

The mission of the Radboud Institute for Health Sciences (RIHS) is to improve clinical practice and public health. It does so by providing evidence of the efficacy and efficiency of existing and new tests, treatments and policies, as well as innovative modes of healthcare delivery, by training young researchers in methodologies for obtaining such evidence and by developing new methodologies for improved research programmes in this field.

As evidence is typically obtained in probabilistic and qualitative rather than deterministic and mechanistic ways, research tends to be done among patients or the general population rather than through laboratory-based models. The Institute's focus is on developing methodologies that optimize personalized healthcare and on the application of these tools in disease-oriented research themes. In line with the Radboudumc's mission of having 'a significant impact on healthcare', the Institute aims to bridge the gap between science and society. Societal impact is at the core of the Institute's ambitions.

Training of young researchers within the Institute is organized in a Royal Netherlands Academy of Arts and Sciences (KNAW)-accredited Graduate School.

Research at Radboudumc is organized in 18 themes. Four of these are embedded exclusively in the Donders Centre for Neuroscience and one in the Radboud Institute for Molecular Life Sciences (RIMLS). The theme 'Healthcare improvement science' is exclusive to RIHS. Within the other 12 themes RIHS researchers work closely together with colleagues at RIMLS. We believe that optimal progress can be achieved when molecule, man and population-oriented researchers work together on the same disease-oriented 'playing field'.

Healthcare improvement science

Theme leader: Prof. Gert Westert

The main focus is on the structure, process and outcomes of healthcare in daily practice, with the aim of improving performance and delivery from the perspective of the patient. Researchers study existing and new interventions at the micro and macro level. Their aim is to explore which interventions or structures work in what circumstances. Immediate value for patients is paramount.

Cancer development and immune defence

Theme leader: Prof. Joop Jansen

Researchers working in this theme investigate resistance to therapy, the tumour micro-environment, cancer-cell trafficking and the interaction between the immune system and cancer. This basic knowledge is translated into novel forms of therapy that targets tumour cells. Strategies are also developed for expanding and manipulating immune cells for clinical use, exploiting and boosting the power of the immune system. For the translational part of this work, researchers carry out phase I, II and III clinical trials.

Rare cancers

Theme leader: Dr Carla van Herpen

Despite the rarity of each of the 'rare' cancers (*i.e.* an incidence <6/100,000 per year), they represent in total about 22% of all cases of cancer. Due to their low frequency, rare cancers pose particular challenges. The main aim is to improve diagnosis and prognosis and to perform personalized clinical studies and translational bench-to-bedside research in patients with rare cancers. This is being performed in a national and international collaborative setting and in relationship with patient advocacy groups, where applicable.

Tumours of the digestive tract

Theme leader: Prof. Iris Nagtegaal

Research in this theme is designed to improve the prognosis and treatment of patients with tumours of the digestive tract, with a focus on sporadic and hereditary forms of colorectal and pancreatic cancer. The aim is to achieve better prevention of cancer in highrisk patients and develop and implement new diagnostic tools for staging and therapy response. In addition, researchers are developing treatment innovations, ranging from improved surgical techniques to immunotherapy.

Staff

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Prof. P.M.P. Poortmans (o) Prof. J.B. Prins (o) Prof. W.M. Prokop (o) Prof. P.L.C.M. van Riel (o) Prof. M. Ritskes-Hoitinga (o) Prof. G.A.P.J.M. Rongen (o) Prof. M.M. Rovers (o) Prof. H.M.J. van Schrojenstein Lantman (o) Prof. L.J. Schultze Kool (o) Prof. J.L.R.M. Smeets (o) Prof. P.A.G.M. de Smet (o) Prof. J.W.A. Smit (o) Prof. P. Smits (o) Prof. D. van Soolingen (e) Prof. A.F.H. Stalenhoef (o) Prof. H. Suryapranata (o) Prof. C.G.J. Sweep (o) Prof. D.J.O. Ulrich (o) Prof. J. van der Velden (o) Prof. A.J.A.M. van der Ven (o) Prof. A.L.M. Verbeek (o) Prof. N.J.J. Verdonschot (p) Prof. F.W.A. Verheugt (o) Prof. M.E. Vierhout (o) Prof. K.C.P. Vissers (o) Prof. C.P.M. van der Vleuten (o) Prof. A. Voss (o) Prof. C. van Weel (o) Prof. M.J.P. Wensing (o) Prof. G.P. Westert (o) Prof. J.F.M. Wetzels (o) Prof. M.H.W.A. Wijnen (o) Prof. J.H.W. de Wilt (o) Prof. J.R.L.M. Wolf (o) Prof. G.A. Zielhuis (o)

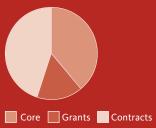
Tenured

Full Professors 24.7 FTE
Associate Professors 9.1 FTE
Assistant Professors 46.9 FTE
Researchers 76.9 FTE

Non-tenured

Researchers 149.0 FTE Doctoral candidates 141.5 FTE

Research funding



(o), (e) and (p) see Glossary

Sanden (o)

Prof. H.J. Out (e) Prof. A.J.P.M. Overbeke (e)

Urological cancers

Theme leader: Prof. Jack Schalken

Research involves identifying and evaluating the usefulness of new biomarkers and imaging techniques for risk, diagnostic, prognostic and predictive assessment in prostate, bladder and kidney cancer. In addition, new and existing prevention and treatment modalities in these types of cancer are evaluated. Synergistic multidisciplinary research collaboration – from molecular life sciences to population sciences – ensures a focus on 'utility' for patients and public health.

Women's cancers

Theme leader: Prof. Leon Massuger

The goal of this theme is to improve the patient-centred quality of care in women's cancers (breast, ovary, cervix, vulva, endometrium and pregnancy-related cancer) in partnership with patients through prevention, early diagnosis or implementation of new management strategies supported by a better understanding of carcinogenesis and tumour development, paying special attention to hereditary causes, preservation of fertility and individual post-treatment care.

Infectious diseases and global health

Theme leader: Prof. Mihai Netea

Researchers within this theme aim to have a significant and global impact on the control, treatment and elimination of infectious diseases. The theme combines cutting-edge research in immunology, microbiology, pharmacology and novel 'omics' methodology with translational and implementation research in immunology and infectious diseases. There are two research lines: Infectious diseases & host defence, and poverty-related infectious diseases.

Inflammatory diseases

Theme leader: Prof. Irma Joosten

Chronic inflammation is currently among the leading causes of morbidity and mortality in the Western world. Researchers working within this theme aim to translate results from the molecular and population level to the individual patient in order to improve diagnosis, disease management and the treatment of (chronic) inflammatory disorders.

Mitochondrial diseases

Theme leader: Prof. Jan Smeitink

The mission within this theme is to better understand the cellular bio-energetics in health and disease at all levels of complexity. Knowledge thus gained will enable the development of preventive measures and help to make substantial contributions to the development of rational treatment strategies for mitochondrial diseases.

Reconstructive and regenerative medicine

Theme leader: Prof. Wout Feitz

The focus within this theme is on the development and clinical translation of innovative diagnosis and therapies, including

regenerative medicine and nano-medicine, for personalized care and cure of patients needing reconstruction of lost or damaged tissues. This will be achieved through transdisciplinary research by leading research groups in medicine, dentistry, biochemistry, chemistry, biology and materials science.

Renal disorders

Theme leader: Prof. Joost Hoenderop

Current and future care of patients with renal and renal-related disorders can be considerably improved. To achieve this, researchers working on this theme aim to increase knowledge of the molecular and immunological basis of rare glomerular and tubular disorders; they develop biomarkers for optimal prediction of disease prognosis; and apply strategies for preventing and improving renal replacement therapy.

Vascular damage

Theme leader: Prof. Gerard Rongen

In this theme the aim is to increase understanding of the causes and consequences of vascular injury and to translate this knowledge into improved personalized cardiovascular healthcare. Early detection of atherosclerosis, primary and secondary prevention of atherosclerosis, optimal treatment of atherosclerosis to preserve end organ function, and implementation of effective diagnostics and therapies in practice are key focus areas.

Sensory disorders

Theme leader: Prof. Anneke den Hollander

The research focus of this theme is to improve our understanding of the molecular mechanisms of retinal diseases, hearing impairment and deaf-blindness. By developing and improving diagnostic and predictive tests for sensory diseases, researchers aim to bring new personalized rehabilitation strategies and therapies into the clinic, including gene therapy and retinal and auditory implants.

Research facilities

RIHS hosts some of the 18 formal Radboudumc Technology Centers (www.radboudumc.nl/Research/TechnologyCenters), which offer research facilities for internal and external researchers:

- The Radboudumc Biobank, an infrastructure for collecting, storing and managing biomaterial and associated clinical data in a standardized manner. It contains large databases and biobanks of general population samples (e.g. the Nijmegen Biomedical Study) and of specific patient groups (e.g. congenital malformations, cancer, rheumatoid arthritis and inflammatory bowel disease).
- A clinical trial centre offering logistics and data management for adult and paediatric human intervention studies.
- Consultation facilities for biostatistics, health economics and research with electronic health records.
- The Minimal Invasive Technology expert Center (MITeC) field lab, which is used to evaluate surgical innovations.



The group led by Mireille Broeders (Associate Professor of Health Evidence) is evaluating tailored follow-up schedules for patients treated for breast or colorectal cancer with curative intent, based on the length of the preclinical detectable phase and taking into account benefits and harm as well as patients' and health professionals' views. The same group is also investigating options for personalized breast cancer screening.

• The Technology Center Data stewardship (start planned early in 2016), which will provide practical knowledge, services and solutions to ensure good research practice according to the FAIR criteria (Findable, Accessible, Interoperable, and Re-usable), in a way that suits each individual study and researcher. In order to support this, a new Digital Research Environment (DRE) will be created in 2016.

In addition to these technology centres, the RIHS has the following are research facilities:

- Academic networks of GP practices (including the GP Continuous Morbidity Registration), nursing homes, institutions for people with an intellectual disability, municipality health services, care facilities for homeless people and dental care sites.
- The 'Koploper programme', a healthcare innovation in which professionals in primary care, public health, allied healthcare workers and the hospital jointly develop new approaches to prevention and care.
- A SYstematic Review Centre for Laboratory animal Experimentation (www.syrcle.nl), affiliated to the Technology Center 'Central Animal Laboratory'.
- Consultation services for quality of care (IQ healthcare).
- $\bullet \ \ Online \ platform \ for \ Personal \ Health \ Communities \ (Mijn Zorgnet).$

In December 2015, the new cyclotron was opened by the Dutch Minister of Health, Welfare & Sport, Mrs. Edith Schippers. The cyclotron will give a boost to research with medical isotopes done by several RIHS researchers (www.radboudtranslationalmedicine.nl).

Collaboration

Although several research lines in the RIHS play a leading role worldwide, the Institute as a whole is best known in the Netherlands. To secure a transition to a more international level,

RIHS offers two junior researcher positions annually for projects proposed by a RIHS researcher, together with an international partner. Appointed PhD candidates carry out at least one year of the research abroad. Furthermore, a researcher or teacher from abroad is annually honoured with the 'Richard Grol Visiting Scientist Award'.

There are formal collaborations with the Universities of Twente, Eindhoven and Groningen for, *e.g.* MITeC. At the Institute level, there is a formal partnership in the KNAW-accredited research school CaRe, together with CAPHRI (UM), NIVEL and EMGO+ (VUmc).

The Institute has formal ties with the HAN University of Applied Sciences, specifically in nursing sciences, physical therapy and musculoskeletal and neurohabilitation therapy, and with the Nederlands Paramedisch Instituut. The Institute is also a formal partner in 'Sterker op eigen benen', a consortium of five service providers for people with intellectual disabilities. Within the Academic Collaborative Centre AMPHI the Institute collaborates with seven Dutch Community Health Services (GGDs) and within UKON, the university network for long term care Nijmegen, RIHS collaborates with 14 care organizations (including 60 nursing homes). RIHS has collaborated with the Netherlands Comprehensive Cancer Organisation (IKNL), the National Expert and Training Centre for Breast Cancer Screening (LRCB), the RIVM, NIVEL, and the Dutch Ministry of Public Health, Welfare and Sports (VWS) for many years.

The RIHS collaborates in research and/or faculty exchanges with many universities around the world and with the European Union/ECDC, the WHO, UNESCO, the Centre on Birth Defects and Developmental Disabilities, various Centres for Disease Control and Prevention, INSERM (Paris), several Cochrane Centres, the

Key publications

Berg, S.W. van den, Gielissen, M.F., Custers, J.A., van der Graaf, W.T., Ottevanger, P.B., Prins, J.B. (2015). BREATH: Web-Based Self-Management for Psychological Adjustment After Primary Breast Cancer--Results of a Multicenter Randomized Controlled Trial. *J Clin Oncol*, 33, 2763-71.

Bosch, C.M. van den, Geerlings, S.E., Natsch, S., Prins, J.M., Hulscher, M.E. (2015). Quality indicators to measure appropriate antibiotic use in hospitalized adults. *Clinical Infectious Diseases*, *60*, 281-291.

Breukels, V., Jansen, K.C., van Heijster, F.H., Capozzi, A., van Bentum, P.J., Schalken, J.A., Comment, A., Scheenen, T.W. (2015). Direct dynamic measurement of intracellular and extracellular lactate in small-volume cell suspensions with 13 C hyperpolarised NMR. NMR Biomed, 30, doi: 10.1002/nbm.3341

Coenen, M.J., de Jong, D.J., van Marrewijk, C.J., Derijks, L.J., Vermeulen, S.H., Wong, D.R., Klungel, O.H., Verbeek, A.L., Hooymans, P.M., Peters, W.H., Te Morsche, R.H., Newman, W.G., Scheffer, H., Guchelaar, H.J., Franke, B. (2015). Identification of Patients With Variants in TPMT and Dose Reduction Reduces Hematologic Events During Thiopurine Treatment of Inflammatory Bowel Disease. *Gastroenterology*, 149, 907-917.

Cremers, R.G., Galesloot, T.E., Aben, K.K., van Oort, I.M., Vasen, H.F., Vermeulen, S.H., Kiemeney, L.A. (2015). Known susceptibility SNPs for sporadic prostate cancer show a similar association with "hereditary" prostate cancer. *Prostate*, 75, 474-83.

Eijsvogels, T.M., Thompson, P.D. (2015). Exercise Is Medicine: At Any Dose? *JAMA*, 314, 1915-1916.

Eppenga, W.L., Kramers, C., Derijks, H.J., Wensing, M., Wetzels, J.F., De Smet, P.A. (2015). Individualizing pharmacotherapy in patients with renal impairment: the validity of the Modification of Diet in Renal Disease formula in specific patient populations with a glomerular filtration rate below 60 ml/min. A systematic review. *PLoS One*, 10, e0116403.

Gameiro, S., Boivin, J., Dancet, E., de Klerk, C., Emery, M., Lewis-Jones, C., Thorn, P., Van den Broeck, U., Venetis, C., Verhaak, C.M., Wischmann, T., Vermeulen, N. (2015). ESHRE guideline: routine psychosocial care in infertility and medically assisted reproduction-a guide for fertility staff. *Hum Reprod*, 30, 2476-85.

Herwaarden, N. van, van der Maas, A., Minten, M.J., van den Hoogen, F.H., Kievit, W., van Vollenhoven, R.F., Bijlsma, J.W., van den Bemt, B.J., den Broeder, A.A. (2015). Disease activity guided dose reduction and withdrawal of adalimumab or etanercept compared with usual care in rheumatoid arthritis: open label, randomised controlled, non-inferiority trial. *BMJ*, 350, h1389.

van Kempen, J.A.L., Schers, H.J., Philp, I., Olde Rikkert, M.G.M., Melis, R.J.F. (2015). Predictive validity of a two-step tool to map frailty in primary care. *BMC Medicine*, 13, 287.

Koetsenruijter, J., Lieshout, J. van, Lionis, C., Portillo, M.C., Vassilev, I., Todorova, E., Foss, C., Gil, M.S., Knutsen, I.R., Angelaki, A., Mujika, A., Roukova, P., Kennedy, A., Rogers, A. & Wensing, M. (2015). Social Support and Health in Diabetes Patients: An Observational Study in Six European Countries in an Era of Austerity. *PLoS ONE*, *10* (8), e0135079. doi: 10.1371/journal.pone.0135079

Lechanteur, Y.T., van de Camp, P.L., Smailhodzic, D., van de Ven, J.P., Buitendijk, G.H., Klaver, C.C., Groenewoud, J.M., den Hollander, A.I., Hoyng, C.B., Klevering, B.J. (2015). Association of Smoking and CFH and ARMS2 Risk Variants With Younger Age at Onset of Neovascular Age-Related Macular Degeneration. *JAMA Ophthalmol.*, 133, 533-41.

Maas, M.J.M., Wees, P.J. van der, Braam, C., Koetsenruijter, J., Heerkens, Y.F., Vleuten, C.P.M. van der & Nijhuis-Van der Sanden, M.W.G. (2015). An innovative peer assessment approach to enhance guideline adherence in physical therapy: single-masked, clusterrandomized controlled trial. *Physical Therapy*, *95* (4), 600-12. doi: 10.2522/ptj.20130469

Marra, M.A., Vanheule, V., Fluit, R., Koopman, B.H., Rasmussen, J., Verdonschot, N., Andersen, M.S. (2015). A subject-specific musculoskeletal modeling framework to predict in vivo mechanics of total knee arthroplasty. *Biomech Eng*, 137, 020904.

Ouédraogo, A.L., Bastiaens, G.J., Tiono, A.B., Guelbéogo, W.M., Kobylinski, K.C., Ouédraogo, A., Barry, A., Bougouma, E.C., Nebie, I., Ouattara, M.S., Lanke, K.H., Fleckenstein, L., Sauerwein, R.W., Slater, H.C., Churcher, T.S., Sirima, S.B., Drakeley, C., Bousema, T. (2015). Efficacy and safety of the mosquitocidal drug ivermectin to prevent malaria transmission after treatment: a double-blind, randomized, clinical trial. *Clin Infect Dis*, *60*, 357-65.

Poortmans, P.M., Collette, S., Kirkove, C., Van Limbergen, E., Budach, V., Struikmans, H., Collette, L., Fourquet, A., Maingon, P., Valli, M., De Winter, K., Marnitz, S., Barillot, I., Scandolaro, L., Vonk, E., Rodenhuis, C., Marsiglia, H., Weidner, N., van Tienhoven, G., Glanzmann, C., Kuten, A., Arriagada, R., Bartelink, H., Van den Bogaert, W. (2015). EORTC Radiation Oncology and Breast Cancer Groups. Internal Mammary and Medial Supraclavicular Irradiation in Breast Cancer. *N Engl J Med*, 373, 317-27.

Sailer, A.M., van Zwam, W.H., Wildberger, J.E., Grutters, J.P.C. (2015). Cost-effectiveness modelling in diagnostic imaging: a stepwise approach. *Eur Radiol*, *25*, 3629-37.

Schünemann, H.J., Al-Ansary, L.A., Forland, F., Kersten, S., Komulainen, J., Kopp, I.B., Macbeth, F., Phillips, S.M., Robbins, C., van der Wees, P., Qaseem, A. (2015). Board of Trustees of the Guidelines International Network. Guidelines International Network: Principles for Disclosure of Interests and Management of Conflicts in Guidelines. *Ann Intern Med*, 163,: 548-53.

Thijssen, W.A., Miero,, E. van Willekens, M., Rebel, J., Sandel, M.H., Giesen, P. & Wensing, M. (2015). Complaints and Diagnoses of Emergency Department Patients in the Netherlands: A Comparative Study of Integrated Primary and Emergency Care. *PLoS ONE*, 10 (7), e0129739. doi: 10.1371/journal.pone.0129739

Thoonsen, B.A., Vissers, K.C., Verhagen, S., Prins, J.B., Bor, H., van Weel, C., de Groot, M & Engels, Y. (2015). Training general practitioners in early identification and anticipatory palliative care planning: a randomized controlled trial. *BMC Family Practice*, *16* (1), 126. doi: 10.1186/s12875-015-0342-6

Tierney, J.F., Vale, C., Riley, R., Smith, C.T., Stewart, L., Clarke, M. & Rovers, M.M. (2015). Individual Participant Data (IPD) Meta-analyses of Randomised Controlled Trials: Guidance on Their Use. *PLoS Medicine*, 12 (7), e1001855. doi: 10.1371/journal.pmed.1001855

Verseveld, M., de Graaf, E.J.R., Verhoef, C., van Meerten, E., Punt, C.J.A., de Hingh, I.H.J.T., Nagtegaal, I.D., Nuyttens, J.J.M.E., Marijnen, C.A.M., de Wilt, J.H.W. (2015). Chemoradiation therapy for rectal cancer in the distal rectum followed by organ-sparing transanal endoscopic microsurgery (The CARTS study). *Br J Surg*, 102, 853-860.

Vlenterie, M., Ho, V.K., Kaal, S., Vlenterie, R., Haas, R., van der Graaf, W.T. (2015). Age as an independent prognostic factor for survival of localised synovial sarcoma patients. Br J Cancer, 113, 1602-6.

Dissertations: 83
Scientific publications: 2043
Patents: 1

MRC in London and deCODE Genetics in Reykjavik, Iceland. Within the scope of the EU 7th Framework and Horizon 2020 Programmes TICD, IMPACT, EuroTARGET, EU-WISE, INTEGRATE-HTA, EURENOMICS, InSup-C, ASSURE, PACE, FAPIC, EYE-RISK, ENSAT-HT, MURAB, the Institute collaborates with numerous public and private organizations.

Research results

In 2015, three PhD theses received the predicate *cum laude*: Dr Nicolien Kuper ('Secondary caries, mind the gap!'), Dr Nicole Saksens ('Familial macular disease. Clinical and genetic studies on age-related macular degeneration and inherited macular dystrophies') and Dr Dennis Vriens ('Quantitative characterisation of solid tumours by 18F-FDG PET. What's in a number?'). Some other research highlights are listed below.

Healthcare improvement science

Dr René Melis and colleagues showed that General Practitioners (GPs) applying the EASY-Care Two step Older people Screening procedure, which uses information that is readily available to GPs, can predict negative health outcomes in their older populations efficiently and almost as accurately as a complete specialist Comprehensive Geriatric Assessment (van Kempen *et al. BMC Medicine*, 2015).

Rare cancers

The group led by Prof. Winette van der Graaf showed that the outcome of synovial sarcoma patients significantly decreases with age regardless of primary tumour site, size, and treatment (Vlenterie *et al. British Journal of Cancer*, 2015).

Tumours of the digestive tract

A Dutch multi centre study by Prof. Hans de Wilt and colleagues demonstrated that chemoradiation followed by organ-sparing transanal endoscopic microsurgery is feasible in early rectal cancer patients. Almost 60% of patients thus treated have their rectum in situ with excellent function, without the need of a colostomy (Verseveld et al. British Journal of Surgery, 2015).

Urological cancers

Dr Ruben Cremers showed that known susceptibility to single nucleotide polymorphisms (SNPs) for sporadic prostate cancer shows a similar association with hereditary prostate cancer (HPC), warranting a reconsideration of HPC and a restrictive policy toward prostate-specific antigen testing in men with a positive family history (Cremers *et al. Prostate*, 2015).

Women's cancers

A large international study of over 4,000 patients with breast cancer (stage1-3), coordinated by Prof. Philip Poortmans, showed that regional radiation therapy after surgery improves survival (Poortmans *et al. New England Journal of Medicine*, 2015).

The first results of the Breast Cancer E-Health (BREATH) trial, a web-based self-management intervention to support the psychological adjustment of women after primary treatment, by reducing distress and improving empowerment, demonstrated that the intervention had an additional effect (van den Berg et al. Journal of Clinical Oncology, 2015).

Infectious diseases and global health

Dr Teun Bousema and colleagues showed that the mosquitocidal drug ivermectin can be safely given in combination with a standard antimalarial and can reduce the likelihood of malaria transmission by reducing the life span of feeding mosquitoes (Ouédraogo *et al. Clinical Infectious Diseases*, 2015).

The group led by Prof. Marlies Hulscher developed quality indicators (QIs) that can be used to measure the appropriateness of antibiotic use in the treatment of all bacterial infections in hospitalized adult patients (van den Bosch *et al. Clinical Infectious Diseases*, 2015).

Inflammatory diseases

The trial carried out by Dr Marieke Coenen and colleagues showed for the first time that thiopurine dosing based on the genotype of thiopurine S-methyltransferase (TPMT) results in less haematological side effects in inflammatory bowel disease patients (Coenen *et al. Gastroenterology*, 2015).

Dr Alfons den Broeder and co-authors demonstrated that using a disease activity-guided, dose reduction strategy of tumour necrosis factor (TNF) inhibitors adalimumab or etanercept to treat rheumatoid arthritis is as good as continuing treatment unaltered with regard to major flaring, while resulting in successful dose reduction or stopping treatment altogether in two thirds of patients (van Herwaarden *et al. British Medical Journal*, 2015).

Mitochondrial diseases

Together with international colleagues Dr Chris Verhaak formulated guidelines for the optimal management of routine psychosocial care at infertility and medically assisted reproduction clinics (Gameiro *et al. Human Reproduction*, 2015).

Reconstructive and regenerative medicine

The Orthopaedics research group presented a methodology for developing subject-specific models that are able to simultaneously predict muscle, ligament, and knee joint contact forces along with secondary knee kinematics. With this work Verdonschot's group won the international grand challenge competition, a global endeavour in which researchers are challenged to predict loads in the knee joint of a patient with a total knee replacement (Marra et al. Journal of Biomechanical Engineering, 2015).

Renal disorders

The Modification of Diet in Renal Disease (MDRD) formula is widely used in clinical practice to assess the correct drug dose. Profs Jack Wetzels, Michel Wensing and Peter de Smet determined the validity of this formula in specific patient populations with renal impairment such as elderly, hospitalized and obese patients, patients with cardiovascular disease, cancer, chronic respiratory diseases, diabetes mellitus, liver cirrhosis and human immunodeficiency virus. They showed that in several specific patient populations with renal impairment the use of the MDRD formula is not valid or has uncertain validity (Eppenga et al. PLoS One, 2015).

Vascular damage

Dr Thijs Eijsvogels demonstrated that 15 minutes of exercise a day at a moderate intensity or 8 minutes exercise a day at a vigorous intensity significantly reduces the risk of all-cause mortality. Higher amounts of moderate-intensity physical activity are related to larger health benefits, whereas physical activity beyond the lowest effective dose for high-intensity exercise is not associated with further reduced mortality rates. Also, no evidence for an upper limit of exercise-induced health benefits was found (Eijsvogels et al. Journal of the American Medical Association, 2015).

Sensory disorders

Dr Jeroen Klevering and colleagues reported that patients with certain risk alleles develop neovascular age-related macular degeneration (AMD) on average 12 years earlier than persons without these risk alleles. A history of smoking makes the age at onset even earlier (Lechanteur et al. Journal of the American Medical Association Ophthalmology, 2015).

Awards and acknowledgements

- Dr Teun Bousema was among the top five nominees for the 2015 New Scientist Research Talent award for his research into malaria medicine.
- Dr Richard ten Broek was awarded the Catharina Pijls
 Dissertation Prize for his research on the formation of
 adhesions after reoperations in abdominal surgery.
 Ten Broek also received the 2015 RIHS PhD Award.
- Dr Philip van der Wees received the Najoua Mlika Cabanne
 Innovation Award from the Guidelines International Network
 (G-I-N) for his pivotal role into the multidisciplinary
 development and implementation of guidelines within
 healthcare.
- Dr Iris van Rooij received the 'Marco Tonini Award' from the Italian patient/parent organisation for anorectal malformations.
- Prof. Judith Prins received the 2015 NVPO (Dutch Psychooncology society) award for her contribution to psychosocial oncology.



On 12 November 2015 Her
Majesty Queen Máxima officially
opened the Medical Innovation
& Technology expert Center
(MITeC) operating rooms at
Radboudumc. MITeC is a partnership that includes Radboudumc,
TU Eindhoven, University of
Twente, Health Valley, and
a number of companies.

Societal impact

Societal impact is at the heart of RIHS research. Much – if not most – RIHS research has direct societal impact and is implemented in clinical care or public health. For this, RIHS encourages researchers to act in close collaboration with public organizations on topics with high societal relevance. RIHS research leads, e.g., to more personalized treatment, to better cooperation between healthcare providers, to more efficient diagnostic protocols, and through all this to better and more efficient healthcare. Research results are shared with the professional and lay community through contributions to guidelines or protocols, professional and popular publications, newspaper and broadcasting items, board membership of (inter)national public (societal) advisory groups and policy institutes, outreach activities and public-private collaborations.

Some highlights in 2015 were:

- On November 12th her Majesty Queen Máxima opened the three innovative operating theatres of MITeC.
- Dr Philip van der Wees was one of the two senior authors of the paper in which the Guidelines International Network released principles for disclosure of interests and management of conflicts

- in published guidelines (Schünemann et al. Annals of Internal Medicine, 2015).
- Prof. Maria Hopman was a member of the Health Council committee that wrote the guidelines 'Goede Voeding 2015' (good diets 2015) that were handed to the Minister of Health, Welfare and Sport.
- Dr Janneke Grutters was one of the authors of a practical guideline on the use of decision modelling in diagnostic imaging (Sailer et al. European Radiology, 2015).
- Spin-off SPL Medical, an enterprise for the production and registration (commercialization) of the contrast material Combidex, was founded with the involvement of Prof. Jelle Barentsz. Combidex-enhanced magnetic resonance imaging (MRI) is more effective than more invasive surgical processes for revealing small and otherwise undetectable lymph node metastases in patients with cancer.
- IQ healthcare coordinates a nationwide research project set up by the Netherlands Federation of University Medical Centers (NFU) that aims to learn how to de-implement ineffective healthcare.
- As president of the Dutch Society of Haematology Prof. Nicole Blijlevens appeared as an expert in the media (Interview on Radio 1 and several items in national newspapers) about the 'no

pay no cure' deal arranged with several insurance companies, a pharmaceutical company and the Dutch Society of Haematology.

- Prof. Bart Kiemeney wrote an opinion column in the newspaper the Volkskrant about an alternative for scientific publishing which received a lot of attention.
- Prof. Nico Verdonschot gave an orthopaedic biomechanics course in India as part of the Global Initiative of Academic Networks (GIAN) scheme, aimed to boost the quality of the country's higher education through international collaboration.
- Prof. Pim Assendelft is the national ambassador for community-based prevention, which is supported by National Institute for Public Health and the Environment ('RIVM') and the Dutch College of General Practitioners. Furthermore, he is chair of the Health Council committee on reorientation of financing university medical research.
- Prof. Jan Kremer is a member of the National Council for Public Health and Society ('Raad voor de Volksgezondheid en Zorg'), which advises the Dutch government and parliament, and he is Chairman of the Advisory Committee Quality of the Dutch Health Care Institute ('Zorginstituut Nederland').
- Dr Eddy Adang, Prof. Pim Assendelft, Prof. Wil van den Bosch, Prof. Maria Hopman, Prof. Jan Keunen, Dr Nel Roeleveld, Prof. André Verbeek and Prof. Gerhard Zielhuis are members of the Health Council of the Netherlands.
- Prof. Hans Kaanders, Prof. Pim Assendelft, Prof. Ellen Kampman, Prof. Bart Kiemeney Prof. Koos van der Hoeven, Prof. Judith Prins and Prof. Peter Siersema are members of the scientific council of the Dutch Cancer Society.
- Prof. Pim Assendelft, Prof. Judith Prins, Prof. Maroeska Rovers, Dr Tom Scheenen, Prof. Michel Wensing and Prof. Gerhard Zielhuis are board members of the Dutch Innovational Research Incentives Scheme (Rubicon-Veni – Vidi-Vici).
- Prof. Nicole Blijlevens is chair of the committee Costs and Effects of the ZonMw Cost and Effectiveness programme (DoelmatigheidsOnderzoek).
- Prof. Gerard Rongen is a member of the Central Committee on Research Involving Human Subject ('CCMO: Centrale Commissie Mensgebonden Onderzoek').

Future research

The Institute will continue to invest in research facilities such as biobanks as well as in large national and international networks. The focus of research will increasingly be on personalized healthcare and patient-centred interventions. For example, the research within MITeC will start and the ambition is to further revolutionize surgical clinical science, so that surgical procedures will become more patient-tailored, safer and efficient. Furthermore, Dr Mireille Broeders' group is evaluating tailored follow-up schedules for patients treated for breast or colorectal cancer with curative intent, based on the length of the preclinical

detectable phase and taking into account benefits and harms as well as patients' and health professionals' views. The same group is also investigating the possibilities of personalised breast cancer screening. Prof. Judith Prins will start a new research line on blended psychotherapy (face-to-face combined with e-health) for cancer survivors.

Dr Teun Bousema will extend his malaria research with a prestigious NWO Vidi grant for the project 'Malaria gametocytes – seeds of dispersion'. Malaria spreads by mosquitoes that become infected after biting malaria infected humans. His research will determine when humans are first infectious and what strategies malaria parasites use to maximize their spread. Uncovering parasite and human factors that influence the spread of malaria may lead to new opportunities for malaria elimination.

With a Kolff postdoc grant from the Dutch Kidney Foundation for the project 'Chronic kidney disease causes progressive decline of kidney function', Dr Jan van den Brand will use novel statistical models to describe and predict commonly occurring trajectories of decline in kidney function. These trajectories give a more informative patient phenotype. Moreover, the trajectory for an individual patient can be extrapolated to make a detailed prognosis. With a Horizon 2020 Marie-Curie Fellowship for the project 'CARDI-ACHE: The cardiovascular consequences of endurance exercise', Dr Thijs Eijsvogels aims to elucidate the clinical importance of exercise-induced cardiac troponin elevations and myocardial fibrosis in endurance athletes. Better understanding of the clinical relevance of these adaptations is important to differentiate between the beneficial and the potentially harmful effects of exercise.

The ageing of the Dutch population will present enormous quality and efficiency challenges in healthcare. Cost-effectiveness will be central to healthcare policy for the next few decades. Four research groups will perform research on healthcare costs and effectiveness with grants from the ZonMw programme 'Doelmatigheids-Onderzoek': Dr Rianne Gerritsen (*In vivo* reflectance confocal microscopy, a novel non-invasive tool for diagnosing skin cancer – a randomized controlled trial), Dr Willem de Boode (BeNeDuctus Trial), Prof. Maroeska Rovers and Prof. Fred Witjes (RACE – RAdicale Cystectomy Evaluation. Comparative Effectiveness Study of Open versus Robot Assisted Laparoscopic Surgery), Prof. Camiel Rosman en Prof. Maroeska Rovers (iCAN trial. Intrathoracic versus Cervical esophagogastric ANastomosis after minimally invasive esophagectomy for oesophageal cancer).

Prof. Barentsz and colleagues will investigate whether multiparametric MRI should be implemented in prostate cancer screening with an Alpe d'HuZes grant. Other projects that received awards from the Dutch Cancer Society are: 'Uniform FDG PET-guided GRAdient Dose prescription to reduce late Radiation Toxicity

Director: Prof. Bart Kiemeney

After a short career as a physiotherapist, Bart Kiemeney was trained as an epidemiologist at Radboud university medical center (Radboudumc). From 1992-1994 he received further training in clinical epidemiology at the University of Washington, Seattle WA and in genetic epidemiology at Johns Hopkins University, Baltimore MD. In 2003 he was appointed Professor of Cancer Epidemiology at Radboud University. His research focuses on the genetic causes and pharmacogenetics of urological cancers.



Radboud Institute for Health Sciences

Postal address
148 RIHS
Radboud university medical center
PO Box 9101
6500 HB Nijmegen
The Netherlands

Visiting address
Geert Grooteplein 21
Route 148, Nijmegen

T: +31 (o)24 361 46 39 E: RIHS@radboudumc.nl I: www.rihs.nl

(UPGRADE-RT): a randomised controlled trial with dose reduction to the elective neck in head and neck squamous cell carcinoma' (Prof. Hans Kaanders), 'Evaluation of bladder cancer care in the Netherlands; a solid foundation for evidence-based quality improvement' (Dr Katja Aben, Prof. Bart Kiemeney, Prof. Fred Witjes), 'Personalised RISk-based MAmmography screening (PRISMA) - from one-size-fits-all to a tailored approach' (Dr Mireille Broeders), 'Minimal invasive breast cancer excision using breast lesion excision system under ultrasound guidance - a feasibility study' (Dr Ritse Mann), 'Aptamer-based multivalent cancer therapeutics: the road to efficient breast cancer detection and treatment' (Dr Paul Span), 'Body composition in renal cell cancer: associations with survival outcomes, tumour characteristics, lifestyle habits, and circulating biomarkers' (Dr Alina Vrieling, Prof. Ellen Kampman, Prof. Peter Mulders).

These are just some examples of ongoing and new research in the Institute. In the short term, the Institute aims to strengthen its expertise in, *e.g.*, data engineering / big data in health sciences, in data integrity with the start of a digital research environment, and in healthcare research among refugees and low-income subgroups in the population. Also, in 2016 the Institute will implement the link between the Biomedical Sciences MSc Programme and the research in the Institute. Every MSc student will choose a principal investigator group in one of the three Radboudumc research institutes as a training environment. Students will be increasingly seen as new colleagues. The longer-term policy of the Institute, along with those of the other two Radboudumc Institutes, has been described in a recent publication: Research Agenda 2025 (www.rihs.nl/about-us/reports).