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Pneumonia prevention: Cost-effectiveness analyses of two vaccines among refugee children aged under two years, *Haemophilus influenzae* type b-containing and pneumococcal conjugate vaccines, during a humanitarian emergency, Yida camp, South Sudan

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ABSTRACT

By September 2013, war between Sudan and South Sudan resulted in >70,000 Sudanese refugees and high pneumonia incidence among the 20,000 refugees in Yida camp, South Sudan. Using Médecins Sans Frontières (MSF)-provided data and modifying our decision-tree models, we estimated if administering *Haemophilus influenzae* type b (Hib)-containing (pentavalent vaccine, also with diphtheria pertussis and tetanus [DPT] and hepatitis B) and pneumococcal conjugate (PCV) vaccines were cost-effective against hospitalized pneumonia. Among children <2 years old, compared with no vaccination, one- and two-doses of combined Hib-containing and PCV would avert an estimated 118 and 125 pneumonia cases, and 8.5 and 9.1 deaths, respectively. The cost per Disability-Adjusted-Life-Year averted for administering combined one- and two-doses was US$125 and US$209, respectively. MSF demonstrated that it was possible to administer these vaccines during an emergency and our analysis found it was highly cost-effective, even with just one-dose of either vaccine. Despite unknown etiology, there is strong field and now economic rationale for administering Hib and PCV during at least one humanitarian emergency.
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1. Introduction

War has occurred between South Sudan and Sudan for decades and continues today despite the 2011 independence, which was expected to bring stability to the country. On 2 August 2012, an international health non-governmental organization, Médecins Sans Frontières (MSF), announced a health catastrophe for Yida camp, in northern South Sudan because of increasing arrivals of Sudanese refugees from across the border, overstretched camps, and the high numbers of children with malnutrition, who were further weakened by diarrhea, malaria and respiratory infections [1]. Black et al. (2010) found that pneumonia and diarrhea are the leading causes of childhood deaths globally and the major causes of lower respiratory-associated or pneumonia deaths are *Haemophilus influenzae* type b (Hib) and *Streptococcus pneumoniae* [2]. Through the end of 2012 in Yida camp, respiratory infections continued and even increased for acute respiratory infections (ARI) among outpatients. Therefore, MSF prepared in the ensuing months to vaccinate against Hib and *Streptococcus pneumoniae* with all training and logistics completed and the vaccine finally arriving the first of July 2013 to provide three rounds each of Hib and pneumococcal conjugate (PCV) vaccines. From their data reported December 2013, we performed a cost-effectiveness analysis from the perspective of MSF [3].

2. Methods

Using the MSF data (Table 1), we used our previously developed decision-tree models (Fig. 1) for one- and two-dose Hib-containing and PCV vaccinations separately and in combination to estimate the vaccines' impact and cost-effectiveness following the target population in their first 2 years of life [4]. We did not include indirect non-medical costs as the MSF report provided neither indirect costs, e.g., time lost to parents, nor non-medical costs, e.g., transportation.

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Table 1
2013 supplemental immunization activity of MSF, Yida refugee camp, South Sudan.

Parameter	Base-case estimate	Sensitivity range	References
Target population	5781	NA	[3]
Epidemiologic			
Hib pneumonia rate (per 100,000, annual)	2925	2194–3656 (±25%)	[3,5]
Pneumococcal pneumonia rate (per 100,000, annual)	5850	4388–7313 (±25%)	Doubled Hib [5,6]
Clinical			
Children's healthcare utilization, %	75	94–56 (±25%)	Assumption
Vaccine coverage per survey, %			
1 dose	89.2	NA	[3]
2 doses	66.1	NA	[3]
Hib vaccine efficacy for radiologically defined pneumonia,%			
1 dose	20.0	0.5–25.0 (+25%)	Assumption [4]
2 doses	22.4	1.9–38.6	[7]
PCV vaccine efficacy for clinical or severe clinical pneumonia, %			
1 dose	29.0	0.5–36.25 (+25%)	Assumption [4]
2 doses	37.0	25.0–48.0	[8]
Case Fatality Rate (CFR, aged < 5 years), %			
Care	6	4–8	[5,6]
No care	11	7–18	[5,6]
Length of inpatient stay, days	4	3–6	[10]
Vaccine wastage (%)	1	NA	[3]
Economic, US$			
Hib vaccine price/dose	2.10	NA	[3]
PCV price/dose	7.97	NA	[3]
Cost/dose delivered, excluding expatriate staff	3.45	NA	[3]
Total care cost/day	1.01	NA	[9]
Medication costs/case of pneumonia	12.34	NA	[11]

Costs were adjusted to 2013 levels.

From the MSF report using estimates provided from the United Nations High Commissioner for Refugees (UNHCR), the mid-2012 total population was 20,000 [3]. Given 585 persons were hospitalized with ARI [3], presumptively mainly pneumonia, the annual incidence was 2925/100,000 total population. This rate would be higher among young children; however, is similar to double the estimated African childhood Hib pneumonia incidence (3448/100,000 children aged <5 years) [5]. Doubling the reported childhood Hib incidence was done because of the high degree of malnutrition and overcrowding, inadequate shelter and blankets during a humanitarian emergency [4]. Comparing the annual African childhood Hib pneumonia rate, pneumococcal pneumonia has double the incidence [6]. Therefore, the childhood pneumococcal pneumonia incidence was assumed to be 5850/100,000 children aged <5 years (Table 1). Invasive disease, such as meningitis or sepsis, was not considered. Table 1 provides other MSF report data for target population, vaccine coverage/wastage, and vaccination program costs that were used.

We assumed 75% of children would use healthcare services. Vaccine effectiveness data for South Sudan were unavailable. From a Gambian study, Hib vaccine efficacy against radiologically defined pneumonia was 22.4% (95% confidence interval [95%CI] 1.9–38.6) [7]; we assumed one-dose efficacy was 20% [3]. From another Gambian trial, two-dose PCV efficacy against clinical or severe clinical pneumonia was 37% (95% CI 25–48) [8]; one-dose was assumed to be 29% [3].

We used World Health Organization (WHO) estimates for Africa-specific childhood case fatality rates (CFR) for Hib and pneumococcal pneumonia [5,6]. Because Hib and pneumococcal CFRs were similar we used one rate. We estimated the medical visit cost at US$1.01/day using the average cost for Ethiopia and Kenya—neighboring countries [9] and multiplied it by the average stay of 4 days [10]. Medication costs ($12.34)/pneumonia case were estimated from previous reports (Table 1) [11].

We compared the costs and benefits of the July-September 2013 MSF conducted Hib-containing and PCV campaigns under base-case scenarios: (1) no vaccination, (2–5) one- and two-dose Hib-containing vaccine or PCV, and (6–7) one-dose or two-doses of combined Hib-containing vaccine and PCV using Microsoft® Excel 2010 (Redmond, WA). We estimated the incremental cost-effectiveness ratio (ICER) as cost per Disability-Adjusted-Life-Year (DALY) averted expressed in 2013 US dollars. DALYs used were WHO life expectancy data weighted by years lost and disability from pneumonia, with the mean duration of four hospital-days and no long-term sequel among survivors [12]. To determine if intervention was cost-effective, we used the WHO threshold for highly cost-effective intervention of less than the country's gross domestic product (GDP)/capita vs. the cost/DALY averted [13]; South Sudan 2013 GDP/capita was US$1045 [14].

A one-way sensitivity analysis was conducted to evaluate the impact of changing values of several parameters on ICER for two-doses of each vaccine or both vaccines combined (Table 1). These one-way sensitivity analyses were examined using tornado diagrams. A threshold analysis was done to decipher the break-even price of two-doses of Hib-containing and PCV vaccines when all other variables are held at their base-case value. Finally, a probabilistic sensitivity analysis (PSA) was done on those variables that indicated an impact on the cost result after performing the one-way sensitivity analysis. This allowed us to limit the number of variables selected for this analysis. Up to 5000 iterations were performed to obtain the cost distribution results. All future costs and DALY estimates were discounted at an annual rate of 3%.

3. Results

Tables 2 and 3 summarize all findings. For no vaccination, estimated total pneumonia cases and associated deaths were 507 and 37, respectively, with 380 medical visits costing US$6232.

One-dose and two-dose Hib-containing vaccination prevented an estimated 30 and 33 Hib pneumonia cases, and estimated 2 and 3 deaths, respectively while reducing medical costs by approximately US$400 for each scenario (Table 2). One- and two-dose PCV would avert an estimated 98 and 105 pneumococcal pneumonia cases, and estimated 7 and 8 deaths averted, respectively. For one- and two-dose PCV, the medical cost averted was about $1100 and $1300, respectively. The greatest impact was seen with combined one- and two-doses of Hib-containing and PCV; they averted 118 and 125 pneumonia cases, and 8.5 and 9.1 deaths, respectively with the largest medical cost reductions of approximately US$1500 for each scenario.

Table 3 shows administering one- and two-doses of Hib-containing vaccines yield ICER/DALY averted of US$211 and US $310, while costing US$945 and US$1388 per case averted, respectively. One- and two-doses of PCV yield ICER/DALY averted of US $148 and US$210, respectively and $664 and $942, respectively, for cost per case averted. The combined one- and two-doses of Hib-containing and PCV campaigns would yield ICER/DALY averted of US$125 and US$209, respectively and $559 and $936, respectively, for cost per case averted. Therefore given the South Sudan 2013 GDP/capita of US$1045, all six scenarios had a cost/DALY averted ranging from $125 (one-dose combined vaccines) to $310 (2 doses of PCV) that are highly cost-effective.

In one-way sensitivity analysis, the base-case estimates for the two-doses of each or combined vaccines were most affected by

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