



# Research Annual Report 2009



## Netherlands Institute for Health Sciences (NIHES)

Biology and technology of reconstructive surgery

Epidemiology of diseases

Basic epidemiologic research

Clinical epidemiology

Biostatistics

Effects of screening and clinical interventions on population health

Determinants and primary prevention

Clinical research in general practice

Implementation of diagnostic and interventional imaging technology

Assessment of diagnostic and interventional imaging technology

Development of acquisition and processing techniques for diagnostic imaging

Structuring of medical knowledge

Structuring of medical data

Assessment, aetiology and course of child and adolescent psychiatry



# Research Annual Report 2009



## Netherlands Institute for Health Sciences (NIHES)

Adaptation of (future) patients to disease and treatment in order to improve counselling and guidance

Competition and regulation in health care (theme 1)

Quality and efficiency in health care (theme 2)

Health care management (theme 3)

## EMC NIHES-01-50-01-A - Biology and technology of reconstructive surgery

### Programme design in brief

In reconstructive surgery, closing of bone-, nerve-, muscle-, vascular- and skin defects of either teratological, traumatological or pathological disposition, is endeavoured by transposition, transplantation or replantation of tissue. In all cases the final outcome largely is determined by the process of tissue regeneration as *de novo* synthesis of fibrous tissue (scar tissue) has a strong negative impact on functional and aesthetic final outcome (tissue adhesions, scar formation, fibrosis, loss of function).

The purpose of this program is the development, registration and evaluation of new reconstructive techniques to repair tissue defects. Furthermore, strategies to decrease the synthesis of fibrous tissue are developed and tested.

1. Short and long term evaluation of peripheral nerve regeneration: electromagnetic registration to measure axonal activity (co-operation with Clin Neurofysiol), functional outcome studies, adhesion studies, neuroma treatment. The pathogenesis of cold intolerance.
2. Short and long term evaluation of tendon repair: functional outcome studies, adhesion studies. Biomechanics of Tendon Repair.
3. Tissue engineering of autologous mucosa and/or fat for facial post-oncology reconstructions: tissue engineering, in vivo angiogenesis, functional outcome.
4. Post mastectomy breast reconstruction; a study of the psychological implications of DIEP flap and implant procedures.
5. Wound regeneration: understanding and improving the process of wound repair. In experimental animals by influencing the extracellular matrix in a wound bed and studying its effects on wound regeneration, immune response and scar tissue formation. In humans by studying the effects of vacuum-assisted wound closure and the treatment with heparan sulfate mimics.
6. Pathogenesis, treatments and imaging of craniofacial malformations and associated brain malformations (isolated and syndromic craniosynostosis and facial clefts), combined with short-term and long-term functional evaluation (with participation of the Departments within Erasmus MC of Clinical Genetics, Orthodontics, Bioinformatics, Neurosurgery, Radiology, Maxillofacial Surgery, ENT, ophthalmology, intensive care-pediatrics, Medical Psychology and Psychotherapy, and Paediatric Psychiatry and outside the Erasmus MC with Prof. Dr. J. Oosterlaan, dept clinical neuropsychology VU Amsterdam; Prof dr P.R. Luijten, dept radiology UMC Utrecht; dr R. Hayward and dr D. Dunaway Great Ormond Street London; prof. A.O.M. Wilkie, Oxford; dr E. Arnaud and D. Renier, Hopital des Enfants Malades Paris).
7. Genetic and embryologic aspects of congenital malformations of the extremities (with participation of the Departments of Clinical Genetics).
8. Aesthetic, functional, surgical, and quality of life outcomes after reconstructive (micro)surgery following treatment of different malignant tumours.
9. General evaluation of new techniques following hand and general microsurgery (changes in bold)

### Keyfigures

Department	SP1	SP2	SP3	SP4	SPtot	T1	T2	T3	Ttot	IS	FS	OP	Ptot
oral and maxillofacial surgery	0,2	0	0	0	0,2								
pediatric psychiatry	0,1	0	0	0	0,1								
plastic and reconstructive surgery	4,95	0	0	5,95	10,9								
rehabilitation	0	0	0	0,5	0,5								
<b>Total</b>	<b>5,25</b>	<b>0</b>	<b>0</b>	<b>6,45</b>	<b>11,7</b>	<b>4</b>	<b>0</b>	<b>0</b>	<b>4</b>	<b>36</b>	<b>3</b>	<b>9</b>	<b>52</b>

### Thesis

Meulen, J.J.N.M. van der (2009, december 08). On trigonocephaly. EUR. Prom./coprom.: Prof.Dr. S.E.R. Hovius & J.M.E. Okkerse.

Moolenburgh, S.E. (2009, november 20). Psychological, functional and aesthetic outcome after nasal reconstruction. EUR. Prom./coprom.: Prof.Dr. S.E.R. Hovius, Dr. M.A.M. Mureau & Dr. S.O.P. Hofer.

Moues, C.M. (2009, december 17). Topical negative pressure therapy in wound care. Effectiveness and guidelines for clinical application. EUR. Prom./coprom.: Prof.Dr. S.E.R. Hovius & F. Heule.

Ruijs, A.C.J. (2009, november 11). Post-traumatic cold intolerance in median and ulnar nerve injury patients. EUR. Prom./coprom.: Prof.Dr. S.E.R. Hovius, Dr. R.W. Selles & Drs. J.B. Jaquet.

### Article/Letter to the editor

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## EMC NIHES-01-64-01 - Epidemiology of diseases

### Programme design in brief

This program includes scientific research in cardiovascular epidemiology, neuroepidemiology and ophthalmologic epidemiology. Cardiovascular epidemiologic research focuses on the determinants of atherosclerosis and coronary heart disease in the elderly, and on cardiovascular diseases in women. The research is based on the Rotterdam Study and addresses inflammation markers and hemostasis as determinants of cardiovascular diseases in the elderly, and the effects of menopause, endogenous hormones and hormone replacement therapy in women. Neuroepidemiologic research focuses on the etiology of neurodegenerative and cerebrovascular diseases, including dementia and Alzheimer's disease, Parkinson's disease, stroke and cerebral white matter lesions. The research emphasizes the role of vascular factors in the etiology of these diseases, with use of state of the art neuroimaging techniques. Ophthalmological epidemiologic research focuses on determinants of macula degeneration and glaucoma. The emphasis is on the putative role of genetic factors and vascular factors in etiology of these diseases.

### Key figures

Department	SP1	SP2	SP3	SP4	SPtot	T1	T2	T3	Ttot	IS	FS	OP	Ptot
epidemiology	5,22	7,24	3,65	0,96	17,07								
internal medicine	0	2	0	0	2								
neurology	0,08	0	0	0	0,08								
radiology	0,42	0	0	0	0,42								
Total	5,72	9,24	3,65	0,96	19,57	4	0	0	4	71	4	1	80

### Thesis

Haag, M.D.M. (2009, februari 13). NSAIDs and Cardiovascular Drugs In Neurodegenerative and Cerebrovascular Diseases. EUR (182 pag.). Prom./coprom.: Prof.Dr. M.M.B. Breteler & Prof.Dr. B.H.C. Stricker.

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### Article/Letter to the editor

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## EMC NIHES-01-64-02 - Basic epidemiologic research

### Programme design in brief

This program includes research in the fields of genetic epidemiology and endocrinologic epidemiology. Genetic epidemiologic research aims at quantifying the population risk of disorders associated with genetic risk factors and at identifying new genetic factors involved in complex genetic disorders. For the empirical studies, the emphasis is on neurodegenerative and neurovascular disorders. The work in endocrinologic epidemiology focuses on the question whether circulating hormone levels are associated with incident diseases of the elderly and with parameters of frailty. The emphasis is on determinants of locomotor diseases (osteoporosis, osteoarthritis) and on sex hormones and thyroid hormones as determinants of disease.

### Key figures

<i>Department</i>	<i>SP1</i>	<i>SP2</i>	<i>SP3</i>	<i>SP4</i>	<i>SPtot</i>	<i>T1</i>	<i>T2</i>	<i>T3</i>	<i>Ttot</i>	<i>IS</i>	<i>FS</i>	<i>OP</i>	<i>Ptot</i>
epidemiology	1,92	5,16	1,7	0,75	9,53								
Generation R	0	0,11	0	0	0,11								
gynaecology/obstetrics	0,2	0	0	0	0,2								
Total	2,12	5,27	1,7	0,75	9,84	5	1	0	6	86	4	1	97

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## EMC NIHES-01-64-03 - Clinical epidemiology

### Programme design in brief

This program comprises three parts: clinical epidemiology in collaboration with radiology, biostatistics and pharmaco-epidemiology. The clinical epidemiology group collaborates with the department of radiology in a joint research program for the Assessment of Radiological Technology (ART program). This program's research focuses on the assessment of medical imaging technology, especially diagnostic imaging but also image-guided therapies, with an emphasis on cardiovascular disease. Methodological research in the ART program focuses on developing the methods for evaluating diagnostic imaging procedures using stochastic modeling and utility assessment related to diagnostic testing and therapeutic outcomes. The biostatistics group provides quantitative support for various studies in the Erasmus MC. For its own research, the biostatistics group focuses on the application of new developments in statistics, such as new analytic methods for dependent observations, like random effect models, Bayesian methods and sequential analysis. Pharmaco-epidemiologic research focuses on intended effects of medications, and the effects of medication use under common circumstances in large populations.

### Key figures

Department	SP1	SP2	SP3	SP4	SPtot	T1	T2	T3	Ttot	IS	FS	OP	Ptot
epidemiology	3,52	2,84	1	1,31	8,67								
immunology	1	0	0	0	1								
internal medicine	0,5	0	0	0	0,5								
medical ethics and philosophy of medicine	0	0,8	0	0	0,8								
Total	5,02	3,64	1	1,31	10,97	5	0	0	5	44	2	0	51

### Thesis

Becker, M.L. (2009, november 04). Individualizing pharmacotherapy. Genetic factors and co-prescribed drugs affecting pharmacotherapy. EUR (253 pag.). Prom./coprom.: Prof.Dr. B.H.C. Stricker, Dr. A.G. Vulto & Dr. L.E. Visser.

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### Article/Letter to the editor

Becker, M.L., Visser, L.E., Newton-Cheh, C., Hofman, A., Uitterlinden, A.G., Witteman, J.C.M. & Stricker, B.H.C. (2009). A common NOS1AP genetic polymorphism is associated with increased cardiovascular mortality in users of dihydropyridine calcium channel blockers. *British Journal of Clinical Pharmacology*, 67(1), 61-67.

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## EMC NIHES-01-66-01 – Biostatistics

### Programme design in brief

This program comprises two parts: general medical statistics and genetic statistics. The activities of the general medical statistics group are research in biostatistics on topics such as statistical modeling of complex data structures, clinical trial methodology, Bayesian methods, meta-analyses, smoothing approaches, survival analysis, etc. Monthly seminars, working groups on specific methodological topics, two courses/year and a yearly symposium are activities of the group to promote statistical research together with quantitative researchers from the whole of Erasmus MC, but also to make publicity for the department outside Erasmus University. Further, the group provides statistical consultancy to and collaborates with various clinical departments and the department of epidemiology. There is also a strong participation of the group in the Nihes and Erasmus Winter and Summer teaching programs.

In addition, the activities on genetic statistics concentrate on high-throughput methods: microarrays, SNPs, proteomics and metabolomics. Of special interest is also the cooperation with the Bioinformatics Department, to integrate data bases, friendly interfaces and standard tools for data visualization with existing and newly developed statistical methods.

### Key figures

<i>Department</i>	<i>SP1</i>	<i>SP2</i>	<i>SP3</i>	<i>SP4</i>	<i>SPtot</i>	<i>T1</i>	<i>T2</i>	<i>T3</i>	<i>Ttot</i>	<i>IS</i>	<i>FS</i>	<i>OP</i>	<i>Ptot</i>
biostatistics	2,5	0	0	0,3	2,8								
gastroenterology & hepatology	0,3	0	0	0	0,3								
Total	2,8	0	0	0,3	3,1	0	0	0	0	72	9	11	92

### Article/Letter to the editor

Bannink, E.M.N., Palen, R.L.F. van der, Mulder, P.G.H. & Muinck Keizer-Schrama, S.M.P.F. (2009). Long-term follow-up of GH-treated girls with Turner Syndrome: BMI, blood pressure, body proportions. *Hormone Research*, 71, 336-342.

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**Part of book - abstract**

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## EMC NIHES-02-65-01 - Effects of screening and clinical interventions on population health

### Programme design in brief

The research programme, originally titled - Effects of interventions on population health-aims to contribute to improved population health by evaluating the favourable and unfavourable effects and the cost-effectiveness of health care interventions, particularly screening for diseases and clinical interventions, and tropical disease control.

Our commitment to the improvement of population health is combined with a strong emphasis on quantitative research methods, thereby maximising quality and public health impact. We conduct observational as well as experimental studies and often use advanced statistical methods and computer simulation models. A shared research focus includes development and application of dynamic age-structured population health models; standardization of research methodology with respect to descriptive health status measurement, development and application of statistical methods and use and optimization of micro-simulation modelling.

This programme consists of 3 sections: evaluation of screening, medical decision-making, and infectious diseases control (Prof.dr. H.J. de Koning, Prof.dr. E.W. Steyerberg, Dr. JH Richardus, Dr. A. van der Heide, Prof.dr. J.D.F. Habbema).

In evaluation of screening, three types of study are undertaken:

(1) Monitoring and evaluation of ongoing screening programmes and randomised trials. (2) Prospective evaluation and prediction of screening strategies, with emphasis on impact on morbidity and mortality and on cost-effectiveness.

(3) Mathematical modelling of new developments and research questions. Specific fields are cancer, cardiovascular disease, prenatal screening and child health surveillance, developmental disorders and child abuse, and genetic disorders.

In evaluation of clinical care, three questions are studied: what is wrong with the patients? (diagnostics), what can be done about it? (therapy choice), and what will happen? (prognosis). Emphasis is on studying prognosis and on methodological issues, and on medical decisions concerning the end of life.

In infectious disease control, research is focused on collection and analysis of empirical data, and development and application of models for the epidemiology and control of important infectious diseases of the tropical zone (onchocerciasis, lymphatic filariasis, schistosomiasis, leprosy, tuberculosis, malaria and sexually transmitted diseases), and in the Western context like Hepatitis A, B and C, and STD's.

### Key figures

<i>Department</i>	<i>SP1</i>	<i>SP2</i>	<i>SP3</i>	<i>SP4</i>	<i>SPtot</i>	<i>T1</i>	<i>T2</i>	<i>T3</i>	<i>Ttot</i>	<i>IS</i>	<i>FS</i>	<i>OP</i>	<i>Ptot</i>
public health	3,79	12,91	6,34	9,78	32,82								
Total	3,79	12,91	6,34	9,78	32,82	13	3	0	16	176	12	12	216

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#### **Book - monograph - book editorial**

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## EMC NIHES-02-65-02 - Determinants and primary prevention

### Programme design in brief

The research programme 'Determinants of Population Health' aims to contribute to a better understanding of the specific role of social and physical determinants in population health and to develop effective primary preventive interventions that will enhance population health.

The research on determinants of population health addresses the specific contribution of a wide array of factors to population health, often by applying novel quantitative methods that are able to capture the complex interrelationships among individual characteristics and behaviours and the living and working environment. This knowledge is subsequently used to develop and evaluate the effectiveness of primary preventive interventions and associated costs and benefits. These interventions are conducted in variety of environments, such as schools, workplaces, and neighbourhoods. The research programme combines 5 research groups: determinants of health-related behaviours, social determinants of population health, occupational health, cancer surveillance, and youth health care (Prof.dr. A. Burdorf, Prof.dr. JW Coebergh, Dr. F.van Lenthe, Dr. H. Raat, Prof.dr. J. Mackenbach)

Important contributions to public health addressed in this research programme include:

- healthy growth and development of youth
- healthy ageing
- reducing health inequalities
- work and health
- combatting the obesity epidemic
- improved cancer surveillance
- tailored lifestyle interventions
- improving health in cities
- international health.

### Key figures

Department	SP1	SP2	SP3	SP4	SPtot	T1	T2	T3	Ttot	IS	FS	OP	Ptot
addiction research institute Rotterdam (IVO)	0	0	0	0,8	0,8								
epidemiology	0	0,71	0,24	0,28	1,23								
public health	4,47	9,08	5,85	3,52	22,92								
Total	4,47	9,79	6,09	4,6	24,95	12	1	0	13	112	10	18	153

### Thesis

Baars, J.E. (2009, januari 16). Hard to reach?: hepatitis B vaccination among high-risk groups. EUR (159 pag.). Prom./coprom.: Prof.Dr. H. van de Mheen, Prof.Dr. H.F.L. Garretsen & B. Boon.

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Roskam, A.J.R. (2009, mei 14). Cross-national comparisons of socioeconomic differences in overweight and obesity. EUR (210 pag.). Prom./coprom.: Prof.Dr. J.P. Mackenbach & Dr. A.E. Kunst.

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### Article/Letter to the editor

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#### **Book - monograph - book editorial**

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## EMC NIHES-02-67-01 - Clinical research in general practice.

### Programme design in brief

The aim of research activities of the Department of General Practice is to do research of academic quality, based on and derived from issues in general practice, aimed at the enhancement of the quality of general practice and supporting the academic workplace of general practice. The research encompasses the scientific basis and quality improvement of general practice. The most important components are studies of occurrence and course of disease and clinical research into the effects of preventive, diagnostic, and therapeutic strategies in general practice by clinical epidemiologic studies and randomised trials. The results of these studies are used in decision analysis and guideline development. Within this research programme patient-centered studies in the field of musculoskeletal disorders and diseases in childhood dominate. In view of the comprehensive approach of general practice other fields are occasionally addressed as well. Main research themes of the chair of Intellectual Disability Medicine (Prof Evenhuis) are 'Cerebral visual impairment', 'Comorbidity in children with severe generalized cerebral palsy' and, since 2008, 'Healthy Ageing and intellectual disabilities.

### Key figures

Department	SP1	SP2	SP3	SP4	SPtot	T1	T2	T3	Ttot	IS	FS	OP	Ptot
family practice	8,45	4,05	0	4,89	17,39								
Total	8,45	4,05	0	4,89	17,39	3	0	0	3	57	7	2	69

### Thesis

Belo, J.N. (2009, juli 01). Non-traumatic knee complaints in adults in general practice. EUR (168 pag.). Prom./coprom.: Prof.Dr. B.W. Koes & Prof.Dr. S.M.A. Bierma-Zeinstra.

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### Article/Letter to the editor

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## EMC NIHES-03-30-01 - Implementation of diagnostic and interventional imaging technology

### Programme design in brief

The research program focuses on the implementation of new techniques used for diagnostic and interventional imaging technology. Specific topics of interest within the program are Magnetic Resonance (MR) technology (including interventional MRI), Multidetector Spiral Computed Tomography (MSCT), and interventional radiology. Projects involve high-speed MR-angiography of coronary/carotid arteries and veins, MRI of organ perfusion (e.g. brain perfusion in stroke, perfusion in transplant organs), real-time imaging of catheter and needle manipulations, MRI-temperature mapping (to monitor thermo-ablative treatment of localized heat-induced gene therapy), and percutaneous treatment of vascular disease. Emphasis is placed on carotid artery stenting, percutaneous treatment of aortic aneurysmal disease in elective and acute situations, creation of Transjugular Intrahepatic Portosystemic Shunts (TIPS), thermo-ablation with laser or focused percutaneous ultrasound, and non-invasive coronary angiography with MSCT.

A parallel line of investigation implements molecular imaging techniques developed in EMC NIHES-03-30-03. Although we principally use MRI (3T) imaging techniques, the potential exists to use MSCT for molecular imaging for projects for which this would be advantageous. Possible future directions include quantification of tumor perfusion and angiogenesis, heat-induced local drug delivery or gene therapy, and/or applying heat-sensitive contrast agents.

There is extensive collaboration with clinical groups within Erasmus MC  $\zeta$  including the Departments of Internal Medicine, Pediatrics, Vascular Surgery, Cardiology, Neurology, and Surgical Oncology  $\zeta$  and with Erasmus MC basic science groups  $\zeta$  including the Department of Experimental Cardiology/Thorax Center and the Department of Medical Informatics

### Key figures

Department	SP1	SP2	SP3	SP4	SPtot	T1	T2	T3	Ttot	IS	FS	OP	Ptot
cardiology	0,11	0	0	0	0,11								
epidemiology	0,03	0	0	0	0,03								
neurosciences	0,2	0	0	0	0,2								
pediatrics	1,04	0	0	0	0,2								
radiology	6,32	1,27	0,75	0,3	8,64								
surgery	0,03	0	0	0	0,03								
Total	7,73	1,27	0,75	0,3	10,05	7	0	0	7	101	30	6	144

### Thesis

Meijboom, W.B. (2009, maart 18). Diagnostic performance of 64- slice ct coronary angiography. EUR. Prom./coprom.: Prof.Dr. P.J. de Feyter & Prof.Dr. G.P. Krestin.

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### Article/Letter to the editor

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**Part of book - abstract**

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Dongen, KWA van, Bakker, J.F., Paulides, M.M., Obdeijn, A.I.M. & Rhoon, G.C. van (Eds.). (2009). *Design of an ultrasound cylindrical phased-array for hyperthermia breast cancer treatment*. NAG/DAGA: International Conference on Acoustics.

## EMC NIHES-03-30-02 - Assessment of diagnostic and interventional imaging technology

### Programme design in brief

The research program focuses on the assessment of diagnostic imaging technology and image-guided therapies. The assessment includes clinical efficacy, patient outcomes, and costs-effectiveness. There is a special interest in the assessment of new imaging technology for cardiovascular disease, including such techniques as magnetic resonance angiography, computed tomography angiography, imaging of vulnerable plaque, and molecular imaging. The research methods employed are from clinical epidemiology, decision sciences, and medical technology assessment. The methodological research of the group focuses on developing the methods and study design for evaluating diagnostic imaging technology. The long-term goal of the program is to provide relevant information for implementing evidence-based clinical services

### Key figures

Department	SP1	SP2	SP3	SP4	SPtot	T1	T2	T3	Ttot	IS	FS	OP	Ptot
epidemiology	2,78	0	0	0	2,78								
radiology	2,47	0	0	0	2,47								
radiotherapy	0,5	0	0	0	0,5								
Total	5,75	0	0	0	5,75	2	0	0	2	17	1	0	20

### Thesis

Groot Koerkamp, B. (2009, december 01). Uncertainty in medical decision making. Knowing how little you know. EUR (232 pag.). Prom./coprom.: Prof.Dr. M.G.M. Hunink, Prof.Dr. T. Stijnen & M.C. Weinstein.

Oei, E.H.G. (2009, maart 04). Magnetic resonance imaging for traumatic knee injury. EUR (219 pag.). Prom./coprom.: Prof.Dr. M.G.M. Hunink & A.Z. Ginai.

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## EMC NIHES-03-30-03 - Development of acquisition and processing techniques for diagnostic imaging

### Programme design in brief

The general goal of this research program is to investigate and validate new diagnostic and therapeutic imaging techniques for both Computed Tomography (CT) and Magnetic Resonance Imaging (MRI). We focus on image acquisition, processing and segmentation of three (or higher) dimensional image data in order to be able to enhance patient care.

The main research focuses are the improvement of existing and development new computerized techniques for the segmentation of high-dimensional diagnostic images. Specific goals are (a) to increase the outcome of image segmentation techniques, (b) to develop new ways of visualizing high-dimensional data sets by combining existing techniques (surface and volume rendering) with newly developed methods (virtual reality), and (c) to improve user-interfaces and develop automated procedures to assist the end-user with the post-processing, segmentation and visualization of radiological image data.

Furthermore, image registration, data fusion and measurements in diagnostic images will be developed and validated.

We are also interested in optimizing acquisition protocols so that region-of-interest imaging makes use of the maximum capabilities of our imaging systems. This will benefit both diagnosis and therapeutical monitoring tasks. The initial target is enhanced direct visualization of the epicardial coronary anatomy, by which we can establish the presence, site, severity, and/or status of coronary atherosclerotic disease. Further targets are assessment of ventricular function and characterization of atherosclerotic plaque composition. We will than use the optimized protocols to investigate the diagnostic possibilities and diagnostic accuracy of MR cardiac and coronary imaging and to determine the possible clinical indications for MR imaging of both native coronary artery disease and coronary bypass disease.

Molecular Imaging is an area demanding international attention. Acquisition of information on the cellular and molecular level and subsequent analysis is expected to have a profound impact on the diagnosis, monitoring and treatment of diseases that have the potential of being redefined in terms of their characteristics genetic or molecular abnormalities. We are optimizing our imaging systems (with an emphasis on MRI) to provide near-cellular resolution and expect to move into animal studies soon.

### Key figures

<i>Department</i>	<i>SP1</i>	<i>SP2</i>	<i>SP3</i>	<i>SP4</i>	<i>SPtot</i>	<i>T1</i>	<i>T2</i>	<i>T3</i>	<i>Ttot</i>	<i>IS</i>	<i>FS</i>	<i>OP</i>	<i>Ptot</i>
Epidemiology	0	0,38	0	0	0,38								
medical informatics	2,45	6,71	0,44	0,13	9,73								
nuclear medicine	0	0	0,5	0	0,5								
Orthopaedics	0	0	0	0,38	0,38								
Radiology	5,06	9,24	0,5	0,57	15,37								
Total	7,51	16,33	1,44	1,08	26,36	1	0	0	1	18	10	10	39

### Thesis

Smal, I. (2009, juni 10). Particle filtering methods for subcellular motion analysis. EUR (155 pag.). Prom./coprom.: Prof.Dr. W.J. Niessen & Dr.Ir. H.W. Meijering.

### Article/Letter to the editor

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**Book editorship**

Brown, M., Bruijne, M. de, Ginneken, B van, Kiraly, A, Kuhnigk, JM, Lorenz, CH., McClelland, J., Mori, K, Reeves, A. & Reinhardt, J (Eds.). (2009). *Second International Workshop on Pulmonary Image Analysis*. --: CreateSpace.

## EMC NIHES-03-77-01 - Structuring of medical knowledge

### Programme design in brief

Our first line of research deals with the formalization of medical knowledge, that is the description of knowledge according to a formal representation so that the knowledge can be made operational in a computer system. We do not limit ourselves to knowledge that is provided by experts or is described in journals or books, but also focus on the (semi)automatic extraction of knowledge from documented databases. With respect to documented databases, attention is paid to automated learning techniques for modeling medical knowledge, tailored to the specific problems in the medical domain. This includes research in the representation and use of uncertainty in medical knowledge, and *learning* by computers in interaction with human experts so that the specific strengths of both human and machine are utilized. It is of great importance to test the results of our research (both methodology and prototypes of systems) in the diverse application domains for their usability, in close collaboration with other investigators and clinical partners.

### Key figures

Department	SP1	SP2	SP3	SP4	SPtot	T1	T2	T3	Ttot	IS	FS	OP	Ptot
medical informatics	1	4,01	0	0,7	5,71								
Total	1	4,01	0	0,7	5,71	0	0	0	0	19	1	0	20

### Article/Letter to the editor

Atsma, F, Schouw, Y.T. van der, Grobbee, D.E., Kors, J.A. & Bartelink, MLEL (2009). Lifetime endogenous estrogen exposure and electrocardiographic frontal T axis changes in postmenopausal women. *Maturitas*, 63(4), 347-351.

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## EMC NIHES-03-77-02 - Structuring of medical data

### Programme design in brief

Medical data recorded in the context of clinical care should not only be available for patient care, but also be accessible for other purposes, such as scientific research, quality assurance, or management. The use of computers to record medical data is a necessary first step to allow data to be used for multiple purposes. Scientific research, however, has shown that the purpose of data collection is closely related to the nature and content of the data recorded. Different usage of the data creates different demands: data requirements in the context of a clinical trial are different than those in the context of management or quality assurance.

In the research theme Structuring of Medical Data, the department of Medical Informatics studies methodologies that allow recording of data for multiple purposes. Our research is focused on generic models for medical data. The scientific challenge is to formulate generic models that are applicable to different specialties. The models, however, have to be usable in daily practice. An essential part of this research, therefore, is the validation of these models in daily care. Once electronic patient records are available, our research focus shifts to on the actual use of the data for multiple purposes. Together with clinicians, we study systems aimed at improving the quality of care. Together with other disciplines we also analyze observational databases and study issues involved in naturalistic trials

### Key figures

Department	SP1	SP2	SP3	SP4	SPtot	T1	T2	T3	Ttot	IS	FS	OP	Ptot
epidemiology	0	0,73	0	0,19	0,92								
medical informatics	0,52	4,95	0	5,05	10,52								
Total	0,52	5,68	0	5,24	11,44	1	0	0	1	45	3	0	49

### Thesis

Trifiro, G. (2009, juni 26). Use and safety of psychotropic drugs in elderly patients. EUR (266 pag.). Prom./coprom.: Prof.Dr. M.C.J.M. Sturkenboom.

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## EMC NIHES-04-55-01 - Assessment, aetiology and course of child and adolescent psychiatry

### Programme design in brief

The main objective of this program is to study the frequency, determinants and course of child psychiatric disorders, such as anxiety, depression, somatoform disorders, aggressive and antisocial behaviours, hyperactivity, and developmental problems (autism, learning disorders, mental retardation). The program uses epidemiological methods to study psychopathology in general population, at risk, and clinical samples. These studies aim to develop assessment instruments and diagnostic procedures; assess the prevalence and incidence of child and adolescent disorders; study the onset and course of psychopathology from infancy to young adulthood using longitudinal and genetically sensitive research designs; assess the effectiveness of preventive and treatment approaches.

#### General population studies

The prevalence and course of child and adolescent psychiatric conditions has been studied in Dutch general population samples across the age range from 2 to 30 years. The influence of life events and personal and social-environmental determinants has been studied, and cross-cultural and secular trend analyses have been performed. These studies confirmed the high prevalence (7%) of serious psychiatric problems in Dutch children and adolescents as well as the cross-cultural similarity of child/adolescent psychopathology, and indicated that the use of mental health services at this age is mainly determined by severity of psychopathology, additional handicaps, and family burden. Longitudinal studies showed that earlier psychopathology is the strongest predictor of later psychopathology from childhood up to early adulthood, and is a strong predictor of later functional problems. Recently, the transgenerational transmission of psychopathology is being studied in a 24-year longitudinal design in which parental ratings of children's problem behaviour is compared with ratings on the same instrument obtained for the offspring 24 years later. Studies in general population samples also yielded improvements in the standardized assessment of psychopathology, as well as contributions to the methodology of longitudinal studies (accelerated designs; developmental pathway analysis). The second generation of longitudinal studies in which determinants of the emergence and continuity of child psychopathology is being studied is well on its way. The focus is on two new large-scale longitudinal studies. The first, Generation R, is a multidisciplinary cohort study following 10.000 children from prebirth into young adulthood. The second, Trails, is a cohort study of 2.500 10-year-olds in the northern provinces. The Rotterdam group focuses on anxiety disorders, illegal substance use, and conduct disorders. Both Generation R and Trails aim to unravel etiological mechanisms, with a special focus on biological determinants and gene-environment interactions and correlations. The first results of Generation R show the effects of smoking (both cannabis and cigarettes) on intrauterine growth and on early brain development. In Trails the associations between autonomous nervous functioning and HPA axis functioning with both externalizing and internalizing problems have been studied.

#### At risk and clinical populations

We have assessed the prevalence and longitudinal course of problem behaviours and quality of life in ethnic minority groups, adopted children, children and adolescents with mental retardation, children with psychiatric conditions, and children with medical conditions (e.g. craniofacial abnormalities, congenital cardiac conditions, meningococcal sepsis). Several studies on referred samples showed a very strong continuity of psychopathology up to 10 years after referral. Only few factors (learning problems, temperament, stress, family functioning) showed predictive power of later psychopathology over and above severity of earlier psychopathology. However, (chronic) physical problems appear to have considerable power in the prediction of later psychopathology (e.g. in mentally retarded children and adolescents). Studies on samples with chronic somatic disorders show the importance of cerebral involvement in child development, as well as the important role of psychological and personality factors in coping with these conditions. Intervention studies aiming anxiety disorders have started.

#### Genetics

In collaboration with the Free University Amsterdam, we have conducted (longitudinal) twin and adoption studies to determine genetic and environmental influences on problem behaviours in young children. Recent findings show changes in genetic influences on psychopathology from preschool- to school age, differential genetic and environmental influences on co-morbid psychopathological problems as well as genetic influences on the stability of problem behaviours. Considerable contributions have been made to the development of estimation methods in quantitative behavioural genetics (e.g. rater bias models). The behavioural genetic studies continue the study of large genetically sensitive samples (twins; adopted children) well into puberty using longitudinal designs and now include the detection of genetically sensitive syndromes of psychopathology (e.g. disruptive disorders). We are currently expanding this research by looking at the association between child psychiatric disorders (ADHD, anxiety disorders) and presynaptic gene networks.

### Key figures

Department	SP1	SP2	SP3	SP4	SPtot	T1	T2	T3	Ttot	IS	FS	OP	Ptot
Generation R	0	0,39	0	0	0,39								
pediatric psychiatry	2,45	6,71	0	10,53	19,69								
Total	2,45	7,1	0	10,53	20,08	5	0	0	5	60	3	21	89

### Thesis

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**Article/Letter to the editor**

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#### **Book - monograph - book editorial**

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#### **Part of book - abstract**

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## EMC NIHES-04-56-01 - Adaptation of (future) patients to disease and treatment in order to improve counselling and guidance

### Programme design in brief

This programme investigates the emotional response to disease and treatment, and the ways to influence these emotions positively. The principal medical topics addressed are: 'pain', 'quality of life', 'clinical genetics', 'psychotherapy' and 'reproductive medicine'. The programme is part of NIHES and carried out with many clinical departments of the Erasmus MC.

### Key figures

<i>Department</i>	<i>SP1</i>	<i>SP2</i>	<i>SP3</i>	<i>SP4</i>	<i>SPtot</i>	<i>T1</i>	<i>T2</i>	<i>T3</i>	<i>Ttot</i>	<i>IS</i>	<i>FS</i>	<i>OP</i>	<i>Ptot</i>
medical psychology & psychotherapy	3,41	1,45	1,93	1,67	8,46								
Total	3,41	1,45	1,93	1,67	8,46	3	0	0	3	37	2	0	42

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## EMC NIHES-05-63-03 - Competition and regulation in health care (theme 1)

### Programme design in brief

The programme "structure and finance of health care" has a strong economic perspective as well as a judicial perspective. Research focuses on some fundamental aspect of the market-oriented health care reforms that are taking place in the Netherlands as well as in many other countries. The risk-adjuster "Pharmacy Cost Group", developed by the health economics group, is considered to be in the forefront of the international risk adjustment research. The Dutch government has implemented this new risk-adjuster in the Dutch health insurance system in 2002. Research activities are currently dealing with the following topics: structure of health care systems, legal aspects of health care reform, uncertainty and equilibrium on the market for health insurers, regulated competition in health care, competition policy, risk adjusted premium subsidies for health insurance, determinants of consumer choice of health plan, consumer information, bonuses for GPs, equity in the finance and delivery of health care and the consequences of the European Union for structure and finance for the Dutch Health care system. The research programme on "equity in health and health care" focuses on the national and international assessment of health equity and inequality. The scope of the research activities has broadened over the period under consideration from the developed world (OECD countries) to the less developed world. In collaboration with the World Bank the methods for measuring inequality and inequity have been adapted to low-income countries and equity objectives, and have been applied to data from a number of developing nations. The measurement methods of the ECuity Project, which is co-ordinated by the group, have now become adopted as a worldwide standard for assessing the equity performance of health systems and the consequences of reforms, as witnessed by their adoption or explicit reference in all major efforts at system (equity) performance evaluation such as the Rockefeller Foundation's Global Health Equity Initiative, the WHO's World Health Report, the World Bank's World Development Report and the OECD's Framework for Health System Performance

### Key figures

<i>Department</i>	<i>SP1</i>	<i>SP2</i>	<i>SP3</i>	<i>SP4</i>	<i>SPtot</i>	<i>T1</i>	<i>T2</i>	<i>T3</i>	<i>Ttot</i>	<i>IS</i>	<i>FS</i>	<i>OP</i>	<i>Ptot</i>
health policy and management	4,41	4,98	0	8,23	17,62								
Total	4,41	4,98	0	8,23	17,62	2	0	0	2	12	3	27	44

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#### **Book - monograph - book editorial**

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## EMC NIHES-05-63-02 - Quality and efficiency in health care (theme 2)

### Programme design in brief

The programme health technology assessment, which is organised and carried out within iMTA, has grown considerably in the period '97/2004. An important impetus at the start of the development in this period was a large grant from the Ministry of Health for iMTA to support medical associations in their development of practice guidelines. In these guidelines for medical practice not only effectiveness but also the cost-effectiveness of various preventive or curative strategies is considered when making recommendations on how to deal with a specific health problem. Furthermore, important methodological topics have been studied, such as the measurement and valuation of productivity costs, the analysis of models describing patients' preferences, the valuation of informal care in economic evaluation, statistical methods of economic evaluation, efficacy-effectiveness issues, and valuation of quality of life. The NWO-subprogram on methodology of 'health technology assessment' as part of the larger program on cost effectiveness of health care programs provided the opportunity to carry out new methodological projects. Furthermore, a large number of practical, often international, projects have been carried out for various diseases and health care programs. An innovative example is a large multinational trial on the management of BPH-treatment in 6 European countries. This is the first large-scale naturalistic prospective economic evaluation in Europe. Finally, a number of projects in low-income countries have been carried out, some of which in close cooperation with WHO Geneva. Almost 100% of the research in this programme is externally funded

### Key figures

<i>Department</i>	<i>SP1</i>	<i>SP2</i>	<i>SP3</i>	<i>SP4</i>	<i>SPtot</i>	<i>T1</i>	<i>T2</i>	<i>T3</i>	<i>Ttot</i>	<i>IS</i>	<i>FS</i>	<i>OP</i>	<i>Ptot</i>
health policy and management	4,53	7,21		26,72	38,46								
Total	4,53	7,21	0	26,72	38,46	3	0	0	3	55	19	24	101

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**EMC NIHES-05-63-01 - Health care management (theme 3)****Programme design in brief**

This research line focuses on the social, legal and organisational aspects of management of professional knowledge, quality systems, information and communication technology in health care and health care management. The programme aims to translate theories of organisation, management and policy into practical guidelines and recommendations for health care organisations. Case studies are undertaken to gain insight in the dynamics of inter- and intra-organisational networks and in opportunities for network management. Special emphasis is put on the quality and accessibility of health care for ethnic minorities. Finally the programme evaluates effects of new health care legislation

**Key figures**

<i>Department</i>	<i>SP1</i>	<i>SP2</i>	<i>SP3</i>	<i>SP4</i>	<i>SPtot</i>	<i>T1</i>	<i>T2</i>	<i>T3</i>	<i>Ttot</i>	<i>IS</i>	<i>FS</i>	<i>OP</i>	<i>Ptot</i>
health policy and management	6,28	5,08	0	11,11	22,47								
Total	6,28	5,08	0	11,11	22,47	3	0	0	3	26	7	39	75

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