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Measles in Kazakhstan:

Overview of the Health System and Root Cause Analysis of the 2019–2020 Outbreak

Acknowledgements

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List of Abbreviations and Acronyms

Adverse event following immunization	AEFI
Centers for Disease Control and Prevention	CDC
Commonwealth of Independent States	CIS
Coronavirus Disease 2019	COVID-19
European Centre for Disease Prevention and Control	ECDC
Expanded Programme on Immunization	EPI
Health Care Worker	HCW
International Heath Regulations	IHR
Infection Prevention and Control	IPC
Measles-containing-vaccine	MCV
Measles-Mumps-Rubella Vaccine	MMR
Ministry of Health	MoH
Non-Governmental Organization	NGO
Outbreak Response Immunization	ORI
Public Health Emergencies of International Concern	PHEIC
Sanitary-epidemiological services	SES
Standard Operating Procedures	SOPs
Supplementary Immunization Activities	SIAs
United Nations Children's Fund	UNICEF
Vaccine Preventable Disease	VPD
World Health Organization	WHO

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PART A. COUNTRY HEALTH SYSTEM AND 2019-2020 MEASLES OUTBREAK

1. Country background

The Republic of Kazakhstan is the ninth largest country in the world, covering 2.7 million square meters. It has been classified as an upper-middle income country by the World Bank since 2006.

The country is divided into 14 regions (Oblasts) and three cities of republican importance (Shymkent, Almaty, and the capital Nur-Sultan) totaling 17 administrative divisions (figure 1).

Figure 1. *Administrative map of Kazakhstan (source: United Nations Cartographic Section)*

According to the Committee on Statistics of the Ministry of National Economy of the Republic of Kazakhstan, as of December 2019 the country has a population of 18,448,000 people, with a median age of 30.9 years and a life expectancy at birth of 66 years for males and 75 years for females.

The age structure of the country is composed as follow: 0-14 years: 26.1%; 15-24 years: 13.5%; 25-54 years: 42.3%; 55-64 years: 10.1%; 65 years and over: 7.9%.

Table 1 shows the number people by administrative division according to the population census 2019.

Table 1. *Population of Kazakhstan by Oblasts / Cities, December 2019. (source)*

Entity	Administrative center	Area (km²)	Population (2009 census)	Population Density
Turkistan	Turkistan	117,249	2,469,357	21.06
Almaty	Taldykorgan	223,924	1,807,894	6.099
East Kazakhstan	Oskemen	283,226	1,396,593	4.931
Almaty	Almaty	319	1,365,632	4281
Karaganda	Karaganda	427,982	1,341,700	3.135
Jambyl	Taraz	144,264	1,022,129	7.085
Kostanay	Kostanay	196,001	885,570	4.518
Aktobe	Aktobe	300,629	757,768	2.521
Pavlodar	Pavlodar	124,800	742,475	5.948
Akmola	Kokshetau	146,219	737,495	5.044
Kyzylorda	Kyzylorda	226,019	678,794	3.003
Nur-Sultan	Nur-Sultan	710	613,006	863.4
Shymkent	Shymkent	1,170	603,499	515.81
West Kazakhstan	Oral	151,339	598,880	3.957
North Kazakhstan	Petropavl	97,993	596,535	6.088
Atyrau	Atyrau	118,631	510,377	4.302
Mangystau	Aktau	165,642	485,392	2.930
Baikonur	Baikonur	57	36,175	644.6

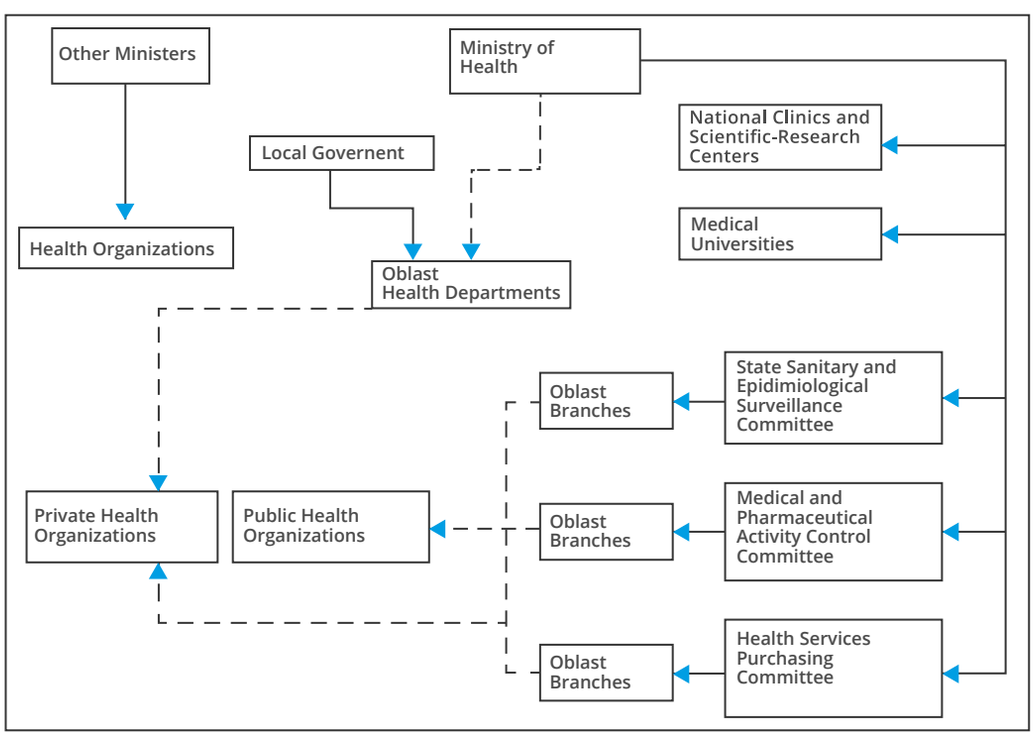
2. Health System

While the administrative set-up of Kazakhstan's health system is highly centralized compared to some federal or highly decentralized systems in western Europe, but it is less centralized than that of most other countries in Central Asia, and the oblasts have a great amount of autonomy.

Figure 2 provides a broad overview of the health system of Kazakhstan. The Ministry of Health (MoH) is responsible for developing national health policies, while oblasts governors are key players in decisions relating to the health system, as are the financing departments at oblasts level. Health fund is pooled at the national and oblast level, with health revenue coming from two main sources: the governmental budget (at national and oblast level) and out-of-pocket payments.

The Ministry of Health established two committees, that have a vertical structure with representation in all oblasts, to implement health policy at the national and regional level: The Committee of Medical and Pharmaceutical Activity Control, and the Committee of State Sanitary-Epidemiological Surveillance.

Figure 2. *overview of the health system of Kazakhstan (source).*
Dotted lines indicate regulatory oversight, solid lines indicate administration and reporting.



According to the Code on People's Health and the Health Care System, approved by President's Decree No. 360-IV of 7 July 2020, among the MoH key functions there are:

• implementation of national health policies and development of health plans

• development and approval of health care legislation, regulations and standards

• monitoring and evaluation

• coordination of health system activities

• organization of continuous education and training of medical and pharmaceutical staff

• ensuring the preparedness of organizations responsible for the prevention and management of emergency situations.

The oblasts and cities health departments are the key bodies administering health services in Kazakhstan and run most hospitals and polyclinics; they own and manage all state-owned health care providers in their territory.

2.1 Provision of services

The Code on People's Health and the Health Care System and the Concept on the Unified National Health Care System, have defined five levels of care in the Republic of Kazakhstan:

1. "pre-physician care" includes all types of health services that can be provided without participation of physicians

2. "qualified health care" is provided without special diagnostic and treatment methods, typically in rural areas

3. "primary health care" is provided in outpatient settings. It includes preventive examinations, immunizations, health promotion activities, the follow-up of chronic patients and the surveillance of communicable and non-communicable diseases

4. "specialized health care" includes the provision of consultative and diagnostic services by polyclinics and of hospital care by specialists (such as urologists, neurologists, cardiologists and neurosurgeons)

5. "tertiary care" includes the use of resource-intensive medical technologies

The delivery of primary care differs between rural and urban areas. Urban polyclinics provide both primary and secondary ambulatory care. For the rural population health services are provided by (a) rural physician ambulatories, (b) medical posts and (c) feldsher-midwifery posts which run immunizations.

The WHO underlines differences in the quality of healthcare provisions between urban and rural areas, with the latter suffer of equipment and supplies shortfalls, lack of health workers and accessibility issues for the population.

2.1.1 Public Health

In Kazakhstan the responsibility for public health and health promotion activities is shared by the following major actors: Oblasts/Cities health departments and their sanitary-epidemiological services (SES), the MoH, the National Center for Public Health, and primary health care providers.

The Ministry of Health is in charge of the following main functions with regard to public health:

• developing national policies, plans and programmes on public health

• regulating the registration of infectious, parasitic, occupational and other diseases and poisonings

• establishing the rules for sanitary-epidemiological surveillance

• ensuring intersectoral coordination in implementation of national and sectoral programmes on health protection and the promotion of healthy lifestyles.

All SES under Oblast and City administrations were placed under the control of the national Committee of State Sanitary-Epidemiological Surveillance. SES are responsible for the following main functions with regard to public health:

• initiating restrictive measures to contain the spread of infectious diseases, including quarantine

• overseeing the organization and implementation of vaccinations against infectious diseases

• undertaking state sanitary-epidemiological surveillance
• monitoring laboratory safety

• monitoring the quality of water and food products

There are currently 17 sanitary-epidemiological services, one per each administrative division. According to the WHO, they have significant laboratory resources and, jointly with Oblast/City health departments, they are responsible for implementing immunization campaigns.

3. Infectious Disease Surveillance System

The Rules for registration, keeping records of cases of infectious, parasitic, occupational diseases and poisoning, and the Rules for reporting on them (September 16, 2019 No. KR DSM-127) define procedures for surveillance of infectious diseases in the Republic of Kazakhstan.

Diagnosis and registration of cases of infectious

and parasitic diseases is carried out at the place of detection of the disease, regardless of the patient's place of residence. Notification is sent within 12 hours to the territorial SES competent. In all medical organizations, a register of infectious diseases is kept in the form No. 060 / y, approved by order No. 907, which is used to record patient information.

According to the order of the MoH October 4, 2019 No. KR DSM-135, each case of vaccine preventable infectious diseases is subject to epidemiological investigation:

• the medical organization reporting the case ensures the completeness, reliability, and timeliness of registration and recording of cases, as well as prompt and full information about them to the territorial-competent SES

• during the epidemiological investigation, the circle of persons who were in contact with the patient is determined

• these contacts undergo clinical examination for symptoms and signs of illness and are under daily medical supervision for the duration of the incubation period. In addition, their vaccination and epidemiological anamnesis is analyzed

The order of the MoH October 4, 2019 No. ҚR DSM-135 also defines the following reporting mechanism, including zero reporting:

The 1st day of each month, all sanitary-epidemiological services under Oblast and City health departments, conduct reconciliation of the number of infectious and parasitic diseases occurred on their territory, and on 3rd day of the month submit a report to the Oblast/City health department. On the 5th day of the month, the Oblast/City health department submits the received report to the National Committee of State Sanitary-Epidemiological Surveillance.

3.1 Measles surveillance

Measles case definitions and classifications in the Republic of Kazakhstan are employed according to the "Order of the Chairman Committee for Quality Control and Safety of Goods and Services of the Ministry of Health Republic of Kazakhstan of 2019 No 200" (table 2).

Table 2. *Measles case definitions in the Republic of Kazakhstan*

Clinical Criteria	**Any person with fever AND Maculo-papular rash AND at least one of the following three:** • Cough • Coryza • Conjunctivitis
Laboratory Criteria	**At least one of the following four:** • Isolation of measles virus from a clinical specimen • Detection of measles virus nucleic acid in a clinical specimen • Measles virus specific antibody response characteristic for acute infection in serum or saliva • Detection of measles virus antigen in a clinical specimen using measles specific monoclonal antibodies Laboratory results need to be interpreted according to the vaccination status. If recently vaccinated, investigate for wild virus
Epidemiological criteria	**An epidemiological link* of human to human transmission**
Case Classification	**A. Possible case** Any person meeting the clinical criteria **B. Probable case** Any person meeting the clinical criteria with an epidemiological link **C. Confirmed case** Any person not recently vaccinated and meeting the clinical and the laboratory criteria

**Epidemiologic linkage is established when there is:*

Contact between two people involving a plausible mode of transmission at a time when:
a. one of them is likely to be infectious (approximately four days before to four days after onset of the rash),
AND
b. the other has an illness that starts usually within 10–14 days (range 7–23 days) days after this contact
AND
At least one case in the chain of epidemiologically linked cases (which may involve many cases) is laboratory confirmed

The National Committee of State Sanitary-Epidemiological Surveillance and Oblast/City health departments, are responsible for declaring the beginning and the end of a measles outbreak using the following criteria:

• **Criterion for Measles Outbreak declaration:** two or more laboratory-confirmed cases that are temporally related (with dates of rash onset occurring 7–23 days apart) and epidemiologically- or virologically-linked, or both

• **Criterion to declare the end of a Measles outbreak:** no further epidemiologically- or virologically-linked cases for two incubation periods (46 days) from the date of onset of the last case

For public health measles surveillance purposes, definitions reported in table 3 are employed by The National Committee of State Sanitary-Epidemiological Surveillance in order to analyze and report surveillance data.

Table 3. *Measles case definitions to be used for public health surveillance*

Epidemiologically linked measles	A probable case of measles that has not been laboratory confirmed, but was geographically and temporally related with dates of rash onset occurring 7–23 days apart from a laboratory-confirmed case or another epidemiologically linked measles case.
Discarded case	**A suspected measles case that has been investigated and discarded as non-measles through::** • Negative laboratory testing in a proficient laboratory on an adequate specimen collected during the proper time after rash onset • Epidemiological linkage to a laboratory-confirmed outbreak of another communicable disease that is not measles • Confirmation of another etiology • Failure to meet the clinically compatible measles case definition
Endemic measles case	**Confirmed case of measles resulting from endemic transmission of measles.** Endemic transmission is defined as a chain of measles virus transmission that is continuous for ≥ 12 months within a country
Imported measles case	**A returning traveller or visitor exposed to measles outside the country during the 7–23 days prior to rash onset and supported by epidemiological or virological evidence.** For cases that were outside the country for only a part of the 7–23 days period prior to rash onset, investigate whether the exposure to another measles case likely occurred outside or within the country to determine the source of infection and whether the case can be considered imported. Imported cases are defined by the place where the case was infected, not the country of residence or origin of the case.
Importation-related measles case	Locally acquired infection that occurs as part of a chain of transmission originating from an imported case as supported by epidemiological or virological evidence. If transmission of measles from cases related to importation persists for ≥12 months within a country, cases are no longer considered imported but endemic.
Unknown source measles case	A confirmed case for which no epidemiological or virological link to importation or endemic transmission can be established after a thorough investigation.
Measles vaccine-associated reaction	**A suspected case that meets all five of the following criteria:** 1. The patient had a rash illness, but did not have cough or other respiratory symptoms related to the rash 2. The rash began 7–14 days after vaccination with a measles-containing vaccine 3. The blood specimen, which was positive for measles IgM, was collected 8–56 days after vaccination 4. A thorough field investigation did not identify any secondary cases 5. Field and laboratory investigations failed to identify other causes, or genotype A was isolated from the suspected case (genotype A is only vaccine-related and does not occur as wild-type infection)
Acute measles-related death	For cases that were outside the country for only a part of the 7–23 days period prior to rash onset, investigate whether the exposure to another measles case likely occurred outside or within the country to determine the source of infection and whether the case can be considered imported. Imported cases are defined by the place where the case was infected, not the country of residence or origin of the case.

In all cases with suspected measles, an epidemiological investigation is carried out with the collection of samples (blood, urine) for laboratory analysis. The order No. KR DSM-135 indicates that laboratory confirmation must be carried out by taking the following samples, and details personal protective equipment and procedures for health professionals managing biological samples:

• blood serum is taken from 4 to 28 days after rash onset. If negative results are obtained when examining a sample taken before the 4th day of the onset of the rash, a second sample is taken from 4 to 28 days after rash onset to re-test for antibodies to immunoglobulin M, as well as to determine the increase in levels antibodies to immunoglobulin G;

• samples of nasopharyngeal discharge, urine and whole blood are taken within the first 3 days from the moment of the appearance of the rash, which were stored and transported at temperatures from + 4 to - 80C within 24 hours from the moment of collection; if blood delivery is not possible within 24 hours, then the whole blood is centrifuged, the serum is transferred to another sterile tube with a screw cap, the tube is labeled accordingly for transportation to the laboratory.

The order of the MoH October 4, 2019 No. KR DSM-135, also defines indicators reported in table 4, for the quality of measles epidemiological and laboratory surveillance.

Table 4. *Indicators for the quality of measles epidemiological and laboratory surveillance.*

Indicator	Target
Measles case detection rate with adequate clinical specimens for laboratory testing	at least 2 cases per 100,000 population
Percentage of laboratory confirmed cases	80%
Percentage of sample collected from 4 to 28 days after the onset of the rash	80%
Proportion of detected transmission-chains with data on the genotype of the virus	90%
Proportion of measles cases investigated by 48 hours from notification	80%

3.2 Procedures for outbreak investigation

Procedures for outbreak investigation in the Republic of Kazakhstan are defined by the Order 2019 No. 200 of the Chairman Committee for Quality Control and Safety of Health Services, which outlines roles and responsibilities of involved institutions as following.

All SESs within Oblasts/Cities are responsible for:

• collect preliminary data

• analyze weekly data

• prepare and maintain a line-list of outbreak-cases

• conducts operational risk assessment

• organize, if necessary, the initial response and preventive measures

The SESs provide the following information to the respective Oblast/City health department in the course of an outbreak investigation:

• Preliminary information. Describes all the available data on the outbreak, including the control measures implemented, which is sent within 24 hours from outbreak-detection to the Oblast/City health department

• Intermediate information. Interim epidemiological reports are sent to the Oblast/City health department when there are new cases. Information should be constantly updated as new facts emerge
During the outbreak the Oblast/City health department is in charge of:

• supervising outbreak investigations and implementation of control and preventive measures

• providing remote support and methodological assistance, and if necessary, provide field support

• oversee communication with other Oblast/City health departments to determine whether other measles cases have been reported

• update regularly the national Committee of State Sanitary-Epidemiological Surveillance on the evolution of the outbreak

The national Committee of State Sanitary-Epidemiological Surveillance:

• provides remote support, methodological assistance and, if necessary, goes in the field

• analyses the situation in other Oblasts/Cities and neighboring countries to determine whether similar outbreaks have been reported

• within 24 hours sends information on all events which constitutes «Public Health Emergencies of International Concern (PHEIC)» to the national coordinator of the International Health Regulations (IHR)

4. Immunization Programme

The Order of the Government of the Republic of Kazakhstan dated December 30, 2009 No. 2295 defines the legal framework for the implementation of the immunization programme in the country.
The Ministry of Health of the Republic of Kazakhstan and Oblast/City administrations are in charge of organizing and providing immunization according to the national vaccinations schedule (Table 5), also with the use of mobile vaccination teams to reach populations living in the settlements without access to medical services.

Table 5. *Kazakhstan immunization calendar for children (source:)*

	At birth	2 months	3 months	4 months	12-15 months	18 months	2 years	2.5 years	6 years	16 years	Every 10 years
BCG	●								●		
HBV	●	●		●							
DTP		●	●	●		●			●		
Hib		●	●	●		●					
IPV		●	●	●		●					
OPV					●						
Pneumo		●		●	●						
MMR					●				●		
DT										●	●
HAV							●	●			

Immunizations are administered by legal entities with licenses to provide primary health care. Persons with higher and secondary medical education, trained in vaccine administration techniques and management of Adverse Event Following Immunization (AEFI), are allowed to administer vaccines.

According to MoH, there are 6,565 licensed vaccination clinics in 5,516 healthcare organizations. To provide immunizations to populations living in the remote areas, there are 1,161 mobile vaccination teams serving 2,460 settlements. Quality control of immunization services is carried out by local-competent SESs.

The order 2009 No. 2295 defines detailed procedures for vaccine administration (e.g. quality check, vial monitor, collection of anamnestic data, etc.) and registration of administered doses.

Infants' vaccinations are administered upon the consent of the parents, and must be registered in the following documents:

• child card of preventive vaccinations (form 063/y)

• register of preventive vaccinations for newborns (form 064-1/y)

For adults, the vaccinations must be registered in the outpatient's medical record (form 025/y)
Subsequently, the immunization card is presented when children' parents apply for kindergarten or school. Each educational institution has its own rules for admission: the availability of the vaccination card is a mandatory requirement for some, while it is not necessary for others.

4.1 Surveillance of Adverse Event Following Immunization

Surveillance and investigation of Adverse Event Following Immunization (AEFI), is regulated by the "Algorithm for the detection, registration and epidemiological investigation of cases of adverse manifestations after immunization" (order of the President of the Public Health Security Committee - Ministry of Health Republic of Kazakhstan).

In case of suspicion of AEFI, the medical worker sends a notification to the territorial-competent SES within 24 hours from the moment of AEFI detection. SES in turn submits a report to the "National Center for Expertise of Medicines, Medical Products and Medical Equipment". The detection of AEFI is carried out by health workers who vaccinate. AEFI cases are then investigated by a commission of specialists. Based on the results of the investigation, a report on AEFI cases is drawn up and submitted to the national Committee of State Sanitary-Epidemiological Surveillance within 10 days from AEFI detection.
The results of the investigation are then brought to the attention of each health worker involved in the immunization programme at all levels of the health care system.

In the event that a link between the AEFI and the quality of the vaccine used is established, the information is notified to the manufacturer and supplier of the vaccine. Samples of the vaccine can be sent to an independent laboratory to confirm its quality. Until the results are received, the national Committee of State Sanitary-Epidemiological Surveillance can decide on the temporary suspension of the implicated vaccine.

4.2 Vaccines procurement, storage and transposition

Procurement of vaccines in the Republic of Kazakhstan is centralized. In February 2009, the Government established SK-Pharmacy Company as part of the National Welfare Fund Samruk-Kazyna JSC (Government Decree No. 134, dated February 11, 2009). Since 2011, in accordance with the Decree of the Government of the Republic of Kazakhstan dated October 30, 2009, no. 1729, SK-Pharmacy Company acts as the organizer of purchases of the medical equipment acquired at the expense of the republican budget as well as for further transfer to health care organizations on the terms of financial leasing.

Purchased vaccines are then distributed to each Oblast/City health department that has an accredited storage warehouse and that then distributes vaccines at the local level according to The Rules for "storage, transportation and use of prophylactic (immunobiological, diagnostic, disinfectant) drugs" - Order of the Minister of National Economy of the Republic of Kazakhstan dated February 4, 2015 No. 76 - which provides detailed procedures and requirements for vaccine storage and transportation. The Order details quality criteria to run immunizations, including structural requirements, equipment, professionalisms needed, procedures related to cold-chain maintenance, vaccine quality check, injection safety and vaccine waste management.

5. Measles immunization coverage profile

Measles vaccine was included in the national calendar of immunization in 1964 providing a first dose at 12-15 months of age. The 2nd dose was included in the national calendar of routine immunization in 1999. Currently the immunization calendar against measles include: vaccination at 12-15 months and revaccination at 6 years. Therefore, young people born before 1999 did not receive the second dose.

The Sanitary Rules "Sanitary and epidemiological requirements for prophylactic vaccinations to the population" (Order of the acting Minister of Health of the Republic of Kazakhstan dated June 13, 2018 No. 361) set the target of MMR first and second dose immunization coverage at 95%.

To ensure full coverage, the target infant population is registered by medical workers of medical organizations (feldsher-obstetric station, medical outpatient clinic, polyclinic) twice a year (spring-autumn).
Sources to calculate MMR vaccine coverage are paper-based, and represented by the official administrative reports at the sub-national level on the

number of vaccinated children, and the population of children according to annually updated data from the Agency of Statistics, which takes into account monthly adjustments.

During the last decade the Government of Kazakhstan is consistently reporting immunization coverage with MCV1 and MCV2 close to 100%, with observed problems of over reporting (figures 3 and 4).

Figure 3. *MCV1 coverage, Kazakhstan, 2000-2019 (source)*

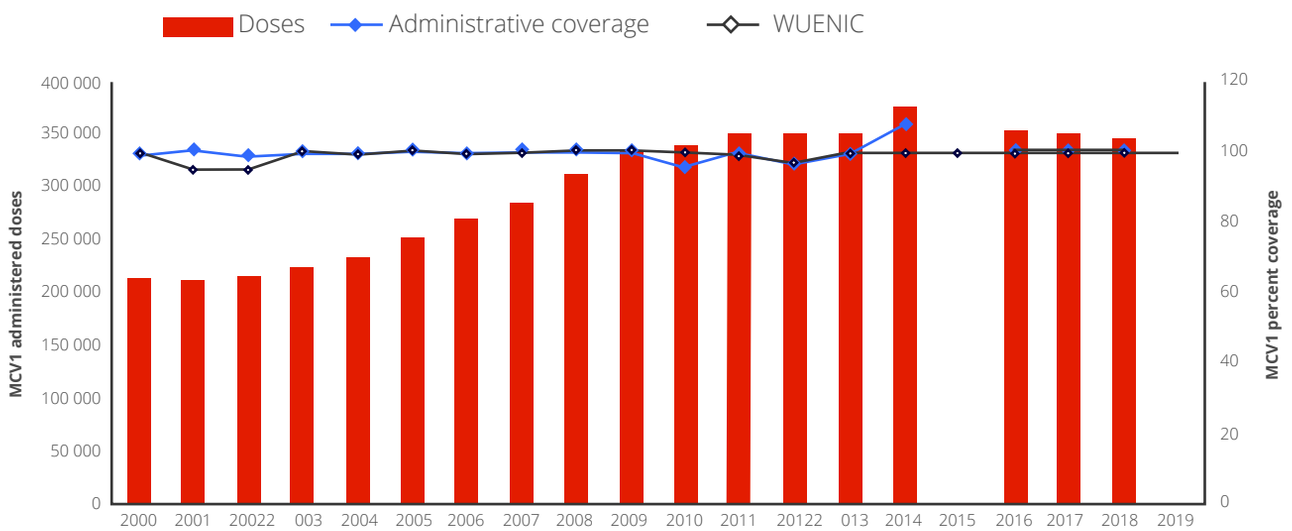
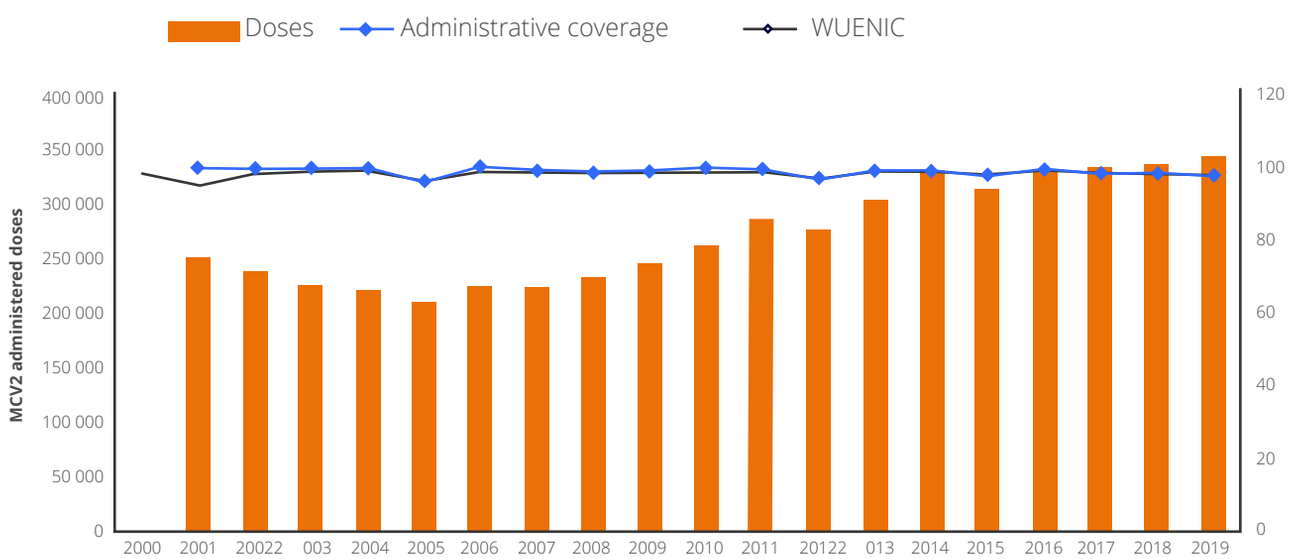


Figure 4. *MCV2 coverage, Kazakhstan, 2000-2019 (source)*



Also at the Oblast/City level Kazakhstan shows optimal values during 2017-2019 for both MCV1 and MCV2 coverage (Table 6), with observed over-reporting problems from the majority of subnational divisions.

Table 6. *MCV-1/2- coverage by Oblast/City, Kazakhstan, 2017-2019.*

Oblast/City	2017		2018		2019	
	MCV1	MCV2	MCV1	MCV2	MCV1	MCV2
Akmola	99.2	97.4	99.3	98.3	100	92.2
Aktubinsk	98.5	97.9	97.9	97.7	99.7	97.1
Almaty	105.2	100.1	100.0	98.4	99.3	100
Almaty City	99.9	98.7	99.5	98.7	99.7	96.4
Astana City	99.6	95.7	99.9	99.9	99.2	95.3
Atyrau	99.1	98.6	97.7	95.7	99.4	97.3
Jambyl	99.2	99.3	99.1	97.2	99.2	97.4
Karaganda	102.9	100.3	99.9	98.9	97.4	100
Kostanai	99.2	98.5	99.5	98.3	97.8	96.8
Kyzyl-Orda	100.5	100.9	98.5	100.0	99.5	100
Mangystau	92.9	89.9	99.9	98.5	98.6	100
Pavlodar	99.5	97.2	96.6	96.6	98.8	95.3
North Kazakhstan	101.2	99.2	100.0	95.9	100	100
East Kazakhstan	99	100	99.4	98.1	98.3	96.8
South Kazakhstan (Turkestan region + Shymkent City)	99.5	99.5	99.0	98.3	97.6	97.1
West Kazakhstan	101.4	99.4	98.6	98.3	99.4	99
Shymkent City	No data	No data	No data	No data	97.6	94

6. Measles Epidemiology Profile

According to the WHO, Kazakhstan is classified as a country with endemic transmission of Measles.
In the past 5 years, two measles epidemics have been registered: in 2015 with 2,340 lab-confirmed cases, and in 2019 with 16,871 cases, of which 13,326 (78.9%) were laboratory confirmed.

The 2019 outbreak begun on January, with around 2,000 monthly cases reported until June, when the epidemic curve started to decline (Figure 5). A recrudescence was then observed from November 2019 with the last outbreak-case reported on May 2020, in concomitance with the increase of COVID-19 cases and the implementation of restrictive public health measures that had a positive impact on the circulation of measles. On the other hand, the two SIAs implemented in April and September 2019, seems to have had little impact on the outbreak.

According to MoH data there have been 21 measles-related deaths during the 2019 outbreak leading to a case fatality rate of 0.15%.

Figure 5. *Number of measles cases by case-classification. Kazakhstan, September 2018 - January 2021 (source:)*

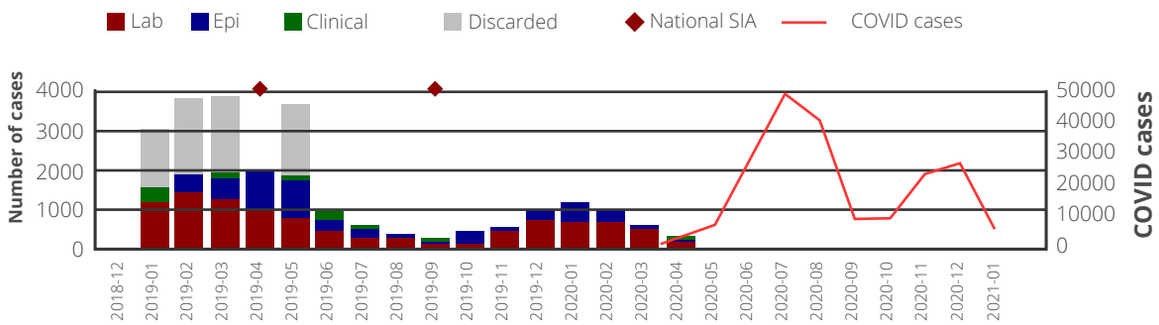


Figure 6 shows the incidence rate of measles cases during the 2019 outbreak by age group and vaccination status. The highest incidence rate was observed among children <1 year of age that are not targeted by the MMR immunization programme. The higher number of cases was instead observed among those aged 1-4 years and so within the MMR target, but among them, the majority did not receive MCV1.

Figure 6. *Incidence of measles cases by age-group and MMR vaccine status. Kazakhstan, September 2019 - August 2020*

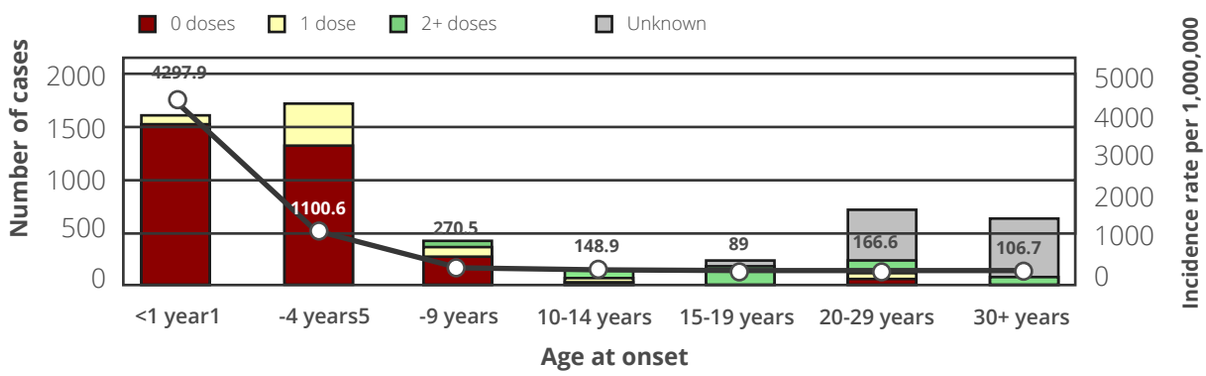


Table 7 shows a detailed analysis of the number of lab-confirmed measles cases occurred during the 2019 outbreak by age group and immunization status.

Table 7. *Number of measles cases by age-group and MMR vaccine status. Kazakhstan, 2019.*

	< 1 year	1-4 years	5-9 years	10-14 years	15-19 years	20-29 years	30+ years	Total
0 doses	3825	3189	543	92	29	71	26	7775
1 dose	53	869	192	40	33	57	29	1273
2 or more doses	0	24	138	210	199	478	83	1132
No data	1	179	44	18	93	1358	1453	3146
Total	3879	4257	917	356	360	1965	1592	13326

Despite most of the cases older than 1 year of age were not vaccinated, it should also be noted that across all target age-groups and Oblasts/Cities a high-burden of vaccine failures was reported:

• among measles cases occurred in children aged 1-4 years, 20.9% received the first MMR dose

• among measles cases occurred in children aged 5-9 years, 15% received 2 MMR doses

• among measles cases occurred in the age group 10-14 years, 59.9% received 2 MMR doses

• among measles cases occurred in teenagers 15-19 years, 55.3% received 2 MMR doses

• among measles cases occurred in people aged 20-29 years, 24.3% received 2 MMR doses

The analysis of the measles outbreak by territorial sub-division is showed in table 8. Incidence rate per 100,000 population ranged from 3.3/100,000 in EKO to 331.6/100,000 in Shymkent. Other sub-divisions that reported a high incidence rate were Nur-Sultan (276.6/100,000) and Mangistau (201.7/100,000).

Table 8. *Number of measles cases and incidence rate (per 100,000 population) by territorial sub-division, Kazakhstan, 2019.*

Oblast/City	Number of cases	incidence per 100,000
Akmola	282	39.4
Aktobe	282	35.4
Almaty	601	29.2
Almaty city	804	45.2
Atyrau	774	139.1
EKO	86	6.3
Karaganda	354	25.7
Kostanay	193	93.2
Kyzylorda	535	90.7
Mangistau	1,422	210.7
NKO	280	48.3
Nur-Sultan city	2,772	276.6
Pavlodar	207	27.4
Shymkent city	3,091	331.6
Turkestan	1,090	40.6
WKO	122	18.6
Zhambyl	431	40.2

During the measles outbreak, to assess the molecular genetic characteristics of measles viruses, 502 biological samples from laboratory-confirmed cases were sent to the National Reference Laboratory for the Control of Viral Infections. According to the data of phylogenetic analysis, all the strains belonged to the B3 genotype of the genetic line «MVs / Kabul. AFG / 20.14 / [B3]», with the exception of one sample from the North Kazakhstan region, which was assigned to the D8 genotype of the genetic line «MVs / Gir Somnath.IND / 42.16 / [D8]». According to these results, no new genotypes were imported into the territory of the Republic of Kazakhstan; genotype B3 variant of the virus began to circulate actively since the end of 2018 and continued circulation throughout 2019 determining the outbreak.

7. Analysis of the Measles outbreak response

With the Resolution of the Chief State Sanitary Doctor of the Republic of Kazakhstan No. 1 dated March 28, 2019 «On the organization and conduct of sanitary-anti-epidemic and sanitary-preventive measures for measles» supplementary MMR immunization activities were implemented among:

• children aged 9 - 10 months with a re-vaccination at 12-15 months;

• medical workers under 40 years old;

• contacts of measles cases under 30 years old.

During the 2019 outbreak, 262,628 children aged 9-10 months were vaccinated reaching a coverage of 89.2%. Moreover, 100% of medical workers and 96.6% of measles contacts were provided with MMR (11,275 people).

To increase MCV coverage among adults, the Decree of the Chief State Sanitary Doctor No. 6-PGVr dated 08/07/2019 «On additional immunization against measles and rubella for persons aged 20 to 29 years in the Republic of Kazakhstan», established the immunization of persons aged 20-29 years with a bivalent vaccine against measles and rubella (MR).

During 2019, coverage reached in the age-group 20-29 years was 90.3%.

Table 9 details the results of Measles Supplementary Immunization activities carried out at the national level in the frame of the outbreak response.

Table 9. *Operational details and results of MMR SIAs implemented in Kazakhstan, 2019-2020.*

Dates of the SIAs	Targeted group	Size of the target population	Number of people vaccinated and coverage (%)
01.04.2019-01.04.2020	9-10 months	262,628	234,142 (89.1%)
01.04.2019-01.04.2020	Medical professionals	73,148	73,148 (100%)
01.04.2019-01.04.2020	Contacts of measles cases	11,666	11,275 (96.6%)
15.09.2019-31.12.2019	20-29 years	1,814,372	1,656,427 (90.3%)

To better response to the outbreak, medical workers were trained during an annual scientific and practical conference on topical issues of immunization. According to the conference program, training focused on measles epidemiology, strengthening surveillance, ensuring high-quality epidemiological investigation, laboratory analysis, and risk communication. Overall, only 230 people were trained, including epidemiologists, infectious disease specialists, pediatricians, general practitioners, laboratory workers, teachers of universities and colleges.

Table 10 provides a summary of measles outbreak response measures implemented by each institution of the Republic of Kazakhstan.

Table 10. *Measles Outbreak response measures implemented by each institution of the republic of Kazakhstan.*

Activity	Responsible institution	Timing
Organizational and preventive measures for measles		
Obtaining approval from the Advisory Commission on Immunization to vaccinate children aged 9 months with MCV (until the epidemiological situation stabilizes)	DPHP	03.01.2019
Ensure that measles diagnostic workshops are held at different levels of care, reaching all health workers	DOHO UZ	05.01.2019
Conduct constant supervision on the organization and implementation of anti-epidemic measures	COOP	Daily
Strengthen supervision on (a) the reported coverage of routine MMR vaccination, (b) the cold chain management	COOP DOHO	Monthly
Measles' contacts management; ensuring their vaccination	UZ DOHO	Constantly
Interaction with international organizations		
Request of support to the WHO and CDC	COOP	29.12.2018
Establish interaction with the ministries of health of the Commonwealth of Independent States (CIS) countries on the state of the measles epidemiological situation and measures taken	COOP	Monthly

Activity	Responsible institution	Timing
Organization and implementation of MCV SIAs		
Calculate the country MCV need taking into account the increase in morbidity and the need for additional funds for the purchase of additional MCV doses	COOP	05.01.2019
Request for measles vaccine to SK-Pharmacia LLP	COOP	05.01.2019
Distribute vaccine to Oblast/City health departments	COOP	05.01.2019
Organize vaccination of children aged 9 months of age	UZ COOP	01.04.2019
Organize SIAs for people aged 20-29	COOP DOHO	15.04.2019
Conduct weekly monitoring of SIAs	COOP SPCSE UZ	Constantly
Organization of measles case management		
Ensure timely collection and delivery of biological samples from measles patients to the laboratory in compliance with transportation requirements	UZ	When registering a case
Ensure the delivery of biological samples from measles patients to the National Reference Laboratory for the Control of Viral Infections for molecular genotyping	UZ	When registering a case
Ensure the provision of qualified medical care to patients with measles in medical organizations, and ensure staff training	UZ Astana	Constantly during the epidemic
Consider the issue of providing methodological and practical assistance to specialists of infectious diseases in the hospital of Astana	Astana Medical University	For the period of the epidemic
Ensure an increase bed capacity for 100% of patients with suspect measles with the re-organization of hospitals in the city of Astana	UZ Astana	For the period of the epidemic
Ensure monitoring of patients with measles after discharge from the hospital on an outpatient basis	UZ Astana	Constantly
Organize a separate admission for patients with high fever and rash in multidisciplinary hospitals in Astana	UZ Astana	For the period of the epidemic
Consider a temporary suspension of admissions of patients to the oncohematology department and referring children for hospitalization to other hospitals of the republic	NCMD	For the period of the epidemic
Risk communication		
Strengthen advocacy on the role of vaccination in the prevention of infectious diseases, including measles	NCPH UZ DOHO	Constantly
Strengthen communication with parents who refuse vaccinations	NCPH UZ DOHO	Constantly
Prepare videos about the benefits of vaccine prevention to be shown in public places, social networks, medical and educational organizations	NCPH DOHO	01.02.2019

Table 10. **LEGEND:**
COOP - Committee for Public Health Protection of the Ministry of Health of the Republic of Kazakhstan
NCPH - National Center for Public Health of the Ministry of Health of the Republic of Kazakhstan
DPHP - Department of Public Health Policy of the Ministry of Health of the Republic of Kazakhstan
DOHO - Departments of Public Health Protection of the Committee for Public Health Protection of the Ministry of Health of the Republic of Kazakhstan regions, Astana, Almaty, Shymkent
UZ - Regional Health Department, Shymkent, Almaty, Public Health Department of Astana
NCMD - Branch of the Corporate Fund «University Medical Center» «National Scientific Center for Motherhood and Childhood»
SKF - SK-Pharmacy LLP
SPCSE - Scientific and Practical Center for Sanitary and Epidemiological Expertise and Monitoring

7.1 Surveillance system performance during the outbreak

Out of the 16,871 cases suspected measles cases occurred during the 2019 outbreak, 13,326 (79.9%) were laboratory-confirmed.

Table 11 shows the results of measles surveillance indicators. Overall, optimal performances were reported during the measles outbreak in terms of epidemiological and laboratory surveillance.

Table 11. *Epidemiological and laboratory surveillance performances of measles during the 2019 outbreak.*

Indicator	Level reached (%)
Timeliness of reporting (national level)	100
Completeness of reporting (national level)	100
Proportion of laboratory confirmed cases	79.9
Sampled collected and tested	100
Rates of excluded (rejected) cases	17,1
Source of infection identified	100

PART B. ROOT CAUSES ANALYSIS OF THE MEASLES OUTBREAK

The root causes analysis (RCA) of the measles outbreak occurred in Kazakhstan in 2019-2020, is carried out following the 2020 WHO Guidance on Measles outbreak preparedness and response (draft 2020). The RCA is conducted through a series of "why" questions, where the answer to each "why" question leads to another "why" question that reveals the chain of causality down to the most fundamental causes.

According to the WHO Guidance, the analysis of a measles outbreak root causes includes the assessment of the following components:

Surveillance, *i.e. the analysis of:*

• inadequate/insensitive and/or untimely case detection and notification

• inadequate and/or untimely case investigation (completion of case investigation form, specimen collection and/or shipping to the national measles laboratory)

• Inadequate and/or untimely specimen testing and providing results to all levels

Response, *i.e. the analysis of:*

• inadequate and/or untimely searching, identifying and investigating additional cases through intensified surveillance

• inadequate and/or untimely source identification and contact tracing for those that may have infected the case and those that the case may have infected

• inadequate and/or untimely isolation for cases and quarantine measures for contacts

• inadequate and/or untimely Outbreak response immunization (ORI) activities with respect to target age-group, target area, type of ORI

Immunity gaps, *that are categorized in:*

► **Provider-based reasons for Vaccine failure, that evaluate aspects as cold-chain management, vaccine quality, administration practices, and may include:**

• administration of spoiled vaccine due to cold chain defects or inappropriate vaccine handling practices, including exposure to sunlight

• administration of an insufficient dose (i.e. volume) of reconstituted vaccine

• administration of expired vaccine

► ***Client-based reasons for Vaccine failure that*** evaluate host factors that are not modifiable as immunity and biological-immunocompromising issues, and may include:

• primary vaccine failure due to vaccination of individuals who biologically do not produce an adequate immune response because of:

1. immaturity of the immune system

2. maternal antibody

3. congenital or acquired immunodeficiency disorders

4. recent administration of high dose steroids, immunosuppressive drugs, or antibody containing blood products, including immunoglobulin

• secondary vaccine failure that occurs with waning antibody and T-cell mediated immunity levels among previously vaccinated and protected individuals after a long period of time

► ***Policy-based reasons for Failure to vaccinate,*** as specific policies such as the national vaccination schedule and eligibility criteria for vaccination.

► ***Policy-based reasons for Failure to vaccinate,*** which includes the capacity of Oblasts/Cities to provide immunizations; as the frequency and location of immunization clinics, the use of mobile teams, the

capacity to invite eligible persons, the availability of enough amount of vaccines, the implementation of communication campaigns (demand generation), false contraindications that determines missed opportunities, sessions not being planned and/or conducted, etc.

► ***Client-based reasons for Failure to vaccinate,*** which include practical obstacles as the distance from immunization services and the capability to reach them, lack of knowledge regarding vaccination, vaccine hesitancy due to complacency, convenience and or confidence.

1. Material and Methods

Because the Measles outbreak affected the whole territory of the Republic of Kazakhstan, the RCA included all the sub-national divisions, and employed a mixed methods study design with the analysis of a wide range of written documents collected by the UNICEF Country Office of Kazakhstan, in depth key informant interviews and surveys with different stakeholders, including groups of parents' pro-vaccination and vaccine hesitant.

1.1 Documents desk review

Documents aimed to assess root causes related to the **Surveillance** component included: national legislations on measles surveillance, case definition and classification; standard operating procedures (SOPs) on public health management of measles cases and their contacts; SOPs on sample collection, transportation and laboratory analysis; SOPs for outbreak investigation; surveillance performance indicators; SOPs defining the measles surveillance reporting mechanism and related tools (i.e. investigation forms quality).

Gaps in the **Response** component were assessed through the analysis of documents pertaining to SIA monitoring reports including MMR-ORI coverage by Oblast/City and target age-groups. Timeliness and appropriateness of legislations employed for the outbreak response was also evaluated (i.e. measles outbreak response measures implemented by each institution of the republic of Kazakhstan), together with response performance monitoring reports.

Reviewed documents also included information for **Provider-based reasons for Vaccine Failure,** as the analysis of available legislations and SOPs for appropriate vaccine cold-chain and stock management, vaccine handling and administration practices, etc.

The analysis of available measles seroprevalence data was used to assess root causes related to **Client-based reasons for Vaccine Failure.**

Routine immunization MMR coverage data were analyzed over the time, at the subnational level and by age-group, to assess **Provider-based reasons for Failure to Vaccinate,** together with surveillance and outbreak data to evaluate the affected ages and their vaccination status.

The MoH Immunization Plan was analyzed to identify **Policy-based reasons for Failure to Vaccinate,** together with available micro-plans to assess if the components of the MMR immunization programme at the local level have been effectively planned, including workforce capacity, communication campaigns, etc.

1.2 Surveys, interviews and focus groups

Data from a survey conducted among health departments of Oblasts/Cities aimed to identify gaps in the implementation of MMR SIAs were analyzed to identify **Provider-based reasons for Failure to Vaccinate** (i.e. the lack of human resources to ensure immunization sessions, the capacity to invite eligible persons for immunization, shortage of vaccines, etc.) and **Provider-based reasons for Vaccine Failure** (i.e. cold-chain defects, power outages on vaccine storage, etc.).

Data on **Client-based reasons for Failure to Vac-**

cinate were analyzed from a survey conducted by the Ministry of Health of the Republic of Kazakhstan through a questionnaire administered by Oblast/Cities health department to parents, that sought for reasons behind parental refusal of vaccines.

Focus groups were conducted with national-level stakeholders and Oblast/City managers of health departments, involved in policy-making, design, planning, and implementation of the immunization programme. Mover, interviews were carried out with field health-staff involved in vaccinations and measles surveillance, as well as with groups of vaccine-hesitant parents and groups of parents' pro-vaccination.

Focus group with the national level healthcare managers, aimed to assess gaps in the **surveillance** and **response** components, including issues in reporting mechanisms. **Provider-based reasons for Failure to Vaccinate** that involved the national level were also assessed during focus groups with national healthcare managers, as the timely and amount-appropriate delivery of vaccines to Oblast/Cities health departments, the planning and implementation of nation-wide communication campaigns for demand generation, etc.

Also national-level Provider-based reasons for Vaccine Failure were evaluated during focus groups with national healthcare managers, i.e. cold chain and storage defects that affected the national vaccine warehouse or that occurred during vaccines' transportation to Oblast/City health departments, etc.

Managers of Oblast/City health departments were interviewed in regard to the level of training

2. Results

Figures 7 and 8 summaries root causes of the 2019-2020 measles outbreak and chapters from 2.1 to 2.7 provides deep insights on each analyzed component. A mix of root causes contributed to the outbreak determining low MMR coverage levels that remain undetected due to a chronic problem of over-reporting that affect all the sub-national divisions. Such root causes have been acknowledged and concurred during the confirmatory focus group with experts from the WHO and CDC country office of Kazakhstan.

Figure 7. *Fishbone diagram of root causes determining the 2019-202 Measles outbreak in Kazakhstan*

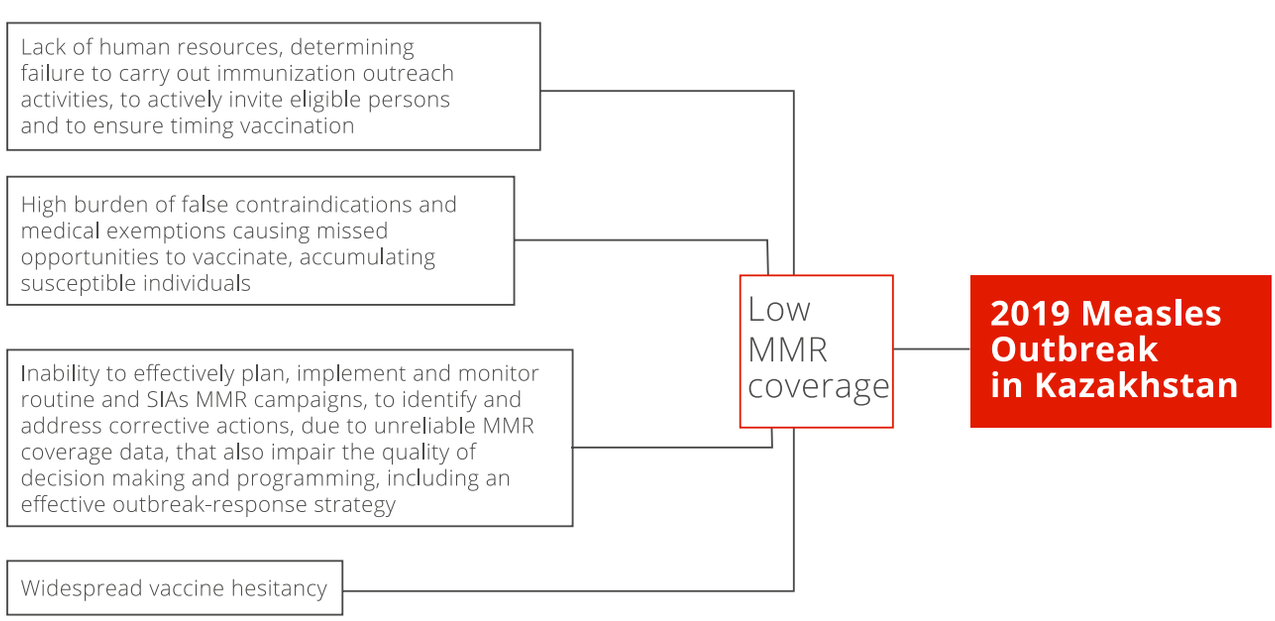
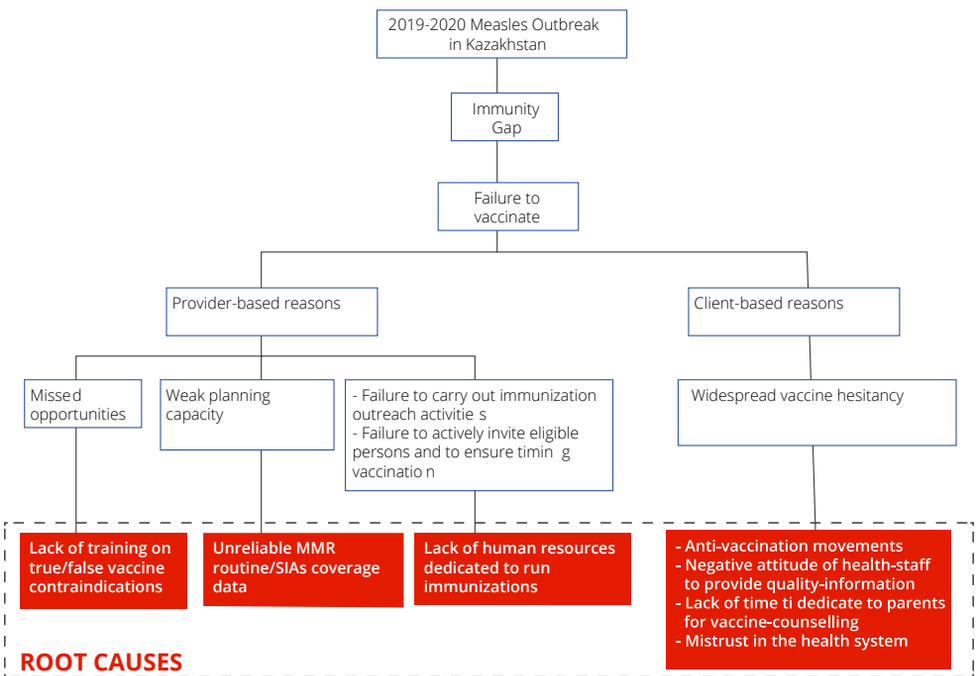


Figure 8. *Measles Outbreak Root Cause Analysis Flow Chart.*



Root causes pertained to **Provider-based reasons for Failure to Vaccinate and Client-based reasons for Failure to vaccinate:**

1. Lack of human resources dedicated to run immunizations, that determines:

• Failure to carry out immunization outreach activities

• Failure to actively invite eligible persons and to ensure timing vaccination

2. High burden of false contraindications and medical exemptions determining missed opportunities to vaccinate, accumulating susceptible individuals. This issue is due to a lack of training on true/false vaccine contraindications.

3. Weak capacity to effectively plan and monitor routine and SIAs MMR programme/campaigns, to identify and address corrective actions, due to unreliable MMR routine/SIAs coverage data, that also impair the quality of decision making and programming, including an effective outbreak-response strategy.

4. Widespread vaccine hesitancy, fueled by:
Mistrust in the health system that leads parents to get information about immunizations on the web where the anti-vaccination sites are masters and there is poor presence of official institutions. This mistrust in the health system is due to reasons mainly related to the negative attitude of health-staff to provide quality-information and lack of time to dedicate to parents for vaccine-counselling, that in turn is due to a lack of training of healthcare workers on communication skills and a lack of human resources that determine low quality of work, a high rate of stress and no space for vaccine-counseling.

2.1 Surveillance component

In response to the Measles outbreak, the MoH of Republic of Kazakhstan reinforced current laws, defining procedures, roles and responsibilities for measles surveillance, investigation and response (e.g. Rules for registration, keeping records of cases of infectious, parasitic, occupational diseases and poisoning, and the Rules for reporting on them (September 16, 2019 No. ҚR DSM-127).

According to data provided in chapter 7 (page 15), optimal epidemiological and laboratory surveillance performances were reached with ≃80% of measles cases laboratory confirmed, 100% of timeliness and completeness of reporting, all sources of infection identified, and 100% of collected samples that were tested.

The Republic of Kazakhstan also adopt international standard case definitions for measles (chapter 3.1 page 5), together with SOPs for case/outbreak investigation and laboratory confirmation (chapter 3.2 page 8).

Focus groups conducted with national, mid-level (i.e. Oblasts/Cities) and field stakeholders, indicated that infectious disease surveillance is well-conducted in the country as confirmed by the ability to detect the outbreak, to collect and analyze case-based data by age, place and immunization status, as well as to collect biological samples for laboratory-confirmation and to carry out genotyping analysis to assess the origin of the outbreak (see chapter 6 page 15).

2.2 Response component

As reported in table 10 (page 18), in response to the measles outbreak, The Government of the Republic of Kazakhstan implemented specific laws in line with the IHR (see references 6,7,13,14) and comprehensive work plans indicating roles and responsibilities to conduct outbreak response activities and related-timelines.

Moreover, with the Resolution of the Chief State Sanitary Doctor of the Republic of Kazakhstan No. 1 dated March 28, 2019 «On the organization and conduct of sanitary-anti-epidemic and sanitary-preventive measures for measles», MMR SIAs were implemented to target the most affected age-groups.

First MMR dose was anticipated at 9-10 months (upon permission of the Advisory Commission on Immunization) to reduce the high incidence rate among children under 1 year, that are not targeted by the routine MMR immunization programme. Following WHO recommendations, these children were revaccinated at 12-15 months. In both age groups a high level of coverage was achieved, with 89.1% and 99.2% among children aged 9-10 and 12-15 months, respectively. Moreover, high MCV coverage rates were reached among medical professionals (100%), contacts of measles cases (96.6%) and people aged 29-29 years (90.3%).

Despite the high level of MMR coverage reached thanks to the implemented SIAs, the outbreak was only partially controlled (fig 5 page 16), and the survey conducted among health departments of Oblasts/Cities to assess SIAs capacity, revealed important gaps that seems to be in contrast with the postivie MMR coverage performances reached (table 12):

- Four health departments report lack of human resources: Aqmola, Almatinskaya, East-Kazakhstan, West-Kazakhstan

- Only two health departments (Aqmola and Aktobe) conducted outreach immunizations activities through mobile immunization teams

- Only four health departments (Shymkent city, West-Kazakhstan, Kyzylorda, Pavlodar, Nur-Sultan) report to have the capacity to invite eligible persons for immunization, and only one (Mangystau) reports to be able to ensure compliance with timing of the immunization schedule. Moreover, only two health departments conduct AEFI surveillance (Aktobe and Zhambyl), and other two stated they have not received the necessary amount of vaccines (Aqmola and North-Kazakhstan).

Table 12. *Result of the MMR SIAs questionnaire administered to Health Departments of Oblasts/cities (in red critical situations).*

Oblast/ City / Question	Aqmola	Aktobe	Almaty	Atyrau	East-Kazakhstan	Zhambyl	West-Kazakhstan	Karaganda	Kostanai	Kyzylorda	Mangystau	Pavlodar	North-Kazakhstan	Turkestan	Almaty city	Nur-Sultam city	Shymkent city
Lack of Human Resources	Yes	No	Yes	No	Yes	No	Yes	No	No	No	No	No	No	No	No	No	No
Outreach immunizations activities	Yes	Yes	No	No	No	No	No	No	No	No	No	No	No	No	No	No	No
Active invitation of eligible persons for immunization	No	No	No	No	No	No	Yes	No	No	Yes	No	Yes	No	No	No	Yes	Yes
Ensuring compliance with vaccine time intervals	No	No	No	No	No	No	No	No	No	No	Yes	No	No	No	No	No	No
Conduct AEFI monitoring	No	Yes	No	No	No	Yes	No	No	No	No	No	No	No	No	No	No	No
Adequate supply with the necessary amount of vaccines	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes
Communication activities to promote vaccine campaigns	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Communication activities targeting vaccine hesitant parents	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Presence of a management group to coordinate immunization activities	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes

The above survey' findings were confirmed during focus groups, where stakeholders from Oblast/City health departments reported that particularly in rural areas there are limited supplies and facilities to carry out the immunization programme; in these areas there is also a shortage of human resources. National stakeholders themselves reported during focus groups of being not confident in MMR immunization data received from the sub-national level that may over-report to reach established vaccine-coverage targets due to fear of penalties.

Additionally, as showed in chapter 7 (page 17), a gap in the response was found in the training of health-staff in charge to conduct measles epidemiological investigation, case management, laboratory procedures and risk communication activities, with only 230 people trained during 2019.

2.3 Provider-based reasons for Vaccine Failure

As reported in chapter 4.2 (page 13), The Rules for "storage, transportation and use of prophylactic (immunobiological, diagnostic, disinfectant) drugs" (Order of the Minister of National Economy of the Republic of Kazakhstan dated February 4, 2015 No. 7), provides detailed SOPs and requirements for vaccine storage and transportation. The order details quality criteria to run immunizations, including structural requirements, equipment, professionalisms needed, procedures for cold-chain maintenance, vaccine quality check, injection safety and waste management.

Moreover, from all-level of stakeholders' consultation, it was reported that no cold-chains defect occurred in 2018-2019. Interviews with field health-workers also revealed that they are confident with vaccine storage and cold-chain management procedures, quality check and administration practices.

2.4 Client-based reasons for Vaccine Failure

To assess this aspect, data from an available Measles seroprevalence survey conducted in 2019 among 3,685 people were analyzed. The survey revealed low prevalence of measles IgG, being:

- 79.2% in Almaty, Nur-Sultan, Shymkent, Mangistau region

- 82.9% among pregnant women and mothers of babies under 1-year-old

- 73.9% among teenagers aged 15-19 years

Taking into account that detailed information on the study were not available, as the precise period of survey-implementation, SOPs for collection and analysis of biological materials, sample representativeness, sample size and sampling procedures, data collection/analysis methods etc., it is however worth noting that these findings contrasts with the high MMR coverage rates reported by all territorial sub-divisions of Kazakhstan both in the frame of the routine MMR immunization programme and in the frame of MMR SIAs, confirming the clue of the over-reporting issue.

2.5 Policy-based reasons for Failure to Vaccinate

The Republic of Kazakhstan has an articulated body of laws to address all the aspects of the immunization programme, including vaccine procurement, cold-chain and waste management, AEFI surveillance, accreditation of immunizations clinics, as well as a National Immunization Plan.

The Order of the Government of the Republic of Kazakhstan dated December 30, 2009 No. 2295 defines the legal framework for the implementation of the immunization programme in the Republic of Kazakhstan indicating roles and responsibilities.

Concerning the MMR vaccination schedule, Kazakhstan follows international recommendations providing the first dose at 12-15 months and the second dose at 6 years. During the 2019 outbreak, due to the high incidence among children <1 year of age, the first MMR dose was anticipated at 9-10 months (upon permission of the Advisory Commission on Immunization), and these children were revaccinated at 12-15 months, reaching in both age-groups high coverage rates.

Nevertheless, due to unreliable MMR coverage data, Policy-based reasons for Failure to Vaccinate may have been occurred and caused by the inability to detect territories with low coverage levels and to address corrective actions with targeted immunization activities. Unreliable MMR coverage data may have also impaired and currently impairing, the quality of decision making and programming, including an effective outbreak-response strategy.

2.6 Provider-based reasons for Failure to Vaccinate

Immunization coverage time-trends data for both MMR-1/2 indicates that top performances have been achieved, even at the Oblast/City levels (figures 3 and 4; table 6; pages 14-15). Also during the MMR SIAs high coverage rates were reported among all targeted age-groups. So, from this data do not emerge low-immunization coverage levels among specific-population pockets and territories that may have contributed to the outbreak.

Despite this, it worth noting that a chronic over-reporting problem is present with the majority of Oblasts/Cities declaring MMR coverage rates close-to or over 100% (table 6 page 15). As said, this issue was confirmed during interviews with national stakeholders that are not confident in immunization coverage data received from the sub-national level. Field health workers did not state openly to over-report coverage data but they replied indirectly underling that the quality of data-reporting is burdened by double data entry work (paper and electronic) that increases the risk of errors.

Other clues confirm the over-reporting problem, as the low seroprevalence of measles IgG (chapter 2.4 page 27), and the important gaps related to SIAs capacity revealed from the survey conducted among health departments of Oblasts/Cities, that contrasts with the high MMR coverage rates reported from themselves.

Moreover, the high burden of vaccine failures observed across all age-groups also among people who received 2 MMR doses (table 7 page 16), suggest for a chronic over-reporting issue more than for provided-based reasons for vaccine failures (i.e. cold-chain and/or storage defects) that are instead episodic rather than chronic.

The survey conducted by the MoH among health departments of Oblasts/Cities to assess SIAs capacity (table 12, page 26), revealed several Provider-Based reasons for Failures to Vaccinate, as the lack of human resources, incapability to run immunization outreach activities, to actively invite eligible persons and to ensure timing vaccination. These issues were confirmed during focus groups with field vaccinators, that reported the problem of human resources shortage that determines low quality of work and high rate of stress / burn out. The lack of human resources, has also an impact on the quality of communication with parents and time to dedicate to them for vaccine-counselling, as well as on the quality of data-reporting which is also burdened by double data entry work (paper and electronic) that increases the risk of errors. Field health workers also confirmed problems in giving immunization on time due human resources insufficiency.

Focus groups with both parents' pro-vaccination and vaccine-hesitant revealed that they never experienced vaccine shortages that caused the impossibility to vaccinate their children, or the absence of planned immunization sessions. This point was also confirmed during focus groups with vaccine providers, were did not emerge vaccine-shortage issues. Nevertheless, parents stated to have experienced delays in receiving timely MMR and other vaccines according to the immunization schedule.

Another reason for provider-based failure to vaccinate emerged from data provided by the MoH showing a growing number of those unvaccinated due to medical contraindications. According to these data, 36,740 temporaries and 581 permanent contraindications were reported for the MMR vaccine in 2019. This suggests that general practitioners and pediatricians over-release medical exemptions, and that field-vaccinators tend to postpone immunizations due to lack of knowledge on true/false contraindications.

2.7 Client-based reasons for Failure to Vaccinate

According to data provided by the MoH of Kazakhstan, in 2019, 16,998 vaccine-refusals have been registered in the country. The largest proportion of refusals regarded children under the age of 1 year (62.8%), followed by children in the age group 1-2 years (13.5%), 3-5 years (14.2%), 6-15 years (9.2%), and over 16 years (0.3%). The main reasons for refusals were personal (51.8%) and religious (30.8%) beliefs. Most of refusals were recorded in Shymkent city (n=979) that also registered the highest attack rate during the measles outbreak. In addition, 10.8% of interviewed parents expressed distrust on immunizations, while 6.5% of those who refused vaccination indicated they received negative information through the media (internet resources, social-networks, TV). This finding was confirmed during focus groups with all level stakeholders, that in particular underlined the internet-channel as the main one to spread miss-information about vaccinations.

Practical obstacles in reaching immunization clinics did not emerge from interviews with parents, whilst a widespread mistrust in the health system was reported even from pro-vaccination parents. They underlined communication problems from vaccine-providers with limited time for counseling, lack of info and open discussion about possible side effects, as well as uncertainty of responsibilities and procedures in case of AEFI. This mistrust in the health system, brings parents to get information on the web where there is poor presence of official institutions and were anti-vaccination web sites are masters.

Parents asked for more commitment from the health system in providing full information on immunizations, together with availability of public data on adverse effects, documentation and clarification about legal responsibility in case of AEFI. This widespread vaccine hesitancy among population contrasts again with the high MMR routine and SIAs coverage rates reported by all Oblasts/Cities, feeding the clue that the over-reporting' problem actually masks a low protection of the population against measles.

3. Conclusion and recommendations

According to results emerged from the RCA, the measles outbreak occurred in the Republic of Kazakhstan during 2019-2020 was influenced by a combination of factors that negatively affected MMR coverage, where real rates are masked by a chronic problem of over-reporting from Oblasts/Cities. These unreliable MMR coverage data also impaired an effective outbreak-response strategy, and the capacity to effectively plan, implement and monitor routine and SIAs MMR programme/campaigns, to identify and address corrective actions, ultimately affecting negatively the quality of decision making and programming.

Many Oblasts/Cities in the country also failed to establish good governance for providing effective and quality immunization services, with lack of human resources and training that determined the inability to carry out outreach immunization activities, to actively invite eligible persons and to ensure timing vaccinations.

Additionally, a growing vaccine hesitancy across the country negatively affected MMR coverage. This seems to be due to a mistrust in the health system (also from pro-vaccination parents), that is fueled by different reasons, including lack of communication skills from vaccinators, insufficient time for counselling to provide the necessary information, and to address parents' fears, false beliefs and concerns. This mistrust in the health system brings parents to get information on the web where they can incur in false information related to the vaccines' safety, myths and misconceptions, and where there is poor presence of institutions to provide evidence-based and clear information about vaccinations.

Moreover, have been emerged from the RCA that health professionals discourage parents to vaccinate their children due to false contraindications, determining an accumulation of susceptible individuals. This is complemented with poor in-country capacity to prepare for and respond in immunization-related crisis situations, which diminishes public trust in the health system.

Table 13 summarizes the root causes that negatively affected MMR coverage levels, determining the 2019-2020 measles outbreak in Kazakhstan, together with potential recommendations to address them.

Table 13. *Measles outbreak Root Causes and recommendations.*

Root Cause	Recommendation
Lack of human resources dedicated to run immunizations	Conduct a Human Resource Gaps Analysis and develop a National Health Workforce Plan, by using the different tools provided by the WHO (https://www.who.int/hrh/tools/planning/en/) in order to define the type, amount and distribution of health-workers involved in the immunization programme.
Weak capacity to effectively plan and monitor routine and SIAs MMR programme/campaigns due to unreliable immunization coverage data	• Conduct an independent immunization coverage survey following the 2018 WHO guidance on Vaccination Coverage Cluster Surveys (https://www.who.int/immunization/documents/who_ivb_18.09/en/), which should also assess for determinants of vaccination • Develop a strategic plan for an electronic-based immunization monitoring system, linked with birth registries and other population-denominator databases
Missed opportunities	• mmediately conduct trainings targeting the Standard Competencies Framework for the Immunization Workforce, with particular focus on true/false vaccine-contraindications and communication skills. These trainings must be provided to the largest possible number of vaccinators, pediatricians and general practitioners. An annual refresh training should be also conducted with an official and certified assessment. • Immediately prepare and disseminate a SOP and/or an algorithm on true false contraindication, preparing and conducting training on this SOP • Based on the Workforce Plan, develop a training programme aimed to address the largest possible number of field health-workers involved in providing vaccinations.
Widespread vaccine hesitancy	Develop a national communication plan on immunization, including strategies to increase and improve the presence of institutions on the web, mainstreaming demand generation for immunization into health programs and budgets, capacity building of health professionals on interpersonal communication on immunization.

To address the root cause related to the lack of human resources dedicated to run immunizations that determined the inability to carry out outreach immunization activities, to actively invite eligible persons and to ensure timing vaccinations, it is necessary to Conduct a Human Resource Gaps Analysis and develop a National Health Workforce Plan in order to define the type, amount and distribution of health-workers involved in the immunization programme. The WHO provides different tools to help countries to develop a comprehensive Health Workforce Plan (https://www.who.int/hrh/tools/planning/en/).

The growing number of those unvaccinated due to medical contraindications, that determines an accumulation of susceptible individuals, needs to be immediately addressed through targeted training programmes focused on true/false vaccine-contraindications. These trainings must be provided to the largest possible number of vaccinators, pediatricians and general practitioners. An annual refresh training should be also conducted with an official and certified assessment.
Moreover, once developed the National Health Workforce Plan, annual trainings (with assessment and certification) must be provided targeting the WHO Standard Competencies Framework for the Immunization Workforce and focusing again on true/false vaccine-contraindications, as well on communication skills related to vaccine-counselling. Reliable MMR coverage data are of vital importance to effectively plan, implement and monitor routine and SIAs MMR programme/campaigns, to identify and address corrective actions, as well as to plan and implement an effective outbreak-response strategy. For this reasons a first effort should be done to have a quick picture of the real MMR-1/2 coverage in all Oblasts/Cities.

To reach this goal, the 2018 WHO guidance on Vaccination Coverage Cluster Surveys (https://www.who.int/immunization/documents/who_ivb_18.09/en/) should be followed, assessing also for determinants of vaccination.

After having obtained a first-picture from the survey of the real immunization coverage, a long-term strategy to monitor immunization coverage (and so the EPI programme) should be planned. This mainly consist in developing an interconnected national and sub-national electronic-based immunization monitoring system, linked with birth registries and other population-denominator databases. A plan to train health-workers that will use the electronic-based immunization monitoring system, needs also to be developed and implemented.

In parallel to the above described recommendations, a national communication plan on immunization, including strategies to increase and improve the presence of institutions on the web, needs to be developed in order to address the widespread vaccine-hesitancy. To reach this goal, several gold-standard guidance can be followed, provided by different organizations, i.e. UNICEF (https://lnct.global/wp-content/uploads/2019/11/UNICEF-ECARO-Immunization-Resource-Pack.pdf; https://www.unicef.org/eca/media/8566/file/interpersonal-communication-immunization.pdf), ECDC (https://www.ecdc.europa.eu/en/publications-data/communication-toolkit-immunisation-how-increase-immunisation-uptake), etc.

The communication plan has the objective to build and maintain public trust and credibility on the health system with the aim to increase vaccine uptake.

The hereby Root Causes Analysis has some limitations related to possible reporting biases from different stakeholders regarding the occurrence of provider-based reasons for vaccine failure as local vaccine supply and cold-chain defects. Nevertheless, all levels stakeholders seemed to be open to report other issues as the lack of human resources, the inability to carry out outreach immunization activities, to invite eligible children in due time, etc. Therefore, is present a good degree of credibility regarding the answers provided from surveys, interviews and focus groups.

Another limit of the RCA is related to the impossibility to perform in-country visits due to the current COVID-19 pandemic. This could have allowed to check health-facility registers in order to identify evidence of low MMR coverage, as well as vaccination report forms and EPI registration books to determine MCV1 coverage and drop-out rates. In-country visits could have allowed these data to be cross-checked with other birth data sources such as birth registries and family planning records in order to assess the number of potentially left out (i.e., never vaccinated) children, and actual coverage by birth cohort, EPI target population (i.e., denominator). In-country visits could also have allowed to review stock ledgers, vaccination session records, staff attendance, etc. in order to detect other Provider-Based reasons for Failure to Vaccinate. Also the analysis of surveillance registers may have allowed to identify gaps of this component related to timeliness and completeness of case-based measles surveillance data, sensitivity of the surveillance system and the quality of investigation and response to measles cases. Finally, in-country visits could have allowed to review health facility outpatient and inpatient logbooks or registers for suspected measles cases and comparing them with the list of cases reported, noting any discrepancies.

Despite such limits, the in depth analysis of a wide range of documents collected by the UNICEF Country Office of Kazakhstan together with interviews and surveys with different key stakeholders, allowed to identify potential root-causes that negatively affected MMR coverage levels, determining the measles outbreak. On these root causes, costed action plans need to be built in order improve the immunization programme in the Republic of Kazakhstan, avoiding future VPDs outbreaks, including measles.

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