ANNUAL REPORT 2020
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The CISMAC consortium was established in 2013 as a Centre of Excellence in intervention science to generate evidence for interventions that would effectively and equitably improve maternal and child health (MNCH) and development in low- and middle-income countries (LMICs). We conduct randomized controlled trials to identify strategies to improve MNCH and development; disseminate and facilitate the use of new evidence for LMIC health programme action; and strengthen the research capacity of the host institutions and their national and international partners to promote their position in MNCH research.

2020 was an unusual year, tragically affected by the COVID-19 pandemic. From the first reports of an unusually severe infection detected in specific locations and hopes for its rapid containment, the situation evolved beyond control into a full-blown pandemic that changed lives and livelihoods around the world. By the end of 2020, over 80 million COVID-19 cases and almost 2 million deaths were recorded. In addition to the misery of disease and loss of lives, the disruption of health services and economic hardship compounded its devastating impact. The pandemic and measures to contain it threaten to reverse decades of progress in maternal and child health and have turned the achievement of the Sustainable Development Goals (SDGs) a more distant target than it was a year ago.

CISMAC partners engaged in the response to COVID-19 at international and national levels. Internationally, we joined WHO-coordinated COVID-19 Research Networks and will participate in the Data and Safety Monitoring Committee for WHO’s COVID-19 SOLIDARITY Vaccine Trials. At the national levels, we lent support to advisory boards; set up studies, using opportunities created by our projects, to understand the epidemiology of COVID-19 and try to identify approaches to control its spread; and assisted our study populations in coping with the hardship brought by the pandemic. Data collection was adjusted to respond to new national guidelines, aiming to protect the health of our study participants and teams. Processes for remote exchanges between the partners were developed and strengthened to allow education programmes and monitoring of study progress to continue and ensure that our studies and teams had support for sustained motivation and quality.

CISMAC continues to be committed, through its network, to increase the quantity and improve the quality of evidence on interventions that promote maternal, newborn and child health and development with the aim to reduce health inequities. The objectives of conducting and supporting cutting-edge research, creating mechanisms for sustained and expanded collaboration, strengthening research and leadership capacity, and influencing policy and programme action have continued to guide us during this turbulent year. CISMAC’s active research agenda now includes 22 studies. They focus on interventions that primarily affect the critical period from conception up to the child’s third year of life, aiming to equitably improve survival and give babies the best opportunities for optimal development.
You will find in this report a selection of our achievements during 2020. They include the completion of data collection in intervention studies in Zambia, Uganda and Nepal— all with high quality and with follow-up exceeding 90%. They also include important publications in high impact international journals, such as the New England Journal of Medicine, Epidemiology as well as successes in procuring external funding, amounting to more than 40 mNOK secured in 2020.

Strengthening research capacity is a key component of CISMAC’s strategy and activity.

Strengthening research capacity enhances the quality of our outputs and promotes the sustainability of our partner groups and of our mission. An important part of CISMAC’s postgraduate training is done as an integrated part of our research. Such capacity strengthening has been affected less than that of some of our research projects. For the PhD candidates and postdoctoral fellows whose projects have been affected, we do our utmost to uphold training activities, now almost exclusively through digital interaction, including our webinar series. Our partners have invested significantly in successfully strengthening the capacity of their staff, using CISMAC support but also other financing opportunities as well as their own funds. Of the 25 PhD candidates enrolled since 2013, 9 have completed and 10 out of 17 postdocs have also completed their terms.

The development of effective vaccines against COVID-19 heightened our hope that a kind of normalcy will start to be restored in 2021. We look forward to a brighter year. Important new studies are planned, analyses of our completed studies will result in impactful papers, new courses and education activities will be implemented.

We express our deep appreciation and gratitude to all the CISMACers who so diligently have kept up their excellent work, continuing the studies despite the many hurdles and securing the safety of all participants as well as the scientific integrity of our studies. We are also deeply indebted to the members of our Data Safety and Monitoring Boards, including Drs. Vinod Paul, Simon Cousens, Nigel Rollins, Lars-Åke Persson, Max Petzold, and Sven-Arne Silfverdal, for their important work in following our trials and advising us. We are confident that the diligence and endurance with which all this important work is done will make 2021 into an even more productive year. We hope that together we can contribute to soften the blow that the pandemic and its countermeasures have given to mothers and children in LMICs.

Halvor Sommerfelt,
Director
CISMAC INTERACTS WITH HEALTH AUTHORITIES

CISMAC’s mission includes carrying out high-quality research to estimate disease burden and evaluate interventions to improve maternal, newborn and child health in low- and middle-income countries.

CISMAC goes beyond just describing disease patterns and measuring how well interventions work. We also aim to translate our findings into policy and practice. We therefore engage with local, regional, national and international health authorities early, not only when we have completed our research and have results to present, but from the very start of conceptualizing, planning, and implementing our studies.

Our completed Kangaroo Mother Care (KMC) trial in the state of Haryana, India, showed that engaging and supporting mothers to keep their low birth weight babies in skin-to-skin contact close to their chest and exclusive breast feeding improves infant survival and reduces their risk of falling seriously ill. We started working with the health authorities in Haryana already when planning the study and have communicated our findings both to the local health administration, the Haryana State health authorities, and all the way to the World Health Organization whose experts are using the study findings for updating guidelines for a global strategy to promote KMC worldwide.

Similarly, our recently completed trial in Uganda examined the effect of applying the disinfectant chlorhexidine to the umbilical cord stump of babies born in three government health facilities in Kampala. This study was inaugurated by the Ugandan State Minister of Public Health who expressed...
her government’s keen interest in the trial. Once we have analyzed the data, we will provide a detailed report both to the local health authorities as well as to the Ugandan Ministry of Health, so they can quickly utilize our study findings in their aim to improve neonatal health and survival in Kampala and in Uganda. We will also communicate our findings quickly to the WHO.

Finally, our recently initiated study of SARS-CoV-2 infection and COVID-19 in HIV-1-positive and HIV-1-negative mothers and their infants in Kampala is also being carried out in collaboration with Ugandan health authorities. Thus, our application to the Ugandan National Drug Authority was not only cleared by the Ugandan Ministry of Health; in its approval letter, the Director of Health Services, Curative services, Dr. Charles Olaro, stated that “The Ministry of Health, Uganda, strongly supports the project entitled ‘SARS-CoV-2 infection and COVID-19 in women and their young infants in Kampala, Uganda’ to be conducted by Makerere University School of Public Health and Uganda Virus Research Institute (UVRI) in collaboration with the University of Bergen, Norway.” His letter ends with: “The proposed project will be of great interest to public entities central to public health promotion in our city…” Now that the study is rolling, we will be providing the Ministry with monthly reports on the evolving SARS-CoV-2 epidemic. We will be informing the Ministry about how COVID-19 affects mothers and children, with a special emphasis on the vulnerable women living with HIV-1 infection and their HIV-1-exposed babies.
Children growing up in poverty face multiple biological and psychosocial risks, some of which are primarily found in low- and middle-income countries (LMIC). Unfavourable biological circumstances such as inadequate nutrition and childhood illnesses, as well as inadequate psychosocial stimulation and learning opportunities put children at risk for compromised development early in life.
Early child development is a precursor for later cognitive functioning, and children that are prevented from fulfilling their potential due to poverty-related risks early in life are less likely to succeed with educational achievements and to become healthy, productive adults. There are estimates suggesting that around 250 million children worldwide fail to reach their development potential. Critical developmental building blocks are established early in life. Identifying modifiable causes of poor developmental outcomes will facilitate focus on interventions that will enable more children globally to achieve their developmental potential.

In Nepal, India and Pakistan, CISMAC partners have been engaged in studies evaluating the effect of such modifiable causes of poor development and investigating the effects of specific interventions to address them in the field of nutrition, early infections and stimulation and responsive caregiving. Their efforts are summarized in the following sections.

**Studies in Nepal**

For more than 10 years, our research group has undertaken studies on the relationship between nutrition, infections, growth and neurodevelopment in our field site in Nepal. The results from our cohort studies demonstrated that suboptimal vitamin B₁₂ status is associated with poor developmental outcomes. These findings motivated randomized controlled trials (RCTs) with vitamin B₁₂ supplementation from infancy or pregnancy where neurodevelopment is the main outcome. The first of these trials, in infants, started in 2015 and enrolled 600 participants. In terms of vitamin status, infants who were randomized to receiving 2 recommended allowances of vitamin B₁₂ responded well to the intervention. However, there were no clinical effects as measured by neurodevelopment, growth or the hemoglobin concentration. In another RCT, 800 women in early pregnancy were enrolled and supplemented with a placebo or vitamin B₁₂ throughout pregnancy until 6 months postpartum. In this trial, which started recruitment in 2017, the main neurodevelopment outcome will be assessed at 6 and 12 months of age.
In 2020 there are 3 postdoctoral fellows and 1 PhD student working in these two RCTs.

In these 2 RCTs, the primary outcome is measured using the Bayley Scales of Infant and Toddler Development (Bayley). We have, however, also included a wide range of other measures of neurodevelopment and mental health in the follow-up of our study children. In addition, we will examine other important questions of early child development in associated studies with observational designs, that will increase our knowledge and generate hypotheses for other RCTs.

**Early childhood development and neurodevelopment studies in India**

The Mental Health and Cognitive Sciences unit at the Centre for Health Research and Development, Society for Applied Studies (CHRD-SAS) conducts research that primarily aims to understand ways to improve neurodevelopment in young children from resource limited settings. Much of this research is supported by CISMAC. The intervention studies we conducted have varied from nutritional interventions, such as Vitamin B12/folic acid supplementation or fortified milk cereal-based supplements, to behavioural interventions, such as Kangaroo Mother Care.
In an ongoing, large community-based trial, the team is documenting the effect of an intervention package on neurodevelopment. The package is delivered from preconception to when the child is 24 months of age. The intervention consists of improved nutrition, clean water, sanitation and hygiene (WASH), enhanced medical care and psychosocial support, which is delivered to mothers and children. Another trial of similar nature but directed at low-birth-weight infants is currently being considered for support by CISMAC. The team is working on newer tools such as eye-tracking assessment and global scale for early development (GSED). The team is also involved in conducting systematic reviews and meta-analyses in order to maximize the use of existing data to generate new insights and identify critical knowledge gaps for future research.

CISMAC has been active in fostering collaborative work between its partner institutes. This has led to quite a few shared research outputs between the India and Nepal sites. Using high quality data from Nepal, we have shown that the
association between linear growth and neurodevelopmental outcomes during infancy is influenced by parental height. Furthermore, using data on low-birth-weight infants, we have analysed determinants of neurodevelopment at the end of infancy. Analysing follow-up data from a Delhi-based cohort, we have shown that linear growth in the first 2 years of life, but not later catch-up growth happening between early and middle childhood, was significantly associated with positive cognitive outcomes in late childhood.

**SCALE-8 Longitudinal follow-up of a birth cohort at age 7–8 years in Pakistan**

SCALE-8 is a follow-up of the Pakistan Early Development Scale-up Trial, to assess children at seven to eight years old. The follow-up evaluates the continuity of the effects of early responsive stimulation and enhanced nutrition on children’s developmental trajectories. Researchers are especially interested in assessing the effects of the interventions on early primary education (grade 1). The children studied were evaluated at 2 years of age, capturing information of the distinct developmental period of infancy through early toddlerhood, and again at 4 years, revealing the development of the cohort prior to any formal exposure to the education system. SCALE-8 follow-up evaluates a third distinct period of children’s development when environmental influences around the child have shifted significantly from a largely home environment to include more educational environments. The follow-up also contributes to our understanding of the predictive nature of assessment at age two years, especially for the Bayley Scale of Infant Development-III, which is considered a gold standard assessment for child development in disadvantaged contexts.

The Sustainable Development Goals call us to action to create a world where no one is left behind. Research on how we can protect children from impaired development and promote the achievement of their full potential is our contribution to responding to this call.
THE IMPACT OF THE COVID-19 PANDEMIC ON MATERNAL AND CHILD HEALTH

The spread of the COVID-19 pandemic made 2020 a very special year. The virus spread to most continents within a couple of months. The pandemic has severely delayed and even reversed work on many of the Sustainable Development Goals (SDGs), a set of global goals developed by the UN for a better future for all.
Since reports from China indicated that the virus was highly contagious and might carry a high fatality risk, in March or April 2020 countries worldwide introduced the strictest measures ever for infectious disease control to slow down its spread. Complete or partial lockdowns were instituted even in countries where the initial number of infected individuals was low because of fears that the health system would not be able to handle a surge in the number of patients in need of intensive care.

**Resources shifted from other healthcare services to COVID-19**

The severity of the lockdowns that were introduced varied between countries, and so did the measures instituted to alleviate the effects on poor families. The control measures in India were particularly stringent and received much media attention all over the world. With 4 hours’ notice, the Indian government announced that shops, schools and transport systems would close down. Millions of poor people lost their source of income with immediate effect and with trains and buses being cancelled, migrant workers and families with children had to walk back to their villages for days since the government had not planned measures to help them survive through this period.

To ensure that health facilities would have sufficient capacity to receive a high number of COVID-19 patients, governments in many countries reacted by restricting health care to emergency services, thus affecting non-emergency health care such as outpatient care and elective surgery. This meant that personnel and resources were diverted away from preventing and treating maternal or childhood conditions, HIV/AIDS, malaria and other common diseases. Considering that many low- and middle-income countries already faced health system challenges with inadequate numbers of qualified health care personnel and severe financial, supply and logistical constraints, immunization programmes were halted in many countries, and the number of women coming for antenatal care and delivery at health facilities declined dramatically during the lockdown periods. Travel restrictions affected the supply of essential medicines and personal protective equipment. In addition, patients in many countries have had difficulties seeking health care due to transport restrictions, curfew, and fear of contracting the virus in healthcare facilities. Loss of work and income opportunities has also affected people’s ability to pay user fees or other costs related to health care. Thus, the risk of complications and deaths from common diseases is expected to have increased. For example, Cameroon and Zimbabwe have reported an increase in the number of deaths due to malaria during the COVID-19 pandemic.

Unfortunately, due to lack of good vital registration systems that collect data in real time and difficulties in collecting data during periods of lockdown, there is still insufficient data to accurately estimate how the pandemic has affected maternal and child health. However, experiences from previous epidemics of public health importance have shown us...
that such indirect effects of an epidemic often have dramatic impact on mortality from other diseases. For example, during the Ebola outbreak in the Democratic Republic of the Congo in 2019, there were more deaths from measles than Ebola because the childhood immunization programme was severely affected.

Reversal of achievements made towards the Sustainable Development Goals

Projections of the probable impact of the COVID-19 pandemic and the instituted control measures on maternal and child health indicate a dramatic reversal of improvements that were achieved in the last two decades. The number of deaths due to malaria is expected to have doubled compared to 2019. Food shortages are expected to have led to increases in the number of malnourished children. Maternal mortality is reported to have increased in some countries that introduced strict lockdowns with travel restrictions, such as Uganda.

Similar reversals appear to have taken place in relation to the other Sustainable Development Goals. Reduced opportunities for income-generating activities have increased poverty levels, and the proportion living in extreme poverty is estimated to have increased by at least 140 million. More than 1.5 billion students worldwide have been affected by school or university closures.

UNESCO estimates that 2/3 of an academic year has been lost on average worldwide so far due to COVID-19 school closures and 11 million girls may not come back after schools reopen. One year into the pandemic, schooling for over 800 million students is still not back to normal. These disruptions in children’s education will adversely affect their health and well-being as well as the health and well-being of their children, particularly those from poorer backgrounds.

The COVID-19 pandemic is a reminder of the importance of investing in stronger health systems that can sustain essential health services such as immunization programmes and delivery services even when new public health threats emerge. Without such investments, further progress towards the Sustainable Development Goals will remain vulnerable to major setbacks from future pandemics or other types of crises.
CISMAC AND THE COVID-19 PANDEMIC

CISMAC is a Norwegian Centre of Excellence and an international consortium. Most of its research and training activity is centred with its partners in low- and middle-income countries.

Travel, fieldwork, teaching, training and re-prioritising medical personnel in the context of the ongoing pandemic have been the greatest CISMAC challenges in 2020. While many of our projects had completed data collection before the start of the pandemic, those engaged in active recruitment, data collection, and participant follow-up, had to adopt new strategies to continue their work, some after weeks or even months of suspended activity.

“… some community meetings had to be delayed, and more interview precautions had to be taken …” (RISE study team, Zambia)

The challenges faced by many of CISMAC’s partners highlighted the weakness of local health systems, aggravated the wealth divide, and many study participants experienced reduced access to infrastructures, resources and health care.

Another challenge was that many CISMAC researchers are medical doctors or other health workers and were thus drafted into service to help with national efforts to fight the pandemic. In addition, many medical facilities were re-prioritised as COVID-19 treatment centres.

While restricted local transport and abolished international travel represented serious drawbacks for CISMAC’s many activities, most meetings and training activities continued to function by migrating to digital platforms. We are proud that, despite the challenges of COVID-19 and lockdowns, CISMAC’s year-end reporting for 2020 showed that most...
of our projects are still on track. This is a testament to the diligence of everyone involved.

“Hard work by the study team enabled us to complete follow-up of over 90% of our study participants…” (BCG study team, Uganda)

CISMAC partners have not only strived to reduce the negative impact of the pandemic on ongoing projects and the study participants, they have also been actively involved in contributing to local, national and international efforts to combat COVID-19.

While COVID-19 brought significant challenges to projects, it also created opportunities. The BCG trial, was able to secure funding from the Research Council of Norway to expand the study objectives to examine whether another non-specific beneficial effect of giving the BCG vaccine to infants might be to reduce their risk of contracting SARS-CoV-2 infections and falling ill with COVID-19. The expanded version of this study re-started enrolling babies in December 2020. In their ethical clearance, the Ugandan Ministry of Health expressed specific appreciation of this important work.

We are now seeing positive signs in pandemic control with vaccines becoming available and countries gearing up to vaccinate their vulnerable populations. CISMAC consortium members began 2021 with a strengthened commitment to ensuring the high quality of their studies – and to contributing to improving maternal, neonatal, child and adolescent health.
RESEARCH PROJECTS
RISE
BCG
CCF instead of RCT?

Zinc-Sepsis
Chlorhexidine
Girl Power

B₁₂ in pregnancy
eRegistry and care
SCALE-8
The CAP trial

Child B₁₂ Follow-up
eRegistry support
SAFEZT
NeoSupra
COMAC
Since March 2020, also Uganda has been facing the COVID-19 pandemic. A high urban population density and extensive and necessary social interaction along with challenging hygienic conditions represent major impediments to the country’s battle against COVID-19. The COMAC study seeks to understand the spread and impact of the COVID-19 pandemic on vulnerable groups in Uganda. The project will have a particular focus on HIV-1 positive women and their babies.

Principal Investigators: Victoria Nankabirwa and Halvor Sommerfelt.

RISE
In Zambia, approximately one third of young girls in rural areas have given birth by the age of 18. Adolescent pregnancies pose significant risks to both mothers and their babies. The Research Initiative to Support the Empowerment of girls (RISE) aims to measure the effect of interventions that include economic support, education and reproductive health programmes on early childbearing in rural Zambia. Nearly 5 000 7th grade girls from 157 rural schools are enrolled in the 5-year study.

Principal Investigator: Ingvild Fossgard Sandøy / Co-Principal Investigator: Patrick Musonda

Cost-Benefit RISE
Adolescent pregnancy is one of the greatest development challenges facing low- and middle-income countries, not only because it represents a danger to mother and child, but also because of its profound social and economic consequences. It is a particular challenge in rural Zambia. This study investigates the short- and long-term benefits of providing cash support to adolescent girls and their guardians / parents, as well as community dialogue in CISMAC’s RISE trial to delay pregnancy and childbearing to an appropriate age.

Principal Investigators: Patrick Musonda, Ingvild Sandøy / Study Lead: Amani Thomas Mori

B₁₂ in Pregnancy
Worldwide, vitamin B₁₂ deficiency is common, affecting people of all ages. It can lead to a wide variety of health problems and can, without prompt treatment, result in permanent damage. In this study, we measure the effect of giving daily oral vitamin B₁₂ supplements to pregnant women and during a 6-month period after they have given birth on the neurodevelopment and growth of their children. The results may help revise dietary guidelines for South Asian women, and could lead to improved pregnancy outcomes as well as improved child neurodevelopment.

Principal Investigators: Ram Krishna Chandyo, Laxman Prasad Shrestha / Co-Principal Investigator: Tor A Strand
Child B$_{12}$ Follow-up

Vitamin B$_{12}$ deficiency is common and can occur at all ages. This study follows up children who participated in a placebo-controlled randomized trial in Nepal, assessing effects on child growth and neurodevelopment, one and two years beyond supplementation with vitamin B$_{12}$ to infants. If persistent improvements in growth and development are found, our results will guide international nutrition recommendations and can potentially improve the well-being of many children.

Principal Investigator: Tor Strand / Co-Principal Investigators: Laxman Shrestha, Prakash S Shrestha

$cKMC$

Nearly 80% of infant deaths occur in babies born with low birth weight (LBW). According to hospital-studies, up to 40% of these deaths could be prevented with Kangaroo Mother Care (KMC), where the baby is kept for several hours every day on the mother’s chest, giving them warmth and access to life-saving breast milk. Almost all evaluations of KMC have been carried out in health facilities. This study evaluated KMC initiated in the homes, also called community-initiated KMC (cKMC). The study took place in India, where over one quarter of babies are born with LBW, and included 8 402 LBW babies. Promotion of and support for cKMC increased the survival chances of infants with 25%.

Principal Investigators: Sarmila Mazumder, Sunita Taneja / Co-Principal Investigator: Halvor Sommerfelt

Biological effects of cKMC

Training mothers in community initiated Kangaroo Mother Care (cKMC) may be an effective way to reduce mortality and morbidity of low birth weight babies (LBW). The current study is a sub-study of CISMAC’s main cKMC trial and investigates some of the pathways with which cKMC can improve infant health and survival.

Principal Investigator: Bireshwar Sinha / Co-Principal Investigators: Nita Bandahari, Halvor Sommerfelt

Poverty and Equity cKMC

As an extension of the completed trial on the survival benefits of promoting Kangaroo Mother Care at home to low birth weight babies (cKMC), this equity study evaluates the impact on fairness outcomes such as survival benefits for the poorest vs. the less poor and the prevention of catastrophic health care expenditures among the poor in two districts in North India.

Principal Investigators: Sarmila Mazumder, Kjell Arne Johansson
**Zinc-Sepsis**

Severe infections, including sepsis and severe pneumonia, contribute to almost one quarter of the deaths in infants up to two months of age. Widely accessible and very cheap, a daily dose of zinc given to young infants under antibiotic treatment for probable serious bacterial infection was shown to increase the success of treatment by 43%. These encouraging results have prompted us to do a much larger study in almost 4 000 infants under two months of age to estimate the efficacy of the treatment to prevent death. The study involves a hospital in Nepal and four hospitals in New Delhi, India.

Principal Investigators: Sudha Basnet, Nitya Wadhwa / Co-Principal Investigator: Tor A Strand

**Zinc Equity**

Low-cost health care interventions that prevent impoverishment and catastrophic health expenditures can be valuable national health initiatives. Zinc Equity is a sub-study of the ongoing zinc-sepsis trial. It evaluates the health and economic consequences for families of zinc given as an adjunct to standard treatment in young infants (age 3-59 days) hospitalized with "clinical severe infection". Zinc may shorten the length of stay and the demand for expensive intensive care for these infants. Comparing the two-arms of the trial will provide information about socio-economic inequalities in infant deaths, cost-effectiveness and financial risk protection.

Principal Investigators: Nitya Wadhwa, Kjell Arne Johansson / Co-Principal Investigator: Debjani Ram Purakayastha

**eRegistry and care**

The Norwegian Institute of Public Health and the World Health Organization have developed a framework and series of tool kits to make it easier for low- and middle-income countries to improve their collection and use of health information to the benefit of women’s and children’s health. This study is the first of its kind to assess the benefits of this type of programme in improving the quality of care in rural Bangladesh where major gaps remain, despite the progress made in reducing maternal and child mortality over the last decade.

Principal Investigator: J. Frederik Frøen / Co-Principal Investigator: Anisur Rahman

**eRegistry support**

eRegistries are designed to increase the availability and timely use of routine maternal and child health (MCH) data. The Palestinian National Institute of Public Health, in close collaboration with the Ministry of Health in Palestine, is currently rolling out a nationwide MCH eRegistry. With support from CISMAC, the Norwegian Institute of Public Health is carrying out randomized controlled trials with 120 health center clusters in Palestine to assess if the eRegistry and its interactive checklists and clinical decision support can improve the quality of antenatal care.

Principal Investigator: J. Frederik Frøen / Co-Principal Investigator: Buthaina Ghanem
BCG

The Bacillus Calmette-Guérin (BCG) vaccine may have non-specific effects in infants, with protection beyond its ability to prevent tuberculosis (TB). In addition, some evidence suggests that giving BCG later in infancy may enhance its effects. This may be particularly important for HIV-1 exposed children who have an increased risk of severe infections. This study randomizes 3,500 HIV-1 exposed Ugandan (expandable to 4,500) infants to receive BCG either within 24 hours of being born or at 14 weeks of age. The results may impact policies concerning timing of BCG administration.

Principal Investigator: Victoria Nankabirwa / Co-Principal Investigator: Halvor Sommerfelt

BCG Immunology

The BCG immunology study is a sub-study of the larger BCG trial. The study seeks to provide additional information of the optimal timing of BCG vaccination among the growing population of HIV-1 exposed infants. Concretely, the substudy will describe possible immunological mechanisms of early vs late BCG vaccination in order to improve protection from infectious diseases in these vulnerable babies. The results will also be important for upcoming studies of new vaccines against tuberculosis in which CISMAC is also engaged.

Principal Investigators: Kurt Hanevik, Victoria Nankabirwa

EcoTime BCG

There is still uncertainty pertaining to when it is best to give the BCG vaccine to babies born to mothers infected with HIV-1. This study evaluates and compares the cost-effectiveness of giving the BCG vaccine to Ugandan HIV-1-exposed babies at birth or at 14 weeks of age. Combined with possible treatment benefits assessed in the main study, the cost implications of the two vaccination strategies will generate information important for vaccine programme development and implementation.

Principal Investigator: Victoria Nankabirwa / Co-Principal Investigator: Bjarne Robbestad / Master student: Steve Kabanda

Chlorhexidine

Infection of the umbilical cord stump (omphalitis) can lead to life threatening illness in the first 28 days of life. The risk of omphalitis is high in low- and middle-income countries. This trial takes place in Uganda and involves nearly 5,000 babies of mothers who are not infected with HIV-1. It assesses the effect of a single cleansing of the umbilical cord stump with an antiseptic solution of 4% chlorhexidine in birth facilities on the risk of omphalitis and severe newborn infections.

Principal Investigator: Victoria Nankabirwa / Co-Principal Investigator: Halvor Sommerfelt
**SCALE-8**

More than 250 million children living in low- and middle-income countries do not achieve their full development potential. This study follows a previous project assessing the effectiveness, feasibility and cost of integrated early stimulation and nutrition interventions delivered by a government community-based health service in Pakistan. It has re-enrolled children at 8 years of age from 80 population clusters to determine which beneficial effects may have endured to school age. The study will identify risks and protective factors that influence outcomes and will inform the development of improved interventions for child development.

Principal Investigator: Muneera A Rasheed / Co-Principal Investigator: Aisha K Yousafzai

**SAFEZT**

This three-year project examines global and national policy discourses surrounding fertility control and abortion, as well as local practices and moralities related to these issues among adolescents in Ethiopia, Zambia and Tanzania. The dynamics between the law, policies and access to fertility control and safe abortion services differ between these countries. The project aims to generate comparative knowledge of the interplay between policy, legislation and socio-cultural conditions framing girls’ and women’s reproductive choices.

Principal Investigator: Astrid Blystad / Co-Principal Investigator: Getnet Tadele

**CCF instead of RCT?**

This study evaluates whether a novel observational epidemiological study design, the case-control with follow-up (CCF), could be an efficient alternative to randomized controlled trials (RCTs), case-control (CC) studies and cohort studies for investigating the association between exposures and rare outcomes. To find out, we did a CCF and a CC study in parallel with the recently completed RCT in Uganda that measures the association between cleansing of the umbilical cord stump with chlorhexidine on the day of birth and the risk of subsequent severe illness in the newborns.

Principal Investigator: Victoria Nankabirwa / Co-Principal Investigator: Hans Steinsland

**Girl Power**

Lack of reproductive health information and lack of economic opportunities may contribute to a high proportion of girls in low- and middle-income countries becoming pregnant at a young age. This study investigates how reproductive health information and entrepreneurship training affect the decision-making of girls when it comes to postponing pregnancy and engaging in economic activities. More than 3 400 Tanzanian school girls drawn from 80 schools across four regions of Tanzania are involved in this now completed cluster randomized controlled trial.

Principal Investigator: Bertil Tungodden
The CAP trial

Low dietary intake of calcium increases the risk of pre-eclampsia and eclampsia, which are serious hypertensive disorders in pregnancy that are dangerous for mother and baby. Although calcium supplementation is recommended by WHO from 20 weeks of pregnancy, no research has evaluated whether starting it before pregnancy can reduce the risk among women with previous pre-eclampsia. This multi-center randomized trial in South Africa, Argentina and Zimbabwe estimated the effect of calcium supplementation before and in the first half of pregnancy on the risk of re-current pre-eclampsia.

Principal Investigator: Justus Hofmeyer

NeoSupra

Globally, many babies are born too exhausted to breathe spontaneously after birth. Such babies need immediate assistance – otherwise they die. At Mulago Hospital, Kampala, Uganda, we conducted a randomized controlled trial to see if the use of a supraglottic airway device instead of a facemask, which is commonly used for ventilation, can reduce the risk of dying of brain damage in newborns who did not breathe after birth. The now published results are important for low- and middle-resourced settings were many such deaths occur.

Principal Investigators: Thorkild Tylleskør, Josaphat Byamugisha

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CISMAC
FACTS
CISMAC MANAGEMENT AND ADMINISTRATION

Halvor Sommerfelt
Director

Ingvild F Sandøy
Deputy Director

Jose Martines
Scientific Coordinator

Ane Straume
Administrative Leader

Filiz Ipek
Economy (until September 2020)

Olga Shangina Williams
Economy (from October 2020)

Anne Berit Kolmanskog
Project administration

Gunhild Koldal
Project administration

Elinor Bartle
Web & communication
University of Bergen (UiB), Chr. Michelsens Institute (CMI) and the Norwegian School of Economics (NHH) launch the Development Learning Lab: Research for Learning and Innovation in Norwegian Development Policy.

The DLL will make it easier for research environments to regularly update NORAD, other Norwegian government agencies as well as NGOs on relevant research findings. DLL will help CISMAC to achieve its mission of translating its research findings into policies and practice that can improve maternal, newborn and child health in LMICs.
Research-based evidence should guide investment in new and existing development initiatives. Norway invests significantly in international development. The current government emphasises the importance of development policies being knowledge-based and effective. However, a 2018 Norad evaluation concluded that this was not the case for Norwegian overseas development cooperation. It found that this funding was only to a limited degree based on systematic evaluations of what actually works. Other donors, such as the Department for International Development (DFID), have established routines for ensuring that the initiatives they fund are knowledge-based. Many Norwegian non-governmental organizations (NGOs) also state that they have insufficient information when they develop their projects.

Why is there a knowledge gap between funding needs and funding programmes?

It takes time to obtain a reliable overview of the research literature in a given field. NGOs and even governmental entities are under time pressure when initiating new development programmes and are unable (or unwilling) to set aside enough time and resources for such reviews. Moreover, evaluations are primarily focused on monitoring the short-term outputs of individual projects. Good data on the baseline situation is rarely collected and large, rigorous evaluations (such as randomized controlled trials) are even rarer. In addition, few studies are undertaken that explore why programmes work or not.

In January 2021, Chr. Michelsen Institute, the University of Bergen, and the Norwegian School of Economics established the Development Learning Lab (DLL). The DLL will be an applied research centre and hub for systematic use of research-based knowledge, learning and innovation in Norwegian aid policy and practice. The aim of the centre will be to improve the understanding of what works well in aid interventions, and what are the facilitating factors for successful programmes. It will also examine programmes that do not achieve their goals and identify impediments to success. The Centre's work will contribute to improving the effectiveness of development cooperation initiatives by bridging and integrating research, policy, and practice. At the University of Bergen, CISMAC has been given the coordinating role for this activity, while the coordinating unit at the Norwegian School of Economics is the Centre for Experimental Research on Fairness, Inequality, and Rationality (FAIR), which is also a Centre of Excellence. The DLL builds on a long-standing, well-established partnership between the three institutions.

**DEVELOPMENT LEARNING LAB**

**THE MAIN ELEMENTS OF DLL WILL BE:**

- **Documentation of what works, what doesn’t, and why. We will:**
  - Summarise research-based knowledge on the effects of development interventions in priority areas for Norwegian development cooperation, such as health and education, thereby making relevant knowledge quickly available when needed.
  - Apply formative research and implementation research to document the impact of development interventions and improve knowledge on factors that contribute to or hinder good results.

- **Learning**
  - We will establish thematic learning arenas that bring together actors from aid organisations, civil society, private sector, and academia on a regular basis to exchange research-based knowledge and practical experience.

- **Innovation**
  - DLL will support the use of research-based knowledge and experience to develop and implement new initiatives.
Since 2018, CISMAC has hosted a webinar series where both established researchers as well as our PhDs candidates and Postdoctoral fellows present research plans and research findings as well as discuss important methodological topics.

The webinars strengthen the links between CISMAC’s partner institutions and between the researchers in our virtual consortium where we live and work in more than 10 different countries.

Our virtual meeting place has never been more important than during 2020, when the pandemic prevented us from meeting both within countries but also between them. The number of participants are on the rise.

We will continue developing our webinars, not only to get through the pandemic, but also for future collaborations where we seek to keep our collaborations strong and our carbon footprint low.
CISMAC was recognized and funded as a Centre of Excellence by the Research Council of Norway (RCN) in 2013. The RCN awarded CISMAC a total of 175 million NOK, whereas the University of Bergen (UiB) supports the Centre with an additional 144 million NOK.

This substantial core funding and the ensuing research activities have formed the basis for CISMAC researchers pursuing additional project funding to sustain and expand our research portfolio and capacity strengthening mission in maternal, neonatal, child and adolescent health. This increasing collateral funding will contribute significantly to our ambition to continue to grow as a centre and to generate awareness and support for maternal and child global health research and training, also beyond the period of core financing by the RCN and UiB.

In 2020 CISMAC researchers secured more than 40 mNOK in external funds.

While we are both proud and appreciative of our researchers’ success in procuring such collateral funding, we have an ongoing concern: the availability of core resources to support the future of the collaborative efforts started by CISMAC and other strong academic initiatives aimed at promoting equitable and sustained health improvements in low- and middle-income countries (LMICs). We hope that our ongoing discussions with the University of Bergen leadership and Norwegian authorities in 2021 will lead to the expansion of mechanisms intended to incentivize research and innovation done in Norway so that they also cover collaborative research in LMICs.
MAIN PUBLICATIONS IN 2020

CISMAC continues to publish its finding in leading international journals.

An important event in 2020 was the publishing of the results from our NEOSUPRA trial in the top-notch scientific journal, the *New England Journal of Medicine*. This large trial conducted in Uganda explored a device, the Laryngeal Mask, and its use in the treatment of neonates who could not breathe when born, a main cause of death in the first week of life. The study showed that midwives were able to safely use this new device but that it was not better than face-mask ventilation in preventing death or brain damage.

We also published the study “Antenatal Uterotonics as a Risk Factor for Intrapartum Stillbirth and First-day Death in Haryana, India” in the prestigious journal *Epidemiology*. This very large study indicates that the extensive use and probable misuse of the drug oxytocin could lead to the death of more than 100,000 babies a year during birth and the first day of life, in India alone. The medication should be given to stop bleeding in women after birth but can be life threatening for the baby if administered as an intramuscular injection before or during delivery to initiate or speed up labor.
Young Indian mother breastfeeding her newborn child.
Credit: iStock.com/Bartosz Hadyniak
LIST OF SCIENTIFIC PUBLICATIONS IN 2020


Namakula, R., de Bree, L. C. J., A. Tvedt, T. H., Netea, M. G., Case, S., & Hanevik, K. Monocytes from neonates and adults have a similar capacity to adapt their cytokine production after previous exposure to BCG and β-glucan. PloS one, 2020; 15(2)

Onarheim, K. H., Moland, K. M., Molla, M., & Miljeteig, I. ‘I wanted to go, but they said wait’: Mothers’ bargaining power and strategies in care-seeking for ill newborns in Ethiopia. PloS one, 2020; 15(6)


Schwinger, C., Chandyo, R.K., Ulak, M., Hysing, M., Shresta,
CISMAC FACTS


TOWARDS A BRIGHTER FUTURE FOR MOTHERS AND CHILDREN

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