Table S1. Inclusion and exclusion criteria for study enrollment by study group

Study group	Inclusion criteria	Exclusion criteria
1. Cerebral malaria (CM)	Coma that is: 1. Unarousable (Blantyre coma score ≤ 2) 2. Not responsive to a glucose bolus one hour after administration if hypoglycemic 3. Lasts at least one hour after termination of seizure or after administration of first line anticonvulsants 4. Has no other known cause – normal cerebral spinal fluid test results	Previous history of: 1. Head trauma or coma 2. Hospitalization for malnutrition 3. Cerebral palsy or other severe neurologic disease prior to episode of CM 4. Known chronic illness requiring medical care
2. Respiratory distress syndrome (RDS)	1. Age-related tachypnea with sustained nasal flaring, deep acidotic breathing or lower chest wall retractions 2. No crepitations on pulmonary examination	1. Same as for CM 2. Meeting inclusion criteria for CM (would be included as CM)
3. Malaria with complicated seizures (MS)	1. Two or more generalized seizures in 24 hours, or 2. Seizure lasting > 30 minutes in duration	1. Same as for CM, plus: 2. Meeting inclusion criteria for CM or respiratory distress (would be included in respective category)
4. Severe malarial anemia (SMA)	1. Serum hemoglobin ≤ 5 g/L	1. Same as for CM, plus: 2. Impaired consciousness on physical exam 3. Meeting inclusion criteria for CM, RDS or MS (would be included in respective category)
5. Prostration (Pros)	1.Unable to sit unsupported or stand although able to before the illness (if 1 year and older) 2. Unable to drink or breastfeed (if <1 year)	1. Same as for CM, plus: 2. Meeting inclusion criteria for CM or RDS or MS or SMA (would be included in respective category)
6. Community children (CC)	1. Children from the neighborhood, extended household or nearby neighborhood of a child with SM 2. Aged between 6 months and 4 years of age	1. Same as for CM, plus: 2. Any illness within the past 4 weeks requiring medical care 3. Medical abnormalities on physical examination 4. Measured temperature of ≥ 37.5 ^{0}C

Table S2. Incidence and risk of study outcomes between children blood smear positive for *P. falciparum* and community children

Outcome	CC (N=120)	SM BS+ (N=401)	CC	SM BS+	Crude HR (95% CI)	P value	Adjusted HR (95% CI)	P value
	no. of children		no. of events (incidence rate per 100 py)					
Hospitalization for any reason	37	225	61 (54.1)	457 (125.4)	1.85 (1.34-2.53)	<0.001	1.87 (1.34-2.62)	<0.001
Death from any cause	1	11	1 (0.88)	11 (3.0)	3.40 (0.44-26.33)	0.24	2.00 (0.21-18.76)	0.54
Hospitalization for severe malaria	30	197	50 (44.3)	379 (103.7)	1.88 (1.33-2.67)	<0.001	1.94 (1.33-2.82)	0.001
Hospitalization for severe malarial anemia or severe anemia	0	30	0 (0)	56 (15.2)	--	--	--	--
Hospitalization for severe malarial anemia	0	27	0 (0)	49 (13.3)	--	--	--	--
Hospitalization for severe anemia	0	4	0 (0)	7 (1.9)	--	--	--	--
Hospitalization for other reasons	10	56	11 (9.7)	71 (19.3)	1.85 (1.01-3.41)	0.048	1.74 (0.92-3.30)	0.09
Clinic visit for any illness	93	279	318 (281.1)	839 (227.7)	1.00 (0.87-1.14)	0.97	0.98 (0.74-1.31)	0.92
Clinic visit for uncomplicated malaria	37	126	62 (54.8)	198 (53.7)	1.25 (0.92-1.70)	0.16	1.28 (0.89-1.82)	0.18
Clinic visit for illness unrelated to malaria	80	243	256 (226.3)	641 (174.0)	0.99 (0.85-1.15)	0.93	0.99 (0.83-1.16)	0.87

Hazard ratios (HR) and 95% confidence intervals (CI) from PWP-TT models for each recurrent outcome. Covariates in the adjusted models included age, study site, height-for-age and weight-for-age z-scores, presence of HIV infection, sickle cell genotype and socioeconomic status at enrollment.
Abbreviations: SM, severe malaria; BS+, blood smear positive; CC, community children; HR, hazard ratio; CI, confidence interval.

Table S3. Incidence and risk of study outcomes between children with severe malaria and community children blood smear negative for *P. falciparum*

Outcome	CC BS- (N=107)	SM (N=551)	CC BS-	SM	Crude HR (95% CI)	P value	Adjusted HR (95% CI)	P value
	no. of children		no. of events (incidence rate per 100 py)					
Hospitalization for any reason	33	312	53 (52.64)	700 (140.48)	2.02 (1.47-2.77)	<0.001	1.90 (1.36-2.66)	<0.001
Death from any cause	1	23	1 (0.99)	23 (4.56)	4.64 (0.63-34.33)	0.13	2.71 (0.33-22.50)	0.36
Hospitalization for severe malaria	26	271	42 (41.68)	575 (115.12)	2.05 (1.43-2.95)	<0.001	1.97 (1.33-2.90)	0.001
Hospitalization for severe malarial anemia or severe anemia	0	60	0 (0)	116 (23.08)	--	--	--	--
Hospitalization for severe malarial anemia	0	55	0 (0)	102 (20.29)	--	--	--	--
Hospitalization for severe anemia	0	9	0 (0)	14 (2.78)	--	--	--	--
Hospitalization for other reasons	10	85	11 (10.90)	111 (22.07)	1.88 (1.04-3.39)	0.04	1.75 (0.97-3.18)	0.07
Clinic visit for any illness	85	375	286 (283.25)	1062 (210.74)	0.97 (0.85-1.11)	0.69	1.08 (0.81-1.43)	0.60
Clinic visit for uncomplicated malaria	31	171	51 (50.51)	261 (51.79)	1.29 (0.93-1.79)	0.12	1.30 (0.92-1.86)	0.14
Clinic visit for illness unrelated to malaria	76	323	240 (237.70)	801 (158.95)	0.96 (0.82-1.11)	0.58	0.98 (0.83-1.16)	0.80

Hazard ratios (HR) and 95% confidence intervals (CI) from adjusted PWP-TT models for each recurrent outcome. Covariates in the adjusted models included age, study site, height-for-age and weight-for-age z-scores, presence of HIV infection, sickle cell genotype and socioeconomic status at enrollment.

Abbreviations: SM, severe malaria; CC, community children; BS-, blood smear negative; HR, hazard ratio; CI, confidence interval.

Table S4. Distribution of severe malaria manifestations and community children according to study site

Group	Study site	
	Kampala (N=374)	Jinja (N=297)
Children with severe malaria	307 (82.1)	244 (82.2)
CM	33 (8.8)	20 (6.7)
RDS	47 (12.6)	61 (20.5)
MS	95 (25.4)	65 (21.9)
SMA	97 (25.9)	58 (19.5)
Pros	35 (9.4)	40 (13.5)
Community children	67 (17.9)	53 (17.9)

Abbreviations: CM, cerebral malaria; RDS, respiratory distress syndrome; MS, multiple seizures; SMA, severe malarial anemia; Pros, prostration.
Data presented as n (%) within study site.

Table S5. Interaction between study site and SM across study outcomes

Outcome	Interaction term: Jinja × SM	
	aHR (95% CI)[a]	P value
Hospitalization for any reason	1.12 (0.58-2.17)	0.74
Death from any cause†	--	--
Hospitalization for severe malaria	1.12 (0.52-2.42)	0.77
Hospitalization for severe malarial anemia or severe anemia	--	--
Hospitalization for severe malarial anemia	--	--
Hospitalization for severe anemia	--	--
Hospitalization for other reasons	1.31 (0.65-1.03)	0.66
Clinic visit for any illness	1.04 (0.79-1.37)	0.77
Clinic visit for uncomplicated malaria	0.38 (0.98-1.45)	0.052
Clinic visit for illness unrelated to malaria	1.05 (0.78-1.43)	0.74

Abbreviations: SM, severe malaria; aHR, adjusted hazard ratio; CI, confidence interval; DNC, did not converge.
[a] Adjusted hazard ratios (aHR) obtained from PWP-TT analysis for each recurring outcome in which study site and SM group were interacted net of age, height-for-age and weight-for-age z-scores, presence of HIV infection, sickle cell genotype and socioeconomic status at enrollment. HR >1 indicates greater effect in Jinja, while HR <1 indicates greater effect in Kampala, when $p<0.05$.
† Estimate for interaction term did not converge likely due to only one death among CC (Jinja).

Table S6. Interaction between age and SM across study outcomes

Outcome	Interaction term: Age × SM	
	aHR (95% CI)[a]	P value
Hospitalization for any reason	1.19 (0.89-1.61)	0.25
Death from any cause†	--	--
Hospitalization for severe malaria	1.09 (0.79-1.50)	0.59
Hospitalization for severe malarial anemia or severe anemia	--	--
Hospitalization for severe malarial anemia	--	--
Hospitalization for severe anemia	--	--
Hospitalization for other reasons	2.18 (1.01-4.72)	0.048
Clinic visit for any illness	1.07 (0.93-1.24)	0.33
Clinic visit for uncomplicated malaria	0.95 (0.70-1.27)	0.72
Clinic visit for illness unrelated to malaria	1.19 (1.03-1.38)	0.02

Abbreviations: SM, severe malaria; aHR, adjusted hazard ratio; CI, confidence interval; DNC, did not converge.
[a] Adjusted hazard ratios (aHR) obtained from PWP-TT analysis for each recurring outcome in which age at enrollment and SM group were interacted net of study site, height-for-age and weight-for-age z-scores, presence of HIV infection, sickle cell genotype and socioeconomic status at enrollment. HR >1 indicates greater effect in Jinja, while HR <1 indicates greater effect in Kampala, when $p<0.05$.
† Estimate for interaction term did not converge likely due to only one death among CC (age 1.1 years).

Table S7. Risk of hospitalizations, death or outpatient and clinic visits among children with severe malaria compared to community children according to treatment of missing covariate data: multiple imputation vs. listwise deletion

Outcome	Multiple imputation (N=671)[a]		Listwise deletion (N=601)[b]	
	aHR (95% CI)[c]	P value	aHR (95% CI)[c]	P value
Hospitalization for any reason	1.91 (1.39-2.63)	<0.001	1.87 (1.34-2.60)	<0.001
Death from any cause	2.98 (0.36-24.82)	0.31	2.15 (0.22-20.74)	0.51
Hospitalization for severe malaria	1.94 (1.36-2.78)	<0.001	1.92 (1.33-2.79)	0.001
Hospitalization for severe malarial anemia or severe anemia	--	--	--	--
Hospitalization for severe malarial anemia	--	--	--	--
Hospitalization for severe anemia	--	--	--	--
Hospitalization for other reasons	1.93 (1.05-3.54)	0.03	1.80 (0.95-3.39)	0.07
Clinic visit for any illness	0.98 (0.85-1.13)	0.75	1.00 (0.86-1.16)	0.99
Clinic visit for uncomplicated malaria	1.24 (0.89-1.73)	0.20	1.35 (0.95-1.93)	0.09
Clinic visit for illness unrelated to malaria	0.98 (0.83-1.16)	0.83	1.00 (0.85-1.19)	0.96

Abbreviations: aHR, adjusted hazard ratio; SM, severe malaria; CC, community children.

[a] SM, N=551; CC, N=120

[b] SM, N=492; CC, N=120

[c] Compares children with SM to CC (reference) using PWP-TT analysis for recurrent events adjusted for age, height-for-age and weight-for-age z-scores, presence of HIV infection, sickle cell genotype and socioeconomic status at enrollment