairman of the Executive Board of the Academic Medical Center*



Periodic external evaluation of scientific research is essential for two reasons: to improve the quality of research and research management, and to provide accountability of the research institute towards fellow universities and university medical centres, funding agencies, government and society at large. Therefore, universities in the Netherlands have agreed to carry out a self-evaluation every three year and an external review every six years. This process is guided by a Standard Evaluation Protocol that has been developed by the Royal Netherlands Academy of Arts and Sciences (KNAW), the Association of Universities in the Netherlands (VSNU) and the Netherlands Organisation for Scientific Research (NWO).

In 2011, the Academic Medical Center (AMC) in Amsterdam had its first external evaluation of its research. A self-evaluation report was prepared by the AMC Research Council under the auspices of the Executive Board. Next, an International Evaluation Committee visited the AMC to review our research performance and answer a number of specific questions. Professor Andre Knottnerus (Chair of the Scientific Council for Government Policy (WRR) and professor of Primary Care and Clinical Epidemiology at the University of Maastricht, The Netherlands chaired the International Evaluation Committee; the other members were Professor Reinhold E. Schmidt, MD, Professor Thomas F. Lüscher, MD, FRCP, Professor Nicholas White, MD and Professor Douglas Green. The positions and affiliations of the members can be found in annex 1. Annex 2 and 3 provide the programme of the site visit and the specific questions that were posed to the Committee.

This report contains the results of the evaluation. Part A encompasses a description of the research organization and policy. Also, key figures on the output and earning capacity in the period 2005-2010 are provided. Next follows a short description of the research performed in each of the seven AMC research themes, including an analysis of the Strengths, Weaknesses, Opportunities and Threats (SWOT) and the future perspectives. Part B is the evaluation of the AMC Graduate School. Part C is the report that was prepared by the International Evaluation Committee on the basis of the information provided in the self-evaluation report and the meetings with research leaders and PhD students during the site visit.

PART A

THE AMC
RESEARCH
INSTITUTE

1. INTRODUCTION

The Academic Medical Center (AMC) is one of the foremost research institutions in the Netherlands, as well as one of its largest hospitals. Over 7000 people provide academic patient care, teach, and perform scientific research. Some 1000 members of staff are either fully or partially employed in (bio)medical research. Many researchers combine their scientific work with day-to-day clinical responsibilities or teaching and training. The AMC has a strong tradition of translational research. Our investigations cover the whole spectrum of biomedical research: from fundamental science and proof of concept studies to applied clinical studies, health services research and medical informatics. In this way, we aim to respond effectively to the current and future medical needs. All research in the AMC is organized in the AMC Research Institute. The mission of the AMC Research Institute is to stimulate excellent (bio)medical research. In our view, outstanding research benefits from a climate of openness and interdisciplinary exchange, international orientation, the facilitation of promising (niche) research and from actively attracting and cherishing of scientific talent.

2. THE AMC RESEARCH ORGANIZATION

Until August 2010, Prof. L.J.Gunning-Schepers has been both the dean of the Faculty of Medicine and the chair of the AMC Executive Board. On September 1, she was succeeded by Prof. M.M. Levi, formerly the chair of the division of Specialisms in Medicine. AMC has 10 Divisions:

- Specialisms in Medicine
- Surgical specialisms
- Paediatrics
- Neurology/Neurosurgery, ENT, Ophthalmology and Dermatology
- Obstetrics and Gynaecology
- Psychiatry
- Laboratory specialisms
- Operating centre and Intensive Care
- Imaging specialisms
- Clinical methodology and Public Health

Each Division is headed by a division chair. The 10 Divisions encompass 71 (sub)departments. Each department head has the integral responsibility for patient care, education and research as well as for management and finances.

In January 2007, the AMC Research Institute was formed out of a merger of seven previously separated thematic research institutes. The board of the Research Institute is formed by the AMC Research Council. The Research Council advises the Executive Board on research policy, including the quality of researchers. Prof. R.A.W. van Lier is the chair of the Research Council and there are 16 members, who together oversee all of the fundamental, translational and clinical research within the AMC. The chair and three members are the executive board of the Research Council. Also since January 2007, the training and supervision of PhD students is coordinated by the AMC Graduate School, chaired by Prof. P. M. Bossuyt. The AMC Graduate School board has 6 members, amongst which a student-member (see Part B).

In order to stimulate interdisciplinary collaboration, the AMC has selected **seven themes** in which it aspires to excel:

- Cardiovascular Diseases (CD)
- Gastrointestinal Diseases (GID)
- Infection and Immunity (I&I)

- Metabolic Disorders (Met)
- Neurological and Psychiatric Disorders (NPD)
- Oncology (Onc)
- Public Health and Epidemiology (PHE).

Each theme covers the whole spectrum from fundamental biomedical research, through translational and clinical research to the evaluation of innovations in actual clinical practice. Within the themes centres have been created that stimulate inter-departmental collaborations and scientific debate. Currently AMC houses the Heart Failure Research Centre, the AMC Liver Centre, CINIMA (Centre for Infection and Immunity Amsterdam), CIA (Centre for Immunology Amsterdam), the Oncology Centre AMC, the Amsterdam Centre for Metabolism and POEHIM (Public, Occupational and Epidemiological Health Issues in Medicine). The AMC is a dynamic organization and new initiatives for supra-departmental collaboration and clustering frequently come into view. Relevant nuclei of research collaboration are emerging in the fields of gynaecological oncology, hemato-oncology, and the fertility lab.

AMC researchers who have shown to be able to develop and sustain their own research line are granted a **'Principal Investigator' (PI)** appointment so that they can take up leadership, create their own group and gain visibility. This system that has been introduced in 2006 has proven to promote the scientific careers especially of young and talented researchers and challenges them to develop their own lines of research and be accountable for it. The AMC board appoints a PI after consultation of the Research Council. The standards used to assess potential Principal Investigators are high, see paragraph 3. AMC's research policy. Currently, there are 202 PIs. The distribution of PIs among the different research themes is given in Figure 1. Please note that PIs can choose to participate in more than one research theme. In 2008 and in 2011 the research performance of the PIs has been evaluated in a 'self-evaluation' procedure.

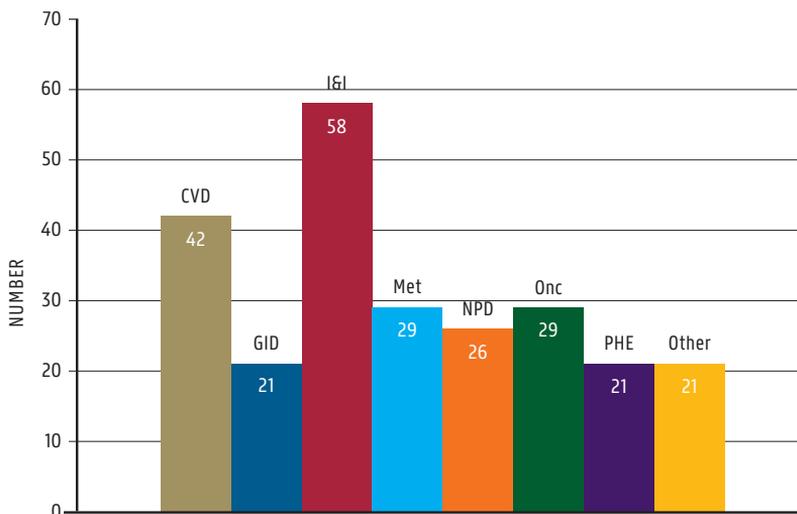


Figure 1: Number of Principal Investigators per theme. CVD=Cardiovascular Diseases; GID=Gastrointestinal Diseases; I&I=Infection and Immunity; Met=Metabolic Disorders; NPD=Neurological and Psychiatric Disorders; Onc=Oncology; PHE=Public Health and Epidemiology.

There is special unit to support the clinical and nursing research carried out at the AMC, the Clinical Research Unit (CRU). The services cover data management, quality control and methodological and statistical supervision during the preparation, conduct and reporting of clinical research. There is also a special support structure for the administration, management and contracting of research projects that are funded by third parties, the AMC Medical Research (AMR Ltd).

The Academic Medical Center in Amsterdam (AMC) complex also houses the Dutch Cochrane Centre, the Netherlands Institute for Neuroscience (NIN) of the Royal Dutch Academy of Sciences (KNAW) and the Amsterdam Institute for Global Health and Development. During the next few years, the Spinoza Centre for Neuroimaging will rise next to the AMC. The AMC has a close collaboration and shared laboratory facility with the Sanquin Blood Supply Foundation. There is also a close and formal relationship with the Netherlands Cancer Institute-Antonie van Leeuwenhoek Hospital (NKI-AvL) and the Public Health Services of Amsterdam (GGD).

3. AMC'S RESEARCH POLICY

AMC's research policies focus on the people (Principal Investigator system, encouragement of scientific collaboration, stimulation of scientific careers), the funding (finances, investments) and the quality system (evaluations, independence and integrity).

Principal Investigator system

AMC's research policy is geared towards stimulating excellence by putting the professional in the lead. Researchers can be nominated to be appointed Principal Investigator by their department head. The Research Council assesses the candidates and upon their advice, PIs are appointed by the AMC Executive Board. Being a multidisciplinary institution, the AMC chooses to assess researchers in fundamental, clinical and para-clinical research against the same set of criteria developed by the Research Council. These criteria include acquisition of funds to sustain one's own research line; having acted as a 'copromotor' (i.e. supervisor of a PhD student); and high quality and quantity output, among which publications as a senior author. A PI appointment is a prerequisite for being eligible for associate professorship.

Encouraging collaboration and visibility

Interdisciplinary exchange is vital for innovative and productive translational research and this is attained by the research themes structure. Retreats, lectures series and other forms of scientific exchange and communication are organized within each theme, in particular by the abovementioned centres. In this way, platforms have been created where fundamental and clinical researchers can meet which furthers our translational research profile. The AMC's research fabric is strengthened by the work of the internal support groups for grant applications under the auspices of the Research Council. Senior researchers are coupled to less experienced researchers or researchers with a related specialty to give feed back on their research proposals with the aim of enhancing the fundability of the proposal. The Research Council also organizes monthly lectures by world class scientists (Ruysch lectures), usually preceded by a master class for AMC scientists. Finally, the Research Council promotes external collaboration and visibility, e.g. by participating in national platforms and contributing to promotional initiatives in the region and in the Netherlands.

Careers

Every five years the Executive Board, with advice of the Research Council and the division chairs, draws up a planning to explicate which research chairs will become available or should be created, taking into account both subject matters of interest and the availability of suitable candidates. Further, the Research Council gives advice on the research profile of new research chairs. For the appointment of associate professors, department heads submit proposals to the dean who decides on the appointments, after having consulted both the Research Council and the Education Council.

AMC wants to be attractive to national and international top researchers and retain our own best researchers, where possible by offering a tenured position. By the means of AMC fellowships and PhD scholarships, AMC aims to exert a pull on international talent and create opportunities for AMC talents. Each year, two AMC fellowships (700 k€ for five years) and two AMC postdoc positions (150 k€ for two years) are awarded to outstanding researchers. Similar to the appointment of PIs and associate professors, excellence is a primary criterion. Awarding these special scholarships is done by the AMC fellowship committee, chaired by Prof. H.R. Büller. Candidates from within the AMC, from other Dutch institutions and from abroad can apply. Also each year, the AMC Graduate School offers six PhD Scholarships to excellent students who completed studies at the Master's level in Medicine, Medical Informatics, Biomedical Sciences or Social Sciences. With an AMC Scholarship, students can develop their own PhD research project (see Part B). Starting in 2009, as part of the AMC Innovation Impulse, 6 extra PhD Scholarships have been made available.

Recently, mid career laureates who have acquired a prestigious personal grant have come into view as an important target group. These researchers are offered a tailor-made training programme to enhance their strategic and management skills.

Quality control

The Research Council periodically evaluates the quality of researchers and their research. For these evaluations, AMC follows an adaptation of the Standard Evaluation Protocol (SEP 2003-2009 and 2009-2015) of the VSNU (Association of Universities in the Netherlands), NWO (Netherlands Organisation for Scientific Research) and KNAW to allow for (inter) national comparison of our achievements. The AMC is keen to use a sole measure for all its Principal Investigators. The SEP definition of scientific quality includes productivity, relevance and viability, and we take into account discipline specific contextual information and societal impact where relevant. The research evaluation is to provide steering information to improve the quality of research and research management to PIs, heads of departments and Divisions, and the Executive Board.

Each year, the heads of department make a research plan for their department as part of the annual plan. In this research plan, they specify their mission and ambitions, the research lines they want to further, the way in which the research at the department is organized, a SWOT analysis and their future perspectives. Thus, the heads of departments are rather self-governing in deciding on future research directions.

All AMC researchers, including PhD students, have annual assessment interviews with their heads of department in which their work is evaluated, tasks and targets are defined and working conditions, personal development and career perspectives are discussed. These interviews are in potential an important way of steering both on the quality and on the content of the research.

Investments

Decision making on investments in research infrastructure has been decentralized and is carried out by the heads of departments. Investments from k€250 or more need approval from the central committee on research investments. In 2006, AMC took the initiative to pursue a major government grant for the String of Pearls Initiative to collect and share amongst the eight other Dutch UMCs clinical data and biomaterial on eight diseases in a coordinated way. The infrastructure is also reinforced by occasional impulses administered by the Executive Board of the AMC. For the period 2009-2011, by means of the Innovation Impulse extra budget has been invested for stimulating innovation in research, education and patient care and about half of the extra budget was assigned to research (translational genetics, utilization of the translational infrastructure String of Pearls Initiative and SPHINX, extra research fellowships for PhDs and postdocs, the project cohorts in the academic population HELIUS and a platform for collaboration and channelling funds on three shared research priorities with the University of Amsterdam Brain and Cognitive Sciences, Global Health and Development and Systems Biology).

Research financing

The direct government funding for research is not earmarked and managed by the heads of departments, who receive an annual lump sum budget for patient care, education and research.

The acquisition of indirect competitive government funding (national and EU) and charity funds is actively stimulated by the Research Council. Relevant grant opportunities are announced in a weekly e-newsletter and on the intranet. Starting researchers who wish to apply for a prestigious personal grant are coupled to experienced expert referees. For prestigious, personal grant proposals the support is compulsory. Application for such prestigious grants is further stimulated by granting an extra PhD student to awardees. In the 2006-2010, 75 of such extra PhD students, 20 AMC scholarships, 4 AMC postdocs and 6 AMC fellowships were granted by the Executive Board.

Research funding from the European Union is becoming increasingly important. Researchers can get support, both for the legal and administrative aspects and to enhance the scientific and technical quality of the grant proposal.

Collaboration with commercial parties is necessary to ensure that the results of scientific research, whenever feasible are rapidly converted into new diagnostic and therapeutic tools. The AMC's Technology Transfer Office advises researchers on these collaborations. The valorisation of results generated by AMC researchers is encouraged.

Independence and integrity

AMC trusts that naming the temptations and potential problems, and specifying the rules helps to avoid conflict of interest and to preserve the independence of the AMC academic community. The guiding principles are laid down in the AMC Research Code, partly based on national laws and regulations and international agreements, and partly the outcome of discussions and experiences at the AMC itself.

All PIs have to make public their 'other research related activities' and their research funding on the personal page on the AMC internet, see www.amc.nl/whoiswho.

Research output per theme

Table 1 reflects key figures on output and project funding acquired by researchers of the seven research themes. Each AMC theme has at least 20 PIs, which appears to be sufficient critical mass for exchange, sharing of knowledge and visibility. Cardiovascular diseases and Infection and immunity are the largest research themes, both in terms of number of PIs and in output (PhD theses and publications). A number of PIs (13) has chosen not to join a research theme. Publications of PIs who participate in more than one research theme are counted for each theme and therefore the total number of publications was deduplicated.

4. KEY FIGURES ON THE AMC RESEARCH THEMES

Research theme	PIs	Number of PhD theses completed 2005-2010	Number of publications in journals with impact factor 2005-2010	Project number of publications 2005-2010	Project funding acquired 2005-2010 (m€)
Cardiovascular diseases	42	239	3861	5034	58.0
Gastro intestinal diseases	21	128	1640	2156	30.0
Infection and Immunity	58	331	4321	5394	90.5
Metabolic disorders	29	114	1699	2121	31.2
Neurological and psychiatric disorders	26	117	2160	2830	31.4
Oncology	29	152	2217	2858	38.6
Public health and epidemiology	28	237	3180	4777	36.0
Other	13	255	3226	4559	
No theme/PI	-	32	1739	2301	
Total (deduplicated)	202	991	15330	21254	367.9

Table 1: Key figures on the output and project funding acquired per AMC research theme.

¹CPP is the average number of citations per publication corrected for self-citations. FCSm (mean Field Citation Score) is the mean citation rate of the fields in which the institute/group is active.

The AMC compared with other UMCs

Dutch biomedical research is highly visible and the AMC is no exception: the CPP/FCSm score¹, a measure for how often publications of an institute are cited compared with other institutes publishing in the same field in 2005-2009, is well above the normalized world average of 1.0, see Figure 2.

Figure 2: CPP/FCSm scores of the eight Dutch UMCs and two other universities. Source: CWTS benchmark analysis 1998-2009; Leiden, Centre for Science and Technology Studies

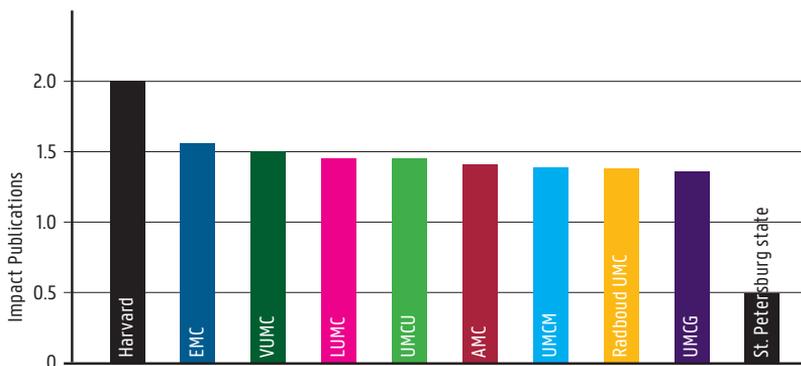
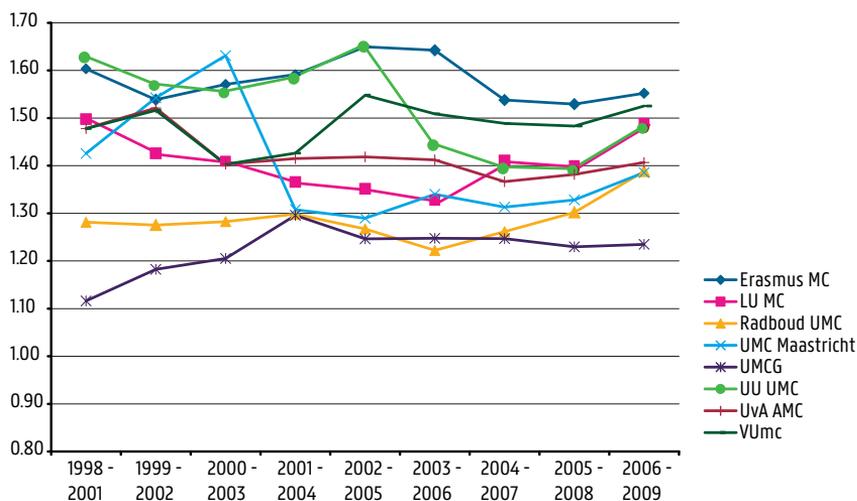
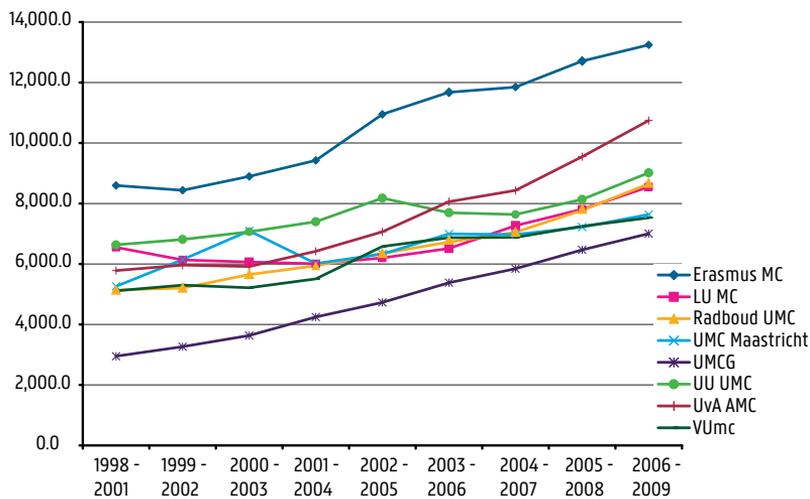


Figure 3: Trends of the field-normalized impact score (CCP/FCSm) for all Dutch UMCs, 1998-2009. Source: CWTS benchmark analysis 1998-2009; Leiden, Centre for Science and Technology Studies.



Scientific output can be measured in different ways and none of the approaches is uncontested. In the comparison of the CPP/FCSm scores of the eight Dutch UMCs, AMC shows a stable position in the mid-segment, see Figure 3. The CWTS as a rule uses only publications with the same address(es) for each UMC in this benchmark analysis. The top position of Erasmus MC partly results from the incorporation of the oncological centre Daniel Den Hoedt Clinic in this UMC, and its affiliation with the Erasmus University. Likewise, the close collaboration between UMC Utrecht and the Hubrecht Laboratory seems to augment the CPP/FCSm of this UMC. At present, AMC has no such close collaborations. The Amsterdam based Netherlands Cancer Institute-Antonie van Leeuwenhoek Hospital (NKI-AvL) shares part of its output with the AMC and three other UMCs.

Another approach is the Brute Force Index. The Brute Force Index is the product of the field-normalized impact score with the total number of publications in a period: $CPP/FCSm * P$.



Because of the high production of the AMC, according to this indicator the AMC holds the second position among the Dutch UMCs (Figure 4).

¹(continued) The Centre for Science and Technology Studies's definition of subfields is based on a classification of scientific journals into categories developed by ISI. Although not perfect, it is at present the only classification that can be automated consistently in their data-system. About 80 percent of all indexed papers are authored by scientists from the United States, Canada, Western Europe, and Japan. Therefore, the 'world' average is dominated by the Western world.

Figure 4: Trends of the Brute Force Index (CPP/FCSm * P) for all Dutch UMCs 1998-2009. Source: CWTS benchmark analysis 1998-2009; Leiden: Centre for Science and Technology Studies.

**5. SHORT
DESCRIPTION
OF THE SEVEN
THEMES**

The descriptions of the AMC research themes below have been written by the members of the Research Council that oversee the specific theme.

CARDIOVASCULAR DISEASES

By: Prof. J.J.P. Kastelein and Prof. A.F.M. Moorman

In the AMC world class expertise exists in the fields of cardiology, vascular medicine and cardiac developmental biology. This theme includes the Heart Failure Research Centre, a leading centre in research on the molecular and genetic basis of heart development and the genetic basis and mechanisms of cardiac arrhythmia, a group that focuses on interventional cardiology, and a vascular medicine group. There are weekly seminars, the Molecular Cardiology seminars, and in order to stimulate the interaction between clinical and preclinical research prominent speakers are invited for the monthly the Vrolijk lecture series.

The Heart Failure Research Centre harbours two major research lines: the genetics of the primary (monogenic) arrhythmia syndromes associated with a high risk of sudden cardiac death, including the genetic variation modulating susceptibility to sudden cardiac death and cardiac development in relation to congenital birth defects. The primary focus of the interventional cardiology group is the coronary circulation. This interdisciplinary research combines biomedical engineering and cardiovascular physiology to advance diagnostic capabilities, in close collaboration with clinical departments. Novel analysis methods applied to intravascular pressure and velocity measurements are utilized together with network models to support the interpretation of experimental and clinical data. The Vascular Medicine group focuses on early diagnostic strategies to detect atherogenic disease in preclinical stages (biomarkers, novel imaging strategies) as well as novel mechanistic pathways in atherothrombotic disease. In addition, the aetiology, diagnosis, prevention and treatment of venous thromboembolism have always been a strong research line. An additional research line aims at the advancement of mechanistic insight and to develop new diagnostic capabilities with the aid of vascular biomechanics and the study of the regulation of vascular function and structure in cardiovascular pathologies.

5 key publications

1. Watanabe H, Koopmann TT, Le Scouarnec S, Yang T, Ingram CR, Schott JJ, Demolombe S, Probst V, Anselme F, Escande D, Wiesfeld AC, Pfeufer A, Kääh S, Wichmann HE, Hasdemir C, Aizawa Y, Wilde AA, Roden DM, Bezzina CR. Sodium channel beta 1 subunit mutations associated with Brugada syndrome and cardiac conduction disease in humans. **The Journal of clinical investigation** 2008; 118: 2260-8.
2. Kastelein JJP, Akdim F, Stroes ES, Zwinderman AH, Bots ML, Stalenhoef AFH, Visseren FL, Sijbrands EJG, Trip MD, Stein EA, Gaudet D, Duivenvoorden R, Veltri EP, Marais AD, De Groot EMD for the ENHANCE investigators. Simvastatin with or without ezetimibe in familial hypercholesterolemia. **The New England journal of medicine** 2008; 358: 1431-43.
3. Van Belle A, Buller HR, Huisman MV, Huisman PM, Kaasjager K, Kamphuisen PW, Kramer MHH, Kruij MJHA, Kwakkel-van Erp JM, Leebeek FWG, Nijkeuter M, Prins MH, Sohne M, Tick LW. Effectiveness of managing suspected pulmonary embolism using an algorithm combining clinical probability, D-dimer testing, and computed tomography. **JAMA: the journal of the American Medical Association** 2006; 295(2): 172-9.
4. Christoffels VM, Grieskamp T, Norden J, Mommersteeg MT, Rudat C, Kispert A. Tbx18 and the fate of epicardial progenitors. **Nature** 2009; 458: E8-E9.

5. Pires NM, Pols TW, de Vries MR, van Tiel CM, Bonta PI, Vos M, Arkenbout EK, Pannekoek H, Jukema JW, Quax PH, de Vries CJ. Activation of nuclear receptor Nur77 by 6-mercaptopurine protects against neointima formation. **Circulation** 2007; 115(4): 493-500.

Highlights

- Coordination of two EU Collaboration projects has led to major breakthroughs in the understanding and modelling of heart formation, as well as an extensive international network in the field.
- We have identified several genes for arrhythmia syndromes and have contributed to the understanding of the underlying pathophysiological mechanisms through studies in cellular systems and mouse models, leading to novel therapies for some disorders.
- Our research on heart development, in particular the transcriptional mechanisms regulating differentiation of cardiac progenitor cells and the formation of structures of the heart, has led to the identification of T-box transcription factors that control development and function of the cardiac conduction system. Research is moving towards the analysis of the complex interactions between morpho-functional factors and regulatory mechanisms for heart development, which, when disturbed, cause congenital heart disease.
- Research into the novel mechanistic pathways in atherothrombotic disease is leading to exciting new developments in the field of clinical glycobiology and cholesterol homeostasis comprising in vivo quantification of tissue cholesterol efflux.
- Major progress has been made in the understanding, prevention, diagnosis and treatment of venous thromboembolism through a series of well designed clinical studies, including the risk of thrombophilia, non-invasive, efficient and patient friendly diagnostic algorithms for both deep venous thrombosis and pulmonary embolism patients as well as simpler, more effective and safe measures, usually pharmacologic, to prevent and treat venous thromboembolism.
- Microvascular adaptation is investigated by detailed 3D structure and perfusion images obtained with a unique self-developed imaging cryo-microtome with a primary focus on the coronary circulation, with extension to other vascular beds.
- Basic research in human primary vascular cell cultures has led to the identification of a sub family of nuclear receptors, the NR4As, with a protective function in the diseased vessel wall inhibiting excessive proliferation of smooth muscle cells, promoting endothelial cell survival and reducing the inflammatory response of macrophages. Dedicated (transgenic) mouse models have been applied to substantiate the in vivo relevance of these nuclear receptors in vascular disease and recent studies revealed the association of genetic variation of NR4As with the risk to develop in-stent restenosis.

SWOT

Strength

The combination of patient care and basic research as well as the close collaborations between clinical cardiologists and basic scientists provide for excellent opportunities for translational research. The departments of Anatomy, Embryology & Physiology and Experimental Cardiology have merged within one centre, providing a synergistic environment to successfully perform the research in collaborations between several specializations, including biophysics, physiological modelling and engineering. Also, a GCP compliant clinical research unit and outstanding expertise in early clinical human research with an extensive international network (academic & industrial) in the cardiovascular field and access to large cohorts with specific rare diseases, including a variety of monogenetic lipid disorders and autosomal dominant premature atherosclerosis guarantees a strong basis for future research.

Weaknesses

The fact that research efforts depend too strongly on accrual of external funding and external referrals is by definition a weakness, but seems unavoidable. Also, the lack of 'structural' supportive personnel supported by funding, leading to loss of build-up expertise is a problem. Furthermore, lack of state-of-the-art facilities within the institution with regards to specialized areas such as vascular radiology is a clear weakness. Facilities for large scale sequencing and genetic modification of mice require attention.

Opportunities

Over the last 14 years, large and well-defined databases and related bio banks of patients have been built up, that will enable the exploitation of new technologies (such as next generation sequencing) for the identification of new genes. Some of these databases (such as the ventricular fibrillation one) are a unique resource.

Basic research, involving molecular biology as well as vascular cell biology and a strong focus on (drugable) nuclear receptors, carries a strong hope for future discoveries.

Threats

The limited availability of bioinformatics and in silico protein modelling is a threat to further progress.

In general, in vascular medicine the presence of only a small team of real experts with funding opportunities in a context of increasing international competition is perceived as a threat.

Future perspectives

The research within this theme will continue to build upon the proven strengths outlined above. International efforts of innovation in health care are directed towards integrative, multi-scale approaches for personalized medical care, with rapid progress in (information) technology and computing power creating excellent opportunities for advancing the imaging and modelling aspects of our research. Development of novel drug-eluting stents based on NR4A-technology involves the implementation of rabbit and pig models in our state-of-the-art large animal facility. Other developing research areas include epigenetic regulation of heart development and arrhythmias, haemostasis, thrombosis and cancer, as well as thrombosis and coagulation in atrial fibrillation and heart failure. Furthermore, the interaction between coagulation and fibrinolysis, the role of the coagulation mechanism in bacterial invasion and novel treatment options for bleeding and thrombosis will be investigated.

The spatial complexity of the tissues and processes involved in heart development has seriously hampered studying the underlying genetic complexity as well as the molecular links between morphogenesis and function. However, 3D computer reconstruction analysis tools have been developed, which, combined with state of the art transgenesis and molecular genetic and electrophysiological analysis tools, have begun to successfully explore these areas. The institute will continue to develop and implement new tools and technology to gain insight into this complex system.

Title	Initials	Name	Department
Prof. dr. ir.	J.M.T.	de Bakker	Experimental Cardiology
Prof. dr.	E.T.	van Bavel	Biomedical Engineering and Physics
Dr.	C.R.	Bezzina	Experimental Cardiology
Prof. dr.	H.R.	Büller	Internal Medicine - Vascular Medicine
Prof. dr.	V.M.	Christoffels	Anatomy, Embryology and Physiology
Dr.	R.	Coronel	Experimental Cardiology
Prof. dr.	B.L.F.	van Eck - Smit	Nuclear Medicine
Prof. dr.	C.A.	Grimbergen	Biomedical Engineering and Physics
Prof. dr.	J.B.L.	Hoekstra	Internal Medicine
Dr.	M.J.B.	van den Hoff	Anatomy, Embryology and Physiology
Prof. dr.	M.W.	Hollmann	Anaesthesiology
Prof. dr.	C.	Ince	Biomedical Engineering and Physics
Prof. dr.	J.J.P.	Kastelein	Internal Medicine - Vascular Medicine
Dr.	R.W.	Koster	Cardiology
Prof. dr.	R.T.	Krediet	Internal Medicine - Nephrology
Dr.	J.A.	Kuivenhoven	Experimental Vascular Medicine
Prof. dr.	A.G.J.M.	van Leeuwen	Biomedical Engineering and Physics
Prof. dr.	D.A.	Legemate	Surgery
Dr.	J.J.	van Lieshout	Internal Medicine
Dr.	M.M.A.M.	Mannens	Clinical Genetics
Prof. dr.	J.C.M.	Meijers	Experimental Vascular Medicine
Prof. dr.	A.F.M.	Moorman	Anatomy, Embryology and Physiology
Prof. dr.	B.J.M.	Mulder	Cardiology
Dr.	R.	Nieuwland	Clinical Chemistry
Prof. dr.	R.J.G.	Peters	Cardiology
Dr.	S.L.M.	Peters	Pharmacology and Pharmacotherapy
Prof. dr.	J.J.	Piek	Cardiology
Prof. dr.	Y.B.W.E.M.	Pinto	Cardiology
Dr.	B.	Preckel	Anaesthesiology
Prof. dr.	J.A.	Reekers	Radiology
Dr.	Y.B.W.E.M.	Roos	Neurology
Prof. dr.	R.O.	Schlingemann	Ophthalmology
Dr.	M.	Siebes	Biomedical Engineering and Physics
Dr. ir.	G.J.	Streekstra	Biomedical Engineering and Physics
Prof. dr.	E.S.G.	Stroes	Internal Medicine - Vascular Medicine
Dr.	H.L.	Tan	Cardiology
Prof. dr.	C.J.M.	de Vries	Medical Biochemistry
Dr.	A.C.	van der Wal	Pathology
Dr.	W.	Wieling	Internal Medicine
Prof. dr.	A.A.M.	Wilde	Cardiology
Prof. dr.	R.J.	de Winter	Cardiology
Dr.	N.	Zelcer	Medical Biochemistry

Pls of the theme
Cardiovascular Diseases

GASTRO-INTESTINAL DISEASES

By: Prof. P.Fockens and Prof. R.P. Oude Elferink

The research theme Gastrointestinal and Liver Diseases encompasses all clinical and translational research from the AMC in this area. This does not only include activities from the department of Gastroenterology and Hepatology, but also important contributions from the departments of Surgery, Radiology and Paediatrics, and close collaboration exists between these departments. Laboratory research is bundled in the Tytgat Institute for Intestinal and Liver Research which was founded in 2009. One of the activities of the theme is to organize regular science and teaching seminars as well as guest lectures. Apart from that, the theme organizes a yearly PhD retreat together with members of the theme Metabolic Diseases. There is overlap between these two themes, both in terms of members and in science.

The research lines that cover the spectrum from clinical to fundamental research include:

- Intestinal immunology (including inflammatory bowel disease and neuro-gastroenterology)
- Gastro-intestinal oncology has a longstanding history on oesophageal, pancreatic and colon cancer. This research line and several of its PIs are embedded in both research themes Oncology and Gastro-Intestinal diseases. Research includes screening, imaging (endoscopy, computed tomography and MRI), endoscopic intervention and oncogenesis.
- Abdominal surgery (including diagnostic imaging, treatment of acute and chronic pancreatitis and liver ischemia/reperfusion).
- Bile formation and cholestasis (including inherited cholestasis, PBC, PSC)
- (Dys)regulation of hepatic metabolism (including NAFLD, amino acid metabolism)
- Gene therapy of inherited liver disease
- Viral hepatitis

5 key publications

1. Kremer AE, Martens JJ, Kulik W, Ruëff F, Kuiper EMM, van Buuren HR, van Erpecum KJ, Kondrackiene J, Prieto J, Rust C, Geenes VL, Williamson C, Moolenaar WH, Beuers U, Oude Elferink RPJ. Lyso-phosphatidic acid is a potential mediator of cholestatic pruritus. **Gastroenterology** 2010; 139: 108-18.
2. Schaap FG, van der Gaag NA, Gouma DJ, Jansen PL. High expression of the bile salt-homeostatic hormone fibroblast growth factor 19 in the liver of patients with extrahepatic cholestasis. **Hepatology** 2009; 49: 1228-35.
3. Curvers W, Baak L, Kiesslich R, Van Oijen A, Rabenstein T, Ragunath K, Rey JF, Scholten P, Seitz U, Ten Kate F, Fockens P, Bergman J. Chromoendoscopy and narrow-band imaging compared with high-resolution magnification endoscopy in Barrett's esophagus. **Gastroenterology** 2008; 134: 670-9.
4. Van Ruler O, Mahler CW, Boer KR, Reuland EA, Gooszen HG, Opmeer BC, de Graaf PW, Lamme B, Gerhards MF, Steller EP, van Till JW, de Borgie CJ, Gouma DJ, Reitsma JB, Boermeester MA; Dutch Peritonitis Study Group. Comparison of on-demand vs planned relaparotomy strategy in patients with severe peritonitis: a randomized trial. **JAMA: the journal of the American Medical Association** 2007; 298: 865-72.
5. De Jonge WJ, Van Der Zanden EP, The FO, Bijlsma MF, van Westerloo DJ, Bennink RJ, Berthoud HR, Uematsu S, Akira S, van den Wijngaard RM, and Boeckxstaens GE. Stimulation of the vagus nerve attenuates macrophage activation by activating the Jak2-STAT3 signaling pathway. **Nature Immunology** 2005; 6: 844-51.

Highlights

- Neuro-gastroenterology: We made several discoveries on the role of the vagal immunomodulation of the intestinal mucosa. Prestigious personal VIDI and VICI grants were acquired in this area.
- Gastrointestinal oncology: Multiple RCT's on imaging and treatment of (pre)neoplastic mucosa in oesophagus and colon are executed.
- Gene therapy of inherited liver disease: We develop gene therapy for the Crigler Najjar syndrome; phase 1 clinical trial within 2 years platform for other inherited liver diseases. This work has led to and benefited from a large NWO grant on translational gene therapy.
- Bile formation and cholestasis: Role of FGF19 in the human adaptive response to cholestasis: Our work on lysophosphatidic as a key factor in cholestatic pruritus has been awarded with five scientific prizes.
- In 2010, the Tytgat Institute for Intestinal and Liver Disease was launched. This is now the largest Dutch research institute in this field and creates a vast extension of our scientific critical mass.

SWOT

Strengths

This theme has a broad research focus which currently fits very well with the clinical profile of the AMC. Although narrowing the focus of research may lead to higher impact, it would at the same time detach a large part of the clinical activities from our research programmes. Currently the patientcare profiles seem to excellently fit the research lines. Only one third of our patient care does not fit research programmes. The scientific output of the past 5 years has been high with very regular publications in journals with impact factors > 10. The research programmes have grown through succesful grant applications with government, foundations and industry. The position of our research in the international research field is for most of our programmes within the top 25%. The broad research focus can be considered a strength and a weakness at the same time. In a busy clinical department it seems to be a strength.

Weaknesses

One of the weaknesses is the relatively small individual research units and lack of synergy between the PIs. Adding more structure to the overall programme without minimizing the feeling of freedom of our researchers, seems to be the challenge for the near future. The loss of expertise in the field of hepatic and gastrointestinal pathology is a weakness. A minor weakness is the relatively long geographical distance between clinical departments and laboratory.

Opportunities

Further integrating our patient care with clinical as well as basic research seems to be a big opportunity which could be achieved by further diminishing our unprofiled patientcare. The recent acquisition of dr. Gijs van der Brink, prof. André Smout, prof. Hans van Goudoever (pediatrics) and dr. Geert D'Haens offers excellent opportunities to further enhance the translational aspects of gastrointestinal research.

Threats

Threats for the coming years seem to be mainly financial with decreasing funds for research from all different providers. Furthermore overpopulation of the Tytgat Institute and clinical department is imminent.

Pls of the theme
Gastrointestinal
Diseases

Title	Initials	Name	Department
Prof. dr.	W.A.	Bemelman	Surgery
Dr.	M.A.	Benninga	Paediatrics - Gastroenterology
Dr.	J.J.G.H.M.	Bergman	Gastroenterology and Hepatology
Prof. dr.	U.H.W.	Beuers	Gastroenterology and Hepatology
Prof. dr.	G.E.E.	Boeckxstaens	Gastroenterology and Hepatology
Dr.	M.A.	Boermeester	Surgery
Dr.	P.J.	Bosma	Tytgat Institute
Dr.	E.	Dekker	Gastroenterology and Hepatology
Prof. dr.	P.	Fockens	Gastroenterology and Hepatology
Prof. dr.	C.A.	Grimbergen	Biomedical Engineering and Physics
Prof. dr.	T.M. van	Gulik	Experimental Surgery
Prof. dr.	P.L.M.	Jansen	Gastroenterology and Hepatology
Dr.	W.J. de	Jonge	Gastroenterology and Hepatology
Dr.	K.K.	Krishnadath	Gastroenterology and Hepatology
Prof. dr.	W.H.	Lamers	Tytgat Institute
Prof. dr.	A.G.J.M. van	Leeuwen	Biomedical Engineering and Physics
Prof. dr.	R.P.J.	Oude Elferink	Tytgat Institute
Dr.	F.G.	Schaap	Biomedical Engineering and Physics
Dr.	J.	Seppen	Tytgat Institute
Prof. dr.	J.	Stoker	Radiology
Dr.	A.A. te	Velde	Centre of Experimental and Molecular Medicine (CEMM)

INFECTION AND IMMUNITY

By: Prof. T. van der Poll and Prof. H. Schuitemaker

The research in the AMC that is captured in the theme of Infection and Immunity covers with more than 60 Principal Investigators the full spectrum from fundamental to clinical research, with a strong emphasis on multidisciplinary approaches and translational research. Research topics include the unravelling of the normal immune response, the epidemiology of infectious diseases such as tuberculosis and HIV, the immunopathology of rheumatoid arthritis, sepsis, asthma, allergy and respiratory infections.

Research within this theme is clustered in two virtual centres: the Centre for Infection and Immunity Amsterdam (CINIMA), which harbours investigators in the field of infectious diseases and the immune response during infections, and the Centre of Immunology Amsterdam (CIA), which harbours investigators studying non-infectious immunology. Each year, the research theme organizes a retreat for all participants. There are monthly lectures (Immunology Hour) with speakers from the Netherlands and abroad.

5 key publications

1. Bunnik EM, Euler Z, Welkers MR, Boeser-Nunnink BD, Grijzen ML, Prins JM, Schuitemaker H. Adaptation of HIV-1 envelope gp120 to humoral immunity at a population level. **Nature Medicine** 2010; 16: 995-7.
2. Gringhuis SI, van der Vlist M, van den Berg LM, den Dunnen J, Litjens M, Geijtenbeek TB. HIV-1 exploits innate signaling by TLR8 and DC-SIGN for productive infection of dendritic cells. **Nature Immunology** 2010; 11: 419-26.
3. Kwakkenbos MJ, Diehl SA, Yasuda E, Bakker AQ, van Geelen CM, Lukens MV, van Bleek GM, Widjoatmodjo MN, Bogers WM, Mei H, Radbruch A, Scheeren FA, Spits H, Beaumont T. Generation of stable monoclonal antibody-producing B cell receptor-positive human memory B cells by genetic programming. **Nature Medicine** 2010; 16:123-8.
van der Neut Kolfschoten M, Schuurman J, Losen M, Bleeker WK,
4. Martinez-Martinez P, Vermeulen E, den Bleker TH, Wiegman L, Vink T, Aarden LA, De Baets MH, van de Winkel JG, Aalberse RC, Parren PW. Anti-inflammatory activity of human IgG4 antibodies by dynamic Fab arm exchange. **Science** 2007; 317: 1554-7.
5. Nolte MA, Arens R, van Os R, van Oosterwijk M, Hooibrink B, van Lier RA, van Oers MH. Immune activation modulates hematopoiesis through interactions between CD27 and CD70. **Nature Immunology** 2005; 6: 412-8.

Highlights

- HIV research has a longstanding history, more specifically in the Amsterdam Cohort Studies on HIV infection and AIDS in homosexual men and injecting drug users, a collaboration between the AMC, the Amsterdam Health Services, and the Sanquin blood supply foundation that covers a multidisciplinary approach by studying the epidemiology, virology, immunology, and clinical aspects of the natural history of this infection as well as treatment and prevention. These cohort studies have resulted in more than 800 articles in peer reviewed journals and 100 PhD theses. The 25th anniversary of these cohort studies were celebrated in November 2009. Recently, the AgeHIV cohort study received funding; this new HIV cohort will investigate the long term consequences of HIV infection and therapy in the ageing population. HIV research has been boosted by the arrival of a new PI with a strong track record on HIV transmission by dendritic and Langerhans cells.

- In collaboration with the AMC theme Neurological and Psychiatric Disorders, meningitis research delivers high profile output. AMC houses the National Reference Laboratory of Bacterial Meningitis. Here all bacteria isolated from patients with confirmed bacterial meningitis are collected. This laboratory has close ties with AMC investigators with a leading role in clinical research on bacterial meningitis. Fundamental research on both the pathogen side and the host side complements this research theme, exemplifying the translational character of research.
- Respiratory tract infections represent another integrated theme covering the full spectrum from bench (including viral discovery programmes and a productive group studying the innate immune response to pneumonia) to bedside (clinical trials in various patient populations).
- The Amsterdam Institute for Global Health and Development (AIGHD) was launched in 2009. AIGHD is a joint effort of several organizations with parent institutions AMC, University of Amsterdam and the Free University. The mission of AIGHD is to provide sustainable solutions to major health problems across the world, by forging synergies between disciplines, health care delivery, research and education. The focus of the Institute is on research, education and policy advice in the context of improving health and the delivery of health care.
- AMC has strong programmes on fundamental immunological research that focus on the molecular pathways regulating the differentiation and effector functions of immune cells including macrophages, dendritic cells, T and B cells and NK cells. Next to state-of-the-art in vitro systems, a number of unique genetically modified mice have been developed that allow characterization of specific regulatory pathways in vivo.
- In the field of clinical immunology, AMC has ample expertise on primary immunodeficiencies, transplant immunology, allergy and immune-mediated inflammatory diseases. We harbour a strong experimental rheumatology group that has a long standing track record experience in phase I/II clinical trials and the pre-clinical development of novel therapies.

SWOT

Strengths

The strength of theme Infection & Immunity is the involvement of AMC researchers in strong international networks. Moreover, AMC research is highly competitive due to the two-directional strong link between clinicians and scientists and the capacity to perform high quality research covering the entire spectrum from fundamental to clinical. The research mindedness of AMC clinicians foresees in a continuous recognition on interesting clinical cases which not only allows top clinical science but, by creating a flow of patient material, also enables fundamental research. The other way around, the short distance to the clinic creates an environment in which new scientific findings can be tested for clinical application, thus resulting in an optimal environment for translational research. PIs affiliated with the theme Infection & Immunity have been very successful in obtaining prestigious funding, not only from the NWO VENI VIDI VICI programme but also from the EU FP6 and FP7 programmes, CTMM, etc.

Weaknesses

The major weakness of I&I is the fractionation of research. The theme I&I holds 61 PIs that are divided over 20 departments. For certain topics, similar types of research are being conducted by different PIs in different departments without optimal collaboration. Although the research output is impressive, with 3671 papers in the past 5 years and several papers in the highest ranking scientific journals (e.g. see key publications), the

average impact factor of all publications is not particularly high. The high production may relate to the high number of PhD theses that have been completed (320) and that require scientific articles.

Opportunities

AMC has invested in state-of-the-art facilities for high throughput sequencing which allows state-of-the-art research on several topics in the I&I theme. Moreover, the AMC funding for the multi-ethnic cohort HELIUS will boost research on the epidemiology of infectious diseases. AMC is the principal partner in a large national sepsis consortium (MARS) which will generate an unprecedented data and bio bank of > 7000 patients in the years to come; this effort will yield a wealth of research opportunities. The Landsteiner laboratory symbolizes the strong and ongoing collaboration with the Sanquin blood supply foundation.

Threats

AMC funding of research is low and possibilities for external funding of fundamental research are limited, especially for established researchers. This situation is a severe threat for the performance of state-of-the-art research on genomics, proteomics, etc. which is extremely expensive.

Future perspectives

The use of high throughput sequencing will boost research on immunological repertoire studies in different infections and autoimmune diseases. It will also be applied in pathogen discovery. Novel immune-based therapies will be explored in the treatment of rheumatoid arthritis, allergy and cancer. AMC will be leading in research on aging, specifically in accelerated (immunological) aging associated with viral infections such as HIV, and associated with immune suppression for organ transplantation. Strong links with African institutions allow excellent research on the prevention and clinical management of infectious diseases, with strong spin-off for fundamental research in the AMC. This will be boosted by the launch of the Amsterdam Institute for Global Health and Development (AIGHD) which is headed by an AMC professor/PI.

Prof. Van Lier and Prof. Schuitemaker were in charge of the Laboratory of Experimental Immunology until September 2010. The departure of both at the same time is a major threat for immunology research at the AMC. Considerations in designing the AMC research strategy in immunological research are:

- Clinical immunology research other than in the sub fields of rheumatoid arthritis, transplantation and paediatrics is largely lacking. This is surprising for an UMC in which Infection and Immunity is a major research theme.
- With the departure of Prof. Schuitemaker, the continuity of the historically strong and highly visible HIV research is endangered. New research leads emerge from research on the interface of HIV and ageing and this is important for the visibility of the AMC in the growing field of ageing research.

Considering the importance of a strong immunological laboratory and the excellent track record of the Laboratory of Experimental Immunology until now, the appointment of a new department head who can oversee, initiate and facilitate fundamental and translational research in immunology is mandatory. In addition, the scientific gap in research on the immunology of HIV infection that came into existence after the departure of Prof. Schuitemaker should be filled in order to guarantee existing valuable links between clinic and laboratory and to continue high level translational research in HIV.

Title	Initials		Name	Department
Prof. dr.	W.M.C.	van	Aalderen	Paediatrics
Dr.	D.		Amsen	Cell Biology and Histology
Dr.	D.L.P.		Baeten	Internal Medicine - Immunology/ Rheumatology
Prof. dr.	R.J.M.	ten	Berge	Internal Medicine - Nephrology
Prof. dr.	B.		Berkhout	Medical Microbiology
Dr.	B.		Blom	Cell Biology and Histology
Dr.	M.A.		Boermeester	Surgery
Prof. dr.	M.W.		Borgdorff	Clinical Epidemiology, Biostatistics and Bioinformatics (KEBB)
Prof. dr.	J.D.		Bos	Dermatology
Dr.	F.G.J.		Cobelens	Internal Medicine - Infec./Trop./Aids
Dr.	A.T.		Das	Medical Microbiology
Dr.	B.		Distel	Medical Biochemistry
Dr.	C.M.	van	Drunen	ENT
Dr.	E.F.		Eldering	Experimental Immunology
Dr.	A.	van der	Ende	Medical Microbiology
Prof. dr.	S.		Florquin	Pathology
Prof. dr.	W.J.		Fokkens	ENT
Prof. dr.	T.B.H.		Geijtenbeek	Centre of Experimental and Molecular Medicine (CEMM)
Dr.	S.I		Gringhuis	Centre of Experimental and Molecular Medicine (CEMM)
Dr.	J.		Hamann	Experimental Immunology
Dr.	C.M.	van der	Hoek	Medical Biochemistry
Dr.	E.C.	de	Jong	Cell Biology and Histology
Prof. dr.	M.L.		Kapsenberg	Cell Biology and Histology
Dr.	N.A.		Kootstra	Experimental Immunology
Prof. dr.	T.W.		Kuijpers	Paediatrics
Prof. dr.	J.M.A.		Lange	Internal Medicine - Infec./Trop./Aids
Dr.	J.C.		Leemans	Pathology
Prof. dr.	R.A.W.	van	Lier	Experimental Immunology
Dr.	R.M.		Luiten	Dermatology
Dr.	V.V.		Lukashov	Medical Microbiology
Dr.	R.		Lutter	Pulmonology
Prof. dr.	J.P.		Medema	Radiotherapy and CEMM
Prof. dr.	M.P.		Mourits	Ophthalmology
Prof. dr.	C.J.M.	van	Noesel	Pathology
Prof. dr.	F.		Nollet	Rehabilitation
Dr.	M.A.		Nolte	Experimental Immunology

Prof. dr.	M.H.J.	van	Oers	Internal Medicine - Clinical Haematology
Prof. dr.	S.T.		Pals	Pathology
Dr.	W.A.		Paxton	Medical Microbiology
Prof. dr.	T.	van der	Poll	Centre of Experimental and Molecular Medicine (CEMM)
Dr.	J.M.		Prins	Internal Medicine - Infec./Trop./Aids
Dr.	M.		Prins	Internal Medicine - Infec./Trop./Aids
Prof. dr.	R.	van	Ree	Experimental Immunology
Dr.	K.		Reedquist	Experimental Immunology
Prof. dr.	P.		Reiss	Internal Medicine - Infec./Trop./Aids
Dr.	G.	ter	Riet	General Practice/Family Medicine
Prof.dr.	M.J.		Schultz	Intensive Care Medicine
Prof. dr.	H.		Schuitemaker	Experimental Immunology
Dr.	M.		Spaargaren	Pathology
Prof. dr.	P.		Speelman	Internal Medicine - Infec./Trop./Aids
Dr.	C.A.		Spek	Centre of Experimental and Molecular Medicine (CEMM)
Dr.	P.H.I.		Spuls	Dermatology
Prof. dr.	J.P		Sterk	Pulmonology
Prof. dr.	P.P.		Tak	Internal Medicine - Immunology/ Rheumatology
Dr.	J.H.H.M.	van de	Wijgert	Internal Medicine- Infec./Trop./Aids
Dr.	A.B.	van 't	Wout	Experimental Immunology
Dr.	S.A.J.		Zaat	Medical Microbiology

PIs of the theme
Infection and Immunity

METABOLIC DISORDERS

By: Prof. J. Aerts and Prof. F.Wijburg

Metabolism and disease is a long-standing topic of interest of the AMC. Several clinical and fundamental researchers from different departments cover pre-clinical and clinical aspects of this research field and participate in the research theme Amsterdam Centre for Metabolism. The core topics of investigation are:

- Selected genetic metabolic disorders, with a strong emphasis on lysosomal and peroxisomal diseases as well as disorders involving fatty acid oxidation;
- Diabetes mellitus and the metabolic syndrome;
- Neural control of metabolism;
- Glycosphingolipid metabolism as key pathway in the pathophysiology of several conditions listed above.

Using a multidisciplinary approach, researchers in the Amsterdam Centre for Metabolism have been successful in the unravelling of genetic and biochemical causes of several inherited and acquired metabolic disorders. Besides offering improved diagnosis, the research has contributed to the development and application of novel therapeutic approaches. Clinical investigators in the Amsterdam Centre for Metabolism have been involved in pivotal clinical drug trials for metabolic disorders.

Research on metabolism intrinsically transcends specific organ systems, and close interactions therefore exist between research lines housed in Amsterdam Centre for Metabolism and those in other AMC research themes. A systems biology approach has recently been initiated to increase insight in the underlying molecular causes of the metabolic syndrome, a complex disorder involving different organs.

The theme organizes a yearly PhD retreat together with members of the theme Gastro-intestinal diseases.

5 key publications

1. Alders M, Hogan BM, Gjini E, Salehi F, Al-Gazali L, Hennekam EA, Holmberg EE, Mannens MMAM, Mulder MF, Offerhaus GJA, Prescott TE, Schroor EJ, Verheij JBG, Witte M, Zwijnenburg PJ, Vikkula M, Schulte-Merker S, Hennekam RC. Mutations in *CCBE1* cause generalized lymph vessel dysplasia in humans. **Nature Genetics** 2009; 41(12): 1272-4.
2. Klieverik LP, Janssen SF, van Riel A, Foppen E, Bisschop PH, Serlie MJ, Boelen A, Ackermans MT, Sauerwein HP, Fliers E, Kalsbeek A. Thyroid hormone modulates glucose production via a sympathetic pathway from the hypothalamic paraventricular nucleus to the liver. **Proceedings of the National Academy of Sciences of the United States of America** 2009; 106(14): 5966-71.
3. Aerts JM, Groener JE, Kuiper S, Donker-Koopman WE, Strijland A, Ottenhoff R, van Roomen C, Mirzaian M, Wijburg FA, Linthorst GE, Vedder AC, Rombach SM, Cox-Brinkman J, Somerharju P, Boot RG, Hollak CE, Brady RO, Poorthuis BJ. Elevated globotriaosylsphingosine is a hallmark of Fabry disease. **Proceedings of the National Academy of Sciences of the United States of America** 2008; 105(8): 2812-7.
4. Waterham HR, Koster J, van Roermund CWT, Mooyer PAW, Wanders RJA, Leonard JV. A lethal defect of mitochondrial and peroxisomal fission. **The New England journal of medicine** 2007; 356(17): 1736-41.
5. Van Maldegeem BT, Duran M, Wanders RJ, Niezen-Koning KE, Hogeveen M, IJlst L, Waterham HR, Wijburg FA. Clinical, biochemical, and genetic heterogeneity in short-chain acyl-coenzyme A dehydrogenase deficiency. **JAMA: the journal of the American Medical Association** 2006; 296(8): 943-52.

Highlights

The theme Metabolic Disorders has witnessed several highlights in the previous years. Some examples are:

- SPHINX, the centre for lysosomal storage disorders (LSDs) in the AMC, harbours a unique concept of multidisciplinary research on LSDs within the broader context of glycosphingolipid biology. Already designated as national centre for evaluation and treatment of LSDs, the innovative translational research in SPHINX involves participation in international clinical trials with new therapeutic agents (small compounds, plant-produced recombinant enzymes) and application of new treatment modalities (bone marrow transplantation, chaperone therapy). The launch of SPHINX in combination with ongoing bio-banking, discovery of biomarkers, identification of potential therapeutic agents, and solid documentation of natural history of LSDs and assessment of optimal use of costly enzyme replacement therapies for these disorders secures the (inter) national leading position.
- Fundamental research on sphingolipids, an element of SPHINX, has also offered new insights in the aetiology of insulin resistance, a major component of the metabolic syndrome. Manipulation of sphingolipid metabolism in appropriate animal models with so-called iminosugars indicates that this approach offers a new therapeutic avenue for prevention/treatment of several aspects of metabolic syndrome.
- The demonstration of the importance of the hypothalamus in the regulation body metabolism has led to a unique translational research line on neural control of metabolism. Using a combination of human/patient studies, the role of the brain and the autonomic nervous system in the pathogenesis of metabolic derangements in schizophrenia, obesity, shift work, and critical illness are studied.
- Strict glucose management has been a major research topic in the Amsterdam Centre for Metabolism. The rapid technical developments in the field of glucose sensors and insulin delivery systems will soon result in an artificial pancreas fit for use at least in an in-hospital setting. In 2009, the AMC received a large FP7 grant for developing an artificial pancreas with a European research network.
- Investigators in the research theme contributed to the development of a complete and validated set of new enzymatic tests allowing rapid discrimination between true and false positives in patients screened 'positive' in the expanded newborn screening programmes (expanded since 2007).
- The work of several researchers in the research theme led to the elucidation of the genetic and mechanistic basis of a number of genetic (metabolic) disorders, for example in the fields of peroxisomal and lysosomal disorders, and generalized lymph vessel dysplasia. These fundamental investigations are a crucial stepping stone for the design of therapeutic interventions and subsequent translational research, as is nicely illustrated by the work on X-ALD.

SWOT

Strengths

The major strength of the theme Metabolic Disorders is the long-standing existence of strong interactions between basic research and the clinic. In the case of selected inherited metabolic disorders the AMC already harbours unique patient cohorts (materials, clinical records) which allow innovative translational research and clinical studies, as is for example nicely illustrated by the lysosomal sphingolipidoses. Technology platforms exist in the AMC for analyses at the level of the genome, transcriptome, proteome and metabolome. Fundamental and translational research is conducted using generated animal and cell models (including yeast). Excellent facilities exist for state-of-the-art metabolic

investigations in humans and animals as well as for clinical trials. Research efforts in the ACM have become increasingly coherent over the last years: close collaborations exist between the Laboratory for Genetic Metabolic Diseases, the AMC Liver Centre, and the departments of Endocrinology and Metabolism, Paediatrics, Clinical Genetics and Medical Biochemistry.

Weaknesses

The research on metabolism is in danger to become scattered. Partly this is caused by the rapidly expanding number of disease conditions that prove to be caused by a metabolic derangement. Especially in the field of metabolism, close interaction between various research lines in the AMC (within and beyond the Amsterdam Centre for Metabolism) is vital for optimal exploitation of joint expertise and technology platforms available in the institute.

The increasing possibilities offered by genetic analyses, in combination with the available collections of materials from individuals suffering from metabolic abnormalities, are not (yet) optimally exploited in the AMC. Attention should also be paid to the introduction of new technologies in this respect. For example, novel methods such as exome sequencing and transformation of fibroblasts to stem cell-like cells are likely to offer new tools for better insight in the causes of heterogeneous disease manifestation among individuals with a similar primary genetic defect.

Opportunities

In essence, the AMC is well prepared for top-quality research on metabolism. In some well defined areas unique patient cohorts and expertise already exist and the institute houses various relevant clinical facilities and laboratory technology platforms, albeit very fragmented throughout the building. This creates interest of industrial and governmental parties to collaborate with the AMC. For example, SPHINX increasingly participates in protocol development and multinational studies to evaluate novel treatments. The tight interaction between fundamental and clinical research allows development of new pathophysiological concepts as well as valuable surrogate markers which are crucial for a better assessment of the impact of costly treatments.

For rare genetic disorders, the formation of expert centres at the European level is presently strongly stimulated. In this respect, the AMC is positioned well for some (lysosomal and peroxisomal) disorders and should attempt to consolidate this.

The research lines on neural control of metabolism and the role of glycosphingolipid metabolism in the metabolic syndrome, in combination with the initiated systems biology approach, offer opportunities for high impact investigations. Given the ethnic diversity of the AMC patient population, this offers an excellent opportunity to study the impact of genetic background in the manifestations of metabolic disorders.

Threats

Metabolic abnormalities are rarely limited to a single organ system. Understanding of pathophysiology, as well as development of interventions, requires detailed insight at the level of the genome, transcriptome, proteome and metabolome in various organs. As a consequence, research on metabolism has become increasingly complex and requires a true multidisciplinary approach. Particularly, the integration and modelling of complex (clinical and laboratory) data sets forms a major challenge.

A clear focus on specific areas of metabolic research and a better integration of novel human genetics technologies will be needed to remain (inter)nationally competitive.

Future perspectives

The interest in metabolism in relation to disease will markedly expand given the increasing incidence of the metabolic syndrome and the rapidly growing number of inherited conditions with a metabolic nature. A clear focus, a multidisciplinary approach and state-of-the-art clinical and laboratory facilities will be essential for the AMC to perform high-impact translational research. The past performance regarding some genetic disorders demonstrates that this is feasible in specific areas.

A particular challenge for future research will be formed by complex multi-organ disease conditions such as the metabolic syndrome. A close interaction of researchers in the Amsterdam Centre for Metabolism with those in other research themes of the AMC studying aspects of the metabolic syndrome (Cardiovascular Diseases, Epidemiology and Public Health, Gastrointestinal Diseases) will be essential for future success.

Title	Initials	Name	Department
Prof. dr.	J.M.F.G.	Aerts	Medical Biochemistry
Dr.	R.G.	Boot	Medical Biochemistry
Dr.	P.J.	Bosma	Tytgat Institute
Dr.	B.	Distel	Medical Biochemistry
Dr.	S.E.J.A.	La Fleur	Internal Medicine - Endocrinology
Prof. dr.	E.	Fliers	Internal Medicine - Endocrinology
Dr.	F.M.H.	Hochstenbach	Medical Biochemistry
Prof. dr.	J.B.L.	Hoekstra	Internal Medicine - Endocrinology
Prof. dr.	C.E.M.	Hollak	Internal Medicine - Clinical Haematology
Dr.	S.M.	Houten	Genetic Metabolic Diseases
Prof. dr.	P.L.M.	Jansen	Gastroenterology and Hepatology
Dr.	A.	Kalsbeek	Internal Medicine - Endocrinology
Prof. dr.	J.J.P.	Kastelein	Internal Medicine - Vascular Medicine
Dr.	S.	Kemp	Genetic and Metabolic Diseases
Dr.	A.B.P.	van Kuilenburg	Genetic and Metabolic Diseases
Prof. dr.	W.H.	Lamers	Tytgat Institute
Dr.	M.M.A.M.	Mannens	Clinical Genetics
Prof. dr.	F.	Nollet	Rehabilitation
Prof. dr.	R.P.J.	Oude Elferink	Tytgat Institute
Dr.	F.G.	Schaap	Tytgat Institute
Prof. dr.	R.O.	Schlingemann	Ophthalmology
Dr.	J.	Seppen	Tytgat Institute
Prof. dr.	E.S.G.	Stroes	Internal Medicine - Vascular Medicine
Prof. dr.	A.	Verhoeven	Medical Biochemistry
Dr.	J.H.	de Vries	Internal Medicine
Prof. dr.	R.J.A.	Wanders	Genetic and Metabolic Diseases
Dr.	H.R.	Waterham	Genetic and Metabolic Diseases
Prof. dr.	F.A.	Wijburg	Paediatrics - Metabolic Diseases
Dr.	N.	Zelcer	Medical Biochemistry

PIs of the theme
Metabolic Disorders

NEUROLOGICAL AND PSYCHIATRIC DISORDERS

By: Prof. F. Baas, Prof. W.A. van Gool and Prof. W. van den Brink

The theme Neurological and Psychiatric Disorders includes a broad range of clinical and translational research in the field of neurology, psychiatry, neuroimaging and genetics. The pathogenesis, diagnostic procedures, treatment and opportunities for prevention of the following conditions are being investigated: addiction, cerebrovascular disease, delirium, dementia, depression, inflammatory and hereditary neuropathies, meningitis (in collaboration with the AMC theme Infection and Immunity), movement disorders, motor neuron disease, obsessive compulsive disorders, posttraumatic stress disorder, and schizophrenia. To enable this, a variety of techniques and designs are used ranging from genome wide analysis through neuroimaging to randomized clinical trials. Collaboration is stimulated between principle investigators originally addressing different clinical problems by exploring common ground between subjects, e.g. the vascular component of dementia, the role of deep brain stimulation in the treatment of movement and psychiatric disorders, neuropsychiatric symptoms in movement disorders and motor neuron disease, and the role of inflammation in depression, obsessive compulsive disorders, delirium and neurodegeneration.

5 key publications

1. Budde BS, Namavar Y, Barth PG, Poll-The BT, Nürnberg G, Becker C, van Ruissen F, Weterman MA, Fluiters K, te Beek ET, Aronica E, van der Knaap MS, Höhne W, Toliat MR, Crow YJ, Steinling M, Voit T, Roelenso F, Brussel W, Brockmann K, Kyllerman M, Boltshauser E, Hammersen G, Willemsen M, Basel-Vanagaite L, Krägeloh-Mann I, de Vries LS, Sztriha L, Muntoni F, Ferrie CD, Battini R, Hennekam RC, Grillo E, Beemer FA, Stoets LM, Wollnik B, Nürnberg P, Baas F. tRNA splicing endonuclease mutations cause pontocerebellar hypoplasia. **Nature Genetics** 2008; 40: 1113-8.
2. De Win MM, Jager G, Booij J, Reneman L, Schilt T, Lavini C, Olabarriaga SD, den Heeten GJ, van den Brink W. Sustained effects of ecstasy on the human brain: a prospective neuroimaging study in novel users. **Brain** 2008; 131: 2936-45.
3. Denys D, Mantione M, Figeo M, van den Munckhof P, Koerselman F, Westenberg H, Bosch A, Schuurman R. Deep brain stimulation of the nucleus accumbens for treatment-refractory obsessive-compulsive disorder. **Archives of general psychiatry**. 2010 Oct;67(10):1061-8.
4. Van de Beek D, Drake JM, Tunkel AR. Nosocomial bacterial meningitis. **The New England journal of medicine** 2010; 362: 146-54.
5. Witlox J, Eurelings LSM, de Jonghe JFM, Eikelenboom P, Kalisvaart KJ, Van Gool WA. Delirium in Elderly Patients and the Risk of Postdischarge Mortality, Institutionalization, and Dementia: A Meta-analysis. **JAMA: the journal of the American Medical Association** 2010; 304: 443-51.

Highlights

- The identification of the genetic basis of neurological disorders by implementation of next generation sequencing is expected to yield more insight in common and rare disorders.
- We lead a prospective and nationwide study to determine the clinical features and prognostic factors in adults with community-acquired acute bacterial meningitis.
- Valuable data are generated in an ongoing study including 3534 participants on the role of vascular care in the prevention of dementia.

- Our group plays a leading role in studies of deep brain stimulation, both in movement disorders and psychiatric diseases such as obsessive compulsive disorder, depression, eating disorders and addiction.
- We have a strong position in research on the aetiology of substance use disorders, treatment of heroin dependent patients, neuroadaptational and neurotoxic processes following the use of addictive and other psychoactive substances and the prediction of relapse.
- Research on the role of inflammation in nerve degeneration has resulted in new insights in regeneration. Two patent applications were filed and Regenesance BV, an AMC spin off focused on nerve regeneration was incorporated in 2009.

SWOT

Strengths

- This research theme covers the entire spectrum from basic preclinical research, through strategic neuroimaging research to clinical research.
- In all fields research groups perform at a competitive level. This is exemplified by two recently awarded prestigious NWO TOP grants: one to M. Olff (Psychiatry) and one to W.A. van Gool (Neurology).
- Research in the fields of neurogenetics, addiction, and clinical neurology (infections, neurodegenerative disease and vascular neurology) have a particularly strong output, they rank in the top of the Netherlands and in Europe.
- The infrastructure for high quality translational research is in place.

Weaknesses

- There is no unifying focus of research among the research lines in this theme.
- There is no steering at the level of the research theme Neurological and Psychiatric Disorders.
- Some research teams are spread too thin, sometimes hardly exceeding a critical threshold with respect to funding and manpower.

Opportunities

- Research in the field of cognitive science is one of the top priorities in medical research in the Netherlands and a top priority of the University of Amsterdam (UvA).
- The UvA Cognitive Science Centre Amsterdam offers opportunities for multidisciplinary research with other UvA faculties.
- The proximity of the Netherland Institute of Neuroscience and collaboration in the newly founded Spinoza Centre for Neuroimaging offer new opportunities.
- Increasing focus within the theme Neurological and Psychiatric Disorders will lead to a top translational research group.

Threats

- Lack of focus, cohesion and steering pose a threat for this theme.
- Within the fields of genetics and imaging the pitfall of 'method-driven' rather than 'hypothesis-driven' research should be averted. The proven, strong and successful other methods used in Neurological and Psychiatric Disorders research (genetics, molecular biology, neuropathology, neuropsychology, clinical epidemiology) should be preserved.
- With collaborations outside the medical faculty, clinical research directly addressing burning clinical questions, directly relevant to patient care, should be preserved.
- No specific funding organisations are as yet active in the field of neurological and psychiatric disorders.

Future perspectives

We plan to build upon our major achievements in recent years and will focus upon the major research lines. Therefore, we will expand our seminal work on the identification of the genetic basis of neurological disorders to more common neurological and psychiatric disorders. In collaboration with the AMC theme Infection and Immunity, the research line on meningitis will be further developed and is expected to secure a leading role in bacterial meningitis research. Responding to major policy concerns, the research on the prevention of dementia is evolving towards a European Dementia Prevention Initiative. The successful neuroimaging work on the early detection and diagnosis of Parkinson's disease will be continued. The research into deep brain stimulation will be extended by both clinically oriented neuroimaging research as well as experimental pre-clinical approaches using a variety of methods (neurophysiology; micro dialysis and animal behaviour studies). Last but not least, our unique and well-built position in the field of addiction research will be further extended.

Title	Initials	Name	Department
Dr.	E.M.A.	Aronica	Pathology
Prof. dr.	F.	Baas	Genome Analysis
Dr.	J.A.J.M.	Beelen	Rehabilitation
Prof. dr.	J.	Booij	Nuclear Medicine
Prof. dr.	W.	van den Brink	Psychiatry
Prof. dr.	P.	Eikelenboom	Neurology
Prof. dr.	E.	Fliers	Internal Medicine - Endocrinology
Prof. dr.	W.A.	van Gool	Neurology
Prof. dr.	C.A.	Grimbergen	Biomedical Engineering and Physics
Dr.	L.	de Haan	Psychiatry
Dr.	T.J.M.	Hulsebos	Genome Analysis
Dr.	S	Kemp	Genetic and Metabolic Diseases
Dr.	M.A.J.	de Koning - Tijssen	Neurology
Dr.	C.B.L.M.	Majoie	Radiology
Prof. dr.	F.	Nollet	Rehabilitation
Dr.	M.	Oloff	Psychiatry
Prof. dr.	B.T.	Poll - The	Paediatrics - Neurology
Dr.	E.A.J.	Reits	Cell Biology and Histology
Dr.	L.	Reneman	Radiology
Dr.	Y.B.W.E.M.	Roos	Neurology
Prof. dr.	A.H.	Schene	Psychiatry
Dr.	W.	Scheper	Genome Analysis
Prof.dr.	R.O.	Schlingemann	Ophthalmology
Prof. dr.	B.A.	Schmand	Neurology
Prof. dr.	J.	Stam	Neurology
Prof. dr.	D.	Troost	Pathology

Pls of the theme
Neurological and
Psychiatric Disorders

ONCOLOGY

By: Prof. H. Caron and Prof. J.P. Medema

Oncology research in the AMC is a typical example of a multidisciplinary approach ranging from fundamental to clinical research, distributed over numerous different departments. Especially in the areas of Gastro-intestinal-, Paediatric- and Haemato-oncology the AMC hosts a spectrum of groups that cover the pre-clinical and clinical areas of research.

Gastro-intestinal oncology has a longstanding history on oesophageal, pancreatic and colon cancer. This research line and several of its PIs are embedded in both research themes Oncology and Gastro-Intestinal diseases. Studies on early detection are combined with excellent clinical trials on novel therapeutic approaches and are linked to several strong fundamental research teams.

Paediatric oncology covers an even broader area focussing specifically on neuroblastoma and medulloblastoma. Basic research is closely linked to clinical trials as well as long term follow up of cancer patients to optimize treatment and minimize side effects.

Haemato-oncology is historically very strong in the area of B cell malignancies. Novel therapies and therapeutic approaches are developed in excellent laboratory settings and combined with clinical trials on specific patient populations.

Besides these three core fundamental-clinical research lines, several smaller research lines focus on the development of new therapies in gynaecological and urological oncology, the optimization of radio therapeutic, immunotherapeutic and hyperthermia treatments as well as on the psychosocial aspects of oncology. Combined, these research lines form a highly active research field organized within the Oncological Research Centre AMC (ORCA). The research theme organizes biweekly OASIS lectures and a yearly ORCA retreat.

5 key publications

These give an overview of the focus areas and types of research within ORCA:

1. Van der Gaag NA, Rauws EA, van Eijck CH, Bruno MJ, van der Harst E, Kubben FJ, Gerritsen JJ, Greve JW, Gerhards MF, de Hingh IH, Klinkenbijnl JH, Nio CY, de Castro SM, Busch OR, van Gulik TM, Bossuyt PM, Gouma DJ. Preoperative biliary drainage for cancer of the head of the pancreas. **The New England journal of medicine** 2010; 362(2):129-37.
2. Van Oers MH, Klasa R, Marcus RE, Wolf M, Kimby E, Gascoyne RD, Jack A, Van't Veer M, Vranovsky A, Holte H, van Glabbeke M, Teodorovic I, Rozewicz C, Hagenbeek A. Rituximab maintenance improves clinical outcome of relapsed/resistant follicular non-Hodgkin lymphoma in patients both with and without rituximab during induction: results of a prospective randomized phase 3 intergroup trial. **Blood** 2006; 108(10):3295-301.
3. Molenaar JJ, Ebus ME, Geerts D, Koster J, Lamers F, Valentijn LJ, Westerhout EM, Versteeg R, Caron HN. Inactivation of CDK2 is synthetically lethal to MYCN over-expressing cancer cells. **Proceedings of the National Academy of Science USA** 2009; 106(31):12968-73.
4. De Gorter DJ, Beuling EA, Kersseboom R, Middendorp S, van Gils JM, Hendriks RW, Pals ST, Spaargaren M. Bruton's tyrosine kinase and phospholipase Cgamma2 mediate chemokine-controlled B cell migration and homing. **Immunity** 2007; 26(1):93-104.
5. Vermeulen L, De Sousa E Melo F, van der Heijden M, Cameron K, de Jong JH, Borovski T, Tuynman JB, Todaro M, Merz C, Rodermond H, Sprick MR, Kemper K, Richel DJ, Stassi G, Medema JP. Wnt activity defines colon cancer stem cells and is regulated by the microenvironment. **Nature Cell Biology** 2010; 12(5):468-76.

Highlights

The Oncological Research Centre AMC has seen several highlights in the previous years, which will clearly boost the research in the different areas.

- The start of the Gastro-Intestinal Oncology Centre Amsterdam GIOCA within the AMC forms a clear highlight. GIOCA was started as a major multidisciplinary effort and is indeed embedded in both research themes Gastro-Intestinal diseases and Oncology with the intention to streamline the treatment of patients. Combined with the early detection and hereditary programme on colorectal cancer this has resulted in an enormous potential for clinical patient research and pre-clinical research on primary cancer samples. This will undoubtedly lead to an even stronger positioning of GI-oncology within the AMC.
- In the field of Paediatric Oncology the multidisciplinary 'Late Effects' research team in the EKZ AMC has established an international leading position by putting together a unique, very complete, single centre cohort of >2000 childhood cancer survivors with active medical follow-up. The EKZ 'Late Effects' team also established national Dutch guidelines for uniform, risk-based follow-up of childhood cancer survivors and leads the DCOG LATER research group, aimed at the entire national cohort of >7000 childhood cancer survivors.
- The collaboration between the departments of Haematology, Experimental Immunology and Pathology has been intensified over the last years to address the selective therapy resistance of chronic lymphocytic leukaemia and multiple myeloma. Basic research into resistance combined with patient material and large clinical trials will provide a solid platform for the development of novel therapies. The start of a Multiple Myeloma Centre, combined with in vivo animal imaging, highlights this development and will further formalize this development.

SWOT

Strength

The clear strength of the Oncological Research Centre AMC is the existence of solid lines between basic research and clinical development. In the three main research areas (GI, Paediatric and Haemato-Oncology) these lines have been secured over the years and form a powerful setting to translate basic findings into clinical research.

Weakness

A major weakness within ORCA is the fragmentation of research. ORCA holds 30 PIs divided over 16 departments and a similar fragmentation in its laboratory efforts. In addition, several research lines are relatively poorly integrated within ORCA. The PIs united in ORCA have produced more than 1000 publications over the last five years, showing that it is an active research area. Although the average impact is 5.4, the number of very high impact publications (>15) only sums up to 41. The research area should therefore aim for more high impact and maybe less quantity publications.

Opportunities

The large number of clinical initiatives (centralization, screening, specific clinics) provide enormous potential for both clinical trials as well as fundamental and translational research. If ORCA would manage to centralize research efforts, or at minimum coordinate research efforts at different departments, the conditions at the AMC would be excellent for top research in the three key areas.

Threats

The foreseen national concentration of oncology clinics in specific areas, such as currently for Paediatric Oncology, holds a clear threat for the future. Depending on the location

of such a concentration, this could prevent or boost further development of research. The position of fundamental oncology research in such a concentration effort is clearly a concern. Another, more internal threat is the fragmentation of research, which clearly complicates interactions between research groups and rather induces department-oriented initiatives. Finally, a large fraction of the research strongly depends on intensive animal experimentation. Limitations in space and finance form a clear threat to this type of research and jeopardize international competitiveness.

Future perspectives

The aging society makes oncology currently the leading cause of death in the Netherlands and thus an increasing health issue. An increasing burden on health care by this disease will likely result in centralization of clinics. The effect of this on research is hard to predict, but will likely also induce more disease focused research areas. The potential of bio banking will make such concentrations interesting from a research point-of-view, but will need to be organized stringently.

Title	Initials	Name	Department
Dr.	J.A.	Aten	Cell Biology and Histology
Prof. dr.	H.N.	Caron	Paediatrics - Oncology
Dr.	H.	Crezee	Radiotherapy
Dr.	E.	Dekker	Gastroenterology and Hepatology
Dr.	E.F.	Eldering	Experimental Immunology
Dr.	N.A.P.	Franken	Radiotherapy
Dr.	H.A.M.	Geerts	Human Genetics
Dr.	M.A.	Grootenhuis	Paediatrics
Dr.	A.	Hagenbeek	Internal Medicine - Clinical Haematology
Dr.	T.J.M.	Hulsebos	Genome Analysis
Prof. dr.	G.G.	Kenter	Obstetrics and Gynaecology
Prof. dr.	C.C.E.	Koning	Radiotherapy
Dr.	M.	Kool	Human Genetics
Dr.	K.K.	Krishnadath	Gastroenterology and Hepatology
Prof. dr.	A.G.J.M.	van Leeuwen	Biomedical Engineering and Physics
Dr.	R.M.	Luiten	Dermatology
Prof. dr.	J.P.	Medema	Radiotherapy and CEMM
Prof. dr.	C.J.M.	van Noesel	Pathology
Prof. dr.	M.H.J.	van Oers	Internal Medicine - Clinical Haematology
Prof. dr.	S.T.	Pals	Pathology
Prof. dr.	D.J.	Richel	Internal Medicine – Oncology
Prof. dr.	J.J.M.C.H.	de la Rosette	Urology
Dr.	M.	Spaargaren	Pathology
Dr.	C.A.	Spek	Centre of Experimental and Molecular Medicine (CEMM)
Dr.	L.J.A.	Stalpers	Radiotherapy
Dr. ir.	G.J.	Streekstra	Biomedical Engineering and Physics
Prof. dr.	R.	Versteeg	Human Genetics
Prof. dr.	M.J.	van de Vijver	Pathology
Dr. ir.	H.	Wijkstra	Urology

Pls of the theme
Oncology

PUBLIC HEALTH AND EPIDEMIOLOGY

By: Prof. P. Bossuyt and Prof. K. Stronks

The research theme Public Health and Epidemiology aims to study disease distribution and the determinants of health and disease risk in human populations, to develop the means for prevention and control in populations, and to study quantitative methods and techniques. The programme does so through an interdisciplinary study of (1) determinants of health, wellbeing and disease in the general and the occupational population, and the effectiveness of measures to promote population health, and (2) the effectiveness of (the organisation of) health care and its impact on population health. In addition (3) quantitative research methods are a subject of research in themselves. Apart from empirical research, also ethical practice issues are addressed.

The ultimate aim of the research within this theme is to contribute to the evidence-base of public and occupational health, primary health care, the organisation of health care, and preclinical and clinical research methods.

The research theme Public Health and Epidemiology encompasses a large and diverse programme of research led by approximately 20 Principal Investigators. Researchers in this theme come from different scientific backgrounds including epidemiology and public health, biostatistics, general practice, occupational/social medicine, psychology, sociology, demography and psychiatry.

5 key publications

1. Agymang C, Kunst A, Bhopal R, Zaninotto P, Unwin N, Nazroo J, Nicolaou M, Redekop WK, Stronks K. A cross-national comparative study of blood pressure and hypertension between English and Dutch South-Asian- and African-origin populations: the role of national context. **American Journal of Hypertension** 2010; 23(6):639-48.
2. Sprangers MA, Sloan JA, Barsevick A, Chauhan C, Dueck AC, Raat H, Shi Q, Van Noorden CJ; GENEQOL Consortium. Scientific imperatives, clinical implications, and theoretical underpinnings for the investigation of the relationship between genetic variables and patient-reported quality-of-life outcomes. **Quality of Life Research** 2010; 19(10):1395-403.
3. Painter RC, Osmond C, Gluckman P, Hanson M, Phillips DI, Roseboom TJ. Transgenerational effects of prenatal exposure to the Dutch famine on neonatal adiposity and health in later life. **British Journal Obstetrics and Gynaecology** 2008; 115(10):1243-9.
4. Leeflang MM, Deeks JJ, Gatsonis C, Bossuyt PM; Cochrane Diagnostic Test Accuracy Working Group. Systematic reviews of diagnostic test accuracy. **Annals of Internal Medicine** 2008; 149(12):889-97.
5. van Dijk PC, Zwinderman AH, Dekker FW, Schön S, Stel VS, Finne P, Jager KJ. Effect of general population mortality on the north-south mortality gradient in patients on replacement therapy in Europe. **Kidney International** 2007; 71(1):53-9.

Highlights

- Although Western societies are becoming increasingly ethnically diverse, ethnic minority populations are usually excluded in health and health care studies. Observed differences between ethnic groups in health have led to a growing awareness of the need to initiate health (care) studies among ethnic minorities as well, particularly longitudinal cohort studies. Therefore, a large (n=60,000) multi-ethnic cohort study is being set up in Amsterdam: HELIUS (Healthy Life in an Urban Setting). This study has been initiated by the AMC, in cooperation with the Amsterdam Municipal Health Service (GGD). HELIUS aims to unravel the causes of (the unequal burden) of (chronic) diseases across ethnic groups. The emphasis will be on the major contributors to the global burden of disease: cardiovascular disease, depression, and infectious diseases. Important themes in relation to these diseases are differences in nutrition, obesity, and health care. The HELIUS study is unique in the Netherlands as well as in Europe. By making use of the variation between different ethnic groups, e.g. related to genetic factors and rapid changes in behaviour and environmental factors, it will be a goldmine for scientific analyses into the causes of (the unequal burden of) chronic diseases.
- Several recent developments have further strengthened the cooperation between research and practice within this theme. These includes the launch of the Research Centre for Insurance Medicine (in cooperation with two other university medical centres), the establishment of an academic workplace between the Amsterdam Municipal Health service and the AMC based on two grants from ZonMw, and the launch of the academic teaching workplace of the Netherlands School of Occupational and Public Health and the AMC.
- In the past years, researchers within this theme received several awards. Prof. Hanneke de Haes was awarded the Wolter Goeman Prize by the Society of Medical Psychologist in General and Academic Hospitals (LVMP/PAZ) for her scientific contribution to advancing the field of medical psychology in the Netherlands. Prof. Bert Schadé was awarded the Muntendam-prize of the KWF Cancer Control for his contribution to developments in the area of cancer control. The programme on 'Developmental origin of health and diseases' (dr. T. Roseboom) was nominated for the Academic Year prize, resulting in international media coverage.

SWOT

Strengths

The PIs have been successful in bringing together researchers with different disciplinary backgrounds. There is a fruitful interaction between researchers with a medical background, statisticians and methodologists, and social scientists in many places.

On average, the research groups have good scientific output, as measured in terms of publications in international scientific journals and compared to their national and international colleagues. Some research groups have very good or excellent scientific productivity, and are among the best in the world in their field. Some research fields are at the international forefront of research.

Many of the Principal Investigators in this research theme have close collaborations with other strong groups in the AMC.

The research groups have been quite responsive to shifts in the clinical and preclinical research activities in AMC, and to changes in the priorities of public health policy and practice.

Most of the researchers within this research theme are working in the Division of Clinical Methods and Public Health. This Division is being reorganized. One of the central aims of this reorganization is a strengthening of the research infrastructure, with better accommodating financial and management support systems, and more flexibility to respond to changes in the research policy of the AMC and the Division.

The recently launched HELIUS cohort initiative provides multiple opportunities for fostering new collaborations and interdisciplinary research teams.

Weaknesses

At present, there is not a strong enough sense of cohesion with the research themes. Collaborations across individual research areas could be intensified, allowing research of even higher scientific and societal impact. Investments in creating multidisciplinary research teams could be better and institutional structures are not sufficiently flexible for such a development.

For some research activities, establishing critical mass may become an issue, as they may have difficulties in achieving or maintaining a competitive position in the international research field. The reorganization of the Division of Clinical Methods and Public Health may help to overcome this, by fostering the clustering of related research activities.

The current funding structure is fragile in relation to long-term research projects, such as cohort studies, and there is a lack of flexible funding for new research areas.

Opportunities

The need for measures to improve prevention and public health in general is still being recognized and receiving renewed interest from several organizations in the field. This may increase the possibilities for funding future research. In addition, there are growing societal concerns that not all innovation and development will come from pharmaceutical companies and industry in general. Universities and, in particular, University Medical Centres, are expected to play a key role in biomedical research.

Threats

If national research assessment exercises are started in the Netherlands, with the aim of eliminating poor groups and concentrating others with limited critical mass in larger research groups, the AMC risks losing some of its research areas to other research organizations, who have a longer history, more research funding and higher visibility.

Future perspectives

In the past few years, the AMC has established a system of Principal Investigators. This system stimulates individual researchers, encouraging them to seek funding for their research ambitions and to find ways for making their research visible and influential. The challenge for AMC research in general, and for this research theme as well, will be to use that new structure to build a better research infrastructure. For that purpose, we expect the development of a more pronounced mission statement, a sharper identification and delineation of key research themes, and stronger collaborative project between researchers from this theme and others.

Title	Initials	Name	Department
Prof.dr.	A.	Abu - Hanna	Clinical Informatics
Prof. dr.	P.M.M.	Bossuyt	Clinical Epidemiology, Biostatistics and Bioinformatics (KEBB)
Prof. dr.	W.	van den Brink	Psychiatry
Prof. dr.	H.N.	Caron	Paediatrics – Oncology
Prof. dr.	F.J.H.	van Dijk	Occupational Health
Dr.	M.L.	Essink-Bot	Social Medicine
Prof. dr.	M.H.W.	Frings - Dresen	Occupational Health
Dr.	K.J.	Jager	Clinical Informatics
Prof. dr.	A.H.C.	van Kampen	Clinical Epidemiology, Biostatistics and Bioinformatics (KEBB)
Dr.	N.F.	de Keizer	Clinical Informatics
Dr.	S.	Kezic	Occupational Health
Dr.	A.E.	Kunst	Social Medicine
Prof. dr.	B.W.J.	Mol	Obstetrics / Gynecology
Prof. dr.	F.	Nollet	Rehabilitation
Prof. dr.	M.	Offringa	Paediatrics - Clinical Epidemiology
Dr.	N.B.	Peek	Clinical Informatics
Dr.	M.	Prins	Internal Medicine - Infec./Trop./Aids
Dr.	J.B.	Reitsma	Clinical Epidemiology, Biostatistics and Bioinformatics (KEBB)
Dr.	G.	ter Riet	General Practice/Family Medicine
Dr.	T.J.	Roseboom	Clinical Epidemiology, Biostatistics and Bioinformatics (KEBB)
Prof. dr.	A.H.	Schene	Psychiatry
Dr.	E.M.A.	Smets	Medical Psychology
Prof. dr.	M.A.G.	Sprangers	Medical Psychology
Dr.	P.H.I	Spuls	Dermatology
Dr.	J.K.	Sluiter	Occupational Health
Prof. dr.	K.	Stronks	Social Medicine
Prof. dr.	D.L.	Willems	General Practice/Family Medicine
Prof. dr.	A.H.	Zwinderman	Clinical Epidemiology, Biostatistics and Bioinformatics (KEBB)

PIs of the theme
Epidemiology and
Public Health

OTHER RESEARCH

About 10% of the AMC PIs have chosen not to join one of the AMC research themes. These PI's perform research in areas such as reproductive health, orthopaedics and other areas.

Title	Initials		Name	Department
Dr. ir.	L.		Blankevoort	Orthopaedics
Dr.	A.P.		Bos	Paediatrics
Prof. dr.	C.N.	van	Dijk	Orthopaedics
Prof. dr.	W.A.		Dreschler	ENT
Prof. dr.	J.C.		Goslings	Surgery
Prof. dr.	C.M.A.M.	van der	Horst	Plastic Reconstructive and Hand surgery
Dr.	E.T.M.		Laan	Obstetrics and Gynaecology
Prof. dr.	M.C.		Michel	Pharmacology and Pharmacotherapy
Dr.	A.M.M.	van	Pelt	Obstetrics and Gynaecology
Prof. dr.	J.A.M.	van der	Post	Obstetrics and Gynaecology
Prof. dr.	S.		Repping	Obstetrics and Gynaecology
Dr.	S.E.J.A.	de	Rooij	Internal Medicine –Geriatrics
Dr. ir.	G.J.		Streekstra	Biomedical Engineering and Physics

PIs of Other Research

PART B

THE PhD
PROGRAMME
OF THE AMC
GRADUATE
SCHOOL

In 2010, 154 PhD theses from the Academic Medical Center (AMC) at the University of Amsterdam were successfully defended. Most of these PhD students were paid employees of AMC Medical Research (AMR Ltd) or the AMC itself. The background field of these students is extremely variable. The PhD programme of the AMC Graduate School accommodates this variability through its flexible and personalized course programme, in which more than 850 PhD students currently participate.

1. OBJECTIVES AND OUTCOMES OF THE PHD PROGRAMME

The aim of the AMC Graduate School is to provide an infrastructure for the training of PhD students at the AMC and to improve and to monitor the quality of the training.

The AMC PhD training programme aims to train PhD students to become independent, original and effective scientists, able to engage in and develop scientifically significant research and to critically evaluate work done by others. Through this training, they can become creative, analytical, critical and autonomous professionals who may also pursue a career within or outside the university.

In this process, the AMC Graduate School supports PhD supervisors in their role as trainers, mentors and supervisors of PhD students, not only regarding the PhD research and the completion of the thesis, but also regarding the training element in PhD projects. Good mentorship of PhD students is expected of all PhD supervisors and other senior researchers.

2. INSTITUTIONAL EMBEDDING OF THE PHD PROGRAMME

Since January 2007, the training of PhD students is coordinated within the AMC Graduate School, which was founded in 2006. The AMC Graduate School merged with AMC Science Education, which had been in existence since 1999. AMC Science Education organized and coordinated training for junior researchers in the AMC.

The AMC Graduate School runs a comprehensive course programme in the AMC. In addition, several students follow courses at other universities and institutions. These include courses, seminars, retreats and other activities organized by KNAW Research Schools, such as the Oncology Graduate School Amsterdam, the Graduate School Neurosciences Amsterdam, and the Netherlands Institute for Health Sciences.

The AMC Graduate School Board members are (October 2010): Prof. Andries Bosch, Prof. Patrick Bossuyt (Chair), Prof. Eric Fliers, Prof. Martien Kapsenberg, Prof. Tom van der Poll, and Drs. Suthesh Sivapalaratnam (PhD Student Member).

The AMC Graduate Board is represented in the AMC Teaching & Training Council, with the other AMC Teaching Institutes: The School of Medicine, The Medical Informatics Programme, the Medical Specialist Training Programmes, and the Amsterdam School of Health Professions. The AMC Teaching & Training Council, founded in 2010, constitutes the link between the education institutes and the AMC Executive Board on aggregated strategic matters in teaching and training.

The AMC Graduate School offers a comprehensive PhD Course Programme. It oversees that the agreed upon conditions for PhD training are met for every AMC PhD student, through the existence of a personalized Training and Supervision Scheme, and that all AMC PhD students are aware of courses and other training activities throughout their PhD training period.

Research

Almost all AMC research projects are led by one of the established AMC Principal Investigators. The heads of department are responsible for developing and running a comprehensive research plan within their department, including finances. The contents, goals and ambitions of all research, including PhD research, are periodically monitored and evaluated within the AMC Research Institute.

AMC PhD Scholarships

Each year, the AMC Graduate School offers a number of PhD Scholarships to excellent students who completed studies at the Master's level. The PhD Scholarships aim to attract and keep talented students as PhD researchers in AMC. Students should have obtained their degree in the AMC, or have spent at least one formally evaluated research training period in AMC as part of their Master level training, or have completed an AMC Summer School programme. Funding for the PhD Scholarships comes from direct government university funding. Each Scholarship covers the costs of a four year appointment as research trainee (*onderzoeker in opleiding*) in the AMC and includes a small bench fee. With an AMC Scholarship, students can develop their own PhD research project. Starting in 2006, 6 PhD Scholarships were granted each year. From 2009 onwards, 6 additional PhD Scholarships were made available as part of the AMC Innovation Impulse 2009-2011.

Training

The AMC Graduate School encourages all PhD students to start their training with a 3 day introductory course "AMC World of Science". This course is offered to all PhD students, regardless their status or background. The aim of this Basic Course is to prepare the student for his or her PhD project at the AMC.

The PhD Course Programme contains 29 more specialized courses. PhD students select courses from this programme with their PhD supervisor based on their prior level of training and their project needs and personal and professional development.

The majority of these courses are organized by the AMC Graduate School itself, and accessible to AMC PhD students only. All AMC courses are offered free of additional charges to AMC PhD students. Other courses are organized by other institutions or organizations, such as the Dutch Heart Foundation, or by KNAW research schools, such as ONWA, OOA, or NIHES. A list of all 30 courses can be found in annex 4.

The AMC Graduate School facilitates the organizations of PhD retreats, where AMC PhD students can discuss their research and that of their colleagues.

All PhD students are invited to subscribe to the AMC Yellow Pages, a weekly email newsletter that announces all research activities in AMC, such as lectures, seminars, or retreats. In 2006, the AMC Research Council started with the Ruysch lectures, plenary lectures for all AMC scientists by internationally recognized researchers who are invited to Amsterdam. Many Ruysch Lectures are accompanied by a master class for scientists, to which PhD students are cordially invited.

Supervision

PhD supervisors (*promotores*) are invited to complete a Training and Supervision Scheme (*Opleidings- en Begeleidingsplan, OBP*) with their PhD students. From 2009, the Training and Supervision Scheme is mandatory and should be signed by both the PhD supervisor and the PhD student.

The Training and Supervision Scheme contains details about the mode and frequency of supervision, as well as details about the training programme. The daily supervision of the PhD student can be delegated by the promotor to other scientists, who then act as *copromotor*.

The PhD supervisor is expected to monitor progress of the PhD project during regular interviews. In addition, all employees of the AMC and the AMC Medical Research (AMR Ltd) have an annual assessment interview, in which work and work methods are evaluated, tasks and targets are defined and working conditions, personal development and career perspectives are discussed.

PhD student Association

In 2006, the AMC Graduate School encouraged and facilitated the foundation of PhD Student Association APROVE, the AMC *Promovendivereniging*. The PhD Student Association organizes additional activities for AMC PhD students year round, including seminars, social programmes, programmes for foreign students, and a web-based PhD social network.

4. INTERNAL QUALITY ASSURANCE

Admission and registration

Decisions about admission to the AMC PhD programme are made individually by one of the full professors in the AMC, who declare his or her willingness to act as PhD supervisor to a qualified student.

The AMC started the comprehensive and obligatory registration of all AMC PhD students in 2009. The registration procedure is organized and supervised by the AMC Graduate School. An AMC PhD student is defined as having a qualified PhD supervisor, having completed a relevant master study and planning to defend his/her PhD thesis at the University of Amsterdam. AMC PhD students are expected to register at the beginning of their PhD training. Registered PhD students subsequently have free access to all PhD programme courses and other facilities of the AMC Graduate School.

On October 18, 2010, this registry contained 862 AMC PhD students, 550 female students (64%) and 312 male students (36%). Of these, 82% are Dutch citizens, whereas 18% are from one of 42 different foreign countries.

Of the PhD students registered, 34% are appointed as research trainee (*oio*); 38% are MD researchers (*arts-onderzoeker*), 3% are medical specialists, and 5% are AMC faculty, whereas 3% have a combined resident and research trainee (*AGIKO*) appointment, see Figure 5.

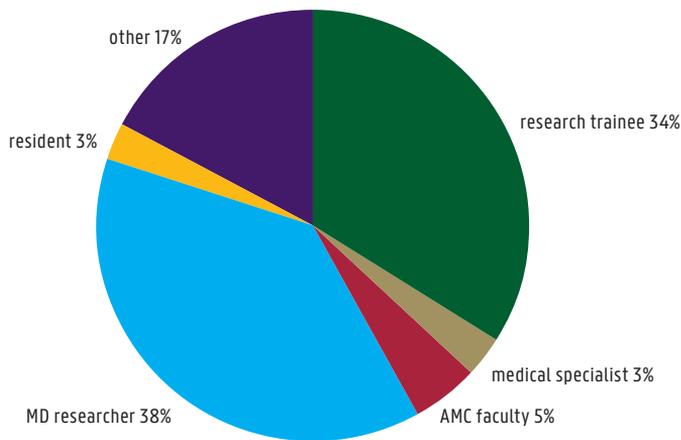


Figure 5: Distribution of the PhD students by appointment.

Thesis requirements

The formal requirements for an AMC PhD thesis are defined in the doctorate regulations of the University of Amsterdam. The informal requirements are regularly discussed in letters from the delegate to the dean for promotion affairs to all AMC Professors. In short, PhD theses should consist of original in extenso papers published or submitted to international peer-reviewed scientific journals. In line with The Zagreb declaration, the minimal requirement for a PhD thesis in medicine and health sciences should be the equivalent of at least three published or accepted publications where the PhD student's contribution is expressed in the candidate being the first author. The vast majority of AMC PhD theses contain six or more scientific papers.

Courses

All courses organized and offered by the AMC Graduate School are systematically evaluated. Course participants complete a standardized evaluation form, which is processed with optical character recognition. Results are summarized and distributed to the course coordinator and the quality officer in the board of the AMC Graduate School. The quality officer and the student-member of the board discuss the results of the evaluation with the course coordinator, the results of which are summarized in minutes. The set of minutes is discussed with the Board of the Graduate School, which annually discusses the findings with the Dean and the AMC Board of Directors.

Supervision

The PhD Student Adviser arranges one personal meeting with each PhD student during their four-year research period. This is scheduled between three and six months after students start their PhD project. PhD students are welcome to approach the adviser at any time with queries or problems concerning the training programme or other matters related to their studentship.

During the meeting, students bring their completed and signed Training and Supervision Scheme form and go through it with the PhD Student Adviser. The PhD Student Adviser then signs it as well. If the student subsequently wishes to make any changes or needs further advice, he or she can contact the Graduate School Office to arrange an appointment with the adviser. The PhD Student Adviser also offers mediation for conflicts about PhD supervision or working conditions for PhD students.

The AMC Graduate School operates in close collaboration with the AMC Ombudsman. The AMC Ombudsman investigates reports of alleged scientific misconduct lodged by one or more persons involved directly or indirectly in scientific research at the AMC. In addition the AMC Ombudsman makes recommendations on good scientific conduct in line with the AMC Research Code, at the request of employees of the AMC. The most recent version of the AMC Research Code contains a separate chapter on Good Mentorship.

5. RESOURCES **Research**

Funding for AMC PhD projects is derived from several sources. These can be classified as direct government funding, indirect government (e.g. NWO, ZonMw, and KNAW) and EU funding, charity funding (e.g. KWF, NHS) and industry funding.

Training

Training of PhD students is defined as one of the core teaching activities of AMC faculty. As of 2011, the work load associated with the PhD courses will be included in calculations of the teaching load for AMC employees and AMC departments.

Additional costs associated with the course programme are covered by the budget of the AMC Graduate School. Registered AMC PhD students do not have to contribute financially. The AMC Graduate School also contributes to the costs of PhD retreats.

The AMC Research Council has a budget for several of the seminars and lectures offered to AMC researchers, including the Ruysch lectures previously mentioned.

6. NUMBER OF PHD-THESES

The number of AMC PhD theses that have been successfully defended in the past five years is listed below.

2005: 111 PhD Theses	2007: 160 PhD Theses	2009: 149 PhD Theses
2006: 130 PhD Theses	2008: 157 PhD Theses	2010: 154 PhD Theses

Of the 861 theses defended in 2005-2010, 440 (51%) were defended by women, see Figure 6. Approximately one out of every five theses was prepared based on research conducted in other institutions or research environments.

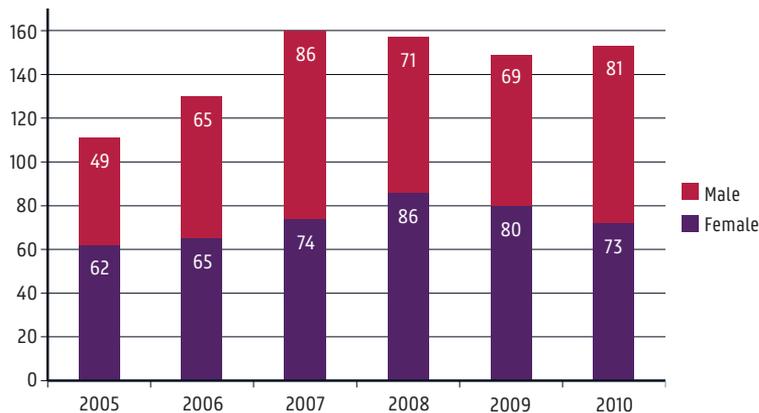


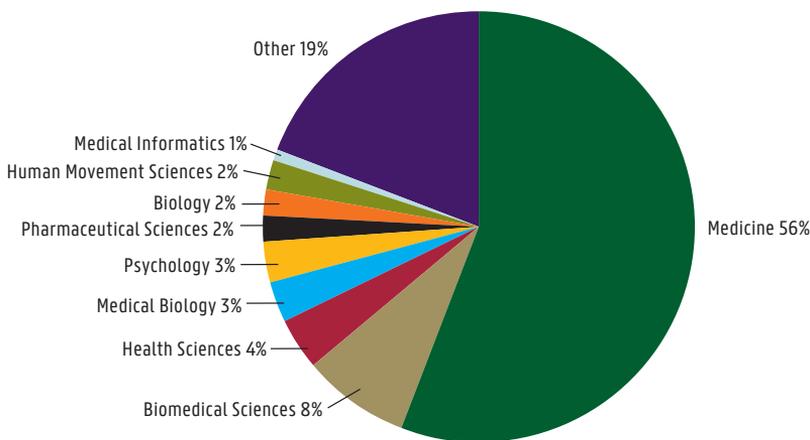
Figure 6: Number of theses defended in 2005-2010 by male and female PhD-students.

A retrospective analysis of 609 completed PhD theses, performed in 2003, revealed that 72% of these theses had been defended within 5 years after the start of the corresponding PhD projects, and 42% within 4 years. Most PhD projects that lasted 6 years or longer had been planned that way, e.g. as part-time programmes. Completion rates are significantly higher for PhD students appointed as research trainee (onderzoeker in opleiding).

These figures seem to have deteriorated somewhat since then. Of the theses defended in 2009 and 2010 for which starting dates of the corresponding PhD projects were available (N=100), 77% were successfully defended within 6 years after the start of the PhD programme, 48% were defended within 5 years, while 19% were defended within 4 years. The mean duration of the PhD projects was 5 years and 3 months.

The AMC Graduate School does not yet keep detailed records of the career destinations of its PhD Graduates.

The AMC Graduate School has a high number of PhD students with a variety in background field and research topics, although the majority of PhD research projects are clinical and the majority of students have a medical background (see Figure 7). The number of PhD students and the number of successfully defended theses are growing. The female to male distribution is changing, with women outnumbering men both in new PhD students and completed PhD projects.



7. SUCCESS RATES OF PHD GRADUATES

8. CAREER DESTINATION OF PHD GRADUATES

9. SWOT ANALYSIS, PERSPECTIVES AND EXPECTATIONS

Figure 7: Distribution of the PhD students by background field.

The AMC has been successful in offering a standardized Training and Supervision Scheme. There is room for improvement in organizing a more standardized way of PhD supervision, with systematic diffusion of best practices within the AMC, and separate training programmes and appraisal instruments for PhD supervisors.

The number of courses offered by the Graduate School has grown systematically, as well as the number of PhD students taking these courses. This testifies to the increasing acceptance of the training programme, also by supervisors of contract research, and growing awareness of the need for additional training by PhD students.

In The Netherlands, all 8 University Medical Centres (UMCs) now have one or more Graduate Schools. The Graduate Schools differ in structure and organisation, but share a common truck of criteria for a PhD degree and PhD training. In 2006, the AMC was one of the first to constitute a Graduate School. In order to promote transparency and the exchange of PhD students, we strive at further collaboration between the Dutch Graduate Schools in the UMCs and in the University of Amsterdam.

On an international level, the University of Amsterdam participates in the League of European Research Universities (LERU). Their position paper *'Doctoral degrees beyond 2010; Training talented researchers for society'* sets out a vision for doctoral education that offers a challenge for universities and doctoral candidates as well as their future employers and society at large: "[...] to train researchers to the highest skill levels to become creative, critical and autonomous intellectual risk takers in pushing the boundaries of frontier research". The AMC Graduate School already set out in the direction indicated by LERU. Our PhD Programme is being broadened to also prepare PhD students for their role in society outside academic research and to equip PhD supervisors for their new role as trainer of PhD students instead of 'just' research supervisor.

Strengths

The AMC Graduate School is firmly grounded in the AMC research community. Its PhD Course programme is comprehensive and well known. The AMC World of Science offers an excellent start for all PhD students. The registration of PhD students has been successfully introduced and is well organized. The PhD Scholarships programme is successful in attracting and preserving talent in the AMC. The overall scientific quality of PhD research seems to be at a very high level.

Weaknesses

The AMC Graduate School monitors PhD students and their supervisors, but lacks in both authority and instruments to give feedback and correct if necessary. The bureau of the delegate of the dean for promotion affairs is not yet integrated in the AMC Graduate School. The registration system is not integrated in the AMC IT infrastructure.

Opportunities

The activities of the AMC Graduate School have contributed to a growing awareness that a PhD project is not just a research project but also a personal training programme, and that the training of PhD students to become independent scientists should also prepare them for a successful professional career in society. This awareness allows AMC to build on the present activities and to develop an even more structured training environment, in close collaboration with our partners in the University of Amsterdam, the other UMC and our international partners. The registration of PhD students offers the opportunity to analyse the success rate of the PhD research.

Threats

Universities are threatened by severe budget cuts, which could make it difficult to expand activities in PhD training up to a level where it fully meets the requirements of the third phase in university training, after the bachelor and master phase. The large variability in positions and background of PhD students will make it difficult to achieve and maintain a common quality level in PhD training programmes.

PART C

REPORT OF THE
INTERNATIONAL
EVALUATION
COMMITTEE

Executive Board of the AMC
Professor M. M. Levi, Chairman
E2-126
Academic Medical Center
PO Box 22700
1100 DE Amsterdam

The Hague, 20 April 2011

Dear Professor Levi,

It is with great pleasure that I send you the final version of the Report on the research performance of the AMC-UvA by the International Evaluation Committee. Overall, the Committee considers the research at AMC to be at a very high level according to international standards, achieving the level of world leadership in various fields. We highly appreciated the quality of the material that was provided to us and the openness of the discussions that we were able to have with AMC research leaders.

On your request, we answered the specific questions that were posed. As to research policy and management, the Committee believes that the role of the AMC Research Council should be strengthened. In our report we have formulated various alternatives on how this could be achieved. The Committee feels that the AMC itself is in the best position to judge which of these alternatives would be most effective in the specific context of the AMC.

We hope that you find our assessments and recommendations helpful and that you will be able to use them to even further increase excellence in research and to advance the research governance of the AMC.

Sincerely,

On behalf of the International Evaluation Committee,



Prof. dr. J.A. Knotttnerus

Annex: Report on the research performance of the AMC-UvA by the International Evaluation Committee

The Executive Board of the Academic Medical Centre of the University of Amsterdam has invited an International Evaluation Committee to review its research performance, and to answer a number of specific questions related to this performance.

The appointed Committee members were:

- **Professor Andre Knottnerus, MD (chair)**
Chair of the Scientific Council for Government Policy (WRR) and professor of Primary Care and Clinical Epidemiology at the University of Maastricht, The Netherlands
- **Professor Reinhold E. Schmidt, MD**
Centre Director of Immunology and Rheumatology and Dean of the Graduate School at the Hannover Medical University, Germany
- **Professor Thomas F. Lüscher, MD FRCP**
Professor and chairman at the Department of Medicine and Cardiology of the University Hospital Zürich, Switzerland
- **Professor Nicholas White, MD FRS**
Professor of Tropical Medicine, Mahidol University, Thailand, and University of Oxford, United Kingdom
- **Professor Douglas Green**
Member and chairman at the Department of Immunology, St. Jude Children's Research Hospital, Memphis, Tennessee, United States

The Committee convened at 15, 16 and 17 March 2011. The full programme of the review session is attached as appendix to this report. In short, at the evening of 15 March, the Committee was welcomed by the chair and the members of the Executive Board of the AMC, who presented background information to the Committee and provided additional explanation regarding the questions that the Committee has been asked to answer. On 16 March, the Committee had a meeting with the AMC Division chairs and reviewed presentations from the leaders of AMC research themes. Also the input from Principal Investigators (PIs) attending the discussions was integrated in the assessment. In addition, the Committee has highly appreciated the meeting with the leadership of the AMC Graduate School and the large delegation of PhD students.

In the morning of 17 March the Committee made its assessment and conclusions, and formulated answers to the questions of the AMC Executive Board. This was summarised in a draft report, which was then presented to the AMC Executive Board and the Research Council of the AMC. After the review session, the draft report was further edited and circulated among the Committee members for possible correction and, subsequently, final approval.

PREAMBLE The Committee was impressed by the quality and quantity of the research presented, the candid discussions with the research representatives, and the supportive material presented in the AMC research self-assessment report (AMC Research Evaluation 2011). It was not possible to conduct a detailed, in depth evaluation of each specific research area within the time available and with the composition of the Committee, but a consistent and clear overview emerged.

In reporting its observations, assessment and conclusions, the International Evaluation Committee will follow the questions of the AMC Executive Board, and formulate recommendations to the Board.

Questions of the AMC Executive Board to the Evaluation Committee

AMC Research Institute as a whole

1. What is your overall judgement of the AMC Research Institute?

– with regard to the research performed:

The research at AMC is performed at a very high level according to international standards, achieving the level of world leadership in various fields.

– with regard to research governance:

While overall substantial efforts are invested in effective research management, there appears to be a deficit in research governance, that is, in transparently relating research resources to research performance. The Committee emphasises that, in order to continuously stimulate progress and to safeguard ongoing competitive top research, there need to be methods of linking budget allocation with research performance. Introducing such a method would also be strongly supported by the key players (e.g., Division chairs and theme leadership).

2. In an international perspective, what do you consider to be the Strengths, Weaknesses, Opportunities, and Threats (SWOT) for the AMC Research Institute?

Based on the material provided and the reviews sessions, the Committee's SWOT analysis of the AMC Research Institute is as follows:

Strengths:

- A very active scientific community in the full range of biomedical, clinical, public health, and primary care research and practice.
- Research is organised into consistent scientific themes, with sufficient flexibility to also conduct promising research outside of themes.
- A large number of active research staff.
- A strong research culture producing high quality research output situated at the top ranks of international science.
- Several groups are clearly recognised as world leaders.
- Multidisciplinary collaboration, aimed at connecting basic and applied research in all the fields mentioned in the first Strength.
- There are strong ties and close links between the basic and clinical research efforts to promote translation of research findings into practice and policy.

Weaknesses:

- Lack of transparency of research budget availability and allocation.
- Lack of a mechanism to assign budgets according to scientific quality and productivity.
- Lack of availability of midcareer opportunities for the top group of talented investigators who can be expected to be future AMC research leaders (recognising the importance of inter-academic and international mobility for young researchers).
- Some core facilities are underfunded, not fully accessible and underdeveloped.

Opportunities:

- Strong interest of young researchers to make a career in biomedical research, and at the interplay of basic and clinical sciences.
- A strengthened AMC Research Council could provide more effective guidance and leadership.
- Strategic planning at the thematic level can benefit research development.
- Stronger links and synergy with research and healthcare institutions in the AMC region would further promote (inter)national competitiveness.

Threats:

- Not rewarding excellent performance in relation to basic academic funding.
- The lack of opportunity for research career development for young talented researchers, with imbalance between the numbers of graduated PhDs and available positions for postdocs and midcareer staff, may lead to a brain drain, and also to difficulty to attract talents from elsewhere.
- Decreased funding both from national and international public funds and from industry.
- Changes in public perception and appreciation of science may affect support for research and research funding and require pro-active measures.

AMC Themes

The Committee highly appreciated the SWOT analyses provided by the different themes as well as the openness of the research representatives in addressing the Committee's questions. The Committee in general agreed with the self-assessments of the themes and Divisions and their strategic plans for further improvement. Due to the composition of the Committee and the time available, detailed advice on each of the areas of research was considered not appropriate, as this would have required specific multidisciplinary teams of experts covering the research fields of each theme in sufficient depth.

3. In an international perspective, what do you consider to be the Strengths, Weaknesses, Opportunities, and Threats of the AMC themes?

AMC Graduate School

The Committee was impressed by the overall quality of the PhD graduates, which is very high according to international standards. The recent founding of the AMC Graduate School is an excellent initiative and its PhD Course Programme is of high quality. As the School is still in its early stages, the Committee recommends the development of a standardised selection, supervisory, monitoring, and evaluation procedure that would strengthen the programme.

4. What is your overall judgement of the AMC Graduate School and what are your recommendations?

Specific questions

5. What in your view is needed if AMC wants to belong to the top-10 of university medical centres in Europe?
- In response to this question, the Committee recommends to focus on the following:
- Strategic planning at the thematic level to promote high impact initiatives.
 - Stronger steering mechanisms to relate research budget to performance.
 - Support collaborative joint research projects and programmes, both between themes and with other strong institutions in the region (e.g., NKI-AvL, NIN, Sanquin, and VUmc).
 - Better internal career perspectives for top talent young researchers who are candidates for future leadership.
 - Further nurturing the close links between clinical and basic research which lead to translational opportunities and connecting resolving basic mechanisms to clinical innovation.
 - Further strengthening of AMC's attractiveness for international top experts to work at or to collaborate with the AMC theme groups.
 - Remain attractive to both biomedical and clinical scientists by safeguarding sufficient room for academic research in a context of increasing pressure to increase clinical care productivity.
6. What do you consider the most effective size of research themes of the AMC, for external recognisability and for adequate focus in the use of research policy instruments (including institutional money and laboratory space)?
- There are no general, evidence-based criteria for size and number of themes, and given the size of the whole AMC, the current number of themes is reasonable, also in an international context. Moreover, for a UMC a reasonably broad coverage over the various educational and clinical domains is important. Performance as to originality and quality of interdisciplinary research, subject-matter related need for focus and mass, finding good niches and complementarities in the national and European arena, and theme governance requirements (including span of control) should be leading. Inter-theme collaboration and cross-fertilization both related to content and to large core infrastructures, can help to develop supra-thematic visibility, coherence, and efficiency. In addition, flexibility and adaptability in relation to developing research challenges and opportunities are important assets.
- As to external recognisability, the exact size of research themes will be less important for the international research community, where only actual domain-specific scientific performance will count. Towards the policy field more general external effects are important, but this should be primarily considered as an executive challenge for effective communication and presentation at the right time and the right place.
7. In which core facilities should AMC invest?
- Based on the AMC self-assessment report and the review sessions, the Committee expects that given the current challenges priority should be given to infrastructural investments in the following areas:
- Genetics: this was identified already in previous research assessments (Advice of the Research Council on the evaluation of the AMC research, 2008) as a weakness, as the availability of top expertise to meet the needs of the various themes is considered highly insufficient. In this 2011 assessment, this need was again indicated as top priority for all themes.

- There is a good bioinformatics group, but its capacity is much too low to meet the increased needs of the various themes.
- Strengthening of the clinical trial and cohort infrastructure would be favourable for efficiently and continuously profiting from the huge AMC potential for inter-thematic clinical and epidemiological research.
- Safeguarding animal facilities and efficiency of procedures in reviewing and approving proposed experiments without unnecessary delay is important.
- Central professional support for Principal Investigators for complex grant applications (e.g., for EU grants) would save time and promote logistic quality (in addition to scientific quality), and accordingly, would increase the chances for success in the international funding arena.

Other recommendations

Overseeing the whole picture arising from the review, the International Evaluation Committee makes the following final recommendations:

1. *As it appeared difficult to obtain clarity regarding the size of research budget and its allocation, the Committee advises that:*
 - the research budget and its allocation should be more transparent.
 - the research budget should be set as a percentage, e.g. 20-25% of the total budget.
 - the research budget allocation should be linked to performance. If starting this would now be hampered by lack of clarity of the current size and allocation status of the research budget, a possible alternative approach to achieve this would be to cut all budgets by, e.g., 20% and to reallocate this money based on performance assessment.
2. *The AMC Research Council could provide more effective guidance and leadership in AMC's research management. In view of this, the Committee advises:*
 - to reconsider the composition and role of the AMC Research Council in order to strengthen its strategic and budgetary role.
 - to intensify the contributions from the AMC Research Council into AMC's research policy, which could be achieved, for example, by:
 - appointing the chair of the AMC Research Council as an advisory ex officio member of the Executive Board, or, even better,
 - by appointing a dean in the Executive Board with specific responsibility for academic tasks including research, who would be directly advised by the AMC Research Council.
3. *To further strengthen the role of the AMC Research Council its task should include:*
 - Assessment, monitoring, and evaluation of the research output.
 - Development of the mechanism for performance based allocation of funding.
 - Giving active input in strategic research planning.
 - Advising the Executive Board on the draft annual AMC research budget.
 - Evaluation of existing and creation of new core facilities: oversee all institutional core facilities and research infrastructures and make budget recommendations for their support.

8. What are your other recommendations to the Executive Board of the AMC?

-
4. *The theme leaders and the Division Chairs should collaborate on the allocation of the research budget to the Principal Investigators.*
 5. *Opportunities to bridge research career gaps for top talent young researchers who are candidates for future leadership should be improved (see also the answer to question 5). In addition, the opportunity for research careers at the interplay of basic and clinical sciences should be promoted.*
 6. *Central support for Principal Investigators in preparing complex, e.g. EU, grant applications should be better organised (see also question 7).*
 7. *AMC should continue to promote academic recognition and opportunities for development in excellent non-theme related research that serves AMC's academic performance and innovation.*
 8. *The inter-thematic coherence and interaction as to content and infrastructure, e.g., genetics, cohort studies, and bioinformatics expertise, etc. should be promoted.*
 9. *Further national and international collaboration (e.g., regarding cohorts, expensive basic facilities, and rare metabolic disorders), based on mutual interest and complementarities should be encouraged.*

ANNEXES

Annex 1
**MEMBERS
OF THE
INTERNATIONAL
EVALUATION
COMMITTEE**

Annex 1: Members of the International Evaluation Committee

The appointed members were:

- **Professor Andre Knottnerus, MD (chair)**
Chair of the Scientific Council for Government Policy (WRR) and professor of Primary Care and Clinical Epidemiology at the University of Maastricht, The Netherlands
- **Professor Reinhold E. Schmidt, MD**
Centre Director of Immunology and Rheumatology and Dean of the Graduate School at the Hannover Medical University, Germany
- **Professor Thomas F. Lüscher, MD FRCP**
Professor and chairman at the Department of Medicine and Cardiology of the University Hospital Zürich, Switzerland
- **Professor Nicholas White, MD FRS**
Professor of Tropical Medicine, Mahidol University, Thailand, and University of Oxford, United Kingdom
- **Professor Douglas Green**
Member and chairman at the Department of Immunology, St. Jude Children's Research Hospital, Memphis, Tennessee, United States

Tuesday March 15th

18.00-19.00 hrs **Meeting with Executive Board**
19.00-21.30 hrs Diner with Executive Board of the AMC and the executive board of the Research Council

Wednesday March 16th

08.00-09.00 hrs **Meeting with the ten Division chairs**
09.00-09.15 hrs commission's wrap up of the meeting

09.15-10.15 hrs **AMC Theme Neurological and Psychiatric Disorders**
Participants: prof. Frank Baas, prof. Pim Van Gool, prof. Wim van den Brink and prof. Damiaan Denys.
Observers: all other Pls of the Theme NPD
10.15-10.30 hrs commission's wrap up of the Theme NPD

10.30-11.30 hrs **AMC Theme Cardiovascular Diseases**
Participants: prof. Antoon Moorman, prof. John Kastelein, prof. Carlie De Vries, prof. Yigal Pinto and prof. Arthur Wilde.
Observers: all other Pls of the Theme CVD
11.30-11.45 hrs commission's wrap up of the Theme CVD

11.45-13.15 hrs **Lunch with board of the Graduate School and PhD students**
Participants: prof. Patrick Bossuyt, prof. Tom van der Poll, prof. Eric Fliers, prof. Andries Bosch, prof. Martien Kapsenberg, dr. Marlies Stouthard and Marije van der Paardt; and the PhD students Joppe Scheiders, Elsmarieke van de Giessen, Zelda Euler, Inge Stegeman, Serge Zweers, Hansje-Eva Teulings, Ronak Delewi, Arvid Schigt, Katja de Jong and David Boerwinkel.

13.15-14.15 hrs **AMC Theme Metabolic Diseases**
Participants: prof. Hans Aerts, prof. Frits Wijburg, prof. Ronald Wanders and prof. Eric Fliers
Observers: all other Pls of the Theme Met
14.15-14.30 hrs commission's wrap up of the Theme Met

14.30-15.30 hrs **AMC Theme Infection and Immunity**
Participants: prof. René van Lier, prof. Tom van der Poll, prof. Ben Berkhout and prof. Paul Peter Tak
Observers: all other Pls of the Theme I&I
15.30-15.45 hrs commission's wrap up of the Theme I&I

15.45-16.45 hrs **AMC Theme Public Health and Epidemiology**
Participants: prof. Karien Stronks, prof. Koos Zwiderman
prof. Monique Frings and prof. Mirjam Sprangers
Observers: all other Pls of the Theme PHE
16.45-17.00 hrs commission's wrap up of the Theme PHE

Annex 2
**PROGRAMME
SITE VISIT
INTERNATIONAL
EVALUATION
COMMITTEE**

AMC research
evaluation,
15-17 March 2011

-
- 17.00-17.15 hrs **AMC Other research – Reproductive Health**
Participants: prof. Maas Jan Heineman, prof. Sjoerd Repping,
prof. Ben Willem Mol and dr. Tessa Roseboom
Observers: all other PIs of Other research
- 17.15-17.30 hrs **AMC Other research – Musculoskeletal and trauma research**
Participants: prof. Thomas van Gulik, prof. Niek van Dijk and
prof. Carel Goslings
Observers: all other PIs of Other research
- 17.30-18.30 hrs Diner
- 18.30-18.45 hrs Catch up time
- 18.45-19.45 hrs **AMC Theme Gastrointestinal Diseases**
Participants: prof. Ronald Oude Elferink, prof. Paul Fockens.
Prof. Ulrich Beuers and dr. Wouter de Jonge
Observers: all other PIs of the Theme GID
- 19.45-20.00 hrs commission's wrap up of the Theme GID
- 20.00-21.00 hrs **AMC Theme Oncology**
Participants: prof. Jan Paul Medema, prof. Huib Caron,
prof. Dick Richel and prof. Steven Pals
Observers: all other PIs of the Theme Onc
- 21.00-21.15 hrs commission's wrap up of the Theme Onc

Thursday March 17th

- 08.30-12.00 hrs Preparation of the advice
12.00-13.00 hrs Presentation of preliminary report to Executive Board and
Research Council and informal lunch

Research Institute as a whole

- 1 What is your overall judgement of the AMC Research Institute?
 - With regard to the research performed
 - With regard to research governance
- 2 In an international perspective, what do you consider to be the Strengths, Weaknesses, Opportunities and Threats of the AMC Research Institute?

AMC research evaluation
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AMC themes

- 3 In an international perspective, what do you consider to be the Strengths, Weaknesses, Opportunities and Threats of the AMC theme:
 - Cardiovascular diseases
 - Gastrointestinal Diseases
 - Infection and Immunity
 - Metabolic Disorders
 - Neurological and Psychiatric Disorders
 - Oncology
 - Public Health and Epidemiology
 - Other research

AMC Graduate School

- 4 What is your overall judgement of the AMC Graduate School and what are your recommendations?

Specific questions

- 5 What in your view is needed if AMC wants to belong to the top-10 of university medical centres in Europe?
- 6 What do you consider the most effective size of research themes of the AMC:
 - for external recognisability (profile for policy makers and/or funding agencies); and
 - for adequate focus in the use of research policy instruments (including institutional money and laboratory space)?Would this have any effect on the number of research themes for the AMC?
- 7 In which core facilities should AMC invest?

Other recommendations

- 8 What are your other recommendations to the Executive Board of the AMC?

Annex 4
**AMC GRADUATE
SCHOOL - LIST OF
COURSES**

- 0 AMC World of Science
- 1 Management of Medical Literature
- 2 Scientific Writing in English
- 3 Oral Presentation in English
- 4 Clinical Data Management
- 5 Basic Course Legislation and Organization for Clinical Researchers (BROK)
- 6 Basic Laboratory Safety
- 7 Radiation Protection
- 8 Practical Biostatistics
- 9 Advanced Biostatistics
- 10 Clinical Epidemiology
- 11 Advanced Topics in Clinical Epidemiology
- 12 Genetic Epidemiology
- 13 Qualitative Health Research
- 14 Introduction to Bioinformatics
- 15 Infectious Diseases
- 16 DNA Technology
- 17 Crash Course: Basic Chemistry, Biochemistry and Molecular Biology for MD's
(re)entering Scientific Research
- 18 Mass Spectrometry, Proteomics & Protein Research
- 19 Systematic Reviews
- 20 Laboratory Animals
- 21 Anatomy of the Mouse
- 22 Bio Business Summer School
- 23 Advanced Immunology
- 24 Basic Course Microscopy
- 25 Advanced Course Microscopy
- 26 Cardiovascular Diseases
- 27 Career Development
- 28 Project Management
- 29 Metabolism Inherited and Acquired Disorders

AIGHD	Amsterdam Institute for Global Health and Development
AMC	Academic Medical Center
AMR Ltd	AMC Medical Research
AvL-NKI	Netherlands Cancer Institute-Antonie van Leeuwenhoek Hospital
CPP/FCSm	CPP is the average number of citations per publication corrected for self-citations. FCSm is the mean Field Citation Score: the mean citation rate of the fields in which the institute/group is active.
CRU	Clinical Research Unit
CVD	Cardiovascular Diseases
CWTS	Centre for Science and Technology Studies
EU	European Union
GGD	Public Health Services of Amsterdam
GID	Gastrointestinal Diseases
I&I	Infection and Immunity
KNAW	Royal Dutch Academy of Sciences
KWF	Dutch Cancer Society
Met	Metabolic Disorders
NHS	Netherlands Heart Foundation
NIN	Netherlands Institute for Neuroscience
NKI	see AvL-NKI
NPD	Neurological and Psychiatric Disorders
NWO	Netherlands Organisation for Scientific Research
Onc	Oncology
PHE	Public Health and Epidemiology
PI	Principal Investigator
RC	Research Council
SEP	Standard Evaluation Protocol
UMC	University Medical Centre
VSNU	Association of Universities in the Netherlands
ZonMw	Netherlands Organisation for Health Research and Development

Colofon

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Lay out and design

ontwerpjanhaandrikman,
Doornenburg

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