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Inpatient and post-discharge mortality among young infants in rural Kenya.

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1 Inpatient and post-discharge mortality among young infants in rural 2 Kenya.

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17 Word count 3810

18 Abstract

19 **Objectives:** to describe admission trends and measure inpatient and post-discharge mortality
20 and its associated exposures, among young infants (YI) admitted to a county hospital in Kenya

21 **Design:** retrospective cohort study

22 **Setting:** secondary level hospital

23 **Participants:** YI aged less than 60 days admitted to hospital January 2009 to December 2019:
24 12,271 admissions in 11,877 individuals. YI who were resident within a health and
25 demographic surveillance system (KHDSS) ; were followed up for 1 year after discharge.

26 **Primary and secondary outcome measures:** Inpatient and 1 year post-discharge mortality

27 **Results:** Of 12,271 YI admissions, 4,421 (36%) were KHDSS-resident. Neonatal sepsis, preterm
28 complications and birth asphyxia accounted for 83% of admissions. The proportion of YI among
29 under-fives admissions increased from 19% in 2009 to 34% in 2019 ($P_{\text{trend}}=0.02$). Inpatient case
30 fatality was 16%, with 66% of deaths occurring within 48 hours of admission. The introduction
31 of free maternity care in 2013 was not associated with a change in admissions or inpatient
32 mortality among YI. During 1-year post-discharge, 208/3625 (5.7%) YI died, 64.3 (95%CI 56.2–
33 73.7) per 1,000 infant-years; 49% of post-discharge deaths occurred within one month of
34 discharge, and 49% of post-discharge deaths occurred at home. Both inpatient and post-
35 discharge deaths were associated with low weight. Inpatient mortality was associated with
36 clinical signs of disease severity, while post-discharge mortality was associated with length of
37 hospitalization, leaving against advice and referral to a specialized hospital.

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3 38 **Conclusions:** Young infants accounted for an increasing proportion of paediatric admissions and
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6 39 inpatient deaths. The post-discharge mortality rate of YI is more than twice that of children aged
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8 40 2-59 months. The proportion of deaths occurring post-discharge is lower than among older
9
10 41 children, but similarly, almost half of post-discharge deaths occur in the first month, and half
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12
13 42 occurred at home.

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15 43 **Key words**

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19 44 Young infant; mortality; inpatient; post-discharge; Africa; Kenya
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22 45 290 words
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10 **Article summary**11
12 **Strengths and limitations of this study**

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- 15 62
- Large sample size with systematic collection of data
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- 17 63
- Linkage to a well-established demographic surveillance system, with few losses to follow
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- 19 up.

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- 22 65
- Lack of accurate gestational age estimation and unknown birthweight of most
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- 24 participants.

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- 27 67
- Data are from a single hospital
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70 Background

71 The United Nations Sustainable Development Goal 3 aims to ensure healthy living and promote
72 wellbeing for all ages, with all countries aiming to reduce neonatal and under-five mortality to
73 below 12 and 25 per 1,000 live births by 2030 respectively. In sub-Saharan Africa, child mortality
74 has declined by ~58% in the last 30 years. However, the estimated neonatal and under-five
75 mortality rates in sub-Saharan Africa remained high in 2019 (27 and 76 per 1,000 live births
76 respectively) with a similar neonatal mortality rate of 27 per 1,000 live births in Kenya.(1)
77 Combined neonatal and post-neonatal infant mortality accounts for over three quarters of all
78 under-five deaths in Kenyan children.(2)

79 Young infants aged <60 days old (YI) comprise around half of hospital admissions in sub-Saharan
80 Africa and continue to face high risk of in-hospital mortality and long-term neuro-disability.(3-6)
81 Post-discharge mortality is emerging as a major problem in children in low- and middle-income
82 countries (LMICs),(7) however, there are limited data among YI. A systematic review of paediatric
83 post-discharge mortality in developing countries included 24 studies published up to July 2017
84 with 19 from Africa.(8) Four studies included YI. Although young age was reported as a risk factor
85 of mortality, no studies specifically identified deaths among infants aged <60 days. We have
86 previously demonstrated excess post-discharge mortality among all hospitalised children,
87 suggesting that hospitalisation itself selects vulnerable children with a sustained increased risk
88 of dying over the longer term.(7, 9)

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3 89 Better understanding of YI deaths occurring during hospitalisation and after discharge from
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6 90 hospital is vital for development and use of targeted interventions aimed at improving survival.
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9 91 This analysis aimed to describe admission trends and measure inpatient and post-discharge
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11 92 mortality and its associated exposures, including the introduction of free maternity care, among
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14 93 YI admitted to Kilifi County Hospital (KCH), Kenya and followed up through the Kilifi Health and
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16 94 Demographic Surveillance System (KHDSS).
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96 **Methods**

97 Study participants and design

98 KCH is a secondary-level referral hospital situated in Kilifi county along the Kenyan coast. It serves
99 a rural and peri-urban population. It has a maternity unit. with approximately 6,000 deliveries
100 per year, a general paediatric ward with a newborn unit for babies aged less than 1 month, and
101 a paediatric High Dependency Unit (HDU) that also admits YIs. The year 2009 was selected as a
102 starting point, because a previous analysis of mortality among YI covered admissions from 1990
103 to 2008(10). Free maternity care was introduced by the Kenyan government on 1st June 2013 and
104 led to a marked increase in health facility births.(11)

105 The KHDSS, established in 2002, covers a population of 279,158 within an area of 900km² centred
106 on KCH.(12) Census rounds visit each household every four months to ascertain vital status and
107 migration in and out of the hospital catchment area.

108 We conducted a retrospective cohort study of YIs resident within the KHDSS who were admitted
109 to KCH between January 1st, 2009 and December 31st, 2019. Children discharged alive and
110 followed up in KHDSS census rounds until March 2021 were eligible for analyses of post-discharge
111 mortality. During the study period, there were 9 health workers' strikes with the last nurses'
112 strike lasting for 150 days (5 June to 2 November 2017).(13) **Supplementary Table S1.** For
113 comparison, we also examined admissions aged 60 days to 59 months during the same period.

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3 115 Procedures
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7 116 At admission, standardised medical history, and clinical examination, including anthropometric
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9 117 measurements were obtained by trained clinical staff. Blood samples were systematically taken
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11 118 for complete blood count, slide for malaria microscopy, and clinical chemistry, Human
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13 119 Immunodeficiency Virus (HIV) antibody test and blood culture at hospital admission, as described
14
15 120 previously.(14) A lumbar puncture for cerebrospinal fluid (CSF) analysis was done at admission in
16
17 121 infants in whom sepsis was suspected and deferred in those seriously ill or with other
18
19 122 contraindications. Clinical and laboratory data were recorded in real time on a ward surveillance
20
21 123 database linked to the KHDSS database. Empiric antibiotics were initiated according to national
22
23 124 guidelines(15) with ampicillin/benzylpenicillin plus gentamicin as first-line intravenous therapy.
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25 125 Second-line and subsequent antimicrobial therapy was guided by blood culture results and
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27 126 clinical progress. Mechanical ventilation was not available at KCH.
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34 127 Statistical methods
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37 128 *Study variables*
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41 129 Outcomes of interest were death in hospital and during 1 year after discharge. Exposures of
42
43 130 interest were demographic, nutritional, clinical features, and haematological, biochemical, and
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45 131 microbiological findings at the time of admission. De-identified study data were deposited in the
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47 132 Harvard Dataverse depository.(16)
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6 136 Weight at admission and mid-upper arm circumference (MUAC) were categorised as shown on
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9 137 **Table 1.** Because approximately 40% of the YI were underweight (<2.5kg), and 60% were aged ≤2
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11 138 days at admission, admission weights rather than anthropometric Z scores using WHO standards
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13 139 were reported. Furthermore, most YI who were born at home or in other hospitals and referred
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16 140 to KCH were missing gestational age estimates and birth weight to be able to estimate gestational
17
18 141 age at birth using the INTERGROWTH 21st Newborn Size Standards (INSS).

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21 142 Prematurity was defined as gestation age <37 weeks and LBW as birth weight <2500 grams for
22
23 143 YIs born at KCH. Admission blood glucose was categorized into <2.6, 2.6 to 7.0 and ≥7.0 mmol/l
24
25 144 representing low, normal and high levels respectively.(15) Missing data were not assumed to be
26
27 145 missing at random. We, therefore, created categorical variables and added a missing category
28
29 146 which was included in the regression analysis.

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32 147 Demographic, anthropometric, and clinical data are presented as frequencies and proportions
33
34 148 for categorical variables and means (standard deviation (sd)) or median (interquartile range
35
36 149 (IQR)) for continuous variables depending on the underlying distribution. Proportions of missing
37
38 150 data for each variable are shown on **Supplementary Table S2.**

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41 151 Monthly admissions and case fatality were plotted against time (month of admission) to visually
42
43 152 inspect the trend from 2009 to 2019 and the predicted trend line superimposed on the curves.
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45 153 We used the Augmented Dickey Fuller test (ADF test) to test if the time series were stationary
46
47 154 (no trend or seasonal effects). We also presented annual absolute admissions, proportion of YI
48
49 155 among all admissions <60 months and case fatality. Monthly admissions and case fatality were

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3 156 tested for annual linear trend using an extension of the Wilcoxon rank-sum test of trend across
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6 157 ordered groups.(17)
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8
9 158 We used interrupted time series analysis to estimate the level and trend changes before and
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11 159 after introduction of free maternity care (1st June 2013). We created a time variable coded
12
13 160 sequentially from 1 to 132 representing the months from January 2009 to December 2019 and
14
15
16 161 free maternity care was coded as 0 before June 2013 and 1 from June 2013. We defined seasonal
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18 162 effect variable using month of the year modelled on harmonic terms using the fourier code in
19
20
21 163 STATA. To measure the effect of free maternity care, we used the negative binomial regression
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23 164 model because of presence of overdispersion in the trends and reported regression coefficients
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26 165 transformed into incidence rate ratios (IRR). All the negative binomial regression models included
27
28 166 the dependent variable of interest e.g. the monthly number of admissions, and the following
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31 167 independent variables: the time variable, the binary pre- and post- free maternity care variable
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33 168 and the seasonal effect variable.
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36 169 Since YIs could be admitted more than once whilst <60 days old, we included multiple admissions
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39 170 using unique IDs and adjusted for clustering by individual with robust standard errors. To identify
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41 171 exposures associated with inpatient death, we treated being discharged alive as a competing
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44 172 event and fitted the proportional sub-distribution hazard model using the Fine-Gray competing
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46 173 risk model.(18) The measure of effect reported from the model was the sub-distribution hazard
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48 174 ratios (SHR) and their respective 95% confidence intervals (CI). To build the multivariable
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51 175 regression model, a backward stepwise approach was used where all the independent variables
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53 176 assessed in the univariate models were included in the model and only those with a P-value <0.1
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56 177 retained in the final multivariable model.
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3 178 For the post-discharge analysis, only data from those YI discharged alive and resident within the
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6 179 KHDSS were analysed. Time at risk was defined from date of discharge to 365 days later or
7
8 180 censure at date of death or outmigration from the KHDSS. We performed a ‘multiple discharges’
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11 181 analysis where YI with multiple admissions had their follow-up time reset at each successive
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13 182 discharge date. Exposures associated with post-discharge assessed using a Cox proportional
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15 183 hazards regression model with robust standard errors accounting for YI with multiple discharges.
16
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18 184 The proportional hazards assumption was assessed using the scaled Schoenfeld residuals test
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20 185 **(Supplementary Tables S3 and S4)**. All exposures assessed in the univariate models were
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22
23 186 considered for inclusion in the multivariable Cox proportional hazards regression model using a
24
25 187 backward stepwise approach. Both the inpatient and post-discharge multivariable regression
26
27
28 188 models’ discrimination performance were assessed using bootstrapped area under receiver
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30 189 operating characteristic curves (AUC) replicated 1000 times.

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33 190 As sensitivity analysis, we assessed the YI born at KCH and enrolled to the Kilifi Perinatal and
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36 191 Maternal Research Project (KIPMAT), which had collected comprehensive birth data including
37
38 192 birth weight and gestational age (weeks).⁽¹⁹⁾ We estimated their birthweight Z scores using the
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41 193 INTERGROWTH Newborn Size Standards (INSS) and ran the regression models replacing
42
43 194 admission weight with birthweight Z score.⁽²⁰⁾

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46 195 Statistical significance was evaluated using 95% CI and a two-tailed *P*-value <0.05. Statistical
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49 196 analyses were conducted using STATA Version 17.0 (College Station, TX, USA).

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51 197 *Study size*

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3 198 With 3,625 YIs discharged alive and included in the post-discharge analysis, a post-discharge
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6 199 mortality of 5.7% and a two-sided alpha of 0.05, the study had greater than 80% power, to detect
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8 200 hazard ratio of ≥ 2.0 of death between YIs with admission weight < 1.5 Kg compared to those with
9
10 201 weight ≥ 2.5 Kg.

11 12 13 202 Ethical considerations

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16 203 Written consent was provided by the caregivers of all the surveillance study participants. Ethical
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18 204 approval to conduct this analysis was granted by the Kenya Medical Research Institute (KEMRI)
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21 205 National Ethics Review Committee (SCC 2778).

22 23 24 206 Patient and public involvement

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27 207 There was no patient and public involvement in the planning or execution of this retrospective
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29 208 cohort study.

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210 Results

211 Baseline characteristics

212 During the study period, there were 42,742 paediatric admissions to KCH, of which 12,271 (29%)
213 admission events among 11,877 individuals were aged <60 days. Of the 12,271 YI admission
214 events, 4,421 (36%) were resident in the KHDSS and included in the analysis (**Figure 1**). This
215 comprised 4,272 individual YI: 4,131 with one admission, 133 two admissions and 8 three
216 admissions within the first 60 days of life.

217 KHDSS-resident admissions

218 Among the 4,421 YI admission events among KHDSS residents, 2,731 (62%) were ≤ 2 days old and
219 1,900 (43%) were female. Reported prematurity and low birth weight were 1,019 (23%) and 581
220 (13%) respectively. Low weight (<2.5kg) was observed in 1694 YIs (38%) while 1342 (30%) had
221 MUAC <9.0cm. Common presenting clinical signs were lower chest wall indrawing (46%) and
222 breathing difficulty (49%). Thirty percent had fever, 31% had hypothermia and 30% tachycardia.
223 Nine hundred and thirty-two YI (21%) had hypoxia ($\text{SaO}_2 < 90\%$) at admission and 250 (5.7%) had
224 impaired consciousness. Presenting signs at admission for all the YI stratified by KHDSS residence
225 are shown on **Table 1**. Malaria was very rare ($n=4$, 0.09%) whilst 142 (3.2%) and 170 (3.9%) YI
226 were HIV antibody positive and had bacteraemia respectively. **Supplementary Table S5** lists the
227 bacterial isolates that were presumed pathogens, led by *Klebsiella pneumoniae*, *Escherichia coli*,
228 *Staphylococcus aureus* and Group B Streptococcus.

229

230 **Table 1. Study participants characteristics at admission.**

	All young infant admissions (N=12,271) ^a	Young infant admissions KHDSS residents (N=4,421)	Young infant admissions non-KHDSS residents (N=7,850)	p-value
Demographics				
Age in days				
0 to 2	7856 (64)	2731 (62)	5125 (65)	<0.001
3 to 7	1384 (11)	468 (11)	916 (12)	
8 to 28	1506 (12)	587 (13)	919 (12)	
>28	1525 (12)	635 (14)	890 (11)	
Sex (female)	5245 (43)	1900 (43)	3345 (43)	0.70
Reported born premature	2970 (24)	1019 (23)	1951 (25)	0.005
Reported low birth weight	1782 (15)	581 (13)	1201 (15)	<0.001
Anthropometry				
Weight (kg)				
<1.5	1767 (14)	566 (13)	1201 (15)	<0.001
1.5 to <2.5	3211 (26)	1128 (26)	2083 (27)	
≥2.5	7193 (59)	2684 (61)	4509 (57)	
Missing	100 (0.8)	43 (1.0)	57 (0.7)	
MUAC (cm)				
<9	3933 (32)	1342 (30)	2591 (33)	<0.001
9 to 10	2492 (20)	862 (20)	1630 (21)	
10 to 11	2926 (24)	1035 (23)	1891 (24)	
≥11	2622 (21)	1056 (24)	1566 (20)	
Missing	298 (2.4)	126 (2.9)	172 (2.2)	
Clinical features				
Axillary temperature				
<36°C	3553 (29)	1358 (31)	2195 (28)	<0.001
36 to 37.5°C	4692 (38)	1711 (39)	2981 (38)	
>37.5°C	3948 (32)	1318 (30)	2630 (34)	
Respiratory rate/min ^b				
Bradypnoea	540 (4.4)	188 (4.3)	352 (4.5)	0.56
Normal	7333 (60)	2647 (60)	4686 (60)	
Tachypnoea	4158 (34)	1490 (34)	2668 (34)	
Missing	240 (2.0)	96 (2.2)	144 (1.8)	
Heart rate/min ^c				
Bradycardia	396 (3.2)	158 (3.6)	238 (3.0)	0.11
Normal	8162 (67)	2910 (66)	5252 (67)	
Tachycardia	3667 (30)	1331 (30)	2336 (30)	
Missing	46 (0.4)	22 (0.5)	24 (0.3)	
Hypoxia ^d	2668 (22)	932 (21)	1736 (22)	0.19
Lower chest wall indrawing	5562 (45)	2051 (46)	3511 (45)	0.13
Wheeze	112 (0.9)	46 (1.0)	66 (0.8)	0.41

Stridor	62 (0.5)	19 (0.4)	43 (0.6)	0.48
Breathing difficulty	5966 (49)	2172 (49)	3794 (48)	0.44
Cyanosis	560 (4.6)	210 (4.8)	350 (4.5)	0.54
Capillary refill >2 seconds	301 (2.6)	105 (2.4)	196 (2.5)	0.81
Temperature gradient	710 (5.8)	258 (5.8)	452 (5.8)	0.73
Weak pulse	463 (3.8)	157 (3.6)	306 (3.9)	0.05
Lethargy	971 (7.9)	325 (7.4)	646 (8.2)	0.15
Impaired consciousness ^e	792 (6.5)	250 (5.7)	542 (6.9)	0.007
Bulging fontanel	111 (0.9)	32 (0.7)	79 (1.0)	0.21
Stiff neck	48 (0.4)	10 (0.2)	38 (0.5)	0.05
Convulsions	689 (5.6)	197 (4.5)	492 (6.3)	<0.001
Sunken eyes	134 (1.1)	44 (1.0)	90 (1.2)	0.44
Reduced skin turgor	308 (2.5)	97 (2.2)	211 (2.7)	0.19
Pallor	633 (5.2)	221 (5.0)	412 (5.3)	0.55
Laboratory features				
Meningitis ^f	98 (0.8)	33 (0.8)	65 (0.8)	0.87
Haemoglobin <11 g/dl) ^g	1207 (9.8)	476 (11)	731 (9.3)	0.02
HIV antibody positive	441 (3.6)	142 (3.2)	299 (3.8)	0.11
Malaria slide positive	5 (0.04)	4 (0.09)	1 (0.01)	0.02
Bacteraemia	590 (4.8)	170 (3.9)	420 (5.4)	<0.001
White blood cells (10 ¹² cells/L) ^h				
<4	134 (1.1)	54 (1.2)	80 (1.0)	<0.001
4–20	8738 (71)	3228 (73)	5510 (70)	
>20	2202 (18)	690 (16)	1512 (19)	
unavailable	1197 (9.8)	449 (10)	748 (9.5)	
Platelets (10 ⁹ cells/L) ⁱ				
<150 cells/L	1615 (13)	586 (13)	1029 (13)	0.59
≥150	9455 (77)	3387 (77)	6068 (77)	
unavailable	1201 (9.8)	448 (10)	753 (9.6)	
Blood glucose (mmols/L)				
<2.6	2479 (20)	882 (20)	1597 (20)	0.29
2.6 to 7.0	5086 (41)	1875 (42)	3211 (41)	
>7.0	688 (5.6)	231 (5.2)	457 (5.8)	
unavailable	4018 (33)	1433 (32)	2585 (33)	

^a-Eligible admissions were young infants aged <60days admitted from 2009 to 2019, ^b- Tachypnoea: respiratory rate ≥60 breaths/min, Bradypnoea: respiratory rate <30 breaths/min, ^c-Tachycardia: heart rate>160 beats/min, Bradycardia: heart rate<100 beats/min, ^d-Hypoxia: oxygen saturation<90%,^e- Impaired consciousness level if 'prostrate' or 'unconscious', ^f Meningitis: positive CSF culture, or positive CSF microscopy, or positive CSF antigen test, or elevated CSF WBC count (≥20 in young infants aged 0-28 days OR, ≥10 in young infants aged 29-59 days) PLUS a positive blood culture for a known pathogen, ^g Anaemia: haemoglobin <11 g/dl, ^h Normal values WBC 4-20 x 10¹² cells/L, Leucopenia WBC <4 x 10¹² cells/L, Leucocytosis WBC >20 x 10¹² cells/L, ⁱ Normal values Platelets ≥150x10⁹ cells/L, Thrombocytopenia <150x10⁹ cells/L, KHDSS: Kilifi Health and Demographic Surveillance System, MUAC: Mid-upper arm circumference.

231 Admissions over time

232 The annual number of admissions are shown in **Supplementary Table S6**. The overall proportion
233 of YI among all admissions under 5 years old was 28% (95%CI 27–29%), increasing from 19% in
234 2009 to 34% in 2019 (test of linear trend $P=0.02$) **Figure 2**. **Figure 3A** shows the upward trend of
235 absolute YI admissions and downward trends for 2 to 59-month-olds and all admissions <60
236 months old (all P-values for tests for stationarity <0.05). There was no significant difference in
237 monthly YI admissions before introduction of free maternity care in June 2013 (monthly median
238 [IQR] of 76 [66–96] admissions) and after June 2013 (monthly median [IQR] of 95 [78–125]
239 admissions) season-adjusted IRR 1.06 (95%CI 0.54–2.09) $P=0.86$ (**Supplementary Figure S1A**).
240 The mean monthly YI admissions on day of birth did not differ before and after June 2013; season-
241 adjusted IRR 0.88 (95%CI 0.44 to 1.76), $P=0.72$. The proportion of YI admissions to total
242 admissions aged <60 months before and after June 2013 were not different; season-adjusted IRR
243 1.02 (95%CI 0.28–3.71) $P=0.97$ **Figure 3D**. We found no significant difference in monthly absolute
244 admissions (all admissions <60 months old), before and after June 2013; season-adjusted IRR
245 1.01 (95%CI 0.51–2.00) $P=0.97$ (**Supplementary Figure S1B**).

246 Inpatient deaths

247 Overall, 1,914/11,877 (16%) of YI died in hospital. The risk of inpatient death was not significantly
248 different between 645/4,272 (15%) KHDSS residents and 1,269/7,605 (17%) non-residents of
249 KHDSS (age- and sex-adjusted SHR 0.93 (95%CI 0.85–1.02) $P=0.12$) (**Figure 1**). The annual YI
250 inpatient case fatality ratio was stable (11% in 2009 and 13% in 2019. P-value for trend=0.80),
251 **Figure 2**. Monthly inpatient case fatality for YI, 2 to 59 months old and all <60 months old children
252 are shown in **Figure 3B**.

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3 253 During the study period there were 3,119 inpatient deaths among admissions <60 months old
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6 254 admitted at KCH, with YI admissions accounting for 61% (95%CI 60–63%) of the deaths and no
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8 255 significant linear trend from 2009 to 2019 (trend P=0.29). The mean monthly YI inpatient case
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10 256 fatality was 16% (sd 0.86) and 16% (sd 1.23) before and after June 2013 respectively; season-
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12
13 257 adjusted IRR 0.77 (95%CI 0.39–1.52) P=0.45 **Figure 3C**. The mean monthly case fatality for all
14
15 258 admissions aged <60 months and admissions 2–59 months old did not differ before June 2013
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17
18 259 and after June 2013; season-adjusted IRR 0.79 (95%CI 0.39–1.58) P=0.50 and IRR 0.81 (95%CI
19
20 260 0.39–1.69) P=0.57 respectively **Supplementary Figure S1 C and D**.

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23 261 Among the 4,421 KHDSS-resident YI admissions, median [IQR] time to death was 2 [1–4] days,
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26 262 while the survivors were admitted for 5 [3–8] days. A total of 423/645 (66%) deaths occurred
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28 263 within the first 48 hours following admission. Forty-one YI left against medical advice, and 55
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31 264 were referred to other hospitals for further care.

32 33 34 265 Admission diagnosis & case fatality ratio

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37 266 The commonest reasons for hospital admission were neonatal sepsis (47%), preterm
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39 267 complications (20%) and birth asphyxia (16%) accounting for 83% of all YI admissions (**Table 2**).
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42 268 The case fatality ratios for YI with respiratory distress syndrome, preterm complications and birth
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44 269 asphyxia were 52%, 29% and 28% respectively (**Table 2**).

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275 **Table 2. Discharge diagnosis assigned by clinician.**

276	Discharge diagnosis ^a	No. (%)	
		Diagnosis assigned by clinician at discharge	
277		All admissions (N=4421)	Inpatient Deaths (N=645)
278	Neonatal sepsis	2097 (47)	201 (9.6)
279	Preterm complications	889 (20)	262 (29)
	Birth asphyxia	724 (16)	201 (28)
	Neonatal jaundice	611 (14)	56 (9.2)
280	Lower respiratory tract infection	486 (11)	41 (8.4)
	Respiratory distress syndrome	263 (6.0)	136 (52)
281	Congenital anomalies	215 (4.9)	55 (26)
	Meningitis ^b	112 (2.5)	11 (9.8)
282	Anaemia	78 (1.8)	14 (18)
	Malnutrition	36 (0.8)	1 (2.8)
283	None specified	69 (1.6)	4 (5.8)
	Others	266 (6.0) ^c	13 (4.9)

^aYoung infant could be assigned up to 2 diagnoses

^bMeningitis: positive CSF culture, or positive CSF microscopy, or positive CSF antigen test, or elevated CSF WBC count (≥ 20 in young infants aged 0-28 days OR, ≥ 10 in young infants aged 29-59 days) PLUS a positive blood culture for a known pathogen

^cAccidents-3, Acute abdominal obstruction-15, bronchiolitis-12, burns-1, Candidiasis-1, Cellulitis abscess-21, Chickenpox-1, Chromosomal abnormality-5, CNS abscess-1, Conjunctivitis-2, Dehydration-2, Dental problems-1, Diabetes-1, Elective surgery-5, Encephalopathy-9, Epilepsy-7, Extra pulmonary TB-1, Febrile convulsions-5, Feeding difficulty-1, Gastroenteritis-15, Haemolytic uraemic syndrome-1, Hydrocephalus-11, LTB/croup-1, Immunosuppression-17, Malaria-2, Male genital problem-1, Meconium aspiration-33, Neonatal haemorrhage-14, Neonatal tetanus -10, Other skin disease-3, Otitis media-1, Poisoning (organophosphates)-1, Pyogenic arthritis-1, Rabies-1, Rash-4, renal failure-6, trauma/fractures/RTA-11, Urinary tract infection-10, upper respiratory tract infection (URTI)-24, Viral hepatitis-2, Viral infection-3.

287 Exposures associated with inpatient death

288 Variables assessed for association with inpatient death in univariate models are shown in

289 **Supplementary Table S3**. In the multivariable analysis (**Table 3**), admissions at age ≤ 2 days and

290 3–7 days, compared to ≥ 28 days old, were associated with inpatient deaths. Very low admission

291 weight (< 1.5 kg) and weight 1.5-2.4kg compared to ≥ 2.5 kg were positively associated with

292 inpatient deaths. Signs of clinical severity (bradypnoea, tachypnoea, bradycardia, hypoxia, lower

293 chest wall indrawing, breathing difficulty, weak pulse, impaired consciousness and hypothermia,

294 but not fever), meningitis, bacteraemia, leucopenia and leucocytosis but not an HIV antibody

295 positive test (aSHR 1.15 (95%CI 0.81–1.63)) were positively associated with inpatient death. The
 296 multivariable model bootstrapped AUC was 0.88 (95%CI 0.86–0.89) **Table 3**.

297 **Table 3. Multivariable regression analysis of factors associated with inpatient and post-**
 298 **discharge mortality.**

	Inpatient analysis		Post-discharge analysis	
	Adjusted SHR*	P-value	Adjusted HR	P-value
Demographics				
Age in days				
0 to 2	2.12 (1.46–3.06)	<0.001	0.78 (0.50–1.21)	0.27
3 to 7	3.88 (2.46–6.10)	<0.001	0.57 (0.30–1.08)	0.08
8 to 28	1.42 (0.90–2.25)	0.13	1.19 (0.73–1.93)	0.48
>28	Reference		Reference	
Sex (female)	0.91 (0.78–1.07)	0.26	0.98 (0.74–1.31)	0.91
Admission days (log)	¶		1.93 (1.52–2.46)	<0.001
Type of discharge				
Normal	¶		Reference	
Absconded	¶		2.73 (1.04–7.18)	0.04
Transferred/referred	¶		14.4 (9.22–22.6)	<0.001
Anthropometry				
Weight (kg)				
<1.5	2.16 (1.75–2.67)	<0.001	2.01 (1.41–2.87)	<0.001
1.5 to <2.5	1.42 (1.16–1.74)	0.001	0.88 (0.47–1.65)	0.69
≥2.5	Reference		Reference	
Missing weight	3.85 (2.59–5.71)	<0.001	-	
Clinical features				
Axillary temperature				
<36°C	1.44 (1.17–1.78)	0.001	1.06 (0.72–1.57)	0.76
36 to 37.5°C	Reference		Reference	
>37.5°C	1.09 (0.84–1.41)	0.53	0.67 (0.46–0.99)	0.04
Missing temperature	1.03 (0.38–2.75)	0.96	0.94 (0.09–9.30)	0.96
Respiratory rate/min				
Bradypnoea	1.45 (1.09–1.93)	0.01	1.72 (0.81–3.65)	0.16
Normal	Reference		Reference	
Tachypnoea	0.80 (0.67–0.95)	0.01	1.33 (0.98–1.79)	0.07
Missing	1.51 (0.64–3.56)	0.34	0.82 (0.10–6.49)	0.85
Heart rate/min				
Bradycardia	1.40 (1.08–1.82)	0.01	¶	
Normal	Reference			
Tachycardia	1.14 (0.94–1.37)	0.18	¶	
Missing	0.41 (0.03–5.13)	0.49	¶	
Hypoxia (SaO ₂ <90%)	1.62 (1.37–1.92)	<0.001	¶	
Capillary refill >2 seconds	1.34 (0.97–1.86)	0.08	¶	

Lower chest wall indrawing	1.41 (1.14–1.75)	0.002	¶	
Stridor	1.93 (0.92–4.03)	0.08	¶	
Breathing difficulty	1.45 (1.15–1.82)	0.001	¶	
Weak pulse	1.61 (1.19–2.17)	0.002	2.33 (1.13–4.82)	0.02
Bulging fontanel	2.45 (0.91–6.65)	0.08	3.41 (1.49–7.79)	0.004
Impaired consciousness	2.21 (1.72–2.84)	<0.001	¶	
Pallor	1.30 (0.98–1.71)	0.07	¶	
Laboratory features				
Meningitis	5.45 (2.50–11.8)	<0.001	2.21 (0.95–5.13)	0.07
HIV antibody positive	1.15 (0.81–1.63)	0.43	1.09 (0.50–2.35)	0.83
Bacteraemia	2.21 (1.51–3.22)	<0.001	¶	
White blood cells (10 ¹² cells/L)				
<4	2.17 (1.30–3.62)	0.003	¶	
4-20	Reference		¶	
>20	1.71 (1.43–2.04)	<0.001	¶	
unavailable	1.09 (0.82–1.44)	0.57	¶	
Model performance				
Bootstrapped AUC (95% CI)	0.88 (0.86–0.89)		0.76 (0.72–0.79)	
<p>SHR; sub-distribution hazard ratios; *the SHR are from the Fine and Gray's proportional sub-hazards model, HR-Hazard ratio from the Proportional Cox regression model, ¶; variables not selected for inclusion in the multivariable model, AUC; area under receiver operating characteristics. Meningitis: positive CSF culture, or positive CSF microscopy, or positive CSF antigen test, or elevated CSF WBC count (≥ 20 in young infants aged 0-28 days OR, ≥ 10 in young infants aged 29-59 days) PLUS a positive blood culture for a known pathogen</p>				

299

300 Post-discharge death

301 There were 3,776 live discharges from 3,640 YI residents of KHDSS, of which 3,760 (from 3,625
302 individual YI) were followed up for 3,233 infant-years (**Figure 1**). During one-year follow-up, there
303 were 208/3625 (5.7%) deaths: 64.3 (95%CI 56.2–73.7) deaths per 1,000 infant-years. The median
304 [IQR] time to death after discharge was 35 [7–92] days. Of the 208 post-discharge deaths, 101
305 (49%), 160 (77%), 179 (86%) and 193 (93%) occurred within 1, 3, 6 and 9 months after discharge
306 respectively. The annual YI post-discharge case fatality was 5.4% in 2009 and 6.3% in 2019
307 without evidence of linear trend (P-value for trend=0.77) (**Figure 2**).

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3 308 One hundred and one (49%) of the 208 post-discharge deaths occurred at home without hospital
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6 309 readmission, 67 (32%) occurred during readmission to KCH and 40 (19%) occurred at other health
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8 310 facilities. The five leading assigned causes of deaths for the 67 deaths at KCH were: neonatal
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10 311 sepsis (24%), preterm complications (22%), congenital heart disease (15%), neonatal jaundice
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13 312 (7.4%) and meningitis (7.4%) which were similar to index admission diagnosis **Supplementary**
14
15 313 **Table S7**. Causes of other deaths were unknown.

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18 314 Overall, we observed 853 (20%) deaths among 4,272 individual YIs: 645 inpatient and 208 post-
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20 315 discharge, hence 24% of deaths were post-discharge.

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24 316 Exposures assessed for association with post-discharge mortality are shown on **Table 3**. In the
25
26 317 multivariable Cox regression model, log days of hospital admission, leaving against advice, and
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28 318 referral to more specialized hospital were positively associated with post-discharge mortality.
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30 319 Other exposures associated with post-discharge mortality were low admission weight, fever,
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32 320 weak pulse, and bulging fontanel, whilst a meningitis diagnosis at admission had borderline effect
33
34 321 (**Table 3**). The multivariable model bootstrapped AUC was 0.76 (95%CI 0.72–0.79).

322 Subgroup analysis

323 In a subgroup analysis including 1,358 admissions of YIs born at KCH, their median [IQR]
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35 324 gestational age was 38 (36–40) weeks and birth weight 2,778 (2,000–3,195) grams respectively.

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39 325 In the univariate regression model, born premature, born low birth weight and birth weight Z
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41 326 score <-2 were positively associated with inpatient mortality (**Supplementary Table S8**). In the
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43 327 multivariable model, low birth weight, admission age <8 days, bacteraemia and signs of clinical
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45 328 severity were associated with inpatient mortality (**Supplementary Table S9**).

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329 Among the 1,142 YI followed up for 1,021 child-years of which 41/1,142 (3.6%) died, low birth
330 weight (aHR 2.76 (95%CI 1.30–5.82)) was positively associated with post-discharge mortality in
331 the multivariable model (**Supplementary Table S9**).

332

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333 Discussion

334 Trends in admissions and proportions of young infants

335 During the study period, we observed a marked increase in YI admissions and proportion of YI
336 among admissions in under-fives increased from around a fifth in 2009, to more than one-third
337 in 2019. However, this did not seem to be associated with the introduction of free maternity care
338 in 2013. Lack of observable effect may be due to challenges faced during policy implementation
339 arising from inadequate expansion of quality health care facilities and resources. Several authors
340 reported an increase in mothers attending Kenyan health facilities for antenatal care and
341 delivery,(11, 21) however our results suggest this occurred in the context of a general trend which
342 we previously observed during 1990-2008.(10)

343 Conversely, the number of admitted children older than 60 days decreased alongside a reduction
344 in local malaria transmission,(22) introduction of routine childhood pneumococcal conjugate and
345 rotavirus immunisation,(23) and expansion in numbers of health facilities in Kilifi County.(24)
346 Variation in annual admissions over the years was due to multiple health workers' strikes.(13)
347 During these periods, the general paediatric ward was closed and only the sickest children were
348 admitted to the paediatric HDU due to limited staffing and bed capacity. The time series analysis
349 indicated an increase in inpatient mortality during strikes (**Figure 3C**).

350 The leading diagnoses at admission in our analysis were neonatal sepsis, preterm complications,
351 and birth asphyxia, similar to the period 1990–2008.(10) Over a third of admissions from KCH
352 maternity were preterm and the hospital also received referrals of preterm and very low
353 birthweight infants from sub-county hospitals and local health centres. There are few African

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3 354 published datasets of neonatal or YI inpatient diagnoses; in a network of 7 Nigerian and Kenyan
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6 355 hospitals, prematurity accounted for over half (52%), and birth asphyxia almost a quarter (24%)
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8 356 of neonatal admissions.(25) The leading bacterial isolates from blood cultures in our study
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10 357 (*Klebsiella pneumoniae*, *Escherichia coli*, *Staphylococcus aureus*) were similar to those among YI
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13 358 in rural settings of Tanzania and Burkina Faso.(26) Kenya attained elimination status of maternal
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15 359 and neonatal tetanus in 2018, following immunisation campaigns in high-risk regions.(27)
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18 360 Compared to 1990–2008,(10)neonatal tetanus was uncommon at our centre with only 10 cases
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20 361 in 11 years.

21 22 23 362 Inpatient deaths

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26 363 The WHO has reported that in 2019, “47% of all under-5 deaths occurred in the newborn period
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29 364 with about one third dying on the day of birth and close to three quarters dying within the first
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31 365 week of life”.(28) We found YI accounted for more than 60% of under-fives inpatient deaths,
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34 366 similar to a retrospective study of 16 Kenyan public hospitals in which neonatal deaths comprised
35
36 367 66% of inpatient paediatric deaths.(5) We found respiratory distress syndrome, birth asphyxia
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39 368 and preterm complications had the highest inpatient mortality. Improvements in peripartum care
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41 369 of mothers and infants together with appropriate technology such as non-invasive ventilation for
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44 370 management of respiratory complications of preterm birth are priorities for reduction in
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46 371 neonatal mortality in hospitals in LMICs.(5)

47 48 49 372 Post-discharge deaths

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52 373 Less than a quarter (24%) of all deaths during 1-year of follow up occurred post-discharge. This
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55 374 reflects a high inpatient (16%) case fatality rate with many very early inpatient deaths compared

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3 375 to 6.6% in children aged ≥ 60 days.(7) Nevertheless, the post-discharge YI mortality rate (64.3 per
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6 376 1,000 child/years) was more than twice that of a cohort of children aged 2–59 months admitted
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8 377 to KCH between 2007- 2015.(29) This reflects post-discharge mortality rates being highest in
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11 378 younger age groups, such as in Tanzania among under 1-year olds: 72 per 1,000 child/years
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13 379 (95%CI. 67.2–77.2) falling to 6.9 (95%CI. 5.5–8.7) per 1,000 child/years in 4 to <5 year olds.(30)
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15
16 380 A greater proportion of YI post-discharge deaths occurred in hospital than among older
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18 381 children,(7) implying that caregivers may be more likely to seek re-admission for YI or may live
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21 382 closer to KCH. About half of post-discharge deaths occurred within the first month, highlighting
22
23 383 the need for formal ‘down-referral’ for continuity of care after discharge in high risk YI.
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26 384 Analysis of exposures revealed that some were common for both inpatient and post-discharge
27
28 385 mortality: low admission weight, axillary temperature, and respiratory rate. Birth weight was
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30
31 386 not available for most YI but low admission weight <2.5kg was common (40%) in our
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34 387 participants. Of known causes of post-discharge deaths, leading ones were related to problems
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36 388 in the early neonatal period. Meningitis was among the top 5 causes and bulging fontanel noted
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39 389 at admission was associated with increased risk of post-discharge death, suggesting that
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41 390 current treatment guidelines may not be sufficiently effective.
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391 **Strengths and limitations of the study**

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47 392 Strengths of this study are large sample size, systematic collection of data and linkage to a well-
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49 393 established demographic surveillance system, with few losses to follow up. Limitations are lack
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52 394 of accurate gestational age estimation and unknown birthweight of most participants. We did
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55 395 not have data collected at discharge, which may be of value in taking a risk-based approach to
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3 396 post-discharge care. This analysis is from a single hospital and outcomes in other settings with a
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6 397 different patient profile and facilities may vary.
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9 398 **Conclusions**

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12 399 Neonatal and YI admissions account for an increasing proportion of inpatient paediatric
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14 400 admissions, and their mortality rate remains high. Mortality reduction will depend on
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17 401 improvements in antenatal, peripartum and postpartum care of mothers and infants, as well as
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19 402 implementation of standardized neonatal care and paediatric protocols. Post-discharge mortality
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22 403 rates are higher, but account for a lower proportion of all deaths than among children age ≥ 60
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24 404 days, likely because of the predominance of fatal conditions soon after birth with a
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26 405 correspondingly substantial proportion of infant mortality occurring in the first week of life.
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3 443 **Figures**
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6 444 **Figure 1. Flow of study participants.**
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9 445 **Figure 2. Annual proportion of YI admissions to all admissions <60 months, inpatient case**
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12 446 **fatality ratio (CFR) and post-discharge CFR.**
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15 447 Proportions are plotted with 95% confidence intervals.
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18 448 **Figure 3. A: Monthly hospital admissions (with predicted mean temporal trend), B: Monthly**
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21 449 **case fatality rates (with predicted mean temporal trend), C: Monthly young infant inpatient**
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23 450 **case fatality before and after June 2013 and D: Monthly proportions of young infants to**
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25 451 **admissions <60 months old.**
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35 454 Ethics approval and consent to participate

36 455 Written consent was provided by the caregivers of all the surveillance study participants. Ethical
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39 456 approval to conduct this analysis was granted by the Kenya Medical Research Institute (KEMRI)
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42 457 National Ethics Review Committee (SCC 2778).
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45 458 Consent for publication – not applicable
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48 459 Availability of data and materials

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50 460 Data are available in a public, open access repository. Deidentified participant data and analysis
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52 461 code have been deposited and may be requested at the Harvard Dataverse via this
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55 462 link <https://doi.org/10.7910/DVN/OXJVFX>
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3 463 Competing interests
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6 464 JAB declares the following: Chair of the DSMB for “**Efficacy and safety of whole-body chlorhexidine**
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8 **cleansing in reducing bacterial skin colonisation of hospitalised neonates - a pilot trial**”. *St George’s,*
9
10 *University of London and global sites*; Treasurer of the Commonwealth Society for Paediatric
11
12 Gastroenterology & Nutrition Other authors declare they have no competing interests.
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15

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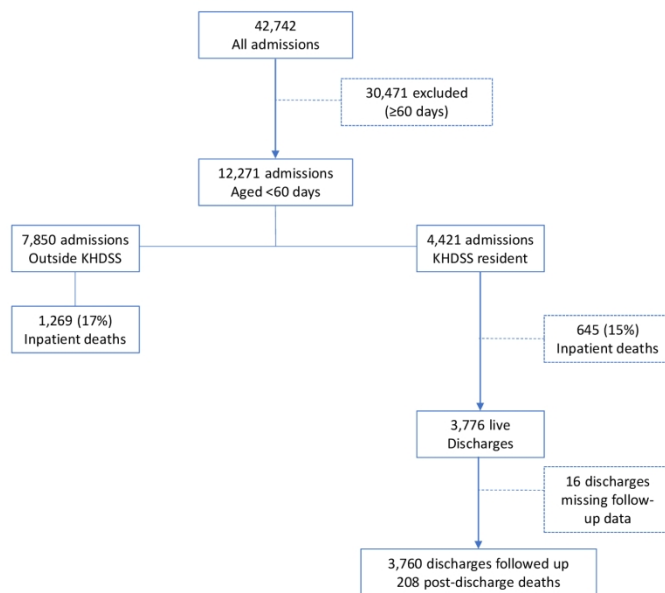
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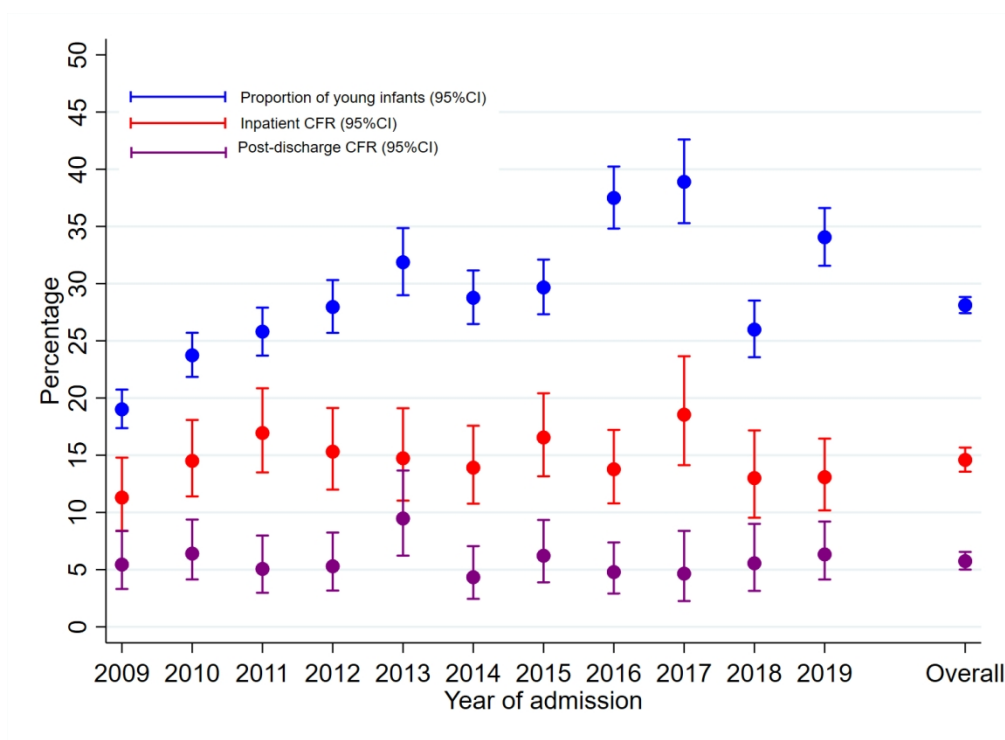
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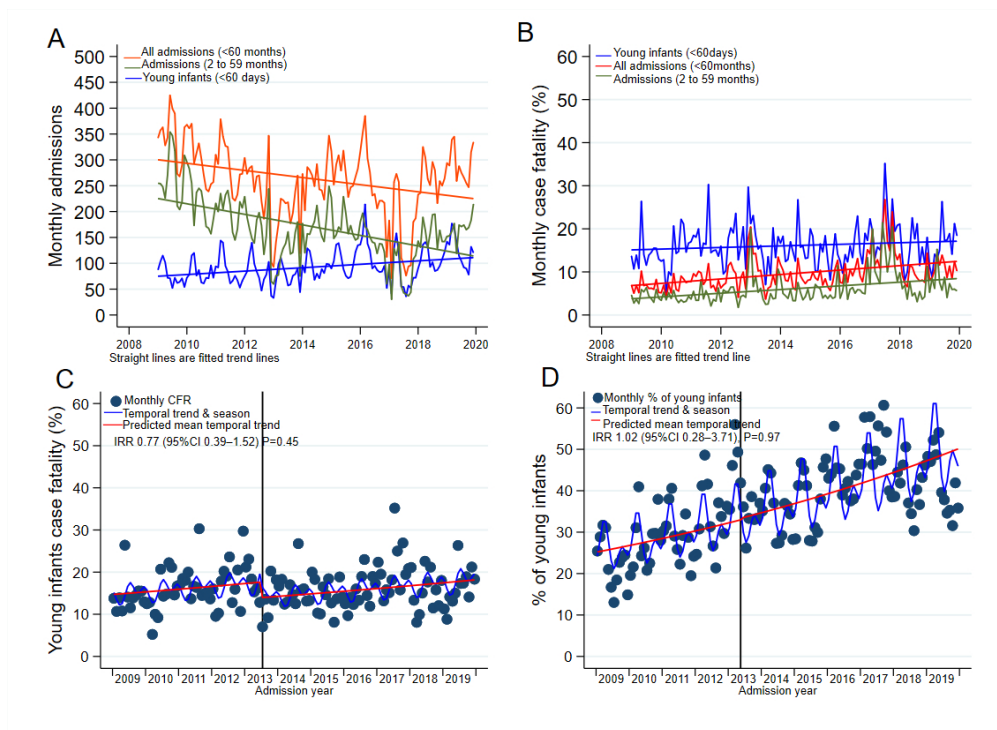
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3 **Supplementary materials**
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Table S1. List of health workers strikes during study period.

Strike dates	Health workers on strike	Duration of strike in days
5 to 13 December 2011	Doctors	9
1 to 15 March 2012	Nurses	15
13 September to 4 October 2012	Doctors	22
3 December 2012 to 13 January 2013	Nurses	42
16 January to 11 February 2013	Nurses	26
10 to 23 December 2013	Doctors & nurses	14
5 to 14 December 2016	Nurses	11
5 December 2016 to 15 March 2017	Doctors	102
5 June to 2 November 2017	Nurses	150

Table S2. Proportion of missing data

N=4,421	N missing	% missing
Demographics		
Age in days	0	
Sex (female)	0	
BCG scar	76	1.7
Reported born premature	321	7.3
Reported low birth weight	322	7.3
Anthropometry		
Weight (kg)	43	1.0
MUAC (cm)	126	2.9
Clinical features		
Axillary temperature	34	0.8
Tachypnea	208	4.7
Tachycardia	43	1.0
Hypoxia (SaO ₂ <90%)	20	0.5
Lower chest wall indrawing	68	1.5
Wheeze	69	1.6
Stridor	71	1.6
Breathing difficulty	64	1.5
Cyanosis	70	1.6
Capillary refill ≥ 2 seconds	34	0.8
Temperature gradient	81	1.8
Weak pulse	71	1.6
Lethargy	70	1.6
Impaired consciousness	70	1.6
Bulging fontanel	72	1.6
Stiff neck	71	1.6
Convulsions	64	1.5
Sunken eyes	73	1.7
Reduced skin turgor	71	1.6
Pallor	70	1.6
Laboratory features		
HIV antibody positive	756	17
Malaria slide positive	372	8.4
Bacteraemia	2281	52

Haemoglobin	448	10
WBC	449	10
Platelets	448	10
Blood glucose (mmols/L)	1433	32

Table S3. Univariate analysis of admission features associated with inpatient deaths.

N=4,421	Deaths (N=645) N (%)	Crude SHR	P-value	Scaled Schoenfeld residuals P-value
Demographics				
Age in days				
0 to 2	511 (19)	3.31 (2.39–4.58)	<0.001	0.14
3 to 7	56 (12)	2.07 (1.38–3.11)	<0.001	
8 to 28	40 (6.8)	1.15 (0.74–1.78)	0.54	
>28	38 (6.0)	Reference		
Sex (female)	268 (14)	0.99 (0.91–1.09)	0.93	0.77
Reported born premature	294 (29)	2.53 (2.32–3.77)	<0.001	0.06
Reported low birth weight	222 (38)	3.25 (2.97–3.56)	<0.001	0.18
Anthropometry				
Weight (kg)				
<1.5	213 (38)	4.95 (4.13–5.93)	<0.001	0.09
1.5 to <2.5	174 (15)	1.86(1.53–2.26)	<0.001	
≥2.5	229 (8.5)	Reference		
Missing weight	29 (67)	10.7 (7.60–14.9)	<0.001	
MUAC (cm)				
<9.0	333 (25)	3.57 (3.07–4.15)	<0.001	0.08
9 to 10	106 (12)	1.73 (1.45–2.07)	<0.001	
10 to 11	96 (9.3)	1.48 (1.24–1.77)	<0.001	
≥11	75 (7.1)	Reference		
Missing MUAC	35 (28)	3.89 (3.02–5.00)	<0.001	
Clinical features				
Axillary temperature				
<36°C	390 (29)	3.13 (2.82–3.47)	<0.001	0.34
36 to 37.5°C	159 (9.3)	Reference		
>37.5°C	84 (6.3)	0.77 (0.67–0.88)	<0.001	
Missing temperature	12 (35)	3.78 (2.65–5.39)	<0.001	
Respiratory rate/min				
Bradypnoea	108 (57)	6.09 (4.98–7.46)	<0.001	0.71
Normal	329 (12)	Reference		
Tachypnoea	197 (13)	1.07 (0.90–1.27)	0.45	
Missing	11 (11)	0.91 (0.51–1.65)	0.76	
Heart rate/min				
Bradycardia	74 (47)	4.05 (3.21–5.11)	<0.001	0.50
Normal	403 (14)	Reference		
Tachycardia	163 (12)	0.88 (0.73–1.05)	0.15	
Missing	5 (23)	1.68 (0.72–3.93)	0.23	
Hypoxia (SaO2 <90%)	309 (33)	3.91 (3.58–4.26)	<0.001	0.48
Lower chest wall indrawing	448 (22)	2.86 (2.60–3.15)	<0.001	0.41

1	Wheeze	0	-		
2	Stridor	6 (32)	1.48 (0.89–2.47)	0.13	0.23
3	Breathing difficulty	481 (22)	3.62 (3.26–4.02)	<0.001	0.28
4	Cyanosis	98 (47)	4.01 (3.55–4.53)	<0.001	0.14
5	Capillary refill >2 seconds	61 (58)	5.61 (4.41–7.14)	<0.001	0.54
6	Temperature gradient	98 (38)	2.85 (2.51–3.23)	<0.001	0.36
7	Weak pulse	108 (69)	5.85 (5.21–6.57)	<0.001	0.71
8	Lethargy	64 (20)	1.20 (1.04–1.40)	0.02	0.34
9	Impaired consciousness	140 (56)	5.43 (4.91–6.00)	<0.001	0.42
10	Bulging fontanel	6 (19)	1.34 (0.90–1.99)	0.15	0.08
11	Stiff neck	4 (40)	2.08 (1.30–3.32)	0.002	0.17
12	Convulsions	16 (8.1)	0.75 (0.61–0.93)	0.01	0.53
13	Sunken eyes	5 (11)	1.04 (0.69–1.56)	0.85	0.52
14	Reduced skin turgor	21 (22)	1.18 (0.91–1.52)	0.22	0.56
15	Pallor	72 (33)	2.47 (2.15–2.83)	<0.001	0.63
16	Laboratory features				
17	Meningitis	8 (24)	8.06 (3.96–16.4)	<0.001	0.13
18	Anaemia (haemoglobin <11 g/dl)	50 (11)	0.67 (0.51–0.90)	0.007	0.51
19	HIV antibody positive	29 (20)	1.39 (1.13–1.71)	0.002	0.28
20	Malaria slide positive	0	-		
21	Bacteraemia	63 (37)	2.92 (2.10–4.06)	<0.001	0.13
22	Blood glucose (mmols/L)				
23	<2.6	137 (16)	1.18 (1.04–1.33)	0.009	0.42
24	2.6 to 7.0	229 (12)	Reference		
25	>7.0	71 (31)	2.85 (2.47–3.29)	<0.001	
26	Missing blood glucose	208 (15)	1.18 (1.06–1.32)	0.002	
27	White blood cells (10 ¹² cells/L)				
28	<4	14 (26)	2.43 (1.47–4.03)	0.001	0.70
29	4-20	362 (11)	Reference		
30	>20	210 (30)	2.97 (2.52–3.50)	<0.001	
31	Missing	59 (13)	1.19 (0.91–1.57)	0.20	
32	Platelets (10 ⁹ cells/L)				
33	<150	139 (24)	1.89 (1.57–2.27)	<0.001	0.10
34	≥150	447 (13)	Reference		
35	Missing	59 (13)	1.01 (0.77–1.32)	0.95	
36	SHR: sub-distribution hazard ratios; the SHR are from the Fine and Gray's proportional sub-hazards model.				
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Table S4. Univariate analysis of admission features associated with post-discharge deaths.

N=3625	Deaths (N=208)	Crude HR	P-value	Scaled Schoenfeld residuals P-value
Demographics				
Age in days				
0 to 2	124 (5.6)	0.98 (0.67–1.44)	0.92	0.10
3 to 7	15 (3.7)	0.63 (0.34–1.16)	0.14	
8 to 28	36 (6.6)	1.17 (0.73–1.87)	0.52	
>28	33 (5.5)	Reference		
Sex (female)	89 (5.5)	0.98 (0.74–1.28)	0.86	0.79
Reported born premature	58 (8.0)	1.79 (1.32–2.44)	<0.001	0.07
Reported low birth weight	33 (9.3)	1.99 (1.37–2.90)	<0.001	0.13
Length of hospitalization (days)-log transformed	-	1.96 (1.68–2.27)	<0.001	0.38
Discharged over weekend				
No	173 (5.7)	Reference		
Yes	35 (4.8)	0.85 (0.59–1.23)	0.39	0.16
Type of discharge				
Normal discharge	180 (4.9)	Reference		0.75
Absconded	5 (12)	2.60 (1.07–6.33)	0.04	
Transferred/referred	23 (44)	11.8 (7.64–18.2)	<0.001	
Anthropometry				
Weight (kg)				
<1.5	30 (8.5)	2.49 (1.65–3.77)	<0.001	0.17
1.5 to <2.5	87 (9.2)	2.64 (1.97–3.54)	<0.001	
≥2.5	91 (3.7)	Reference		
Missing weight	0	-		
MUAC (cm)				
<9.0	88 (8.8)	4.05 (2.56–6.41)	<0.001	0.17
9 to 10	44 (5.8)	2.56 (1.55–4.24)	<0.001	
10 to 11	42 (4.5)	1.92 (1.15–3.18)	0.01	
≥11	23 (2.4)	Reference		
Missing MUAC	11 (12)	5.83 (2.84–12.0)	<0.001	
Clinical features				
Axillary temperature				
<36°C	78 (8.1)	1.45 (1.07–1.96)	0.02	0.80
36 to 37.5°C	88 (5.7)	Reference		
>37.5°C	41 (3.3)	0.57 (0.40–0.83)	0.003	
Missing temperature	1 (5.0)	0.99 (0.14–7.12)	0.99	
Respiratory rate/min				
Bradypnoea	7 (8.8)	1.92 (0.90–4.13)	0.09	0.30
Normal	108 (4.7)	Reference		
Tachypnoea	87 (6.8)	1.44 (1.09–1.92)	0.01	
Missing	6 (7.2)	1.65 (0.72–3.76)	0.23	
Heart rate/min				
Bradycardia	9 (11)	2.10 (1.07–4.13)	0.03	0.73
Normal	137 (5.5)	Reference		
Tachycardia	62 (5.3)	0.97 (0.72–1.31)	0.85	

Missing	0	-		
Hypoxia (SaO ₂ <90%)	51 (8.2)	1.68 (1.23–2.31)	0.001	0.54
Lower chest wall indrawing	108 (6.8)	1.54 (1.17–2.02)	0.002	0.18
Wheeze	2 (4.4)	0.77 (0.19–3.10)	0.71	0.20
Stridor	0	-		
Breathing difficulty	109 (6.5)	1.40 (1.07–1.85)	0.02	0.26
Cyanosis	7 (6.3)	1.14 (0.54–2.43)	0.73	0.17
Capillary refill ≥2 seconds	4 (9.4)	1.81 (0.67–4.87)	0.24	0.40
Temperature gradient	12 (7.5)	1.44 (0.80–2.57)	0.23	0.22
Weak pulse	7 (15)	3.10 (1.46–6.59)	0.003	0.38
Lethargy	14 (5.8)	1.06 (0.63–1.80)	0.82	0.19
Impaired consciousness	6 (5.5)	0.98 (0.44–2.21)	0.96	0.50
Bulging fontanel	4 (15)	3.04 (1.13–8.18)	0.03	0.06
Stiff neck	1 (17)	2.84 (0.40–20.2)	0.30	0.15
Convulsions	9 (5.0)	0.88 (0.46–1.75)	0.75	0.31
Sunken eyes	6 (15)	3.31 (1.47–7.45)	0.004	0.20
Reduced skin turgor	8 (11)	2.19 (1.08–4.43)	0.03	0.20
Pallor	15 (10)	2.09 (1.23–3.53)	0.006	0.23
Laboratory features				
Meningitis	4 (16)	3.98 (1.45–10.9)	0.007	0.13
Anaemia (haemoglobin <11 g/dl)	26 (6.2)	1.19 (0.79–1.80)	0.41	0.68
HIV antibody positive	7 (6.2)	1.17 (0.55–2.49)	0.69	0.76
Malaria slide positive	0	-		
Bacteraemia	10 (9.4)	1.02 (0.50–2.06)	0.96	0.28
Blood glucose (mmols/L)				
<2.6	51 (6.9)	1.31 (0.92–1.85)	0.13	0.25
2.6 to 7.0	86 (5.3)	Reference		
>7.0	10 (6.3)	1.21 (0.63–2.32)	0.57	
Missing blood glucose	61 (5.0)	0.95 (0.68–1.32)	0.75	
White blood cells (10 ¹² cells/L)				
<4	1 (2.5)	0.45 (0.06–3.20)	0.42	0.79
4–20	157 (5.5)	Reference		
>20	29 (6.1)	1.10 (0.74–1.64)	0.63	
Missing	21 (5.4)	0.99 (0.63–1.56)	0.97	
Platelets (10 ⁹ cells/L)				
<150	38 (8.6)	1.69 (1.18–2.41)	0.004	0.70
≥150	149 (5.1)	Reference		
Missing	21 (5.4)	1.08 (0.68–1.70)	0.75	
HR: hazard ratios; the HR are from the Cox proportional hazards model.				

Table S5 Pathogens isolated from blood and CSF culture of young infants resident of KHDSS during inpatient period.

Blood culture Isolates		CSF culture isolates	
Pathogen full names (N=178)	No. (%)	Pathogen full names (N=24)	No. (%)
<i>Klebsiella pneumoniae</i>	53 (30)	<i>Escherichia coli</i>	6 (25)
<i>Escherichia coli</i>	25 (14)	Group B Streptococcus	6 (25)
<i>Staphylococcus aureus</i>	22 (12)	<i>Klebsiella pneumoniae</i>	3 (13)
Group B Streptococcus	19 (11)	<i>Streptococcus pneumoniae</i>	3 (13)
Non-typhoidal Salmonella species	9 (5.1)	<i>Enterobacter cloacae</i>	3 (13)
<i>Enterobacter cloacae</i>	8 (4.5)	Non-typhoidal Salmonella species	2 (8.2)
<i>Pseudomonas aeruginosa</i>	6 (3.4)	<i>Acinetobacter lwoffii</i>	1 (4.2)
<i>Streptococcus pneumoniae</i>	5 (2.8)		
<i>Streptococcus pyogenes</i>	3 (1.7)		
Acinetobacter species	3 (1.7)		
<i>Aeromonas hydrophila</i>	3 (1.7)		
Group A Streptococcus	3 (1.7)		
<i>Serratia marcescens</i>	2 (1.1)		
<i>Acinetobacter calcoaceticus/baumannii</i>	2 (1.1)		
<i>Acinetobacter lwoffii</i>	1 (0.6)		
<i>Aeromonas sobria</i>	1 (0.6)		
<i>Chryseobacterium indologenes</i>	1 (0.6)		
<i>Enterobacter aerogenes</i>	1 (0.6)		
Enterococci species	1 (0.6)		
<i>Haemophilus influenzae</i>	1 (0.6)		
<i>Proteus mirabilis</i>	1 (0.6)		

CSF; cerebrospinal fluid, Out of the 33 Meningitis cases, only the 24 presented had positive CSF culture.

Table S6. Annual admissions and case fatality ratios (CFR).

Admissions/Year	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019
<60 days	407	455	425	418	319	424	429	472	275	323	474
2 to 59 months	1734	1462	1222	1177	682	1050	1017	787	432	920	918
Proportion of YI admissions	19%	24%	26%	28%	32%	29%	30%	37%	39%	26%	34%
YI inpatient deaths	46	66	72	64	47	59	71	65	51	42	62
YI inpatient CFR	11%	15%	17%	15%	15%	14%	17%	14%	19%	13%	13%
YI post-discharge 1-year deaths	19	24	17	18	25	15	21	19	10	15	25
YI Post-discharge 1- year CFR	5.4%	6.4%	5.1%	5.3%	9.5%	4.3%	6.2%	4.8%	4.7%	5.6%	6.3%

Table S7. Estimated causes of post-discharge deaths during readmission at KCH (67 deaths).

Index admission diagnosis (N=67)	No. (%)	Causes of post-discharge deaths (N=67)	No. (%)
Neonatal sepsis	15 (22)	Neonatal sepsis	16 (24)
Preterm complications	15 (22)	Preterm complications	15 (22)
Heart disease-Congenital	9 (13)	Heart disease-Congenital	10 (15)
Neonatal jaundice	5 (7.5)	Neonatal jaundice	5 (7.4)
Meningitis	4 (6.0)	Meningitis	5 (7.4)
Birth asphyxia	4 (6.0)	Birth asphyxia	5 (7.4)
Lower respiratory tract infection	4 (6.0)	Lower respiratory tract infection	4 (6.0)
Encephalopathy - unknown	0	Encephalopathy - unknown	1 (1.5)
Hydrocephalus	1 (1.5)	Hydrocephalus	1 (1.5)
Malnutrition	1 (1.5)	None specified	5 (7.4)
None specified	9 (13)		

Index admission diagnosis and causes of death were assigned by treating clinician.

Table S8. Univariate analysis of admission features associated with inpatient deaths among babies born at KCH only.

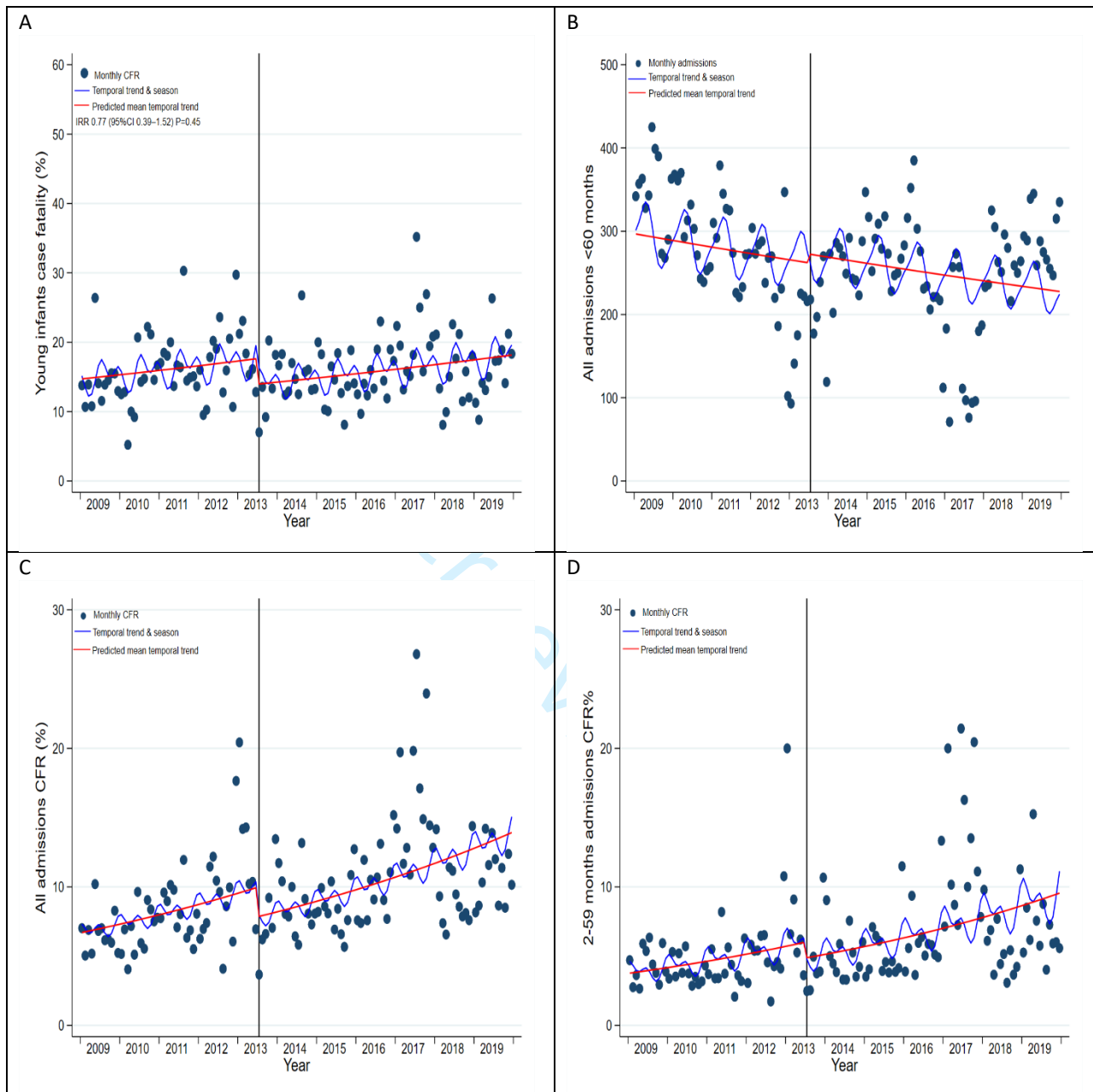
N=1,358	Deaths (N=174) N (%)	Crude SHR	P-value	Scaled Schoenfeld residuals P- value
Demographics				
Age in days				
0 to 2	151 (15)	2.48 (1.19–5.16)	0.02	0.26
3 to 7	8 (7.0)	1.22 (0.45–3.30)	0.69	
8 to 28	8 (6.8)	1.21 (0.46–3.23)	0.70	
>28	7 (5.5)	Reference		
Sex (female)	84 (14)	1.11 (0.83–1.48)	0.50	0.31
Born premature	101 (21)	2.65 (1.97–3.56)	<0.001	0.10
Born low birth weight	107 (21)	2.74 (2.03–3.71)	<0.001	0.44
Anthropometry				
Weight z score at birth				
<-2.0	32 (17)	1.49 (1.02–2.17)	0.04	0.12
≥-2.0	142 (12)	Reference		
MUAC (cm)				
<9.0	97 (23)	3.14 (2.05–4.83)	<0.001	0.17
9 to 10	26 (9.9)	1.26 (0.74–2.17)	0.40	
10 to 11	25 (7.3)	0.91 (0.53–1.57)	0.73	
≥11	26 (7.9)	Reference		
Missing MUAC	0	-		
Clinical features				
Axillary temperature				
<36°C	113 (26)	3.02 (2.13–4.27)	<0.001	0.30
36 to 37.5°C	41 (9.2)	Reference		
>37.5°C	18 (3.9)	0.42 (0.24–0.72)	0.002	
Missing temperature	2 (50)	6.90 (1.84–25.8)	0.004	
Respiratory rate/min				
Bradypnoea	32 (52)	6.44 (4.39–9.45)	<0.001	0.17
Normal	91 (10)	Reference		
Tachypnoea	50 (12)	1.21 (0.86–1.69)	0.28	
Missing	1 (5.3)	0.49 (0.07–3.37)	0.47	
Heart rate/min				
Bradycardia	21 (43)	4.76 (3.06–7.43)	<0.001	0.81
Normal	98 (10)	Reference		
Tachycardia	55 (15)	1.48 (1.07–2.05)	0.02	

Missing	0	-		
Hypoxia (SaO ₂ <90%)	79 (29)	3.62 (2.71–4.83)	<0.001	0.81
Lower chest wall indrawing	125 (21)	3.57 (2.57–4.95)	<0.001	0.47
Wheeze	0	-		
Stridor	5 (63)	6.96 (3.09–15.7)	<0.001	0.60
Breathing difficulty	481 (22)	5.40 (3.69–7.88)	<0.001	0.18
Cyanosis	29 (48)	5.15 (3.54–7.50)	<0.001	0.18
Capillary refill >2 seconds	14 (64)	7.22 (4.43–11.7)	<0.001	0.58
Temperature gradient	26 (30)	2.69 (1.81–4.01)	<0.001	0.49
Weak pulse	25 (58)	6.52 (4.44–9.56)	<0.001	0.77
Lethargy	17 (16)	1.29 (0.79–2.10)	0.31	0.56
Impaired consciousness	48 (52)	6.75 (4.93–9.24)	<0.001	0.13
Bulging fontanel	1 (25)	2.03 (0.31–13.2)	0.46	0.59
Stiff neck	1 (5.3)	-		0.31
Convulsions	1 (2.9)	0.21 (0.03–1.48)	0.12	0.21
Sunken eyes	1 (17)	1.35 (0.19–9.77)	0.77	0.57
Reduced skin turgor	1 (5.9)	0.44 (0.06–3.19)	0.42	0.56
Pallor	21 (42)	4.00 (2.61–6.12)	<0.001	0.59
Laboratory features				
Meningitis	2 (29)	9.95 (2.37–41.8)	0.002	0.12
Haemoglobin <11 g/dl	11 (13)	0.92 (0.51–1.66)	0.78	0.25
HIV antibody positive	8 (21)	1.68 (0.84–3.33)	0.14	0.14
Malaria slide positive	0	-		
Bacteraemia	14 (33)	3.00 (1.48–5.95)	0.002	0.20
Blood glucose (mmols/l)				
<2.6	33 (12)	1.02 (0.67–1.56)	0.91	0.95
2.6 to 7.0	58 (12)	Reference		
>7.0	11 (21)	1.88 (1.00–3.54)	0.05	
Missing blood glucose	72 (13)	1.11 (0.79–1.56)	0.53	
White blood cells (10 ¹² cells/L)				
<4	3 (33)	3.52 (1.25–9.91)	0.02	0.08
4-20	100 (10)	Reference		
>20	59 (28)	3.10 (2.27–4.24)	<0.001	
Missing	12 (8.2)	0.82 (0.45–1.48)	0.50	
Platelets (10 ⁹ cells/L)				
<150	35 (20)	1.69 (1.18–2.44)	0.005	0.50
≥150	127 (12)	Reference		
Missing	12 (8.2)	0.66 (0.37–1.19)	0.17	
SHR; sub-distribution hazard ratios; the SHR are from the Fine and Gray's proportional sub-hazards model.				

Table S9. Multivariable regression analysis of factors associated with inpatient and post-discharge mortality among children born at KCH only.

	Inpatient analysis		Post-discharge analysis	
	Adjusted SHR*	P-value	Adjusted HR	P-value
Demographics				
Age in days				
0 to 2	3.03 (1.33–6.94)	0.009	¶	
3 to 7	4.08 (1.48–11.3)	0.007	¶	
8 to 28	2.57 (0.90–7.29)	0.08	¶	
>28	Reference			
Anthropometry				
Low birth weight	1.55 (1.10–2.20)	0.01	2.76 (1.30–5.82)	0.008
Clinical features				
Axillary temperature				
<36°C	1.49 (0.97–2.28)	0.07	1.44 (0.71–2.95)	0.31
36 to 37.5°C	Reference		Reference	
>37.5°C	0.67 (0.39–1.13)	0.13	0.22 (0.06–0.78)	0.02
Missing temperature	3.37 (0.85–13.4)	0.09	0.48 (0.09–2.64)	0.40
Respiratory rate/min				
Bradypnoea	2.22 (1.36–3.63)	0.001	¶	
Normal	Reference			
Tachypnoea	0.78 (0.55–1.11)	0.17	¶	
Missing	-			
Heart rate/min				
Bradycardia	1.88 (1.14–3.12)	0.01	3.56 (1.14–11.2)	0.03
Normal	Reference		Reference	
Tachycardia	1.57 (1.11–2.21)	0.01	1.54 (0.77–3.07)	0.22
Missing	0.25 (0.02–3.00)	0.28	-	
Hypoxia (SaO ₂ <90%)	1.60 (1.14–2.24)	0.006	¶	
Lower chest wall indrawing	1.42 (0.91–2.22)	0.12	¶	
Stridor	3.74 (1.87–7.49)	<0.001	¶	
Breathing difficulty	2.13 (1.25–3.64)	0.005	¶	
Capillary refill >2 seconds	1.94 (1.06–3.56)	0.03	¶	
Weak pulse	2.15 (1.27–3.65)	0.004	1.60 (0.24–10.5)	0.63
Pallor	2.36 (1.46–3.83)	<0.001	¶	
Laboratory features				
Bacteraemia	2.50 (1.20–5.22)	0.02	0.21 (0.03–1.81)	0.16
Model performance				
AUC (95% CI)	0.85 (0.82–0.88)		0.79 (0.72–0.85)	
SHR; sub-distribution hazard ratios; *the SHR are from the Fine and Gray's proportional subhazards model, HR-Hazard ratio from the Proportional Cox regression model, ¶; variables not selected for inclusion in the multivariable model, AUC; area under receiver operating characteristics.				

Figure S1. **A: Monthly all young infant admissions, B: all admissions (<60 months old), C: all admissions (<60 months old) case fatality and D: 2–59 months old case fatality before and after July 2013.**



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4 1 **Trends in inpatient and post-discharge mortality among young infants**
5 2 **admitted to Kilifi County Hospital Kenya, a retrospective cohort**
6 3 **study.**

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19 Abstract

20 **Objectives:** to describe admission trends and estimate inpatient and post-discharge mortality
21 and its associated exposures, among young infants (YI) admitted to a county hospital in Kenya

22 **Design:** retrospective cohort study

23 **Setting:** secondary level hospital

24 **Participants:** YI aged less than 60 days admitted to hospital January 2009 to December 2019:
25 12,271 admissions in 11,877 individuals. YI who were resident within a health and demographic
26 surveillance system (KHDSS): n= 3,625 with 4,421 admissions were followed up for 1 year after
27 discharge.

28 **Primary and secondary outcome measures:** Inpatient and 1-year post-discharge mortality, the
29 latter in KHDSS residents.

30 **Results:** Of 12,271 YI admissions, 4,421 (36%) were KHDSS-resident. Neonatal sepsis, preterm
31 complications and birth asphyxia accounted for 83% of admissions. The proportion of YI among
32 under-fives admissions increased from 19% in 2009 to 34% in 2019 ($P_{\text{trend}}=0.02$). Inpatient case
33 fatality was 16%, with 66% of deaths occurring within 48 hours of admission. The introduction
34 of free maternity care in 2013 was not associated with a change in admissions or inpatient
35 mortality among YI. During 1-year post-discharge, 208/3625 (5.7%) YI died, 64.3 (95%CI 56.2–
36 73.7) per 1,000 infant-years. 49% of post-discharge deaths occurred within one month of
37 discharge, and 49% of post-discharge deaths occurred at home. Both inpatient and post-
38 discharge deaths were associated with low admission weight. Inpatient mortality was

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3 39 associated with clinical signs of disease severity, while post-discharge mortality was associated
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6 40 with length of hospitalization, leaving against advice and referral to a specialized hospital.
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9 41 **Conclusions:** YIs accounted for an increasing proportion of paediatric admissions and their overall
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11 42 mortality remains high. Post-discharge mortality accounts for a lower proportion of deaths but
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13 43 mortality rate is higher than among children aged 2-59 months. Services to address post-
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16 44 discharge mortality are needed and should focus on infants at higher risk.
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19 45
20 46 **Key words**

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24 47 Young infant; neonatal; mortality; inpatient; post-discharge; Africa; Kenya
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27 48 291 words
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15 63 **Article summary**16
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18 64 **Strengths and limitations of this study**

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- 21 65
- Large sample size with systematic data collection
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- Linkage of hospital admissions to a well-established demographic surveillance system,
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- 25 with low loss to follow up.

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- Lack of accurate gestational age estimation or birthweight of most participants.

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- Data are from a single hospital and only the population covered by demographic

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73 Background

74 The United Nations Sustainable Development Goal 3 aims to ensure healthy living and promote
75 wellbeing for all ages, with all countries aiming to reduce neonatal and under-five mortality to
76 below 12 and 25 per 1,000 live births by 2030 respectively. In sub-Saharan Africa, child mortality
77 has declined by ~58% in the last 30 years. However, the estimated neonatal and under-five
78 mortality rates in sub-Saharan Africa remained high in 2019 (27 and 76 per 1,000 live births
79 respectively) with a similar neonatal mortality rate of 27 per 1,000 live births in Kenya.¹
80 Combined neonatal and post-neonatal infant mortality accounts for over three quarters of all
81 under-five deaths in Kenyan children.²

82 Young infants aged <60 days old (YI) comprise around half of hospital admissions in sub-Saharan
83 Africa and continue to face high risk of in-hospital mortality and long-term neuro-disability.³⁻⁶
84 Post-discharge mortality is emerging as a major problem in children in low- and middle-income
85 countries (LMICs),⁷ however, there are limited data among YI. A systematic review of paediatric
86 post-discharge mortality in developing countries included 24 studies published up to July 2017
87 with 19 from Africa.⁸ Four studies included YI. Although young age was reported as a risk factor
88 of mortality, no studies specifically identified deaths among infants aged <60 days. We have
89 previously demonstrated excess post-discharge mortality among all hospitalised children,
90 suggesting that hospitalisation itself selects vulnerable children with a sustained increased risk
91 of dying over the longer term.^{7,9}

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3 92 Better understanding of YI deaths occurring during hospitalisation and after discharge from
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6 93 hospital is vital for development and use of targeted interventions aimed at improving survival.
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9 94 This analysis aimed to describe admission trends and measure inpatient and post-discharge
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11 95 mortality and its associated exposures, including the introduction of free maternity care, among
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14 96 YI admitted to Kilifi County Hospital (KCH), Kenya and followed up through the Kilifi Health and
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16 97 Demographic Surveillance System (KHDSS).
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99 **Methods**

100 *Study participants and design*

101 KCH is a secondary-level referral hospital situated in Kilifi County along the Kenyan coast. It serves
102 a rural and peri-urban population. It has a maternity unit. with approximately 6,000 deliveries
103 per year, a general paediatric ward with a newborn unit for babies aged less than 1 month, and
104 a paediatric High Dependency Unit (HDU) that also admits YIs. The year 2009 was selected as a
105 starting point, because a previous analysis of mortality among YI covered admissions from 1990
106 to 2008¹⁰. Free maternity care was introduced by the Kenyan government on 1st June 2013 and
107 led to a marked increase in health facility births.¹¹

108 The KHDSS, established in 2002, covers a population of 279,158 within an area of 900km² centred
109 on KCH.¹² Census rounds visit each household every four months to ascertain vital status and
110 migration in and out of the hospital catchment area.

111 We conducted a retrospective cohort study of YIs resident within the KHDSS who were admitted
112 to KCH between January 1st, 2009, and December 31st, 2019. Children discharged alive and
113 followed up in KHDSS census rounds until March 2021 were eligible for analyses of post-discharge
114 mortality. During the study period, there were 9 health workers' strikes with the last nurses'
115 strike lasting for 150 days (5th June to 2nd November 2017).¹³ **Supplementary Table S1.** For
116 comparison, we also examined admissions aged 60 days to 59 months during the same period.

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3 118 *Procedures*
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7 119 At admission, standardised medical history, and clinical examination, including anthropometric
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9 120 measurements were obtained by trained clinical staff. Blood samples were systematically taken
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11 121 for complete blood count, slide for malaria microscopy, and clinical chemistry, Human
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13 122 Immunodeficiency Virus (HIV) antibody test and blood culture at hospital admission, as described
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15 123 previously.¹⁴ A lumbar puncture for cerebrospinal fluid (CSF) analysis was done at admission in
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17 124 infants in whom sepsis was suspected and deferred in those seriously ill or with other
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19 125 contraindications. Clinical and laboratory data were recorded in real time on a ward surveillance
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21 126 database linked to the KHDSS database. Empiric antibiotics were initiated according to national
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23 127 guidelines¹⁵ with ampicillin/benzylpenicillin plus gentamicin as first-line intravenous therapy.
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25 128 Second-line and subsequent antimicrobial therapy was guided by blood culture results and
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27 129 clinical progress. Mechanical ventilation was not available at KCH.
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34 130 *Statistical methods*
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37 131 *Study variables*
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41 132 Outcomes of interest were death in hospital and during 1 year after discharge. Exposures of
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43 133 interest were demographic, nutritional, clinical features, and haematological, biochemical, and
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45 134 microbiological findings at the time of admission. De-identified study data were deposited in the
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47 135 Harvard Dataverse depository.¹⁶
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6 139 Weight at admission and mid-upper arm circumference (MUAC) were categorised as shown on
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9 140 **Table 1.** Because approximately 40% of the YI were underweight (<2.5kg), and 60% were aged ≤2
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11 141 days at admission, YI's admission weights rather than anthropometric Z scores using WHO
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13 142 standards were reported. Furthermore, most YI who were born at home or in other hospitals and
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15 143 referred to KCH were missing gestational age estimates and birth weight to be able to estimate
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17 144 gestational age at birth using the INTERGROWTH 21st Newborn Size Standards (INSS).

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21 145 Prematurity was defined as gestation age <37 weeks and LBW as birth weight <2500 grams for
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23 146 YIs born at KCH. Admission blood glucose was categorized into <2.6, 2.6 to 7.0 and ≥7.0 mmol/l
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25 147 representing low, normal and high levels respectively.¹⁵ Missing data were not assumed to be
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27 148 missing at random. We, therefore, created categorical variables and added a missing category
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29 149 which was included in the regression analysis.

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34 150 Demographic, anthropometric, and clinical data are presented as frequencies and proportions
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36 151 for categorical variables and means (standard deviation (sd)) or median (interquartile range
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38 152 (IQR)) for continuous variables depending on the underlying distribution. Proportions of missing
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40 153 data for each variable are shown on **Supplementary Table S2.**

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45 154 Monthly admissions and case fatality were plotted against time (month of admission) to visually
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47 155 inspect the trend from 2009 to 2019 and the predicted trend line superimposed on the curves.
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49 156 We used the Augmented Dickey Fuller test (ADF test) to test if the time series were stationary
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51 157 (no trend or seasonal effects). We also presented annual absolute admissions, proportion of YI
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53 158 among all admissions <60 months and case fatality. Monthly admissions and case fatality were
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3 159 tested for annual linear trend using an extension of the Wilcoxon rank-sum test of trend across
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6 160 ordered groups.¹⁷
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9 161 We used interrupted time series analysis to estimate the level and trend changes before and
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11 162 after introduction of free maternity care (1st June 2013). We created a time month variable
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13 163 coded sequentially from January 2009 to December 2019 and a binary variable coded as 0 and 1
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15 164 for admissions before and after June 2013 respectively to represent to represent introduction of
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17 165 free maternity care . We defined seasonal effect variable using month of the year modelled on
18
19 166 harmonic terms using the Fourier code in STATA. To measure the effect of free maternity care,
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21 167 we used the negative binomial regression model because of presence of overdispersion in the
22
23 168 trends and reported regression coefficients transformed into incidence rate ratios (IRR). All the
24
25 169 negative binomial regression models included the following independent variables: the time
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27 170 month variable, the binary pre- and post- free maternity care variable and the seasonal effect
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29 171 variable.
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36 172 Since YIs could be admitted more than once whilst <60 days old, we included multiple admissions
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38 173 using unique IDs and adjusted for clustering by individual with robust standard errors. To identify
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40 174 exposures associated with inpatient death, we treated being discharged alive as a competing
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42 175 event and fitted the proportional sub-distribution hazard model using the Fine-Gray competing
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44 176 risk model.¹⁸ The measure of effect reported from the model was the sub-distribution hazard
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46 177 ratios (SHR) and their respective 95% confidence intervals (CI). To build the multivariable
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48 178 regression model, a backward stepwise approach was used where all the independent variables
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50 179 assessed in the univariate models were included in the model and only those with a P-value <0.1
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52 180 retained in the final multivariable model.
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3 181 For the post-discharge analysis, only data from those YI discharged alive and resident within the
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6 182 KHDSS were analysed. Time at risk was defined from date of discharge to 365 days later or
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8 183 censure at date of death or outmigration from the KHDSS. We performed a ‘multiple discharges’
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11 184 analysis where YI with multiple admissions had their follow-up time reset at each successive
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13 185 discharge date. Exposures associated with post-discharge were assessed using a Gamma
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15 186 distribution shared frailty Cox proportional hazards regression model accounting for YI with
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18 187 multiple discharges. The proportional hazards assumption was assessed using the scaled
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20 188 Schoenfeld residuals test (**Supplementary Tables S3 and S4**). All exposures assessed in the
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23 189 univariate models were considered for inclusion in the multivariable Cox proportional hazards
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25 190 regression model using a backward stepwise approach similar to the inpatient analysis. Both the
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28 191 inpatient and post-discharge multivariable regression models’ discrimination performance were
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30 192 assessed using bootstrapped area under receiver operating characteristic curves (AUC) replicated
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33 193 1000 times.

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35 194 As sensitivity analysis, we assessed the YI born at KCH and enrolled to the Kilifi Perinatal and
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38 195 Maternal Research Project (KIPMAT), which had collected comprehensive birth data including
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41 196 birth weight and gestational age (weeks).¹⁹ We estimated their birthweight Z scores using the
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43 197 INTERGROWTH Newborn Size Standards (INSS) and ran the regression models replacing
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45 198 admission weight with birthweight Z score.²⁰

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48 199 Statistical significance was evaluated using 95% CI and a two-tailed *P*-value <0.05. Statistical
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51 200 analyses were conducted using STATA Version 17.0 (College Station, TX, USA).

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54 201 *Study size*

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3 202 We used all available eligible YI data from 2009 to 2019 (4,421 for inpatient and 3,625 for post-
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6 203 discharge analyses) regardless of sample size.

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10 205 *Ethical considerations*

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13 206 Written consent was provided by the caregivers of all the surveillance study participants. Ethical
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16 207 approval to conduct this analysis was granted by the Kenya Medical Research Institute (KEMRI)
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18
19 208 National Ethics Review Committee (SCC 2778).

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21 209 *Patient and public involvement*

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24 210 There was no patient and public involvement in the planning or execution of this retrospective
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27 211 cohort study.

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213 Results

214 *Baseline characteristics*

215 During the study period, there were 42,742 paediatric admissions to KCH, of which 12,271 (29%)
216 admission events among 11,877 individuals were aged <60 days. Of the 12,271 YI admission
217 events, 4,421 (36%) were resident in the KHDSS and included in the analysis (**Figure 1**). This
218 comprised 4,272 individual YI: 4,131 with one admission, 133 two admissions and 8 three
219 admissions within the first 60 days of life.

220 *KHDSS-resident admissions*

221 Among the 4,421 YI admission events among KHDSS residents, 2,731 (62%) were ≤ 2 days old and
222 1,900 (43%) were female. Reported prematurity and low birth weight were 1,019 (23%) and 581
223 (13%) respectively. Low weight (<2.5kg) was observed in 1694 YIs (38%) while 1342 (30%) had
224 MUAC <9.0cm. Common presenting clinical signs were lower chest wall indrawing (46%) and
225 breathing difficulty (49%). Thirty percent had fever, 31% had hypothermia and 30% tachycardia.
226 Nine hundred and thirty-two YI (21%) had hypoxia (SaO₂ <90%) at admission and 250 (5.7%) had
227 impaired consciousness. Presenting signs at admission for all the YI stratified by KHDSS residence
228 are shown on **Table 1**. Malaria was rare (n=4, 0.09%) whilst 142 (3.2%) and 170 (3.9%) YI were
229 HIV antibody positive and had bacteraemia respectively. **Supplementary Table S3** lists the
230 bacterial isolates that were presumed pathogens, led by *Klebsiella pneumoniae*, *Escherichia coli*,
231 *Staphylococcus aureus* and Group B Streptococcus.

232

233 **Table 1. Study participants characteristics at admission.**

	All young infant admissions (N=12,271) ^a	Young infant admissions KHDSS residents (N=4,421)	Young infant admissions non-KHDSS residents (N=7,850)	p-value
Demographics				
Age in days				
0 to 2	7856 (64)	2731 (62)	5125 (65)	<0.001
3 to 7	1384 (11)	468 (11)	916 (12)	
8 to 28	1506 (12)	587 (13)	919 (12)	
>28	1525 (12)	635 (14)	890 (11)	
Sex (female)	5245 (43)	1900 (43)	3345 (43)	0.70
Reported born premature	2970 (24)	1019 (23)	1951 (25)	0.005
Reported low birth weight	1782 (15)	581 (13)	1201 (15)	<0.001
Born at KCH				
Yes	6757 (55)	2743 (62)	4014 (51)	<0.001
No	5514 (45)	1678 (38)	3836 (49)	
Anthropometry				
Weight (kg)				
<1.5	1767 (14)	566 (13)	1201 (15)	<0.001
1.5 to <2.5	3211 (26)	1128 (26)	2083 (27)	
≥2.5	7193 (59)	2684 (61)	4509 (57)	
Missing	100 (0.8)	43 (1.0)	57 (0.7)	
MUAC (cm)				
<9	3933 (32)	1342 (30)	2591 (33)	<0.001
9 to 10	2492 (20)	862 (20)	1630 (21)	
10 to 11	2926 (24)	1035 (23)	1891 (24)	
≥11	2622 (21)	1056 (24)	1566 (20)	
Missing	298 (2.4)	126 (2.9)	172 (2.2)	
Clinical features				
Axillary temperature				
<36°C	3553 (29)	1358 (31)	2195 (28)	<0.001
36 to 37.5°C	4692 (38)	1711 (39)	2981 (38)	
>37.5°C	3948 (32)	1318 (30)	2630 (34)	
Respiratory rate/min ^b				
Bradypnoea	540 (4.4)	188 (4.3)	352 (4.5)	0.56
Normal	7333 (60)	2647 (60)	4686 (60)	
Tachypnoea	4158 (34)	1490 (34)	2668 (34)	
Missing	240 (2.0)	96 (2.2)	144 (1.8)	
Heart rate/min ^c				
Bradycardia	396 (3.2)	158 (3.6)	238 (3.0)	0.11
Normal	8162 (67)	2910 (66)	5252 (67)	
Tachycardia	3667 (30)	1331 (30)	2336 (30)	
Missing	46 (0.4)	22 (0.5)	24 (0.3)	

Hypoxia ^d	2668 (22)	932 (21)	1736 (22)	0.19
Lower chest wall indrawing	5562 (45)	2051 (46)	3511 (45)	0.13
Wheeze	112 (0.9)	46 (1.0)	66 (0.8)	0.41
Stridor	62 (0.5)	19 (0.4)	43 (0.6)	0.48
Breathing difficulty	5966 (49)	2172 (49)	3794 (48)	0.44
Cyanosis	560 (4.6)	210 (4.8)	350 (4.5)	0.54
Capillary refill >2 seconds	301 (2.6)	105 (2.4)	196 (2.5)	0.81
Temperature gradient	710 (5.8)	258 (5.8)	452 (5.8)	0.73
Weak pulse	463 (3.8)	157 (3.6)	306 (3.9)	0.05
Lethargy	971 (7.9)	325 (7.4)	646 (8.2)	0.15
Impaired consciousness ^e	792 (6.5)	250 (5.7)	542 (6.9)	0.007
Bulging fontanel	111 (0.9)	32 (0.7)	79 (1.0)	0.21
Stiff neck	48 (0.4)	10 (0.2)	38 (0.5)	0.05
Convulsions	689 (5.6)	197 (4.5)	492 (6.3)	<0.001
Sunken eyes	134 (1.1)	44 (1.0)	90 (1.2)	0.44
Reduced skin turgor	308 (2.5)	97 (2.2)	211 (2.7)	0.19
Pallor	633 (5.2)	221 (5.0)	412 (5.3)	0.55
Laboratory features				
Meningitis ^f	98 (0.8)	33 (0.8)	65 (0.8)	0.87
Haemoglobin <11 g/dl ^g	1207 (9.8)	476 (11)	731 (9.3)	0.02
HIV antibody positive	441 (3.6)	142 (3.2)	299 (3.8)	0.11
Malaria slide positive	5 (0.04)	4 (0.09)	1 (0.01)	0.02
Bacteraemia	590 (4.8)	170 (3.9)	420 (5.4)	<0.001
White blood cells (10 ¹² cells/L) ^h				
<4	134 (1.1)	54 (1.2)	80 (1.0)	<0.001
4–20	8738 (71)	3228 (73)	5510 (70)	
>20	2202 (18)	690 (16)	1512 (19)	
unavailable	1197 (9.8)	449 (10)	748 (9.5)	
Platelets (10 ⁹ cells/L) ⁱ				
<150 cells/L	1615 (13)	586 (13)	1029 (13)	0.59
≥150	9455 (77)	3387 (77)	6068 (77)	
unavailable	1201 (9.8)	448 (10)	753 (9.6)	
Blood glucose (mmols/L)				
<2.6	2479 (20)	882 (20)	1597 (20)	0.29
2.6 to 7.0	5086 (41)	1875 (42)	3211 (41)	
>7.0	688 (5.6)	231 (5.2)	457 (5.8)	
unavailable	4018 (33)	1433 (32)	2585 (33)	

^a-Eligible admissions were young infants aged <60days admitted from 2009 to 2019, ^b- Tachypnoea: respiratory rate ≥60 breaths/min, Bradypnoea: respiratory rate <30 breaths/min, ^c-Tachycardia: heart rate>160 beats/min, Bradycardia: heart rate<100 beats/min, ^d-Hypoxia: oxygen saturation<90%,^e- Impaired consciousness level if 'prostrate' or 'unconscious', ^f Meningitis: positive CSF culture, or positive CSF microscopy, or positive CSF antigen test, or elevated CSF WBC count (≥20 in young infants aged 0-28 days OR, ≥10 in young infants aged 29-59 days) PLUS a positive blood culture for a known pathogen, ^g Anaemia: haemoglobin <11 g/dl, ^h Normal values WBC 4-20 x 10¹² cells/L, Leucopenia WBC <4 x 10¹² cells/L, Leucocytosis WBC >20 x 10¹² cells/L, ⁱ Normal values Platelets ≥150x10⁹ cells/L, Thrombocytopenia <150x10⁹ cells/L, KHDSS: Kilifi Health and Demographic Surveillance System, MUAC: Mid-upper arm circumference.

234 *Admissions over time*

235 The annual number of admissions are shown in **Supplementary Table S4**. The overall proportion
 236 of YI among all admissions under 5 years old was 28% (95%CI 27–29%), increasing from 19% in
 237 2009 to 34% in 2019 (test of linear trend P=0.02) **Figure 2**. **Figure 3A** shows the upward trend of
 238 absolute YI admissions and downward trends for 2 to 59-month-olds and all admissions <60
 239 months old (all P-values for tests for stationarity <0.05). There was no significant difference in
 240 monthly YI admissions before introduction of free maternity care in June 2013 (monthly median
 241 [IQR] of 76 [66–96] admissions) and after June 2013 (monthly median [IQR] of 95 [78–125]
 242 admissions) season-adjusted IRR 1.06 (95%CI 0.54–2.09) P=0.86 (**Supplementary Figure S1A**).
 243 The mean monthly YI admissions on day of birth did not differ before and after June 2013; season-
 244 adjusted IRR 0.88 (95%CI 0.44 to 1.76), P=0.72. The proportion of YI admissions to total
 245 admissions aged <60 months before and after June 2013 were not different; season-adjusted IRR
 246 1.02 (95%CI 0.28–3.71) P=0.97 **Figure 3D**. We found no significant difference in monthly absolute
 247 admissions (all admissions <60 months old), before and after June 2013; season-adjusted IRR
 248 1.01 (95%CI 0.51–2.00) P=0.97 (**Supplementary Figure S1B**).

249 *Inpatient deaths*

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3 250 Overall, 1,914/11,877 (16%) of YI died in hospital. The risk of inpatient death was not significantly
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6 251 different between 645/4,272 (15%) KHDSS residents and 1,269/7,605 (17%) non-residents of
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8 252 KHDSS (age- and sex-adjusted SHR 0.93 (95%CI 0.85–1.02) P=0.12) (**Figure 1**). The annual YI
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10 253 inpatient case fatality ratio was stable (11% in 2009 and 13% in 2019. P-value for trend=0.80),
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13 254 **Figure 2**. Monthly inpatient case fatality for YI, 2 to 59 months old and all <60 months old children
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15 255 are shown in **Figure 3B**.

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18 256 During the study period there were 3,119 inpatient deaths among admissions <60 months old
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21 257 admitted at KCH, with YI admissions accounting for 61% (95%CI 60–63%) of the deaths and no
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23 258 significant linear trend from 2009 to 2019 (trend P=0.29). The mean monthly YI inpatient case
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26 259 fatality was 16% (sd 0.86) and 16% (sd 1.23) before and after June 2013 respectively; season-
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28 260 adjusted IRR 0.77 (95%CI 0.39–1.52) P=0.45 **Figure 3C**. The mean monthly case fatality for all
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31 261 admissions aged <60 months and admissions 2–59 months old did not differ before June 2013
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33 262 and after June 2013; season-adjusted IRR 0.79 (95%CI 0.39–1.58) P=0.50 and IRR 0.81 (95%CI
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35 263 0.39–1.69) P=0.57 respectively **Supplementary Figure S1 C and D**.

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38 264 Among the 4,421 KHDSS-resident YI admissions, median [IQR] time to death was 2 [1–4] days,
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41 265 while the survivors were admitted for 5 [3–8] days. A total of 423/645 (66%) deaths occurred
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43 266 within the first 48 hours following admission. Forty-one YI left against medical advice, and 55
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46 267 were referred to other hospitals for further care.

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49 268 *Admission diagnosis & case fatality ratio*
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269 The commonest reasons for hospital admission were neonatal sepsis (47%), preterm

Discharge diagnosis ^a	No. (%) Diagnosis assigned by clinician at discharge	
	All admissions (N=4421)	Inpatient Deaths (N=645)
Neonatal sepsis	2097 (47)	201 (9.6)
Preterm complications	889 (20)	262 (29)
Birth asphyxia	724 (16)	201 (28)
Neonatal jaundice	611 (14)	56 (9.2)
Lower respiratory tract infection	486 (11)	41 (8.4)
Respiratory distress syndrome	263 (6.0)	136 (52)
Congenital anomalies	215 (4.9)	55 (26)
Meningitis ^b	112 (2.5)	11 (9.8)
Anaemia	78 (1.8)	14 (18)
Malnutrition	36 (0.8)	1 (2.8)
None specified	69 (1.6)	4 (5.8)
Others	266 (6.0) ^c	13 (4.9)

270 complications (20%) and birth asphyxia (16%) accounting for 83% of all YI admissions (**Table 2**).

271 The case fatality ratios for YI with respiratory distress syndrome, preterm complications and birth
 272 asphyxia were 52%, 29% and 28% respectively (**Table 2**).

274 **Table 2. Discharge diagnosis assigned by clinician.**

^a Young infant could be assigned up to 2 diagnoses

^b Meningitis: positive CSF culture, or positive CSF microscopy, or positive CSF antigen test, or elevated CSF WBC count (≥ 20 in young infants aged 0-28 days OR, ≥ 10 in young infants aged 29-59 days) PLUS a positive blood culture for a known pathogen

^c Accidents-3, Acute abdominal obstruction-15, bronchiolitis-12, burns-1, Candidiasis-1, Cellulitis abscess-21, Chickenpox-1, Chromosomal abnormality-5, CNS abscess-1, Conjunctivitis-2, Dehydration-2, Dental problems-1, Diabetes-1, Elective surgery-5, Encephalopathy-9, Epilepsy-7, Extra pulmonary TB-1, Febrile convulsions-5, Feeding difficulty-1, Gastroenteritis-15, Haemolytic uraemic syndrome-1, Hydrocephalus-11, LTB/croup-1, Immunosuppression-17, Malaria-2, Male genital problem-1, Meconium aspiration-33, Neonatal haemorrhage-14, Neonatal tetanus -10, Other skin disease-3, Otitis media-1, Poisoning (organophosphates)-1, Pyogenic arthritis-1, Rabies-1, Rash-4, renal failure-6, trauma/fractures/RTA-11, Urinary tract infection-10, upper respiratory tract infection (URTI)-24, Viral hepatitis-2, Viral infection-3.

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281

282 *Exposures associated with inpatient death*

283 Variables assessed for association with inpatient death in univariate models are shown in

284 **Supplementary Table S5**. In the multivariable analysis (**Table 3**), admissions at age ≤ 2 days and

285 3–7 days, compared to ≥ 28 days old, were associated with inpatient deaths. Being born at KCH

286 was not associated with inpatient death, so was not included in the multivariate analysis. Very

287 low admission weight (< 1.5 kg) and weight 1.5–2.4 kg compared to ≥ 2.5 kg were positively

288 associated with inpatient deaths. Signs of clinical severity (bradypnoea, tachypnoea, bradycardia,

289 hypoxia, lower chest wall indrawing, breathing difficulty, weak pulse, impaired consciousness,

290 and hypothermia, but not fever), meningitis, bacteraemia, leucopenia and leucocytosis but not

291 an HIV antibody positive test (aSHR 1.15 (95%CI 0.81–1.63)) were positively associated with

292 inpatient death. The multivariable model bootstrapped AUC was 0.88 (95%CI 0.86–0.89) **Table 3**.

293 Performance of a multivariable model including only 4,272 single admissions did not differ from

294 the model with multiple admissions (bootstrapped AUC 0.88 (95%CI 0.86–0.89) **Supplementary**

295 **Table S6**.

296 **Table 3. Multivariable regression analysis of factors associated with inpatient and post-**
297 **discharge mortality.**

	Inpatient analysis		Post-discharge analysis	
	Adjusted SHR*	P-value	Adjusted HR	P-value
Demographics				
Age in days				
0 to 2	2.12 (1.46–3.06)	<0.001	1.30 (0.73–2.31)	0.37
3 to 7	3.88 (2.46–6.10)	<0.001	0.80 (0.38–1.68)	0.56
8 to 28	1.42 (0.90–2.25)	0.13	1.45 (0.81–2.59)	0.21
>28	Reference		Reference	
Sex (female)	0.91 (0.78–1.07)	0.26	0.98 (0.74–1.31)	0.94
Born at KCH				
Yes	¶		Reference	
No	¶		1.59 (1.18–2.14)	0.003
Admission days (log)	¶		1.87 (1.54–2.26)	<0.001
Type of discharge				
Normal	¶		Reference	
Absconded	¶		3.01 (1.22–7.46)	0.02
Transferred/referred	¶		12.8 (8.11–20.2)	<0.001
Anthropometry				
Weight (kg)				
<1.5	2.16 (1.75–2.67)	<0.001	1.95 (1.38–2.74)	<0.001
1.5 to <2.5	1.42 (1.16–1.74)	0.001	0.82 (0.48–1.42)	0.49
≥2.5	Reference		Reference	
Missing weight	3.85 (2.59–5.71)	<0.001	-	
Clinical features				
Axillary temperature				
<36°C	1.44 (1.17–1.78)	0.001	1.06 (0.74–1.53)	0.75
36 to 37.5°C	Reference		Reference	
>37.5°C	1.09 (0.84–1.41)	0.53	0.69 (0.47–0.99)	0.04
Missing temperature	1.03 (0.38–2.75)	0.96	1.09 (0.15–8.22)	0.93
Respiratory rate/min				
Bradypnoea	1.45 (1.09–1.93)	0.01	1.66 (0.76–3.63)	0.21
Normal	Reference		Reference	

Tachypnoea	0.80 (0.67–0.95)	0.01	1.24 (0.93–1.66)	0.14
Missing	1.51 (0.64–3.56)	0.34	0.80 (0.11–5.82)	0.82
Heart rate/min				
Bradycardia	1.40 (1.08–1.82)	0.01	¶	
Normal	Reference			
Tachycardia	1.14 (0.94–1.37)	0.18	¶	
Missing	0.41 (0.03–5.13)	0.49	¶	
Hypoxia (SaO ₂ <90%)	1.62 (1.37–1.92)	<0.001	¶	
Capillary refill >2 seconds	1.34 (0.97–1.86)	0.08	¶	
Lower chest wall indrawing	1.41 (1.14–1.75)	0.002	¶	
Stridor	1.93 (0.92–4.03)	0.08	¶	
Breathing difficulty	1.45 (1.15–1.82)	0.001	¶	
Weak pulse	1.61 (1.19–2.17)	0.002	2.22 (1.01–4.89)	0.04
Bulging fontanel	2.45 (0.91–6.65)	0.08	2.59 (0.92–7.26)	0.07
Impaired consciousness	2.21 (1.72–2.84)	<0.001	¶	
Pallor	1.30 (0.98–1.71)	0.07	¶	
Laboratory features				
Meningitis	5.45 (2.50–11.8)	<0.001	2.16 (0.73–6.37)	0.17
HIV antibody positive	1.15 (0.81–1.63)	0.43	0.94 (0.43–2.05)	0.87
Bacteraemia	2.21 (1.51–3.22)	<0.001	¶	
White blood cells (10 ¹² cells/L)				
<4	2.17 (1.30–3.62)	0.003	¶	
4-20	Reference		¶	
>20	1.71 (1.43–2.04)	<0.001	¶	
unavailable	1.09 (0.82–1.44)	0.57	¶	
Model performance				
Bootstrapped AUC (95% CI)	0.88 (0.86–0.89)		0.76 (0.73–0.80)	
<p>SHR; sub-distribution hazard ratios; *the SHR are from the Fine and Gray's proportional sub-hazards model, HR-Hazard ratio from the shared frailty Cox regression model, ¶; variables not selected for inclusion in the multivariable model, AUC; area under receiver operating characteristics. Meningitis: positive CSF culture, or positive CSF microscopy,</p>				

or positive CSF antigen test, or elevated CSF WBC count (≥ 20 in young infants aged 0-28 days OR, ≥ 10 in young infants aged 29-59 days) PLUS a positive blood culture for a known pathogen

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299 Post-discharge death

300 There were 3,776 live discharges from 3,640 YI residents of KHDSS, of which 3,760 (from 3,625
301 individual YI) were followed up for 3,233 infant-years (**Figure 1**). During one-year follow-up, there
302 were 208/3625 (5.7%) deaths: 64.3 (95%CI 56.2–73.7) deaths per 1,000 infant-years. The median
303 [IQR] time to death after discharge was 35 [7–92] days. Of the 208 post-discharge deaths, 101
304 (49%), 160 (77%), 179 (86%) and 193 (93%) occurred within 1, 3, 6 and 9 months after discharge
305 respectively. The annual YI post-discharge case fatality was 5.4% in 2009 and 6.3% in 2019
306 without evidence of linear trend (P-value for trend=0.77) (**Figure 2**).

307 One hundred and one (49%) of the 208 post-discharge deaths occurred at home without hospital
308 readmission, 67 (32%) occurred during readmission to KCH and 40 (19%) occurred at other health
309 facilities. The five leading assigned causes of deaths for the 67 deaths at KCH were: neonatal
310 sepsis (24%), preterm complications (22%), congenital heart disease (15%), neonatal jaundice
311 (7.4%) and meningitis (7.4%) which were similar to index admission diagnosis **Supplementary**
312 **Table S7**. Causes of other deaths were unknown.

313 Overall, we observed 853 (20%) deaths among 4,272 individual YIs: 645 inpatient and 208 post-
314 discharge, hence 24% of deaths were post-discharge.

315 Exposures assessed for association with post-discharge mortality are shown on **Supplementary**
316 **Table S8**. In the multivariable Cox regression model, born outside KCH, log days of hospital

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3 317 admission, leaving against advice, and referral to more specialized hospital were positively
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6 318 associated with post-discharge mortality. Other exposures associated with post-discharge
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8 319 mortality were low admission weight, fever and weak pulse(**Table 3**). The multivariable model
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10 320 bootstrapped AUC was 0·76 (95%CI 0·73–0·80).

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14 321 *Subgroup analysis*

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17 322 In a subgroup analysis including 1,358 admissions of YIs born at KCH, their median [IQR]
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19 323 gestational age was 38 (36–40) weeks and birth weight 2,778 (2,000–3,195) grams respectively.

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22 324 In the univariate regression model, born premature, low birth weight and birth weight Z score
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24 325 <-2 were positively associated with inpatient mortality (**Supplementary Table S9**). In the
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26 326 multivariable model, low birth weight, admission age <8 days, bacteraemia and signs of clinical
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28 327 severity were associated with inpatient mortality (**Supplementary Table S10**).

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32 328 Among the 1,142 YI followed up for 1,021 child-years of which 41/1,142 (3·6%) died, low birth
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34 329 weight (aHR 2·76 (95%CI 1·30–5·82)) was positively associated with post-discharge mortality in
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36 330 the multivariable model (**Supplementary Table S10**).

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332 Discussion

333 *Trends in admissions and proportions of young infants*

334 During the study period, we observed a marked increase in YI admissions and proportion of YI
335 among admissions in under-fives increased from around a fifth in 2009, to more than one-third
336 in 2019. However, this did not seem to be associated with the introduction of free maternity care
337 in 2013. Lack of observable effect may be due to challenges faced during policy implementation
338 arising from inadequate expansion of quality health care facilities and resources. Several authors
339 reported an increase in mothers attending Kenyan health facilities for antenatal care and
340 delivery,^{11 21} however our results suggest this occurred in the context of a general trend which
341 we previously observed during 1990-2008.¹⁰

342 Conversely, the number of admitted children older than 60 days decreased alongside a reduction
343 in local malaria transmission,²² introduction of routine childhood pneumococcal conjugate and
344 rotavirus immunisation,²³ and expansion in numbers of health facilities in Kilifi County.²⁴
345 Variation in annual admissions over the years was due to multiple health workers' strikes.¹³
346 During these periods, the general paediatric ward was closed and only the sickest children were
347 admitted to the paediatric HDU due to limited staffing and bed capacity. The time series analysis
348 indicated an increase in inpatient mortality during strikes (**Figure 3C**).

349 The leading diagnoses at admission in our analysis were neonatal sepsis, preterm complications,
350 and birth asphyxia, similar to the period 1990–2008.¹⁰ Over a third of admissions from KCH
351 maternity were preterm and the hospital also received referrals of preterm and very low
352 birthweight infants from sub-county hospitals and local health centres. There are few African

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3 353 published datasets of neonatal or YI inpatient diagnoses; in a network of 7 Nigerian and Kenyan
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6 354 hospitals, prematurity accounted for over half (52%), and birth asphyxia almost a quarter (24%)
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8 355 of neonatal admissions.²⁵ The leading bacterial isolates from blood cultures in our study
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10 356 (*Klebsiella pneumoniae*, *Escherichia coli*, *Staphylococcus aureus*) were similar to those among YI
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13 357 in rural settings of Tanzania and Burkina Faso.²⁶ Kenya attained elimination status of maternal
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15 358 and neonatal tetanus in 2018, following immunisation campaigns in high-risk regions.²⁷
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18 359 Compared to 1990–2008,¹⁰ neonatal tetanus was uncommon at our centre with only 10 cases in
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20 360 11 years.

21 22 23 361 *Inpatient deaths*

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26 362 The WHO has reported that in 2019, “47% of all under-5 deaths occurred in the newborn period
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29 363 with about one third dying on the day of birth and close to three quarters dying within the first
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31 364 week of life”.²⁸ Delivery by a skilled health worker has been shown to be effective in reducing
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34 365 perinatal mortality.²⁹ We did not collect data on delivery by a skilled birth attendant but in 2018/9
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36 366 69% of births in Kilifi County were reported to be attended by skilled health personnel which is
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39 367 slightly higher than the national average.³⁰ We found YI accounted for more than 60% of under-
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41 368 fives inpatient deaths, similar to a retrospective study of 16 Kenyan public hospitals in which
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44 369 neonatal deaths comprised 66% of inpatient paediatric deaths.⁵ We found respiratory distress
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46 370 syndrome, birth asphyxia and preterm complications had the highest inpatient mortality.
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49 371 Mechanical ventilation was not available in Kilifi County Hospital. Improvements in peripartum
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51 372 care of mothers and infants together with appropriate technology such as non-invasive
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53 373 ventilation for management of respiratory complications of preterm birth are priorities for
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56 374 reduction in neonatal mortality in hospitals in LMICs.⁵

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3 375 *Post-discharge deaths*
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6 376 Less than a quarter (24%) of all deaths during 1-year of follow up occurred post-discharge. This
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8 377 reflects a high inpatient (16%) case fatality rate with many very early inpatient deaths compared
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11 378 to 6.6% in children aged ≥ 60 days.⁷ Nevertheless, the post-discharge YI mortality rate (64.3 per
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13 379 1,000 child/years) was more than twice that of a cohort of children aged 2–59 months admitted
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16 380 to KCH between 2007– 2015.³¹ This reflects post-discharge mortality rates being highest in
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18 381 younger age groups, such as in Tanzania among under 1-year olds: 72 per 1,000 child/years
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21 382 (95% C.I. 67.2–77.2) falling to 6.9 (95% C.I. 5.5–8.7) per 1,000 child/years in 4 to <5 year olds.³²
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24 383 A greater proportion of YI post-discharge deaths occurred in hospital than among older children,⁷
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26 384 implying that caregivers may be more likely to seek re-admission for YI or may live closer to KCH.
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29 385 About half of post-discharge deaths occurred within the first month, highlighting the need for
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31 386 formal ‘down-referral’ for continuity of care after discharge in high risk YI.
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34 387 Analysis of exposures revealed that some were common for both inpatient and post-discharge
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36 388 mortality: low admission weight, axillary temperature, and respiratory rate. Birth weight was
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39 389 not available for most YI but low admission weight <2.5kg was common (40%) in our
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42 390 participants. In young infants it is difficult to distinguish low birth weight from malnutrition, but
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44 391 we have reported the higher case fatality rates in the lower admission weight categories
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46 392 (Tables S3 and S4). Of known causes of post-discharge deaths, leading ones were related to
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49 393 problems in the early neonatal period.
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52 394 *Strengths and limitations of the study*
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3 395 Strengths of this study are large sample size, systematic collection of data and linkage to a well-
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6 396 established demographic surveillance system, with few losses to follow up. Limitations are lack
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8 397 of accurate gestational age estimation, unknown birthweight of most participants and that
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10 398 individual socioeconomic data were unavailable. We did not have clinical data collected at
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13 399 discharge, which may be of value in taking a risk-based approach to post-discharge care. This
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15 400 analysis is from a single hospital and excludes residents outside KHDSS who may have different
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18 401 exposures and risks.
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21 402 *Conclusions*

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24 403 Neonatal and YI admissions account for an increasing proportion of inpatient paediatric
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26 404 admissions, and their overall mortality rate remains high. Post-discharge mortality accounts for
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29 405 a lower proportion of all deaths than hospital admissions aged 2 to 59 months but the post-
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31 406 discharge mortality rate among young infants is higher.^{31 33} This is likely because of the
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34 407 predominance of fatal neonatal conditions such as extreme prematurity or birth asphyxia.
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36 408 Services to address post-discharge mortality are needed and should focus on infants at higher
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5 442 **Figures**

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8 443 **Figure 1. Flow of study participants.**

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11 444 **Figure 2. Annual proportion of YI admissions to all admissions <60 months, inpatient case**
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14 445 **fatality ratio (CFR) and post-discharge CFR.**

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17 446 Proportions are plotted with 95% confidence intervals.

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20 447 **Figure 3. A: Monthly hospital admissions (with predicted mean temporal trend), B: Monthly**
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22 448 **case fatality rates (with predicted mean temporal trend), C: Monthly young infant inpatient**
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24 449 **case fatality before and after June 2013 and D: Monthly proportions of young infants to**
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26 450 **admissions <60 months old.**

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36 453 Ethics approval and consent to participate

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38 454 Written consent was provided by the caregivers of all the surveillance study participants. Ethical
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40 455 approval to conduct this analysis was granted by the Kenya Medical Research Institute (KEMRI)
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42 456 National Ethics Review Committee (SCC 2778).

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46 457 Consent for publication – not applicable

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50 458 Availability of data and materials

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3 459 Data are available in a public, open access repository. Deidentified participant data and analysis
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6 460 code have been deposited and may be requested at the Harvard Dataverse via this
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8 461 link <https://doi.org/10.7910/DVN/OXJVFX>
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15
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8 482 visualisation , writing – original draft, writing– review & editing; CWO: Conceptualization,
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10 483 investigation, methodology, formal analysis, validation, writing – original draft, writing– review
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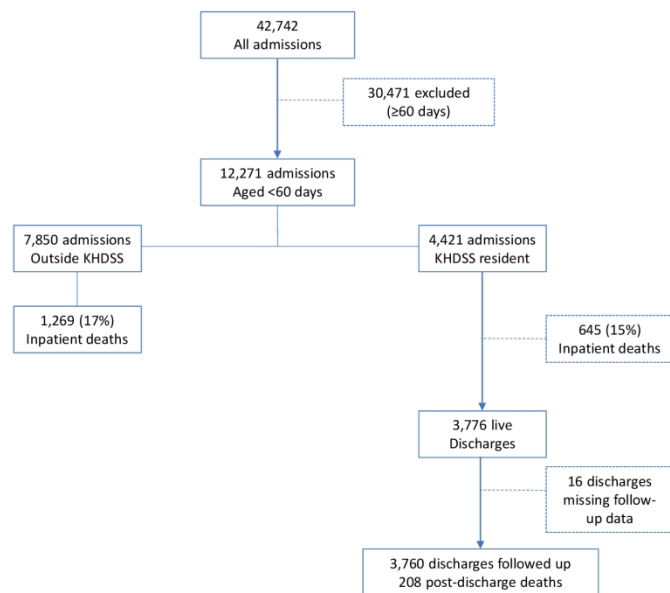
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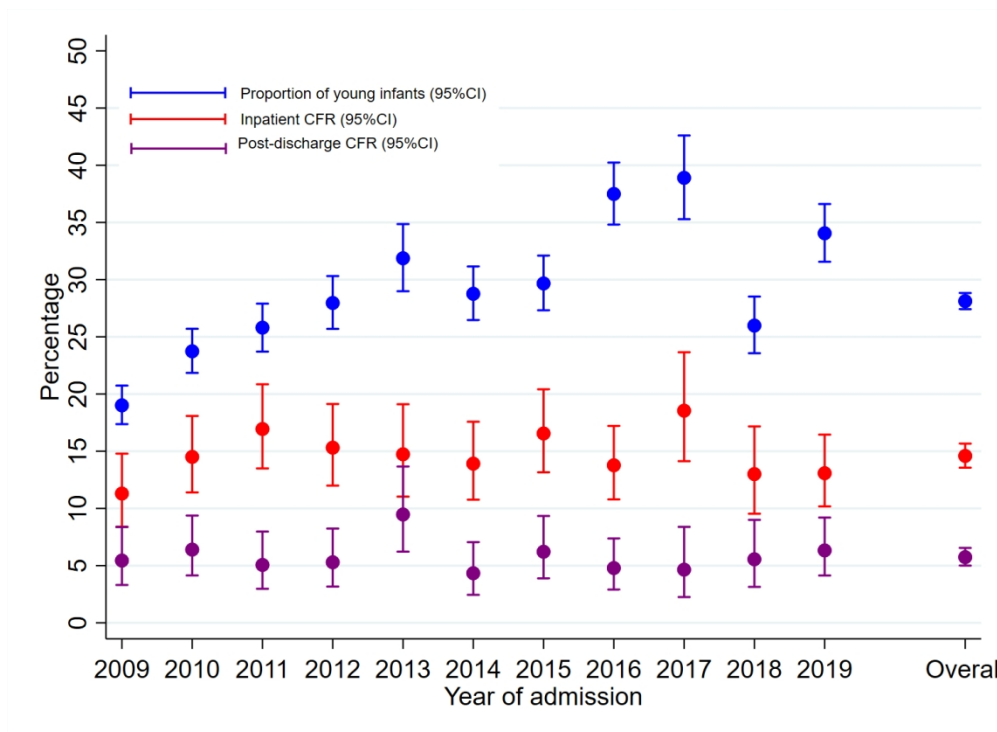
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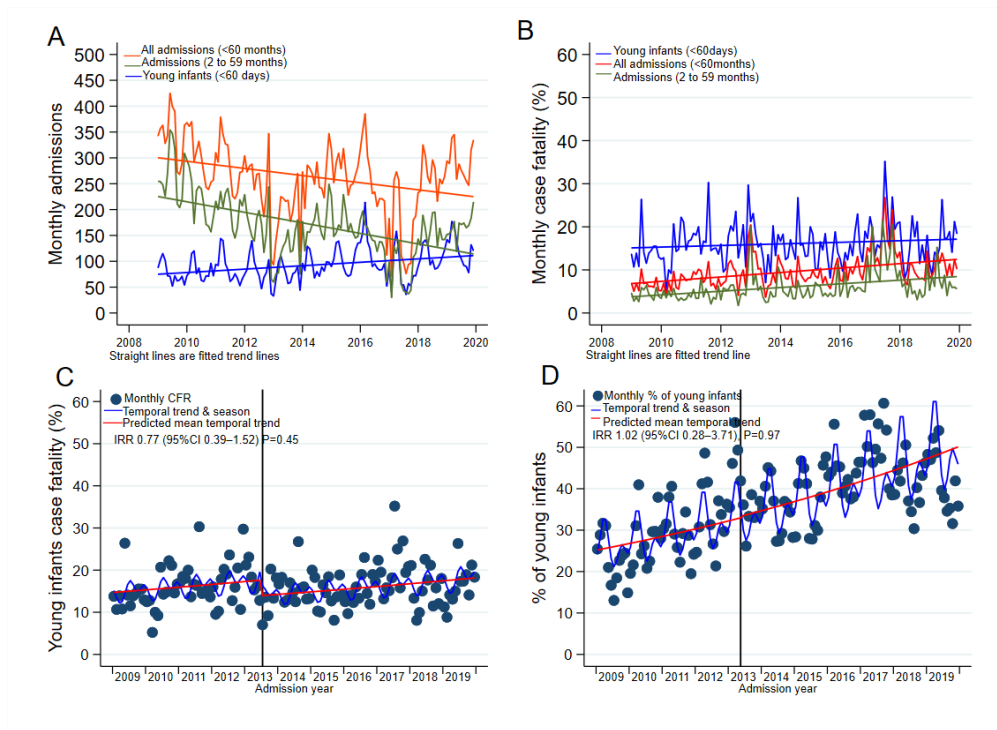
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3 **Supplementary materials**
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Table S1. List of health workers strikes during study period.

Strike dates	Health workers on strike	Duration of strike in days
5 to 13 December 2011	Doctors	9
1 to 15 March 2012	Nurses	15
13 September to 4 October 2012	Doctors	22
3 December 2012 to 13 January 2013	Nurses	42
16 January to 11 February 2013	Nurses	26
10 to 23 December 2013	Doctors & nurses	14
5 to 14 December 2016	Nurses	11
5 December 2016 to 15 March 2017	Doctors	102
5 June to 2 November 2017	Nurses	150

For peer review only

Table S2. Proportion of missing data

N=4,421	N missing	% missing
Demographics		
Age in days	0	
Sex (female)	0	
BCG scar	76	1.7
Reported born premature	321	7.3
Reported low birth weight	322	7.3
Anthropometry		
Weight (kg)	43	1.0
MUAC (cm)	126	2.9
Clinical features		
Axillary temperature	34	0.8
Tachypnea	208	4.7
Tachycardia	43	1.0
Hypoxia (SaO ₂ <90%)	20	0.5
Lower chest wall indrawing	68	1.5
Wheeze	69	1.6
Stridor	71	1.6
Breathing difficulty	64	1.5
Cyanosis	70	1.6
Capillary refill \geq 2 seconds	34	0.8
Temperature gradient	81	1.8
Weak pulse	71	1.6
Lethargy	70	1.6
Impaired consciousness	70	1.6
Bulging fontanel	72	1.6
Stiff neck	71	1.6
Convulsions	64	1.5
Sunken eyes	73	1.7
Reduced skin turgor	71	1.6
Pallor	70	1.6
Laboratory features		
HIV antibody positive	756	17
Malaria slide positive	372	8.4
Bacteraemia	2281	52
Haemoglobin	448	10
WBC	449	10
Platelets	448	10
Blood glucose (mmols/L)	1433	32

Table S3 Pathogens isolated from blood and CSF cultures of young infants resident in KHDSS during inpatient period.

Blood culture Isolates		CSF culture isolates	
Pathogen (N=178)	No. (%)	Pathogen (N=24)	No. (%)
<i>Klebsiella pneumoniae</i>	53 (30)	<i>Escherichia coli</i>	6 (25)
<i>Escherichia coli</i>	25 (14)	Group B Streptococcus	6 (25)
<i>Staphylococcus aureus</i>	22 (12)	<i>Klebsiella pneumoniae</i>	3 (13)
Group B Streptococcus	19 (11)	<i>Streptococcus pneumoniae</i>	3 (13)
Non-typhoidal Salmonella species	9 (5.1)	<i>Enterobacter cloacae</i>	3 (13)
<i>Enterobacter cloacae</i>	8 (4.5)	Non-typhoidal Salmonella species	2 (8.2)
<i>Pseudomonas aeruginosa</i>	6 (3.4)	<i>Acinetobacter lwoffii</i>	1 (4.2)
<i>Streptococcus pneumoniae</i>	5 (2.8)		
<i>Streptococcus pyogenes</i>	3 (1.7)		
Acinetobacter species	3 (1.7)		
<i>Aeromonas hydrophila</i>	3 (1.7)		
Group A Streptococcus	3 (1.7)		
<i>Serratia marcescens</i>	2 (1.1)		
<i>Acinetobacter calcoaceticus/baumannii</i>	2 (1.1)		
<i>Acinetobacter lwoffii</i>	1 (0.6)		
<i>Aeromonas sobria</i>	1 (0.6)		
<i>Chryseobacterium indologenes</i>	1 (0.6)		
<i>Enterobacter aerogenes</i>	1 (0.6)		
Enterococci species	1 (0.6)		
<i>Haemophilus influenzae</i>	1 (0.6)		
<i>Proteus mirabilis</i>	1 (0.6)		

CSF; cerebrospinal fluid, Out of the 33 Meningitis cases, only the 24 presented had positive CSF culture.

Table S4. Annual admissions and case fatality ratios (CFR).

Admissions/Year	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019
<60 days	407	455	425	418	319	424	429	472	275	323	474
2 to 59 months	1734	1462	1222	1177	682	1050	1017	787	432	920	918
Proportion of YI admissions	19%	24%	26%	28%	32%	29%	30%	37%	39%	26%	34%
YI inpatient deaths	46	66	72	64	47	59	71	65	51	42	62
YI inpatient CFR	11%	15%	17%	15%	15%	14%	17%	14%	19%	13%	13%
YI post-discharge 1-year deaths	19	24	17	18	25	15	21	19	10	15	25
YI Post-discharge 1- year CFR	5.4%	6.4%	5.1%	5.3%	9.5%	4.3%	6.2%	4.8%	4.7%	5.6%	6.3%

Table S5. Univariate analysis of admission features associated with inpatient deaths.

N=4,421	Deaths (N=645) N (%)	Crude SHR	P-value	Scaled Schoenfeld residuals P-value
Demographics				
Age in days				
0 to 2	511 (19)	3.31 (2.39–4.58)	<0.001	0.14
3 to 7	56 (12)	2.07 (1.38–3.11)	<0.001	
8 to 28	40 (6.8)	1.15 (0.74–1.78)	0.54	
>28	38 (6.0)	Reference		
Sex (female)	268 (14)	0.99 (0.91–1.09)	0.93	0.77
Reported born premature	294 (29)	2.53 (2.32–3.77)	<0.001	0.06
Reported low birth weight	222 (38)	3.25 (2.97–3.56)	<0.001	0.18
Born at KCH				
Yes	382 (14)	Reference		
No	263 (16)	1.13 (0.97–1.32)	0.12	0.61
Anthropometry				
Weight (kg)				
<1.5	213 (38)	4.95 (4.13–5.93)	<0.001	0.09
1.5 to <2.5	174 (15)	1.86(1.53–2.26)	<0.001	
≥2.5	229 (8.5)	Reference		
Missing weight	29 (67)	10.7 (7.60–14.9)	<0.001	
MUAC (cm)				
<9.0	333 (25)	3.57 (3.07–4.15)	<0.001	0.08
9 to 10	106 (12)	1.73 (1.45–2.07)	<0.001	
10 to 11	96 (9.3)	1.48 (1.24–1.77)	<0.001	
≥11	75 (7.1)	Reference		
Missing MUAC	35 (28)	3.89 (3.02–5.00)	<0.001	
Clinical features				
Axillary temperature				
<36°C	390 (29)	3.13 (2.82–3.47)	<0.001	0.34
36 to 37.5°C	159 (9.3)	Reference		
>37.5°C	84 (6.3)	0.77 (0.67–0.88)	<0.001	
Missing temperature	12 (35)	3.78 (2.65–5.39)	<0.001	
Respiratory rate/min				
Bradypnoea	108 (57)	6.09 (4.98–7.46)	<0.001	0.71
Normal	329 (12)	Reference		
Tachypnoea	197 (13)	1.07 (0.90–1.27)	0.45	
Missing	11 (11)	0.91 (0.51–1.65)	0.76	
Heart rate/min				
Bradycardia	74 (47)	4.05 (3.21–5.11)	<0.001	0.50
Normal	403 (14)	Reference		
Tachycardia	163 (12)	0.88 (0.73–1.05)	0.15	
Missing	5 (23)	1.68 (0.72–3.93)	0.23	
Hypoxia (SaO ₂ <90%)	309 (33)	3.91 (3.58–4.26)	<0.001	0.48
Lower chest wall indrawing	448 (22)	2.86 (2.60–3.15)	<0.001	0.41
Wheeze	0	-		

Stridor	6 (32)	1.48 (0.89–2.47)	0.13	0.23
Breathing difficulty	481 (22)	3.62 (3.26–4.02)	<0.001	0.28
Cyanosis	98 (47)	4.01 (3.55–4.53)	<0.001	0.14
Capillary refill >2 seconds	61 (58)	5.61 (4.41–7.14)	<0.001	0.54
Temperature gradient	98 (38)	2.85 (2.51–3.23)	<0.001	0.36
Weak pulse	108 (69)	5.85 (5.21–6.57)	<0.001	0.71
Lethargy	64 (20)	1.20 (1.04–1.40)	0.02	0.34
Impaired consciousness	140 (56)	5.43 (4.91–6.00)	<0.001	0.42
Bulging fontanel	6 (19)	1.34 (0.90–1.99)	0.15	0.08
Stiff neck	4 (40)	2.08 (1.30–3.32)	0.002	0.17
Convulsions	16 (8.1)	0.75 (0.61–0.93)	0.01	0.53
Sunken eyes	5 (11)	1.04 (0.69–1.56)	0.85	0.52
Reduced skin turgor	21 (22)	1.18 (0.91–1.52)	0.22	0.56
Pallor	72 (33)	2.47 (2.15–2.83)	<0.001	0.63
Laboratory features				
Meningitis	8 (24)	8.06 (3.96–16.4)	<0.001	0.13
Anaemia (haemoglobin <11 g/dl)	50 (11)	0.67 (0.51–0.90)	0.007	0.51
HIV antibody positive	29 (20)	1.39 (1.13–1.71)	0.002	0.28
Malaria slide positive	0	-		
Bacteraemia	63 (37)	2.92 (2.10–4.06)	<0.001	0.13
Blood glucose (mmols/L)				
<2.6	137 (16)	1.18 (1.04–1.33)	0.009	0.42
2.6 to 7.0	229 (12)	Reference		
>7.0	71 (31)	2.85 (2.47–3.29)	<0.001	
Missing blood glucose	208 (15)	1.18 (1.06–1.32)	0.002	
White blood cells (10 ¹² cells/L)				
<4	14 (26)	2.43 (1.47–4.03)	0.001	0.70
4-20	362 (11)	Reference		
>20	210 (30)	2.97 (2.52–3.50)	<0.001	
Missing	59 (13)	1.19 (0.91–1.57)	0.20	
Platelets (10 ⁹ cells/L)				
<150	139 (24)	1.89 (1.57–2.27)	<0.001	0.10
≥150	447 (13)	Reference		
Missing	59 (13)	1.01 (0.77–1.32)	0.95	
SHR: sub-distribution hazard ratios; the SHR are from the Fine and Gray's proportional sub-hazards model.				

Table S6. **Multivariable regression analysis of factors associated with inpatient mortality (single vs multiple admissions).**

	Multiple admissions (N=4421)		Single admissions (N=4272)	
	Adjusted SHR*	P-value	Adjusted SHR*	P-value
Demographics				
Age in days				
0 to 2	2.12 (1.46–3.06)	<0.001	2.14 (1.49–3.10)	<0.001
3 to 7	3.88 (2.46–6.10)	<0.001	3.92 (2.48–5.16)	<0.001
8 to 28	1.42 (0.90–2.25)	0.13	1.50 (0.95–2.38)	0.08
>28	Reference		Reference	
Sex (female)	0.91 (0.78–1.07)	0.26	0.90 (0.77–1.06)	0.20
Anthropometry				
Weight (kg)				
<1.5	2.16 (1.75–2.67)	<0.001	2.26 (1.83–2.79)	<0.001
1.5 to <2.5	1.42 (1.16–1.74)	0.001	1.43 (1.17–1.76)	<0.001
≥2.5	Reference		Reference	
Missing weight	3.85 (2.59–5.71)	<0.001	3.78 (2.56–5.58)	<0.001
Clinical features				
Axillary temperature				
<36°C	1.44 (1.17–1.78)	0.001	1.45 (1.17–1.79)	0.001
36 to 37.5°C	Reference		Reference	
>37.5°C	1.09 (0.84–1.41)	0.53	1.07 (0.83–1.39)	0.57
Missing temperature	1.03 (0.38–2.75)	0.96	0.92 (0.33–2.51)	0.87
Respiratory rate/min				
Bradypnoea	1.45 (1.09–1.93)	0.01	1.44 (1.08–1.92)	0.01
Normal	Reference		Reference	
Tachypnoea	0.80 (0.67–0.95)	0.01	0.79 (0.66–0.94)	0.009
Missing	1.51 (0.64–3.56)	0.34	1.48 (0.62–3.55)	0.38
Heart rate/min				
Bradycardia	1.40 (1.08–1.82)	0.01	1.42 (1.09–1.85)	0.008
Normal	Reference		Reference	
Tachycardia	1.14 (0.94–1.37)	0.18	1.15 (0.96–1.39)	0.14
Missing	0.41 (0.03–5.13)	0.49	0.45 (0.04–5.14)	0.52
Hypoxia (SaO ₂ <90%)	1.62 (1.37–1.92)	<0.001	1.60 (1.36–1.90)	<0.001
Capillary refill >2 seconds	1.34 (0.97–1.86)	0.08	1.31 (0.94–1.83)	0.11
Lower chest wall indrawing	1.41 (1.14–1.75)	0.002	1.42 (1.14–1.77)	0.002
Stridor	1.93 (0.92–4.03)	0.08	1.85 (0.89–3.85)	0.10
Breathing difficulty	1.45 (1.15–1.82)	0.001	1.44 (1.15–1.81)	0.002
Weak pulse	1.61 (1.19–2.17)	0.002	1.61 (1.18–2.18)	0.002
Bulging fontanel	2.45 (0.91–6.65)	0.08	2.41 (0.90–6.55)	0.08
Impaired consciousness	2.21 (1.72–2.84)	<0.001	2.17 (1.68–2.78)	<0.001
Pallor	1.30 (0.98–1.71)	0.07	1.28 (0.97–1.69)	0.08
Laboratory features				
Meningitis	5.45 (2.50–11.8)	<0.001	5.18 (2.39–11.2)	<0.001
HIV antibody positive	1.15 (0.81–1.63)	0.43	1.14 (0.80–1.62)	0.47

Bacteraemia	2.21 (1.51–3.22)	<0.001	2.20 (1.51–3.20)	<0.001
White blood cells (10^{12} cells/L)				
<4	2.17 (1.30–3.62)	0.003	2.11 (1.27–3.50)	0.003
4-20	Reference		Reference	
>20	1.71 (1.43–2.04)	<0.001	1.70 (1.43–2.03)	<0.001
unavailable	1.09 (0.82–1.44)	0.57	1.06 (0.79–1.41)	0.71
Model performance				
Bootstrapped AUC (95% CI)	0.88 (0.86–0.89)		0.88 (0.86–0.89)	
SHR; sub-distribution hazard ratios; *the SHR are from the Fine and Gray's proportional sub-hazards model, AUC; area under receiver operating characteristics. Meningitis: positive CSF culture, or positive CSF microscopy, or positive CSF antigen test, or elevated CSF WBC count (≥ 20 in young infants aged 0-28 days OR, ≥ 10 in young infants aged 29-59 days) PLUS a positive blood culture for a known pathogen				

Table S7. Estimated causes of post-discharge deaths during readmission at KCH (67 deaths).

Index admission diagnosis (N=67)	No. (%)	Causes of post-discharge deaths (N=67)	No. (%)
Neonatal sepsis	15 (22)	Neonatal sepsis	16 (24)
Preterm complications	15 (22)	Preterm complications	15 (22)
Heart disease-Congenital	9 (13)	Heart disease-Congenital	10 (15)
Neonatal jaundice	5 (7.5)	Neonatal jaundice	5 (7.4)
Meningitis	4 (6.0)	Meningitis	5 (7.4)
Birth asphyxia	4 (6.0)	Birth asphyxia	5 (7.4)
Lower respiratory tract infection	4 (6.0)	Lower respiratory tract infection	4 (6.0)
Encephalopathy - unknown	0	Encephalopathy - unknown	1 (1.5)
Hydrocephalus	1 (1.5)	Hydrocephalus	1 (1.5)
Malnutrition	1 (1.5)	None specified	5 (7.4)
None specified	9 (13)		

Index admission diagnosis and causes of death were assigned by treating clinician.

Table S8. Univariate analysis of admission features associated with post-discharge deaths.

N=3625	Deaths (N=208)	Crude HR	P-value	Scaled Schoenfeld residuals P-value
Demographics				
Age in days				
0 to 2	124 (5.6)	0.98 (0.67–1.44)	0.92	0.10
3 to 7	15 (3.7)	0.63 (0.34–1.16)	0.14	
8 to 28	36 (6.6)	1.17 (0.73–1.87)	0.52	
>28	33 (5.5)	Reference		
Sex (female)	89 (5.5)	0.98 (0.74–1.28)	0.86	0.79
Reported born premature	58 (8.0)	1.79 (1.32–2.44)	<0.001	0.07
Reported low birth weight	33 (9.3)	1.99 (1.37–2.90)	<0.001	0.13
Born at KCH				
Yes	102 (4.3)	Reference		
No	106 (7.6)	1.75 (1.34–2.30)	<0.001	0.12
Length of hospitalization (days)-log transformed	-	1.96 (1.68–2.27)	<0.001	0.38
Discharged over weekend				
No	173 (5.7)	Reference		
Yes	35 (4.8)	0.85 (0.59–1.23)	0.39	0.16
Type of discharge				
Normal discharge	180 (4.9)	Reference		0.75
Absconded	5 (12)	2.60 (1.07–6.33)	0.04	
Transferred/referred	23 (44)	11.8 (7.64–18.2)	<0.001	
Anthropometry				
Weight (kg)				
<1.5	30 (8.5)	2.49 (1.65–3.77)	<0.001	0.17
1.5 to <2.5	87 (9.2)	2.64 (1.97–3.54)	<0.001	
≥2.5	91 (3.7)	Reference		
Missing weight	0	-		
MUAC (cm)				
<9.0	88 (8.8)	4.05 (2.56–6.41)	<0.001	0.17
9 to 10	44 (5.8)	2.56 (1.55–4.24)	<0.001	
10 to 11	42 (4.5)	1.92 (1.15–3.18)	0.01	
≥11	23 (2.4)	Reference		
Missing MUAC	11 (12)	5.83 (2.84–12.0)	<0.001	
Clinical features				
Axillary temperature				
<36°C	78 (8.1)	1.45 (1.07–1.96)	0.02	0.80
36 to 37.5°C	88 (5.7)	Reference		
>37.5°C	41 (3.3)	0.57 (0.40–0.83)	0.003	
Missing temperature	1 (5.0)	0.99 (0.14–7.12)	0.99	
Respiratory rate/min				
Bradypnoea	7 (8.8)	1.92 (0.90–4.13)	0.09	0.30
Normal	108 (4.7)	Reference		
Tachypnoea	87 (6.8)	1.44 (1.09–1.92)	0.01	
Missing	6 (7.2)	1.65 (0.72–3.76)	0.23	
Heart rate/min				

Bradycardia	9 (11)	2.10 (1.07–4.13)	0.03	0.73
Normal	137 (5.5)	Reference		
Tachycardia	62 (5.3)	0.97 (0.72–1.31)	0.85	
Missing	0	-		
Hypoxia (SaO ₂ <90%)	51 (8.2)	1.68 (1.23–2.31)	0.001	0.54
Lower chest wall indrawing	108 (6.8)	1.54 (1.17–2.02)	0.002	0.18
Wheeze	2 (4.4)	0.77 (0.19–3.10)	0.71	0.20
Stridor	0	-		
Breathing difficulty	109 (6.5)	1.40 (1.07–1.85)	0.02	0.26
Cyanosis	7 (6.3)	1.14 (0.54–2.43)	0.73	0.17
Capillary refill ≥2 seconds	4 (9.4)	1.81 (0.67–4.87)	0.24	0.40
Temperature gradient	12 (7.5)	1.44 (0.80–2.57)	0.23	0.22
Weak pulse	7 (15)	3.10 (1.46–6.59)	0.003	0.38
Lethargy	14 (5.8)	1.06 (0.63–1.80)	0.82	0.19
Impaired consciousness	6 (5.5)	0.98 (0.44–2.21)	0.96	0.50
Bulging fontanel	4 (15)	3.04 (1.13–8.18)	0.03	0.06
Stiff neck	1 (17)	2.84 (0.40–20.2)	0.30	0.15
Convulsions	9 (5.0)	0.88 (0.46–1.75)	0.75	0.31
Sunken eyes	6 (15)	3.31 (1.47–7.45)	0.004	0.20
Reduced skin turgor	8 (11)	2.19 (1.08–4.43)	0.03	0.20
Pallor	15 (10)	2.09 (1.23–3.53)	0.006	0.23
Laboratory features				
Meningitis	4 (16)	3.98 (1.45–10.9)	0.007	0.13
Anaemia (haemoglobin <11 g/dl)	26 (6.2)	1.19 (0.79–1.80)	0.41	0.68
HIV antibody positive	7 (6.2)	1.17 (0.55–2.49)	0.69	0.76
Malaria slide positive	0	-		
Bacteraemia	10 (9.4)	1.02 (0.50–2.06)	0.96	0.28
Blood glucose (mmols/L)				
<2.6	51 (6.9)	1.31 (0.92–1.85)	0.13	0.25
2.6 to 7.0	86 (5.3)	Reference		
>7.0	10 (6.3)	1.21 (0.63–2.32)	0.57	
Missing blood glucose	61 (5.0)	0.95 (0.68–1.32)	0.75	
White blood cells (10 ¹² cells/L)				
<4	1 (2.5)	0.45 (0.06–3.20)	0.42	0.79
4-20	157 (5.5)	Reference		
>20	29 (6.1)	1.10 (0.74–1.64)	0.63	
Missing	21 (5.4)	0.99 (0.63–1.56)	0.97	
Platelets (10 ⁹ cells/L)				
<150	38 (8.6)	1.69 (1.18–2.41)	0.004	0.70
≥150	149 (5.1)	Reference		
Missing	21 (5.4)	1.08 (0.68–1.70)	0.75	
HR: hazard ratios; the HR are from the Cox proportional hazards model.				

Table S9. Univariate regression analysis of factors associated with inpatient and post-discharge mortality among children born at KCH only.

N=1,358	Deaths (N=174) N (%)	Crude SHR	P-value	Scaled Schoenfeld residuals P- value
Demographics				
Age in days				
0 to 2	151 (15)	2.48 (1.19–5.16)	0.02	0.26
3 to 7	8 (7.0)	1.22 (0.45–3.30)	0.69	
8 to 28	8 (6.8)	1.21 (0.46–3.23)	0.70	
>28	7 (5.5)	Reference		
Sex (female)	84 (14)	1.11 (0.83–1.48)	0.50	0.31
Born premature	101 (21)	2.65 (1.97–3.56)	<0.001	0.10
Born low birth weight	107 (21)	2.74 (2.03–3.71)	<0.001	0.44
Anthropometry				
Weight z score at birth				
<-2.0	32 (17)	1.49 (1.02–2.17)	0.04	0.12
≥-2.0	142 (12)	Reference		
MUAC (cm)				
<9.0	97 (23)	3.14 (2.05–4.83)	<0.001	0.17
9 to 10	26 (9.9)	1.26 (0.74–2.17)	0.40	
10 to 11	25 (7.3)	0.91 (0.53–1.57)	0.73	
≥11	26 (7.9)	Reference		
Missing MUAC	0	-		
Clinical features				
Axillary temperature				
<36°C	113 (26)	3.02 (2.13–4.27)	<0.001	0.30
36 to 37.5°C	41 (9.2)	Reference		
>37.5°C	18 (3.9)	0.42 (0.24–0.72)	0.002	
Missing temperature	2 (50)	6.90 (1.84–25.8)	0.004	
Respiratory rate/min				
Bradypnoea	32 (52)	6.44 (4.39–9.45)	<0.001	0.17
Normal	91 (10)	Reference		
Tachypnoea	50 (12)	1.21 (0.86–1.69)	0.28	
Missing	1 (5.3)	0.49 (0.07–3.37)	0.47	
Heart rate/min				
Bradycardia	21 (43)	4.76 (3.06–7.43)	<0.001	0.81
Normal	98 (10)	Reference		
Tachycardia	55 (15)	1.48 (1.07–2.05)	0.02	

Missing	0	-		
Hypoxia (SaO ₂ <90%)	79 (29)	3.62 (2.71–4.83)	<0.001	0.81
Lower chest wall indrawing	125 (21)	3.57 (2.57–4.95)	<0.001	0.47
Wheeze	0	-		
Stridor	5 (63)	6.96 (3.09–15.7)	<0.001	0.60
Breathing difficulty	481 (22)	5.40 (3.69–7.88)	<0.001	0.18
Cyanosis	29 (48)	5.15 (3.54–7.50)	<0.001	0.18
Capillary refill >2 seconds	14 (64)	7.22 (4.43–11.7)	<0.001	0.58
Temperature gradient	26 (30)	2.69 (1.81–4.01)	<0.001	0.49
Weak pulse	25 (58)	6.52 (4.44–9.56)	<0.001	0.77
Lethargy	17 (16)	1.29 (0.79–2.10)	0.31	0.56
Impaired consciousness	48 (52)	6.75 (4.93–9.24)	<0.001	0.13
Bulging fontanel	1 (25)	2.03 (0.31–13.2)	0.46	0.59
Stiff neck	1 (5.3)	-		0.31
Convulsions	1 (2.9)	0.21 (0.03–1.48)	0.12	0.21
Sunken eyes	1 (17)	1.35 (0.19–9.77)	0.77	0.57
Reduced skin turgor	1 (5.9)	0.44 (0.06–3.19)	0.42	0.56
Pallor	21 (42)	4.00 (2.61–6.12)	<0.001	0.59
Laboratory features				
Meningitis	2 (29)	9.95 (2.37–41.8)	0.002	0.12
Haemoglobin <11 g/dl	11 (13)	0.92 (0.51–1.66)	0.78	0.25
HIV antibody positive	8 (21)	1.68 (0.84–3.33)	0.14	0.14
Malaria slide positive	0	-		
Bacteraemia	14 (33)	3.00 (1.48–5.95)	0.002	0.20
Blood glucose (mmols/l)				
<2.6	33 (12)	1.02 (0.67–1.56)	0.91	0.95
2.6 to 7.0	58 (12)	Reference		
>7.0	11 (21)	1.88 (1.00–3.54)	0.05	
Missing blood glucose	72 (13)	1.11 (0.79–1.56)	0.53	
White blood cells (10 ¹² cells/L)				
<4	3 (33)	3.52 (1.25–9.91)	0.02	0.08
4-20	100 (10)	Reference		
>20	59 (28)	3.10 (2.27–4.24)	<0.001	
Missing	12 (8.2)	0.82 (0.45–1.48)	0.50	
Platelets (10 ⁹ cells/L)				
<150	35 (20)	1.69 (1.18–2.44)	0.005	0.50
≥150	127 (12)	Reference		
Missing	12 (8.2)	0.66 (0.37–1.19)	0.17	
SHR; sub-distribution hazard ratios; the SHR are from the Fine and Gray's proportional sub-hazards model.				

Table S10. Multivariable regression analysis of factors associated with inpatient and post-discharge mortality among children born at KCH only.

	Inpatient analysis		Post-discharge analysis	
	Adjusted SHR*	P-value	Adjusted HR	P-value
Demographics				
Age in days				
0 to 2	3.03 (1.33–6.94)	0.009	¶	
3 to 7	4.08 (1.48–11.3)	0.007	¶	
8 to 28	2.57 (0.90–7.29)	0.08	¶	
>28	Reference			
Anthropometry				
Low birth weight	1.55 (1.10–2.20)	0.01	2.76 (1.30–5.82)	0.008
Clinical features				
Axillary temperature				
<36°C	1.49 (0.97–2.28)	0.07	1.44 (0.71–2.95)	0.31
36 to 37.5°C	Reference		Reference	
>37.5°C	0.67 (0.39–1.13)	0.13	0.22 (0.06–0.78)	0.02
Missing temperature	3.37 (0.85–13.4)	0.09	0.48 (0.09–2.64)	0.40
Respiratory rate/min				
Bradypnoea	2.22 (1.36–3.63)	0.001	¶	
Normal	Reference			
Tachypnoea	0.78 (0.55–1.11)	0.17	¶	
Missing	-			
Heart rate/min				
Bradycardia	1.88 (1.14–3.12)	0.01	3.56 (1.14–11.2)	0.03
Normal	Reference		Reference	
Tachycardia	1.57 (1.11–2.21)	0.01	1.54 (0.77–3.07)	0.22
Missing	0.25 (0.02–3.00)	0.28	-	
Hypoxia (SaO ₂ <90%)	1.60 (1.14–2.24)	0.006	¶	
Lower chest wall indrawing	1.42 (0.91–2.22)	0.12	¶	
Stridor	3.74 (1.87–7.49)	<0.001	¶	
Breathing difficulty	2.13 (1.25–3.64)	0.005	¶	
Capillary refill >2 seconds	1.94 (1.06–3.56)	0.03	¶	
Weak pulse	2.15 (1.27–3.65)	0.004	1.60 (0.24–10.5)	0.63
Pallor	2.36 (1.46–3.83)	<0.001	¶	
Laboratory features				
Bacteraemia	2.50 (1.20–5.22)	0.02	0.21 (0.03–1.81)	0.16
Model performance				
AUC (95% CI)	0.85 (0.82–0.88)		0.79 (0.72–0.85)	
SHR; sub-distribution hazard ratios; *the SHR are from the Fine and Gray's proportional subhazards model, HR-Hazard ratio from the Proportional Cox regression model, ¶; variables not selected for inclusion in the multivariable model, AUC; area under receiver operating characteristics.				

Figure S1. **A: Monthly all young infant admissions, B: all admissions (<60 months old), C: all admissions (<60 months old) case fatality and D: 2–59 months old case fatality before and after July 2013.**

