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Threats to the child's brain in resource-poor countries

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ABSTRACT

Children in low and middle-income countries are 16 times more likely to die before 5 years of age compared to children in high-income countries. More than 200 million children under five in the developing world do not fulfil their potential, the major reasons appear to be poor nutrition, and limited access to education in the setting of extreme poverty. Three major factors with multiple sub-headings result in threats to the child's brain. Namely, the background setting the child is born into and grows up in, the acquired influences of the local setting, and the available interventions for the child. The following text is an overview of these key issues and their subheadings, for children residing in low and middle-income countries. Whilst many influencers are beyond the control of health practitioners, such as conflicts of war and impact of famine, there are relatively cost-effective interventions which can have a massive ripple effect in reducing diseases of high burden such as effective vaccination programs, insectide immersed nets for beds, and effective pigs' pens. There is need for viable protocols to be adapted for the local setting, for simple, cost effective diagnostic tools to be developed and for health practitioners to be equipped with the skills to cope with neurological disorders, especially those prevalent in and specific to low and middle-income countries.

Keywords: child's brain, resource-poor settings

INTRODUCTION

Threats to the child's brain in resource-poor countries include the over-arching and intersecting impact from environmental and socioeconomic issues, the specific aetiologies, lack of prevention, treatment and rehabilitation, as well as limited capacity to implement best practices required to permit nervous system health for these children. Many challenges are unique to low and middle-income countries (LMIC).

WHAT ARE THE PRIORITIES?

The World Health Organisation (WHO) estimates that children in low and middle-income countries are 16 times more likely to die before 5 years of age compared to children in high-income countries [1]. Almost 75% of childhood deaths are due to 6 conditions: neonatal causes (preterm birth, asphyxia and infections), pneumonia, diarrhoea, malaria, Human Immunodeficiency Virus (HIV) and measles. In resource limited settings the burden is heavily skewed towards Africa where almost half of these childhood deaths occur and many of the survivors suffer long-term complications often with neurological sequelae [1]. The Lancet series report in 2007 on Early Child Development, estimated that more than 200 million children under five in the developing world do not fulfil their potential [2]. The major reasons related to poor nutrition and limited access to education in the setting of extreme poverty. The WHO's Commission on the Social Determinants of Health acknowledged the role of early childhood development in the achievement of equity, adult health, well-being and productivity.

Three major factors with multiple sub-headings can result in threats to the child's brain. Namely – the background setting the child is born into and grows up in, the acquired influences of the local setting, and the available interventions for the child.

The background setting that the child is born into and grows up in, extends from the health of the mother, the home environment (e.g. orphan or child led households), socioeconomic challenges (leading to poor nutritional state, chronic ill-health), environment influences (e.g. rural, famine, war, toxins) and the predestined genetic influences. **The direct acquired** influences that impact on the child include those from hypoxic insults typically at the time of delivery, the exposure to infections (direct neuroinfections and secondary impact from system compromise e.g. diarrhoea, pneumonia), effects of trauma (motor vehicle accidents, the conflict of war), toxins (farm pesticides, dietary influences e.g. cassava). **The available interventions** for neurological disorders are affected by the lack of capacity to prevent (e.g. through vaccinations), diagnosis (e.g. through trained staff, basic blood work-up, infection screens, neuroimaging, electrophysiology), treat (e.g. through the lack of access to or sustainable supply of antiepileptic drugs, antibiotics, antiret-

roviral agents) and management (e.g. through rehabilitation therapists, nursing care) these complications.

THE BACKGROUND SETTING

IN THE BEGINNING…

The health of the mother is crucial to that of the offspring. Maternal ill-health, inclusive of chronic infections (e.g. HIV, tuberculosis), toxin exposure (e.g. alcohol and substance abuse) and poor nutrition, iron deficiency, along with poor access to obstetric services, are major influences that lead to the legacy of an "at risk" or frankly neurologically compromised child [3]. In the 2015 the WHO reported neonatal mortality at 28 per 1000 live births in Africa and 24.3 in South East Asia, compared to 7.7 in America and 6.0 in Europe [4]. In resource poor settings most babies are delivered at home without access to skilled birth attendance services [5,6]. Proportionally of those who survive delivery, the number of infants with neurodisability related to prematurity, birth asphyxia and infections will be far higher than in resource equipped settings.

Some 80–85% of the world's population reside in LMICs [7,8]. Of these 5.8 billion people, 1 billion live in extreme poverty which has major influences on cognitive profile [9]. About 3 billion people lack piped drinking water in their home and about one billion proper sanitation [10,11]. The degradation of farming systems further affects food supply [1,12,13,14]. Armed conflicts and population displacements are additional stressors [15]. Quarantines such as during Ebola outbreaks in the Democratic Republic of the Congo created conditions that exacerbated the risk of environmental exposure and brain disease [16]. Similar challenges occurred with the collapse of vaccine programs and other health services in Sierra Leone following the recent Ebola outbreak [17].

The **specific location** that a child grows up in may also influence their course – regions of India and Africa are endemic for neurocysticercosis, malaria, rabies and tuberculosis. Children in rural settings may have less access to routine and emergency health care, missing immunisation programs and early detection of reversible disorders. The impact of orphans and child-led households has also become an issue in Africa due to the HIV pandemic [18,19]. Overlying these issues are the child's **genetic make-up** which, whilst influenced by environmental factors, will result in the overall phenotype of the child. Increasingly, understandings and subsequent management is guided by concepts of the genetics of diseases based on data from resource equipped world populations. Such data is lacking as to whether the same genetics are expressed in many parts of the world, especially from LMIC [20]. In low and middle-income countries, the risk of environmentally mediated brain disease is augmented by lack of infrastructure, poor health and safety regulations, and limited measures for environmental protection.

Diarrhoea in the first 2 years of life is associated with an 8 cm drop in height and a 10 point reduction in IQ by the time children reaches 7 to 9 years of age [21]. The mechanism that diarrhoea relates to this cognitive dysfunction is not understood, but may be linked to the resultant stunting [22]. Catch-up growth is seen if there is control of diarrhoea in this early period, emphasising the importance of effective interventions to promote a child's developmental potential [23]. Pathogenic microbes can cause brain disorders and the microbial population harboured in the human body, termed the human microbiome, can, as a whole, influence brain activity [24]. Associations are reported between the microbiome and neurological diseases, including multiple sclerosis and autism spectrum disorder (ASD) [25]. In a mouse model, probiotics alleviated some behavioural symptoms of ASD [26]. The composition of the human microbiome differs markedly between countries and further research may led to possible treatment interventions [27].

The burden of conventional neurodevelopmental stressors (for example, lead) on children is exacerbated by unique environmental challenges, including malnutrition and enteric infections [21,28,29,30] and, possibly, a diet of neurotoxicant-containing plants such as cassava (*Manihot esculenta*; also known as tapioca), the grass pea *Lathyrus sativus* or the seeds from the cycad plants, which are associated with a high burden of neurodisability [31-36]. Populations with unique exposures and risks include those living in the tropical cassava belt of Angola, the Central African Republic, Cameroon, Congo, Tanzania, Uganda, Nigeria and Mozambique;[37-43] and those reliant on *L. sativus* as a staple food in Ethiopia, Eritrea, India and Bangladesh[34,44-46].

That genetic and epigenetic factors, including the effect of maternal stress on brain function, influence the effect of environmental exposure [47,48]. As an example, the E4 allele of the *APOE* gene is reportedly associated with increased risk of late-onset Alzheimer's disease, although not in people from sub-Saharan Africa and with a mild association among Hispanic people, is also associated with protection against early childhood diarrhoea and its related cognitive impairment [49,50]. Gene–environment interactions are illustrated through the relationship between air pollution components and the gene encoding the MET receptor tyrosine kinase. *MET* has been implicated as an autism risk gene [51,52]. Early-life exposure to pollutants is hypothesised to reprogram global gene expression in old age through epigenetic mechanisms [53-56]. Variation in exposure response, even among individuals exposed to the same environment could be due, not only to early-life exposures, but also to differences in genetic make-up [57-59]. Clinical implications of exposure-related neurological deficits in LMICs include, but are not limited to, neural tube defects, learning disabilities, behavioural problems, psychiatric disorders, cognitive decline and the occurrence of distinct entities such as tropical ataxic neuropathy, and konzo [42,60,61].

DIRECT ACQUIRED INFLUENCES

THE GLOBAL BURDEN OF DISEASE

The proportion of the global burden of disease (GBD) that is attributable to neurological, mental health, developmental and substance-use (NMDS) disorders is expected to rise worldwide, in part due to prolonged survival [62,63].

Before the implementation of measures such as the disability-adjusted life year (DALY), the global burden of disease was primar¬ily quantified in terms of mortality [63]. Use of the DALY permitted the importance of neurological and psychiatric disorders to be evident, confirming that they account for about 28% of the GBD [63-65]. The highest-ranked causes of death in the GBD 2010 study included malaria (ranked 11th), neonatal encephalopathy (ranked 24th) and meningitis (ranked 29th) [63]. These conditions fall under other categories and are not included in the neurological category, despite their contribution to global disability [66]. Three of the seventeen World Health Organization (WHO) reported Neglected tropical disorders (NTD) are primarily due to neurological infections (rabies, human African trypanosomiasis and leprosy), further severe manifestations result from ner-

vous-system involvement can occur from other NDTs including central nervous system schistosomiasis and Chagas-related stroke [67]. Many of the most common and disabling neurological conditions are preventable or remedial with inexpensive therapies. Treatment for epilepsy and secondary stroke prevention are ranked by the World Bank among the best investments in global health [68]. In May 2015 the World Health Assembly approved the Epilepsy Resolution to address the "*global burden of epilepsy and the need for coordinated action at the country level to address its health, social and public knowledge implications*" [69]. This should lead to focus greater attention on improving the care for people with epilepsy.

COMMUNICABLE DISEASES

VIRAL INFECTIONS [70]

Rabies and Japanese encephalitis virus (JEV) are responsible for an estimated annual mortality of 60,000 and 17,000 people, respectively [71,72]. People contracting JEV encephalitis are restricted to Asia. Rabies is prevalent throughout Southeast Asia, Africa, Latin America and further afield. Long-term cognitive or neurological impairment is present in as many as 70% of those who survive herpes simplex virus encephalitis (HSV encephalitis) [73] and 30–50% of those with JEV encephalitis [74]. Incidence of CMV is higher in LMICs than in high-income countries and the same is suspected for congenital cytomegalovirus (CMV) infection. The impact from symptomatic CNS disease and hearing loss in LMICs is mostly unknown [75]. Dengue, and to a lesser extent chikungunya, viruses will probably become leading global causes of arboviral encephalitis in the next decade [72,76,77]. Whilst encephalitis affects a small proportion of those with dengue virus, the large number of infections worldwide would lead to significant overall numbers of encephalitis cases. **Zika virus** was first identified in primates in 1947 in the Zika forest of Uganda and human cases were reported in the 1960s in Africa and Southeast Asia. In December 2014 Zika was detected in Brazil affecting potentially millions of people [78,79]. The first indication was an increase in patients with Guillain-Barré syndrome (GBS), often with a history of a febrile rash illness in the week before preceding symptoms of weakness. Some 80% of cases are clinically asymptomatic and in most, symptoms are mild. Eight to 9 months after the first cases of Zika were reported, a dramatic increase in babies born with microcephaly was seen, with some 3500 reported cases. By April 2016 Zika virus transmission by the Aedes mosquito species was evident in 62 countries and territories with the geographical distribution of the virus continuing to steadily and rapidly expand. The virus has been isolated from the amniotic fluid of pregnant women and blood and tissues of newborns, suggesting materno-fetal transmission. Affected babies have widespread calcification on computed tomography imaging. Other malformations, such as anencephaly and lissencephaly, might also occur and could be related to earlier the infection occurs during gestation [80]. There are many differential causes for microcephaly and these must still be considered and excluded. Patients with microcephaly may have legacy of neurodisabilities including developmental delay, difficulty with gait and balance, mental retardation, seizures and hyperactivity. The socio-economic impact of the infection, particularly if the association between Zika virus and microcephaly is confirmed, will be large and felt for decades. The Centers for Disease Control and Prevention (CDC) has issued guidelines for the testing of infants born with possible Zika virus infection [81].

HIV AND OPPORTUNISTIC INFECTIONS

At the end of 2014 there were an estimated 2.6 million children less than 15 years of age worldwide living with HIV infection, with approximately 88% living in sub-Saharan Africa [82]. Neurological disease is common in infected children due to primary HIV infection, secondary or opportunistic infection, and treatment-related complications. In LMICs, where only one third of patients requiring antiretroviral therapy (ART) receive it, the opportunistic infections cryptococcal meningitis, tuberculous meningitis, cerebral toxoplasmosis, progressive multifocal leukoencephalopathy and CNS cytomegalovirus infection remain common [83]. Poor nutritional status further compromises neurocognitive development of children infected with HIV [84]. However widespread roll-out of combination antiretroviral therapy (cART) has resulted in changes to the presentation, manifestation and epidemiology of many co-morbidities related to HIV. Further increased prevalence of cognitive impairment is evident, which maybe relatively subtle in these patients who are now living longer [83,85]. Children infected with HIV illustrate the layering effect seen with this condition, where multiple complications occur, and compound the diagnosis, management and outcome of this complex disease.

BACTERIAL INFECTIONS

The most common bacterial infections affecting the nervous system are sepsis and meningitis in neonates; bacterial meningitis due to Streptococcus pneumoniae, Haemophilus influenzae type b and Neisseria meningitides occur in children and adults; and tuberculous meningitis in children and adults. In LMICs, it is estimated that 23% of neonates who survived meningitis have moderate to severe neurodevelopmental impairment [86]. Drug resistance among Gram-negative organisms infecting neonates from Africa and India is increasing and effective immunization programs in LMICs are variable [87,88]. Tuberculous meningitis (TBM) occurs in around 1% of all cases of tuberculosis, and results in death or severe disability in about 50% of those TBM [89]. Hydrocephalus, a potential complication of bacterial meningitis, and particularly TBM, often cannot be managed in LMICs due to lack of capacity. Prevalence of syphilis remains high with approximately 10.6 million new cases reported by the WHO in 2008, but number of affected people with neurosyphilis is not known [90].

PARASITIC INFECTIONS

One in four children with cerebral malaria develops long-term cognitive impairment [91,92]. Children often present with acute convulsive seizures and the carry a poor prognosis [93]. Neurocysticercosis, which is endemic in areas with poor pig management practices and sanitation, occurs when the larval stages of Taenia solium infect the brain. In LMICs in which neurocysticercosis is endemic, it is the leading identified cause of seizures [94]. Neuroschistosomiasis brain involvement may result in acute schistosomal encephalopathy (acute phase) or cerebral schistosomiasis or pseudotumoral encephalic schistosomiasis (chronic phase). The spinal cord may also be involved [95]. Soil-transmitted helminths (STH) affect millions, most frequently children. Infants and children under 5 years of age with anaemia and STH infection show disturbed social and emotional behaviour, and treating school-aged children with antiparasitic drugs and iron sup-

plementation improves attention, memory and processing speed [96].

TRAUMA [97]

There is a need for established protocols to be adapted for LMICs. Such a standardized trauma-care protocol decreased in-hospital mortality of patients with severe TBI in a LMIC teaching hospital [98]. Adherence to the protocol was limited at about 60%, not because of lack of resources or technology, but due to resistance to change established practices. Similar to decompressive craniectomy, prophylactic hypothermia for the treatment of ICP is a relatively low-technology option available in LMICs [99-101].

THE AVAILABLE INTERVENTIONS

PHYSICAL, OCCUPATIONAL AND COGNITIVE REHABILITATION

Whereas physical, occupational and cognitive rehabilitation for individuals with sequelae of CNS events are routine in resource equipped countries, such interventions are lacking in LMICs owing to a lack of trained personnel and high costs. In the community, home stimulation, parenting education and support, and provision of financial support or nutritional support for children enrolled in early child development centres have shown some benefit in improving children's cognition [102,103]. Interventions that target both the carer and the child are more effective than those that include either one [103]. In tertiary centres, computer-based cognitive training programmes were effective in improving cognition in African children surviving CNS infections [104,105].

TRAINING [106]

The workforce equipped with the skills to address neurological disease is lacking in Africa [107-109]. The density of paediatricians practicing in countries in the continent ranges between 0.03 and 0.8 per 100 000 of the population [4,110,111]. Compared to European figures, which range from 11 to 86 paediatricians per 100 000 of the population in the United Kingdom and Germany respectively.

Migration of skilled personnel, referred to as the "brain drain", has resulted in adaptation and development of training programs, whereby trainees are sent to other centres based in Africa to gain skills relevant to practice in the continent and to equip these health practitioners with the necessary knowledge to be effective on their return to their home centres [111,112]. To achieve these goals, it is important to identify key health challenges by setting priorities; strengthening national health systems and building capacity; and consolidating links between health research and action (translation and evidence-based implementation). The implications of the Zika virus pandemic is likely to result in a large number of children with developmental disorders, and highlights for the pressing need to train personnel in a wide variety of health disciplines, including neurology, rehabilitation, specialized nursing, social services, and so on to care for and treat this population and so many other children with neurodisability in LMICs.

Beyond the limitations of trained staff in LIMCs, additional compounding factors include distance to travel to access health care facilities, lack of infrastructure within such facilities, unreliable access to diagnostics tools and subsequent treatments, which often burden families with untenable costs. In addition, management of neurological conditions in some LMICs, especially Africa, are based in psychiatric units, further compounding the stigma associated with neurological disease.

ADOLESCENTS AND SUBSTANCE ABUSE [113]

Adolescents in LMIC face enormous environmental threats, from the effects of poverty, war, local conflicts, sex trafficking and slavery, early marriage and/or pregnancy, as well as inadequate education. Worldwide, the primary causes of years lost due to disability (YLD) for adolescents include neuropsychiatric disorders (45%), unintentional injuries (12%) and infectious diseases (10%) [114]. Adolescence is regarded as a high priority by the United Nations programme UNICEF and other agencies [115,116]. In LMICs 20% of mothers have their first child by 18 years of age [117].

In wars, despite international agreements and conventions, child soldiers are recruited and are at risk of physical trauma with lasting disability, post-traumatic stress disorder (PTSD) and addiction [118]. Similar outcomes are found from the impact of post-conflict displacement of adolescents, who are often separated from their family and community [119]. Treatments for refugee children, including cognitive behavioural therapy (CBT) and narrative exposure therapy, can reduce psychological problems such as depression and PTSD [120]. Alcohol use, particularly binge drinking, inhibits neuronal development in adolescence [121] and has a greater impact on motor and executive impairment in adolescents than in adults, thus conferring greater risk of injury or risky behaviour in adolescents [122].

Untreated HIV infection is associated with disabling cognitive impairment, depression and behavioural disorders in adolescence [123]. Following the scale-up of ART, survival of perinatally infected children in sub-Saharan Africa has dramatically improved. The population of adolescents with HIV is now estimated at 2 million with more than 90% of those living in sub-Saharan Africa. A study in South Africa evaluated a community participatory approach to adapt a family-based intervention (originally developed in the United States) to promote mental health awareness in adolescents receiving HIV ART [123]. Short-term results showed improvements in mental health, behaviour and adherence to the drug regimen with a decrease in stigma experience [123].

REGIONAL INFLUENCES [124]

SUB-SAHARAN AFRICA

Malnutrition, from birth through to adulthood, is the most significant contributor to disease burden and disability in sub-Saharan Africa [125]. Maternal malnutrition, including micronutrient deficiencies such as vitamins and iodine, impairs the development and function of the nervous system of offspring, and negative effects can persist in the next generation. Other forms of maternal and environmental trauma during the perinatal period affect brain development and cause long-term changes in brain function. Neurological disorders caused by eating toxic foodstuffs are unique to sub-Saharan Africa for example cassava. Lathyrism that presents as spastic paraparesis is an equally debilitating neurological disorder caused by excessive ingestion of the grass pea *Lathyrus sativus* that contains the excitotoxic amino acid, βN-oxalyl amino-L-alanine [125].

Use of psychostimulants is another major contributor to the burden of brain disorders in sub-Saharan Africa [126]. Of particular concern is the high prevalence of maternal alcohol and methamphetamine use in areas such as the Western

Cape of South Africa. The incidence of fetal alcohol syndrome in some locations within this region is the highest in the world [127]. The increase of methamphetamine use in pregnant women in the Western Cape is of concern given the negative effects that the drug has on the developing fetus [128].

The prevalence and incidence of epilepsy in sub-Saharan Africa countries is two-fold higher than in other countries [93,129-133]. The prevalence varies between 4.5 and 20.8 per 1,000 people, owing to the localized and high incidence of parasitic infections, poor perinatal care and poor access to treatment. The full burden of epilepsy in sub-Saharan Africa is difficult to assess and is likely to be under-reported because people with epilepsy are stigmatized and frequently left untreated [133].

Sub-Saharan Africa has the highest burden of infectious diseases and the poorest public health infrastructure in the world [125,134]. Parasitic infections are also highest in this region and often have neurocognitive sequelae. HIV-associated neurological disorders area major burden, with more than 1.5-million children living with HIV and at risk of developing HIV-associated cognitive impairment and dementia [135,136]. Little is known of the effects of HIV and ART on the developing brain. Further research is needed on the longitudinal trajectory of neurodevelopment among children and adolescents who are perinatally infected with HIV [135]. Neuroimaging and neurocognitive testing are established in several regions within sub-Saharan Africa and are used in cross-country collaborations to further understanding of the spectrum of neurocognitive disorders in patients with HIV and to determine the effect of antiretroviral therapy on these individuals [137]. Subtle changes in white-matter integrity have been used for early diagnosis and monitoring of progression of neurological disease in individuals with HIV [137].

MIDDLE EAST AND NORTH AFRICA

Many of the aetiological and treatment features of psychiatric disorders in the Middle East and North Africa are due, in part, to the unique environmental and cultural influences within the region. Over the past few decades, communities have been exposed to traumatic events including anti-government uprisings and wars, leaving many populations vulnerable to mood disorders, such as PTSD and major depressive disorder (MDD). In comparison with the global estimate of 4.4%, [138] depression prevalence in Iraq is 7.2% and in the Palestinian territories, is 15.3% [139,140]. Owing to the high rate of consanguinity in the region, the incidence of several recessively inherited genetic disorders, such as inherited deafness, is increasing [141-143]. The prevalence of substance-use disorders varies between 7.25% and 14.5%, with cannabis being the most commonly used drug followed by alcohol [144,145]. Khat is also widely used as a stimulant in Yemen and the neighbouring countries within the Arabian Peninsula.

LATIN AMERICA AND CARIBBEAN

The overall weighted prevalence of 12.7% for mental health disorders in children in the region is significantly more than the prevalence of 9.7% seen in United Kingdom [146]. There is inadequate information on risk and protective factors that affect the incidence of mental health disorders in children living in LMICs in general, and Latin America and the Caribbean in particular [147].

The annual incidence of epilepsy in Latin America and the Caribbean is 77.7 to 190 per 100,000 people each year [148] compared with 30 to 50 per 100,000 people in high-income countries. Distribution of epilepsy across sub-regions of Latin America and the Caribbean also differs, in part due to the direct association between epilepsy and the distribution of neurocysticercosis [149].

ASIA

An epidemiological study of epilepsy in 23 Asian countries revealed the lifetime prevalence of epilepsy to be 1.5 to 14 per 1,000 people [150]. Infections of the nervous system often contribute to epilepsy and prevention of these infections is needed to reduce the burden of the condition.

FUTURE PERSPECTIVES

PRIMARY PREVENTION

Effective immunisation programs are essential, along with avoidance of nutritional deficiencies and malnutrition, but also measures such as malaria nets, use of insecticides and effective implementation of pig pens all would contribute to lower the incidence many avoidable conditions [151].

DIAGNOSIS

LMICs are faced with significant diagnostic challenges often unable to do more than the basic of tests and cannot access screens for standard bacterial, fungal or viral cultures, let alone PCR. Similarly, neuroimaging is often unavailable based on access and cost. Development of affordable, easy-to-use, rapid **diagnostic assays**, preferably at the point-of-care, that can identify infections affecting the nervous system are a high priority.

Simple algorithms for conditions that affect the nervous system, coupled with the ability to provide effective therapy following diagnosis, or appropriate referral for screening algorithms, have the potential to substantially reduce morbidity and possibly mortality from these infections.

INTEGRATION OF TRADITIONAL METHODS OF TREATMENT

Assessing the efficacy of indigenous, traditional Chinese medicine and Indian Ayurveda medicine for brain disorders is important as well exploring resources such as collaboration with traditional healers across LMICs [152,153].

The unique environmental structure, disease profile and health needs of LMIC settings, mean that interventions and approaches developed and tested in high-income countries may not be practical if directly introduced into LMICs and if used must be adapted at a local level. In fact, solutions which have been developed in LMICs may have global applications, such as kangaroo care and bubble CPAP for neonates [154].

IN CONCLUSION

The brain develops most rapidly in the first few years of a child's life. The ongoing interchange between genes and different environments shapes the developing brain. During these early critical years, foundations are laid for a child's physical and mental health, inclusive of how long they live for, their ability to learn, to adapt to change and their resilience against adverse circumstances.

Target areas include improving maternal obstetric and subsequent neonatal care, providing effective vaccination programs to prevent respiratory, diarrhoeal and measles diseases and supporting good nutrition and sanitation. Mother to child intervention programs are effective and have reduced the incidence of HIV in the paediatric population, but despite this the number of affected children in sub-Saharan Africa remains huge. Malaria nets and avoidance of putting children where they are at risk can influence risk of infection. To improve early child development, governments as well as the global communities need to continuously work towards ways to improve these conditions for all children regardless of where they reside.

Competing interests

The author is not aware of any financial or non-financial competing interests which affect the content of this report.

Author Contributions

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