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Nepal measles outbreak response immunization during COVID-19: A risk-based intervention strategy

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ABSTRACT

In 2020, National Immunization Programme (NIP) of Nepal implemented a measles outbreak response immunization (ORI) campaign, which was additional to an ongoing preventive measles-rubella SIA campaign. Both campaigns were implemented during ongoing COVID-19 transmission. By April, 220 measles cases and two deaths were confirmed from eight districts of Nepal. The NIP triangulated information from surveillance (measles and COVID-19), measles immunization performance and immunity profile, programme capacities and community engagement and applied a logical decision-making framework to the collated data to inform ‘Go/No-Go’ decisions for ORI interventions. This was reviewed by the National Immunization Advisory Committee (NIAC) for endorsement. Outbreak response with non-selective immunization (ORI), vitamin-A administration and case management were implemented in affected municipalities of four districts, while in the remaining districts outbreak response without ORI were undertaken. The structure and iterative application of this logical framework has been described. ORI was implemented without interrupting the ongoing measles-rubella vaccination campaign which had targeted children from 9 to 59 months of age. The age group for ORI was same as SIA in one sub-district area, while for the other three sub-district areas it was from 6 months to 15 years of age. More than 32,000 persons (97% coverage) were vaccinated in ORI response. Overall measles incidence decreased by 98% after ORI. The daily incidence rate of measles was 94 times higher (95% confidence interval: 36.11 – 347.62) before the ORI compared to two weeks after ORI until year end. Close attention to surveillance and other data to inform actions and seamless collaboration between NIP and core immunization partners (WHO, UNICEF), with guidance from NIAC were key elements in successful implementation. This was an example of feasible application of the global framework for implementation of a mass vaccination campaign during COVID-19 through application of a simple decision-making logical framework.

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1. Introduction

Measles is a highly infectious and lethal disease caused by paramyxovirus and usually transmitted through aerosolized respiratory droplets. In 2019, the World Health Organization (WHO) estimated that there were 9.8 million cases and 0.2 million deaths from measles globally [1]. The reported number of cases was highest since 1996, largely driven by major outbreaks in several countries. Strengthening capacities for outbreak response is a strategic priority of the Measles and rubella strategic framework 2021–2030 [2].

In Nepal, substantial progress has been made towards measles elimination. Confirmed measles case occurrence has reduced by 98% between 2003 and 2017 [3]. Confirmed rubella cases had decreased by 97% between 2008 and 2017 which was certified by the WHO Regional Verification Commission [4] However, from 2018 to 2019 confirmed measles cases had increased by 66% (260 to 431). The National Immunization Programme (NIP) of Nepal had planned to conduct a nationwide campaign with measles rubella (MR) vaccine in late 2019, but owing to some operational considerations, MR campaign was shifted to first half of 2020.

The MR campaign had planned to vaccinate 9–59-month-old children in two one-month phases, in February-March and March-April 2020. NIP completed the first phase as scheduled. However, the second phase was extended because of the COVID-19 situation in Nepal.

The first and second COVID-19 cases in Nepal were reported on 23 January and 23 March 2020 respectively. From 23 March till 7 September 2020, 46,257 confirmed cases of COVID-19 with 289 deaths were reported in Nepal [5]. Government of Nepal (GoN) declared a national lockdown starting 24 March 2020 [6]. The sudden declaration of lockdown also impacted on delivery of all routine health services and the MR campaign. The second phase of MR campaign was thus delayed by more than a month and was finally completed by 7 July 2020.

In the first quarter of 2020, the vaccine preventable disease (VPD) surveillance programme in Nepal observed an increasing incidence of measles cases in age groups above five years. At this time, the MR-SIA was interrupted due to nationwide lock-down, while measles outbreaks were occurring in and spreading across several districts. The National Immunization Programme (NIP) continually reviewed surveillance data for measles as well as COVID-19 cases, assessed magnitude of measles outbreak cases, deaths and other epidemiological parameters as described below, and took informed decisions on outbreak-by-outbreak basis to implement outbreak response immunization (ORI) after assessing risk of measles morbidity and mortality vis-a-vis risk of COVID-19 occurrence in the outbreak affected areas.

This report documents the epidemiologic rationale, application of existing policy guidelines, programmatic decision-making processes, and how a simple logical framework was adapted to inform decisions for risk-based ORI. We also describe how the National Immunization Advisory Group (NIAC) which functions as the National Immunization Technical Advisory Group (NITAG) for Nepal provided technical advice and recommendations to guide the NIP.

2. Methods

The case-based measles surveillance system in Nepal investigates and confirms (through serology) every suspected measles case in the country. WHO-Nepal’s Immunization Preventable Disease (WHO-IPD) programme provides technical assistance to the Family Welfare Division (FWD) and to public health laboratories for VPD surveillance. A dedicated team of WHO surveillance medical officers, coordinates with a nationwide reporting network of nearly 1500 health facilities and clinics in public and private sectors for VPD surveillance case reporting and investigation. WHO-Nepal also provided technical assistance during the pandemic for COVID-19 surveillance and response.

**Confirmation of suspected cases and outbreaks:** A suspected measles case was a person of any age with fever and maculopapular (non-vesicular) rash or a person in whom a health care worker suspects measles [7]. Occurrence of five or more suspected measles cases from a municipal ward or contiguous wards of the same or adjoining municipalities (rural or urban) as a rolling total over a period of any four consecutive weeks was the operational definition for a suspected measles outbreak [8].

**Confirmation of suspected cases and outbreaks:** The VPD surveillance programme tests blood samples from every sporadic suspected case and from five to ten cases from each suspected outbreak. WHO accredited (National Public Health laboratory, (NPHL) Kathmandu) and proficient (BP Koirala Institute of Health Sciences (BPKIHS), Dharan) laboratories conduct laboratory tests for Immunoglobulin-M (IgM) antibodies for confirmation of measles, and for rubella IgM antibodies if negative for measles [9].

A suspected case was confirmed (measles or rubella) based on IgM serology result. Please see supplementary information for further details on laboratory procedures followed.

A suspected outbreak was confirmed when at least two suspected cases from an outbreak tested IgM positive for either measles or rubella. Cases from a suspected outbreak from whom no samples were collected were confirmed through epidemiological linkage with other laboratory confirmed or epidemiologically confirmed cases.

Sporadic cases from whom no samples were collected, were confirmed as clinically compatible based on presenting symptoms and signs (along with fever and rash, and either cough, coryza or conjunctivitis at onset for a case to be measles compatible). As per case classification algorithm, a confirmed case in this report is defined as a suspected case that was either laboratory confirmed, or epidemiologically confirmed (i.e. epidemiologically linked) or was clinically compatible.

**A measles death** was defined as a death occurring within 30 days of onset of rash in a confirmed measles case, which was not due to another unrelated cause like trauma etc.

**Outbreak closure and outbreak duration:** As per national surveillance guidelines a suspected measles outbreak was declared closed when at least 21 days had passed without occurrence of any suspected measles cases after onset of rash of the last case [10]. However, in practice public health workers, would follow up until 30 days from onset of last case to ascertain any measles related deaths as well as to validate absence of fresh cases for closure of the outbreak. The duration of an outbreak was the difference between the dates of onset of the first and last detected cases.

**Measles-rubella immunization campaign:** In 2020, a nationwide SIA campaign was planned for all 77 districts with MR vaccine with add-on bivalent oral polio vaccine (bOPV) in 19 districts in two phases. Phase – I was conducted from 13 February to 13 March in provinces 1, 2 and 5 (now renamed Lumbini province). Phase-2 was started on 14 March in the remaining provinces (Bagmati, Gandaki, Karnali and Sudurpaschim) with a plan for completing the activity within a month. It was interrupted from 24 March due to national lockdown because of COVID-19, resumed in May and finally completed by 7 July 2020. The target age-group for the MR-SIA campaign was 9–59-month-old children and for bOPV it was 0–59-month-old children irrespective of their past MR or OPV vaccination status.

**Measles outbreak response mechanisms and decision framework:** WHO-Nepal IPD programme collects and continuously
reviews measles surveillance information (case and lab results) and shares updates with the NIP and Family Welfare Division (FWD) and immunization partners (WHO and UNICEF) and the National immunization Advisory Committee (NIAC).

The Department of Health Services has formulated programme guidelines for responding to measles outbreaks including through ORI [11]. The guidelines have provisions for non-selective ORI for target age groups from six or nine months of age to five, ten or fifteen years of age. However, these guidelines were drawn up in 2019 before the COVID-19 pandemic and thus did not include an explicit logical framework for examining competing risks from another disease or hazard to inform decisions to conduct ORI.

Application of decision framework: To inform the decision to undertake (or withhold or defer) an outbreak response immunization (ORI) the NIP used the following dimensions – programme mandate for ORI, direct risk of measles transmission, competing or indirect risk of COVID-19 transmission, community demand and ownership of ORI, operational feasibility including availability of vaccine supplies and other logistics and local programme capacity for implementing ORI. Under each dimension, the NIP collected quantitative and qualitative information and intelligence as detailed below to help inform the final decision for action.

1. Programme mandate for ORI: Existing mandate and any set procedures for the national immunization programme to undertake ORI.
2. Direct epidemiological risk of measles transmission: Number of measles cases and deaths, risk or evidence of contiguous spread between wards, municipalities, and districts, age group affected (within and beyond SIA target age group) and immunity gap. Disproportionate burden of disease in one or more specific underserved communities.
3. Competing epidemiological risks of COVID-19 transmission: COVID-19 cases, deaths and extent of geographical spread.
4. Community demand and ownership of ORI: Staff from NIP and development partners discussed with local elected representatives and leaders, health facility staff including Female Community Health Volunteer (FCHV), as well as with community members to gauge community demand and acceptance for ORI.
5. Operational feasibility for ORI: This included assessing availability of vaccine supplies and other logistics from central level.
6. Local programme capacity for ORI: Capacity of the local programme functionaries to implement measles ORI safely and effectively was assessed. This assessment also included operational feasibility like availability of trained human resources, vaccine, ancillary equipment including personal protective equipment and waste management.

The sequential list above is for descriptive purposes only. The process was undertaken by updating available data and analyses through multiple iterations. On 30 April 2020, NIP along with partners, WHO and UNICEF presented all collated information to the NIAC including a competing risk analysis for each outbreak or cluster of outbreaks and sought its concurrence on actions undertaken and recommendations and guidance for future response.

Statistical methods: Surveillance data were extracted from the web-based surveillance database module developed by WHO-IPD and used by NIP. Immunization coverage data was extracted from reports available with NIP. Descriptive statistical measures (per cent age distribution and vaccination status, spatial distribution maps for cases, per cent coverage etc.) were used to describe the epidemiology of the outbreaks.

Daily incidence rate (DIR) of confirmed measles cases per million persons was computed for a district as below:

\[ \text{No. of confirmed measles cases in district in time period} \times \frac{1,000,000}{\text{Population of district}} \times \frac{\text{No. of days in time period}}{365} \]

Confirmed measles cases were partitioned into three mutually exclusive time periods as per dates of rash onset. Period A was from 1 January 2020 to end date of ORI for the district. The buffer period was from end date of ORI to 14 days after ORI for that district. Period B was from end date of buffer period for a district to 31 December 2020.

The DIR of measles were compared between two time-periods A and B by computing DIR ratios for each district and overall, by dividing DIR in period A by DIR in period B. Cases occurring during the buffer period were excluded as we assumed it would take at least 14 days from the time of vaccination to develop immunity. Similar exclusion of cases during buffer periods of two or three weeks have been reported by other authors [12,13].

DIR ratios between the two time periods were tested for statistical significance at 95% level. The statistical software package, Stata version 15.0 was used for statistical tests for computing incidence rate ratio and 95% confidence interval for hypotheses testing for impact of ORI on risk of measles.

Consent and ethical clearance: Measles surveillance is part of the national surveillance programme for diseases of public health importance. Being part of a national programme, explicit individual consent is not sought for investigation and blood sample collection, but individual and/or community participation is coordinated by local public health authorities. Participation in the surveillance programme is entirely voluntary. All data collected are stored securely and individual identifiers are not shared publicly. Laboratory results are usually communicated back to individuals (for sporadic cases) and to the community (for outbreaks) through local public health teams.

3. Results

Between 1 January and 29 April 2020, VPD surveillance programme notified 11 laboratory confirmed measles outbreaks in eight districts of Nepal including the largest number of cases from a cluster of four outbreaks in Dhading district (Table 1 and Fig. 1). Two measles deaths occurred in the Dhading cluster. No measles deaths were reported from any of the other outbreaks.

Initial analysis showed that as many as 78% (172/220) of the confirmed measles cases were beyond the age group targeted through the MR SIA campaign. Of these, 60% (104/172) were in the 5–14-year-old age group, in which only about 10% of cases gave a history of vaccination with measles containing vaccine.

Timeline and spread of Dhading outbreak cluster: The Dhading district outbreak cluster (138 cases) had the earliest onset of cases in February and continued for the longest period of 72 days. The first two clusters of cases were detected on 4 February 2020 and 29 February 2020 from two wards of Benighat-Rorang rural municipality in the district, spreading quickly to other wards of the rural municipality. In addition, there were few cases in neighbouring municipalities (Palika) too.

Analyses of case-based surveillance data revealed that some underserved communities were being disproportionately affected with 95% (131/138) of cases from underserved ethnic groups. In April, the outbreak spread beyond Dhading to contiguous municipalities in Gorkha and Chitwan districts and all the outbreak related cases were from the same underserved groups in these districts (Table 1).

A separate measles outbreak occurred in Kathmandu district amongst workers and their family members in a carpet factory of Kageshwori-Manahara Municipality, from 03 to 20 April 2020. This outbreak confirmed 14 measles cases mainly affecting workers
In four other outbreak affected districts during this time, the outbreaks were either of very short duration (Lalitpur – four days), or of small size (Morang and Sarlahi – eight and seven cases). In Jhapa (22 cases) the outbreak continued for 60 days. However, no other alarm signals (deaths, underserved community etc.) were observed.

Based on this initial rolling review of surveillance data, the NIP determined that the ongoing MR SIA intervention will not impact on the outbreak transmission as a large proportion of the cases (range 60% to 91% between outbreak affected districts) were from an underserved community (86%) and majority (76%) of cases were above five years of age.

Table 1: Confirmed measles outbreaks from 1 January to 29 April 2020 by district and cases by age group affected with vaccination status.

| District       | No. of outbreak Cases* | Outbreak period in 2020 | Outbreak Duration (days) | Number (%) of cases from underserved community | <9 months | 9 month - <5 years | 5 - <15 years | >=15 years |
|----------------|------------------------|-------------------------|--------------------------|-----------------------------------------------|-----------|-------------------|--------------|-----------|
|                |                        |                         |                          |                                               | No. of cases | Proportion of cases vaccinated | No. of cases | Proportion of cases vaccinated |
| DHADING        | 138                    | 04-Feb to 16-April      | 72                       | 131 (95%)                                     | 9          | 35                | 66%          | 77        | 6%          | 17          |
| CHITWAN        | 8                      | 15 to 24 April          | 9                        | 8 (100%)                                      | 1          | 2                 | 0%           | 3         | 33%         | 2           |
| GORKHA         | 5                      | 23 to 28 April          | 5                        | 5 (100%)                                      | 1          | 2                 | 50%          | 1         | 0%          | 1           |
| KATHMANDU      | 14                     | 03 to 20 April          | 17                       | 12 (86%)                                      | 1          | 2                 | 50%          | 2         | 0%          | 9           |
| LAITPUR        | 18                     | 15 to 19 March          | 4                        | 0                                             | 0          | 3                 | 0%           | 7         | 0%          | 8           |
| JHAPA          | 22                     | 24 Feb to 24 March      | 60                       | 0                                             | 2          | 2                 | 50%          | 10        | 40%         | 8           |
| MORANG         | 8                      | 15 to 27 April          | 12                       | 0                                             | 0          | 1                 | 0%           | 0         | –           | 7           |
| SARLAHI        | 7                      | 25 Feb to 16 March      | 20                       | 0                                             | 1          | 1                 | 0%           | 4         | 0%          | 1           |
| Grand Total    | 220                    | –                       | –                        | 156 (71%)                                     | 15         | 48                | 54%          | 104       | 10%         | 53          |

* Two measles deaths were reported from the Dhading outbreak cluster. No other deaths were reported.

**: No cases were vaccinated in this age group as the age group was below eligible age for MR vaccination in routine immunization schedule.

@: No vaccination or unknown vaccination status for all cases.

Fig. 1. Map of Nepal showing confirmed measles outbreak and COVID-19 cases between 1 January and 30 April 2020.
side the age groups targeted through the SIA. (Table 2) Moreover, the second phase of SIA campaign was interrupted from 23 March 2020 in Bagmati and Gandaki provinces (including Dhading, Chitwan, Kathmandu, Lalitpur, and Gorkha districts) because of the national lockdown declared to tackle COVID-19.

NIP considered implementing an outbreak response immunization (ORI) at the local level with measles containing vaccine (MCV). At the same time NIP was also closely coordinating with COVID-19 surveillance system and observed increasing incidence of COVID-19 cases in Nepal. NIP inferred that any ORI intervention had to be balanced against the competing risks of measles as well as COVID-19 infection and spread.

NIP consulted with core VPD surveillance and immunization partners (WHO and UNICEF) to develop a set of parameters incorporated in a multi-dimensional logic framework to help inform decisions regarding need, feasibility, time and extent of implementing an ORI response. With the help of partners, NIP captured the relevant information in the logic frame (Table 2). The information was populated in the logical framework through multiple iterations involving several formal and semi-formal discussion sessions. NIP considered implementing an ORI in Dhading (Benighat-Rorang municipality) as this was the largest outbreak cluster with two deaths and there was an urgency to intervene. Further the risk of triggering COVID-19 transmission because of MR-ORI was considered low as Bagmati and Gandaki provinces were in sporadic stage of COVID-19 transmission at that time with little active transmission of COVID-19 as the most recent cases had occurred at least two weeks earlier.

There were also demands from other outbreak affected districts like Kathmandu and Jhapa for an ORI. NIP decided to seek advice from NIAO on a logical framework for Go/No-go decisions for measles ORI in COVID-19 context. All available information was placed before the National Immunization Advisory Committee in its meeting on 30 April 2020.

To facilitate structured progression to an informed decision, the logical framework considered the following dimensions – (1) programme mandate, (2) direct epidemiological risk, (3) competing epidemiological risk, (4) community demand and ownership, (5) operational feasibility including logistics at central level and (6) local programme capacity. The evaluation of these criteria except the first and fifth criteria are captured in Table 2. The criteria of programme mandate and availability of logistics were evaluated and applied uniformly from the central level and thus have not been captured in the matrix used for district specific Go/No-go decisions as described below.

1. Programme mandate (not captured in matrix): ORI guidelines were already endorsed by Ministry of Health and Population (MOHP) in 2019. Hence NIP had a clear mandate to conduct ORI as per need. However, the uppermost age limit prescribed in the guidelines was up to the age of 15 years.

2. Direct epidemiological risk of measles: The VPD surveillance programme supported by WHO-IPD provided core epidemiological data on incidence of measles cases and deaths, risk or evidence of contiguous spread between wards, municipalities, and districts, age group affected (within and beyond SIA target age group) and vaccination status with at least one dose of measles containing vaccine. The programme also captured the proportional burden of disease in one or more specific under-served communities.

3. Competing epidemiological risks of COVID-19: This VPD surveillance programme collated the data on COVID-19 cases, type of transmission and occurrence of last case in province from COVID-19 surveillance into the matrix. At the time of eval-

### Table 2

Logical framework decision matrix on selected criteria for ORI response for measles outbreaks – observation period – 1 January to 29 April 2020.

| Province, District | Direct risk (measles) | Indirect risk (COVID-19) | Community demand | Local capacity | Decision for ORI |
|--------------------|-----------------------|--------------------------|------------------|---------------|------------------|
|                     | Sporadic measles cases| Outbreak cases from under-served community | Outbreak affected Palika | Risk or evidence of contiguous spread of measles? | Outbreak cases outside MR SIA target age group (%) | Cases (outbreak & sporadic) outside MR SIA target age group (%) |ORI COVID-19 cases in Province (date of last case in 2020) |
|                    | 4 | 138 | 131 | Benighat Rorang RM § ** | Yes | 103 (75%) | 114 (74%) | 7 (15 Apr) | Yes | Yes | Yes |
| Bagmati, Dhading   | 9 | 8 | 8 | Rapti RM § | Yes | 6 (75%) | 11 (65%) | 7 (15 Apr) | Yes | Yes | Yes |
| Bagmati, Chitwan   | 2 | 5 | 5 | Gandaki RM | Yes | 3 (60%) | 3 (51%) | 7 (15 Apr) | Yes | Yes | Yes |
| Gandaki, Gorkha    | 23 | 14 | 12 | Kageshwoori Mahahara UM | Yes | 12 (86%) | 31 (74%) | 7 (15 Apr) | Yes | Yes | Yes |
| Bagmati, Kathmandu | 19 | 18 | 0 | Lalitpur MA | No | 15 (83%) | 39 (78%) | 7 (15 Apr) | No | Yes | No |
| Bagmati, Lalitpur  | 10 | 22 | 0 | Damak UM | No | 20 (91%) | 28 (88%) | 31 (26 Apr) | Yes | Yes | No |
| Province-1, Jhapa  | 19 | 8 | 0 | Urlabari UM | No | 7 (83%) | 31 (78%) | 31 (26 Apr) | No | Yes | No |
| Province-1, Morang | 3 | 7 | 0 | Bagmati UM | No | 6 (86%) | 9 (90%) | 12 (29 Apr) | No | Yes | No |
| Province-2, Sarlahi|                    |                         |                  |                |                         |                          |                          |                          |                |               |             |

§: RM/UM/MA = Rural Municipality/Urban Municipality / Metropolitan Area; ** Four outbreaks were detected in sequence from wards numbers 6, 1, 4 and 2 of Benighat-Rorang rural municipality of Dhading district. The first outbreak onset was from 4 February 2020 till 16 April 2020 and fourth outbreak was from 29 February 2020 till 12 May 2020. 1 case was detected from Dhunibesi UM.

#: At that time, COVID-19 transmission was considered sporadic in Bagmati and Gandaki provinces, and clustered in Provinces 1 and 2.
nation, of the eight measles-outbreak affected districts in four provinces, the COVID-19 surveillance system classified COVID-19 transmission as sporadic in Bagmati and Gandaki provinces, and clustered in Provinces 1 and 2.

4. Community demand and ownership: This was assessed through formal and informal discussions mentioned above. NIP staff and partners garnered active support from political leaders especially at the local municipality level as well as community members by actively engaging them from the planning stage and sought their commitment to support ORI. Once such commitment was obtained, this criterion was recorded in the affirmative.

5. Operational feasibility including vaccine doses and other logistics from central level (not captured in matrix): logistics: NIP determined that MR vaccine and syringes would be available from existing national stock, and ancillary equipment including personal protective equipment and waste management support would be available for a limited scale ORI in selected municipalities.

6. Local programme capacity: NIP assessed availability of trained human resources at the local level and their capacity to implement measles ORI or SIA campaign safely and effectively. NIP determined that the training for the MR-SIA was already completed in the municipalities including training on managing adverse events following immunization. In addition, NIP in collaboration with partners, WHO and UNICEF, conducted an additional two-day training programme for local health workers and supervisors who would conduct the ORI.

On 30 April 2020, the NIAC meeting endorsed the ORI response for the Dhading outbreak cluster (Dhading, Chitwan and Gorkha districts) and the Kathmandu outbreak by NIP with support from core immunization partners (WHO and UNICEF). NIAC considered the risk of further spread of measles quite high and the risk of COVID-19 transmission to be low in the two provinces (Bagmati and Gandaki) as at that time there were only sporadic COVID-19 transmission and these two provinces had remained free of new COVID-19 cases for 14 days or longer. NIAC also asked NIP to communicate clearly the rationale behind such Go/No-go decisions to selected municipalities.

On 30 April 2020, the NIAC meeting endorsed the ORI response for the Dhading outbreak cluster (Dhading, Chitwan and Gorkha districts) and the Kathmandu outbreak by NIP with support from core immunization partners (WHO and UNICEF). NIAC considered the risk of further spread of measles quite high and the risk of COVID-19 transmission to be low in the two provinces (Bagmati and Gandaki) as at that time there were only sporadic COVID-19 transmission and these two provinces had remained free of new COVID-19 cases for 14 days or longer. NIAC also asked NIP to communicate clearly the rationale behind such Go/No-go decisions to the appropriate levels and nodes of the health service delivery system.

Based on this advice, NIP decided to implement ORI for the Dhading cluster. NIP also decided to implement ORI against the Kathmandu outbreak as cases were also occurring in other parts of the municipality too. The COVID-19 risk in Kathmandu was quite low at that time. However, NIP did not propose ORI for the other outbreaks. These decisions were taken because either (a) the risk of measles cases and deaths was low (as in outbreaks in Jhapa, Morang and Sarlahi), or (b) there was no demand for ORI (Lalitpur), and/or (c) the risk of COVID-19 was too high or there was very recent transmission of COVID-19 (Jhapa, Morang and Sarlahi). For all outbreaks, case management, therapeutic Vitamin-A administration to under-five children and referral of complicated cases were carried out irrespective of ORI decisions.

**Extent of ORI:** ORI was conducted as per NIP guidelines for non-selective vaccination with MR vaccine. The area for ORI, dates of ORI and target populations etc. are in Table 3.

### 3.1. Implementing outbreak response immunization and impact

NIP and immunization partners (WHO, UNICEF) provided dynamic technical support for microplanning sessions, training, communications, coordinating adequate supply of vaccines with ancillary items in time, including personal protective equipment (PPE), soap, hand sanitizers, masks and gloves for vaccinators and immunization session support staffs. Other voluntary organizations also supported the activities.

Effective communication and social mobilization for ORI was done through FCHV, local leaders and social media. Simultaneously, measles surveillance was strengthened to identify suspected measles cases in affected and adjacent wards of municipalities. During ORI, crowd management was given high priority and infection prevention and control (IPC) measures were maintained to mitigate risk of COVID-19 transmission. To ensure vaccine safety as well as to prevent overcrowding at session sites, the maximum number of persons to be vaccinated per vaccinator per day was kept at 50 or less. Immunization session sites also provided handouts on COVID-19 prevention measures. In addition, supportive supervision and monitoring was conducted by FWD, provinces and districts and partners.

The target age group was 9 months to 5 years of age in Gandaki rural municipality, Gorkha district, Gandaki province. In the remaining areas (municipalities in Dhading, Chitwan and Kathmandu districts – Bagmati province) the target age group for ORI was 6 months to 15 years of age. The total target was 32,150 and 97% of the target age group was immunized (Table 3).

The national measles ORI guideline was adapted for this ORI response during active COVID-19 transmission. These included a) Close coordination with Provincial Health Directorate (PHD), Health Offices (HO) and Municipality health section; b) ORI information dissemination through local media supported by active involvement of local leaders, health workers, FCHV and stakeholders; c) Increased public awareness and demand for vaccination enhanced through counselling from local FCHV; and d) High ownership of ORI demonstrated through active involvement of local leaders to bring all eligible children through mobilization of local youth club, mothers’ group etc.

**Impact of ORI:** ORI was effective in reducing measles cases by 98% (Table 4 and Fig. 2). The ratio of daily incidence rates of measles cases per million population between two time periods pre-ORI (period A) and post-buffer (period B) showed that the daily incidence was significantly reduced overall in each district sepa-

### Table 3

| District | Municipality with ORI done | Number of municipal wards with ORI (Total no. of wards) | Period of ORI in Palika | Period of MR SIA in Palika | Target age group for ORI * | Target Pop for ORI | Persons vaccinated in ORI | Coverage (%) |
|----------|-----------------------------|--------------------------------------------------------|-------------------------|-----------------------------|---------------------------|-------------------|--------------------------|--------------|
| Dhading  | Benighat Rorang             | 10 (10)                                                 | 29 April – 5 May        | 14–22 March                 | 6 mo – 15 yrs             | 20,276            | 21,343                   | 105%         |
|          | Gajuri                      | 8 (8)                                                   | May                     |                             |                           |                   |                          |              |
| Chitwan  | Rapti                       | 4 (13)                                                  | 5–10 May                | 18–23 May                   | 6 mo – 15 yrs             | 6,931             | 5,641                    | 81%          |
| Gorkha   | Gandaki                     | 8 (8)                                                   | 8–13 May                | 9 mo – 5 yrs                | 1,740                     | 3,203             | 1,693                    | 97%          |
| Kathmandu| Kageshwori                  | 1 (9)                                                   | 4 May                   | 18–26 March                 | 6 mo – 15 yrs             | 3,203             | 2,652                    | 83%          |
| Manahora |                             |                                                         |                         |                             |                           |                   |                          |              |
| Total    |                             |                                                         |                         |                             |                           | 32,150            | 31,329                   | 97%          |

* ORI age group in Gorkha outbreak was 9 months to 5 years. Gandaki Rural Municipality had planned to conduct SIA from 08 to 13 May 2020. So, municipality conducted ORI in outbreak affected areas during the same time.
rately at 95% level of confidence. For all four districts combined, the incidence risk ratio was 94 times higher in pre-ORI period compared to the post buffer period (95% CI: 36.11 – 347.62).

### 4. Discussion

This report describes the systematic application of a logical decision-making framework to inform the Nepal NIP for taking ‘Go/No Go’ decisions for measles outbreak response immunization in several districts during unfolding COVID-19 transmission.

Delays in implementing outbreak response immunization often increase the risk of spread of measles and associated mortality as observed in Demographic Republic of Congo (DRC), Central African Republic (CAR), Chad. Measles outbreak spread from May 2018 in Chad, from June 2019 in DRC and from January 2020 in CAR.

Measles epidemic in these countries infected hundreds of thousands of children and killed thousands [14].

The ORI decision in Nepal was optimally timed for stopping expansion of outbreaks. The first confirmed outbreak from one ward of Benighat-Rorang Rural Municipality of Dhading district spread across several wards of same municipality and later to two adjacent districts - Gorkha and Chitwan making a contiguous block of three districts. This outbreak cluster continued from 4 February to end of April 2020 resulting in total of 166 measles cases including two deaths. ORI was conducted in affected municipalities in these three districts between 29 April to 13 May 2020 (Tables 2 and 3).

However, no ORI response was conducted for outbreaks in several other districts (Jhapa, Morang, Sarlahi and Lalitpur). While more than 80% of cases in these outbreaks were beyond SIA target

### Table 4

Impact of ORI: confirmed measles cases before ORI, during buffer period and after buffer period until end of year; daily incidence rate (DIR) per million persons and incidence risk ratio by district before ORI and after buffer period.

| District       | Population | ORI end date in 2020 | No. of days in period A* | Confirmed measles cases in period A | Confirmed measles cases in buffer period # | Confirmed measles cases in period B# | DIR per million persons in period A | DIR per million persons in period B | DIR ratio A/B | 95% confidence interval of DIR ratio § |
|----------------|------------|-----------------------|--------------------------|-------------------------------------|------------------------------------------|-------------------------------------|-----------------------------------|-----------------------------------|----------------|----------------------------------|
| Dhading        | 353,434    | 5-May                 | 125                      | 142                                 | 1                                        | 3                                   | 3.214                             | 0.038                             | 85.58          | 28.70 – 419.91                   |
| Chitwan       | 691,674    | 10-May                | 130                      | 24                                 | 0                                        | 0                                   | 0.267                             | –                                 | ^                | 10.23 - ^                        |
| Gorkha        | 247,845    | 13-May                | 133                      | 7                                  | 1                                        | 0                                   | 0.212                             | –                                 | ^                | 2.36 - ^                         |
| Kathmandu     | 2,214,130  | 4-May                 | 124                      | 37                                 | 1                                        | 1                                   | 0.135                             | 0.002                             | 67.73          | 11.43 – 2746.74                  |
| All districts | 3,507,083  | –                     | ——                      | 210                                | 3                                        | 4                                   | 0.476                             | 0.005                             | 93.84          | 36.11 – 347.62                   |

* Period A: From 1 January 2020 to end date of ORI for district; #: Buffer period: up to 14 days from end date of ORI per district;

# Period B: From end of buffer period for each district to 31 December 2020; ^: Undefined as DIR in period B (denominator) was zero.

§: All DIR ratios were statistically significant at 95% level of significance as the lower bound was greater than one for each district.

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Fig. 2. Incidence of confirmed measles cases by week of onset from week-1 of 2020 through 90 days after ORI end in four outbreak affected districts – Dhading (A), Chitwan (B), Gorkha (C) and Kathmandu (D). * Green horizontal bar: Duration of MR SIA in district; Red horizontal bar: Duration of ORI in district. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)
age group, no underserved community was affected and there was no community demand for ORI response and there were no measles deaths.

The success of this program experience and the processes followed clearly demonstrated that this approach was feasible and practicable within existing resources at country level when decisions needed to be taken and choices made in a complex environment faced with two lethal infectious diseases simultaneously. Of note, these decisions were based on triangulating surveillance data (for both measles and COVID-19) and programmatic data from different sources like real time epidemiological data, immunization programme information and community related information and these were taken collectively and iteratively with close collaboration between the NIP, core immunization partners (WHO and UNICEF) and the NIAC, which is the mandated national immunization technical advisory group in Nepal. COVID-19 surveillance data was also accessed. The WHO-IPD immunization team was also supporting COVID-19 surveillance.

By the end of May 2020, the World Health Organization published a framework document for decision-making regarding implementation of mass vaccination campaigns in the context of COVID-19 [15]. The logical decision-making approach described here predated publication of this WHO document. However, there is a close alignment between Nepal NIP experience and practice and the global framework demonstrating that the WHO framework document is indeed adaptable and implementable in a country context. In fact, the Nepal experience can well serve as an example of application of the principles laid out in the WHO framework document, as adapted to small-scale ORI responses which were right sized to respond to the outbreaks. The NIP, core immunization partners (WHO and UNICEF) and the NIAC, which is the mandated national immunization technical advisory group in Nepal. COVID-19 surveillance data was also accessed. The WHO-IPD immunization team was also supporting COVID-19 surveillance.

The Nepal NIP applied multiple iterative decision-making loops to reach a proposed solution that was finally endorsed by NIAC rather than a rigidly sequential algorithmic approach. Community engagement, acceptance and demand for ORI including from local opinion leaders was taken as an integral component of the decision process for a Go/No-go decision for ORI. Federal level staff of NIP and partners were in regular contact with local level public health staff and opinion leaders to gauge such acceptance and demand. Past programme experience in Nepal had informed NIP that community demand and support from local leaders were essential elements for success in the bottom-up planning and implementation of such public health interventions in current federal governance system of Nepal. This approach was thus a practical application of the four core principles of the Immunization Agenda 2030 and the measles and rubella strategic framework 2021–2030 being “people-focused, country-owned, partnership-based and data-enabled” [2,16].

WHO-IPD supported NIP with rapid analysis of case based VPD surveillance data linking up with laboratory results and quickly picked up the occurrence of the outbreaks with laboratory confirmation and identified key epidemiological characteristics of some of the outbreaks which weighed in on the decision making for the ORI interventions. In the four outbreaks where the ORI intervention was done, about 75% of the cases were beyond the age group targeted by the nationwide MR-SIA who were mostly without a history or record of measles vaccination. Further, some underserved communities who had historically lacked access to health services were being disproportionately affected in the outbreaks. Detailed analysis of case-based surveillance data identified preponderance of measles cases in underserved ethnic groups who are categorized as “Mountain/Hill Janajati” or indigenous population of Nepal. As per 2011 Nepal Census data, these affected ethnic groups constituted only about six percent of Nepal population with literacy level of below the national average [17].

The MR-SIA would thus have had little direct impact on the age group being affected by the outbreaks. Pockets of susceptible population often remain within underserved communities even in countries with relatively well performing childhood immunization programmes as observed in Nepal as well as in other countries [18]. Surveillance programmes should be able to pick up such data flags to help inform programme intervention decisions.

By June 2020, while several countries had postponed measles SIA campaigns faced with the COVID-19 pandemic, Nepal implemented planned SIA campaigns. In addition, faced with these relatively circumscribed outbreaks, the NIP of Nepal guided by NIAC was able to respond swiftly with targeted measles ORI and was thus able to opportunistically utilize a narrow window of time before COVID-19 transmission increased in the districts where the outbreaks occurred. In contrast, some countries, had decided against a mass immunization response when faced with the dilemma of managing two lethal infectious diseases simultaneously [19].

ORI response was successful in several ways. Measles case incidence was reduced by 98% and only a few cases but no measles associated deaths occurred after ORI. Through this ORI, local municipalities were also able to decrease measles immunity gap of underserved communities in age groups beyond the preventative SIA target group. The ORI also increased political support and community participation in outbreak response as well as generally for immunization.

Experience of implementing measles ORI in Africa has shown that for optimal impact ORI implementation should be contextualized to local epidemiology [20]. In Nepal, ORI implementation was contextualized based not only on risk of measles but also considered COVID-19 transmission risk. All outbreak affected districts had greater than 95% reduction in measles cases and the difference was statistically significant (Table 4).

This report has several limitations. Because of COVID-19 induced lockdown, mobility restrictions, and other programmatic considerations, population-based age specific attack rates could not be ascertained in outbreak affected areas. As per existing surveillance protocols only IgM ELISA tests were done to confirm measles and rubella cases. Gene sequencing was not attempted, and thus it was not possible to ascertain if the outbreaks in the different districts were genetically linked and part of the same outbreak or were caused by different lineages of the measles virus. It is possible that because of social and programme disruptions on account of COVID-19 in 2020, some fever and rash cases were missed by the surveillance system. However, this was unlikely to have been significant because the detection rate of non-measles non-rubella (NMNR) cases was above the target of 2 per 100 000 persons in 2019 and 2020 in all four outbreak affected districts except for Kathmandu where it was 4.92 per 100 000 persons in 2019 but 1.4 in 2020. In Dhading, the district with the largest outbreak, the NMNR case detection rate was between 8 and 13 per 100 000 persons from 2018 to 2020. In 2020, Chitwan and Kathmandu districts confirmed one and three cases of rubella while the other two outbreak affected districts had no rubella cases.

5. Conclusion

The Nepal NIP, through this effective outbreak response, was able to reduce measles morbidity and mortality. By keeping an eye on VPD as well as COVID-19 case-based data from laboratory supported surveillance and triangulating multiple strands of information from surveillance, immunization programme as well as community acceptance and demand, the NIP and immunization partners rapidly processed necessary information through a logical framework and obtained NIAC endorsement to implement ORI.
There are several lessons for future from this experience. First, measles outbreak response is context specific. This was demonstrated by the advice for Go/No-Go decisions by NIAC and a differential approach for outbreak response immunization in different districts. Second, data from different sources need to be collected and collated rapidly and processed through a structured iterative logical framework for appropriate response. The logical framework outlined here pre-dated the WHO framework guidance for mass vaccination in COVID-19 context. However, it is closely aligned with the guidance in the framework and can be adapted to other country contexts. Third, close collaboration between the NIP, core immunization partners (WHO and UNICEF) and NIAC was key to the successful response. Fourth, proactively engaging with the community prior to ORI intervention and obtaining support from local opinion leaders are needed for smooth and successful operations. This is not explicitly stipulated in WHO framework document and may be considered in its future iterations. Fifth, having a pre-existing guideline from MOHP for measles outbreak response including immunization response helped the programme division to obtain internal approvals quickly. The current guideline in Nepal was drawn up prior to the COVID-19 pandemic. This would need to be modified considering the logical framework described here incorporating assessment of competing risks from different diseases and added flexibility to respond up to the right age group as indicated by surveillance data. Finally, the target age group for preventive SIA campaigns should be guided by epidemiological data collected through population-based surveillance. Nepal surveillance data had shown that in 2017, 2018 and 2019 54% (52/97), 43% (113/260) and 51% (220/431) of confirmed measles cases were five years or older indicating that there was susceptible population in these age groups [21]. Such data should inform decisions regarding target age groups for preventive SIA campaigns (rather than pre-determined target age groups) on the path to measles elimination for Nepal and the WHO South East Asia Region.

Disclaimer

The opinions expressed by the authors are their own, and do not necessarily reflect that of their organizations. Any proprietary names mentioned in this manuscript do not indicate endorsement of the product(s) by any of the authors or their respective organizations.

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Author Contributions

PR and ASB wrote up the initial draft of the manuscript. ASB conceptualized the manuscript and the analysis. ML, SS and PR provided surveillance and other data analyses, graphical outputs, and maps. PR, RP, DS, AG, ML, SS, BC, JSG, BB, BS, SB and PS provided immunization data and other relevant programme information. RJ and BK provided lab results. JSG coordinated the ORI planning and activities on behalf of NIP. All authors were closely involved with the programme activities described here and all of them reviewed the manuscript and provided important intellectual inputs.

Appendix A. Supplementary data

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