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Incidence and Severity of Respiratory Syncytial Virus Pneumonia in Rural Kenyan Children Identified through Hospital Surveillance

D. James Nokes,[1,2] Mwanajuma Ngama,[1] Anne Bett,[1] John Abwao,[1] Patrick Munywoki,[1] Mike English,[1,3] J. Anthony G. Scott,[1,4] Patricia A. Cane,[5] and Graham F. Medley[2]

[1]Kenya Medical Research Institute, Centre for Geographic Medicine Research-Coast, Kilifi, Kenya; and [2]Department of Biological Sciences, University of Warwick, Coventry, [3]Department of Paediatrics, Oxford University, and [4]Nuffield Department of Medicine, University of Oxford, Oxford, and [5]Health Protection Agency, London, United Kingdom

Background. Although necessary for developing a rationale for vaccination, the burden of severe respiratory syncytial virus (RSV) disease in children in resource-poor settings remains poorly defined.

Methods. We conducted prospective surveillance of severe and very severe pneumonia in children aged <5 years admitted from 2002 through 2007 to Kilifi district hospital in coastal Kenya. Nasal specimens were screened for RSV antigen by immunofluorescence. Incidence rates were estimated for the well-defined population.

Results. Of 25,149 hospital admissions, 7359 patients (29%) had severe or very severe pneumonia, of whom 6026 (82%) were enrolled. RSV prevalence was 15% (20% among infants) and 27% during epidemics (32% among infants). The proportion of case patients aged ⩾3 months was 65%, and the proportion aged ⩾6 months was 43%. Average annual hospitalization rates were 293 hospitalizations per 100,000 children aged <5 years (95% confidence interval, 271–371 hospitalizations per 100,000 children aged <5 years) and 1107 hospitalizations per 100,000 infants (95% confidence interval, 1012–1211 hospitalizations per 100,000 infants). Hospital admission rates were double in the region close to the hospital. Few patients with RSV infection had life-threatening clinical features or concurrent serious illnesses, and the associated mortality was 2.2%.

Conclusions. In this low-income setting, rates of hospital admission with RSV-associated pneumonia are substantial; they are comparable to estimates from the United States but considerably underestimate the burden in the full community. An effective vaccine for children aged >2 months (outside the age group of poor responders) could prevent a large portion of RSV disease. Severity data suggest that the justification for RSV vaccination will be based on the prevention of morbidity, not mortality.

Respiratory syncytial virus (RSV) is a major cause of severe pneumonia and bronchiolitis in infants and children worldwide and is seen as an important target for a pediatric vaccine [1–3]. Much attention has focused on developing a live, attenuated RSV vaccine for administration during early infancy, with some encouraging results reported on the safety and immunogenicity of recent candidates [1, 4, 5]. In addition to research in vaccine design and development, a successful intervention program needs (1) an accurate estimate of disease burden in the target population and (2) a comprehensive description of the epidemiology of infection and disease to optimize control strategies and estimate their potential impact. Both of these objectives can be reached through hospital-based surveillance for RSV disease within a well-defined population. Furthermore, long-term disease monitoring establishes the necessary baseline information by which to assess the impact and effectiveness of interventions. In the developing world, hospital-based surveillance of RSV disease has been performed infrequently, mainly without an accurate population base, and surveillance has rarely been sustained [6–8]. In this study, we present the results of prospective population-based surveillance for RSV disease spanning 6 years at a rural district hospital typical of tropical sub-Saharan Africa.

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Reprints or correspondence: Dr D. James Nokes, KEMRI-Wellcome Trust Collaborative Research Programme, PO Box 230, Kilifi, Kenya (jnokes@kilifi.kemri-wellcome.org).

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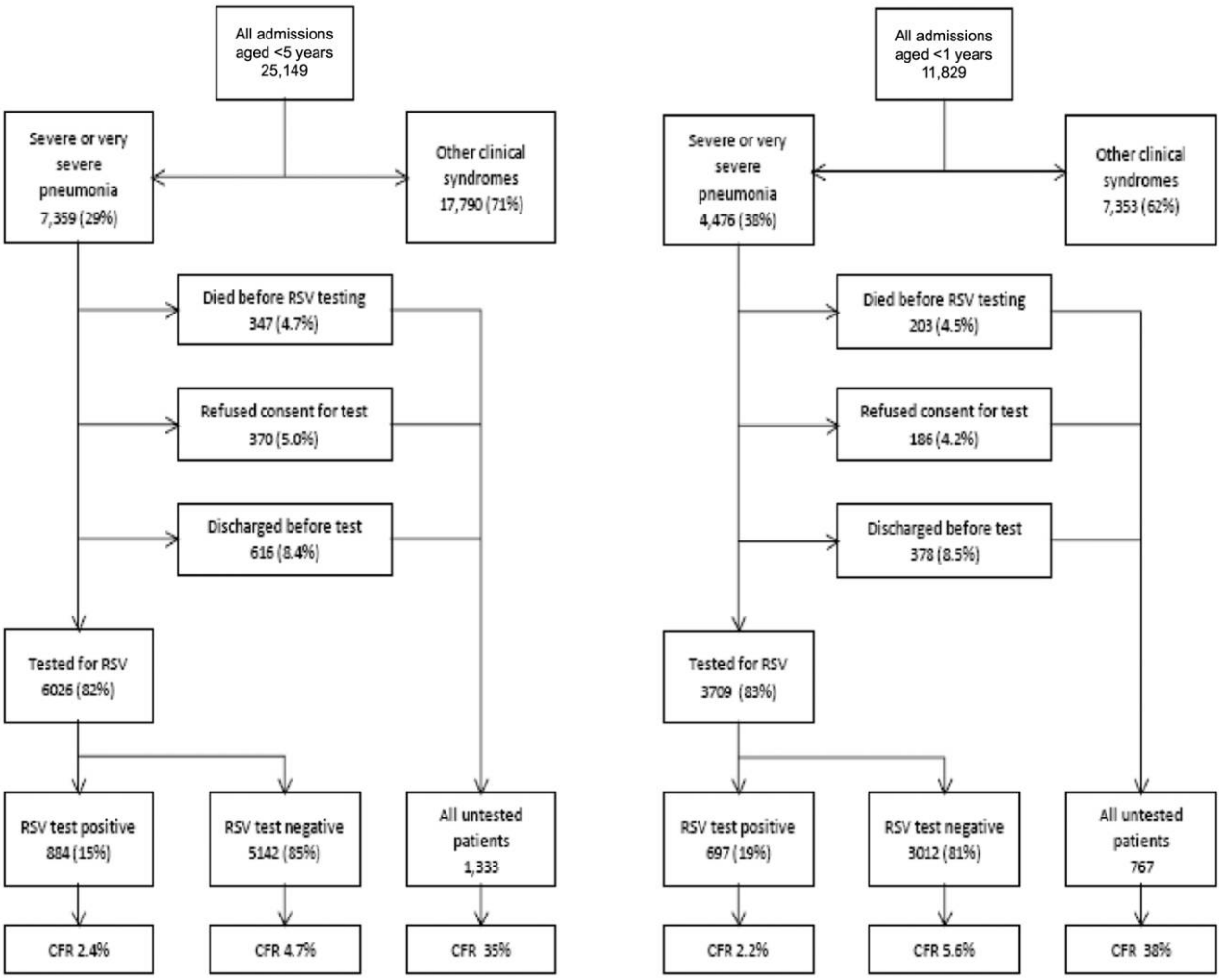

Figure 1. Flow diagram of recruitment and sample testing of children aged <5 years *(left)* and infants *(right)* admitted to Kilifi District Hospital from January 2002 through December 2007. Tested children refers to those who were enrolled and had a sample collected and tested, with the remainder either not enrolled or enrolled with a sample not taken and tested. Percentages in brackets within a box refer to the proportion of individuals from the preceding box. Note that, among those who were untested who refused participation, 121 children aged <5 years and 90 infants subsequently died, and these patients contribute to the denominator of the case fatality ratio (CFR). RSV, respiratory syncytial virus.

METHODS

Study location and population. Surveillance was undertaken at Kilifi District Hospital (KDH), which is situated in the town of Kilifi in coastal Kenya and serves as a primary care and referral facility for the predominantly rural farming population of around 500,000 persons, of whom 18% are aged <5 years [9]. The District has one of the lowest average per capita incomes in Kenya, and mortality rates among those aged <5 years and infants (aged <1 year) are high (141 and 85 deaths per 100,000 persons, respectively [9]), although there is considerable geographical variability. Malaria is transmitted throughout the year, with peaks in transmission during November-January and May-August following the rainy season, but the incidence of malaria has decreased sharply in recent years [10]. Human immunodeficiency virus type 1 (HIV-1) prevalence in women attending KDH antenatal care in 2004 was ~5% [11]. There are ~5000 pediatric hospital admissions (upper age, 12 years) each year. Each child is investigated with a standard computerized clinical history and examination and standard set of investigations on hospital admission, including a full hemogram, blood culture, and among febrile children, a Giemsa-stained blood sample slide [12]. In 2000, a demographic surveillance study was established in an area of 891 km^2 close to KDH, to monitor births, deaths, and migration events in a population of ~240,000 persons through 4-monthly enumeration rounds. From 16 April 2002, the residency sta-

The figure is available in its entirety in the online edition of *Clinical Infectious Diseases*.

Figure 2. Seasonal variation in monthly admissions to Kilifi District Hospital of children aged <5 years over the period from January 2002 through December 2007 and corresponding meteorological recordings.

tus of each child presenting to KDH was established on hospital admission through linkage to the population register of the Kilifi Epidemiological and Demographic Surveillance Study (EpiDSS) [12].

Patients. Surveillance for RSV was initiated on 1 January 2002. We report on all children aged 1 day to 59 months who presented with the clinical syndrome of pneumonia, either severe or very severe, excluding babies with neonatal tetanus. Clinical definitions, which follow, have been described elsewhere [12, 13]. A history of cough or difficulty in breathing for <30 days, when accompanied by lower chest wall indrawing, was defined as severe pneumonia. A history of cough or difficulty in breathing for <30 days, when accompanied by any 1 of prostration, coma, or hypoxemia was defined as very severe pneumonia. Prostration included the inability to feed or drink. Hypoxemia was defined by an oxygen saturation level (pO_2) of <90% determined by finger tip Oxymeter (Nelcor). All children with hypoxemia at hospital admission are given supplemental oxygen. Malaria was defined by *Plasmodium falciparum* parasitemia observed on the blood sample slide. Severe malnutrition was defined as a small value (≤10th percentile by age group) for mid-upper arm circumference, bipedal edema, or visible severe wasting. Shock was determined by a peripheral-central temperature gradient, a capillary refill time of >3 s, or a weak peripheral pulse volume. A history of premature birth was elicited for all infants at hospital admission, and a history of heart disease was established from diagnosis-on-discharge data. Bronchiolitis as a specific condition is not reported; in this setting, it has little influence on patient management and, despite the long-term surveillance, remains poorly recognized by clinicians at hospital admission (in the absence of laboratory confirmation of RSV). HIV diagnostic counseling and testing was not in place for most of the period of surveillance covered in this report and is not considered here. Written informed consent was obtained for all eligible participants.

Nasal specimens were collected as soon as possible after hospital admission by nasal washing; in children who were too unwell to undergo nasal washing, a nasaopharyngeal aspirate was performed [14]. Sample collection was postponed to the following Monday for children admitted over the weekend (beginning Friday at 5 PM). Specimens were processed as described elsewhere [15] and were screened for RSV antigen by use of a Direct Immunofluorescent Antibody Test (Light Diagnostics RSV screen; Chemicon), according to the manufacturer's protocol. The Kenyan National Research Ethical Committee and the Coventry Research Ethics Committee (United Kingdom) granted ethical approval for the study.

Data analysis. Data obtained at hospital admission and demographic data were entered into FileMaker, version 5.5 (FileMaker), and were cleaned and analyzed using STATA, version 10.1 (StataCorp). Throughout, the term pneumonia refers to all cases of clinically severe or very severe pneumonia. The pattern of admission to the hospital with RSV-associated pneumonia was determined from January 2002 through December 2007, and the incidence of admission to the hospital with RSV-associated pneumonia was determined from May 2002 through April 2007. The incidences and 95% confidence intervals (CIs) were calculated as the mean annual number of resident children admitted with each case definition divided by the resident population size at the mid-point of the study period (29 October 2004), adjusted for the estimated proportion of these patients with detectable RSV in their nasal specimens. This assumes that the proportion of children with pneumonia who had RSV in their nasal specimens was the same in both the tested and untested groups. Annual period incidence estimates (eg, for the year from May 2002 through April 2003) were calculated using

Table 1. Age Distribution of Admissions due to Respiratory Syncytial Virus (RSV)–Associated Pneumonia at Kilifi District Hospital, 2002–2007, Stratified by Severity

	Severe pneumonia				Very severe pneumonia				All cases			
Age class, months	No. tested	Positive result	Percentage positive in age class	Percentage positive overall	No. tested	Positive result	Percentage positive in age class	Percentage positive overall	No. tested	Positive result	Percentage positive in age class	Percentage positive overall
0–2	1210	255	21.1	33.0	311	57	18.3	50.9	1521	312	20.5	35.3
3–5	761	169	22.2	21.9	151	19	12.6	17.0	912	188	20.6	21.3
6–11	1023	183	17.9	23.7	253	14	5.5	12.5	1276	197	15.4	22.3
12–23	994	101	10.2	13.1	258	14	5.4	12.5	1252	115	9.2	13.0
24–35	388	47	12.1	6.1	198	4	2.0	3.6	586	51	8.7	5.8
36–59	307	17	5.5	2.2	172	4	2.3	3.6	479	21	4.4	2.4
All	4683	772	16.5	100.0	1343	112	8.3	100.0	6026	884	14.7	100.0

Table 2. Estimated Rates of Hospitalization (Hospitalizations per 100,000 Persons per Year) with Respiratory Syncytial Virus (RSV)–Associated Pneumonia to Kilifi District Hospital over the Period from 1 May 2002 through 30 April 2007, by Age and Severity

Age class and pneumonia severity	No. of cases	No. of persons tested for RSV	No. (%) of persons positive for RSV	Person-years of observation	LRTI incidence	RSV incidence (95% CI)
<1 year						
Severe	1889	1644	348 (21.2)	42960	4397	931 (844–1027)
Very severe	486	344	50 (14.5)	42960	1131	164 (130–208)
Severe or very severe	2375	1988	398 (20.0)	42960	5528	1107 (1012–1211)
<5 years						
Severe	3037	2647	447 (16.9)	209075	1453	245 (225–267)
Very severe	961	680	63 (9.3)	209075	460	43 (35–52)
Severe or very severe	3998	3327	510 (15.3)	209075	1912	293 (271–317)

NOTE. The estimated resident population for the specified age class was estimated by multiplying the estimated population at the midpoint of the study (ie, 29 October 2004) by 5 (ie, the number of years in the study period). See the Methods section for the definitions used for pneumonia categories and the incidence estimation procedure. CI, confidence interval; LRTI, lower respiratory tract infection.

the resident population denominator for the mid-point of each period (eg, 30 October 2002). Incidence rates and 95% CIs were estimated using a normal approximation of the likelihood profile [16].

Geographical variation in the incidence of RSV-associated admissions was calculated for each administrative sub-location (of which there are 40 in Kilifi EpiDSS) and was presented as a categorical variable with use of ArcView ArcMap, version 9.2 (ESRI), and Adobe Illustrator CS2, version 12.1 (Adobe). The incidence was calculated separately for sub-locations that are close to the hospital, meaning that at least part of the sub-location fell within a radius of 5 km of KDH [12]. RSV epidemic periods were empirically defined to begin when at least 10% of tested samples were RSV positive or with the observation of at least 2 cases of RSV infection per week in each of 2 consecutive weeks and were defined to continue as long as these conditions were satisfied, with the requirement that an epidemic must last for $\geqslant$4 weeks. Proportions were compared using Fisher's exact or χ^2 tests (2 tailed), and equality of distributions was evaluated using the Wilcoxon rank-sum test. Adjusted risk ratios were determined using binomial regression.

RESULTS

From 1 January 2002 through 31 December 2007, 25,149 children aged <5 years, including 11,829 infants, were admitted to KDH (Figure 1). Of the 7359 eligible children, 6026 (82%) were enrolled, of whom, 884 (15%) had positive test results for RSV (there was no difference by sex). The reasons for nonenrollment were early discharge, refusal, and death, in an approximate ratio of 2:1:1. Comparing children who were and who were not enrolled, there was no difference in the median age (9 months) or in the percentage with male sex (56%), and the proportion of infants was higher in the enrolled group (59% vs 56%; $P = .037$). The rate of nonenrollment was higher not during than during RSV epidemics (20% vs 16%; $P < .001$, by Fisher's exact test). Among the enrolled patients, 4.4% died in the hospital, compared with 9.9% of all eligible children. Furthermore, for those enrolled in the study, there was a lower proportion with malaria parasitemia at hospital admission (16% vs 21%; $P < .001$), with a pathogenic bacterial isolate (5.4% vs 11%; $P < .001$, by Fisher's exact test), and with very severe pneumonia (22% vs 46%; $P < .001$, by Fisher's exact test), but there was no difference in the proportion with severe malnutrition (14% vs 16%; $P = .058$, by Fisher's exact test).

Epidemiology. Epidemics of RSV-positive case patients were periodic with a starting date from November through February, a peak month from January through May, and an average duration of 18 weeks (range, 13–27 weeks). Epidemics appear not to have a simple annual pattern, but rather, the interepidemic period (from peak month to peak month) alternates between 9 and 15 months (Figure 2). Of all hospital admissions of patients with RSV-associated pneumonia, 815 (92%) occurred during an epidemic period. The number of RSV cases occurring during each epidemic ranged from 68 (17% of samples tested) in the epidemic of 2002–2003 to 202 (30% of samples tested) in 2005–2006, with an overall proportion of 27%. Seasonal variation in hospital admissions with RSV infection roughly coincided with the variation in total

Table 3. Hospitalization Rates per 100,000 Children by Year of Surveillance and Stratified by Age Group for Cases of Severe or Very Severe Pneumonia and Cases of Respiratory Syncytial Virus (RSV)–Associated Severe or Very Severe Pneumonia

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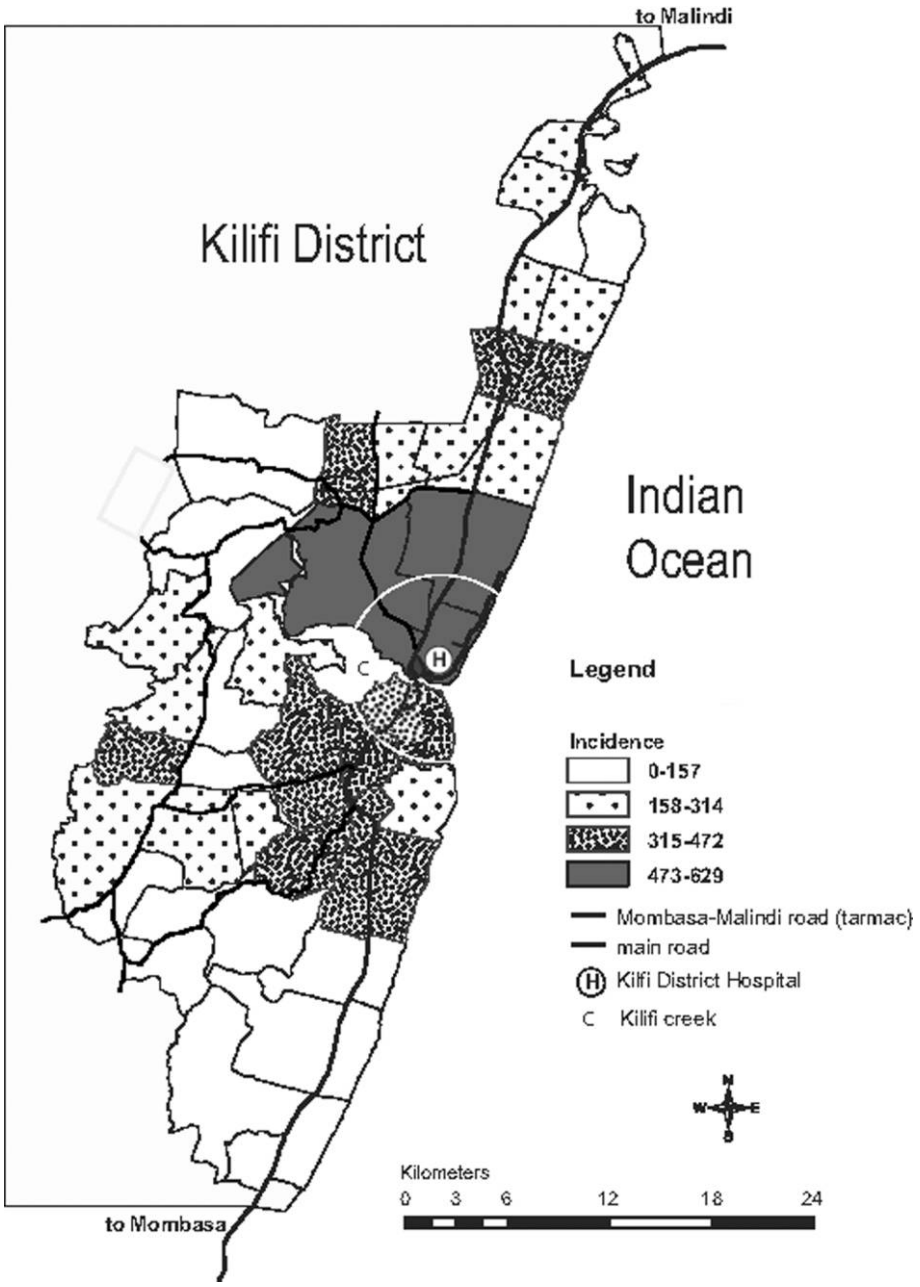

Figure 3. Geographical variation within the Kilifi Health and Demographic Surveillance System in the incidence of respiratory syncytial virus (RSV)–associated severe or very severe pneumonia among children aged <5 years admitted to Kilifi District Hospital (KDH). Incidence is presented as the number of hospitalizations per 100,000 children aged <5 years admitted per year for the 5-year period from May 2002 through April 2007, categorized into 4 levels (see numerical ranges) and stratified by administrative sublocation. Main roads, Kilifi Creek *(C),* and KDH *(H)* are identified. The zone marked by a white perimeter has a 5-km radius from its central point (KDH).

pneumonia admissions. No temporal association with any meteorological measure or other disease syndrome was observed (Figure 2).

The distribution of hospital admissions with RSV-associated pneumonia by age and severity is presented in Table 1. The proportion of patients with positive results for RSV within an age class was highest among children aged 0–5 months (~21%), decreased with increasing age, and was higher among children with severe pneumonia than among those with very severe pneumonia (16.5% vs 8.3%; $P < .001$). The proportions of case patients aged <3, <6, and <12 months were 35%, 57%, and 79%, respectively. The age distribution of case patients differed

Table 4. Prevalence of Features among Respiratory Syncytial Virus (RSV)–Positive and -Negative Children Aged <5 Years Admitted to Kilifi District Hospital with Severe or Very Severe Pneumonia, 2002–2007

Characteristic	Percentage of RSV-positive patients (n = 884)[a]	Percentage of RSV-negative patients (n = 5142)[a]	Adjusted RR[b] (95% CI) (95%)
Clinical			
Crackles	66.7	44.1	1.43 (1.34–1.52)
Wheezing	15.2	11.2	1.43 (1.18–1.73)
Nasal flaring	61.8	48.2	1.16 (1.09–1.24)
Indrawing	98.3	90.2	1.04 (1.03–1.05)
Shock[c]	13.5	19.4	0.68 (0.56–0.82)
Hypoxemia	10.3	13.7	0.73 (0.59–0.91)
Postrate/unconscious	4.1	13.8	0.36 (0.26–0.50)
Concurrent illness			
Slide-positive malaria	4.6 (n = 864)	18.3 (n = 5073)	0.36 (0.26–0.49)
Malnutrition[d]	6.6	15.4	0.47 (0.36–0.61)
Bacteremia	2.3 (n = 864)	6.0 (n = 5071)	0.4 (0.25–0.63)
Risk factors			
Premature (infants)	4.6 (n = 697)	6.7 (n = 3005)	0.67 (0.45– 0.97)
Heart disease	1.0	2.1	0.49 (0.24–1.00)
Outcome			
Duration of inpatient stay >12 days	3.8	8.8	0.46[e] (0.32–0.66)
Died	2.4	4.7	0.41 (0.26–0.64)

NOTE. CI, confidence interval; RR, relative risk.

[a] Denominator for percentage calculations, unless otherwise specified in parentheses.

[b] RR of feature in RSV-positive patients, relative to RSV-negative patients, adjusted for age class (with 95% CI).

[c] Temperature gradient, capillary refill >3 s, or weak pulse volume.

[d] Small mid-upper arm circumference for age, bipedal edema, or visible severe wasting. Small mid-upper arm circumference was defined as ⩽10th percentile calculated for all patients admitted to Kilifi District Hospital during 2002–2007, which generated the following cut-off values by age: 0–5 months, ⩽7.8 cm; 6–23 months, ⩽11.0 cm; 24–35 months, ⩽11.6 cm; 36–59 months, ⩽12.2 cm [12].

[e] RR was also adjusted for differential mortality between RSV-positive and RSV-negative children.

significantly by clinical category ($P < .001$). In particular, the proportion of patients admitted with RSV-associated disease who were aged 0–2 months was higher (51%) among the subset of children with very severe pneumonia.

Hospitalization rates. Over the 5 year period from 1 May 2002 through 30 April 2007, the mean annual number of hospital admissions from the community of Kilifi EpiDSS residents was 2661 for patients aged <5 years and 1188 for patients aged <1 year. The annual rate of hospital admissions of patients with severe or very severe pneumonia was 1912 hospitalizations per 100,000 persons for children aged <5 years and 5528 hospitalizations per 100,000 persons for infants aged <1 year. The annual incidence of hospital admission with RSV-associated severe or very severe pneumonia was 293 hospitalizations per 100,000 persons (range by year of study, 202–373 hospitalizations per 100,000 persons) for children aged <5 years and 1107 hospitalizations per 100,000 persons (range, 692–1587 hospitalizations per 100,000 persons) for infants (Table 2). Incidence estimates by year of study and finely stratified by age are provided in Table 3.

The geographical distribution of RSV-associated severe and very severe pneumonia incidence in children aged <5 years, presented in Figure 3, reveals considerable variation between administrative sub-locations, with incidence apparently decreasing with distance from the District hospital. For the population of children aged <5 years living within the region defined as close to KDH, the annual hospitalization rate for severe or very severe pneumonia was 3169 hospitalizations per 100,000 persons (95% CI, 3023–3323 hospitalizations per 100,000 persons) and for RSV-associated severe or very severe pneumonia was 574 hospitalizations per 100,000 persons (95% CI, 507–650 hospitalizations per 100,000 persons). Among infants in the sub-locations closest to the hospital, the annual incidence of severe or very severe pneumonia and RSV-associated severe or very severe pneumonia were 8828 (95% CI, 8297–9393 hospitalizations per 100,000 persons) and 2112 hospitalizations per 100,000 persons (95% CI, 1835–2431 hospitalizations per 100,000 persons), respectively.

Severity and concurrent illnesses. Among patients with severe or very severe pneumonia, the clinical signs crackles, wheezing, nasal flaring, and lower chest-wall indrawing were all associated with RSV infection, whereas shock, hypoxemia,

prostration, and coma were inversely associated with RSV infection (Table 4). Concurrent malaria parasitemia, severe malnutrition, and bacteremia were all significantly less common among RSV-positive children with pneumonia. Furthermore, a history of premature birth among infants and a discharge diagnosis including heart disease were marginally less frequent among RSV-positive children. Patients with RSV-associated pneumonia had a significantly shorter inpatient stay and lower case fatality rates than did patients with RSV-negative pneumonia. RSV-positive patients were significantly younger than RSV-negative patients (median age, 4.9 vs 19.1 months; $z = 11.34$, by Wilcoxon rank-sum test; $P < .001$). Adjusting the relative risk of each feature in Table 4 for age did not alter these associations. The proportion of RSV-associated pneumonia cases in children aged <5 years that were very severe did not differ by distance from KDH (11.2% near KDH vs 13.5% far from KDH; $P = .501$, by Fisher's exact test).

Bacterial pathogens were identified in the blood samples of 20 (2%) of 864 RSV-positive patients with pneumonia. Isolates cultured were Group A β-hemolytic streptococci ($n = 5$), *Streptococcus pneumoniae* ($n = 5$), *Acinetobacter* species ($n = 5$), *Haemophilus influenzae* ($n = 4$), *Pseudomonas* species ($n = 1$), and *Escherichia coli* ($n = 1$). In 1 instance, there was a coinfection with *S. pneumoniae* and *H. influenzae*. Three of the children with confirmed bacterial coinfection subsequently died; 2 were infected with *H. influenzae*, and 1 was infected with *Acinetobacter*. In comparison, 6% (302) of RSV-negative patients had positive blood culture results, with similar mortality (15%) and species distribution relative to RSV-positive patients.

DISCUSSION

Our surveillance at a district hospital in coastal Kenya spanning 6 years provides a highly detailed description of the burden of severe RSV disease among young children in a typical rural developing country setting. Over the period 2002–2007, we identified clinically severe or very severe pneumonia in roughly one-third of children aged <5 years and 38% of infants admitted to KDH, of which an estimated 15% and 19%, respectively, had pneumonia associated with RSV infection. The rate of hospital admissions with RSV-associated pneumonia within the demographically well-defined population was 293 cases per 100,000 patients per year among children aged <5 years and 1107 cases per 100,000 patients per year among infants. These data are similar in magnitude to those reported for an intensively monitored birth cohort within the same population (1300 cases of RSV-associated severe pneumonia in infants admitted to KDH per 100,000 child-years of observation) [13] and are similar to the data reported for the small number of other denominator-based studies of hospital admissions in resource-poor countries [6, 7]. Furthermore, our reported rates mirror closely population-based hospitalization rates recently described for various locations in the United States [17].

Thus, our data indicate that an effective pediatric RSV vaccine could prevent a sizeable proportion of hospital admissions attributable to pneumonia. A useful reference point is afforded by comparison with severe rotavirus diarrhea (targeted for vaccination [18]), which exhibited an annual rate of hospitalization at KDH for the period 2002–2004 of 478 cases per 100,000 patients among children aged <5 years and 1431 cases per 100,000 patients among infants [12]. Furthermore, the distance decay in rates of hospitalization (Figure 3), reported elsewhere in The Gambia [8], indicates a large (~2-fold) additional burden of severe pneumonia due to RSV present in the community but not recorded through inpatient surveillance. If we assume the estimates for areas that are close to the hospital are more realistic of the community burden and representative of Kenya as a whole, the annual number of cases of RSV-associated severe or very severe pneumonia among children aged <5 years and infants throughout the country are estimated to be 37,000 and 29,500, respectively (based on population estimates for children aged <5 years and births in 2008 of 6.5 and 1.4 million, respectively [19]).

Further, we point out an additional burden of severe pneumonia due to RSV in the community, missed by hospital surveillance, in the form of patients presenting to outpatient health facilities who are not admitted, which was shown in our report of a birth cohort in the same setting as the present study [13]. A potential additional source of underestimation of RSV disease in our study arises from the immunofluorescence assay used to detect the virus, which has been shown to be less sensitive than molecular detection methods [20, 21].

A clear impediment to vaccine intervention is the absence of an effective candidate for use in the key target age group of 0–2 months [4, 22]. Nevertheless, studies consistently show good safety and immunogenicity of live, attenuated RSV vaccines in older infants and young children [5, 23]. Data from the present study show that approximately two-thirds of RSV-associated pneumonia that results in hospitalization occurs in children aged ⩾3 months, and therefore, delayed vaccine delivery has the potential to prevent a significant fraction of RSV disease. Reduced transmission from older, vaccinated infants to vulnerable infants may enhance the benefit of delayed vaccination.

Our data show that the incidence of RSV disease varies considerably year-by-year, particularly among infants, where incidence varied by a factor of >2 between the lowest and highest incidence years, suggesting that short-term studies may present a biased picture of RSV disease burden. Interestingly the distribution of disease by age was roughly constant over time (in contrast to observations made in The Gambia [24]).

In relation to pneumonia severity, our study shows that non–

life-threatening clinical features were more strongly associated with being RSV positive than RSV negative, whereas the risks of very severe conditions, risk factors, and concurrent illness were significantly higher among RSV-negative patients. A similar clinical pattern was reported in an in-patient study performed in Mozambique [25]. The low case fatality rate of 2.2% for RSV-positive patients (in line with most other reports [6, 26, 27]), compared with 4.7% for RSV-negative patients, is therefore not surprising. These data support the rationale for an RSV vaccine on the basis of prevention of morbidity rather than mortality. Nevertheless, as in other studies, there is some concern regarding bias in sampling of less severe cases [6], because 18% of eligible children were not tested, and the case fatality among the enrolled patients was less than one-half that observed among all eligible children (4.4% vs 9.9%). In our setting, faced with a child undergoing emergency treatment, it was not a clear priority for the clinician to collect a nasal sample. Therefore, it is possible that the true case fatality rate associated with RSV is significantly higher than that observed, and consideration should be given to collecting a specimen post-mortem to address this unknown factor.

The prospect of widespread use of vaccines against *H. influenza* type b and *S. pneumoniae* across the developing world is set to substantially alter the landscape of pneumonia etiology [3]. Surveillance for a broad etiology of the remaining significant burden of childhood pneumonia is of increasing importance. Arguably, the most important remaining cause of childhood pneumonia that is potentially preventable by vaccine intervention is RSV. The present study reports a substantial burden of RSV-associated severe pneumonia in a low-income setting that is equivalent to that identified in the high-income setting. This argues for a need to investigate the potential use of vaccines for both developed and developing countries. This study also demonstrates the power of long-term surveillance in understanding the role of RSV in morbidity and mortality patterns in children in a low-resource setting and the requirement for population evidence in developing a rational strategy for future RSV vaccine intervention.

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