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Paediatric postdischarge mortality in developing countries: a systematic review

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ABSTRACT

Objectives To update the current evidence base on paediatric postdischarge mortality (PDM) in developing countries. Secondary objectives included an evaluation of risk factors, timing and location of PDM.

Design Systematic literature review without meta-analysis.

Data sources Searches of Medline and EMBASE were conducted from October 2012 to July 2017.

Eligibility criteria Studies were included if they were conducted in developing countries and examined paediatric PDM. 1238 articles were screened, yielding 11 eligible studies. These were added to 13 studies identified in a previous systematic review including studies prior to October 2012. In total, 24 studies were included for analysis.

Data extraction and synthesis Two independent reviewers extracted and synthesised data using Microsoft Excel.

Results Studies were conducted mostly within African countries (19 of 24) and looked at all admissions or specific subsets of admissions. The primary subpopulations included malnutrition, respiratory infections, diarrhoeal diseases, malaria and anaemia. The anaemia and malaria subpopulations had the lowest PDM rates (typically 1%–2%), while those with malnutrition and respiratory infections had the highest (typically 3%–20%). Although there was significant heterogeneity between study populations and follow-up periods, studies consistently found rates of PDM to be similar, or to exceed, in-hospital mortality. Furthermore, over two-thirds of deaths after discharge occurred at home. Highly significant risk factors for PDM across all infectious admissions included HIV status, young age, pneumonia, malnutrition, anthropometric variables, hypoxia, anaemia, leaving hospital against medical advice and previous hospitalisations.

Conclusions Postdischarge mortality rates are often as high as in-hospital mortality, yet remain largely unaddressed. Most children who die following discharge do so at home, suggesting that interventions applied prior to discharge are ideal to addressing this neglected cause of mortality. The development, therefore, of evidence-based, risk-guided, interventions must be a focus to achieve the sustainable development goals.

Strengths and limitations of this study

- ► Extensive literature search of Medline and Embase with independent screening of all abstracts and eligible full-text publications by two investigators.
- ► Extensive data extraction on risk factors for mortality within each study population.
- ► Few studies were prospective and focused on measurement of post-discharge mortality as a primary outcome.
- ► Heterogeneity in populations, duration of follow-up and high proportion of loss to follow-up may limit the external validity and underestimate outcome rates.
- ► No optimal method to assess the risk of bias in included studies.

INTRODUCTION

The third of 17 United Nations sustainable development goals (SDGs) emphasises preventable deaths of newborns and children under 5 years of age, with all countries aiming to reduce under-5 mortality to at least as low as 25 deaths per 1000 live births by the year 2030.[1] Although significant progress was made during the Millennium Development Goal era (1990–2015), preventable childhood deaths remain high in Southern Asia and sub-Saharan Africa.[2] These deaths result largely from infectious diseases (including malaria, pneumonia, diarrhoea, etc), which lead to sepsis.[3] Children are particularly vulnerable in the months following hospital discharge, with a growing body of research demonstrating that postdischarge deaths occur in similar numbers as during hospital admission. Despite the staggering burden of postdischarge mortality, this issue has been largely neglected when examining paediatric mortality from infectious disease. The 2017 United Nations World Health Assembly (WHA) resolution calling for improvement in prevention, diagnosis and management of sepsis is timely as it emphasises the need for improved follow-up care, particularly for developing countries, within their recommended actions for reducing the burden of sepsis globally.[4] Member states are urged to emphasise the impact of sepsis on public health, of which postdischarge mortality is a crucial aspect.[2] Thus, as the international community works towards achieving the WHA resolution and the third SDG, addressing the

burden of paediatric postdischarge mortality is of utmost importance.

A systematic literature review conducted in 2012 examined the burden of paediatric postdischarge mortality in resource-poor countries.[5] This systematic review found that the rate of paediatric postdischarge death is often as high as in-hospital mortality rates, with two-thirds of these deaths occurring outside the health system, usually at home. Common risk factors for postdischarge mortality included young age, malnutrition, HIV, pneumonia and recent prior admissions.

Despite the high burden of postdischarge death, this issue continues to receive insufficient recognition at either national or international levels. The lack of research and data highlighting the burden of postdischarge mortality relegates care following discharge as a low priority to policy makers. Additional studies published since the last systematic review contribute to the growing evidence base that can galvanise both researchers and policy makers to action.

The purpose of this systematic review, therefore, is to update the literature addressing the critical nature of paediatric postdischarge mortality in resource-poor settings, propelling research and interventions towards the goal of reduced child mortality.

METHODS

Objective and study eligibility criteria

The primary objective was to determine the risk factors and rates of mortality in children following discharge from hospitals in developing countries. Table 1 outlines the study inclusion eligibility, determined through the Population, Interventions, Comparisons, Outcomes and Study Design format.

Patient and public involvement

Patients and the public were not involved in the design or conduct of this study.

Search strategy

Articles published and indexed between 1 January 2012 and 18 July 2017 were identified using the MEDLINE and EMBASE databases within the OVID platform. The detailed search strategy for each database is outlined in online supplementary appendix 1. Studies conducted prior to 2012 were identified from a prior publication, using a similar search strategy.[5] Articles were included if the study was conducted in a developing country (defined as countries currently (2016) classified by the United Nations Development Programme as having a low Human Development Index plus those countries

Table 1 Population, Interventions, Comparisons, Outcomes and Study Design

Population	Paediatric patients discharged from hospitals in developing countries, as defined as those countries currently (2016) classified by the United Nations Development Programme as having a low Human Development Index plus those countries included previously (2011) as having a low Human Development Index.[6 7] Exclusion criteria: ► No paediatric data or paediatric data not differentiated from adult populations. ► No postdischarge information or patients not discharged from a hospital setting. ► Discharge was following a non-admission (eg, following birth). ► Studies representing a specific non-infectious disease population where postdischarge care and outcomes would likely be different than that following acute (primarily infectious) illness including: – Surgical population; – Specific congenital disease (cardiac, renal, etc); – Cancer; – Specific non-infectious admission including trauma, kidney disease, cardiac disease, ophthalmic disease, sickle cell disease, liver disease, epilepsy, burns, poisoning, asthma, etc. ► Study was unpublished, published only in abstract form or in a language other than English, or provided no original data.
Interventions	Studies may or may not include an interventional arm (ie, both arms of an RCT will be included).
Comparisons	NA
Outcomes	Primary outcome: ► Postdischarge mortality assessed >7 days following discharge. Secondary outcomes: ► In-hospital mortality; ► Risk factors for postdischarge mortality.
Study design	Eligible study designs include the following: ► Randomised controlled trials (RCTs); ► Prospective or retrospective cohort studies; ► Studies using surveillance data; ► Study designs which include a population discharged and then followed up (including case-control, mixed-methods).

NA, not applicable.

included previously (2011) as having a low Human Development Index[6 7]), included children admitted to hospital for medical reasons, and included follow-up to capture vital status during the postdischarge period.[5 6] Furthermore, references of all included articles were reviewed to identify other potentially eligible studies not captured in the systematic search.

Study selection and data extraction

Two investigators (BN, LE) independently screened articles during two rounds of review. The first round consisted of reviewing all abstracts for the presence of specific exclusion criteria. The second round of review consisted of a detailed review of remaining articles in full-text format. In both rounds, any discrepancies were resolved through discussion and consensus. A third investigator (MOW) provided arbitration for any discrepancies not resolved through consensus.

For eligible studies, the characteristics extracted included author, title and year of publication, year of study, country, study design, facility, population (diarrhoea, malaria, all admissions, etc), time of enrolment (admission or discharge), number of subjects, age, sex and study eligibility criteria. Outcomes extracted included total number of subjects who died both in-hospital and following discharge, timing and location of postdischarge deaths, follow-up method and losses to follow-up, number of postdischarge rehospitalisations and health seeking, timing of rehospitalisations and health seeking and risk factors for postdischarge mortality. When extracting data on risk factors, the results of multivariate analysis were preferentially extracted over univariate analyses.

Risk of bias

A formal risk of bias assessment, such as the Newcastle Ottawa Quality Assessment Scale for Cohort Studies, was not conducted since the primary outcome of the rate of postdischarge mortality was not exposure related among included studies. Primary factors leading to potential bias include the per cent follow-up as well as whether inclusion criteria were correctly applied to enrolled subjects, leading to a representative sample of the population. While the former was included in the outcome characteristics, the latter was not defined in any study. Thus, proportion of children successfully followed remains the primary indicator of risk of bias.

Data analysis and outcomes

Microsoft Excel (Redmond, Washington, USA) was used to compile extracted data. Due to varying populations, risk factors, definitions and types of results (eg, OR, HR), a formal meta-analysis was not deemed possible. Therefore, the analysis was descriptive in nature. The primary outcome was the proportion of discharged subjects who died during the postdischarge period. Secondary outcomes included the proportion of total deaths (in-hospital and postdischarge), which occurred following discharge, as well as risk factors associated with postdischarge mortality. Given that several distinct populations were evaluated, results were reported according to the underlying study population. Studies were grouped according to five underlying populations: (1) all admissions including those for infectious diseases, (2) malnutrition, (3) respiratory infection, (4) diarrhoeal diseases and (5) malaria/anaemia.

RESULTS

Summary of included articles

A total of 1238 articles were identified through the systematic searches, with two additional articles identified independently. Of these, 1174 were excluded at the abstract stage and a further 55 were excluded during the full-text screening stage, resulting in 11 eligible studies (figure 1, online supplementary appendix 2). These 11 studies were added to the 13 studies identified prior to 2012 through a similar systematic search,[5] resulting in a total of 24 included studies (table 2). Studies were grouped according to underlying population. Three studies examined either all admissions or all infectious admissions, five examined malnutrition, seven respiratory infection, three diarrhoeal diseases and six included children with malaria and/or anaemia. Seven randomised controlled trials, 12 prospective cohorts, 2 retrospective cohorts and 3 case-control studies were included. Two studies examined those admitted to a health centre, whereas the remaining 22 were conducted at various types and levels of hospitals. All studies were performed in a single country, and Bangladesh was the only non-African country in which included studies were conducted.

All admissions, including unspecified infectious admissions

The three studies within this population were conducted between 1991 and 2013 in Guinea-Bissau, Kenya and Uganda, and enrolled between 1307 and 10 277 subjects (table 2).[8–10] Follow-up periods ranged from 6 months to 1 year, with postdischarge mortality ranging from 4.9% to 8% (table 3). Two studies reported postdischarge readmission, measured rates between 16.5% and 17.7%.[9–11] Inpatient mortality was recorded by two studies, finding rates of 4.9% and 15%.[8 10] These same studies recorded that most postdischarge deaths (67% and 77%) occurred outside of the hospital setting. The majority of postdischarge deaths occurred relatively early in the follow-up period, with 63% occurring within 13 (of 52) weeks in one study and 50% within 8 (of 24) weeks in the other study.[8 10] Several variables were included in risk factor analyses for postdischarge mortality (table 4). Increasing age was shown to be a protective factor in all three studies. Parasitaemia was found to be associated with lower PDM compared with other diagnoses in two studies, with the third study showing lower PDM compared with diarrhoea, anaemia and other less common diagnoses. Bacteraemia, severe or very severe pneumonia, severe malnutrition, meningitis and HIV were all associated with a higher probability of postdischarge death.[9 10] In the study by Veirum *et*

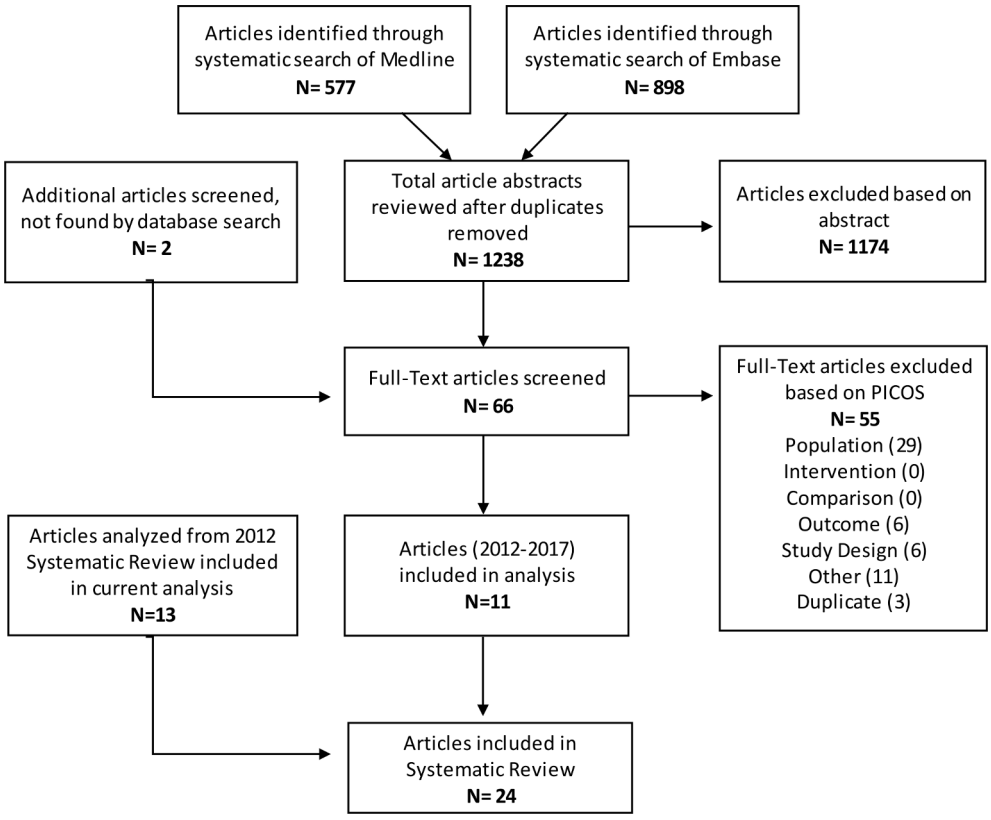

Figure 1 Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow diagram.

al that evaluated discharge against medical advice (AMA), those who left AMA were eight times more likely to die after discharge.[8] Anthropometric factors (including mid-upper arm circumference (MUAC), weight-for-age, weight-for-height and height-for-age z-scores), hypoxia, respiratory rate, jaundice, hepatomegaly and Blantyre coma scale rating were all associated with a statistically significant increase in the probability of PDM.[9 10] Those who had been hospitalised prior to the index admission were also at increased risk for death, with each additional hospitalisation compounding the risk.[9 10]

Malnutrition

Five studies focusing on a malnourished population were identified. These studies were conducted in the Democratic Republic of the Congo, Malawi, Bangladesh, Kenya and Uganda between 1970 and 2015 and and enrolled between 171 and 1778 children (table 2). The period of follow-up varied widely in this subpopulation, ranging from 8 weeks to 5 years (table 3). Postdischarge mortality rates were observed to be between 1.8% and 24%. Where hospital mortality rates were measured (n=2), mortality following discharge was comparable to that observed during hospital admission, with one study reporting an inpatient mortality rate of 23.2% (24% after discharge), and a second study of 8.6% (8.7% after discharge).[12 13] Three of four studies specified the timing of deaths during the follow-up period with all finding that the majority of deaths following discharge occurred early during the follow-up period (relative to total follow-up). In one study, 59% of those who died after discharge did so within 52 weeks (of 5 years),[14] another found that 44% died within 13 (of 52) weeks,[12] and the third study observed 88% dying within 9 (of 26) weeks of discharge.[13] A study conducted in Bangladesh reporting the location of postdischarge death found that 80% of deaths occurred at home, while another conducted in Kenya found 53% occurring in the community.[13 15] Anthropometric parameters including MUAC, weight-for-age and weight-for-height z-scores were among the highly significant predictors for death postdischarge (table 5).[12 13] Age <12 months was associated with mortality in one study, but was found not to be significant in another, although wide CIs could not rule out an important effect.[12 13] Highly significant associations variables included positive HIV status (HR 4.03; 95% CI 3.08 to 5.25), unknown HIV status (HR 16.90; 95% CI 12.10 to 23.70) and discharge AMA (HR 4.68; 95% CI 2.01 to 10.85).

Respiratory infection

Seven studies examining respiratory infections were identified. These included children with a variety of inclusion criteria, including pneumonia, acute lower respiratory tract infection and tuberculosis. Studies were conducted between 1992 and 2014 in the Gambia, Tanzania, Bangladesh, Malawi and Kenya (table 2). Mortality rates postdischarge ranged widely, from 1.3% to 35% across the studies. These rates, however, remained consistently comparable to inpatient mortality when both were measured (table 3). As with other populations, mortality

Table 2 Study characteristics

Author ID	Years of study	Country	Design	Facility type	Population	Number of subjects	Age range	Age estimate and dispersion (months): mean (SD) or median (IQR)	Female proportion (%)
All admissions/unspecified infectious admissions									
Veirum *et al*[8]	January 1991–December 1996	Guinea-Bissau	Prospective cohort	National Referral Hospital	All admissions	3373	<6 y		
Moisi *et al*[9]	January 2004–December 2008	Kenya	Retrospective cohort	District Hospital	All admissions	10277	<15 y		
Wiens *et al*[10]	March 2012–December 2013	Uganda	Prospective cohort	Regional Referral Hospital	Proven or suspected infection	1307	6 m-5 y	18.10 (10.8–34.6)	45.1
Malnutrition									
Hennart *et al*[14]	1970	Democratic Republic of the Congo (Zaire)	Prospective cohort	Hospital	Severe protein-energy malnutrition	171	0–6+ y	Mean=46	
Kerac *et al*[12]	July 2006–March 2007	Malawi	Prospective cohort	National Referral Hospital	Malnutrition	1024	5–168 m	21.5 (15.0–32.0)	47
Chisti *et al*[13]	April 2011–June 2012	Bangladesh	Prospective cohort	Hospital	Severe malnutrition and radiological pneumonia	405	0–59 m	10 (5–18)	44.2
Berkley *et al*[15]	November 2009–March 2013	Kenya	RCT	Hospital	Severe acute malnutrition—cotrimoxazole	887	2–59 m	11.2 (7.2–16.7)	50%
					Severe acute malnutrition—placebo	891		10.8 (6.9–16.7)	48%
Grenov *et al*[32]	March 2014–October 2015	Uganda	RCT	National Referral Hospital	Severe acute malnutrition—probiotics	200	6–59 m	17.5 (8.5)	42.5
					Severe acute malnutrition—placebo	200		16.5 (8.4)	42.5
Respiratory Infection									
West *et al*[33]	May 1992–November 1994	The Gambia	Case-control	Hospital	Acute lower respiratory tract infection	118	<5 y	Mean=9.7	43.2
Villamor *et al*[17]	1993–1997	Tanzania	Prospective cohort	Hospital	Pneumonia	687	6–60 m	17.6 (12.1)	45.8
Ashraf *et al*[34]	September 2006–November 2008	Bangladesh	Prospective cohort	Hospital	Severe pneumonia	180	2–59 m	7.3 (6.8)	34.4
Reddy *et al*[35]	November 2008–July 2009	Tanzania	RCT	Regional Referral Hospital	Tuberculosis—standard diagnostics	10	<6 y	21 (5–47)	70
					Tuberculosis—intensified diagnostics	13		10.5 (6.0–18.0)	38.5
Chhibber *et al*[16]	May 2008–May 2012	The Gambia	Prospective cohort	Health Centre	Pneumonia, sepsis or meningitis	3952	2–59 m		
Ngari *et al*[18]	January 2007–December 2012	Kenya	Prospective cohort	District Hospital	Severe pneumonia	2461	1–59 m	9.3 (3.9–20.4)	43.2
					No pneumonia	5270		19.5 (11.0–28.5)	43.6

Continued

Table 2 Continued

Author ID	Years of study	Country	Design	Facility type	Population	Number of subjects	Age range	Age estimate and dispersion (months): mean (SD) or median (IQR)	Female proportion (%)
Newberry *et al*[36]	April 2012–August 2014	Malawi	RCT	Hospital	Pneumocystis jirovecii pneumonia (PJP)—intervention (corticosteroids)	36	2–6 m	3.1 (2.7–3.9)	66.7
					PJP—placebo	42		3.4 (2.9–4.4)	50
Diarrhoea									
Roy *et al*[19]	1979–1980	Bangladesh	Prospective cohort	Health Centre	Diarrhoea	551	3–36 m		
Stanton *et al*[37]	October 1983–December 1983	Bangladesh	Retrospective cohort	Hospital	Diarrhoea	112	24–72 m		27
Islam *et al*[20]	November 1991–December 1992	Bangladesh	Prospective cohort	Hospital	Diarrhoea	427	1–23 m		39.1
Anaemia/Malaria									
Zucker *et al*[24]	March 1991–September 1991	Kenya	Case-control	District Hospital	Anaemia (case)	293	<60 m	9.8 (8.6)	50
					No anaemia (control)	291		13.5 (11.3)	50
Biai *et al*[21]	December 2004–January 2006	Guinea-Bissau	RCT	National Referral Hospital	Malaria—intervention	460	3–60 m	24 (13–36)	45.4
					Malaria—no intervention	491		24 (14–39)	43
Phiri *et al*[25]	July 2002–July 2004	Malawi	Longitudinal case-control	Hospital	Severe anaemia	377	6–60 m	20.4 (12.8)	53.6
					No anaemia	377		22.5 (12.1)	47.7
Phiri *et al*[23]	June 2006– August 2009	Malawi	RCT	Hospital	Severe malarial anaemia	1414	4–59 m	23.9 (13.4)	51.6
Olupot-Olupot *et al*[26]	2014	Uganda	RCT	Hospital	Severe anaemia—higher blood transfusion volume (30 mL/kg)	78	60 d–12 y	31 (11–48)	51
					Severe anaemia—standard blood transfusion volume (20 mL/kg)	82		36 (19–54)	50
Opoka *et al*[22]	November 2008–October 2013	Uganda	Prospective cohort	National Referral Hospital	Cerebral malaria	269	18 m–12 y	3.9 (2.7–6.0)	35.2
					Severe malarial anaemia	233		2.8 (2.1–3.9)	39.9

d, day; m, month; RCT, randomised controlled trial; y, year.

Table 3 Outcome characteristics

Author ID	Intervention/Exposure	IPM (%)*	Follow-up times	Loss to follow-up (%)*	PD rehospitalised (%)*	PDM (%)*	Place of PD death	PDM statistics†
All admissions/unspecified infectious admissions								
Veirum *et al*[8]		15	Days 1, 14, 30, 91, 182, 365	–		8	77% at home 23% in hospital	63% at 13 w
Moisi *et al*[9]		–	1 year	–	17.7	5.2		
Wiens *et al*[10]		4.9	2, 4, 6 months	1.7	16.5	4.9	67% out of hospital 33% in hospital	50% at 4 w
Malnutrition								
Hennart *et al*[14]		–	Every year for 5 years	–		15.9		59% at 52 w
Kerac *et al*[12]		23.2	90 days and 1 year	17.2	6.62	24.0		44% at 13 w
Chisti *et al*[13]		8.6	Weekly for 2 weeks then monthly until 6 months	15.0		8.7	80% at home 16% in hospital 4% on transport	59% at 4 w 88% at 9 w
Berkley *et al*[15]	Oral cotrimoxazole prophylaxis	3.4	Once per month until 6 months, then once every 2 months until 12 months	5.3	296 non-fatal admissions	11.1	(32%) in readmission to a study hospital (15%) in other hospitals (53%) in the community	
	Placebo			5.1	320 non-fatal admissions			
Grenov *et al*[32]	Probiotics	11.5	At 8–12 weeks	10.4		1.8		
	Placebo	8.0		7.9		2.4		
Respiratory infection								
West *et al*[33]	Hypoxaemia	–	Mean length of follow-up 41 months	36.1		9.6		
	Non-hypoxaemic	–	Mean length of follow-up 34.1 months	39.3		3.7		
Villamor *et al*[17]		3.1	Every 2 weeks for a year then every 4 months Mean duration of follow-up 24.7 months (SD=12.3, median=28.2)	11.4		10.4		80% by 52 w
Ashraf *et al*[34]		0	Every 2 weeks for 3 months	6.4	6.4	1.7		
Reddy *et al*[35]	Standard and intensified diagnostic arms analysed together	–	2 and 8 weeks post-enrolment	–		17.4		50% at 2 w 'postenrolment deaths'; IP or PD not specified
Chhibber *et al*[16]		3.9	180 days	–		2.8		55% at 6 w
Ngari *et al*[18]	Pneumonia	5.6	Every 4 months until 1 year	1.9		3.1	37% in hospital	44% at 13 w 74% at 26 w
	No pneumonia	2.4		0.9		1.3		
Newberry *et al*[36]	Corticosteroids	27.8	1, 3, 6 months	11.5		19.2		
	Placebo	52.4		10.0		35.0		
Diarrhoeal diseases								
Roy *et al*[19]		–	Monthly for 12 months	–		4		52% at 4 w 70% at 9 w
Stanton *et al*[37]		1.8	At 4–5 months	6.8		2.9		

Continued

Table 3 Continued

Author ID	Intervention/Exposure	IPM (%)*	Follow-up times	Loss to follow-up (%)*	PD rehospitalised (%)*	PDM (%)*	Place of PD death	PDM statistics†
Islam *et al*[20]		14.6	At 6 and 12 weeks	–		7.5		94% at 6 w
Anaemia/Malaria								
Zucker *et al*[24]	Anaemia	13	4 and 8 weeks	4.0		18.8		
	No anaemia; figures include the analysed 'no-anaemia cohort' from study plus additional children	9		4.0		10.3		
Biai *et al*[21]	Intervention: improved management and free emergency drugs for malaria, financial incentive	4.6	28 days	3.9		1.8		
	Control	9.4		4.9		0.9		
Phiri *et al*[25]	Severe anaemia	6.4	1, 3, 6, 12, 18 months	17.8	18.1	11.6		71% at 26 w
	No anaemia	0		19.6	9.3	2.7		60% at 26 w
Phiri *et al*[23]	Artemether–lumefantrine	–	1, 3, 6 months	5.0	21.5	2.5		50% at 4 w
	Placebo	–		4.9	24.4	2.3		50% at 9 w
Olupot-Olupot *et al*[26]	Severe anaemia—higher blood transfusion volume (30 mL/kg)	0	28 days postadmission	0		1.3		
	Severe anaemia—standard blood transfusion volume (20 mL/kg)	7.3		0		0		
Opoka *et al*[22]	Cerebral malaria	12.6	6 months	2.5	3.1	0.6		
	Severe malarial anaemia	0.4		3.6	9.4	2.2		

*Indicates cumulative rates as of the last follow-up time.
†Indicates specified mortality statistics in regard to per cent of total postdischarges by a certain number of weeks, in relation to entire duration of follow-up.
IP, inpatient; IPM, inpatient mortality; PD, postdischarge; PDM, postdischarge mortality; w,week.

Table 4 Risk factors for PDM in all admissions/unspecified infectious admission studies

Article	Risk factor category	Mortality risk factor on admission	Estimate type	Estimate (95% CI)	Adjusted
Veirum *et al*[8]	Age	Age at discharge>5 years (ref: age 1–12 months)	RR	**0.15 (0.07 to 0.30)**	Yes
		Age at discharge 4 years (ref: age 1–12 months)	RR	**0.23 (0.10 to 0.59)**	Yes
		Age at discharge 3 years (ref: age 1–12 months)	RR	**0.14 (0.06 to 0.35)**	Yes
		Age at discharge 2 years (ref: age 1–12 months)	RR	**0.52 (0.33 to 0.81)**	Yes
		Age at discharge 1 year (ref: age 1–12 months)	RR	0.82 (0.59 to 1.13)	Yes
		Neonatal (ref: age 1–12 months)	RR	0.69 (0.31 to 1.55)	Yes
	Diagnosis	Diagnosis: other—includes chronic diseases which cannot be treated in Bissau (ref: malaria)	RR	**1.65 (1.08 to 2.55)**	Yes
		Anaemia (ref: malaria)	RR	**1.97 (1.07 to 3.63)**	Yes
		Diarrhoea (ref: malaria)	RR	**1.82 (1.21 to 2.74)**	Yes
		Bronchopneumonia (ref: malaria)	RR	0.98 (0.65 to 1.51)	Yes
		Measles (ref: malaria)	RR	0.77 (0.36 to 1.64)	Yes
	Hospital stay	Leaving against medical advice	RR	**8.51 (5.32 to 13.59)**	Yes
	Maternal influence	Mother educated (ref: no maternal education)	RR	**0.74 (0.55 to 0.99)**	Yes
Moisi *et al*[9]	Age	Age 1–5 months	HR	1.34 (0.93 to 1.92)	Yes
		Age 6–11 months	HR	0.82 (0.57 to 1.18)	Yes
		Age 2–5 years	HR	**0.57 (0.36 to 0.90)**	Yes
		Sick young infant	HR	**2.67 (1.98 to 3.58)**	Yes
	Diagnosis	Parasitaemia	HR	**0.45 (0.29 to 0.71)**	Yes
		Bacteraemia	HR	**1.77 (1.15 to 2.74)**	Yes
		Mild pneumonia	HR	2.30 (1.00 to 5.28)	Yes
		Severe pneumonia	HR	**1.37 (1.05 to 1.79)**	Yes
		Very severe pneumonia	HR	**4.09 (2.25 to 7.46)**	Yes
		Severe malnutrition	HR	**4.37 (2.73 to 7.01)**	Yes
		Meningitis	HR	**2.29 (1.57 to 3.32)**	Yes
	Growth parameters	WAZ < −3	HR	**3.42 (2.50 to 4.68)**	Yes
		WAZ < −4	HR	**6.53 (4.85 to 8.80)**	Yes
	Hospital stay	Hospitalisation>13 days	HR	**1.83 (1.33 to 2.52)**	Yes
		One prior discharge (occurring within 1 year of index discharge)	HR	**2.83 (2.04 to 3.92)**	Yes
		Two prior discharges	HR	**7.06 (4.09 to 12.21)**	Yes
		≥3 prior discharges	HR	**23.55 (10.70 to 51.84)**	Yes
	Symptoms	Hypoxia	HR	**2.30 (1.64 to 3.23)**	Yes
		Jaundice	HR	**1.77 (1.08 to 2.91)**	Yes
		Hepatomegaly	HR	**2.34 (1.60 to 3.24)**	Yes

Continued

Table 4 Continued

Article	Risk factor category	Mortality risk factor on admission	Estimate type	Estimate (95% CI)	Adjusted
Wiens *et al*[10] 2015	Age	Age (months)	OR	**0.97 (0.97 to 0.97)**	No
	Comorbid conditions	HIV positive	OR	**5.21 (2.55 to 10.65)**	No
	Growth parameters	MUAC (mm)	OR	**0.97 (0.96 to 0.98)**	No
		Weight-for-age z-score	OR	**0.66 (0.57 to 0.76)**	No
		Weight for length/height z-score	OR	**0.81 (0.72 to 0.91)**	No
		Length/height-for-age z-score	OR	**0.79 (0.70 to 0.89)**	No
	Hospital stay	Illness>7 days prior to admission	OR	**0.50 (0.30 to 0.83)**	No
		Time since last hospitalisation (ordered as <7 days, 7–30 days, 30 days to 1 year, >1 year and never (analysed as continuous and coded as 1–5, respectively)	OR	**0.75 (0.62 to 0.90)**	No
	Labs/Assessments	Haemoglobin (g/dL)	OR	0.95 (0.87 to 1.03)	No
		Blantyre coma scale<5 (ref: 5)	OR	**2.40 (1.27 to 4.57)**	No
		Positive blood smear	OR	**0.33 (0.16 to 0.68)**	No
	Maternal influence	Maternal age (years)	OR	1.00 (0.97 to 1.04)	No
		Maternal HIV positive (ref: HIV negative)	OR	1.79 (0.87 to 3.67)	No
		Maternal HIV status unknown (ref: HIV negative)	OR	1.27 (0.64 to 2.52)	No
		Maternal education primary 3–7 (ref: maternal education<P3)	OR	1.18 (0.62 to 2.23)	No
		Maternal education some secondary (ref: maternal education<P3)	OR	0.72 (0.31 to 1.70)	No
		Maternal education postsecondary (ref: maternal education<P3)	OR	1.18 (0.41 to 3.36)	No
	Sex	Male	OR	0.90 (0.54 to 1.51)	No
	Social determinants of health	Bed net use—sometimes (ref: never)	OR	1.00 (0.48 to 2.09)	No
		Bed net use—always (ref: never)	OR	0.85 (0.46 to 1.58)	No
		Siblings death	OR	1.54 (0.89 to 2.65)	No
		Number of children in the family	OR	1.02 (0.92 to 1.13)	No
		Boil all drinking water	OR	0.82 (0.47 to 1.42)	No
		Distance from hospital 30–60 min (ref: distance<30 min)	OR	0.71 (0.31 1.64)	No
		Distance from hospital>60 min (ref: distance<30 min)	OR	1.30 (0.70 to 2.41)	No

Continued

Table 4 Continued

Article	Risk factor category	Mortality risk factor on admission	Estimate type	Estimate (95% CI)	Adjusted
	Vital signs	HR for age z-score	OR	**0.86 (0.74 to 0.99)**	No
		HR (raw)	OR	1.00 (0.99 to 1.01)	No
		RR for age z-score	OR	0.99 (0.92 to 1.06)	No
		RR (raw)	OR	1.01 (1.00 to 1.03)	No
		SBP z-score	OR	0.94 (0.79 to 1.12)	No
		SBP (raw)	OR	0.98 (0.96 to 1.00)	No
		DBP (raw)	OR	0.99 (0.97 to 1.01)	No
		Temperature (transformed)	OR	1.02 (0.90 to 1.16)	No
		Temperature (raw)	OR	**0.76 (0.62 to 0.93)**	No
		SpO_2 (raw)	OR	**0.94 (0.92 to 0.96)**	No
		SpO_2 (transformed)	OR	**1.04 (1.02 to 1.05)**	No

Bolded values are statistically significant.
DBP, diastolic blood pressure; PDM, postdischarge mortality; RR, relative risk; SBP, systolic blood pressure; WAZ, weight for age z-score.

rates generally occurred early during follow-up. A large prospective cohort study by Ngari *et al* including children aged 1–59 months with severe pneumonia found that 74% of postdischarge deaths occurred by 26 (of 52) weeks with 63% occurring outside of the hospital. Chhibber *et al*[16] conducted a study of 3952 children admitted primarily with pneumonia in rural Gambia, and sought to identify specific comorbidities and physiologic factors predictive of mortality after discharge. This study found that physiologic factors, including neck stiffness, oxygen saturation, temperature and haemoglobin concentration were associated with postdischarge mortality. Malnutrition-related variables (clinical malnutrition and low MUAC) were the strongest predictors of postdischarge mortality, producing HRs ranging from 18.4 to 43.7 (table 6). Although individual studies differed in regard to whether risk factors were measured continuously, categorically or dichotomously, it is clear that the directionality of certain risk factors such as low haemoglobin and low MUAC continue to be associated with higher PDM in children admitted for respiratory illness.[16–18] When examining the timing of mortality, most cases occurred relatively early during follow-up. One study found that 80% had occurred by 12 months (mean duration of follow-up 24.7 months),[17] another study had 55% by 6 (of 26) weeks[16] and yet another reported 74% by 26 (of 52) weeks.[18] Low MUAC, stunting, HIV-positive status, jaundice, low haemoglobin, under 24 months of age and availability of water were significant predictors of postdischarge mortality among children with respiratory illness.[17 18]

Diarrhoeal diseases

Three studies of paediatric patients with diarrhoea conducted between 1979 and 1992 were included, all three of which were conducted in Bangladesh (table 2). Included studies enrolled children aged 1–72 months and found postdischarge death rates of between 2% and 8%, all being generally comparable to in-hospital rates (table 3). Deaths occurred within the first few weeks after discharge, with one study reporting 52% by 4 (of 52) weeks,[19] and a second reporting 94% of deaths occurring by 6 (of 12) weeks postdischarge.[20] Significant risk factors for death after discharge identified in this set of studies included young age (<6 months), not having been breast fed, malnutrition (based on Height for age z-score (HAZ) and WAZ scores), low levels of maternal education and immunisation status of the child (table 7).

Anaemia and/or malaria

Six studies were conducted between 1991 and 2014 in Kenya, Guinea-Bissau, Malawi and Uganda in children with anaemia and/or malaria (table 2). Studies were heterogeneous in their specified populations, including children with various illness severity, with mortality postdischarge ranging from 0.9% to 18.8%, and with follow-up periods ranging from 1 to 18 months (table 3). In the only study looking

Table 5 Risk factors for PDM in malnutrition studies

Article	Risk factor category	Mortality risk factor on admission	Estimate type	Estimate (95% CI)	Adjusted
Hennart *et al*[14]	No data				
Kerac *et al*[12]	Age	Age>60 m (ref: age 48–60 m)	HR	1.22 (0.63 to 2.36)	Yes
		Age 36–48 m (ref: age 48–60 m)	HR	1.66 (0.84 to 3.29)	Yes
		Age 24–36 m (ref: age 48–60 m)	HR	1.38 (0.76 to 2.49)	Yes
		Age 12–24 m (ref: age 48–60 m)	HR	1.57 (0.89 to 2.78)	Yes
		Age<12 m (ref: age 48–60 m)	HR	**2.49 (1.38 to 4.51)**	Yes
	Comorbid conditions	HIV positive (ref: HIV negative)	HR	**4.03 (3.08 to 5.25)**	Yes
		HIV unknown status (ref: HIV negative)	HR	**16.90 (12.10 to 23.70)**	Yes
	Growth parameters	Oedema	HR	**0.58 (0.47 to 0.72)**	Yes
		MUAC per cm unit increase	HR	**0.80 (0.74 to 0.86)**	Yes
		Weight-for-height: per 1 unit z-score increase	HR	**0.75 (0.68 to 0.83)**	Yes
		Weight-for-age: per 1 unit z-score increase	HR	**0.73 (0.66 to 0.81)**	Yes
		Height-for-age: per 1 unit z-score increase	HR	**0.92 (0.86 to 0.99)**	Yes
	Sex	Male	HR	0.89 (0.73 to 1.08)	Yes
Chisti *et al*[13]	Age	Age<12 m	OR	2.05 (0.90 to 4.90)	No
	Comorbid conditions	Confirmed TB	OR	1.74 (0.40 to 6.90)	No
		Clinical TB—not confirmed	OR	0.15 (0.01 to 1.10)	No
		History of previous pneumonia prior to present episode	OR	**3.4 (1.1 to 10.2)**	No
	Growth parameters	Severe wasting* (z-score <–4 weight-for-height/length)	OR	**3.4 (1.5 to 7.8)**	No
		Severe underweight* (z-score <–5 weight-for-age)	OR	**3.05 (1.4 to 6.8)**	No
		Severe wasting (z-score <–4 weight-for-height/length)	OR	**2.74 (1.2 to 6.2)**	No
		Severe underweight (z-score <–5 weight-for-age)	OR	**2.82 (1.2 to 6.7)**	No
		Nutritional oedema	OR	2.34 (0.5 to 9.6)	No
	Hospital stay	Left against medical advice*	OR	**4.16 (1.5 to 11.3)**	No
	Sex	Male	OR	0.68 (0.3 to 1.5)	No
	Social determinants of health	Live outside Dhaka district	OR	1.69 (0.7 to 4)	No
		Poor socioeconomic condition–income<US$125 per month	OR	0.73 (0.3 to 2)	No
	Symptoms	Lower chest wall in-drawing	OR	0.86 (0.4 to 1.9)	No
		Hypoxaemia (arterial oxygen saturation<90% in room air)	OR	1.23 (0.3 to 4.7)	No
Berkley *et al*[15]	Intervention	Cotrimoxazole vs placebo	HR	**0.90 (0.71 to 1.16)**	No
Grenov *et al*[32]		No data			

Bolded values are statistically significant.
*Risk factor for mortality assessed on discharge.
m, month; PDM, postdischarge mortality; TB, tuberculosis.

specifically at acute malaria, postdischarge mortality (1.8% intervention; 0.9%% control) was lower than inpatient mortality (4.6% intervention; 9.4% control) over a follow-up period of 28 days.[21] Another study that followed children with cerebral malaria or severe malarial anaemia for 6 months following discharge reported that although children with cerebral malaria experienced higher inpatient mortality (13% compared with 0.4%), those with severe malarial anaemia had a higher rate of death after discharge (2.2% compared with 0.6%).[22] A large study (n=1414) by Phiri *et al* examining severe malarial anaemia found high rates of postdischarge readmission (approximately 22%), with rates of death at approximately

Table 6 Risk factors for PDM in respiratory infection studies

Article	Risk factor category	Mortality risk factor on admission	Estimate type	Estimate (95% CI)	Adjusted
West *et al*[33]	No data				
Villamor *et al*[17]	Age	Age 6–11 m (ref: >24 m)	HR	**3.70 (1.72 to 7.95)**	Yes
		Age 12–23 m (ref: >24 m)	HR	**3.14 (1.44 to 6.88)**	Yes
	Comorbid conditions	HIV positive	HR	**3.92 (2.34 to 6.55)**	Yes
	Diagnosis	Severe pneumonia on admission	HR	**2.47 (1.59 to 3.85)**	Yes
	Growth parameters	Stunted at baseline (2 z-scores (NCHS/WHO reference) in height-for-age Wasted children were 2 z-scores in weight-for-height)	HR	**2.12 (1.31 to 3.42)**	Yes
		Low MUAC at baseline (25th percentile of the population age-specific distribution)	HR	**1.88 (1.16 to 3.03)**	Yes
	Labs/Assessments	Haemoglobin (Hgb) concentration<7.00 (g/dL) (ref: Hgb concentration>10 g/dL)	HR	**2.55 (1.13 to 5.77)**	Yes
		Hgb concentration 7.01–8.50 g/dL (ref: Hgb concentration>10 g/dL)	HR	**2.81 (1.24 to 6.37)**	Yes
		Hgb concentration 8.51–10.00 g/dL (ref: Hgb concentration>10 g/dL)	HR	1.76 (0.75 to 4.10)	Yes
	Maternal influence	Maternal education—elementary (ref: no maternal education)	HR	0.84 (0.48 to 1.49)	Yes
		Maternal education—secondary or higher (ref: no maternal education)	HR	0.27 (0.06 to 1.17)	Yes
		Mother works outside home	HR	0.61 (0.36 to 1.03)	Yes
		Mother not living with partner	HR	1.60 (1.00 to 2.57)	Yes
	Sex	Male	HR	0.98 (0.65 to 1.48)	Yes
	Social determinants of health	Water tap in compound (ref: water tap in house)	HR	1.40 (0.60 to 3.29)	Yes
		Water tap outside compound (ref: water tap in house)	HR	**2.27 (1.02 to 5.03)**	Yes
		Public well (ref: water tap in house)	HR	**2.92 (1.03 to 8.30)**	Yes
Ashraf *et al*[34]	No data				
Reddy *et al*[35]	Intervention	Not receiving anti-TB medication (predictor of death within 2 weeks of admission)	OR	**0.25 (0.03 to 2.00)**	No
		Not receiving anti-TB medication (predictor of death within 8 weeks of admission)	OR	**0.20 (0.04 to 0.96)**	No
Chhibber *et al*[16]	Age	Age (m)	HR	1.00 (0.98 to 1.03)	Yes
	Comorbid conditions	Sepsis with clinically severe malnutrition (CSM); (ref: pneumonia without CSM)	HR	**18.4 (11.3 to 30.0)**	Yes
		Meningitis with CSM (ref: pneumonia without CSM)	HR	**13.7 (4.2 to 44.7)**	Yes
		Pneumonia with CSM (ref: pneumonia without CSM)	HR	**8.1 (4.4 to 14.8)**	Yes
		Meningitis without CSM (ref: pneumonia without CSM)	HR	**2.6 (1.2 to 5.5)**	Yes
		Sepsis without CSM (ref: pneumonia without CSM)	HR	**2.2 (1.1 to 4.3)**	Yes
	Growth parameters	MUAC 11.5–13.0 cm (ref: MUAC>13 cm)	HR	**7.19 (3.04 to 17.01)**	Yes
		MUAC 10.5–11.4 cm (ref: MUAC>13 cm)	HR	**24.2 (9.4 to 61.9)**	Yes
		MUAC<10.5 cm (ref: MUAC>13 cm)	HR	**43.7 (17.7 to 108.0)**	Yes
	Hospital stay	Non-medical discharge	HR	**4.68 (2.01 to 10.85)**	Yes
	Labs/Assessments	Hgb concentration (g/dL)	HR	**0.82 (0.73 to 0.91)**	Yes

Continued

Table 6 Continued

Article	Risk factor category	Mortality risk factor on admission	Estimate type	Estimate (95% CI)	Adjusted
	Social determinants of health	Dry season	HR	**1.96 (1.16 to 3.32)**	Yes
	Sym	Neck stiffness	HR	**10.4 (3.1 to 34.8)**	Yes
	Vital signs	Axillary temperature (°C)	HR	**0.71 (0.58 to 0.87)**	Yes
		SpO_2 (%)	HR	**0.96 (0.93 to 0.99)**	Yes
Ngari *et al*[18]	Age	Age 12–23 m (ref: age>24 m)	HR	1.0 (0.1 to 9.6)	Yes
		Age 6–11 m (ref: age>24 m)	HR	5.8 (0.8 to 40.5)	Yes
		Age<6 m (ref: age>24 m)	HR	4.8 (0.7 to 34.1)	Yes
	Comorbid conditions	Reported preterm/low birth weight	HR	0.7 (0.2 to 2.8)	Yes
		HIV antibody test positive	HR	**6.5 (2.3 to 18.4)**	Yes
		HIV test not performed	HR	0.4 (0.1 to 3.6)	Yes
		RSV test positive	HR	0.3 (0.1 to 1.2)	Yes
		RSV test not performed	HR	**2.7 (1.2 to 6.3)**	Yes
		Malaria slide positive	HR	0.5 (0.1 to 5.2)	Yes
		Bacteraemia	HR	0.8 (0.1 to 5.2)	Yes
	Growth parameters	MUAC per cm	HR	**0.6 (0.5 to 0.8)**	Yes
	Hospital stay	Duration of hospitalisation (per day)	HR	1.1 (1.0 to 1.2)	Yes
	Hospital stay	Year of admission 2008 (ref: 2007 admission year)	HR	0.9 (0.3 to 3.1)	Yes
		Year of admission 2009 (ref: 2007 admission year)	HR	0.5 (0.1 to 2.1)	Yes
		Year of admission 2010 (ref: 2007 admission year)	HR	0.7 (0.2 to 2.5)	Yes
		Year of admission 2011 (ref: 2007 admission year)	HR	1.7 (0.5 to 5.3)	Yes
		Year of admission 2012 (ref: 2007 admission year)	HR	1.8 (0.2 to 15.7)	Yes
	Labs/Assessments	Severe anaemia (Hgb<5 g/dL)	HR	0.8 (0.1 to 7.5)	Yes
	Sex	Female	HR	0.5 (0.3 to 1.1)	Yes
	Social determinants of health	Residence distance from hospital (per km)	HR	1.0 (0.9 to 1.1)	Yes
	Symptoms	Capillary refill>2 s	HR	2.4 (0.5 to 12.1)	Yes
		Impaired consciousness	HR	1.1 (0.2 to 7.8)	Yes
		Wheezing	HR	0.5 (0.1 to 2.4)	Yes
		Cough for>14 days	HR	0.2 (0.1 to 5.5)	Yes
		Jaundice	HR	**12.5 (1.1 to 13.7)**	Yes
	Vital signs	Hypoxia (SaO_2<90%)	HR	1.9 (0.7 to 5.4)	Yes
		Axillary temperature<36°C (ref: axillary temperature 36°C–39°C)	HR	0.3 (0.1 to 2.8)	Yes
		Axillary temperature>39°C (ref: axillary temperature 36°C–39°C)	HR	1.1 (0.4 to 3.0)	Yes
Newberry *et al*[36]	Intervention	Prednisone (ref: placebo)	RR	**0.63 (0.41 to 0.95)**	

Bolded values are statistically significant.
m, month; NCHS, National Center for Health Statistics; PDM, postdischarge mortality; RR, relative risk; TB, tuberculosis.

Table 7 Risk factors for PDM in diarrhoea studies

Article	Risk factor category	Mortality risk factor on admission	Estimate type	Estimate (95% CI)	Adjusted
Roy *et al*[19]	No data				
Stanton *et al*[37]	No data				
Islam *et al* [20]	Age	Age<6 months	RR	**4.57 (2.90 to 7.18)**	Yes
	Growth parameters	Weight-for-age median<60%	RR	1.04 (0.57 to 1.89)	Yes
		Length-for-age median<85%	RR	**2.97 (1.43 to 6.16)**	Yes
	Maternal influence	Mother's education (no school vs >1 year)	RR	**2.12 (1.37 to 3.28)**	Yes
		No breast feeding	RR	**2.35 (1.44 to 3.84)**	Yes
	Sex	Female	RR	**1.73 (1.14 to 2.65)**	Yes
	Social determinants of health	Immunisation not up-to-date	RR	**1.36 (1.25 to 1.48)**	Yes

Bolded values are statistically significant.
PDM, postdischarge mortality; RR, relative risk.

2.4%.[23] Children with anaemia experienced higher rates of inpatient (13% anaemia; 9% no anaemia) and postdischarge mortality (18.8% anaemia; 10.3% no anaemia).[24] In both cohorts, death after discharge was greater than death in-hospital. Rates of readmission to hospital within 18 months were quantified in one study (18.4% severe anaemia; 9% no anaemia) and postdischarge mortality rates (11.6% anaemia; 2.7% no anaemia) exceed those of inpatient mortality rates (6.4% anaemia; 0% no anaemia).[25] Although this study had approximately 18% loss to follow-up, 71% of anaemic and 60% of non-anaemic total postdischarge deaths had occurred by 26 (of 78) weeks.[25] An RCT conducted in Uganda studied the effect of transfusion volume (30 mL/kg vs the standard 20 mL/kg) in severely anaemic children, which showed reduced inpatient mortality rates but no difference for deaths after discharge (table 8).[26] Rates of death were consistently higher after discharge than in hospital in paediatric patients presenting with

Table 8 Risk factors for PDM in anaemia/malaria studies

Article	Risk factor category	Mortality risk factor on admission	Estimate type	Estimate (95% CI)	Adjusted
Biai *et al*[21]	No data				
Phiri *et al*[25]	Age	Age (months)	HR	**0.92 (0.87 to 0.97)**	Yes
	Comorbid conditions	HIV positive	HR	**10.49 (4.05 to 27.20)**	Yes
		Bacteraemia	HR	2.17 (0.84 to 5.64)	Yes
	Diagnosis	Malaria (any parasite/mL blood)	HR	1.25 (0.67 to 2.34)	No
	Growth parameters	Wasting (<–2 z-score weight-for-height)	HR	0.74 (0.31 to 1.80)	No
		Stunting (<–2 z-score height-for-age)	HR	0.61 (0.30 to 1.22)	No
	Labs/Assessments	Iron deficiency (>5.6 sTfR/log ferritin)	HR	0.91 (0.41 to 2.03)	No
	Maternal influence	Mother education (some)	HR	1.63 (0.72 to 3.70)	No
	Sex	Male	HR	1.54 (0.68 to 3.52)	Yes
	Social determinants of health	Rural residency	HR	1.63 (0.63 to 4.20)	Yes
		Parents unemployed	HR	**4.15 (1.61 to 10.74)**	Yes
	Symptoms	Splenomegaly	HR	**0.36 (0.16 to 0.80)**	Yes
Phiri *et al*[23]	No data				
Zucker *et al*[24]	Intervention	PS, quinine, TS treatment x5d (ref: chloroquine or no antimalarial)	RR	**0.33 (0.19 to 0.65)**	Unspecified
	Labs/Assessments	Severe anaemia (Hgb<5 g/dL)	RR	**1.52 (1.22 to 1.90)**	Unspecified
Olupot-Olupot *et al*[26]	Intervention	30 mL/kg transfusion vs 20 mL/kg transfusion	RR	0.18 (0.02 to 1.42)	Unspecified
Opoka *et al*[22]	Diagnosis	Severe malarial anaemia*	HR	**16.26 (2.03 to 130.34)**	Yes
		Cerebral malaria*	HR	4.45 (0.51 to 38.55)	Yes

*Risk factor for readmission.
Hgb, haemoglobin; PDM, postdischarge mortality; RR, relative risk.

malaria and/or anaemia. Of risk factors identified throughout these studies, severe anaemia was found to be highly significant for postdischarge death[24] and readmission to the hospital.[22] HIV status profoundly influenced mortality, with a HR of 10.49 (95% CI 4.05 to 27.20) for death postdischarge in children who tested positive.[25]

DISCUSSION

Twenty-four studies examining postdischarge mortality in paediatric populations in developing countries were included in this systematic review, together substantiating the significant and unaddressed challenge continuing to plague children around the world. Significant heterogeneity in study characteristics was noted, within inclusion criteria, study design, length of follow-up, interventions (if any), risk factors and risk factor definitions. Studies were conducted primarily in African countries, and examined a variety of populations, including all admissions, infectious disease admissions, malnutrition, respiratory infections, diarrhoea, malaria and anaemia. Studies examining anaemia and/or malaria had the lowest PDM rates, while those of malnutrition and respiratory infections had the highest. Results from the studies identified through the updated search generally reflected the results from the earlier systematic review; rates of postdischarge mortality continued to be high and comparable to (sometimes exceeding) in-hospital mortality, with most postdischarge deaths occurring at home.[5] With so many deaths occurring after discharge, it is critical that effective interventions be developed and evaluated as a means to addressing this neglected cause of childhood deaths. Furthermore, no analysis of cause for death postdischarge was identified within any of the reviewed studies, highlighting this as an important area for further research.

When reported, over two-thirds of postdischarge deaths were noted to occur outside of the hospital, generally at home. In order to develop interventions to reduce the burden of PDM, an understanding of circumstances and barriers to care following discharge is of utmost importance. In a recent qualitative study, mothers of children who died postdischarge identified barriers to seeking care prior to their child's death; barriers included lack of access to health facilities and services, poor health-seeking behaviour, finances, transportation and a lack of recognition of symptoms and perceptions of recovery in children recently discharged even in the midst of persisting illness.[27] Additional factors that contribute to poor socioeconomic conditions may relate to deaths after discharge, as they further disadvantage children and families. Socioeconomically disadvantaged children continue to be served by health sectors that are poorly resourced and lack the resilience to be able to deal with large numbers of patients seen every day. Follow-up care after initial hospitalisation is an important and yet largely ignored aspect of comprehensive healthcare in both developing countries.[2] With so few patients returning to the healthcare system after discharge, identifying and understanding the barriers and targeted interventions required to enhance outcomes must be initiated during the original hospitalisation.

Risk factors consistently identified across all types of infectious admissions as highly associated with postdischarge mortality included HIV status, young age, pneumonia, malnutrition, anthropometric factors, hypoxia, anaemia, leaving the hospital against medical advice and previous hospitalisations. An important observation, therefore, is that regardless of the underlying infectious aetiology, certain risk factors consistently identify vulnerability. These observations suggest that vertical, disease-based, approaches to addressing postdischarge mortality are likely to be ineffective in comparison to simple, broadly applicable interventions. Specific illness (ie, pneumonia, diarrhoea, malaria) are often both difficult to differentiate clinically and often co-exist, especially in children in low-resource settings.[28] Sepsis, therefore, as the final common pathway for the majority of infectious disease-related deaths, may be a helpful framework within which to explore paediatric postdischarge mortality and to develop interventions. Instead of focusing on a specific body system or infectious agent, pragmatic interventions towards time-sensitive treatment can be focused towards sepsis as the overarching syndrome, increasing the potential for impactful results.[28] The Integrated Management of Childhood Illness (IMCI) pocketbook by the WHO uses a similar approach through their identification of danger signs and treatments as opposed to individual diseases. Addressing sepsis through clinical management is an important component in the reduction of preventable childhood death, requiring sustained efforts by the global community including healthcare providers, patients, pharmaceutical companies and policy makers if large-scale change is to occur.[29]

While knowledge of risk factors alone has only moderate utility in the identification of vulnerable children, the development of robust prediction models can provide a more reliable means of risk evaluation. In resource-limited environments, the use of prediction modelling is appealing, especially in relation to interventions aimed at improving postdischarge outcomes. A recent proof-of-concept study found that a simple discharge intervention including education and routine postdischarge follow-up could substantially improve postdischarge health seeking and health outcomes.[30] Such approaches, if focused primarily on the most vulnerable children, can ensure that limited resources are most effectively used and have the highest possible level of cost-effectiveness.

This systematic review is subject to several important limitations. First, it is possible that some relevant articles may not have been identified through the systematic search. Although the search was comprehensive, including both Medline and EMBASE, no MeSH/Emtree terms currently exist for postdischarge mortality and even so, many studies measure postdischarge mortality as a secondary end point. A further limitation of this review

is that the studies included were predominantly based in African countries. Therefore, these results may not be as applicable to countries outside of this setting. This highlights the continued need for ongoing research in resource-poor settings both within and outside of Africa. Significant heterogeneity in duration of follow-up, as well as when postdischarge mortality was assessed, was noted between the studies, potentially leading to a decreased ability to compare mortality rates. Many studies included in this review had high losses to follow-up (ranging between 0% and 39.3%), and very few were conducted prospectively with the stated intent of exploring postdischarge mortality. Studies with significant attrition due to follow-up likely underestimate the true rate of postdischarge mortality as these losses undoubtedly represent a more vulnerable population. While one study focused on barriers to care following discharge among those children who died in the community, one important remaining gap is that studies did not evaluate the causes of postdischarge mortality, which is difficult to measure given that most deaths occur in the community.[10 27] The ongoing, multicountry, Childhood Acute Illness and Nutrition (CHAIN) network, is attempting to understand the specific reasons for deaths postdischarge among malnourished children.[31] It is through contributions such as this that further interventions can be developed and implemented that target the specific and causal factors affecting paediatric mortality rates in developing countries.

CONCLUSIONS

In conclusion, the studies identified emphasise the significant burden of postdischarge mortality in countries where overextended and resource-limited health systems serve millions of socioeconomically disadvantaged children. The scale of this burden continues to be under-recognised, in part due to the inability of health systems to observe patient outcomes after discharge. Addressing these issues with specific regard to the identification of vulnerable children, and the development of effective postdischarge interventions, will be an essential component towards the achievement of the child mortality targets of the SDGs.

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