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TROPICAL DISEASES OF MOZAMBIQUE (B GRAU-PUJOL, SECTION EDITOR)

# Child Mortality in Mozambique: a Review of Recent Trends and Attributable Causes

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## Abstract

**Purpose of Review** In the last 25 years, child mortality has significantly dropped at a global level. Understanding particularities of child mortality at the national level is useful to tailor health policy to those conditions requiring more attention. In Mozambique, a variety of efforts have been made to better characterize the overall child mortality and to describe the main contributors for death. In this review, we attempt to contextualize current knowledge on causes of pediatric deaths in Mozambique.

**Recent Findings** The available data regarding the principal causes of death in Mozambican children point out to infectious diseases and neonatal causes as the principal causes of preventable deaths, with important variations in recent years in line with the epidemiological changes seen in the country as a result of reductions in malaria transmission and the impact of the nationwide introduction of different conjugate vaccines.

**Summary** Data regarding the main causes of death among children in Mozambique are patchy, outdated, and in many cases based on methodologies with many underlying limitations, which make them unreliable. More robust postmortem methodologies to study the underlying causes of mortality, currently being introduced in a surveillance sentinel site of the country, will surely contribute to improve our understanding of what is really killing children in this country.

**Keywords** Mozambique · Children · Mortality · Cause of death · Verbal autopsy · Postmortem methods

**Abbreviations**

| | |
|---|---|
| 5q0 | Under five mortality |
| AfDB | African Development Bank |
| CHAMPS | Child Health and Mortality Prevention Surveillance |
| CHERG | Child Health Epidemiology Reference Group |
| CISM | Centro de Investigação em Saúde de Manhiça |
| CoD | Cause of death |
| DHIS2 | District Health Information System, version 2 |
| GNI | Gross national income |
| HMIS | Health Management Information System |
| IBI | Invasive bacterial infections |
| IHME | Institute of Health Metrics and Evaluation |
| INE | Instituto Nacional de Estatística |
| INS | Instituto Nacional de Saúde |
| MCEE | Maternal Child Epidemiology Estimation |
| MDG | Millennium development goals |
| MITS | Minimally invasive tissue sampling |
| WHO | World Health Organization |

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## Introduction

The last quarter of a century can indisputably be characterized by a global health revolution that has led to massive improvements in health outcomes, particularly in terms of child survival. Indeed, never before in the history of mankind have the chances of surviving for any newborn in this world been

greater, with child mortality becoming minimal in many high-income regions, and the number of child deaths decreasing globally at a fast pace, from over 13 million annual deaths in 1990 to around 5.9 million in 2015 [1]. Reductions in child mortality have been documented all over the planet, although global progress has been unequal, and many countries, particularly in Sub-Saharan Africa, have failed to achieve in the 1990–2015 period the two-thirds reduction in child mortality stipulated by millennium development goal (MDG) 4. As a result, many children still die from preventable conditions [2].

Understanding that regions and countries have their specific idiosyncrasies, it appears relevant to attempt to look at child mortality on a more focalized manner. In this respect, exploring national mortality patterns and associated available statistics regarding causes of child mortality within country boundaries can provide a more granular understanding of the principal causes and determinants of death, enabling a more accurate calculation of specific burden and the evaluation of the quality of the data available for that country. In this paper, we have attempted to summarize current knowledge on child mortality in Mozambique, in the Southern African region.

## Mozambique: Country Profile and Mortality Trends

Mozambique is a paradigmatic example of an emerging country in Sub-Saharan Africa having shown in the last two decades substantial progress in many fronts, such as for instance economically, with an average 1.54% increase in its gross domestic product (GDP) in the period 2007–2017, but still facing significant challenges in terms of poverty, access to health, child morbidity (including malaria, malnutrition, etc.), and mortality. According to the World Bank, the country had in the year 2016 an estimated population of 28,829,476 inhabitants, 70% of which lived in rural areas [3]. The population pyramid remains heavily skewed towards young ages, with fertility rates of 5.2 per woman, approximately 1,125,000 annual births, and an estimated 4,950,000 (17.2%) of its inhabitants being under 5 years of age, in 2016 [4]. In this same year, the gross national income (GNI) per capita was 480 US$/person, for the first time declining after an uninterrupted upwards annual trend which started in the year 1992 [3]. Figure 1 summarizes trends in child mortality estimates for Mozambique since the year 1965 and compares them to the rest of the African continent. Impressive advances have been witnessed, with country-wide under five mortality rates (5q0) having dropped from the circa 275 deaths per 1000 live births in the 1960s, to the latest estimates ranging from 71.8 to 78/1000 in the year 2016 [4, 5]. Decreases have been continuous throughout the last several decades, but the slope of the curve significantly increased from the year 1992 onwards, coinciding with the end of a 15-year-long civil war. Infant mortality was estimated to be 53 deaths/1000 live births in the year 2016, and neonatal mortality, at 27 deaths/1000 live births in 2016, also has shown uninterrupted decreasing trends, albeit at a much slower pace, and now accounts for 35% of all under five deaths [3].

## Limitations of Methods Used to Characterize Causes of Child Mortality in Mozambique

The last decade has seen a proliferation of death estimates (overall and by general cause) at national, regional, and global levels. In spite of an estimated ~ 60% of all child deaths occurring outside of the health system in Mozambique, there have been significant improvements in "counting the dead" [6], as a result of strong efforts to develop the country's' death registration system and augment its coverage [7]. Beyond counting the dead, characterizing what is killing children is a much harder but necessary leap forward to address child survival challenges. Historically, the country has used different methods to describe CoD in children, which include clinical diagnoses provided at the health system level (generally from secondary and tertiary levels of care, and as a result of either pre-mortem clinical diagnoses or death certificate diagnoses), and mortality surveys conducted using a "verbal autopsy" tool, a post-mortem questionnaire given to parents or caretakers [8]. The major limitation of clinical data, beyond its poor reliability (as recurrently shown by the high amount of discrepancies in clinico-pathological comparisons against the gold standard complete diagnostic autopsy [9–11]), is the fact that only deaths reaching the health system will have a diagnosis, therefore excluding more than half of all child deaths occurring in country. In contrast, verbal autopsies can be used to investigate any kind of death, but their performance is even more uncertain than that of clinical data, and therefore estimates provided from this source need to be interpreted with skepticism, as they rely on information provided by non-clinicians and can generally only identify broad syndromes rather than specific precise diagnoses. Nonetheless, while specificity is obviously a problem, given the approach, verbal autopsies are known to provide somewhat credible results at a population—rather than at an individual—level, and often there is no other cause of death information available [12, 13].

## Characterization of Causes of Child Mortality in Mozambique

Data regarding child deaths in Mozambique have traditionally been generated by national and international institutions. From a national point of view, the Ministry of Health (MoH) conducts regular assessments, normally once every decade, often in close collaboration with national government-linked

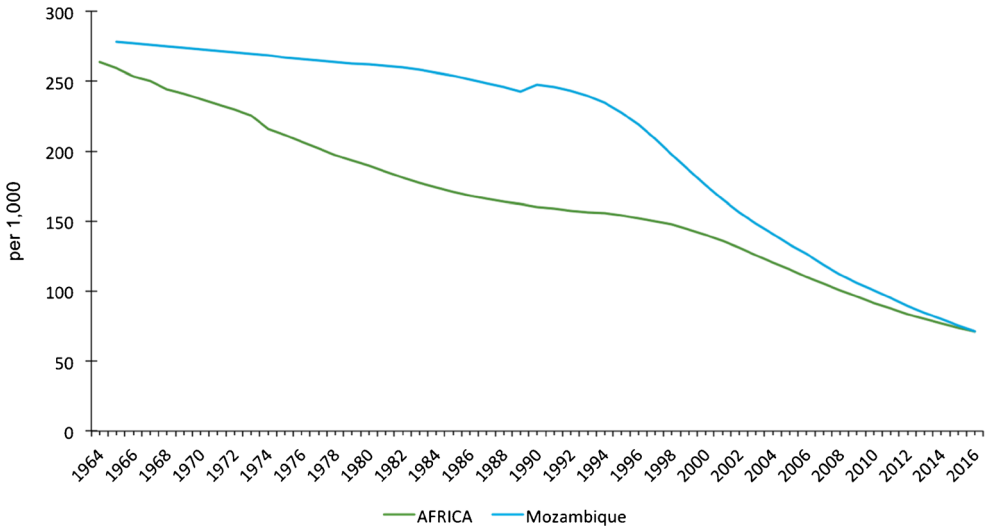


**Fig. 1** Trends in child mortality (5q0) in Mozambique and Africa, 1965–2015, according to the African Development Bank [5]

and/or independent research institutions, such as the *Instituto Nacional de Estatística* (National Institute of Statistics; INE), the *Instituto Nacional de Saude* (National Institute of Health, INS), or the *Centro de Investigação em Saúde de Manhiça* (Manhiça's Health Research Centre, CISM [14]). These institutions have undertaken efforts to characterize mortality causes or at least to provide burden of disease data for certain conditions. The last national review of mortality causes ("Inquérito nacional sobre causas de mortalidade") was published in 2012, but it reports on data from the years 2007–2008. In this report [15], data are inferred from a nation-wide sampling of ~ 16,000 deaths from all age groups, but with up to a quarter of all included deaths being from children aged less than 5 years, in 388 clusters representing the ten provinces and the capital city, all of them studied through verbal autopsy. Main causes of child mortality were determined to be malaria (42% of all deaths), followed by HIV/AIDS (13%), pneumonia (6%), diarrheal diseases (6%), malnutrition (2%), and measles (< 1%) [15]. In the subgroup of neonatal deaths ($n = 719$), the major causes of mortality included bacterial sepsis (35%), obstetric factors and delivery-associated complications (10%), malaria (6%), intrauterine hypoxia and perinatal asphyxia (6%), complications of prematurity (6%), and pneumonia (4%). Interestingly, 74% of all studied deaths (for the total sample size) occurred at the household level, and not in the health system. Relatedly, CISM conducted another exercise using verbal autopsy to describe the CoD of a sample (80%) of all pediatric (< 15 years of age) deaths occurring in the Manhiça District during the period 1997–2006. Of the 3002 deaths studied in this age group, nearly three-quarters (73.6%) were attributed to communicable diseases, whereas non-communicable diseases accounted for 9.5% of the defined causes of death, and injuries for 3.9% of the remaining causes. Malaria was the single individual largest cause, accounting for 21.8% of cases, followed by pneumonia (9.8%), HIV/AIDS (8.3%), and diarrheal diseases (8%) [16]. In this study, 54% of all child deaths occurred outside of a health facility.

Beyond verbal autopsies, Mozambique has recently embarked on an improved morbidity and mortality reporting system, based on the HMIS (health management information system) that utilizes DHIS2 software, which allows data disaggregation by each facility level. Table 1 summarizes cause of death data reported at the hospital level (secondary and tertiary level of care) for the year 2016 ($n = 2213$), whereby malaria, malnutrition, and pneumonia are described as the three primary causes of death in children under the age of 15. Surprisingly, no neonatal conditions appear in the list, but this may be related to the different reporting systems expected in this particular vulnerable group, which are usually linked to maternities and not necessarily pediatric wards. At a lower level of health care (health center and below), DHIS2 also reported from 2016 12,884 additional pediatric deaths from the health center level.

Mortality data for Mozambican children are also routinely estimated by International organizations, as part of their global evaluations of under five mortality. In this respect, two large

**Table 1** Pediatric deaths recorded in the Mozambique HMIS at hospital level (secondary and tertiary) during the year 2016

| Causes of death (not ICD-10) | Ages 0–< 15 years, *n* (%) |
|---|---|
| HIV/AIDS | 151 (6.8) |
| Malaria | 902 (40.8) |
| Pneumonia | 299 (13.5) |
| Measles | 0 (0) |
| Anemia | 249 (11.3) |
| Diarrhea | 120 (5.4) |
| Tuberculosis | 35 (1.6) |
| Malnutrition | 457 (20.7) |
| Total deaths | 2213 (100) |

groups stand out among the rest, which include the Maternal Child Epidemiology Estimation (MCEE) group (formerly Child Health Epidemiology Reference Group, CHERG) from the World Health Organization, which includes partners such as UNICEF, and the Institute of Health Metrics (IHME), from Seattle, USA, which runs the "Global Burden of disease" program. Both groups use complex methodologies [17, 18] that input data from various data sources, such as verbal autopsies, clinical records, and death certificates; estimates from each group have been often observed to differ substantially at the global level [19, 20]. Figure 2 summarizes the principal causes of child mortality in Mozambique as estimated by IHME. This group, which makes their estimates freely available online, highlights the importance of neonatal deaths, which would be responsible for an overall 27.2% of all child mortality in Mozambique. Malaria (16.2%), followed by HIV/AIDS and tuberculosis (altogether 13.7%), and lower respiratory tract infections (12.2%) are the three principal causes of premature non-neonatal child deaths [21]. In Fig. 3, IHME proposes a graphical representation of the changes in the relative importance of the main causes of death in the period 1990–2015. Noteworthy, changes in the last 25 years in the five main causes of mortality have been tiny, with the exception of the increase of HIV-associated deaths (from rank 8 to rank 4) [21]. For WHO-MCEE, although estimates are slightly less recent, neonatal conditions accounted in 2015 for ~ 35% of all deaths, whereas malaria (13%), post-neonatal pneumonia (12%), diarrheal diseases (9%), and HIV/AIDS-associated deaths (5%) would be the main causes of child death [4].

## The "Big Five"

Five conditions are responsible for the majority of child deaths, and it may be worth looking in a bit more detail at their numbers and the current knowledge related to their epidemiology in Mozambique.

### Acute Lower Respiratory Infections

Acute respiratory infections, and pneumonia as their hallmark, remain the number one killer of children globally, claiming the lives of 920,000 children in 2015. More importantly, 99% of all pediatric pneumonia deaths are thought to occur in low- and middle-income countries, as a paradigmatic example of health inequities in the world. In Mozambique, pneumonia is also recognized as a major cause of child mortality, although likely underestimated, as it generally is ranked either in the second or in the third position of child deaths. The introduction of two highly effective conjugate vaccines, against *Haemophilus influenzae* type B (2009), and subsequently against *Streptococcus pneumoniae* (2013), has been associated to a significant impact in decreasing pneumonia cases and deaths [22]. However, a study in Manhiça showed that pneumonia accounted, before vaccine introduction, for up to 16% of all hospital admissions, and whenever present, was associated with a high case fatality rate (11%) [23]. The common circulation in-country of other pathogens responsible for acute and potentially life-threatening respiratory infections, such as respiratory syncytial virus [24, 25], or Pneumocystis [26],

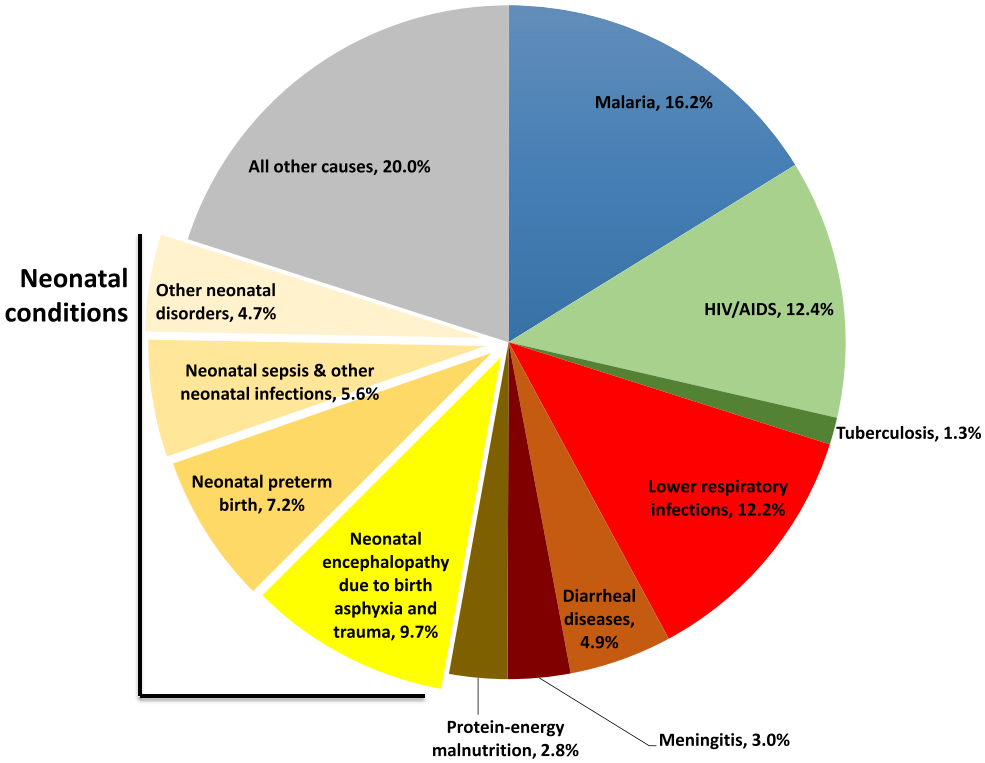


**Fig. 2** Distribution of causes of under-5 deaths in Mozambique (including neonatal deaths), according to IHME estimates, 2016 [21]

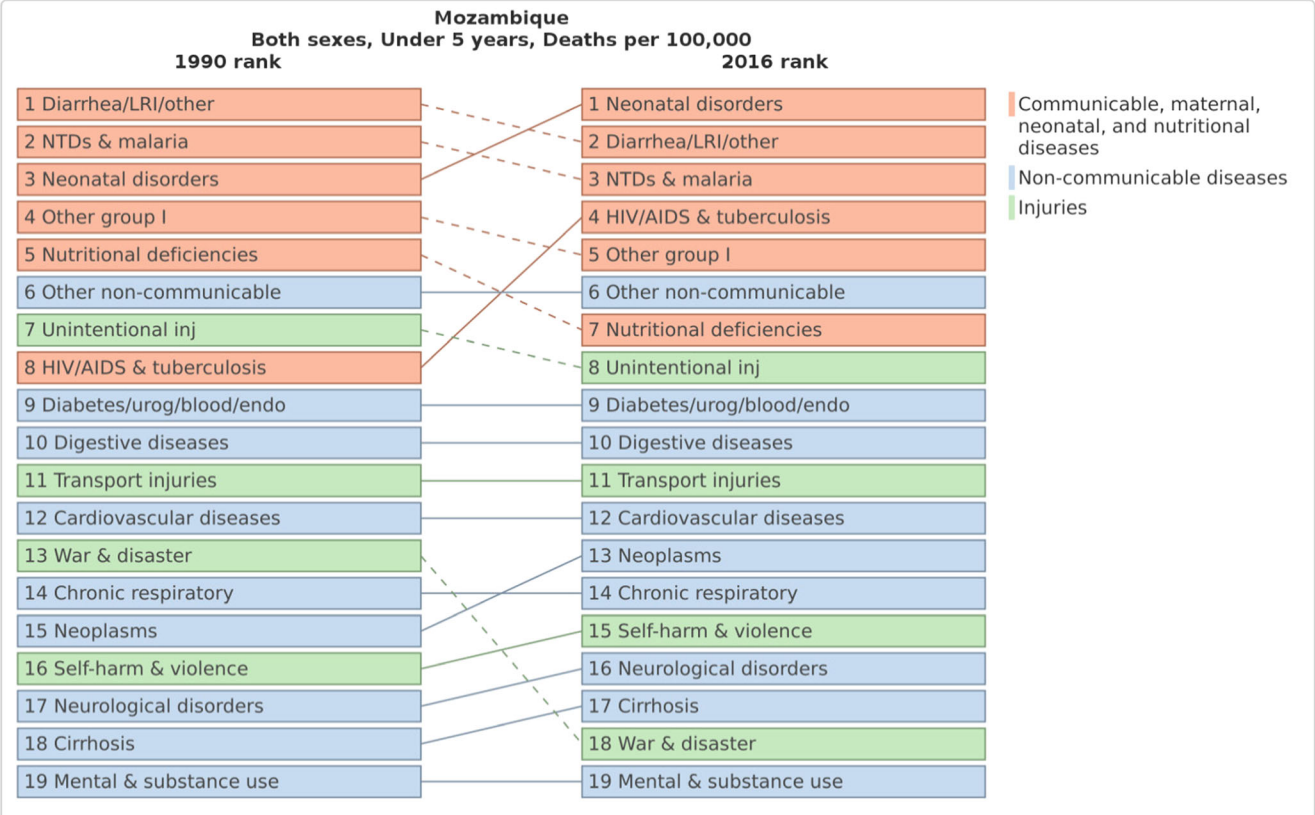


**Fig. 3** Changes in the ranking of principal causes of child mortality, 1990–2015, according to IHME estimates [21]

well documented in surveillance sites in the country, needs also to be emphasized, the latter particularly in the context of the high prevalence of HIV co-infections. Surveillance of other relevant viral or bacterial pathogens, such as influenza and *Bordetella pertussis*, has been patchy, and National burden data in children have not been properly characterized.

## Malaria

Malaria has traditionally been considered the main cause of child mortality in Sub-Saharan Africa, and the number one cause of pediatric deaths in Mozambique, where transmission is perennial and occurring throughout the country. However, the decreases in malaria incidence observed globally during the last 15 years have also been documented in Mozambique, where WHO data reports 14,370 deaths, and 8.87 million episodes, for the year 2015 [27], in comparison for instance. Nonetheless, the northern provinces remain hotspots of global malaria transmission, and recent reports alarmingly portray increases in the incidence of this disease [28]. Data from Mozambique's Malaria National Control program are in line with an increase by 17% since the previous malaria survey in the number of cases but only recognize 1114 malaria deaths in total in 2017, which is likely a substantial underestimation. Data from an ongoing surveillance of malaria incidence and hospitalizations at the Manhiça District suggest a continuous increase of the number of outpatient visits, admissions, and deaths since the year 2011, which signified the nadir of malaria transmission and death in the district, with only three documented fatal episodes in an entire year (Guinovart C, personal communication). In spite of the massive deployment of prevention (like insecticide treated nets) and clinical management (rapid diagnostic treats and therapeutic options) tools, malaria remains, as of 2018, a significant public health problem for Mozambique.

## Diarrheal Diseases

Diarrhea-associated deaths are the only condition that indisputably appear to have decreased in Mozambique during the last decade. Reasons for this include a widespread availability of oral rehydration solution, and the recent introduction of the rotavirus conjugate vaccine nationwide. Whereas in the past, diarrhea was usually the second most common cause of mortality, it now appears to have been relegated to lower ranks (sixth condition according to the DHIS2 reporting system in country, and similar positions when analyzed by GBD and MCEE). The recent Global Enteric Multi-center Study (GEMS), an etiology of diarrhea study in four African countries (including Mozambique) and three in South Asia, characterized the main pathogens and characteristics of diarrheal disease in Mozambique, through data generated from the

Manhiça site. Mortality for cases of moderate to severe diarrhea in the GEMS study was highest for the Mozambican children in relation to the seven participating sites, and rotavirus and cryptosporidium were found to be the commonest pathogens causing diarrhea in infants, perhaps in relation to the high underlying HIV endemicity [29].

### HIV and Tuberculosis

The HIV pandemic has severely affected Mozambique [30], which is currently one of the most HIV-impacted countries in the world, with the nationally reported HIV prevalence in adults being 13.2% [31]. Community cross-sectional studies conducted in the district of Manhiça have repeatedly estimated the HIV prevalence in this specific district to be as high as 40% in the last years [32, 33], and vertical transmission rates in the first month of life of children born from HIV-infected mothers have been estimated in a study that took place in the years 2008–2009 at around 9% [34]. Measures implemented by Mozambique's MoH to reduce the disproportionate burden imposed by HIV have had significant impact, decreasing in particular the number of HIV-infected newborns. However, prevention of mother to child transmission (PMTCT) remains suboptimal, and many incident infections still occur, leading to a relatively high HIV prevalence among children under the age of five, and therefore high associated mortality rates. The MoH estimates that in 2017, 7.9% of children aged 0–< 15 years of age are living with HIV and that nearly 10,000 pediatric deaths still occurred nationally as a result of this disease, a figure that may be an important underestimate due to the particular challenges of diagnosing this disease in early life. Tuberculosis deaths among children are also particularly difficult to recognize, with IHME estimates suggesting 5884 pediatric deaths in Mozambique [21], as opposed to 7334 according to MCEE-WHO [35]. However, the estimated incidence of tuberculosis in a study conducted in children (470 cases/100,000 person-year; among the highest in the world documented) and the high HIV co-infection (present in 44% of the TB cases) [36] are clearly suggestive of an iceberg effect in terms of the real number of tuberculosis deaths among Mozambican children.

### Neonatal Conditions

This is perhaps the area where least is known in relation to the burden and associated mortality of some of these conditions in Mozambique. Although national statistics highlight the importance of these conditions in terms of their association with poor outcomes [15], little information is available on their true burden and associated outcomes. Surveillance studies on specific neonatal conditions, such as bacteremia during the first 28 days of life, suggest that infections in this period are a major cause of perinatal mortality, with group B Streptococcus standing out as the main cause of invasive bacterial infections (IBI) among neonates (incidence of 2.7/1000 live births) and with a high associated case fatality rate [37].

Importantly, the number of annual stillbirths reported in Mozambique is believed to be around 22,900 [38], and national stillbirth incidence has been calculated at 20.67/1000 live births [38]. This indicator, although not formally part of child mortality estimates, and often neglected as part of public health policy, is an important proxy of quality of antenatal and *intrapartum* care and of the importance of the perinatal period in terms of child survival.

## Other Overlapping Conditions and Diagnostic Challenges

Certain conditions are inappropriately absent from the currently available lists of major killers of children globally, and this is also the case for Mozambique. This is in relation to either (1) the generalized belief that they do not play a direct role in the CoD, but rather a contributory one, or (2) the difficulties in currently diagnosing them, and therefore acknowledging their role. A blatant example of the former includes severe acute malnutrition, consisting of severe wasting (marasmus) and/or edematous malnutrition (kwashiorkor), which is thought to be involved in up to 50% of all global child deaths [39]. A study conducted by CISM in Manhiça highlighted that in a 10-year-long period, up to 47% of all pediatric outpatients presented with some indication of malnutrition, and 6% with severe malnutrition. Importantly, case fatality rate of children admitted to hospital with severe malnutrition was high and estimated at 7% [40]. Additional examples also include anemia, often linked to malaria, and considered as the number one killer of malaria patients in Sub-Saharan Africa [41]. In Mozambique, research studies have highlighted the significant burden of morbidity and mortality associated to anemia [42], and its multiplicity of underlying etiologies [43]. For other diseases, such as for instance IBI, of well-established potential to cause life-threatening disease, the challenge relies on identifying them in a context of a fragile health systems and a generalized scarcity of diagnostic tools. In Mozambique, only two laboratories have the capacity of routinely evaluating pediatric patient samples for IBI via blood cultures, explaining why these conditions do not appear as usual culprits of child mortality. In spite of this, surveillance studies have identified IBI as a major killer of Mozambican children, on their own [37, 44], or as

superimposed infections complicating cases of severe malaria [45], anemia [43], or malnutrition [40].

## Future Perspectives and Conclusions

Recent estimates of child mortality causes in Mozambique presented in this review highlight the unreliability of methods currently utilized for the purpose of CoD attribution, and the difficulties in uncovering the real underlying causes of mortality. It is clear that current methods lack sufficient specificity and that as a result provide little granularity on the causes of death, beyond a largely syndromic approximation. In this respect, innovative and more accurate approaches, based on the use of minimally invasive post-mortem sampling methods, currently being introduced in the country in the context of research protocols [46] and the CHAMPS [6] (Child Health and Mortality Prevention Surveillance) program—a large-scale child mortality surveillance endeavor—will likely provide a more solid evidence-base in the sentinel sites where they are conducted to further understand CoD. This approach includes the sampling of key organs (brain, liver, both lungs, among others) and bodily fluids such as blood and cerebrospinal fluid, which are then subject to histopathological and microbiological procedures [47, 48]. Validation of the method when compared against the gold standard complete diagnostic autopsy has shown a significant agreement (89%) and a high concordance (kappa 0.70) in cases of pediatric deaths [49]. The minimally invasive tissue sampling (MITS) and testing methods, although currently limited geographically to six sites in sub-Saharan Africa and one site in south Asia, will, however, ensure quality CoD diagnoses, using a more objective and robust methodology, a first step in the tortuous road towards understanding better child mortality, and to introducing effective interventions to continue reducing it. Comparing verbal autopsy results with MITS-informed cause of death determinations (as "gold-standard") may make it possible to modify interpretation of verbal autopsy findings (and/or to modify questions asked) to improve the specificity of verbal autopsy and to sharpen cause of death determination in areas where post-mortem sampling and testing are not possible.

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## Compliance with Ethical Standards

**Conflict of Interest** The authors declare that they have no conflict of interest.

**Human and Animal Rights and Informed Consent** This article does not contain any studies with human or animal subjects performed by any of the authors.

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