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Supplementary appendix

This appendix formed part of the original submission and has been peer reviewed. We post it as supplied by the authors.

Supplement to: Kwambai TK, Mori AT, Nevitt S, et al. Post-discharge morbidity and mortality in children admitted with severe anaemia and other health conditions in malaria-endemic settings in Africa: a systematic review and meta-analysis. *Lancet Child Adolesc Health* 2022; published online May 20. https://doi.org/10.1016/S2352-4642(22)00074-8.

Supplementary appendix

Supplement to: Kwambai et al., Post-Discharge Morbidity and Mortality in Children Admitted with Severe Anaemia and Other Health-conditions in Malaria-Endemic Settings in Africa: A Systematic Review and Meta-Analysis

Table of Contents

Supplemental methods

Search terms used in PubMed

(((((((((child) OR childhood) OR infant) OR paediatric)) AND ((((((((((anemia) OR "severe anemia") OR "severe malaria") OR "severe malaria anemia") OR "severe malarial anemia") OR "severe malarial anaemia") OR "severe pneumonia") OR "severe malnutrition") OR diarrhea) OR sepsis)) AND (((((((death) OR admission) OR readmission) OR mortality) OR morbidity) OR survival) OR post-discharge health condition)) AND ((((((post-discharge) OR post-discharge) OR post hospitalization) OR longitudinal) OR follow-up) OR discharge follow-up)) AND ((cape verde) OR Gambia) OR Mauritania) OR guinea bissau) OR liberia) OR togo) OR sierra leone) OR benin) OR senegal) OR guinea) OR cote d'ivoire) OR mali) OR ghana) OR burkina fasso) OR niger) OR nigeria) OR zimbabwe) OR zambia) OR swaziland) OR south africa) OR namibia) OR mozambique) OR malawi) OR mauritius) OR madagascar) OR botswana) OR angola) OR egypt) OR uganda) OR tanzania) OR sudan) OR somalia) OR rwanda) OR mayotte) OR kenya) OR ethiopia) OR eritrea) OR djibouti) OR comoros) OR burundi) OR "sao tome") OR ("sao tome and principe")) OR "equatorial guinea") OR gabon) OR "central african republic") OR congo) OR chad) OR cameroon) OR "democratic republic of congo")) OR ((africa) OR sub-saharan africa))) NOT (((((((("aplastic anemia") OR "severe aplastic anemia") OR "acquired aplastic anemia") OR "Fanconi anemia") OR "megaloblastic anemia") OR "maternal anemia") OR "pregnant women") OR "sickle cell anemia").

Outcome definitions

Primary outcomes

All-cause death or all-cause readmission in the first six months post-discharge

Secondary outcomes

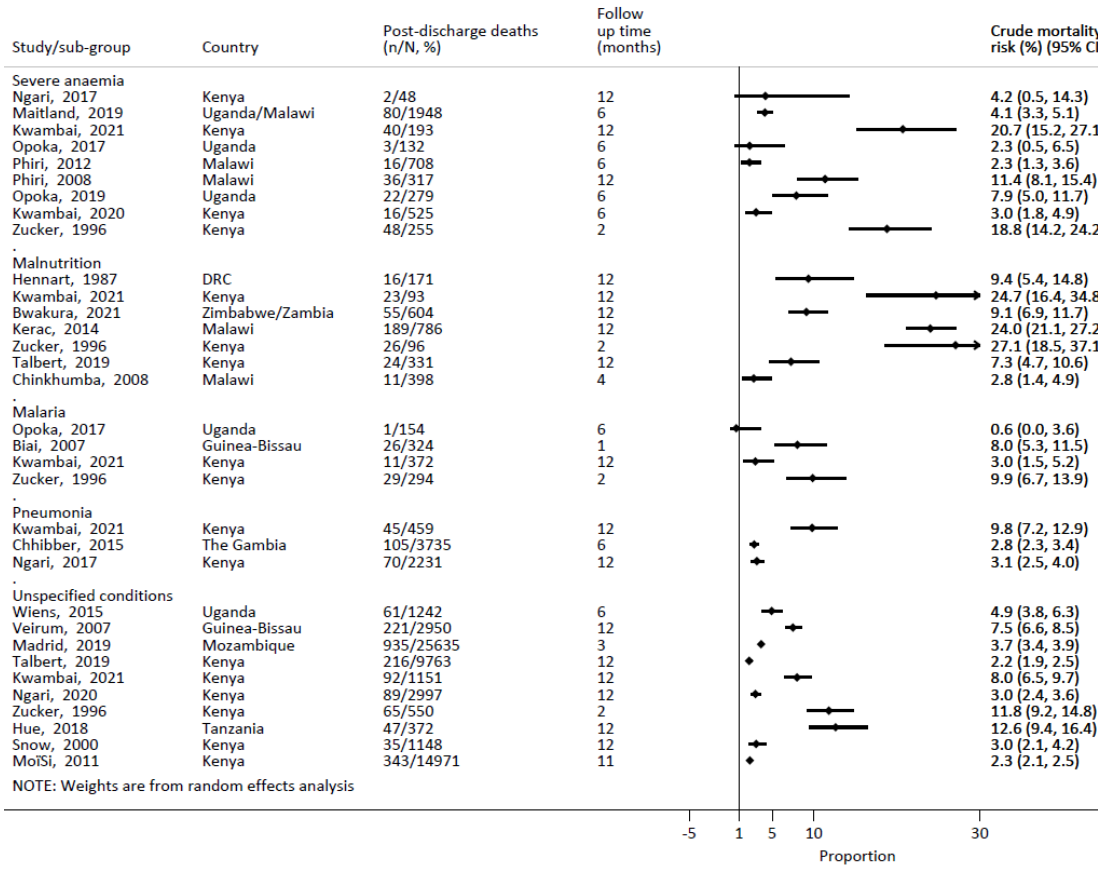
- Deaths due to severe anaemia in the first six months post-discharge
- Deaths due to health conditions other than severe anaemia in the first six months post-discharge
- In-hospital deaths due to severe anaemia
- In-hospital deaths due to health conditions other than severe anaemia
- Readmission due to health conditions other than severe anaemia

Analysis of risk factors

The crude hazard ratios for other risk factors of post-discharge mortality reported in the source studies are summarised in Table S7 and Figure S6. However, no meta-analysis of these other risk factors was conducted due to differences in definitions and scales.

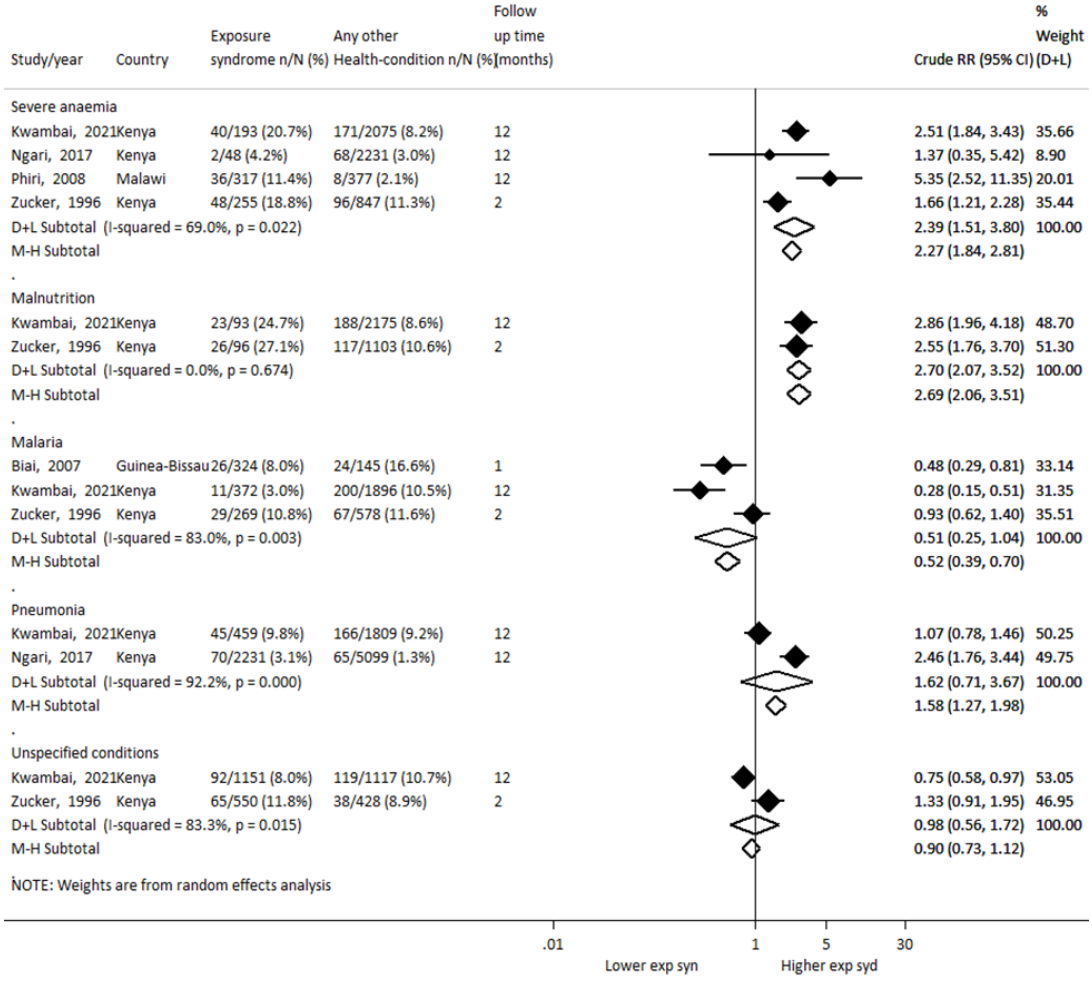
Supplemental figures

Figure S1: Mortality risk by twelve months post-discharge or earlier (all studies)



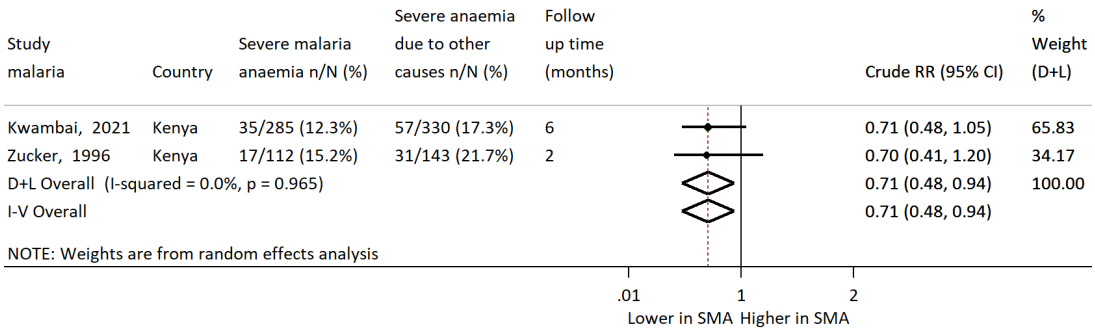
Kwambai 2021, Zucker 1996 and Opoka 2017 are included in more than one sub-group, each representing a mutually exclusive group. Due to considerable heterogeneity (the pooled I^2 is 96·6%) between and within admission health condition groups, the summary statistics are not shown.

Figure S2: Relative Risk of mortality by twelve-month post-discharge among studies reporting results by multiple syndromes



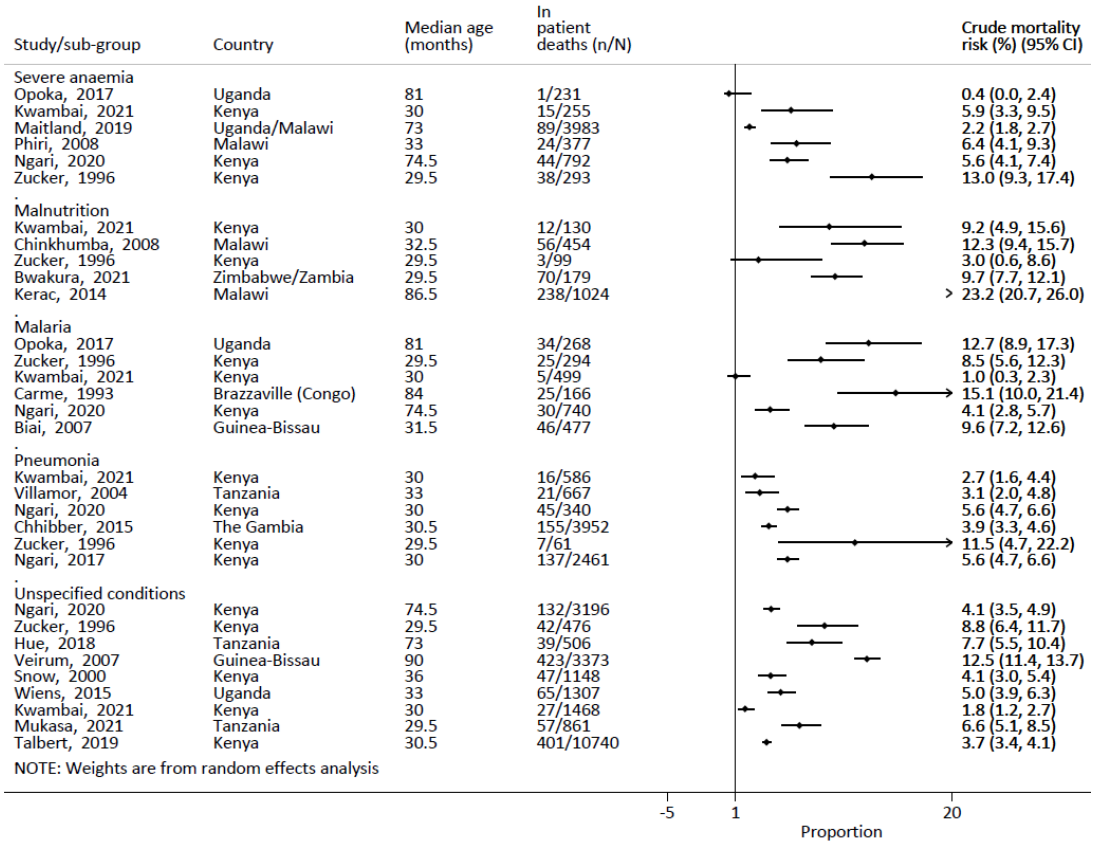
RR=relative risk. CI=confidence interval. D+L=DerSimonian and Laird random effects. M-H=Mantel-Haenszel fixed effect. Includes only studies that reported enough detail to directly compare the post-discharge mortality by health condition among children from the same cohort study.

Figure S3: Post-discharge mortality between severe malaria anaemia vs severe anaemia due to other causes.



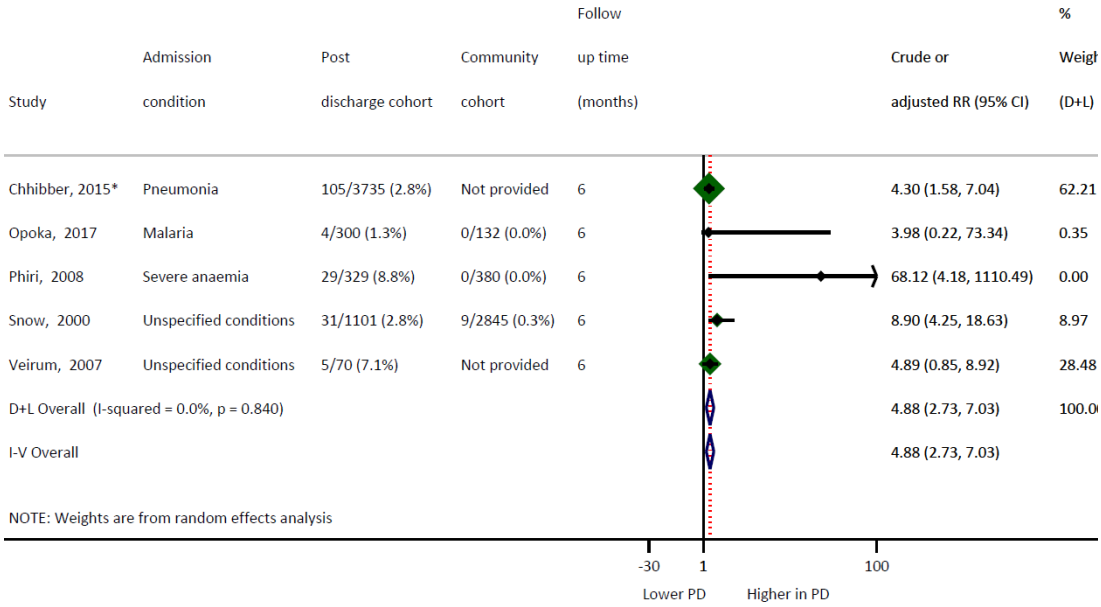
RR=relative risk. CI=confidence interval. D+L=DerSimonian and Laird random effects. I-V=inverse variance fixed effect. SMA=severe malarial anaemia.

Figure S4: Mortality risk in-hospital by health condition.



Kwambai 2021, Zucker 1996 and Opoka 2017 are included in more than one sub-group each representing a mutually exclusive group. The summary statistics are not shown due to considerable heterogeneity (The pooled I^2 is 96·9%) between and within admission health condition groups.

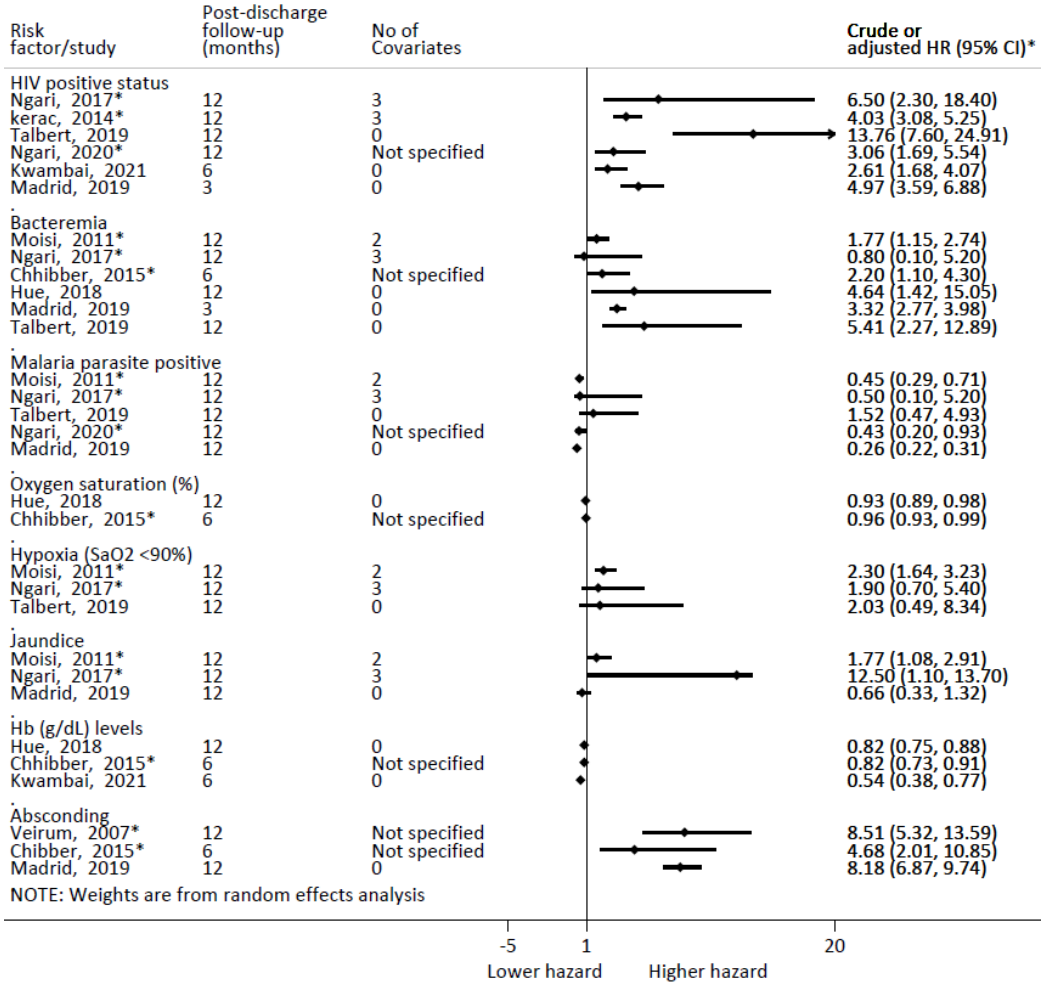
Figure S5: Mortality within six months post-discharge versus community cohorts



RR=relative risk. CI=confidence interval. D+L=DerSimonian and Laird random effects. I-V=inverse variance fixed effect. PD=post-discharge. The data columns towards the left of the forest plot represent n/N (%) for these data points.

*Adjusted effect estimates were used for this data point because the crude effect estimate, or crude data (n/N) were not available

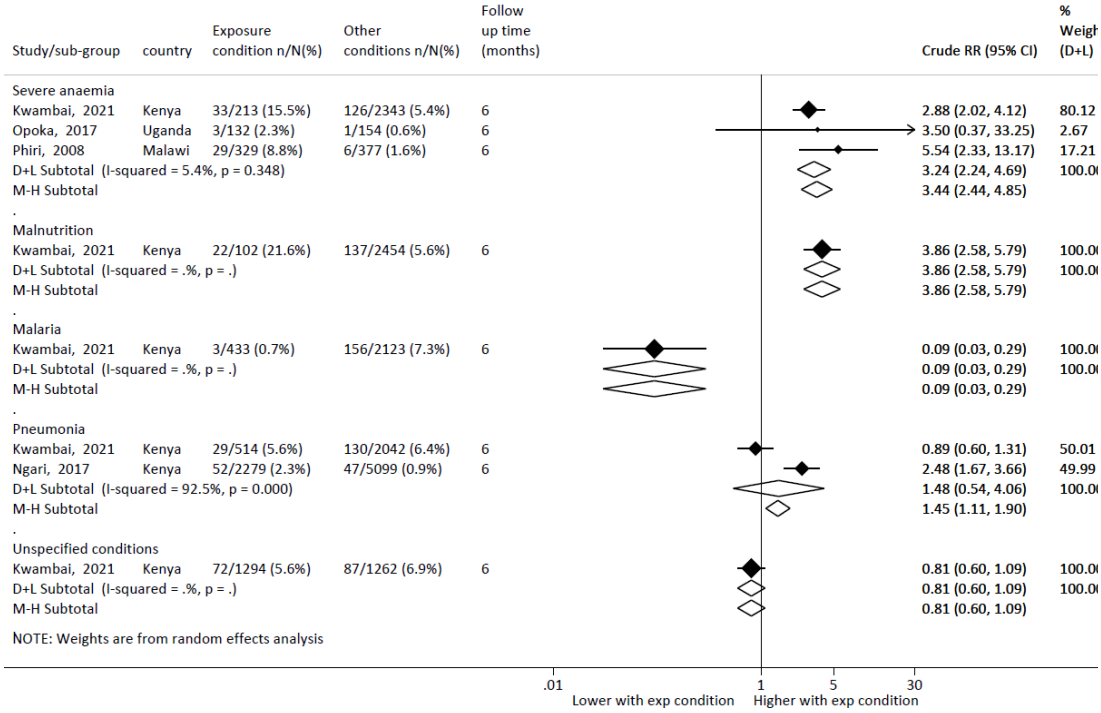
Figure S6: Other risk factors for post-discharge mortality



CI=confidence interval. HR=hazard ratio. Hb=haemoglobin. D+L=DerSimonian and Laird random effects. I-V=inverse-variance fixed-effect. HR=hazard ratio with the absence of the risk factor as the reference group.

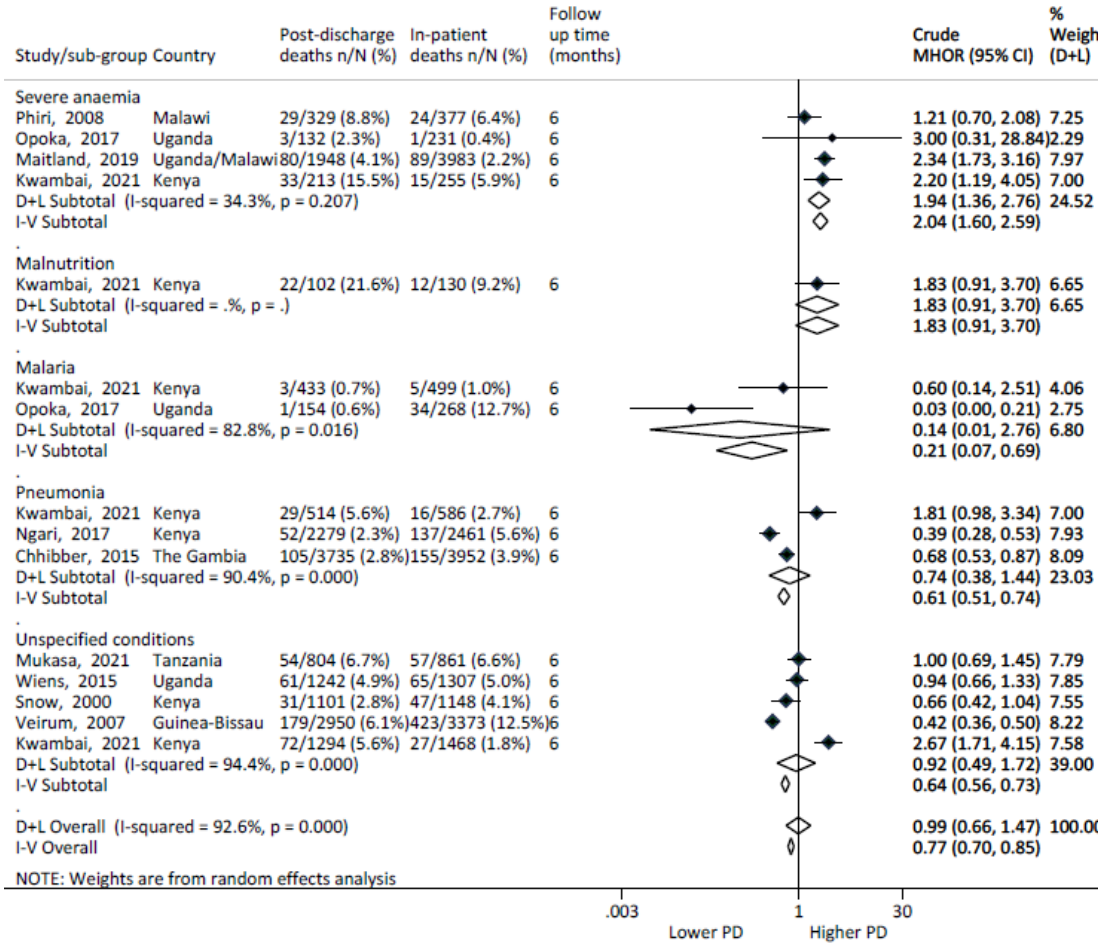
*Adjusted effect estimates were used for these data points because the crude effect estimate, or crude data (n/N) were not available

Figure S7: Sensitivity analysis restricted to studies that included at least six months follow-up for relative risk of mortality by six-month post-discharge among studies reporting results by multiple health conditions



RR=relative risk. CI=confidence interval. D+L=DerSimonian and Laird random effects. M-H=Mantel-Haenszel fixed effect. Exp=exposure group Includes only studies that reported enough detail to allow direct comparisons of the post-discharge mortality by health condition among children from the same cohort study. Diamond shapes depict the pooled effect size. The crude RR is calculated by comparing the "exposure condition" vs "other conditions". For example, in the first section under "Severe anaemia", the random effects summary crude RR of 3.24 (95% CI 2.24-4.69) represents the relative risk of post-discharge mortality comparing children who were recently admitted with severe anaemia versus all other children that were admitted for any other conditions that excluded severe anaemia ("Other conditions"), such as severe acute malnutrition, severe malaria, severe pneumonia or other unspecified conditions). Similarly, the second section under malnutrition (summary random effects RR 3.86) represents the relative risk of post-discharge mortality comparing children who were recently admitted with severe acute malnutrition versus children that were admitted for any other conditions that excluded severe acute malnutrition. In the latter case, "Other conditions" includes children with severe anaemia, severe malaria, severe pneumonia or other unspecified conditions.

Figure S8: Sensitivity analysis restricted to studies that included at least six months follow-up of in-patient vs post-discharge mortality by six months by health condition on admission



D+L=DerSimonian and Laird random effects. I-V=inverse-variance fixed-effect. MHOR=Mantel-Haenszel odds ratio. PD=post-discharge. For each study, the MHOR is obtained by comparing the number of "post-discharge deaths" vs "in-patient deaths" during the initial hospitalisation.This figure is restricted to studies that followed up participants for 6 months after discharge.
D+L=DerSimonian and Laird random effects. I-V=inverse-variance fixed-effect. MHOR=Mantel-Haenszel odds ratio. PD=post-discharge. For each study, the MHOR is obtained by comparing the number of "post-discharge deaths" vs "in-patient deaths" during the initial hospitalisation.

Supplemental tables

Table S1: Characteristics of included studies

Study	Location	Dates	Comparison groups	Age Range	Admission Health-condition	Participants assessed for*	Total Enrolled	IP Death	PD Death	Re-Admission	Loss to follow-up	FUP Time
		Randomized Controlled Trials										
Kwambai et al[1]	Kenya and Uganda	2016-18	Placebo Intervention: Dihydroartemisinin-piperaquine	<5y	Severe anaemia	1, 2	525	NR	3·1%	30·1%	6.7%	6m
Maitland et al[2]	Uganda/Malawi	2014-17	Co-trimoxazole or multivitamin multimineral or iron/folate	2m-12y	Severe anaemia	1, 2, 3, 4	1948	2·2%	4·1%	18·0%	4.2%	6m
Biai et al[3]	Guinea-Bissau	2004-06	Use of malaria treatment protocols Control ward: staff not trained Intervention: staff trained	3m-5y	Malaria	1, 2	491	9·6%	1·0%	NR	5%	28d
Phiri et al[4]	Malawi	2006-09	Placebo Intervention: artemether-lumefantrine	4m-59m	SMA	1, 2, 4	708	NR	2.3%	18·5%	4.9%	6m
Pavlinac et al[5]	Kenya	2016-2019	Placebo Intervention: Azithromyzcin	1-59m	All cause	1, 2, 3, 4	696	NR	2.7%	8.2%	NR	6m
	Cohort studies without a comparator group											
Carme et al[6]	Congo	1988-89	All enrolled	≤ 14	Cerebral malaria	2	170	15·0%	6·7%	NR	37.7%	27m
Chhibber et al[7]	The Gambia	2008-12	All enrolled	2m-59m	Pneumonia+ others	1, 2, 3, 5	3,735	3·9%	2·8%	NR	1.6%	180d
Villamor et al[8]	Tanzania	1993-97	All enrolled	6m-60m	Pneumonia	1, 2, 3, 4, 5	687	3·1%	11·7%	NR	8.7%	Mean 24.7m
Wiens et al[9]	Uganda	2012-13	All enrolled	6m-5y	All cause (Infectious)	1, 2, 3, 4, 5	1,307	5·0%	4·9%	NR	1.7%	

Study	Location	Dates	Comparison groups	Age Range	Admission Health-condition	Participants assessed for*	Total Enrolled	IP Death	PD Death	Re-Admission	Loss to follow-up	FUP Time
Hennart et al[10]	Congo	1970	All enrolled	mean 46m	PEM	3	171	NR	0·2	NR	NR	5y
Kerac et al[11]	Malawi	2006-07	All enrolled	5m-14y	PEM	1, 2, 3, 4	1,024	23·2%	24·0%	7·1%	13%	1y
Opoka et al[12]	Uganda	2016-18	All enrolled	<5 y	Severe anaemia	1, 2, 3, 4	279	NR	7·9%	45·8%	1.1%	6m
Madrid et al[13]	Mozambique	2000-2016	All enrolled	2m-15y	All cause	1, 2, 3, 4, 5	25,635	NR	3·6%	NR	NR	3m
Mukasa et al[14]	Tanzania	2003-2007	All enrolled	0-5y	All cause	-	28,910	6.6%	6.7%	NR	NR	6m
		Cohort studies with comparator groups										
Moisi et al[15]	Kenya	2003-08	Post-discharge group	<15y	All cause	2, 3, 5	14,971	NR	4·5%	8·9%	NR	12m
			Community group	<15y	NR		96,029	NA	NA	NA		
Ngari et al[16]	Kenya	2007-12	Post-discharge group	1m-59m	Severe Pneumonia	1, 2, 3, 4, 5	2,461	5·6%	3·1%	NR	1.9%	1y
			Post-discharge group	1m-59m	No Severe Pneumonia		5,270	2·4%	1·3%	NR	0.9%	
Opoka et al[17]	Uganda	2008-13	Admissions with Cerebral malaria	18m-12y	Cerebral malaria	1, 2, 3, 4	162	12·7%	0·6%	3·1%	4.9%	6m
			Admissions with SMA	18m-12y	SMA		138	0·4%	2·2%	9·4%	4.3%	
			Community (not admitted)	18m-12y	Healthy		133	NA	0·0%	0·0%	2.3%	
Veirum et al[18]	Guinea-Bissau	1991-96	PD Cohort	≤15y	All cause	1, 2, 5	2,950	12·5%	7·5%	15·9%	NR	12m
			Community cohort	≤15y	All cause		8,184	NA	*MRR	0·04	NR	
Zucker et al[19]	Kenya	1991	Exposed group	6m-5y	Severe anaemia	1, 2, 3, 4, 5	293	13·0%	18·8%	NR	4% (overall)	8w
			non-exposed group	6m-5y	Non-severe anaemia		930	8·9%	11·3%	NR		
Snow et al[20]	Kenya	1992-97	Post-discharge group	≤6y	All cause	1, 2, 5	1,148	0·0	2.39/1000 pm	347	NR	1y

Study	Location	Dates	Comparison groups	Age Range	Admission Health-condition	Participants assessed for*	Total Enrolled	IP Death	PD Death	Re-Admission	Loss to follow-up	FUP Time
			Community group	≤6y	NR		2,845	NA	1·1/1000 pm	172	NR	
Phiri et al[21]	Malawi	2002-06	Cases	6-60m	Severe anaemia	1, 2, 3, 4	377	6·4%	11·6%	17·2%	17.8%	18m
			Hospital control	6-60m	No severe anaemia		377	0·0%	2·7%	9·4%	19.0%	
			Community controls	6-60m	Healthy		380	N/A	1·3%	10·0%	15.3%	
Kwambai et al[22]	Kenya	2008-2013	Admitted with severe malaria	≤5y	Severe malaria	1, 2, 3, 4, 5	1,033	1·6%	5·7%	NR	32.8%	12m
			Admitted with severe anaemia	≤5y	Severe anaemia		651	5·5%	16·1%	NR	24.4%	
			Admitted with Pneumonia	≤5y	Pneumonia		996	2·9%	8·9%	NR	24.2	
			Admitted with SAM	≤5y	Severe acute malnutrition		271	8·5%	22·1%	NR	26.9%	
			Admitted with other health conditions	≤5y	Other health conditions		1,521	1·8%	8·2%	NR	25.2%	
Chinkhumba et al[23]	Malawi	2005-06	HIV Positive	6m-59m	SAM	1, 3, 4	79	30·4%	7·3%	NR	NR	4m
			HIV Negative	6m-59m	SAM		375	8·5%	2·0%	NR	NR	
Talbert et al[24]	Kenya	2007-2015	All enrolled	2m-59m	Acute diarrhoea	1, 2, 3, 4, 5	2,626	3·7%	2·3%	NR	NR	12m
Ngari et al[25]	Kenya	2007-2016	All enrolled	5y-12y	All enrolled	1, 2, 3, 4, 5	3,196	4·1%	3·0%	NR	2.2%	12m
Hau et al[26]	Tanzania	2014	All-enrolled	2-12y	All-cause	1, 2, 3, 4, 5	537	7·7%	12·6	NR	2.0%	12m
Bwakura-Dangarembizi et al[27]	Zimbabwe and Zambia	2016-2018	HIV Positive HIV Negative	1-59m	SAM	1, 3, 4,	750	9.7%	9.1%	NR	7.0%	12m

IP=in-patient. PD=post-discharge. FUP=follow-up. SP=sulphadoxine-pyrimethamine. IPTpd=intermittent preventive treatment post-discharge. SpO2=peripheral capillary oxygen saturation. NR=not reported. SMA=severe malarial anaemia. SAM=severe acute malnutrition. NA=not applicable. MRR= mortality rate ratio. PEM=protein-energy malnutrition. Y=years. M=months. w=weeks.

* Participants assessed for 1=Severe anaemia, 2=Severe malaria, 3=Severe acute malnutrition, 4=HIV, 5=Pneumonia

Table S2: Mean and median duration of follow-up per health condition

	Follow up times (upto 6 months)			Follow up times (upto 12 months)		
Main Health Condition	**N**	**Mean (SD)**	**Median (IQR)**	**N**	**Mean (SD)**	**Median (IQR)**
Severe anaemia	8	5.5 (1.4)	6.0 (6.0-6.0)	9	7.6 (3.6)	6.0 (6.0-12.0)
Severe malaria	4	3.8 (1.7)	3.3 (2.5-5.0)	6	9.0 (4.7)	12.0 (4.0-12.0)
Severe malnutrition	4	3.8 (2.6)	4.0 (1.5-6.0)	4	5.3 (5.0)	4.0 (1.5-9.0)
Pneumonia	4	5 (2.0)	6.0 (4.0-6.0)	3	10.0 (3.5)	12.0 (6.0-12.0)
Unspecified conditions	9	4.8 (1.6)	6.0 (3.0-6.0)	11	9.6 (4.0)	12.0 (6.0-12.0)

Table S3: Cochrane collaboration tool for quality assessment of randomised controlled trials

	Random Sequence Generation	Allocation Concealment	Blinding of Participants and Personnel	Blinding of Outcome Assessment	Incomplete Outcome Data	Selective Reporting	Other Bias
Biai et al[3]	+	+	+	+	+	+	+
Phiri et al[4]	+	+	+	+	+	+	+
Kwambai[1]	+	+	+	+	+	+	+
Maitland[2]	+	+	+*	+	+	+	+
Pavlinac[5]	+	+	+	+	+	+	+

+	Low Risk of Bias	?	Unclear Risk of Bias	-	High Risk of Bias

Risk of bias assessment for included studies based on the authors' judgements for each included trial. The scores were classified as 'low risk of bias' if all criteria were met, as 'unclear risk of bias' if insufficient information was available for at least one of the criteria in the study report, or as 'high risk of bias' if at least one of the criteria was not met'. Adapted from the Cochrane Library.

* The trials by Biai[3] and Maitland[2] et al were well designed an open-label trials

Table S4: Newcastle Ottawa scale for quality assessment of cohort studies with comparison groups

Criterion	Number of stars awarded											
	Chinkhumba et al[21]	Kwambai et al[20]	Ngari et al[14]	Opkoka et al[17]	Veirum et al[16]	Zucker et al[17]	Snow et al[18]	Moisi et al[13]	Phiri et al[19]	Talbert et al[22]	Ngari et al[23]	Bwakura-Dangarembizi et al[27]
Selection												
Representativeness of exposed cohort	1	1	1	1	1	1	1	1	1	1	1	1
selection of the non-exposed cohort	1	1	1	1	1	1	1	1	1	1	1	1
Ascertainment of exposure	1	1	1	1	1	1	1	1	1	1	1	1
Demonstration that outcome of interest was not present at the start of the study	1	1	1	1	1	1	1	1	1	1	1	1
Comparability												
Comparability of cohorts on the basis of the design or analysis	2	2	2	2	1	1	1	2	2	2	2	2
Outcome												
Assessment of outcome	1	1	1	1	1	1	1	1	1	1	1	1
Was follow up long enough for outcomes to occur?	1	1	1	1	1	1	1	1	1	1	1	1
Adequacy of follow up of cohorts	0	1	0	1	0	0	0	0	1	1	1	1
Total stars awarded out of 9	8	9	8	9	7	7	7	8	9	9	9	9
Quality Assessment	Good	Good	Good	Good	Good	Good	Good	Good	Good	Good	Good	Good

The Newcastle Ottawa scale is based on a star system where one star is awarded for each item under selection and outcome categories and a maximum of two stars for comparability. A maximum of nine points is assigned for the least risk of bias in three domains: 1) selection of study groups (four points); 2) comparability of groups (two points); and 3) ascertainment of outcomes (three points) for cohort studies. The quality of studies was rated based on the Newcastle Ottawa scale of 0 to 9 as; poor quality (0 -3), fair quality (4 -6) and good quality (7 -9).

Table S5: Modified Newcastle Ottawa scale for quality assessment of cohort studies without comparison

Criterion	**Summary of reviewers scores**									
	Carme et al[6]	Chhibber et al[7]	Hennart et al[10]	Kerac et al[11]	Villamor et al[8]	Wiens et al[9]	Opoka et al[12]	Madrid et al[13]	Hau et al[26]	Mukasa et al[14]
Selection										
Representativeness of exposed cohort	1	1	1	1	1	1	1	1	1	1
Selection of the non-exposed cohort	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Ascertainment of exposure	1	1	1	1	1	1	1	1	1	1
Demonstration that outcome of interest was not present at the start of the study	0	1	1	1	1	0	1	1	1	1
Comparability										
Comparability of cohorts on the basis of the design or analysis	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Outcome										
Assessment of outcome	0	1	1	1	1	1	1	1	1	1
Was follow up long enough for outcomes to occur?	1	1	1	1	1	1	1	1	1	1
Adequacy of follow up of cohorts	0	1	0	1	1	1	1	1	1	1
Total stars awarded out of 6	3	6	5	6	6	5	6	6	6	6
Quality assessment	Poor	Good	Good	Good	Good	Good	Good	Good	Good	Good

This tool was used for cohort studies without a comparison group. A single group of participants with an exposure of interest were followed up to determine the outcome. In the "selection" criteria of the Newcastle Ottawa scale, the "selection of the non-exposed cohort" and the comparability criteria were omitted. The total score is six stars, with quality assessment scored as 1-2 stars (poor quality), 3-4 (fair quality) and 5-6 (good quality).

Table S6: Comparison by health condition of the crude risks of post-discharge mortality and readmissions by six- and twelve-months post-discharge

	By 6 months			By 12 months		
	RR (95% CI, P, I^2, N)	RR (95% CI, P, I^2, N)	RR (95% CI, P, I^2, N)	RR (95% CI, P, I^2, N)	RR (95% CI, P, I^2, N)	RR (95% CI, P, I^2, N)
Mortality	Versus any other health condition	Versus any other health condition, excluding severe anaemia	Versus any other health condition, excluding severe malnutrition	Versus any other health conditions	Versus any other health condition, excluding severe anaemia	Versus any other health condition, excluding severe malnutrition
Severe anaemia	2·69 (1·59-4·53), P<0·0001, 69·2%, 4	NA	2·30 (1·11-4·78), P=0·025, 88·2%, 2	2·39 (1·51-3·80), P<0·0001, 69·0%, 4	NA	Insufficient data
Severe malnutrition	3·12 (2·07-4·68), P<0·0001, 54·7%, 2	3·26 (1·62-6·56), P=0·001, 83·0%, 2	NA	2·70 (2·07-3·52), P<0·0001, 0·0%, 2	3·26 (2·47-4·30), P<0·0001, 0·0%, 2	NA
Severe pneumonia	1·09 (0·44-2·71), P=0·846, 88·7%, 3	0·84 (0·41-1·74), P=0·643, 45·0%, 2	0·88 (0·50-1·53), P=0·641, 25·2%, 2	1·62 (0·71-3·67), P=0·249, 92·2%, 2	1·44 (0·79-2·62), P=0·237, 83·0%, 3	1·12 (0·83-1·50), P=0·454, 0·0%, 2
Not defined	1·02 (0·63-1·670), P=0·929, 75·5%, 2	1·15 (0·90-1·47), P=0·274, 0·0%, 2	1·28 (1·01-1·62), P=0·040, 0·0%, 2	0·98 (0·56-1·72), P=0·949, 83·3%, 2	0·90 (0·72-1·12), P=0·336, 0·0%, 2	1·06 (0·76-1·48), P=0·736, 53·3%, 2
Severe malaria	0·39 (0·14-1·05), P=0·061, 87·8%, 3	0·33 (0·03-3·41), P=0·351, 93·3%, 2	0·32 (0·03-3·44), P=0·348, 93·5, 2	0·51 (0·25-1·04), P=0·066, 83·0%, 3	0·57 (0·18-1·80), P=0·336, 90·1%, 2	0·55 (0·17-1·82), P=0·328, 90·8%, 2
Readmissions						
Severe anaemia	3·05 (1·12-8·35), P<0·0001, 0·0%, 1	NA	Insufficient data	Insufficient data	N/A	Insufficient data

RR=relative risk. CI=confidence interval. The effect estimates shown in the second column from the left is the same as shown in Figure *3* (given for illustration purposes only)

Table S7: Risk factors for post discharge mortality

Author	Risk factor	Effect Measure	EM (95% CI)	Adjusted
Moisi[15]	Age 1–5 months (ref: <1 month)	HR	1·34 (0·93-1·92)	Yes
	Age 6–11 months (ref: <1 month)	HR	0·82 (0·57-1·18)	Yes
	Age 2–5 years (ref: <1 month)	HR	0·57 (0·36-0·90)	Yes
	Weigh for age z-score < −3	HR	3·42 (2·50-4·68)	Yes
	Weigh for age z-score < −4	HR	6·53 (4·85-8·80)	Yes
	Parasitaemia (ref: no parasitaemia)	HR	0·45 (0·29-0·71)	Yes
	Hypoxia (ref: no hypoxia)	HR	2·3 (1·64-3·23)	Yes
	Bacteraemia (ref: no bacteraemia)	HR	1·77 (1·15-2·74)	Yes
	Jaundice (ref: no jaundice)	HR	1·77 (1·08-2·91)	Yes
	Hepatomegaly (ref: no hepatomegaly)	HR	2·34 (1·60-3·42)	Yes
	Hospitalization > 13 d (ref: <13 days)	HR	1·83 (1·33-2·52)	Yes
	1 prior discharge (within a 1 year of index discharge) (ref: no prior discharge)	HR	2·83 (2·04-3·92)	Yes
	2 prior discharges (within a 1 year of index discharge) (ref: no prior discharge)	HR	7·06 (4·09-12·21)	Yes
	≥ 3 prior discharges (within a 1 year of index discharge) (ref: no prior discharge)	HR	23·55 (10·70-51·84)	Yes
	Mild pneumonia (ref: no pneumonia)	HR	2·30 (1·00-5·28)	Yes
	Severe pneumonia (ref: no pneumonia)	HR	1·37 (1·05-1·79)	Yes
	Very severe pneumonia (ref: no pneumonia)	HR	4·09 (2·25-7·46)	Yes
	Severe malnutrition (ref: no malnutrition)	HR	4·37 (2·73-7·01)	Yes
	Meningitis (ref: no meningitis)	HR	2.29 (1.57-3.32)	Yes
	Sick young infant	HR	2·67 (1·98-3·58)	Yes
Wiens[9]	Male sex (ref: female)	OR	0·90 (0·54-1·51)	No
	Age (months) (per unit increase)	OR	0·97 (0·97-0·97)	No
	MUAC (per mm increase)	OR	0·97 (0·96-0·98)	No
	Weight for age z-score (per unit increase)	OR	0·66 (0·57-0·76)	No

Author	Risk factor	Effect Measure	EM (95% CI)	Adjusted
	Weight for length/height z-score (per unit increase)	OR	0·81 (0·72-0·91)	No
	Length/height for age z-score (per unit increase)	OR	0·79 (0·7-0·89)	No
	Heart rate for age z-score	OR	0·86 (0·74-0·99)	No
	Heart rate (raw)	OR	1·00 (0·99-1·01)	No
	Respiratory rate for age z-score	OR	0·99 (0·92-1·06)	No
	Respiratory rate (raw)	OR	1·01 (1·00-1·03)	No
	Systolic blood pressure z-score	OR	0·94 (0·79-1·12)	No
	Systolic blood pressure (raw)	OR	0·98 (0·96-1·00)	No
	Diastolic blood pressure (raw)	OR	0·99 (0·97-1·01)	No
	Temperature (transformed)	OR	1·02 (0·90-1·16)	No
	Temperature (raw)	OR	0·76 (0·62-0·93)	No
	SpO2 (raw) (per 1% increase)	OR	0·94 (0·92-0·96)	No
	SpO2 (transformed) (per 1% increase)	OR	1·04 (1·02-1·05)	No
	HIV positive (ref: negative)	OR	5·21 (2·55-10·65)	No
	Hb (g/dL)	OR	0·95 (0·87-1·03)	No
	Blantyre Coma Scale <5 (ref: 5)	OR	2·40 (1·27-4·57)	No
	Positive blood smear (vs negative)	OR	0·33 (0·16-0·68)	No
	Illness >7 days prior to admission	OR	0·50 (0·30-0·83)	No
	Time since last hospitalisation (Ordered as <7 days, 7 to 30 days, 30 days to 1 year, >1 year and never (analysed as continuous and coded and 1–5, respectively)	OR	0·75 (0·62-0·90)	No
	Sibling deaths	OR	1·54 (0·89-2·65)	No
	Number of children in family	OR	1·02 (0·92-1·13)	No
	Boil all drinking water	OR	0·82 (0·47-1·42	No
	Maternal age (years)	OR	1·00 (0·97-1·04)	No
	Mother HIV positive (ref: negative)	OR	1·79 (0·87-3·67)	No

Author	Risk factor	Effect Measure	EM (95% CI)	Adjusted
	Mother HIV status unknown (ref: negative))	OR	1·27 (0·64-2·52)	No
	Maternal education (Primary) (ref: <primary 3)	OR	1·18 (0·62-2·23)	No
	Maternal education (Some) (ref: <primary 3)	OR	0·72 (0·31-1·70)	No
	Maternal education (Postsecondary) (ref: <primary 3)	OR	1·18 (0·41-3·36)	No
	Bed net use (Sometimes) (ref: never)	OR	1·00 (0·48-2·09)	No
	Bed net use (always) (ref: never)	OR	0·85 (0·46-1·58)	No
	Distance from hospital (30–60 minutes) (ref: <30 min)	OR	0·71 (0·31-1·64)	No
	Distance from hospital (>60 minutes) (ref: <30 min)	OR	1·30 (0·70-2·41)	No
Phiri[21]	Unit increase in age (months)	HR	0·92 (0·87-0·97)	Yes
	Rural residency (ref: urban)	HR	1·63 (0·63-4·20)	Yes
	Sex (Male)	HR	1·54 (0·68-3·52)	Yes
	Maternal education (Some) (ref: none)	HR	1·63 (0·72-3·70)	No
	Parents unemployed (ref: employed)	HR	4·15 (1·61-10·74)	Yes
	Weight-for-height (WHZ) <-2 Z-score (≥-2 Z-score WHZ)	HR	0·74 (0·31-1·80)	No
	Height-for-age (HAZ) <-2 Z-score (≥-2 Z-score HAZ)	HR	0·61 (0·30-1·22)	No
	Splenomegaly (ref: no splenomegaly)	HR	0·36 (0·16-0·80)	Yes
	Iron deficiency ≥5.6 sTfR/Log ferritin (ref: <5.6 sTfR/Log ferritin)	HR	0·91 (0·41-2·03)	No
	Any malaria parasite/µL blood (ref: no parasitaemia)	HR	1·25 (0·67-2·34)	No
	HIV Positive (ref: HIV negative)	HR	10·49 (4·05-27·20)	Yes
	Bacteraemia (ref: no bacteraemia)	HR	2·17 (0·84-5·64)	Yes
Ngari[16]	Age 12–23 months (ref: ≥24 months)	HR	1·02 (0·1-9·6)	Yes
	Age 6–11 months (ref: ≥24 months)	HR	5·8 (0·8-40·5)	Yes
	Age <6 months (ref: ≥24 months)	HR	4·8 (0·7-34·1)	Yes
	Sex (male)	HR	1·45 (0·75-2·83)	Yes
	Reported preterm/low birthweight (LBW) (ref: no preterm/LBW)	HR	0·7 (0·2-2·8)	Yes

Author	Risk factor	Effect Measure	EM (95% CI)	Adjusted
	Residence distance (from study site per KM)	HR	1·0 (0·9-1·1)	Yes
	Duration of hospitalisation per day	HR	1·1 (1·0-1·2)	Yes
	Hypoxia (SaPO2 <90%) (ref: SaPO2 >90%)	HR	1·9 (0·7-5·4)	Yes
	Capillary refill >2 seconds (ref: <2seconds)	HR	2·4 (0·5-12·1)	Yes
	Impaired consciousness (ref: normal consciousness)	HR	1·1 (0·2-7·8)	Yes
	Wheezing (ref: no wheezing)	HR	0·5 (0·1-2·4)	Yes
	Cough for >14 days	HR	0·2 (0·1-5·5)	Yes
	Jaundice (ref: no jaundice)	HR	12·5 (1·1-13·7)	Yes
	Severe anaemia (Hb <5g/dL) (ref: Hb≥5)	HR	0·8 (0·1-7·5)	Yes
	Axillary temperature <36°C (ref: axillary temperature 36 to 39oc)	HR	0·3 (0·1-2·8)	Yes
	Axillary temperature >39°C (ref: axillary temperature 36 to 39oc)	HR	1·1 (0·4-3·0)	Yes
	HIV antibody test positive (ref: HIV negative)	HR	6·5 (2·3-18·4)	Yes
	HIV test not performed (ref: HIV negative)	HR	0·4 (0·1-3·6)	Yes
	Respiratory Syncytial Virus test positive (ref: RSV test negative)	HR	0·3 (0·1-1·2)	Yes
	Respiratory Syncytial Virus test not performed (ref: RSV test negative)	HR	2·7 (1·2-6·3)	Yes
	Malaria slide positive (ref: negative)	HR	0·5 (0·1-5·2)	Yes
	Bacteraemia (ref: no bacteraemia)	HR	0·8 (0·1-5·2)	Yes
	MUAC per cm increase	HR	0·6 (0·5-0·8)	Yes
	Year of admission 2008 (ref: Year of admission 2007)	HR	0·9 (0·3-3·1)	Yes
	Year of admission 2009 (ref: Year of admission 2007)	HR	0·5 (0·1-2·1)	Yes
	Year of admission 2010 (ref: Year of admission 2007)	HR	0·7 (0·2-2·5)	Yes
	Year of admission 2011 (ref: Year of admission 2007)	HR	1·7 (0·5-5·3)	Yes
	Year of admission 2012 (ref: Year of admission 2007)	HR	1·8 (0·2-15·7)	Yes
Villamor[8]	HIV Positive (ref: HIV negative)	HR	3·92 (2·34-6·55)	Yes
	Sex Male	HR	0·98 (0·65-1·48)	No

Author	Risk factor	Effect Measure	EM (95% CI)	Adjusted
	Age 6–11 months (ref: ≥24 months)	HR	3·70 (1·72-7·95)	Yes
	Age 12–23 months (ref: ≥24 months)	HR	3·14 (1·44-6·88)	Yes
	Height-for-age <-2 Z-score (ref: HAZ>-2 Z-score)	HR	2·12 (1·31-3·42)	Yes
	Low MUAC at baseline (MUAC <25th percentile of the population age-specific distribution) (per cm increase)	HR	1·88 (1·16-3·03)	Yes
	Hb ≤7.00 g/dL (ref: Hb >10.00g/dL)	HR	2·55 (1·13-5·77)	Yes
	Hb 7.01–8.50 g/dL (ref: Hb >10.00g/dL)	HR	2·81 (1·24-6·37)	Yes
	Hb 8.51–10.00 g/dL (ref: Hb >10.00g/dL)	HR	1·76 (0·75-4·10)	Yes
	Severe pneumonia on admission (ref: no pneumonia on admission)	HR	2·47 (1·59-3·85)	Yes
	Maternal education (Elementary) (ref: None/illiterate)	HR	0·84 (0·48-1·49)	No
	Maternal education (Secondary or higher) (ref: None/illiterate)	HR	0·27 (0·06-1·17)	No
	Tap in compound (ref: tap in house)	HR	1·40 (0·60-3·29)	Yes
	Tap outside compound (ref: tap in the house)	HR	2·27 (1·02-5·03)	Yes
	Public well (ref: tap in the house)	HR	2·92 (1·03-8·30)	Yes
	Mother works outside home-yes (ref: no)	HR	0·61 (0·36-1·03)	No
	Mother lives with a partner (ref: mother lives without a partner)	HR	1·60 (1·00-2·57)	No
	No household amenity (ref: 1 household amenity) (from a list of five items: car, refrigerator, radio, bicycle, and television)	HR	1·58 (0·92-2·69)	No
	2≤ household amenities (ref: 1 household amenity)	HR	0·95 (0·56-1·60)	No
Kerac[11]	Sex (Male)	HR	0·89 (0·73-1·08)	Yes
	Age >=60 months (ref: age 48 to 60 months)	HR	1·22 (0·63-2·36)	Yes
	Age 36 to 48 months (ref: age 48 to 60 months)	HR	1·66 (0·84-3·29)	Yes
	Age 24 to 36 months (ref: age 48 to 60 months)	HR	1·38 (0·76-2·49)	Yes
	Age 12 to 24 months (ref: age 48 to 60 months)	HR	1·57 (0·89-2·78)	Yes
	Age <12 months (ref: age 48 to 60 months)	HR	2·49 (1·38-4·51)	Yes

Author	Risk factor	Effect Measure	EM (95% CI)	Adjusted
	Oedema (ref: no oedema)	HR	0·58 (0·47-0·72)	Yes
	MUAC per cm increase	HR	0·80 (0·74-0·86)	Yes
	weight-for-height (per 1-unit z-score increase)	HR	0·75 (0·68-0·83)	Yes
	Weight for age (per 1-unit z-score increase)	HR	0·73 (0·66-0·81)	Yes
	height for age z-score (per 1-unit z-score increase)	HR	0·92 (0·86-0·99)	Yes
	HIV Positive (ref: HIV negative)	HR	4·03 (3·08-5·25)	Yes
	HIV status unknown (ref: HIV negative)	HR	16·9 (12·1-23·7)	Yes
Chhibber[7]	Sepsis with clinically severe malnutrition (ref: pneumonia without clinically severe malnutrition)	HR	18·4 (11·3-30·0)	Yes
	Meningitis with clinically severe malnutrition (ref: pneumonia without clinically severe malnutrition)	HR	13·7 (4·2-44·7)	Yes
	Pneumonia with clinically severe malnutrition (ref: pneumonia without clinically severe malnutrition)	HR	8·1 (4·4-14·8)	Yes
	Meningitis without clinically severe malnutrition (ref: pneumonia without clinically severe malnutrition)	HR	2·6 (1·2-5·5)	Yes
	Sepsis without clinically severe malnutrition (ref: pneumonia without clinically severe malnutrition)	HR	2·2 (1·1-4·3)	Yes
	Age in months (mean [SD])	HR	1·00 (0·98-1·03)	Yes
	Neck stiffness (ref: no neck stiffness)	HR	10·4 (3·1-34·8)	Yes
	Non-medical discharge (i.e. discharge against medical advice) (ref: medical discharge)	HR	4·68 (2·01-10·85)	Yes
	Axillary temperature (°C) (mean [SD])	HR	0·71 (0·58-0·87)	Yes
	Oxygen saturation (% increase)	HR	0·96 (0·93-0·99)	Yes
	Hb in g/dL (mean [SD])	HR	0·82 (0·73-0·91)	Yes
	MUAC 11.5–13.0 cm (ref: MUAC>13cm)	HR	7·19 (3·04-17·01)	Yes
	MUAC 10.5–11.4 cm (ref: MUAC>13cm)	HR	24·2 (9·4-61.9)	Yes
	MUAC <10.5 cm (ref: MUAC>13cm)	HR	43·7 (17·7-108)	Yes

Author	Risk factor	Effect Measure	EM (95% CI)	Adjusted
Veirum[18]	Discharge age 5 years+ (ref: 1-12 months)	RR	0·15 (0·05-0·30)	Yes
	Discharge age 4 years (ref: 1-12 months)	RR	0·23 (0·09-0·48)	Yes
	Discharge age 3 years (ref: 1-12 months)	RR	0·14 (0·04-0·39)	Yes
	Discharge age 2 years (ref: 1-12 months)	RR	0·52 (0·25-0·76)	Yes
	Discharge age 1 year (ref: 1-12 months)	RR	0·82 (0·67-1·41)	Yes
	Neonatal (ref: 1-12 months)	RR	0·69 (0·21-1·77)	Yes
	Mothers' education (ref: no education)	RR	0·74 (0·56-1·14)	Yes
	Non-medical discharge (against medical advice) (ref: medical discharge)	RR	8·51 (5·32-13·59)	Yes
	Other (ref: malaria)	RR	1·65 (1·02-2·92)	Yes
	Anaemia (ref: malaria)	RR	1·97 (0·97-4·00)	Yes
	Diarrhoea (ref: malaria)	RR	1·82 (0·83-2·35)	Yes
	Bronchopneumonia (ref: malaria)	RR	0·98 (0·66-1·74)	Yes
	Measles (ref: malaria)	RR	0·77 (0·43-2·22)	Yes
Hue et al[26]	Age 5 – 12 years (ref: <5 years)	HR	1·75 (1·15 – 2·68)	No
	Age 5-12 years (ref: <5 years)	HR	1·01 (1·00-1·01)	Yes
	Pit latrine at home (ref: none)	HR	1·58 (1·00-2·50)	No
	Sex (ref: female)	HR	0·84 (0·55-1·28)	No
	Lake or pond as a water source (ref: no)	HR	1·10 (0·71-1·69)	No
	HIV Status (HIV negative)	HR	1·38 (0·60-3·16)	No
	Decreased urine output (ref: no)	HR	4·95 (2·83-8·66)	No
	Diarrhoea (ref: no diarrhoea)	HR	0·11 (0·39-1·11)	No
	Fever (ref: none)	HR	0·86 (0·54-1·36)	No
	Vomiting (ref: none)	HR	1·02 (0·63-1·63)	No
	Oxygen saturation: per % increase	HR	0·93 (0·91-0·95)	No
	Oxygen saturation: per % increase	HR	0·93 (0·89-0·98)	Yes

Author	Risk factor	Effect Measure	EM (95% CI)	Adjusted
	Glasgow coma scale 13-14 (ref: <13)	HR	0·66 (0·60-0·73)	No
	Bilateral lower extremity oedema (ref: none)	HR	2·31 (1·40-3·81)	No
	Respiratory Rate-bpm (per unit increase) 2-5 years	HR	1·04 (1·02-1·06)	No
	Respiratory Rate-bpm (per unit increase) 6-12 years	HR	1·02 (1·00-1·04)	No
	Diastolic blood pressure, mean mm Hg (per unit increase) 2-5 years	HR	0·99 (0·96-1·02)	No
	Diastolic blood pressure, mean mm Hg (per unit increase) 6-12 years	HR	0·94 (0·91-0·98)	No
	Heart rate, beats per minute, mean (SD) (per unit increase) 2-5 years	HR	1·00 (0·99-1·02)	No
	Heart rate, beats per minute, mean (SD) (per unit increase) 6-12 years	HR	1·01 (0·99-1·02)	No
	Systolic blood pressure, mean mm Hg (per unit increase) 2-5 years	HR	1·00 (0·98-1·02)	No
	Systolic blood pressure, mean mm Hg (per unit increase) 6-12 years	HR	0·97 (0·95-1·00)	No
	Severe Malnutrition (ref: normal)	HR	1·49 (0·83-2·70)	No
	Moderate Malnutrition (ref: normal)	HR	1·07 (0·57-1·98)	No
	Mild Malnutrition (ref: normal)	HR	0·99 (0·55-1·77)	No
	Temperature, Celsius, mean (SD)	HR	1·05 (0·84-1·30)	No
	Hb level, g/dL, mean (SD) (per unit increase)	HR	0·82 (0·75-0·88)	No
	Hb level, g/dL, mean (SD) (per unit increase)	HR	0·79 (0·70-0·88)	Yes
	Proteinuria by urinalysis (ref: none)	HR	2·38 (1·51-3·74)	No
	Proteinuria by urinalysis (ref: none)	HR	2·13 (1·12-4·05)	Yes
	Haematuria by urinalysis (ref: none)	HR	2·81 (1·35-5·81)	No
	Glomerular filtration rate < 60 ml/min/1.73m2 (ref: no)	HR	1·91 (1·21-3·02)	No
	Random blood glucose, mg/dL, mean (SD) (per unit increase)	HR	0·98 (0·90-1·05)	No
	Cancer (ref: respiratory infections & malaria)	HR	11·79 (4·95-28·03)	No
	Heart disease (ref: respiratory infections & malaria)	HR	7·11 (2·89-17·51)	No
	Sickle cell disease (ref: respiratory infections & malaria	HR	3·32 (1·44-7·68)	No
	Neurologic diseases (ref: respiratory infections & malaria)	HR	3·51 (1·35-9·11)	No

Author	Risk factor	Effect Measure	EM (95% CI)	Adjusted
	Septic shock (ref: respiratory infections & malaria)	HR	4·64 (1·42-15·08)	No
	Severe malnutrition (ref: respiratory infections & malaria)	HR	3·19 (1·18-8·57)	No
	Anaemia (ref: respiratory infections & malaria)	HR	2·03 (0·75-5·46)	No
	Diarrheal diseases (ref: respiratory infections & malaria)	HR	1·94 (0·75-5·04)	No
	Diarrheal diseases (ref: respiratory infections & malaria)	HR	0·49 (0·20-1·17)	Yes
	Other (ref: respiratory infections & malaria)	HR	1·96 (0·73-5·27)	No
	Decreased urine output (ref: no)	HR	4·95 (2·83-8·66)	No
	Diarrhoea (ref: no diarrhoea)	HR	0·114 (0·39-1·11)	No
	Fever (ref: none)	HR	0·86 (0·54-1·36)	No
	Vomiting (ref: none)	HR	1·02 (0·63-1·63)	No
Madrid et al[13]	Age 4 to < 1 year (ref: <3 months)	HR	0·86 (0·70 –1·06)	No
	Age 1 to 5 years (ref: <3 months)	HR	0·50 (0·41-0·60)	No
	Age >5 years (ref: <3 months)	HR	0·35 (0·26-0·46)	No
	Female sex	HR	1·01 (0·89-1·15)	No
	Rainy season	HR	1·16 (1·02-1·33)	No
	Weight for height *z* score (mean ± SD)	HR	0·63 (0·57-0·69)	No
	WHZ *z* score, SD (ref:>-1): >−2 to <−1	HR	1·34 (0·88-2·04)	No
	WHZ *z* score, SD (ref:>-1): >−3 to <−2	HR	2·42 (1·58-3·71)	No
	WHZ *z* score, SD (ref:>-1): >−3	HR	5·94 (4·12-8·57)	No
	History of fever	HR	0·54 (0·45-0·64)	No
	History of cough	HR	1·78 (1·53-2·06)	No
	History of diarrhoea	HR	2·36 (2·06-2·69)	No
	History of vomiting	HR	1·32 (1·15-1·52)	No
	History of difficulty in breathing	HR	1·81 (1·58-2·08)	No
	History of anorexia	HR	1·79 (1·46-2·20)	No

Author	Risk factor	Effect Measure	EM (95% CI)	Adjusted
	History of blood in urine	HR	1·43 (0·59-3·44)	No
	History of seizures	HR	0·37 (0·27-0·51)	No
	Axillary temperature <35.5 (ref: 35.5^{0}C-37.4^{0}C)	HR	1·31 (0·90-1·89)	No
	Axillary temperature >37.5 (ref: 35.5^{0}C-37.4^{0}C)	HR	0·67 (0·59-0·77)	No
	Bradycardia	HR	1·10 (0·87-1·40)	No
	Tachycardia	HR	1·05 (0·90-1·21)	No
	Increased respiratory rate	HR	1·37 (1·20-1·57)	No
	Dehydration	HR	2·04 (1·77-2·37)	No
	Pallor	HR	0·90 (0·75-1·07)	No
	Jaundice	HR	0·88 (0·33-1·32)	No
	Oedema (any location)	HR	2·96 (2·46-3·57)	No
	Skin flaking off	HR	2·90 (2·15-3·90)	No
	Depigmented or reddish hair	HR	5·30 (4·55-6·18)	No
	Oral candidiasis	HR	7·44 (6·08-9·09)	No
	Swollen lymph nodes	HR	4·33 (3·56-5·25)	No
	Conjunctivitis	HR	1·62 (1·08-2·43)	No
	Ear discharge	HR	2·59 (1·98-3·38)	No
	Lower chest wall indrawing	HR	1·73 (1·51-1·99)	No
	Nasal flaring	HR	1·48 (1·27-1·73)	No
	Pathologic breathing pattern	HR	1·50 (1·14-1·97)	No
	Auscultatory crackles	HR	2·02 (1·77-2·31)	No
	Wheeze and/or rhonchus	HR	1·15 (0·96-1·39)	No
	Hepatomegaly	HR	1·57 (1·14-2·18)	No
	Splenomegaly	HR	0·69 (0·58-0·82)	No
	Blantyre coma scale (3-4): (ref:5)	HR	1·26 (0·91-1·73)	No

Author	Risk factor	Effect Measure	EM (95% CI)	Adjusted
	Blantyre coma scale (≤2): (ref:5)	HR	1·57 (1·03-2·41)	No
	Malaria positive test: (ref: negative test)	HR	0·26 (0·22-0·31)	No
	Malaria test not done: (ref: negative test)	HR	0·61 (0·51-0·74)	No
	Hypoglycaemia (<2.5): (ref: 2.5-11.0)	HR	0·92 (0·73-1·15)	No
	Hyperglycaemia (>11.0): (ref: 2.5-11.0)	HR	0·78 (0·60-1·03)	No
	Blood culture result positive: (ref: negative)	HR	3·32 (2·77-3·98)	No
	Anaemia mild to moderate: (ref: no anaemia)	HR	1·00 (0·87-1·15)	No
	Anaemia severe: (ref: no anaemia)	HR	1·04 (0·84-1·28)	No
	HIV status negative (ref: test not done)	HR	0·55 (0·37-0·82)	No
	HIV status positive (ref: test not done)	HR	4·97 (3·59-6·88)	No
	Absconded from hospital	HR	8·18 (6·87-9·74)	No
	Transferred to another hospital	HR	6·30 (5·12-7·75)	No
Talbert et al[24]	Age (months)	HR	1·00 (0·97-1·02)	No
	Sex (female): (ref: male)	HR	1·12 (0·64-1·96)	No
	Prior hospital admission: (ref: no prior hospitalization)	HR	4·71 (2·66-8·32)	No
	Prior hospital admission: (ref: no prior hospitalisation)	HR	3·11 (1·57-6·17)	Yes
	Persistent diarrhoea	HR	3·51 (1·11-11·13)	No
	Bloody diarrhoea	HR	0·90 (0·12-6·46)	No
	Some dehydration: (ref: no dehydration)	HR	0.90 (0.40-2.04)	No
	Severe dehydration: (ref: no dehydration)	HR	1·92 (1·02-3·61)	No
	Tachypnoea: (ref: no tachypnoea)	HR	1·50 (0·83-2·68)	No
	Tachycardia: ref: no tachycardia)	HR	0·95 (0·53-1·68)	No
	Lower chest wall indrawing: (ref: no lower chest wall indrawing)	HR	2·90 (1·59-5·26)	No
	Lower chest wall indrawing: (ref: no lower chest wall indrawing)	HR	2·00 (1·03-3·79)	Yes
	Hypoxia (SaO2 < 90%): (ref: SaO2 ≥90%)	HR	2·03 (0·49-8·34)	No

Author	Risk factor	Effect Measure	EM (95% CI)	Adjusted
	Capillary refill > 2 s: (ref: Capillary refill ≤2 seconds)	HR	3·16 (1·35-7·43)	No
	Temperature gradient: (ref: no temperature gradient)	HR	1·85 (0·83-4·12)	No
	Impaired consciousness: (ref: normal conscious level)	HR	2·75 (1·17-6·45)	No
	HIV antibody positive: (ref: HIV antibody negative)	HR	13·76 (7·60-24·91)	No
	HIV antibody positive: (ref: HIV antibody negative)	HR	5·02 (2·31-10·92)	Yes
	Bacteraemia (ref: no bacteraemia)	HR	5·41 (2·27-12·89)	No
	Bacteraemia: (ref: no bacteraemia)	HR	3·69 (1·64-10·14)	Yes
	Malaria slide positive: (ref: malaria slide negative)	HR	0·48 (0·47-4·93)	No
	Severe anaemia (Hb < 5 g/dL)	HR	4·20 (1·78-9·90)	No
	MUAC per centimetre	HR	0·55 (0·47-0·64)	No
	MUAC per centimetre	HR	0·67 (0·56-0·81)	Yes
	Height-for-age z score	HR	0·62 (0·52-0·73)	No
Ngari 2020[25]	Weak pulse: (ref: normal pulse)	HR	3·54 (1·64-7·64)	Yes
	HIV positive: (ref: HIV negative)	HR	3·06 (1·69-5·54)	Yes
	Malaria positive: (ref: malaria negative)	HR	0·43 (0·20-0·93)	Yes
	Moderate anaemia: (ref: no anaemia)	HR	1·38 (0·73-2·61)	Yes
	Severe anaemia: (ref: no anaemia)	HR	2·34 (1·18-4·63)	Yes
	MUAC-for-age Z score -3 to -2: (ref: ≥-2)	HR	1·66 (0·95-2·91)	Yes
	MUAC-for-age Z score <-3: (ref: ≥-2)	HR	3·74 (2·24-6·25)	Yes
Bwakura-Dangarembizi 2021[27]	Sex (male): (ref: female)	HR	1·15 (0·67-1·97)	Yes
	HIV Positive: (ref: Negative)	HR	3·83 (2·15-6·82)	Yes
	Nonoedematous SAM: (ref: oedematous SAM)	HR	2·23 (1·24-4·01)	Yes
	SAM at discharge: (ref: no SAM at discharge)	HR	2·28 (1·22-4·25)	Yes

Author	Risk factor	Effect Measure	EM (95% CI)	Adjusted
	Cerebral palsy: (ref: no Cerebral palsy)	HR	5·60 (2·72-11·50)	Yes
Mukasa 2021[14]	Less poor households: (ref: Least Poor households)	HR	0.55 (0·22-1·37)	No
	Poor households: (ref: Least Poor households)	HR	1·04 (0·48-2·24)	No
	Very poor households: (ref: Least Poor households)	HR	1·13 (0·52-2·44)	No
	Poorest households: (ref: Least Poor households)	HR	0·88 (0·34-2·29)	No
	Anemia: (ref: Malaria)	HR	0·89 (0·37-2·22)	No
	Pneumonia: (ref: Malaria)	HR	1·20 (0·41-3·43)	No
	Diarrhoea: (ref: Malaria)	HR	0·57 (0·16-2·09)	No
	Others: (ref: Malaria)	HR	0·65 (0·31-1·34)	No
	Proximity to hospital, 25‑ < 50 Km: (ref: <25Km)	HR	0·92 (0·43-2·01)	No
	Proximity to hospital, 50‑ < 75 Km: (ref: <25Km)	HR	1·48 (0·68-3·23)	No
	Proximity to hospital, ≥ 75 Km: (ref: <25Km)	HR	3·55 (1·77-7·11)	No

HR=hazard ratio. MUAC=mid-upper arm circumference. SD=standard deviation. Hb=haemoglobin. HIV=human immunodeficiency virus. g/dL=grams per decilitre. mg/dl=milligrams per decilitre. SaO_2<90%=arterial blood oxygen saturation less than 90%. SpO_2, oxygen saturation as detected by the pulse oximeter

Table S8: PRISMA checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review=meta-analysis, or both.	**Error! Bookmark not defined.**
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	**Error! Bookmark not defined.**
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	**Error! Bookmark not defined.** and **Error! Bookmark not defined.**
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	**Error! Bookmark not defined.**
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	**Error! Bookmark not defined.**
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving a rationale.	**Error! Bookmark not defined.**
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	**Error! Bookmark not defined.** and **Error! Bookmark not defined.**
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	S3

Section/topic	#	Checklist item	Reported on page #
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in a systematic review, and, if applicable, included in the meta-analysis).	**Error! Bookmark not defined.**
Data collection process	10	Describe the method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	**Error! Bookmark not defined.**
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	**Error! Bookmark not defined.**, S3
Risk of bias in individual studies	12	Describe methods used for assessing the risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	**Error! Bookmark not defined.**
Summary measures	13	State the principal summary measures (e.g., risk ratio, the difference in means).	**Error! Bookmark not defined.**
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	**Error! Bookmark not defined.**
Risk of bias across studies	15	Specify any assessment of the risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	NA
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	**Error! Bookmark not defined.**
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	**Error! Bookmark not defined.** and, Figure 1
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	Table S1
Risk of bias within studies	19	Present data on the risk of bias of each study and, if available, any outcome level assessment (see item 12).	Table S2, Table S3 Table S4 and Table S5
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	Figure 2, Figure 3, Figure 4, Figure S1, Figure S2, Figure S3,

Section/topic	#	Checklist item	Reported on page #
			Figure S4, Figure S5 , Figure S6, Figure S7, Figure S8
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	Figure 2, Figure 3, Figure 4, Figure S1, Figure S2, Figure S3, Figure S4, Figure S5 , Figure S6, Figure S7, Figure S8
Risk of bias across studies	22	Present results of any assessment of the risk of bias across studies (see Item 15).	NA
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	**Error! Bookmark not defined.**
DISCUSSION			
Summary of evidence	24	Summarise the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policymakers).	**Error! Bookmark not defined.** to **Error!**
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	**Error! Bookmark not defined.**
Conclusions	26	Provide a general interpretation of the results in the context of other evidence and implications for future research.	**Error! Bookmark not defined.**
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., the supply of data); the role of funders for the systematic review.	**Error! Bookmark not defined.** and **Error!**

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