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Effectiveness of COVID-19 Vaccine Doses in Children: Case of Lake Region Economic Bloc-Kenya

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Abstract

Introduction: Vaccination of children has experienced delays due to paucity of information regarding safety, effectiveness, immunogenicity, and reactogenicity. Age wise approval prioritized 12 - 17 years and later 5 - 11 years. Those below 5 years possess naïve immunity and not considered. In Lake Region Economic Bloc children aged 12 - 17 variably received 1, 2, and 3 doses of vaccine. This analysis looks into effectiveness of the doses administered. **Method:** Data providers from 84 LREB facilities submitted patients' vaccination data to Power BI supported dashboard between June 24, 2021 and July 30, 2022. Data of 12 - 17 years old was mined, analyzed and visualized. Sample sizes considered for analysis were 0 dose, n = 8132; 1 dose, n = 271; 2 doses, n = 402, and 3 doses, n = 90. Data used in the analysis was facility operational and not from experimental design. Relative risk analysis of children who received 0, 1, 2, and 3 doses was done using Odds Ratio run on R software. **Results:** The relative risk of infection to a child with one dose against unvaccinated counterpart is 0.92 (95% CI, 0.61 - 1.43). Likewise the relative risk of infection to a child aged 12 - 17 years with 2 doses against another who received no dose is 0.87 (95% CI, 0.63 - 1.24). A child with 3 doses is 46% (95% CI, 27% - 84%) less likely to get infected compared to another not vaccinated. Also, the relative risk between having 2 doses and 1 dose for a child aged 12 - 17 years is 0.95 (95% CI, 0.55 - 1.6). For the same age group the relative risk of having 3 doses of vaccines against 1 dose is 51% (95% CI, 26% - 100%). In addition, a child who receives 3 doses of vaccine is 53% (95% CI, 28% - 100%) less likely to experience breakthrough infection compared to another with 2 doses. Whereas 1st dose offers (5%) marginal protection advantage over the 2nd dose, the 3r dose offers 49% and 47% more protection

over 1st and 2nd doses, respectively, because of incremental reduced risk of infection gained from previous doses. During the period, 15 children at risk were admitted with COVID-19 infections in various regional hospitals, one had 3 doses but confounded with severe comorbidity. **Conclusion:** We found that 2nd dose had marginal protection over the 1st dose. However, the 3rd dose offers extensive protection compared to 1st and 2nd doses, and protects more against hospitalization. Children at risk should receive 3 doses of vaccines.

Keywords

Children Vaccination, Doses, Effectiveness

1. Introduction

In the evolution of COVID-19 pandemic, relevant authorities delayed approval of children's vaccination against SARS-COV-2. Age discriminant approval permitted the use of child-size doses only in 5 - 17 years old [1]. Fortunately, many children who contact coronavirus present mild symptoms and barely end up with severe outcomes. On the other hand, researchers have not sufficiently established vaccine safety, effectiveness, immunogenicity, and reactogenicity in children of all ages, particularly 0 - 5 years old. As such, pediatric vaccine trial in children is crucial in determining safety, effectiveness, immunogenicity, and reactogenicity against COVID-19, including those at high risk because of medical conditions and life threatening illnesses [2]. Although most children infected with COVID-19 do not end up with severe outcomes, they act as reservoirs of SARS-COV-2 virus [3] which is inadvertently transmitted to elderly parents, grandparents, and guardians. It is argued that COVID-19 being age discriminant, vaccinating children is seen as indirect way of protecting adult and elderly population [4] characterized with underlying conditions. However, protecting adults must not come at the risk of adverse outcomes in children [5].

Inevaluating the immunogenicity, safety, and effectiveness of the BNT162b2 vaccine, a randomized clinical trial of two doses on children found no adverse incidents. The vaccine exhibited favorable safety profile among 6 - 11 years olds [6]. In another case, mRNA vaccine tested in 6 - 11 years old was also found safe and immunogenic [7]. Right from the start of vaccination of populations against COVID-19, use in children elicited much debate among medical practitioners, since severe COVID-19 is rare in healthy children [7] Creech, *et al.*, (2022). According to [8], in fewer incidents, there are reported risk of cardiovascular adverse events with certain COVID-19 vaccines

It is important to establish these sensitivities since children form 32% of the global population. WHO reports that 1 in 9 cases of COVID-19 is from children who account for 2% of total hospitalization. Whereas 1 in 60 COVID-19 cases result in death for adult population in absence of vaccination, approximately 1 in 3500 children who get infected with the virus succumb [9]. Moreover, UNICEF

data shows that from the start of the pandemic until November 3, 2022, COVID-19 case mortality of children by age is: 0 - 4 years (5044), 5 - 9 years (2578), 10 - 14 years (3121), and 15 - 19 years (5404). The world lost 16,147 children to coronavirus. But these are only reported and confirmed deaths, [10]. When we factor in excess mortality and unreported deaths, the figure may be higher [11].

In Africa, 9% of total confirmed COVID-19 cases are in children. Also, 2.4% of total death (or COVID death) are accounted for by children. In general, age group 12 - 17 years experiences disproportionate higher infection rates [12]. In Kenya, an estimated number of 37,815 and 136 confirmed cases and fatalities, respectively have been reported in children.

It is estimated that LREB children account for 25% of children's fatality in Kenya, that is, 34 deaths. It is also approximated that 1,971,581, and 788,632 children aged 12 - 17 years nationally, and in Lake Region Economic Bloc, respectively have been vaccinated [13].

Lake Region Economic Bloc-Kenya (LREB) comprises 14 counties of western Kenya: Bomet, Bungoma, Busia, Homa Bay, Kericho, Kisii, Kisumu, Migori, Nandi, Nyamira, Siaya, Trans Nzoia, and Vihiga [14]. The first case of COVID-19 in the region was reported on March 13, 2020 [13]. Vaccine administration in the region started one years later, that is, after March 26, 2021.

Data from LREB showed that infected children presented generally no symptoms (coughs, fever, sore throat, body weakness, headache, running nose, difficulty in breathing, pain, loss of taste and smell among others). Some children, considered to be at high risk of severe outcomes, had the following comorbidities: hypertension, pregnancy, cardiovascular, diabetes, and HIV. Adolescents aged 12 - 17 years old received 1, 2, and 3 COVID-19 vaccine doses from June 24, 2021 to July 30, 2022. Analyzing relative effectiveness of the vaccine doses administered is the subject of this paper.

In all these uncertainties, it is important to investigate the relative effectiveness of doses, 1, 2, and 3 on children [15].

In pursuit of this, LREB operational data collected at facility level is used to analyze the effectiveness of child-size 1, 2, and 3 doses.

2. Method

Data used in this analysis is facility operations data. Patients who turn up in 84 LREB facilities for treatment between June 24 2021 and July 30, 2022 had their data recorded. The process of data collection involved official Kenyan COVID-19 case investigation form (CCIF) being configured and digitalized in CommCareapplication. Then 192 LREB facility data providers in 84 health facilities were trained on online data submission using internet enabled tablets and/or mobile phones to Power BI supported COVID-Dxdashboards. Vaccination data of children aged 12 - 17 years was mined, visualized, and analyzed. In this LREB operational research, vaccination data from 8895 participants aged 12 - 17 years

was and used in the analysis. Other than the number of vaccine doses administered to this cohort, data is neither categorized by gender not by type of vaccine received. The sample sizes used variably is as follows: 0 dose, n = 8132; 1 dose, n = 271; 2 doses, n = 402; and 3 doses, n = 90.

The odds ratio analysis on relative risk of receiving 0, 1, 2, and 3 doses was done using R software. The results obtained are interpreted and presented.

Data used was not experimentally generated but from facility operations. Unintended biases may be possible based on collection method as most patients came for treatment.

3. Ethical Clearance

Ethical clearance and approval number IERC/JOOTRH/581/22 was obtained from Jaramogi Oginda Odinga Teaching and Referral Hospital on 21st February 2022. At the same time data sharing agreement was signed by participating facilities in compliance with national and international Data Protection Acts. Only patients identification numbers were used and not names such that they remained anonymous.

4. Results

The sample sizes used meet central limit theory from which a general conclusion can be drawn. Among the children whose data was collected 67 or 0.75% presented comorbidities as follows: hypertension (3), pregnant (10), cardiovascular (8), diabetes (43), and HIV (28). As such, HIV and diabetes form bulk of comorbidities (see **Figure 1**).

During that period, only some children with comorbidities were hospitalized as follows: diabetes (4), HIV (3), cardiovascular disease (2), hypertension (1), diabetes mellitus (1), and pregnancy (1) (see **Figure 2**).

Results from odds ration analysis are presented in the tables below.

4.1. Effectiveness of Dose 1

The ratio of likelihood of COVID-19 infection to a child with 1 dose of vaccine

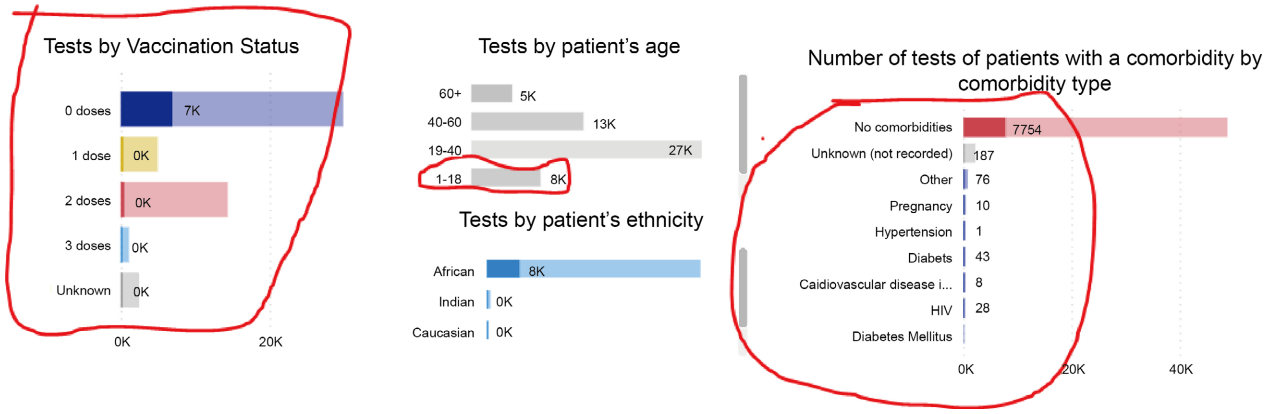

Figure 1. Children vaccination status and comorbidities.

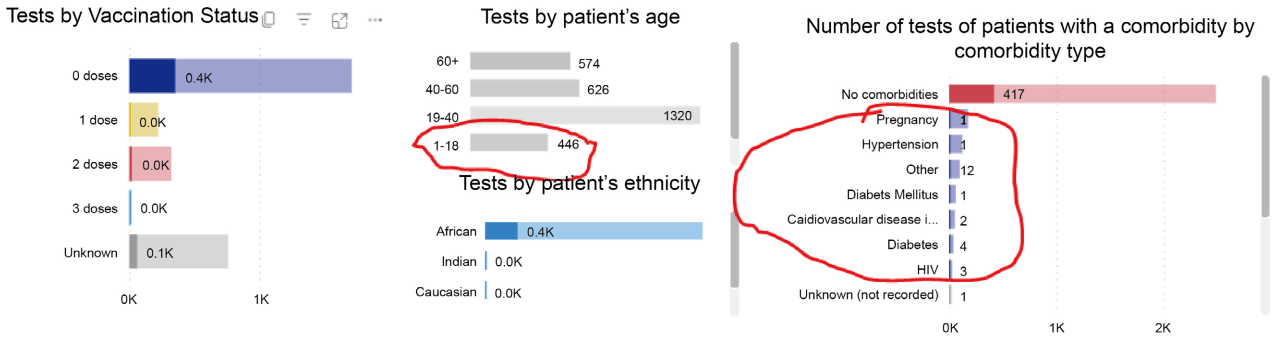

Figure 2. Visualization of hospitalized children and comorbidities.

against no dose is 0.92 [95% CI, 0.61, 1.43]. The protection ratio ranges from 0.61 to 1.43. It implies that the protection of a child aged 12 - 17 years who receive 1 dose ranges from 39% less likely to 43% more likely to be infected. As such, the protection one dose offers a child aged 12 - 17 years is weak, at least according to LREB operations data (see Table 1).

Table 1. Effectiveness of one dose results.

vaccine	Estimate	Lower	Upper
1 dose	1.000	NA	NA
0 dose	0.92	0.61	1.43
p-value	0.054	0.051	0.05

4.2. Effectiveness of Dose 2

The ratio of likelihood of infection after 2 doses against zero dose to a child aged 12 - 17 years is 0.87 [95% CI, 0.63, 1.24]. The protection two doses of vaccine offer to children 12 - 17 years old ranges from 37% less likely to 24% more likely to get infected. According to these results, the 2nd dose offers slightly more protection than the 1st dose, *i.e.*, 19% more protection (see Table 2).

Table 2. Effectiveness of 2 doses.

Impact of 2 doses results			
Vaccine doses	Estimate	Lower	Upper
2 doses	1.000	NA	NA
0 dose	0.87	0.63	1.24
p-value	0.042	0.041	0.043

4.3. Effectiveness of Dose 3

A child with 3 doses of vaccine is 46% [95% CI, 27%, 84%] less likely to be infected compared to one not vaccinated. This implies that the protection offered by the 3rd dose to a child aged 12 - 17 years ranges from 27% to 84% less likely to

experience breakthrough infection. Considered individually, the 3rd dose offers 46% and 41% more protection than 1st and 2nd doses, respectively. In that regard, the 3rd doses offers extensive protection over both 2nd and 1st doses (see Table 3).

Table 3. Effectiveness of three doses results.

Vaccination Status	Estimate	Lower	Upper
3 doses	1.000	NA	NA
0 dose	0.46	0.27	0.84
p-value	0.01266019	0.01182676	0.005724581

4.4. Comparing Doses 2 and 1

The likelihood of infection between a child aged 12 - 17 years with 2 doses and a counterpart with 1 dose is 0.95 [95% CI, 0.55, 1.6], that is, the child with 2 doses is 5% less likely to get infected compared to 1st dose. The earlier results estimated 8% advantage over 1st dose. The findings are consistent that 2nd dose has only marginal advantage of the 1st dose (see Table 4).

Table 4. Relative effectiveness of 2 doses against 1 dose.

Doses	Estimate	Lower	Upper
2 dose	1.000	NA	NA
1 doses	0.95	0.55	1.60
p-value	0.051	0.050	0.050

4.5. Comparing Doses 3, and 1

A child aged 12 - 17 years with the 3rd dose is 51% [95% CI, 26%, 100%] less likely to experience breakthrough infection compared to counterpart with the1st dose. The actual estimate is (100 − 51)% = 49% advantage of the 1st dose. The earlier individual results estimated 46% advantages of the 1st dose. These estimates are consistent (see Table 5).

Table 5. Relative effectiveness of 3 doses against 1 dose.

Vaccine Doses	Estimate	Lower	Upper
3 doses	1.000	NA	NA
1 dose	0.51	0.2557567	1.0
p-value	0.0502293	0.0510789	0.05133296

4.6. Comparing 3 Doses to 2 Doses

A child aged 12 - 17 years with 3 doses of vaccine is 53% [95% CI, 28%, 100%] less likely to experience breakthrough infection compared to counterpart with 2 doses. The actual estimate is (100 − 53)% = 47%. In the regard, the 3rd dose offers 47% more protection than the 2nd dose (see Table 6).

Table 6. Relative effectiveness of 3 doses against 2.

Doses	Estimate	Lower	Upper
3 doses	1.000	NA	NA
2 doses	0.53	0.28	1.0
p-value	0.04852	0.05630	0.05060

5. Discussion

In this facility-based study we found that three doses of the vaccine confer significant protection against COVID-19 infection in 12 - 17 year old children attending healthcare facilities in the LREB network. Hence, our analysis can have a selection bias towards symptomatic patients and not possible to generalize to the 12 - 17 year old population of this area. Nevertheless, our findings point that 3 doses protect his cohort of children more.

The data used in this analysis is facility-based operational data and not experimental design. In Kenya, vaccination of children between 12 - 17 years started in early 2022. From this data, the relative risk of 1 dose over zero doses administered to 12 - 17 year olds is 0.95 (95% CI, 0.61, and 1.43). As such, the protection one dose offers a child aged 12 - 17 years is weak and wanes quickly. The relative risk of infection after administration of 2 doses to children against zero dose is 0.87 (95% CI, 0.63, and 1.24). According to these findings, the 2nd dose offers marginal protection over 1st dose, *i.e.*, 8% more protection. However, the relative risk of infection when a 12 - 17 year old child receives 3 doses against zero dose is 54% (95% CI, 27%, 84%). The 3rd dose offers 49% and 41% more protection than 1st and 2nd doses, respectively. In that regard, the 3rd doses offers extensive protection compared to both 2nd and 1st doses considered individually.

Interestingly, the relative risk of infection between 1st and 2nd doses administered to 12 - 17 years old is 0.95 (95% CI, 0.55, 1.6), thus the 2nd dose has 5% marginal protection advantage compared to the 1st. The earlier results estimated 8% advantage over 1st dose. The findings are consistent that the 2nd dose has only marginal advantage over the 1st dose. According to [16] study in Australia, confirmed prior SARS-COV-2 infection with Delta combined with 2 vaccines doses offer more protection against subsequent infection compared to 2 doses without infection. In LREB both 1 and 2 doses were administered after prevalence of Delta infections in the community. The participants were not infection-naiive before the data was collected but had prior exposure. Thus, doses 1 and 2 had the benefit of pre-exposure in LREB making only slight difference in favour of 2nd dose. However, the relative risk of infection for 12 - 17 years old after the 3rd dose compared to the 1st and 2nd doses are 51% (95% CI, 26%, 100%), and 53% (95% CI, 28%, 100%), respectively. The 3rd dose has 49% and 47% more protection compared to 1st and 2nd doses, respectively. According to [17] the reduction in odds of infection after the 3doses is incremental, that is, it accumulates reduction in both 1 and 2 doses in addition to prior infection, where it was expe-

rienced. During the period, 15 children who tested COVID-19 positive were admitted in various hospitals; of whom 11 had no comorbidities, HIV (2), diabetes (1), and cardiovascular (1). Among the 15 hospitalized children, 7 had (0) doses, 2 (1st dose), 3 (2nd dose), 1 (3rd dose), and 2 had vaccination status unknown.

These LREB data results agree with [12] that 12 - 17 year olds experience higher cumulative incidence of COVID-19 infections compared to younger children. Considering children at increased risks of severe outcomes, which include those with comorbidities and underlying conditions (see **Figure 1** and **Figure 2**), we agree with [18] on mandatory vaccination of children, especially those with adverse medical conditions should receive at least 3 doses of vaccine.

Coincidentally, [15] observed that vaccine effectiveness in children was highest against Omicron after the 2nd dose. However, the effectiveness waned in 3 months. The finding agrees with LREB analysis that the 2nd dose offers marginal protection after the 1st dose. The outstanding result of LREB data analysis is that 3rd dose offers effective and extensive protection compared to doses 1, and 2.

6. Conclusion

In terms of comparative advantages in child vaccination, the 2nd dose offers 19% more protection than the 1st dose, considered individually. However, the 3rd dose offers 49% and 47% more protections than 1st and 2nd doses, respectively. Whereas the 2nd dose has marginal advantage over the 1st, it has been found that the 3rd dose has extensive protection compared to 1, and 2 doses.

Limitation of the Study

The data used is based on facility operations data and not experimental design. Issues of representativeness may results in bias however there is general indication of validity of results based on test statistics. Also, the data was not controlled for gender, and type of vaccine administered.

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Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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