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Assessing the relationship between operationally defined zero-dose communities and access to selected primary healthcare services for children and pregnant women in emergency settings

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Abstract

In this study the authors examine the relationship between "zero-dose" communities and access to healthcare services. This was done by first ensuring the first dose of the Diphtheria Tetanus and Pertussis vaccine was a better measure of zero-dose communities than the measles-containing vaccine. Once ensured, it was used to examine the association with access to primary healthcare services for children and pregnant women in the Democratic Republic of Congo, Afghanistan, and Bangladesh. These services were divided into: a) unscheduled healthcare services such as birth assistance as well as seeking care and treatment for diarrheal diseases and cough/fever episodes and b) other scheduled health services such as antenatal care visits and vitamin A supplementation. Using recent Demographic Health Survey data (2014: Democratic Republic of Congo, 2015: Afghanistan, 2018: Bangladesh), data was analyzed via Chi Squared analysis or Fischer's Exact Test. If significant, a linear regression analysis was performed to examine if the association was linear. While the linear relationship observed between children who had received the first dose of the Diphtheria Tetanus and Pertussis vaccine (the reverse to zero-dose communities) and coverage of other vaccines was expected, the results of the regression analysis depicted an unexpected split in behavior. For scheduled and birth assistance health services, a linear relationship was generally observed. For unscheduled services associated with illness treatments, this was not the case. While it does not appear that the first dose of the Diphtheria Tetanus and Pertussis vaccine can be used to predict (at least in a linear manner) access to some primary (particularly illness treatment) healthcare services in emergency/ humanitarian settings, it can serve as an indirect measure of health services not associated with the treatment of childhood infections such as

each DHS Program survey is the owner of the resulting data".

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antenatal care, skilled birth assistance, and to a lesser degree even vitamin A supplementation.

Introduction

In the midst of the ongoing COVID-19 pandemic, much focus has been placed on access to vaccines, specifically for this virus, highlighting global inequities in access to healthcare and vaccination [1]. This problem unfortunately is not novel, having persisted since 1974 and extends beyond COVID-19 vaccines to even the most basic of childhood vaccination services [1]. Communities where children do not receive the suite of basic vaccinations are known as zero-dose communities and are often operationally defined as locations where children have not received the first dose of a Diphtheria, Tetanus and Pertussis vaccine (DTP1), according to GAVI [2].

Vaccination against diseases such as Measles, Polio, Tuberculosis and of course DTP is a critical and cost effective aspect of increasing health protection in early childhood, especially in Low and Middle Income (LMIC) countries where vaccination has accounted for a large decrease in deaths from infectious diseases [3, 4]. As such, studies have looked to elucidate the risk factors associated with children under five not receiving these vaccines and residing in "zero-dose" communities [5-10]. This has been done in an effort to make better informed predictions about where these zero-dose populations may exist as well as the overall size of these communities so as to better understand how vaccination coverage can be improved so that some of the most vulnerable children can be reached [5–10]. Despite the number of studies focused on the risk factors associated with zero dose communities as well as strategies to decrease the size of zero dose communities, only a few studies have focused on using zerodose communities to examine associated impacts on other factors of pediatric healthcare, especially in countries in the midst of health emergencies. The studies that have attempted to fill this gap and have focused on this relationship provided generalized information for grouped LMICs but did so without any specific focus on countries suffering from health emergency settings [11]. Galles et. al have examined the global trend in coverage of various childhood vaccines and reported on association between social demographic index (SDI) and the third dose of DTP (DTP3) noting the sigmoidal relationship between social (SDI) and coverage of DTP3 [12]. Additionally, Figueiredo et. al have examined the key factors that correlate to DTP3 coverage between 1980-2010 and 2001-2010 within Africa, the Americas, Europe, Eastern Mediterranean, South-East Asia Region and Western Pacific Region [13]. Furthermore Figueiredo et. al have noted that not only do these socioeconomic factors correlate with DTP3 vaccine coverage but there is also a link between out-of-hospital births and reduced immunization as well as some socioeconomic factors (such as income) relating to utilization of skilled birth assistance [13]. As such, taken together, these studies only transitively draw direct, regional, higher order relationships between zero-dose communities and these correlated health elements through the establishment of a relationship between DTP1 and DTP3 and then DTP3 and other health factors; these metrics all seem to correlate to each other indirectly through socioeconomic factors but no study seems to have directly look at the correlation between DTP1 and treatment for disease, birth related services or vitamin A supplementation.

While these studies provide a helpful analysis, these insights still assume there is already some degree of vaccination access available as these children examined have already received

prior doses of DTP. Additionally, as noted before, these results were based on aggregated data from various countries grouped together based on geography or economic level [11, 13]. Although zero-dose communities can exist anywhere, many exist in locations in the midst of humanitarian crisis or armed conflicts which have directly or indirectly resulted in health emergencies [14]. As such, with this analysis we aim to begin to fill this gap by directly assessing the association between vaccination and access to other healthcare services using data from nationwide surveys for countries representing emergency settings resulting from different conditions. This includes systemic civil unrest and conflict as seen in countries like Afghanistan, more sub-nationally localized civil unrest and conflict as seen in Democratic Republic of Congo (DRC) and localized, migration-based crisis such as the Rohingya crisis in Bangladesh [15, 16]. Here, we hypothesize that there is a negative correlation between zero dose communities and healthcare access and utilization. These findings may provide insight into using vaccine uptake as a predictive marker for access to both healthcare services related to pregnancy and birth related services and healthcare services related to treatment for common childhood diseases like cough/fever (indicative of possible respiratory infections) and diarrhea.

Materials and methods

Data sources and curation

Data from DRC, Afghanistan and Bangladesh was collected as part of the Demographic and Health Surveys Program which is publicly available through the program's website as the most recent complete DHS report at the time of writing [17]. Survey responses were organized into topical categories of which the Individual's Response and Child's Response categories were specifically examined. These survey responses were collected and reported out at the highest subnational level within each country.

Study design

To create a nationwide picture of childhood healthcare, we used the combination of all subnational data reports from within a country and classified this as "national" data. In a country like DRC where conflict and resulting humanitarian crisis was more localized, the specific subnational regions undergoing a humanitarian crisis (specifically Kasai-Occidental, Kasai-Oriental, Nord-Kivu and Sud-Kivu) were also separately examined and these locations were classified as "local" data.

Statistical analysis

Data was first collected and analyzed by a Chi Squared test or a Fischer's Exact Test for sample sizes less than 10 individuals using the GraphPad Prism statistical software using a two-sided test with one degree of freedom for all cases. For significant differences found via the Chi Squared test which were noted as a p value of less than 0.05, survey data was scored and reported as fraction of total individuals who fit each category. This continuous data was then graphed and analyzed in GraphPad Prism to examine the strength of any linear association between variables. Association was determined via a simple univariate linear regression using the R² value to determine the strength of association and an F-statistic (significant at a p value of less than 0.05) to determine if the slope was non-zero [18]. While we note here our assumption that R squared values of less than 0.2 are considered negligible, 0.2–0.8 weak and 0.8 to 1 as strong, these values are largely arbitrary as various cut off values have been used to demarcate strong vs weak vs negligible degrees of linear associations [19–21].

Estimating zero-dose via vaccination data

The fraction of children under five who specifically received either the measles vaccine (MCV), DTP1, the third dose of DTP (DTP3), the first dose of the Polio vaccine (Polio1), the third dose of the Polio vaccine (Polio3), or the Bacillus Calmette–Guérin vaccine (BCG), was calculated from the Child's Response Survey by tallying the number of responses where a child received the vaccine in question according to either a vaccination card (recorded as a 1 or 3) or their caregiver (recorded as a 2) as recorded in the DHS. We took this categorical data and transformed it into the fraction of coverage by dividing the total number of responses recorded at the provincial administrative level. With the few exceptions of survey responses recorded as an "unknown" or "other" (marked as an 8), this metric is effectively the complementary probability of selecting a child from a zero-dose community out of the region's population.

Linear regression analysis was performed as described in the prior paragraph twice for two different definitions of "vaccinated". For the first analysis, noted as *All Sources*, a child was considered vaccinated if any survey response indicated the child was vaccinated. For the second analysis, noted as *Card-only Sources*, a child was considered vaccinated only if the survey indicated they were vaccinated according to their vaccination card such as having the name of the vaccine received on the card and or having the date of vaccination on the card.

Scheduled health services. *Definition of scheduled health services.* Scheduled health services were defined as any type of healthcare access for services that are designed to be planned in advanced. In this study we examined two services under this category: antenatal care (a non-illness, pregnancy related service) and vitamin A supplements (a non-pregnancy, non-illness related treatment).

Antenatal care definition. Antenatal care was determined as the fraction of recorded responses where a mother had at least one antenatal care visit divided by the total number of recorded responses to the antenatal care questionnaire.

Vitamin A supplements definition. To measure the fraction receiving vitamin A supplementation, the fraction of all living children born in the last five years who received vitamin A in the form of an ampoule, a capsule or a syrup in last six months was recorded in the Children's Response document (noted as a 1). This value was divided by the total number of survey responses in the region to yield the fraction of children under five who had access to vitamin A supplementation in the last six months.

Unscheduled health services. *Definition of Unscheduled Health Services.* Unscheduled health services were defined as any type of healthcare access for services that are needed suddenly. As such, their use is unable to be planned for in advance. Three healthcare services fall under this category: birth assistance (a non-illness, pregnancy related service), access to care for diarrhea (a non-pregnancy, illness related treatment), and access to care for cough/ fever episodes (a non-pregnancy, illness related treatment).

Birth assistance definition. Birth assistance was analyzed based on *Skilled Assistance* or the fraction of mothers who responded that they were assisted by a skilled birth attendant (calculated as the fraction of mothers who received assistance during delivery from either a doctor, nurse, health worker or midwife divided by the total number of responses.

Access to care for diarrhea and cough/fever episodes definitions. Access to care for diarrhea and access to care for cough/fever episodes were measured as Access to Medical Care. This was measured based on the DHS surveys which have direct yes/no responses on if a symptomatic child received medical care which was used to determine this metric. We calculated this as the number of responses where a child received medical care divided by total number of

respondents who were symptomatic. Furthermore, these surveys also broke down the type/ location where treatment was received.

Results

After observing that DTP1 coverage was a better indicator of zero dose communities compared to MCV, a result in line with GAVI's operational definition as mentioned earlier, this metric was selected for further use. [S1–S6 Figs] Next, the relationship with access to care was determined.

Treatment for diarrhea and cough/fever

DRC. In the DRC, a Chi Squared analysis showed there was a significant association between DTP1 and medical treatment for diarrhea at the national level (p = 0.0006) and the specific local regions examined (p = 0.0008). Despite both having significant associations, there was a noticeable difference between the observed relationship with diarrhea treatment when examining the general medical treatment data from facilities and community health workers throughout the country and the relationship when observed only in the previously defined local regions in the country. In these specific subnational areas, a strong linear relationship was seen between the fraction of children under five who received DTP1 and general medical treatment for diarrhea (p = 0.0212, $R^2 = 0.96$). When examined over the whole country however, no linear relationships were observed for diarrhea treatment (p = 0.6901, $R^2 = 0.02$) indicating a split in behavior potentially due to sample size.

For an examination of cough/fever treatment, the chi squared analysis again showed a significant association at the national level (p < 0.0001) but not a significant association at the local level (p = 0.0710). In these cases, no linear relationship between cough/fever treatment and DTP1 coverage was observed in either the "local" data set or the national data set (p = 0.9857, $R^2 = 0.00$ for the national case; p = 0.9376, $R^2 = 0.00$ for the local case).

Afghanistan and Bangladesh. Trends in Afghanistan and Bangladesh, however behaved more akin to the DRC national level data. For Afghanistan, the Chi Squared analysis showed a significant association between DTP1 and medical treatment from facilities and community health workers for diarrhea (p < 0.0001) and medical treatment from facilities and community health workers for cough/fever (p < 0.0001) while for Bangladesh no significant association was seen between DTP1 and medical treatment for diarrhea (p = 0.2923) nor for cough/fever medical treatment (p = 0.3781). While there was an association for Afghanistan, further examination revealed it was not a linear association for diarrhea (Afghanistan p = 0.2360, $R^2 = 0.04$) nor for cough/ fever (Afghanistan p = 0.4708, $R^2 = 0.02$) due to low R^2 values and the slope of the relationship not being significantly different than zero. The lack of linear association for both cases in Bangladesh (diarrhea p = 0.7668, $R^2 = 0.02$ cough/fever p = 0.8648, $R^2 = 0.01$) was expected given the lack of any significant association expected via the Chi Squared results. [Fig 1]

Antenatal care

The results for antenatal care followed the same trend seen for vaccination coverage: as the fraction of children covered by the vaccine in question increased within each subnational region, the fraction of mothers who received antenatal care visits also increased. [Fig 2]

DRC. Chi Squared analysis for antenatal care showed a significant association between DTP1 and antenatal care nationally (p<0.0001) and sub nationally (p<0.0001). Additional examination into the association showed that in the DRC, an almost perfect positive linear association was observed between increasing DTP1 vaccination coverage and increasing the



Fig 1. Linear regression between DTP1 coverage and medical treatment for diarrhea and for cough/ fever. Columns show results for DRC (A, D), Afghanistan (B, E) and Bangladesh (C, F), respectively. When examined at the subnational level throughout the whole country no linear trends were observed. However, specific crisis regions within DRC did show a strong linear relationship between DTP1 and medical treatment for diarrhea.

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fraction of women who received antenatal care visits within the specific subnational regions in DRC (p = 0.0382, $R^2 = 0.93$). When examined throughout all subnational areas in the national DRC dataset, a linear trend with a slope significantly different than zero was still observed (p = 0.0009, $R^2 = 0.72$).

Afghanistan. Likewise in Afghanistan the results from the Chi Squared analysis showed a similarly significant association between DTP1 coverage and antenatal care (p < 0.0001). Despite the similar results in general association to those observed in the DRC, additional analysis for Afghanistan did not produce as strong of a linear trend comparatively, though a linear association with a non-zero slope was still observed (p < 0.0001, $R^2 = 0.49$).

Bangladesh. Lastly, antenatal care results from Bangladesh again showed a significant (albeit less so) association between DTP1 coverage and antenatal care (p = 0.0012). However, unlike both the DRC and Afghanistan data sets, while the line of best fit has an R² value of 0.34



Fig 2. Linear regression between DTP1 coverage and antenatal care in DRC (A), Afghanistan (B), and Bangladesh (C). Local data points in DRC (A) refer to subnational regions in DRC where emergency conditions are more acute, specifically Kasai-Occidental, Kasai-oriental, Nord-kivu and Sud-kivu, while the national set encompasses all subnational data points. The degree of linear association was strongest in these specific regions in the DRC compared to the country as a whole ($R^2 = 0.93$ vs. $R^2 = 0.72$). Meanwhile Afghanistan (B) and Bangladesh (C) still saw weak linear associations between DTP1 coverage and antenatal care visits ($R^2 = 0.49$, and $R^2 = 0.34$ respectively).

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Fig 3. Linear regression between DTP1 and birth assistance in DRC (A), Afghanistan (B), and Bangladesh (C). Skilled birth assistance was considered as receiving assistance from a doctor, nurse, midwife, or healthcare worker. Linear associations were observed in DRC (A), Afghanistan (B) and Bangladesh (C) for skilled birth assistance ($R^2 = 0.79$, 0.32, and 0.43 respectively).

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indicating at least a weak linear association it did not have a slope that was significantly different than zero (p = 0.1306).

Birth assistance

To further examine the potential relationship between unscheduled services and DTP1 vaccination status, birth assistance was also examined with findings similar to those for antenatal care as shown in Fig 3.

DRC. In the data from the DRC, the Chi Squared test returned a significant association at the national level between DTP1 and receiving birth assistance from a skilled medical worker (p<0.001) as well as at the local level (p<0.001).

Afghanistan. In Afghanistan Chi Squared results were analogous to those in the DRC with significant association observed between DTP1 coverage and birth assistance from a skilled medical worker (p<0.001).

Bangladesh. The association in Bangladesh between DTP1 coverage and skilled birth assistance was significant (p = 0.0141). Despite this less significant association, a linear association was still observed for birth assistance from a skilled medical provider though the slope of the line was not significantly different than zero (p = 0.0795, $R^2 = 0.43$).

Vitamin A supplementation

To see if the relationship observed between DTP1 and scheduled services held for those services beyond birth and pregnancy related ones, vitamin A supplementation was also examined with results shown in Fig 4.

DRC. In the DRC as with the prior variables examined, there was a significant association between DTP1 and Vitamin A supplementation via Chi Squared test at the national level (p <0.0001) and local level (p<0.0001). Further examination of the data and the association yielded a strong linear trend when DTP1 was used and compared against the fraction of children who received vitamin A in the last six months. This association was strongest when restricted to the specific regions where conflict was most present, producing an R² value of 0.90 with a p = 0.0464 compared to an R² of 0.80 with p = 0.0002 seen at the national level.

Afghanistan. In Afghanistan, the initial Chi Squared results also indicated a significant association between DTP1 and Vitamin A supplementation (p<0.0001) and the fraction who received Vitamin A supplements in the last six months also demonstrated the association was a weak linear association ($R^2 = 0.22$, p = 0.0046) with the fraction who received DTP1. However, unlike in DRC, the R^2 value was closer to the cutoff between no linear association and a



Fig 4. Linear association between DTP1 coverage and vitamin A supplementation in DRC (A), Afghanistan (B) and Bangladesh (C). This association was seen in the local and national data sets in DRC (A). In Afghanistan (B), the association was weaker, producing an R^2 indicating a weak association ($R^2 = 0.22$). However, the data set for Bangladesh (C) showed no linear association, appearing to be nearly perfectly separate, dissociated variables ($R^2 = 0.00$).

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weak linear association, showing the strength was much weaker in this data set and might ultimately be a more complicated relationship.

Bangladesh. Lastly, in Bangladesh, despite a significant association recorded according to the Chi Squared analysis between DTP1 and Vitamin A supplementation (p<0.0001), the association did not appear to be a linear as it produced an $R^2 = 0.00$ with p = 0.8792. In this case, the two variables were nearly perfectly linearly dissociated.

Discussion

Vaccination coverage

While DTP1 vaccine coverage showed a similar degree of associations (both generally via Chi Squared and linearly via linear regression) to childhood coverage of DTP3, MCV, BCG, Polio1 and Polio3 vaccines in DRC and Afghanistan as MCV vaccine coverage showed, more linear associations were observed in Bangladesh when DTP1 was examined instead of MCV. While this was expected given the operational definition of zero-dose communities, this confirmation combined with the operation definition led to the selection of DTP1 as the main variable for analysis in our work going forward instead of other vaccines such as MCV [2]. In this case it was expected that as DTP1 coverage increased (and therefore as Zero-dose populations decreased) the coverage of routine vaccination would also increase in all three countries. Of particular interest is the breakdown between how vaccination status was assessed, namely either based solely on a vaccine card (which has been notated as Card-only Sources) or supplemented with insight from the mother of the child in question (notated as All Sources). While vaccination card data is the standard approach for assessing if a child has actually received a specific vaccine eliminating the need for a mother to accurately recall which vaccine or which dose of a vaccine her child may have received, we found there was a stronger association and better ability to estimate vaccination coverage from DTP1 coverage if the mother's response was taken into consideration, as in all three countries examined, this All Sources metric resulted in an improved linear fit via a larger R² value. While potentially less accurate in the "actual" vaccination coverage values, this approach within each subnational region still has its benefits for planners as the All Sources metric can act as a sort of "ideal" coverage value where it can be assumed this value represents the best possible vaccination case if every mother's response and memory recall was completely accurate. As such, this provides a useful metric for what proportion of the population in the area is not actively vaccinated (the remaining population) which can help health care workers and planners better prioritize which regions

are more in need of vaccination assistance for a range of vaccines in a timely manner based simply on the coverage of one dose of a single vaccine. While this metric might not provide concrete estimates of vaccination coverage for academic or research purposes, we nonetheless believe such a metric might still be of practical use for fieldworkers on the ground.

Birth assistance

As the goal for improving healthcare access would be for women to receive assistance from a healthcare provider rather than anyone, we examined the relationship between DTP1 coverage and skilled birth assistance. Here, we found that a positive linear relationship was observed, a result largely expected due to prior observations between the correlation of DTP3 and births attended by health staff and is supported additionally by our findings that antenatal care also was linearly related to DTP1 coverage which would likely produce similar results [13]. This seems to indicate that similar types of treatment services will behave in a similar manner to each other even if they are grouped dissimilarly in terms of their more arbitrary timing/schedule classification. That said, explanations behind this relationship are partially complicated by the fact that in addition to socio-economic status and geographical factors there are also a lot of social and behavioral factors which determine whether a woman will seek skilled birth care including education level of her mother-in-law and any "taboos" around birth and pregnancy common in the area as stated in a conversation by V. Buj, MPH [April 2022]. Thus, based on the observations made on this data set, utilization of skilled birth assistance within a subnational region of a country would be able to be estimated by knowing the population size of zero-dose children who reside in this portion of the country.

Unscheduled services vs. scheduled services

With the selection of our metric for a zero-dose community analogue variable determined and confirmed to match prior approaches and the operational definition, we began to examine if there was any relationship between DTP1 coverage and utilization/ access to scheduled ad unscheduled health care services. With this distinction in place, a split in behavior was generally able to be observed between how zero-dose communities relate to access to care for other services. Based on the data sets used in this analysis and the geographical resolution provided, we noticed that while there was an observed linear relationship when scheduled treatment services were examined, the trend was not as clear for unscheduled services. While at least a weak linear relationship was observed for Vitamin A supplementation in two of the three countries examined (notably those that are experiencing a crisis with armed conflict as a key component as opposed to a migration-based crisis as is the case in Bangladesh), the R^2 value was generally lower, indicating that the association was not as prevalent compared to the birth and pregnancy related services observed. That said, in all three countries, there always was a significant association between DTP1 coverage and scheduled services even if the association was not always linear such as with Vitamin A supplementation. This seemed to indicate that not only do zero-dose communities have a different relationship between scheduled and unscheduled services, but these relationships are even more nuanced allowing the linear association to appear more strongly (or even at all) for pregnancy related services compared to other types of services. This was irrespective of a service's classification as a scheduled or unscheduled service. In the conflict regions examined, this contrast was even more stark. We note here though the focus of this manuscript was not to compare the underlying sources of these emergencies nor to compare access to care in emergency settings vs. access to care in non-emergency settings though such result might be useful for further investigation. Overall, for healthcare planners, this means that by knowing the proportion of children in zero-dose communities within a subnational region of a

country, estimates can be made for the degree of access to or utilization of these scheduled services (and birth assistance), with an increasingly more accurate prediction made for antenatal care and skilled birth assistance compared to other services, especially in countries where the crisis is largely conflict driven and more systemic. Furthermore, based on this analysis, it appears that even if the exact size of the zero-dose population is unknown for certain locations, healthcare planners can still work to determine which areas are most in need of assistance in increasing the access to care for scheduled services by determining which locations are likely to have the greatest zero-dose population. This relative, priority order type approach can provide quick insight into the ground situation even in locations where data may be more limited, similar to the "ideal" vaccination approach mentioned earlier in the discussion section. This approach would, however, be insufficient for unscheduled services related to illness treatment due to the lack of observed linearity between zero-dose communities and access to these types of care services based on the data used for this analysis which included both facility and community-based health workers. We note that while a linear relationship was not seen between zero dose communities and services related to illness treatment, for the three samples that did result in significant association by Chi Squared analysis (but not linear regression) this could mean that the relationship at this level is more complicated than a linear relationship or simply that such a linear relationship may only be observable at a more local level. As such, future work can further search for a relationship between zero-dose communities (and by proxy vaccination status) and access to illness treatment healthcare services, especially at an even more local, perhaps district, level.

Limitations

We note that this analysis does have limitations. One such limitation is the DRC specific data. As some of the emergency conditions are more localized to a few specific subregions in the country (the local dataset) the regression analysis on this portion of the data only had four data points. This means each point contributes more heavily to the line of best fit, making it more susceptible to the impact from any outliers. Furthermore, such a small sample set here means that linear relationships (and any statistical findings) could be observed by chance. To help counter these limitations, analysis was done not only within these few specified local regions but also across all areas of the country at this same government level as a means of comparing this smaller sample size against a more statistically robust data set. In many cases the trends seen in the local data set are similar to the national level, but in a few cases (such as the treatment for diarrhea) there is a difference between these two data sets with the local set resulting in an \mathbb{R}^2 that is ~50 times larger, most likely indicating that this behavior is due to the small sample size.

Likewise, we note that in this analysis, even the most statistically robust data set (Afghanistan) had only about 20 data points for the linear analysis. While the data sets could be pooled together to create a supranational data set to increase statistical power, we believe this approach would have added additional complications and limitations. One such example is that since the data was collected within each country separately, combining these data points could possibly result in the addition of country-country confounding factors as well as temporal confounding factors given that although each survey was the most recent version, they were each performed over different timeframes. Thus, we opted to keep each country separate and use all the information provided at this level to make the findings as robust as possible despite the ultimately smaller size.

An additional data-based limitation presents itself during the analysis of illness based treatment services, specifically with regards to treatment of cough/fever. We note that conjoining cough and fever may result in a flawed analysis since "fever" is usually the first symptom for seeking care, especially in the DRC where malaria is such a high burden. In these locations with a large number of malaria cases, cough would be a secondary symptom, which in addition to rapid diagnostic tests would help distinguish between upper respiratory infections and malaria. This cough/fever metric was used as while the DHS data set had information on fever episodes, there was no information specifically regarding treatment for fever or treatment for cough; treatment data was only recorded as "treatment for cough/fever". Based on the region and overlap with Malaria, and the lack of a respiratory infection section, this most likely is done specifically to filter out treatment for Malaria and focus just on potential respiratory infections. Despite this assumption, in an effort to be more direct and clearer in our analysis the name was left unchanged from the titles in the DHS data sets.

Furthermore, while we initial perform a Chi Squared analysis to determine if there is any association between the variables we examined, we note that if there is an association this analysis only looks to see if that association is a simple linear relationship between the variables described. Thus, while linear predictions might not be possible due to a lack of a linear association, that does not necessarily mean that such an analysis using a different regression approach would result in a lack of association; a different relationship may exist that relates the dependent and independent variables examined in this report, which is what would be expected for the comparisons that saw an association via Chi Squared but not linear regression.

Conclusion

In this analysis, we examined the relationship between zero dose communities in healthcare emergency settings and access to healthcare services. To this end, we have observed at the subnational level that DTP1 vaccination status was a good indicator for zero-dose communities and resulted in a stronger set of linear relationships compared to MCV for the prediction of coverage for other vaccines. Furthermore, we noticed a split in behaviors depending on the type of services examined, a distinction we have previously not seen in the literature on this topic. DTP1 coverage saw no linear relationship with unscheduled, illness related treatment services and thus could not be used to make predictions on this facet of health, however linear relationships were observed when examining all scheduled health services as well as birth assistance, a non-illness unscheduled treatment service. Thus, in health emergency/ humanitarian settings, DTP1 coverage is the best proxy for labeling a community as zero-dose and is linearly associated with access and utilization of antennal care, skilled birth assistance, and to a lesser degree vitamin A supplementation. As such DTP1 coverage can be used as an indirect measure of these metrics, even though this was not the case for the treatment for childhood diseases such as diarrhea and cough/fever which saw no linear association with DTP1 coverage.

Supporting information

S1 Fig. Univariate linear regression between DTP1 vaccination coverage and coverage for other common vaccines in DRC. Column A shows how the inclusion of caregivers' responses improve the linear fit compared to the relationships in column B which only considered a child vaccinated if their vaccination card contained the appropriate vaccine information. In this case, a difference was observed between the strength of the relationship observed in regions with conflict compared to the entire country. (TIF)

S2 Fig. Linear regression between MCV vaccination coverage and coverage for other common vaccines in DRC. Column A shows how the inclusion of mothers' responses improve the linear fit compared to the relationships in column B which only considered a child vaccinated if their vaccination card contained the appropriate vaccine information. In this case, a difference was observed between the strength of the relationship observed in regions with conflict compared to the entire country.

(TIF)

S3 Fig. Univariate linear regression between DTP1 coverage and coverage for other common vaccines in Afghanistan. Column A shows how the inclusion of mothers' responses improve the linear fit compared to the relationships in column B which only considered a child vaccinated if their vaccination card contained the appropriate vaccine information. This trend was not observed for either dose of the Polio vaccine, though the strengths of the fit were similar for both metrics used.



S4 Fig. Univariate linear regression between MCV vaccination coverage and coverage for other common vaccines in Afghanistan. Column A shows how the inclusion of mothers' responses improve the linear fit compared to the relationships in column B which only considered a child vaccinated if their vaccination card contained the appropriate vaccine information. Unlike for DTP1 This trend did not breakdown for either Polio vaccine dose. (TIF)

S5 Fig. Univariate linear regression between DTP1 coverage and coverage for other common vaccines in Bangladesh. Column A shows how the inclusion of mothers' responses improve the linear fit compared to the relationships in column B which only viewed a child as vaccinated if their vaccination card contained the appropriate information. This trend was especially apparent for DTP3, MCV, and Polio3 as the *card only* metric led to no linear relationship being observed, while the *all sources* data saw linear relationships for all cases. (TIF)

S6 Fig. Univariate linear regression between MCV vaccination coverage and coverage for other common vaccines in Bangladesh. Column A shows how the inclusion of mothers' responses improved the linear fit compared to the relationships in column B which only viewed a child as vaccinated if their vaccination card contained the appropriate information. This trend was especially apparent for DTP1, Polio1 and Polio3 as the card only metric led to no linear relationship being observed, while the *all sources* data saw linear associations for all of these vaccines.

(TIF)

S1 Text. Additional insight into the results of the supplemental figures. The accompanying supplemental contains additional statistical information for S1-S6 Figs. This is done to present the results of these supplemental figures with a degree of detail similar to the result section of the main manuscript.

(DOCX)

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References

- Ning C, Wang H, Wu J, Chen Q, Pei H, Gao H. The COVID-19 Vaccination and Vaccine Inequity Worldwide: An Empirical Study Based on Global Data. Int J Environ Res Public Health. 2022; 19(9). https:// doi.org/10.3390/ijerph19095267 PMID: 35564661
- Gavi. Zero-Dose Analysis Card [Internet]. 2019. https://lnct.global/wp-content/uploads/2021/08/Gavi_ Zero-dose_AnalysisCard.pdf.
- 3. Li X, Mukandavire C, Cucunubá ZM, Echeverria Londono S, Abbas K, Clapham HE, et al. Articles Estimating the health impact of vaccination against ten pathogens in 98 low-income and middle-income countries from 2000 to 2030: a modelling study. www.thelancet.com [Internet]. 2021 [cited 2022 Dec 1];397.
- Lee LA, Franzel L, Atwell J, Datta SD, Friberg IK, Goldie SJ, et al. The estimated mortality impact of vaccinations forecast to be administered during 2011–2020 in 73 countries supported by the gavi alliance. Vaccine. 2013 Apr 18; 31(SUPPL2). https://doi.org/10.1016/j.vaccine.2012.11.035 PMID: 23598494
- 5. Greenwood B. The contribution of vaccination to global health: Past, present and future. Philos Trans R Soc B Biol Sci. 2014; 369(1645). https://doi.org/10.1098/rstb.2013.0433 PMID: 24821919
- 6. GAVI. Data for Zero-dose: what was done? What did we learn? What next? 2021.
- Johri M, Rajpal S, Subramanian SV. Progress in reaching unvaccinated (zero-dose) children in India, 1992–2016: a multilevel, geospatial analysis of repeated cross-sectional surveys. Lancet Glob Heal [Internet]. 2021 Dec 1 [cited 2022 Mar 18]; 9(12):e1697–706. Available from: www.thelancet.com/ lancetgh PMID: 34798029
- Deshpande A, Miller-Petrie MK, Lindstedt PA, Baumann MM, Johnson KB, Blacker BF, et al. Mapping geographical inequalities in access to drinking water and sanitation facilities in low-income and middleincome countries, 2000–17. Lancet Glob Heal. 2020; 8(9):e1162–85. https://doi.org/10.1016/S2214-109X(20)30278-3 PMID: 32827479
- Arambepola R, Yang Y, Hutchinson K, Mwansa FD, Doherty JA, Bwalya F, et al. Using geospatial models to map zero-dose children: Factors associated with zero-dose vaccination status before and after a mass measles and rubella vaccination campaign in Southern province, Zambia. BMJ Glob Heal. 2021 Dec 30; 6(12).
- Wahl B, Gupta M, Erchick DJ, Patenaude BN, Holroyd TA, Sauer M, et al. Change in full immunization inequalities in Indian children 12–23 months: an analysis of household survey data. <u>https://doi.org/10. 1186/s12889-021-10849-y</u>.
- Santos TM, Cata-Preta BO, Mengistu T, Victora CG, Hogan DR, Barros AJD. Assessing the overlap between immunisation and other essential health interventions in 92 low- and middle-income countries using household surveys: opportunities for expanding immunisation and primary health care. eClinical-Medicine [Internet]. 2021 Dec 1 [cited 2022 Mar 18]; 42:101196. Available from: http:// creativecommons.org/licenses/by/4.0/ PMID: 34805814
- Galles NC, Liu PY, Updike RL, Fullman N, Nguyen J, Rolfe S, et al. Measuring routine childhood vaccination coverage in 204 countries and territories, 1980–2019: a systematic analysis for the Global Burden of Disease Study 2020, Release 1. Lancet. 2021; 398(10299):503–21. https://doi.org/10.1016/ S0140-6736(21)00984-3 PMID: 34273291
- de Figueiredo A Johnston IG, Smith DMD, Agarwal S, Larson HJ, Jones NS. Forecasted trends in vaccination coverage and correlations with socioeconomic factors: a global time-series analysis over 30 years. Lancet Glob Heal [Internet]. 2016 Oct 1 [cited 2021 Sep 9]; 4(10):e726–35. Available from: http:// www.thelancet.com/article/S2214109X1630167X/fulltext.
- UNICEF and WHO. Progress and Challenges with Achieving Universal Immunization Coverage, UNI-CEF and the World Health Organization, July 2020. [Internet]. 2019. https://www.who.int/immunization/ monitoring_surveillance/who-immuniz.pdf.
- Council on Foreign Relations. The U.S. War in Afghanistan [Internet]. [cited 2021 Nov 18]. <u>https://www.cfr.org/timeline/us-war-afghanistan</u>.

- 16. United Nations Office for the Coordination of Humanitarian Affairs. Rohingya Refugee Crisis | OCHA [Internet]. [cited 2021 Nov 18]. https://www.unocha.org/rohingya-refugee-crisis.
- The DHS Program—login_main [Internet]. [cited 2021 Sep 9]. https://dhsprogram.com/data/dataset_ admin/login_main.cfm?CFID=28539468&CFTOKEN=f150420d72cebd9c-1577BB01-F01A-0CAE-BED1E8C2D336A42A.
- Schneider A, Hommel G, Blettner M. Linear Regression Analysis. Dtsch Arztebl. 2010; 107(44):776– 82.
- Akoglu H. User's guide to correlation coefficients. Turkish J Emerg Med. 2018; 18(3):91–3. <u>https://doi.org/10.1016/j.tjem.2018.08.001</u> PMID: 30191186
- Schober P, Schwarte LA. Correlation coefficients: Appropriate use and interpretation. Anesth Analg. 2018; 126(5):1763–8. https://doi.org/10.1213/ANE.00000000002864 PMID: 29481436
- 21. Jost S. Linear Correlation [Internet]. [cited 2021 Nov 24]. https://condor.depaul.edu/sjost/it223/ documents/correlation.htm.