Two Decades of Global Child Health at Amsterdam UMC

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TWO DECADES OF GLOBAL CHILD HEALTH AT AMSTERDAM UMC

1999 - 2019

ACHIEVEMENTS, ACTIVITIES AND FUTURE PERSPECTIVES OF THE AMSTERDAM CENTRE FOR GLOBAL CHILD HEALTH

Reading guidance

For decades Global Child Health (GCH) has been an important component of the paediatric departments of the VUmc and the Emma Children's Hospital, AMC. In 2018 the institutions VUmc and AMC formed an alliance continuing under the name Amsterdam UMC. With the alliance, the two institutes have joined their global child health activities and have established the 'Amsterdam Centre for Global Child Health' (Amsterdam CGCH), which is unique in the Netherlands.

This report describes the achievements and activities over the past two decades and the future perspectives of the paediatric specialists in Global Child Health from both institutions. Unless needed for clarity, the activities described are not specifically linked to the individual institutes.

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Emma Children's Hospital
Amsterdam UMC

EXECUTIVE SUMMARY

Who we are

We are paediatricians with specialisation in different aspects of Global Child Health (GCH) working together at the 'Amsterdam Centre for Global Child Health'. The centre is based at Amsterdam UMC, which forms part of the VU University Amsterdam (VU) and the University of Amsterdam (UvA).

Our aims

Our overarching aim is to contribute to improved health for children worldwide. We try to achieve this by contributing to the training of medical staff working or wanting to work in a GCH setting (capacity building) and by addressing important outstanding scientific research questions in the area of GCH.

Our achievements

Over the past two decades, we have initiated and successfully completed many research initiatives 'overseas', which has involved obtaining funding, setting-up research sites, training local staff, conducting research and reporting the findings in (high impact) medical journals. During this period, we have secured in excess of seventeen million Euros through competitive research funding; we have published over 300 scientific manuscripts (average 15 per year) in peer reviewed (medical) journals; we have supervised mostly locally recruited PhD students, of which fifty-nine have successfully defended their PhD theses at the VU and the UvA; we have developed several training courses in the area of GCH for medical students, for registrars in paediatrics and/or global health, and for medical staff of NGO's. Finally, all projects and activities described in this report, were done by doctors who undertook this work alongside a regular appointment as paediatrician at Amsterdam UMC.

The 'Amsterdam Centre for Global Child Health'

We have taken the initiative to officially launch the Amsterdam Centre for Global Child Health in the second half of 2020. This will allow concentration of GCH knowledge and specialisation which currently is fragmented in many institutes. The objective in establishing this new centre, which is unique in the Netherlands, is to facilitate a central role within the Netherlands: (I) in advising on the care of children with potential tropical disease(s); (II) in teaching and training healthcare workers interested in GCH; (III) in contributing to and advising on the development and evaluation of GCH projects initiated and funded by the Dutch government or NGO's; in advising, communicating and informing the media on new developments in the area of GCH; and in promoting work and collaboration on important outstanding research questions.

INTRODUCTION & ORGANISATION

AMSTERDAM CENTRE FOR GLOBAL CHILD HEALTH

The year 2015 was of importance because at the end of that year the Millennium Development Goals (MDG) should have been achieved. The 4th MDG, reduction in child mortality by 2/3 in comparison with the 1990 mortality rates, was achieved in only a minority of low-income countries with rates remaining up to twenty times higher compared to high-income countries. International organisations including the World Health Organisation, UNICEF and the World Bank, acknowledged that a great deal of work remained to be done which lead to the formulation of the Sustainable Development Goals (SDGs). These are more inclusive and have a target date of 2030. To achieve these new goals, international organisations as well as the medical profession including research communities in developed and developing countries need to increase their efforts and collaborations.

Over the past decades, the Netherlands has developed into a more globalised society in which paediatricians may encounter rare tropical diseases, epidemics of emerging infectious diseases, as well as various cultural perceptions of childhood disease by parents from different ethnic backgrounds. Furthermore, mortality in children from ethnic minorities in the Netherlands is substantially higher than that of Dutch Caucasian children. In view of this changing paradigm, both at the national and at the international level, it is necessary that academia engages actively in research and education on Global Child Health in the Netherlands.

This priority was recognised at the VU by Professor Ed van der Veen who appointed Professor Marceline Tutu-van Furth as the first Professor on the Desmond Tutu Chair in Global Child Health in 2009. The Chair forms part of the Desmond Tutu Training Programme (DTTP), which is an academic cooperation for the joint supervision of PhD students with a focus on 'Bridging Diversities for Academic Advancement'. Tutu van Furth was succeeded in 2017 by Prof. Mirjam van Weissenbruch.

At the UvA, Prof. Hugo Heymans, former head of the Emma Children's Hospital AMC and Dr. Mulder, former Director of 'Stichting Simavi', jointly took the initiative to establish a Chair in Global Child Health at the UvA. In 1999 Professor Bernard Brabin was the first to be appointed on this new chair and established the Global Child Health Group (GCHG) with the aim to develop both an active teaching and research programme. He was succeeded in 2013 by Professor Michaël Boele van Hensbroek who has broadened the scope of the GCHG by attracting experts in important sub-areas within the GCH-field to join the GCHG initiative.

MISSION

IMPROVING GLOBAL CHILD HEALTH THROUGH CLINICAL CARE, SCIENTIFIC RESEARCH AND TRAINING & EDUCATION

Improving Global Child Health (GCH) by (1) consolidating and further improving the Amsterdam CGCH as a knowledge centre on GCH for clinical issues; (2) initiating, leading, conducting and participating in relevant scientific research and (3) training and education (capacity building) in the field of GCH.

VISION

IMPROVING THE HEALTH CARE OF CHILDREN WORLDWIDE

By bundling knowledge and skills, the Amsterdam CGCH will make an important contribution to improving the health care of children worldwide.

THE NUMBERS

11
STAFF

Starting out with 2 FTE in 1999, we've now grown to 11 full-time staff members in 2019

59
COMPLETED PHD

By 2019 we've had 59 completed PhDs, averaging to approximately 3 per year

12
TEACHING & TRAINING

We contribute to 12 courses per annum and give 3 of our own courses each year

307
PUBLICATIONS

Over the past two decades we've published 307 articles, averaging to approximately 15 per year

€ 17.7m
FUNDING

In total, we've been granted € 17.757.201 in competitive funding, on average this equals to € 887.860 per year

OBJECTIVES

1. Amsterdam CGCH as knowledge centre for clinical questions
2. Research in collaboration with international partners
3. To provide a comprehensive teaching and training programme

1. Amsterdam CGCH as knowledge centre for clinical questions

- Through development of a centre for consultation and advice for (paediatric) doctors in the Netherlands offering expertise and experience in different areas of GCH.
- By setting up a 'paediatric task force', in which members of the Amsterdam CGCH can be deployed ad hoc via partners such as Doctors without Borders if international emergencies arise where GCH expertise is required.
- Identifying or interpreting a particular GCH problem to the media or government agencies seeking expertise

2. Research in collaboration with international partners

- Expand research activities within the area of GCH.
- Promote comprehensive research strategies utilising basic research methods, clinical and epidemiological studies and clinical trials.
- Contribute to research capacity building by offering PhD opportunities at the VU and the UvA, and promote local research ownership of collaborative research projects.

3. To provide a comprehensive teaching and training programme

- Creation of training opportunities for medics intending to specialise in GCH.
- Through courses on GCH specifically designed for different user groups (e.g. paediatric registrars, Global Health registrars and NGO staff).
- Contribution to the curriculum, training and exchange-programmes of medical students and the post-graduate training programmes of the VU, UvA and Collaborating Universities overseas.
- Contribution to on-site training of medical staff at paediatric hospitals in resource limited settings.
- Development of suitable training materials

MILLENNIUM DEVELOPMENT GOAL 4

TO REDUCE THE UNDER-FIVE MORTALITY RATE BY TWO-THIRDS BETWEEN 1990 AND 2015

Despite being a millennium development goal, by the end of 2015 the under-five mortality rate in low-income countries still remained up to twenty times higher compared to high-income countries.

"Dutch doctors in the 1980's were everywhere in the tropics, but few were trained in tropical paediatrics"

PROF. BERNARD BRABIN
FOUNDER OF THE GLOBAL CHILD HEALTH GROUP

HISTORY & POSITIONING

Global Child Health at the
VU University Amsterdam

Research Institute

Formerly all translational research performed by Professor Tutu van Furth and her group had a special focus on central nervous system infections and was embedded in the 'Amsterdam Institute for Infection & Immunity'.

Research Themes

The main topic of research was meningitis (viral and bacterial). Studies were conducted from bench to bedside, from fundamental immunological, metabolomics, proteomics, and pathology studies, to a home treatment program for children with tuberculous meningitis. Most studies were performed in collaboration with the department of Child Neurology of Tygerberg Hospital, Cape Town, South-Africa and with the laboratory of metabolomics of the University of Potchefstroom, South-Africa.

For example:

- A large follow-up cohort study (n=580) of bacterial meningitis survivors, 25 years after initial infection (age range between 20-30 years), has recently been completed in South Africa.
- A sepsis study in neonates, with emphasis on innate immunity, treatment and outcomes, is currently being analysed.
- Currently in progress is the project 'Giving Children a Chance for Life', funded by the Dutch 'Postcode Loterij'. An exchange of knowledge between religious leaders and health care workers on treatment adherence in children with HIV in South-Africa has been assessed.

Global Child Health at the
University of Amsterdam

Global Child Health Group

In 1999 Professor Bernard Brabin was appointed to the Chair of Global Child Health and founded the Global Child Health Group. Core members had responsibilities for planning and daily management which included: teaching, supervision of PhD students and administrative and logistic support of research programmes. The member's main research and clinical experience represented: critical paediatric care, maternal and child nutrition, anaemia, malaria, and community child health. These themes represented internationally recognised priority areas in GCH as well as the sub-specialisation of individual group members.

Positioning

With respect to the positioning of the GCHG it is important to note that three groups are responsible for the majority of Global Health activities within Amsterdam UMC location AMC. These are: the GCHG of the Emma Children's Hospital (the Emma); the Department of Tropical Medicine, Infectious Diseases and AIDS of the Division of Internal Medicine (Tropencentrum) and the Amsterdam Institute of Global Health and Development (AIGHD) of the Department of Global Health, also part of the Division of Internal Medicine. All three groups work closely together and have numerous joint activities. Within the Emma the GCHG has established close relationships with the Departments of Paediatric Haematology, Paediatric Infectious Diseases and Immunology, Paediatric Intensive Care, and General Paediatrics.

CORE STAFF

in alphabetical order

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01 PROF. MICHAËL BOELE VAN HENSBROEK (MBVH)

Professor of GCH, Paediatric Infectious Disease specialist and staff member of the Emma Children's Hospital and of the AIGHD. MBvH previously worked in The Gambia (1991-1995), conducting research on the treatment of severe malaria in children at the MRC in collaboration with the University of Oxford. In 2000 he became a Wellcome Trust fellow studying severe anaemia in Malawian children. In 2005 he returned to the Emma Children's Hospital to become an ID specialist and paediatric advisor for Doctors Without Boarders (MSF). In 2013 he was appointed Professor in GCH and head of the GCHG. He is currently involved in several projects globally, is a member of various steering committees (DSMB's and TSC's) and vice-chair of the CCMO (Centrale Commissie Mensgebonden Onderzoek). He combines work with carpentry and writing children's books.

02 PROF. BERNARD BRABIN (BB)

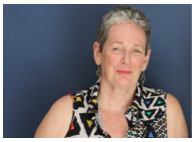
Emeritus Professor in GCH at the UvA and the Liverpool School of Tropical Medicine. His main areas of interest include maternal and child health, focussing on pregnancy infections as they affect birth weight, pre-term birth and child health outcomes in developing countries. In particular, malaria and micro-nutrients and their influence on pregnancy outcomes, the growth and development of young children and nutrition-infection interactions. His initial work formed the basis for the development of the World Health Organisation strategy for treatment and prevention of malaria in pregnancy. He has supervised over 40 PhD students in the Netherlands and United Kingdom and conducted projects in Kenya, Malawi, Nigeria, Tanzania, Zambia, Papua New Guinea, and Burkina Faso. BB has been a member of International Advisory Committees and Working Groups on nutrition and infection. Most recently he acted as Principal Investigator of the NIH (USA) supported PALUFER trial of iron supplementation in non-pregnant adolescents. Apart from continuing his research work he enjoys writing on historical aspects of tropical medicine, ballroom dancing and philately.

03 DR. JOB CALIS (JC)

Paediatric Intensive Care specialist at the Emma Children's Hospital, Amsterdam UMC, with a special interest in Global Child Health. Between 2002-2005 he worked in the department of paediatrics of the Queen Elizabeth Central Hospital, Blantyre, Malawi ("Queens"). During this period he conducted a large study on the aetiology of severe anaemia in Malawian children which led to a PhD with distinction at the University of Amsterdam in 2008. During his Paediatric and Intensive Care training (2008 – 2015) he continued his research and supervised various PhD students, focusing on iron deficiency, anaemia and HIV. From 2017–2019 he returned to Malawi to set up the paediatric intensive care department at Queens and started studies on shock in children in Africa. Besides research, his medical interests include teaching, infectious diseases, electronic data management, and crew resource management. Currently he

is a staff member of both the Department of Paediatric Intensive Care and the Amsterdam Centre for GCH at the Amsterdam UMC. He is a father of four children and balances hard work with running, playing football or cooking.

04 PROF. MARCELINE TUTU-VAN FURTH (MTVF)



Professor of Paediatric Infectious Diseases at the Emma Children's Hospital, Amsterdam UMC. Her vision: "empowerment of children around the world to create a safe and healthy home for each of them". Apart from contributing to this vision on a daily basis she gives advice on infectious or immunological problems in children. In addition, she teaches medical students, paediatric residents, and colleague paediatricians on important topics in the field of paediatric infectious disease. MTvF's research focuses on bacterial meningitis from bench to bedside, including follow-up of these patients. As an Honorary Professor of Tygerberg Hospital in Cape Town she supervises South-African PhD students in their research on tuberculous meningitis and HIV. She holds an MBA and uses this knowledge in initiating innovative projects such as "Giving children a chance for life" on HIV treatment adherence which will have a global impact. Together with her wife (Mpho Tutu van Furth) she has built an e-mentoring platform, for women only, # I Too (www.tututeach.org).

05 DR. MARTIJN VAN DER KUIP (MVDK)

Paediatric Infectious Disease specialist at the Emma Children's Hospital, Amsterdam UMC, and head of the Department of Paediatric Infectious Diseases, Rheumatology and Immunology. He completed his PhD in Paediatric Intensive Care Medicine before he specialised in paediatric ID. His research focusses on tuberculous meningitis (TBM) in children for which he collaborates with the University of Stellenbosch in South Africa. He is working on various models to study mycobacterial brain invasion and granuloma formation (silico based and zebrafish models). He is also involved in a large post-mortem study of brain specimens to study host immune-pathogenesis by means of immune-histopathology, metabolomics and proteomics. Furthermore, he is involved in various studies of TBM patients in Cape Town on the topics of nutritional status, early diagnostics and disease outcome. In the Emma Children's Hospital he does outpatient and clinical consultations and he teaches on a regular base for paediatricians, residents, interns and students.

06 DRS. NINA MEELS (NM)

Project Manager at the Amsterdam CGCH. Equipped with a Master's degree in both Global Health and Healthcare Innovation Management, she supports the Amsterdam CGCH as a project manager. In this role she hopes to unify her curiosity for infectious diseases with her keen interest in the implementation of innovative applications in health care. Aside from her day job at the Amsterdam CGCH, she organises the annual Global Health Film Festival in Rotterdam. A festival that aims to bring people together around issues in global health through film and dialogue.

07 LINDE NIEUWENHUIJS (LN)

HR assistant at AIGHD. LN has been coordinating the administrative aspects of the Amsterdam CGCH over the past 6 years. After completing her College Education (HBO) Linde started as a Secretary/Office Manager at AIGHD. In the past 3 years she has moved on to Human Resource Management (HRM) with a completed degree. Now her main focus is HRM in combination with the supervision of all the PhD students within the Global Health department. Nina Meels has taken over her role within the Amsterdam CGCH.

08 DR. WIEGER VOSKUIJL (WV)

General paediatrician at the Emma Children's Hospital, Amsterdam UMC and since 2018 a senior scientist in Global Child Health at AIGHD. He lived and worked in Malawi between 2012-2015 and since then he co-leads a large Malawian research group looking at the interplay between acute illness and undernutrition in children. Clinical phenotyping of fragile children has his main interest; early risk prediction and triage but also Cause-of-Death with minimally invasive tissue sampling are areas of interest. Since 2015 he is the site-PI for the Childhood Acute Illness and Nutrition (CHAIN) network in Malawi. In the CHAIN network he collaborates with internationally renowned scientists from SickKids Toronto, KEMRI/Wellcome trust and the University of Washington. WV is a honorary Senior Lecturer in Paediatrics and Child Health at the College of Medicine (COM since 2012), University of Malawi, (Queen Elisabeth Central Hospital). He has 3 children and tries to combine the above with running and playing the trumpet.

09 PROF. MIRJAM VAN WEISSENBRUCH (MvW)

Professor of Neonatology, Nutrition and Metabolism and Desmond Tutu Chair; Clinical Pharmacologist, Epidemiologist. Staff member of the Emma Children's Hospital, Amsterdam UMC, VU University. Conducting research on developmental origins of health and disease and on infectious diseases in the Netherlands, in collaboration with Stellenbosch University and Gadjah Mada University. She is currently involved in several projects globally.

10 PROF. JOB VAN WOENSEL (JVW)

Professor in Paediatric Intensive Care, and Head of the Paediatric Intensive Care Unit (PICU), at the Emma Children's Hospital, Amsterdam UMC. JvW, worked in 1991-1992 for Medicine Sans Frontiers (MSF) in a refugee camp on the Thai-Cambodian border, conducting mefloquine trials in (severe) malaria. In addition, in 2007 he worked in an MSF project in Myanmar. JvW supervised

studies in Kenya and Uganda regarding fluid management during shock in malnourished children. He is member of the board of directors of Medical Action Myanmar. Finally, he is involved in a collaboration programme with the Mercy James Center in the Queen Elisabeth Central Hospital, Blantyre, Malawi where he is co-investigator in studies on fluid management in sepsis in children.

NEW MEMBERS

11 DRS. TESSA DE BAAT (TDB)

Paediatrician, Neonatology Fellow in Emma Children's Hospital, Amsterdam UMC. TDB worked as a clinician in Queen Elizabeth Central Hospital in Blantyre, Malawi and conducted research in collaboration with Malawi-Liverpool-Wellcome Trust (MLW). Her research focuses on neonatal sepsis and antibiotic stewardship. She is a lecturer at the Netherlands Course on Global Health and Tropical Medicine (NTC) and certified instructor of Neonatal Life Support.

12 DR. MINKE HUIBERS (MH)

Paediatric specialist with a focus on Global Paediatric Oncology. MH is a general paediatrician trained and graduated in 2018 as a resident in the Emma Children's Hospital, Amsterdam UMC. In 2019 she successfully defended her PhD thesis at the UvA, entitled: "HIV-infection in sub-Saharan Africa; from quantity to quality of care. Currently MH is working as paediatrician for Baylor College of Medicine and Texas Children's Hospital, Houston, USA, based at the Global HOPE (Haematology Oncology Paediatric Excellence) in Lilongwe, Malawi. Her current research focuses on different aspects of paediatric cancer in low and middle-income countries, including the effects of malnutrition on the treatment of childhood cancer, early recognition of childhood cancer and palliative care. Finally, MH is also involved in the paediatric oncology outreach group of the Princess Maxima Centre, the Dutch National Hospital for Paediatric Oncology, in Utrecht, the Netherlands.

13 DR. MENNO SMIT (MS)

Paediatric Registrar at the Emma Children's Hospital, Amsterdam UMC, and an Honorary Associate Professor in Malaria Epidemiology at the Liverpool School of Tropical Medicine (LSTM). Following clinical training in Tropical Medicine (Maternal & Child Health), he obtained an M.Sc. in Public Health (MPH) at the London School of Hygiene & Tropical Medicine (LSHTM), and a Doctor of Philosophy (PhD) at the LSTM. His research, for which he was based in Kenya, has included trials assessing: (i) the risk of malaria infection following iron supplementation in pregnancy, (ii) safety and efficacy of primaquine as a gametocidal drug in children with malaria, and (iii) high-dose ivermectin as a first-in-class mosquitocidal drug. Currently he is involved as an investigator and DSMB member in several trials across the globe that are assessing the use of ivermectin for the elimination of malaria and neglected tropical diseases.

KEY COLLABORATORS

in alphabetical order

Prof. Tahmeed Ahmed	*ICDDR-B, Dhaka, Bangladesh*
Dr. Robert Bandsma	*SickKids, Toronto, Canada*
Prof. Imelda Bates	*Liverpool School of Tropical Medicine, UK*
Prof. Adrie Bekker	*Stellenbosch University, South Africa*
Prof. Jay Berkley	*University of Oxford, UK, and KEMRI, Kenya*
Prof. Louis Bont	*University Medical Centre Utrecht*
Prof. Frank Cobelens	*AIGHD, Department of Global Health, Amsterdam UMC*
Prof. Donna Denno	*Washington University, Seattle, US*
Prof. Angela Dramowsky	*Stellenbosch University, South Africa*
Prof. Mike English	*University of Oxford, UK, and KEMRI, Kenya*
Prof. Martin Grobusch	*Department of Internal Medicine, Amsterdam UMC*
Dr. Lia van der Hoek	*Department of Microbiology, Amsterdam UMC*
Prof. Richard Idro	*Makerere University, Uganda*
Prof. Menno de Jong	*Department of Microbiology, Amsterdam UMC*
Prof. Mohammed Juffrie	*Gadja Mada University, Yogyakarta, Indonesia*
Prof. Mariana Kruger	*Stellenbosch University, South Africa*
Prof. Feiko ter Kuile	*Liverpool School of Tropical Medicine, UK*
Dr. Lisette van Lieshout	*Department of Parasitology, LUMC*
Prof. Rina Madarina	*Gadja Mada University, Yogyakarta Indonesia*
Prof. Kath Maitland	*Imperial College, London, UK, and KEMRI, Kenya*
Dr. Tim de Meij	*Department of Paediatrics, Amsterdam UMC*
Prof. Charles Newton	*University of Oxford, UK, and KEMRI, Kenya*
Prof. Kamija Phiri	*University of Malawi, CoM, Malawi*
Prof. Tobias Rinke de Wit	*AIGHD, Department of Global Health, Amsterdam UMC*
Prof. Constance Schultz	*AIGHD, Department of Global Health, Amsterdam UMC*
Prof. Boy Sebit	*University of Juba, South Sudan*
Prof. Frank Smithuis	*University of Oxford, UK, and Myanmar*

RESEARCH NETWORKS

memberships

CHAIN

Optimizing the management and care of highly vulnerable children in resource-limited settings to improve survival

www.chainnetwork.org

IPT-PD

Intermitted Preventive Treatment-Post Discharge in the prevention of severe malaria anaemia

LYMEPROSPECTKIDS

Clinical presentation and long term outcome of Borrelia infections in children

www.expertisecentrumlyme.nl

SSNSS

South Sudan Nodding Syndrome Study: network to study the aetiology, epidemiology, risk factors and outcome of Nodding Syndrome

TUBERCULOUS MENINGITIS IN SOUTH-AFRICA

TB-meningitis network South Africa

TBM IN SILICO MODELLING

Systems biology of cerebral granuloma formation caused by *Mycobacterium tuberculosis*

METABOLOMICS IN TUBERCULOUS MENINGITIS

Metabolomic (urine) and proteomic (brain) profiling of central nervous system tuberculosis

MORU TROPICAL HEALTH NETWORK

Ivermection Safety in Small Children - Trial network for malaria and neglected tropical diseases

www.tropmedres.ac

ACHIEVEMENTS & ACTIVITIES

TWO DECADES OF GLOBAL CHILD HEALTH

RESEARCH LINES

Over the past 20 years, the Amsterdam CGCH has been involved in nine main research lines. The following section provides a brief review of each of the research lines as listed below.

1 CRITICAL CARE
2 NUTRITION
3 MENINGITIS AND TUBERCULOSIS
4 MALARIA
5 ANAEMIA
6 COMA AND CONVULSIONS
7 HIV
8 NODDING SYNDROME
9 NEONATOLOGY
10 OTHER PROJECTS

1. Critical Care

Childhood mortality in low income countries (LMIC) has dramatically decreased over the last two decades [1,2]. In the 1990's nearly one in five children living in sub-Saharan Africa died before their fifth birthday. The under-five mortality for sub-Saharan Africa has since more than halved and is currently estimated at 7.6%, however it remains eight times higher when compared to high income countries and requires further reduction in the coming decades [1,2]. The question is of course how to achieve this. So far the largest reduction may have been due to preventive medicine, an area that may still have room for improvement [3]. However, we now may have entered an era where further reduction of mortality should (also) come from improved curative services.

Reducing in-hospital mortality means improving care of critically sick children, or in other words developing critical care medicine in low income settings. The WHO acknowledged the importance of critical care in paediatrics by developing the Emergency Triage and Treatment (ETAT) guidelines in the previous decade [4]. These guidelines, developed for healthcare workers in LMIC's, help to timely detect critically sick children, prioritise their care and improve the quality of resuscitation and safe lives [5].

Although this may be seen as the introduction of critical care to LMIC, still much has to be improved in the care we deliver to children following on the acute moment. Focussing attention, means and efforts on the sickest children is ideally done in high-care wards or paediatric intensive care units (PICU), a concept which is relatively new to sub-Saharan Africa. Even in western settings separate paediatric intensive care units were only established in the 70's or 80's. In sub-Saharan Africa these units are not common, but are slowly appearing [6].

In Blantyre, Malawi we opened the first paediatric intensive care unit in July 2017. In the following paragraphs we describe some of the

issues we faced and progress that has been made to inform and possibly help others with similar interests.

Fluid management in critically ill children in resource poor settings has gained renewed interest. Where since decades intra-venous (iv) fluid for (septic) shock has been considered the cornerstone of the first line treatment, the so-called FEAST trial showed that at least in shocked children in a resource poor setting the contrary may be true. In the trial it was demonstrated that iv fluid increased the mortality rate in children with signs of septic shock. However, the pathophysiological explanation for this unexpected outcome remains to be elucidated. This has been the stepping-stone for an intensive observational study to the underlying diseases, the clinical presentations as well the physiological phenomena accompanying circulatory insufficiency in children. Shocked children with malnutrition have historically always taken a particular place in iv fluid treatment. There has been strong reluctance in giving these children iv fluid since the heart was considered to be 'malnourished' too. However, in an observational study with echocardiography studies in Kenya and Uganda we found that the cardial condition of malnourished is good enough to handle fluid boluses (Critical Care, 2017).

Shock due to sepsis is one of the leading causes of childhood mortality, especially in low-resource settings. The mortality rates are high in part due to the delayed diagnosis and treatment in these children. Even in high resource settings, early diagnosis and prompt treatment can reduce mortality substantially. However, in many low-resource settings early diagnosis is hampered by the lack of (qualified) human resources and shortage of suitable high quality diagnostics. Previous research has indicated that monitoring physiological vital signs in combination with smart algorithms could assist clinicians in obtaining the diagnosis earlier and thereby reducing the mortality rates of children under 5.

Currently we are undertaking a feasibility study addressing a threefold aim. First, we want to assess whether tablet assisted patient monitoring is suitable in low-resource settings. Second, we want to investigate if it we can develop an algorithm to assist clinicians in diagnosing sepsis. Third, we want to assess if this system is economically viable in low-income countries.

2. Nutrition

The nutrition research line was initiated by Dr. Wieger Voskuijl during the years he was based at the nutrition rehabilitation unit of the paediatric department of Queen Elizabeth Central Hospital, Blantyre, Malawi (2012-15). Initially he started doing research with funding from 'Stichting Steun Emma Kinderziekenhuis' and 'Ter Meulenfonds'. But with further funding from Thrasher Foundation and collaborating with dr Robert Bandsma (SickKids Hospital, Toronto) and Prof. Jay Berkley (KEMRI/Wellcome trust, Kenya) the research gradually grew and the Malawian research team increased. He further developed this research line as a PI in the CHAIN network, funded by the Bill & Melinda Gates foundation, with collaborators from SickKids hospital in Toronto, Canada (Dr. Robert Brandsma), the Kilifi Research Unit, part of the University of Oxford (Prof. James Berkley), and University of Washington (Prof. Judd Walson and Prof. Donna Denno). This collaboration has already resulted in numerous publications in high impact journals and a completed PhD by Dr. Rosalie Bartels.

- Childhood Acute Illness and Nutrition Network (CHAIN network with 9 sites, in 6 countries in Asia and Africa): Between October 2016 and October 2019, WV was PI for the Malawi site for the CHAIN-network. A prospective cohort in which study both the clinical phenotype of fragile, acutely ill, young children has been investigated using clinical data during admission and 180 days after discharge, and biological samples have been collected and stored in a large bio-repository in Kilifi, Kenya. The first papers from this network will emerge in 2020 (chief PI's prof Jay Berkley and prof Judd Walson). Also see www.chainnetwork.org

Currently, Dr Wieger Voskuijl is coordinating two other lines of research both within and outside the CHAIN network:

- Minimally Invasive Tissue Sampling ("MITS"): In the MITS study causes of death in severely malnourished children admitted to a low resource hospital are studied using MITS

IMPRESSIONS FROM THE NUTRITION RESEARCH LINE

with the primary aim of unravelling pathways underlying death in these vulnerable, sick children. The second aim of the project is to investigate the feasibility of post-mortem endoscopy. The studies are conducted in collaboration with Prof. Donna Denno (University of Washington, Seattle, US) and received 1.400.000,- USD funding from the Gates Foundation.

- Early Risk Prediction & Volatile Organic Compounds (VOCs).

At the Amsterdam Institute of Global Health and Development (AIGHD), Dr. Wieger Voskuijl formed a team with Dr. Daniella Brals, econometrician and basic scientist in Global Child Health, and PhD students from the University of Toronto and have established a model looking at daily 'early warning signs' in children with severe malnutrition (rather than on admission only). This has been followed by organising a workshop on machine learning (early 2020) for junior and early phase senior scientists in Amsterdam and strengthening the collaboration with the International Centre for Diarrhoeal Diseases in Dhaka, Bangladesh Prof. Tahmeed Ahmed, Dr. Chisti Mobayer, and Dr. Subhasish Das, ICDDR,B) and with Dr. Tim de Meij (Amsterdam UMC), to further validate VOCs. The ultimate aim will be to validate these VOC-data and to establish if VOCs can serve as proxies for pathophysiological mechanisms and/or as (an add on to) early risk prediction. This will be done as a sub-study in CHAIN part 2 that will start July 2020 with Daniella Brals (PhD) works as senior statistical advisor on this project.

3. Meningitis and Tuberculosis

The 'central nervous tuberculosis' or 'tuberculous meningitis' studies that take place in South Africa are in collaboration with the University of Stellenbosch and the affiliated Tygerberg academic hospital in Cape Town. It started in 2008 with a review on the burden of TBM: 'Twenty Years of Paediatric Tuberculous Meningitis: A

IMPRESSIONS FROM THE MENINGITIS AND TUBERCULOSIS RESEARCH LINE

Retrospective Cohort Study in the Western Cape of South Africa'. The past and current research projects are subdivided in clinical studies and basic science. The first clinical studies focused on early 'pre-clinical' detection of TBM and the host immune response (Regan Solomons and Douwe Visser). In that line of research, metabolomics profiling of urine samples was undertaken to develop a discriminating biosignature for different kinds of meningitis and to understand the metabolic response in TBM (Shayne Mason and ongoing by Simon Isaiah). A large postportem study of a historical cohort of brain specimens studies the immunohistopathology of TBM (ongoing by Dan Zahari). Proteomic profiling of the brain material was recently added on this topic (ongoing Abisola Shoyele). A prospective observational study is undertaken to monitor the effect of nutritional status and immunological status on the 6 months course of TBM (ongoing by Yajna Kooblal).

The Amsterdam Tuberculosis Centre (Amsterdam TBC) was initiated in 2018 by Prof. Marceline Tutu van Furth, ACGCH, together with Prof. Frank Cobelens, director of the AIGHD. The vision of the centre is: "A world free of tuberculosis", with the following mission: "To build the scientific basis for elimination of tuberculosis through multidisciplinary research and research-based education along the entire research and development chain." The need for the centre is based on the fact that tuberculosis (TB) is among the major global infectious diseases, and worldwide the number-one infectious cause of death. While in rich countries TB incidence rates have fallen dramatically over the past century, the burden of disease in low- and middle-income countries remains high, further compounded by HIV co-infection and increasing rates of anti-tuberculosis drug resistance. There is a global push for eliminating TB as a health problem, supported by the World Health Organization's End TB Strategy, requiring better diagnostics, drugs, vaccines and health service interventions. This calls for massive scale up in research, covering the entire research and development chain from basic science to implementation research. With the alliance of the two universities in Amsterdam merging the existing knowledge on TB into a single centre will provide a major scientific contribution to TB elimination.

The Amsterdam TBC will be complementary to the current Amsterdam UMC structures of research institutes: contrary to these it focuses on a single disease, bringing together various disciplines across the entire R&D chain, including basic microbiology and immunology, clinical/translational research, epidemiology,

IMPRESSIONS FROM THE MALARIA RESEARCH LINE

implementation/social science and health economics. Important added values are strong links with implementation, both clinical and public health, at national (Amsterdam UMC clinical departments, GGD) and international levels (KNCV Tuberculosis Foundation, collaborating clinical sites in low- and middle-income countries), as well as strong links with national and global disease control policy (RIVM, WHO, Stop TB Partnership).

4. Malaria

The malaria research line began with MBvH's "A Trial of Artemether or Quinine in Children with Cerebral Malaria" (NEJM 1996) and Prof. Feiko ter Kuile's (FtK) series of papers on the "Efficacy of permethrin-treated bed nets in the prevention of mortality in young children" (AJTMH 2003). This was followed by multi-centre studies, coordinated by Prof. Kamija Phiri and supervised by MBvH and FtK on the benefit of antimalarial treatment in preventing rebound severe anaemia in African children (Lancet ID 2011). Most recently this research line has been expanded by work by Menno Smit (MS) assessing the safety and efficacy of population-level drug interventions in individuals at risk of malaria in western Kenya. A trial with pregnant women showed that iron supplementation did not increase the risk of malaria infection in the mother's blood, the placenta or the new-born, increased the birth-weight by 234 grams in neonates born to iron deficient mothers, and increased the birthweight by 150 grams in all neonates regardless of maternal iron status (JAMA 2015). A trial with children (1-12 years old) showed that single low dose primaquine with artemisinin combination therapy reduced Plasmodium falciparum gametocyte carriage and reduced transmission to Anopheles mosquitoes (JID 2020), without increasing the risk of haemolysis in both G6PD-normal and G6PD-deficient children (pre-submission). Finally, an initial trial in adults showed that high-doses of ivermectin are safe and kill mosquitoes, which bite treated malaria patients, for at least 28 days after treatment, resulting in a new class of antimalarial drugs (Lancet ID 2018). Population-level modelling showed that in a highly seasonal moderate transmission setting adding high-dose ivermectin to seasonal malaria chemoprevention (SMC) or mass drug administration (MDA) with antimalarials would reduce clinical incidence of malaria in children under 5 years of age by 77% and 75% respectively compared to SMC/MDA without ivermectin (Lancet ID 2020). This work has attracted a lot of attention and led to more than $40 million in combined funding for the research groups helping to take this strategy forward. Currently field trials are ongoing in several countries assessing the impact of high-dose ivermectin with SMC/MDA on malaria incidence and prevalence. Further trials are assessing (i) the antiparasitic, i.e. not mosquitocidal, effect of ivermectin against Plasmodium, and (ii) the safety of (high-dose) ivermectin in children <15kg, whom previously have never been included in ivermectin studies and therefore are currently excluded as per the product label. Menno Smit is currently involved in many of these ongoing studies.

5. Anaemia

The anaemia research line was initiated by MBvH in 2002 as part of a Wellcome Trust career development fellowship awarded to study the aetiology and outcome of severe anaemia in Malawian children. This was the start of a very productive research theme which is still ongoing and had the New England Journal of Medicine paper by Calis et al as the initiating paper reporting on the aetiology of severe anaemia in Malawian children. Other papers on the outcome, risk factors and relationship between iron deficiency and susceptibility to infection followed. Especially the role of iron status and supplementation on haematological recovery and HIV disease progression and infection risk was studied in detailed and gave a new insight into the role of iron in infection and haemoglobin recovery. This research line not only resulted in 6 completed PhD tracks (K. Phiri, J. Calis, M. Esan, F. Jonker, A. Dhabangi and M. Huibers), as well as over thirty publications with several of them in high impact factor journals (e.g. NEJM, Lancet, CID). The leading role in this research line has been taken over by Prof. Kamija Phiri of the University of Malawi. Currently he is coordinating a multi-centre study evaluating the impact of intermittent presumptive treatment of malaria on the post discharge morbidity and mortality following a severe anaemia episode. This includes apart from efficacy, a cost-benefit analysis as well as feasibility component.

6. Coma and Convulsions

The coma and convulsions research line, abbreviated to Coco, was initiated by MBvH and JvW in 2015 and funded by a NWO grant. The focus of this project, much like the anaemia research line, was to study the aetiology of coma and convulsions in children in resource poor settings using conventional and state-of-the-art diagnostic techniques. As a proof of concept study, a pilot study was initiated in Malawi, Uganda and Rwanda, coordinated by Arther Edridge who received a AMC PhD Scholarship to continue this work as a PhD student. This project is still ongoing but has already resulted in several successful results. The preliminary results indicate that a wide range of common, uncommon and even novel viruses are implicated in the aetiology of coma and convulsions. One of these included a novel orthobunyavirus, detected in the cerebrospinal fluid of a Ugandan girl with a fatal encephalitis which was published in CID. A current case-control is currently ongoing in the region where the index case came from to determine the burden of the virus. Besides viruses, novel unbiased techniques such as metabolomics, 16s sequencing, indirect murine immunohistochemistry and gene expression profiling are currently being used to look at metabolic, bacterial, auto-immune and other causes in this cohort. To scale up scope of this study, a Wellcome Trust Collaborative Award in Science was recently applied for with a team of European, African, Asian and American researchers, initiated by MBvH, but was unfortunately rejected.

7. HIV

Antiretroviral treatment for HIV has become increasingly available in South Africa. For the treatment to be successful an adherence level of 95% is required. Especially among children, reaching this high level of adherence can be a challenge, given the complex set of both social and material factors that influence adherence. Among those factors, religion plays an important role: e.g. how people view treatment and illness, which influences their health care seeking and treatment behaviour.

Religious structures have become increasingly involved in the HIV epidemic over the past years. Both negative and positive effects on the HIV epidemic have been reported. Overall, religious structures are a valuable actor when addressing HIV, given their wide reach in communities and influence in daily lives of people. Specifically, religion can support improved paediatric ART adherence.

The research of PhD student Martha Teijmea and Germari Kruger (promotor MTvF) integrates existing literature and previous findings, and collects qualitative and quantitative data in order to better understand and eventually benefit from the interactions between child well-being, the role of religious structures, and HIV health care. This collaborative research can lead to a sustainable intervention involving local stakeholders (community leaders, religious leaders, health care workers, and community members) in Masiphumelele and Gugulethu in the Western Cape. Participants involved include community members, caregivers of children with HIV that receive ART, adolescents, health care workers, policy makers, and other people working in the intersection of health, HIV, and religion. Currently the following three PhD students are working on these project under supervision of promotor MTvF and are expected to defend their PhD's in the coming years:

- T. Msoka. PhD entitled "Effects of long-term use of anti-retroviral drugs and metabolomics changes in patients with HIV infection attending at Kilamanjar Christian Medical Center
- M. Teijema. PhD thesis entitled "Faith initiatives and HIV in the Western Cape Province, South-Africa
- G. Kruger. PhD thesis entitled "Stigma in faith initiatives and HIV in the Western Cape Province, South-Africa

A research line on HIV in Sub-Saharan Africa was initiated in 2010 by Job Calis following the strong link between anaemia and HIV identified in the severe anaemia study. The research line initially focussed on starting HIV treatment and detecting failure in Malawian children (Peter Moons and Minke Huibers). Given the high incidence of treatment failure we joined forces with Prof. Tobias Rinke de Wit and Dr. Cissy Kityo, who also studied resistance in children in Uganda and Nigeria on first and second line HIV treatment. This resulted in several PhD's including the four who were linked to the Global Child

Health Group: Sonia Boender, Ragna Boerma, Michaël Esan, Minke Huibers) and twenty publications including those in journals such as Lancet ID, CID and AIDS. The results of these studies have been used to adjust WHO guidelines for HIV treatment in children.

8. Nodding Syndrome

Nodding syndrome (NS) is a mysterious devastating neurological illness occurring in east African children. The epidemiological burden, disease aetiology and treatment are unknown. In 2016 we started a large case-control study, with a detailed clinical component, in the area surrounding Mundri, South Sudan, with the aim of obtaining a better understanding of the size of the problem, risk factors for disease and disease progression, and aetiology. The study is funded by the Dutch Ministry of Foreign Affairs. So far, our field and hospital teams have screened close to 3,000 households and identified over 500 children with NS of which 70 were taken to hospital for detailed investigations. The data are currently being analysed by PhD student Gasim Abd-Elfarac, supervised by MBvH and Dr. E. Rood of the Royal Tropical Institute (KIT). Results are expected by the end of 2020.

9. Neonatology

Prof. Mirjam van Weissenbruch holds the Desmond Tutu chair (Aim of the chair: ”Bridging Diversities for Academic Advancement” coordinated by SAVUSA (South Africa - VU University - Strategic Alliances). One of the most important targets of this program is the stimulation of exchange and guiding of undergraduate and PhD students. The chair has also created the opportunity to further develop the neonatal research agenda by adding South Africa as a second collaborating site aside from Indonesia.

South African (SA) collaboration: In SA neonatal morbidity and mortality is high, with infectious diseases related sepsis as one of the main causes. However, there is not much data available about the epidemiology, aetiology, diagnosis and management of neonatal-sepsis in Sub-Sahara Africa. There is an urgent need to study the outstanding questions related to the right diagnostic approach and optimal treatment of neonatal

IMPRESSIONS FROM NEONATOLOGY (TOP) & ANAEMIA (BOTTOM) RESEARCH LINES

sepsis in Sub-Saharan Africa. Together with neonatologist Lizel lloyd and Angela Dramowski of the Tygerberg Hospital, we are in the process of developing a bedside scoring system together with a cheap point-of-care (POC) test for pro-calcitonine and CRP in order to predict and/or identify neonatal sepsis at an early stage. This may ultimately lead to an improvement in better short- and long-term outcome.

Neonatal sepsis is also the focus of Tessa de Baat's research in collaboration with the Malawi Liverpool Wellcome Trust. Recognition of true neonatal sepsis amongst the large amount of neonates with presumed sepsis is of essential importance to reduce neonatal mortality and the rising problem of antimicrobial resistance in low and middle income countries.

Indonesian (IND) collaboration: The circumstances in Indonesia are in a way comparable to South-Africa. In Indonesia malnutrition, iron deficiency anaemia and chronic infectious diseases, before, during and after pregnancy, are very common. The incidence of prematurity and low birth weight is very high as well as the related mortality. Those who survive have a higher chance of growth restriction especially in the first 2 years of life.

Together with Prof. Rina Madarina (Paediatric Endocrinologist) and two PhD students at the Dr. Sardjito Hospital, University Gadjah Mada, we study the nutrition, hormone regulation, growth and body composition of preterm infants from birth until the corrected age of 6 months. In addition, we also investigate whether there are differences in DNA methylation, which can play an important part in the development of chronic disease due to malnutrition.

Another aim is to start a collaboration with Prof. Hamam Hadi of the Alma Ata University in Yogyakarta to co-investigate the consequences of malnutrition and iron deficiency anaemia in the mother and child in the city (high-income) as well as in the countryside (low-income). With an intensive intervention program already before marriage, information will be offered regarding optimal nutrition. Mother and the growth and development of the child will be followed until the age of two years.

10. Other Projects

- Fever in children in Burkina Faso: aetiology and development of diagnostic tests. P.I: Dr. H. Schallig. PhD student: Francis Kiemde. Co-investigator: Prof. M. Boele van Hensbroek.
- Microbiome and rotavirus vaccine efficacy in children, adults and a mouse model. Location: Pakistan, Ghana and the Netherlands. PhD student and P.I.: Vanessa Harris.
- MACHS: Evaluation of the impact of the Health Insurance Fund program on maternal and child health in Kwara state, Nigeria. PhD students: Daniella Brals and Deji Aderibigbi.
- 'Giving children a chance for life'. Prof. dr. A. Marceline van Furth (VUmc), Martha Teijema, Sabine van Elsland (Desmond & Leah Tutu Legacy Foundation, Cape Town, South-Africa), Maarten Kok (Faculty of Earth & Life Sciences, VU).
- #ITOO MENTORING PLATFORM - Social responsibility project by Marceline and Mpho Tutu van Furth in 2019: key factors influencing women's participation in leadership. (Ref: Lancet special issue "Advancing women in science, medicine, and global health" (vol 393. Number 10171).

IMPRESSIONS FROM THE NODDING SYNDROME RESEARCH LINE

"It would be amazing if we could find the missing pieces, with which we could reduce infant mortality from malnutrition"

DR. WIEGER VOSKUIJL
GENERAL PAEDIATRICIAN & SENIOR SCIENTIST

PHD PROGRAMME

SUCCESSFULLY DEFENDED PHD'S

59 **TOTAL**

3 **MEAN** PER YEAR

Year	# PhD's
'00	1
'01	0
'02	1
'03	3
'04	1
'05	1
'06	3
'07	2
'08	2
'09	1
'10	3
'11	3
'12	10
'13	3
'14	3
'15	6
'16	2
'17	2
'18	3
'19	6
'20	3*

* Expected number of defences

A total of 59 PhD students have successfully defended their PhD over the past 20 years. All but one at either the Vrije Universiteit or the University of Amsterdam. At the Vrije Universiteit Prof. Tutu-van Furth took seat as promotor (or co-promotor), at the University of Amsterdam Prof. B. Brabin acted as the promotor between 1999 and 2013 while Prof. M. Boele van Hensbroek did so from 2014 onwards.

One student (K. Phiri) defended his PhD at the University of Liverpool. For a full list of all the published PhDs please refer to Appendix A. List of Publications.

Especially for this report, we've reached out to four PhD alumni and asked to share their story after successfully completing their PhD.

FOUR STORIES

THE STORY OF
PROF. KAMIJA PHIRI

Prof. Kamija Phiri completed his PhD from the Liverpool School of Tropical Medicine under the supervision of Prof. Michaël Boele van Hensbroek and Prof. Bernard Brabin in 2006. He returned to his tenured position at the College of Medicine, University of Malawi in Blantyre to lecture and continue with his research career in anaemia. He secured a number of research grants (EDCTP and HRCSI Senior Fellowships) and grew into an independent researcher and established his own research group within the College of Medicine. In 2012 he was presented with the Merle A. Sande African award for leadership, training and research. He also served as Dean for Postgraduate Studies and Research and later founded the School of Public Health. He developed the PhD curriculum for the college and established masters' programs in epidemiology and global health. In 2015 he was made a full Professor in clinical epidemiology and also made a member of several national malaria policy making bodies.

As a researcher he has continued to have interest in strategies to prevent and treat of malaria in pregnant women and children. He has been awarded approximately $30million in grants since his PhD. He has recently established an independent research centre (Training and Research Unit of Excellence) currently supporting 4 postdocs and 10 PhD students, research interns and a 100+ member field team with sites across southern Malawi. He also leads a large consortium on post-discharge management of severe anaemia in children with trial sites in Kenya, Uganda and Malawi and with collaborators in UK (LSTM, LSHTM, Imperial College), Norway and USA. He recently was granted funding to establish a multidisciplinary multinational network to tackle anaemia in Sub-Sahara Africa.

THE STORY OF

DR. FRANCINE VERHOEFF

Two electives in Kenya, whilst being a medical student and foundation doctor in Leiden, gave Dr. Verhoeff the taste for further endeavours in tropical medicine. After following the Tropical Medicine & Hygiene course at the Liverpool School of Tropical Medicine in 1992, she was appointed as field investigator for an EU funded research project based in Malawi where she spent 3 years in the Chikwawa District. The Chikwawa district is known as the hottest and wettest area of the country assuring plenty of malaria to assess the consequences of malaria in pregnancy in mother and child.

In 2001, after completing her paediatric training in the Netherlands, she went back to Liverpool to become coordinator of the newly established PREgnancy and MAlaria network PREMA-EU. She combined this with working part-time as paediatrician in a local hospital. This was a perfect combination for several years but international travel became more difficult with a young family and she decided to focus on her paediatric career. She currently works as a consultant in a large teaching hospital in Liverpool. Her main interest still remains improving health for the many, this may no longer be in Africa, but Liverpool has a diverse population and her years in tropical Medicine taught her the importance of Public Health.

THE STORY OF

PROF. RALF WEIGEL

Prof. Ralf Weigel completed his PhD under the supervison of Prof. Bernard Brabin in 2012. Between 2002 and 2010 he was employed by the Ministry of Health in Lilongwe, Malawi, as clinical advisor for the Lighthouse Trust supported by the German technical cooperation. His role included mentoring, supervision, clinical care and operations research in diagnosis, treatment and prevention of HIV and TB.

Between 2010 and 2017 he worked at LSTM as a Senior Clinical Lecturer under the Education and Scholarship track to lead innovative learning and teaching for the Master's programmes in Clinical Sciences and contribute to LSTM's attainment of independent Higher Education status and Degree Awarding Powers. He was the Director of Studies for the *MSc in Tropical and Infectious Diseases* and *MSc in Tropical Paediatrics* programmes and convened the postgraduate modules *Current clinical challenges, HIV in resource limited settings* and *Development of a disease control programme*. He was also holding a post in the UK's National Health System as an Honorary Consultant Paediatrician at Alder Hey children's hospital in Liverpool.

Since October 2017 Prof. Weigel holds the Friede Springer endowed Professorship of Global Child Health at the Witten/Herdecke University, Faculty of Health, Department of Medicine, Germany.

THE STORY OF

PROF. STEPHEN GRAHAM

Prof. Stephen Graham's PhD studies focused on the devastating impact of the HIV epidemic on the epidemiology of respiratory disease in Malawian children. He was awarded the Leverhulme Medal by Liverpool School of Tropical Medicine for distinguished contribution to tropical medicine in 2007. Since returning to Australia from Malawi in 2008, his research has focussed on important causes of neonatal and child morbidity and mortality in the Asia-Pacific region. A particular commitment to capacity building through research in resource-limited settings – including supervision of PhD studies in Indonesia, Vietnam, Bangladesh and Papua New Guinea as well as conducting operational research training courses in PNG and Fiji. He is now Professor of International Child Health with The University of Melbourne, Group Leader in International Child Health with The Murdoch Childrens Research Institute, and Principal Research Fellow with The Burnet Institute, Melbourne.

He is particularly recognised for global and regional contribution to increasing attention to tuberculosis in children and adolescents – detection, treatment and prevention. Throughout his time in Malawi (1995-2007), Prof. Graham was responsible for inpatient and outpatient care of children and young adolescents with TB, collaborated with the Malawi NTP and conducted TB-related research. He was a founding member of WHO's Child TB sub-group (now Child and Adolescent Working Group), and was Chair from 2011 until 2017, as well as a member of WHO's Strategic Technical Advisory Group on TB. Under his leadership, the attention to child TB globally increased markedly, child-friendly fixed-dose combination treatments were developed, children were integrated with the WHO End TB Strategy (2015) and the first international Roadmap for Child TB was developed. Since 2009, he has been a consultant in child TB and lung health for the International Union Against Tuberculosis and Lung Disease (The Union, France) and was awarded the Karel Styblo Public Health Prize by The Union in 2015.

TEACHING & TRAINING

In the Netherlands

TEACHING AND EDUCATIONAL PROGRAMS ON GLOBAL HEALTH FOR MEDICAL STUDENTS AT THE AMSTERDAM UMC

(Vrije Universiteit and University of Amsterdam).

- Bachelor's students: 2nd and 3rd years.
- Master's students.

CERTIFICATE COURSE IN TROPICAL PAEDIATRICS AND CHILD HEALTH

- Introductory course in Tropical Paediatrics, based at the Emma Children's Hospital, location AMC, coordinated by Linde Nieuwenhuys and Prof. M. Boele v Hensbroek.
- This course offers 5 sessions of 5 hours, the 20th annual course is planned.
- Target group: Paediatric registrars and Tropical Medicine and International Health registrars, based in the Netherlands (average 18 participants/year).

SUMMER SCHOOL GLOBAL CHILD HEALTH - UNIVERSITY OF UTRECHT AND UNIVERSITY OF AMSTERDAM

- One week summer school started in 2018.
- Target groups: Master students and junior doctors from the Netherlands and international.
- The Amsterdam CGCH contributes to the organisation as well as the teaching.

REGULAR CONTRIBUTIONS BY AMSTERDAM CGCH MEMBERS TO OTHER DUTCH TRAINING COURSES:

- Masters in Anthropology (University of Amsterdam)
- NTC-Tropical Medicine Course (Royal Tropical Institute [KIT], Amsterdam)
- Tropical courses for Medical Students (University of Amsterdam, Leiden University)

International

MSF-EMMA CHILDREN'S HOSPITAL TROPICAL PAEDIATRIC COURSE

- Tailor made, 10 days annual course developed and started by M. Boele van Hensbroek and conducted at Queen's Elisabeth General Hospital, Blantyre, Malawi. Started in 2006.
- Target groups: MSF doctors and senior nurses.
- Currently the Amsterdam CGCH contributes teachers, but does not take part in the organisation of the course.

DIPLOMA IN TROPICAL MEDICINE AND HYGIENE.

- Annual diploma course of the Liverpool School of Tropical Medicine (LSTM), England.

POST-GRADUATE TRAINING OF PAEDIATRICS REGISTRARS

- Coordination of a six-months paediatric rotation at the Department of Paediatrics of Queen Elisabeth Central Hospital (Queens), College of Medicine, University of Malawi.
- This long standing relationship has developed into an official collaboration between the Emma Children's Hospital and the Paediatric Department of Queens, Blantyre, Malawi.

PAEDIATRIC SUPPORT ST. DAMIEN HOSPITAL, PORT AUX PRINCE, HAITI.

- Collaboration started on request from the 'Wereld ouders' NGO in 2017.
- The aim is to give sub-specialist support to the medical staff of St. Damien paediatric hospital through short visits by Emma Children's Hospital sub-specialists (nurses as well as doctors).
- The first visit was successfully done by R. Simons, former nursing head of the Emma Children's Hospital-PICU. The following visits will include a HIV and haematology specialist.






IMPRESSIONS FROM TEACHING AND/OR TRAINING

DR. VOSKUIJL AT THE NUTRITION REHABILITATION UNIT

JOURNAL REVIEWS

in alphabetical order

Acta Paediatrica *(MW)*

AIDS *(MBvH)*

L'Agence Nationale de la Recherche projects *(ANR France; MS)*

American Journal of Clinical Nutrition *(BB)*

Annals of Tropical Paediatrics and International Child Health *(MBvH, BB)*

Archives of Diseases of Childhood *(MBvH, BB, WV, MW)*

BMC *(MBvH, WV)*

BMC-ID *(MBvH, JC)*

BMC-Nutrition *(WV)*

BMC-Paediatrics *(WV)*

BMC Pregnancy and Childbirth *(BB)*

BMC-Medicine *(BB)*

BMJ-Open *(MBvH, WV, JC)*

British Medical Journal Infection and Immunology *(MBvH)*

Bulletin World Health Organisation *(BB)*

Clinical Chemistry and Laboratory Medicine *(MW)*

Ebiomedicine *(JC)*

Fertility and Sterility *(MW)*

Gates Open Research *(MS)*

Hormone Research *(MW)*

Human Reproduction *(MW)*

Infection and Immunity *(BB)*

International Journal of Epidemiology *(BB)*

JAMA *(MBvH, BB, MW)*

Journal of Antimicrobial Chemotherapy *(MS)*

Journal of Infectious Diseases *(MBvH)*

Journal of lnfection *(BB)*

JPGN *(WV)*

Journal of Clinical Endocrinology and Metabolism *(MW)*

Journal of Neuroinflammation *(MvdK)*

Journal of Public Health Medicine *(BB)*

Journal of Tropical Paediatrics *(JC)*

Lancet *(MBvH, BB)*

Lancet Global Health *(JC)*

Malaria Journal *(MBvH, BB, MS)*

Malawi Medical Journal *(JC)*

MRC projects *(WV, BB)*

New England Journal of Medicine *(BB, JC)*

Netherlands Journal of Critical Care *(JC)*

Obesity *(MW)*

Parasitology *(MBvH)*

Parasitology Today *(BB)*

Paediatrics *(MBvH, BB, JC)*

Paediatric Research *(MW)*

Paediatric Infectious Diseases Journal *(MBvH)*

PLoS Medicine *(MBvH, WV)*

PLoS NTD *(MS)*

PLoS One *(MBvH, WV, MW)*

Public Health Nutrition *(BB)*

Toxicology *(MW)*

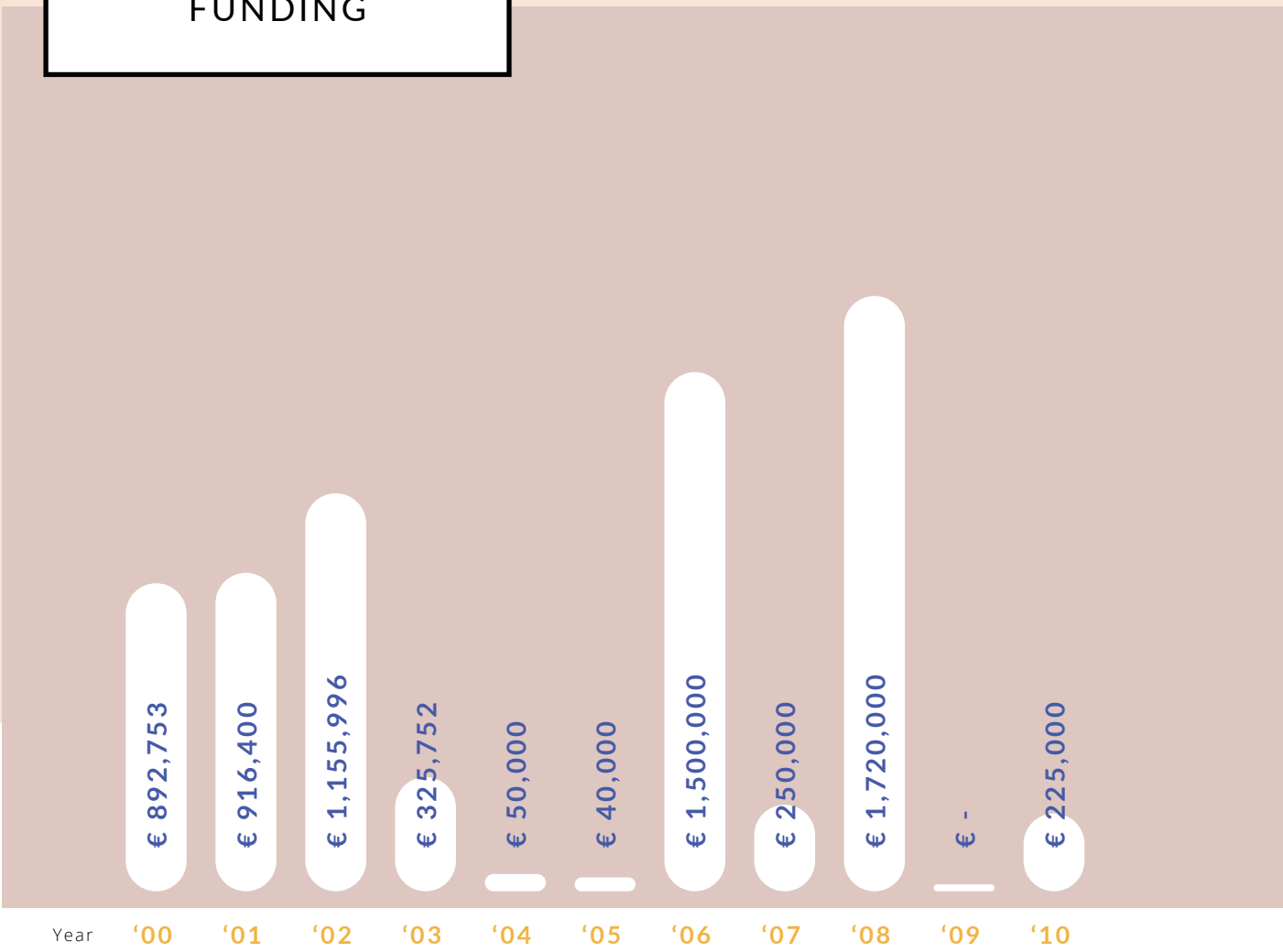
Tropical Medicine and International Health *(MBvH, BB, JC)*

Transactions of the Royal Society of Tropical Medicine and Hygiene *(MBvH, BB)*

Tropical Doctor *(WV)*

Wellcome Trust Population and Health Projects *(BB)*

FUNDING

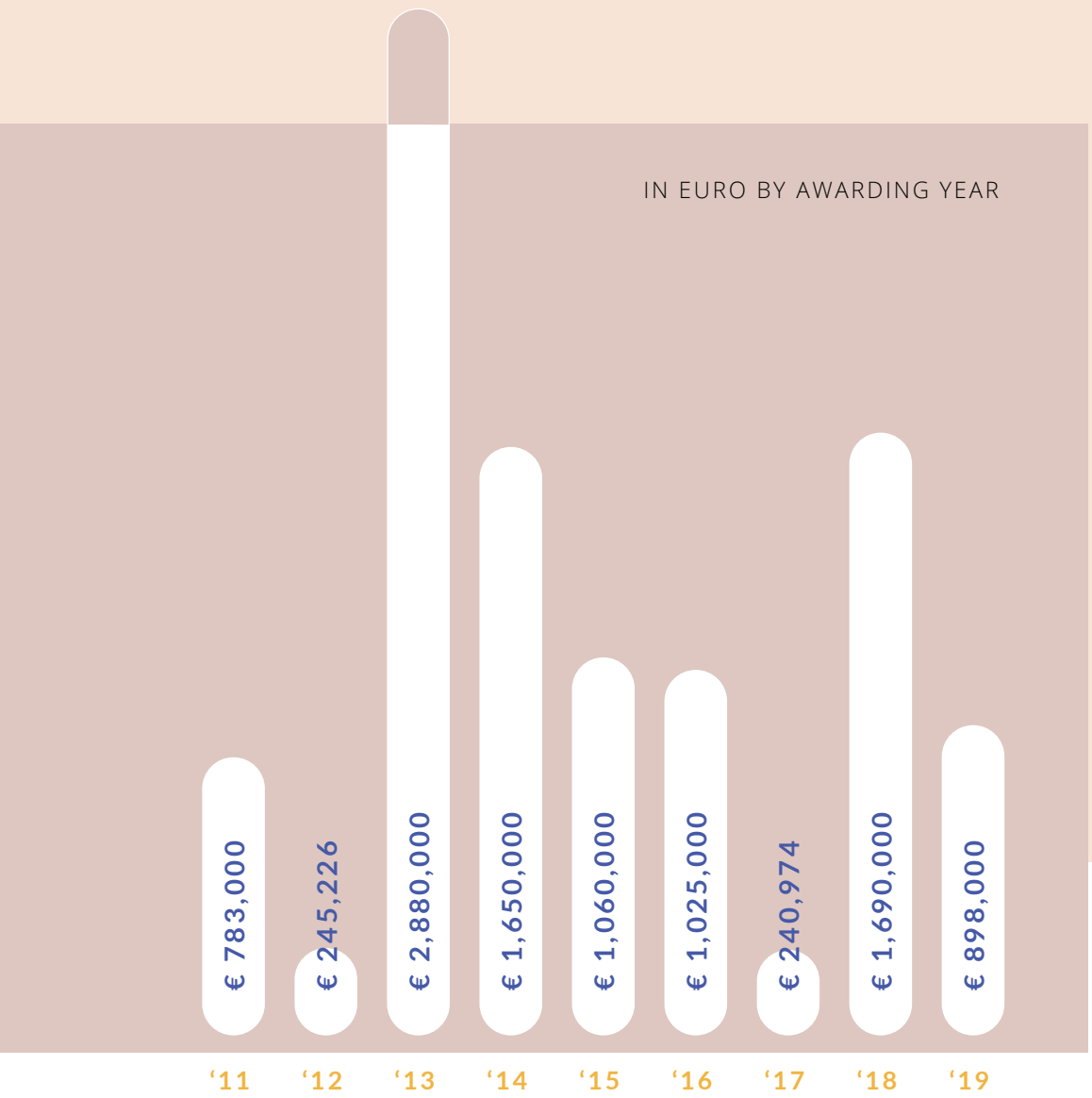


Core funding

- *1999-2013:* Annual remittance to LSTM covering administrative cost Prof. B Brabin and running cost: Emma Children's Hospital-AMC. € 27,000.
- *2013-present:* Salary support secretarial support GCHG: Emma Children's Hospital-AMC. € 20,000/year.
- *2013-present:* Salary support Prof. M. Boele van Hensbroek. Division A (Department of Global Health, AMC), 0,3 FTE.
- *2018-present:* Salary support Dr. W.P. Voskuijl. Division A (Department of Global Health, AMC), 0,2 FTE.

Grants obtained ongoing

- *2016-2020:* South Sudan Nodding Syndrome Study (SSNSS). Ministry of Foreign Affairs, €1.000.000 (M. Boele van Hensbroek).
- *2017-2021:* Encephalopathies of unknown cause in children in resource poor settings. AMC-PhD fellowship A. Edridge €216.064 (M. Boele van Hensbroek).
- *2018-2020:* Minimally Invasive Tissue Sampling in children dying of an acute illness with varying forms of undernutrition; determining Causes of Death within the Malawian 'CHAIN' cohort. "MITS in CHAIN. Bill and Melinda Gates Foundation $1.400.000,- total funding (W.P. Voskuijl).
- *2018-2020:* Shock in children; epidemiology, early recognition and pathophysiology.



€17.7m
TOTAL
OVER 20 YEARS

€887k
MEAN
PER YEAR

€3.7m
GRANTS
OBTAINED
ONGOING

Please refer to Annex B. for a detailed overview of all grants obtained

Stichting Steun Emma: € 30.000 (J.C.J. Calis).

- *2018-2022:* Optimizing strategies for the diagnosis of hospital-acquired neonatal sepsis in low resource settings: Tygerberg Hospital, Stellenbosch University South Africa., €100.000 (M. Weissenbruch.).
- *2018-2022:* Effect of Global DNA Methylation Status At Birth And Early Life Nutrition To The Growth Velocity and Nutritional Status In Low Birth Weight Infants. Gadja Mada University/ Sardjito General Hospital. €80.000 (M. Weissenbruch).
- *2018-2022:* Body Composition of Premature Infants at Term Equivalent Age (2018-2022). Gadja Mada University/ Sardjito General Hospital. €80.000. (M. Weissenbruch).
- *2019-2020:* Monitoring device for children in RPS. NWO, € 40.000 (J v Woensel)
- *2019-2021:* Improving HIV care in Indonesian children through Monitoring, Evaluation and Clinical Research (INDIGO). Ter Meulen foundation and Emma Children's Hospital-GCHG funding. €28.000. (M. Boele van Hensbroek).
- *2019:* AI&I TBM. Doortje Heemskerk: €80.000 (M. Tutu v Furth).
- *2019:* Doctoral training grant for South African PhD. NRF-Nuffic: €80.000 (M. Tutu v Furth).
- *CHAIN-2:* Pancreatic Enzymes and Bile acids: A non-antibiotic approach to treat intestinal dysbiosis in acutely ill severy malnourished children (PB-SMAL). USD 640.000 (W.P. Voskuijl)

PUBLICATIONS

During the reporting period a total of 307 manuscripts were published in peer reviewed medical journals with major contributions by members of the Amsterdam Centre for Global Child Health. This included publications in high impact journals, like the New England Journal of Medicine and The Lancet, but also in journals with a high impact in the local medical communities, like the Malawi Medical Journal. The average number of publications per year, over the reporting period was 15, but there is a steady increase in numbers over time, with over 20 publications per year in the most recent years. When interpreting these numbers, one must realise however, that over the study period the number of scientific staff also increased to eight in recent years.

More important is the fact that we have made major contributions to the general knowledge and understanding in several important areas of Global Child Health. For example, the severe anaemia research line has made major contributions towards our understanding of the aetiology, pathogenesis, treatment and prevention of this often fatal paediatric syndrome. Especially our work on the role of iron-infection interactions and the importance of malaria prevention have had an important impact on treatment and prevention strategies worldwide. The work done on TB meningitis in South African children and animal models has given insight in early diagnosis of TBM patients and treatment adherence and on mycobacterial brain invasion and the brain immune response. Finally, our work on severe malnutrition in Malawian children has made a major contribution towards our understanding of the clinical phenotyping of children with complicated severe malnutrition. In addition much information about gastro-intestinal dysfunction in these children and potential new treatments have been investigated. A complete list of all publications can be found in Annex A.

Summary

307
TOTAL

15
MEAN
PER YEAR

Year	# PhD's
'99	9
'00	3
'01	6
'02	7
'03	10
'04	12
'05	9
'06	18
'07	14
'08	16
'09	13
'10	12
'11	13
'12	15
'13	14
'14	18
'15	20
'16	24
'17	21
'18	25
'19	28

Only global child health relevant papers included from core members

FUTURE PERSPECTIVES

STRATEGIC PLAN 2020- 2024

There is no time to sit back! Despite the progress that has been made over the past two decades, global mortality among young children is still unacceptably high, especially in low-resource settings (LRS). Knowledge of paediatrics and scientific research into the causes, pathophysiology, treatment and disease outcomes in children in LRS are therefore still necessary.

Over the past decades, the Netherlands has developed into a more globalised society in which, paediatricians may encounter rare tropical diseases, epidemics of emerging infectious diseases, as well as various cultural perceptions of childhood disease by parents from different ethnic backgrounds. Furthermore, mortality in children from ethnic minorities in the Netherlands is substantially higher than that of Dutch Caucasian children. Finally, frequent paediatric medical care is required after (natural) disasters, conflicts and massive migration, as recently became clear in the refugee camps on, for example, Lesbos, Greece. The conclusion from the above may therefore only be that good knowledge of Global Child Health (GCH) is essential not only for paediatricians (in training) who want to work in LRS, but also for those who remain working in the Netherlands.

Currently, GCH knowledge is fragmented and spread over many sub-specialists, working in various institutes throughout the Netherlands. This means that it is difficult to find the right specialist if advice is needed about a specific patient, but also if a GCH item (for example, new developments in the field of tuberculosis treatment or malnutrition) must be interpreted in the media. In addition, it can also be a challenge to find the right teacher for the development and / or teaching of modules in the field of GCH. Finally, the fragmented knowledge does not promote the formation of knowledge networks for the development and implementation of GCH related research proposals.

Bringing a wide range of sub-specialists together in one group, the "Amsterdam Centre for Global Child Health (Amsterdam CGCH)", pools knowledge, creates shorter lines and improves effectiveness (for example, if a paediatrician has to contribute to medical teams deployed in international relief actions).

The initiative to further develop an Amsterdam CGCH fits in seamlessly with the name, ambition and international image that the Amsterdam UMC has in the field of Global Health and Internationalisation and which has already taken shape in the Amsterdam Institute for Global Health and Development (AIGHD).

THEME 1

AMSTERDAM CGCH AS KNOWLEDGE CENTRE FOR CLINICAL QUESTIONS

Over the past two decades, expertise in the field of GCH has been built up in the field of GCH in both the (former) VUmc and the (former) AMC. With the alliance of the two institutes the expertise has been merged resulting in at least one expert in each of the following key areas within GCH: neonatology, intensive care, malnutrition, anaemia, oncology, meningitis, malaria, tuberculosis and HIV. The alliance has also brought together education and research experts in low-resource settings. This concentration of GCH expertise in one centre (Amsterdam UMC) is unique for the Netherlands. The experts listed in the table below are affiliated with the Amsterdam CGCH.

In the coming years, the Amsterdam CGCH wants to further distinguish itself as an (inter) national knowledge Centre in the field of GCH and make this knowledge available to the following target groups and situations:

1. Medical professionals inside and outside the Netherlands. The Amsterdam CGCH wants to be the centre for consultation and advice for (paediatric) doctors in the Netherlands with regard to the diagnosis and treatment of children with suspicion of a "tropical disease". It is expected that with more brand awareness both the number of consultations and the number of referred patients to the Amsterdam CGCH will increase in the coming years.
2. The aim of the Amsterdam CGCH is to set up a 'paediatric task force', in which members of the Amsterdam CGCH can be deployed ad hoc via partners such as Doctors without Borders if international emergencies arise where GCH expertise is required.
3. Media or government agencies seeking expertise to identify or interpret a particular GCH health problem.
4. Donors ("Funders") who are looking for opportunities to sponsor paediatric projects in low-research settings.

Experts affiliated with the Amsterdam CGCH

Neonatology	Prof. Mirjam van Weissenbruch Drs. Tessa de Baat
Intensive care	Dr. Job Calis Prof. Job van Woensel
Malnutrition	Dr. Wieger Voskuijl
Anaemia	Dr. Job Calis Prof. Michaël Boele van Hensbroek
Oncology	Dr. Minke Huibers
Meningitis	Prof. Marceline Tutu - van Furth Dr. Martijn van der Kuip
Malaria	Dr. Menno Smit Prof. Michaël Boele van Hensbroek
Tuberculosis	Prof. Marceline Tutu – van Furth Dr. Martijn van der Kuip
HIV	Dr. Job Calis

THEME 2

SCIENTIFIC RESEARCH

The doctors of the Amsterdam CGCH are initiators of, or are very closely involved in, various research projects and programs in low research settings. In this regard, there is close cooperation with the Amsterdam Institute of Global Health & Development (AIGHD) of the Global Health department of the Amsterdam UMC. In recent years, this has resulted in the acquisition of major research grants and the publication of dozens of scientific articles every year. The current research areas of the Amsterdam CGCH are:

Malaria: this infectious disease still has a high morbidity and mortality and the research is aimed at optimising treatment and prevention of new infections and complications.

Tuberculosis (TB): In children, TB can quickly lead to an often life-threatening infection in the brain (TB meningitis). The research into this (in animal models and in humans) aims to gain a better understanding of pathophysiology in order to develop more effective treatments.

HIV: In children, HIV is a treatable disease, but (still) without any prospect of a cure. Good therapy compliance helps to prevent resistance and complications. This can be monitored with the "HIV Monitoring Foundation" (SHM) monitoring system. This system is being evaluated with our partners in Indonesia.

Nodding Syndrome: This is a neurological disease that only occurs in children in East Africa and has nodding as one of the hallmark symptoms. Epidemiology (including the extent of the problem), aetiology and treatment are unknown. The research, in South Sudan, focuses on the first two aspects.

Shock & critical care: Shock is a leading cause of death for (young) children in LRS. Not enough is known about the aetiology of childhood shock in LRS. In Malawi, research is conducted into the aetiology and risk factors in the context of the 'critical care' research line.

Coma & convulsions: These neurological syndromes are very common in LRS and are a frequent reason for hospitalisation, with high mortality rates in this case as well. Cerebral malaria has long been considered the leading cause, but now that malaria is less common and the incidence of coma and convulsions has not decreased proportionately, research into other causes is a priority. This research is carried out by the Amsterdam CGCH in Uganda, Rwanda and Malawi.

Severe anaemia: This syndrome, too, is still associated with high mortality in young childre, in particular after hospital discharge. Prevention and treatment have been subjects of ongoing research for more than a decade, with the most recent research focusing on the prevention of malaria and bacterial infections.

Oncology: it is estimated that two-thirds of children diagnosed with cancer live in a low resource setting. Survival of these children is extremely low. Research in Malawi focuses on improving the treatment of children with cancer in this setting with a special focus on the effect of severe malnutrition on treatment.

The future

An important aspect of the scientific program of the Amsterdam CGCH is research capacity building in the countries where the research is carried out. This is done by setting up research sites, training local researchers and supporting staff, but above all by training local PhD students. In the past two decades, more than 40 local students have successfully defended their dissertations at the UvA or VU and obtained their PhD. Given the current number of

PhD students, it is expected that this successful program will continue in its current size in the next five years.

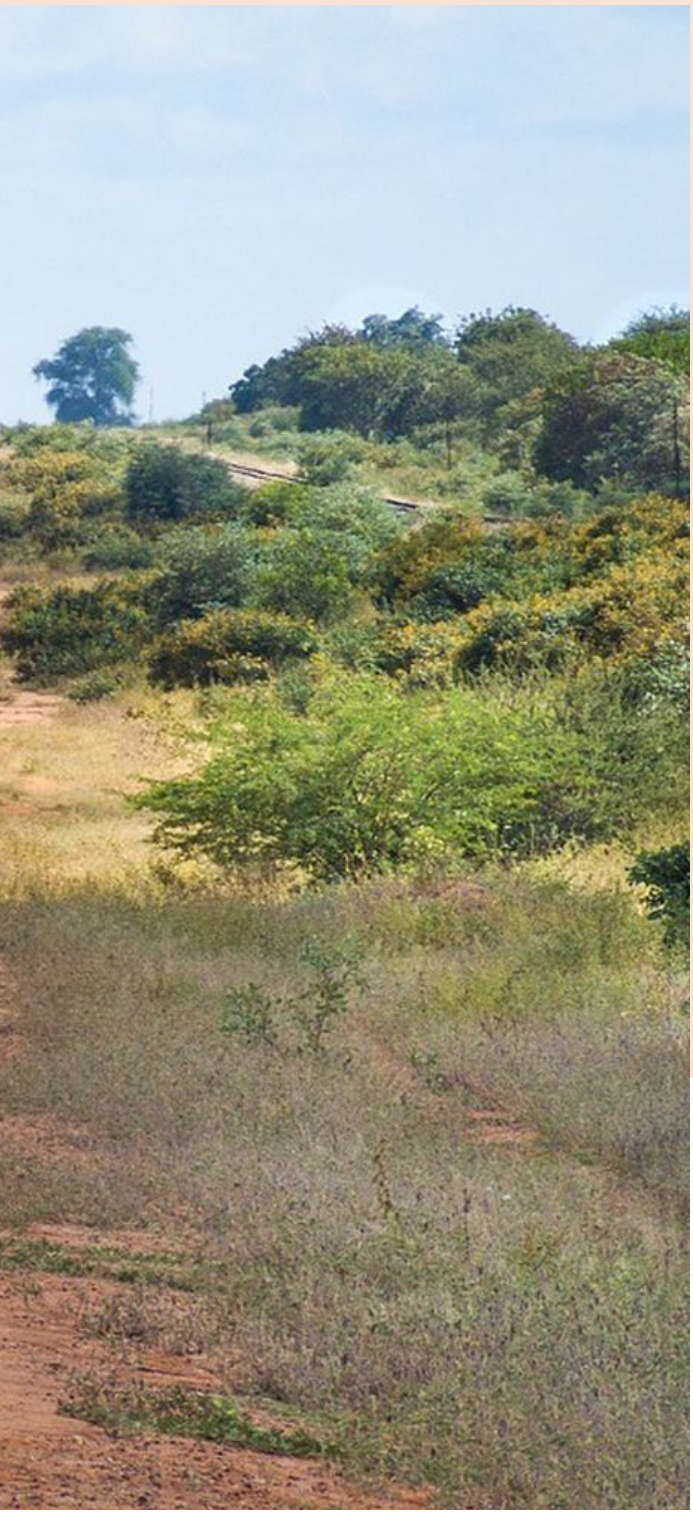
The Amsterdam CGCH wants to further strengthen the existing lines of research, as described above, through cross-pollination and new initiatives. In particular, efforts will be made to further expand the research lines 'critical care' and 'malnutrition'. In addition, there are advanced plans to develop a new line of research with a focus on migration issues, both in the Netherlands and in refugee camps on the borders of Europe. The newly to be established 'Paediatric Task Force' of the Amsterdam CGCH will also have its own line of research.

THEME 3

TRAINING & EDUCATION

Within the Amsterdam UMC, Amsterdam CGCH doctors are involved in the education of medical students in the Bachelors and the Master phase. In addition, for more than twenty years, a multi-day course "Global Child Health" has been given to paediatricians and Doctors of International Health and Tropical Medicine in Training (AIGT). Outside the Amsterdam UMC, Amsterdam CGCH physicians contribute to courses and training in Amsterdam, Leiden, Utrecht and Liverpool (England) and Blantyre (Malawi). In addition, the Amsterdam CGCH organises annual courses and summer schools for (para) medics. The aim is to further expand these educational activities in the coming years, including by offering new courses.

Finally, the Amsterdam CGCH plays a central role in creating opportunities for paediatric registrars to work for at least six months in children's wards in collaborating hospitals in low-resource settings. This offers much-needed paediatric support to local hospitals and allow registrars to develop GCH expertise.



"By training and educating medical students today, I hope to pass on the baton one day"

PROF. MICHAËL BOELE VAN HENSBROEK
HEAD OF THE AMSTERDAM CENTRE FOR GLOBAL CHILD HEALTH

ANNEX

ANNEX A

LIST OF PUBLICATIONS

FULL LIST BY SENIOR STAFF MEMBER

Publications 1999

Brabin B. *Iron pots for cooking: wishful thinking or traditional common sense?* **The Lancet**. 1999;353(9154):690-1. http://doi.org/10.1016/s0140-6736(98)00370-5.

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ANNEX B

OVERVIEW OF GRANTS OBTAINED

GRANTS OBTAINED AND CLOSED

TOTAL € 14.013.137
EXCL. KWARA, AIGHD FUNDING

2000-2004: A cost-shared concerted action on malaria and anaemia control for pregnant women and their infants (PREMU-EU): EU funding: € 658,753 (B. Brabin).

2000-2007: Amsterdam-Liverpool collaborative project on teaching and research in tropical paediatrics. "Child Foundation", The Netherlands and Academic Medical Centre, University of Amsterdam. Cost: €234,000 (B. Brabin)

2001-2006: Studies into the aetiology pathogenesis and long term outcome of severe anaemia in Malawian children (SEVANA) Wellcome Trust: € 815,400 (M. Boele van Hensbroek).

2001-2004: Growth in infants and adolescents in malarious area of rural Malawi. Bill and Melinda Gates Foundation: € 101,000.

2002-2004: Randomised controlled trial of iron cooking pots for prevention of iron deficiency anaemia: Bush Hospital Foundation € 29,500 (B. Brabin)

2002-2004: PhD training costs for Boniface Kalenda. Bill and Melinda Gates Foundation. € 116,570 (B. Brabin).

2002-2004: HIV and anaemia PhD scholarship J.C. Calis. Ter Meulen Foundation € 80,000 (JC Calis & M. Boele van Hensbroek).

2002-2007: New approaches to improve coverage and compliance of antimalarial treatment for pregnant women in rural Africa. EU-INCO € 849,926 (B. Brabin).

2002: The role of inflammatory mediators during experimental tuberculous meningitis. Mr. Willem Bakhuys Roozeboomstichting € 80.000 (M. Tutu v Furth).

2003: The role of inflammatory mediators during experimental tuberculous meningitis. KNCV Tuberculosefonds € 15.000 (M. Tutu v Furth).

2003-2006: The role of zinc and other micronutrients in the aetiology and pathogenesis of malaria. WOTRO € 270,252 (B. Brabin).

2003-07: Studies on infant anaemia and cord clamping practices (Zambia): Liverpool/Amsterdam International Child Health Programme €40,500 (B. Brabin)

2004-2006: HIV and anaemia PhD scholarship J.C. Calis. Numico stipendium € 50,000 (J.C.J. Calis & M. Boele van Hensbroek).

2005: De rol van immunoglobulinen in de behandeling van experimentele meningitis. Baxter BV € 45.000 (M. Tutu v Furth).

2006-2012: College of Medicine, Malawi-Amsterdam-Liverpool partnership for Research Capacity Development through the establishment of a Research Support Centre in the College of Medicine, University of Malawi (COMMAL). NWO-WOTRO € 850,000 (M. Boele van Hensbroek).

2006-2012: Double blind randomised trial to evaluate the use of Coartem as Intermitted Preventive Treatment –post discharge in children following a severe malaria anaemia episode (IPTpd). NWO-WOTRO € 650,000 (Boele van Hensbroek).

2007-2012: Double blind randomised trial to evaluate the effect of iron supplementation in haematological recovery in HIV infected anaemic children. NWO-WOTRO € 250,000 (M. Boele van Hensbroek).

2008: Tuberculeuze meningitis Township project. Turing Foundation, Alexander Ribbink and KIDS Rights. Total € 45.000. (M. Tutu v Furth).

2008-2010: Simple markers to start HAART in children; NWO-NACCAP and Stichting Steun Emma: € 175,000 (150,000 + 25,000), (J.C. Calis).

2008-2013: Malaria risk prior to and during pregnancy in nulliparous women receiving long-term weekly iron and folic acid supplementation (WIFS): a non-inferiority randomised controlled trial. National Institutes of Health (USA) $ 1,500,000 (B. Brabin).

2010: Effects of long-term use of antiretroviral drugs and metabolomics changes in patients with HIV infection attending at Kilimanjaro Christian Medical Center, Tanzania. Nuffic: € 85.000.

2010: Mathematical modelling of tuberculous meningitis. ESPID Fellowship Award MvdK: €80.000.

2010-2011: Hepcidin and other iron markers in Malawian children. Janivo and Stichting Steun Emma € 60,000 (J. Calis).

2011: Metabolomics study and Improving early diagnosis of tuberculous meningitis. Desmond Tutu PhD's € 180.000 (M. Tutu v Furth).

2011: Tuberculous meningitis home treatment program. UBS Optimum Fund € 118.000 (M. Tutu v Furth).

2011: Tuberculous meningitis home treatment program. Lions Noordwijk: € 60.000 (M. Tutu v Furth).

2011: Neonatal infections. Nuts-Ohra Fonds € 225.000 (M. Tutu v Furth).

2011-2019: TBM South Africa: from bench to bedside. Mr Willem Backhuys Roozeboom Stichting € 200.000. (M. Tutu v Furth).

20012-2015: Pancreatic exocrine replacement therapy in severely malnourished children (Optmism trail). Stichting Steun Emma € 68,000 and Ter Meulen foundation €35,900. (W.P. Voskuijl). 2012-2015: Pancreatic exocrine replacement therapy in severely malnourished children. The "OPTIMISM" trial, a pilot study. Ter Meulenfonds, € 38,000 (W.P. Voskuijl).

2012-2016: Appropriate Fluid Resuscitation for Shock in Severely Malnourished Children. Co-applicant (AFRIM). Medicines sans Frontieres (MSF): € 171.326 (J. v Woensel).

Health Insurance Fund – evaluation of impact on child health MinBuza € 1.000.000 (AIGHD-group including J.C.J. Calis & M Boele van Hensbroek, not included in the total sum of funds obtained)

2013-2017: High quality research and sustainable research capacity building through a Research Support & Training Center network for sub-Saharan Africa (RSTC network programme): Ministry of Foreign Affairs. € 2,880,000 (M. Boele van Hensbroek).

2014: Giving Children a Chance for Life; Postcodeloterij: € 1.500.000. (M. Tutu v Furth).

2014-2015: Phase III Randomised, double blind, placebo-controlled trial of a reduced carbohydrate formulation of F75 therapeutic milk among children with severe acute malnutrition, the "F75-trial. The Thrasher Research Fund with $150,000 of $450,000 total funding (W.P. Voskuijl).

2015-2017: Rotavirus vaccine and the microbiome. Stichting Steun Emma: € 60,000 (M. Boele van Hensbroek),

2015-2019: The Childhood Acute Illness and Nutrition (CHAIN) network. Bill and Melinda Gates Foundation $ 1,000,000 for the Malawian site ($12.500.000,- total funding) (W.P. Voskuijl)

2016-2018: Numico stipendium PhD scholarship Iron and anaemia. Numico foundation. € 25,000 (J.C.J. Calis).

2017-2019: Bone marrow iron deficiency in HIV-infected Malawian adults: defining its role in the development of very severe anaemia and identifying the best peripheral blood marker. Nutricia Research Foundation: € 24,910 (J.C.J. Calis).

GRANTS OBTAINED ONGOING

TOTAL € 3.744.064

2016-2020: South Sudan Nodding Syndrome Study (SSNSS). Ministry of Foreign Affairs, € 1,000,000 (M. Boele van Hensbroek).

2017-2021: Encephalopathies of unknown cause in children in resource poor settings. AMC-PhD fellowship A. Edridge € 216,064 (M. Boele van Hensbroek).

2018-2020: Minimally Invasive Tissue Sampling in children dying of an acute illness with varying forms of undernutrition; determining Causes of Death within the Malawian 'CHAIN' cohort. "MITS in CHAIN. Bill and Melinda Gates Foundation $1.400.000,- total funding (W.P. Voskuijl).

2018-2020: Shock in children; epidemiology, early recognition and pathophysiology. Stichting Steun Emma: € 30,000 (J.C.J. Calis). 2018-2022: Optimizing strategies for the diagnosis of hospital-acquired neonatal sepsis in low resource settings: Tygerberg Hospital, Stellenbosch University South Africa. , € 100.000 (M. Weissenbruch.).

2018-2022: Effect of Global DNA Methylation Status At Birth And Early Life Nutrition To The Growth Velocity and Nutritional Status In Low Birth Weight Infants. Gadja Mada University/ Sardjito General Hospital. €80.000 (M. Weissenbruch).

2018-2022: Body Composition of Premature Infants at Term Equivalent Age (2018-2022). Gadja Mada University/ Sardjito General Hospital. €80.000. (M. Weissenbruch).

2019-2020: Monitoring device for children in RPS. NWO, € 40.000 (J v Woensel)

2019-2021: Improving HIV care in Indonesian children through Monitoring, Evaluation and Clinical Research (INDIGO). Ter Meulen foundation and Emma Children's Hospital-GCHG funding. € 28,000. (M. Boele van Hensbroek).

2019: AI&I TBM. Doortje Heemskerk: € 80.000 (M. Tutu v Furth).

2019: Doctoral training grant for South African PhD. NRF-Nuffic: € 80.000 (M. Tutu v Furth).

CHAIN-2: Pancreatic Enzymes and Bile acids: A non-antibiotic approach to treat intestinal dysbiosis in acutely ill severy malnourished children (PB-SMAL). 640.000 USD (W.P. Voskuijl)

CORE FUNDING

1999-2013: Annual remittance to LSTM covering administrative cost Prof. B Brabin and running cost: Emma Children's Hospital-AMC. € 27,000.

2013-present: Salary support secretarial support GCHG: Emma Children's Hospital-AMC. € 20,000/ year.

2013-present: Salary support Prof. M. Boele van Hensbroek. Division A (Department of Global Health, AMC), 0,3 FTE.

2018-present: Salary support Dr. W.P. Voskuijl. Division A (Department of Global Health, AMC), 0,2 FTE.

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