Electronic Journal of General Medicine
2023, 20(1), em429
e-ISSN: 2516-3507
https://www.ejgm.co.uk/

MODESTUM

Original Article

OPEN ACCESS

Epidemiological characteristics and seasonal variation of measles, pertussis, and influenza in Kazakhstan between 2010-2020 years

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Citation: Yerdessov S, Abbay A, Makhammajanov Z, Zhuzzhasarova A, Gusmanov A, Sakko Y, Zhakhina G, Mussina K, Syssoyev D, Alimbayev A, Gaipov A. Epidemiological characteristics and seasonal variation of measles, pertussis, and influenza in Kazakhstan between 2010-2020 years. Electron J Gen Med. 2023;20(1):em429. https://doi.org/10.29333/ejgm/12621

ARTICLE INFO

Received: 09 Oct. 2022

Accepted: 01 Nov. 2022

ABSTRACT

Background: Vaccine-preventable diseases such as pertussis, measles, and influenza remain among the most significant medical and socioeconomic issues in Kazakhstan, despite significant vaccination achievements. Thus, here we aimed to analyze the long-term dynamics and provide information on the current epidemiology of pertussis, measles, and influenza in Kazakhstan.

Methods: A retrospective analysis of the long-term dynamics of infectious diseases was carried out using the data from the statistical collections for 2010-2020 and the Unified Payment System from 2014 to 2020.

Results: During the 2010-2020 years, the long-term dynamics show an unequal distribution of pertussis, measles, and influenza-related morbidity. In comparison with earlier years, registration of infectious disease was the highest in 2019 and 2020. The incidence cases among registered infectious diseases in 2019 were: pertussis-147, measles-13,326, and in 2020: influenza-2,678. High incidence rates have been documented in Pavlodar, North Kazakhstan, Mangystau regions, and the cities of Shymkent and Nur-Sultan. The incidence varies depending on the seasonality: pertussis (summer-autumn), measles (winter-spring), and influenza (mostly in winter).

Conclusion: The findings highlight the importance of focusing more on the characteristics of the epidemic process of vaccine-preventable diseases in order to assess the effectiveness of implemented measures and verify new routes in strengthening the epidemiological surveillance system.

Keywords: communicable diseases, epidemiology, vaccine-preventable diseases, Kazakhstan

INTRODUCTION

Understanding the epidemiology of disease begins with characterizing the geological transmission of infection within a country or area, which helps health services to identify epidemic/endemic zones and susceptible groups at risk. Also, climate drivers may play an important role in the dynamics, distribution, and transmission of the contagious diseases by influencing the evolution of the pathogen and also affect the host environment and its susceptibility. Hence, they can be regarded as early warning signals for epidemics of contagious diseases [1, 2], which enables disease comparisons, analysis of global trends, and identification of climatic factors. Climate can be used to improve our assessment of intercessions for climate-sensitive diseases and human wellbeing [3-6], not just to determine the geographical and sporadic distribution of infectious diseases [7], but also as a plausible determinant of inter-annual inconstancy, including epidemics [8-11], and long-term trends [12, 13].

Vaccination, recognized as one of the most significant public health triumphs [14], has significantly reduced morbidity and death from vaccine-preventable diseases [15]. However, illnesses with cyclical patterns of action such as measles [16-19], pertussis [16], and influenza [20], remain a topic of public health discussion and study due to substantial morbidity and associated healthcare expenditure, despite widely available of vaccines and established public immunization guidelines.

Pertussis, commonly known as "whooping cough", is a highly contagious respiratory disease caused by the bacterium bordetella pertussis [21]. Infection is easily spread from child to child via droplets of infected individuals with pertussis coughing or sneezing [22]. However, pertussis morbidity has decreased significantly since the advent of the vaccine, which has been accessible since the twentieth century [22, 23]. Previous research had indicated a link between weather and pertussis. It was, for example, reported that a 1°C increase in monthly mean minimum temperature was associated with a 3.1% (95% CI 1.3-4.8%) decrease in monthly pertussis morbidity [24]. According to [25], the wet season may significantly impact the seasonal pattern of pertussis transmission.

Measles is a highly contagious virus-borne illness. Since 1963, the usage of measles vaccination has progressively grown, with yearly cases decreasing to less than 500,000. Measles immunizations saved around 21.1 million lives between 2000 and 2017. While increased immunization has significantly lowered measles mortality, the disease is still resurfacing in high-income countries [26].

It is still commonly encountered in many developing countries with low per capita income levels and poor quality of healthcare, where the vast majority of measles deaths occur, particularly in countries of Africa and Asia, including China [27, 28]. The seasonal occurrence of measles is more noticeable in temperate countries, with the highest number of manifestations occurring in winter and spring, which is associated with dry climate, seasonal temperature change, decline in respiratory system tolerance, and easier penetration of viruses [29, 30].

Influenza is an acute viral infection of the respiratory system caused by influenza viruses that circulate globally [31]. Largely, if the single occurrence of measles or pertussis provides lifetime immunity, immunization to influenza is short-lived, attributed to antigenic drift, which drives annual epidemics. According to European research on the burden of communicable illnesses, influenza has the largest burden of all infectious diseases in Europe, with 81.8 disability-adjusted life years per 100,000 people (95% UI: 76.9-86.5) [32].

Studies looking into the burden of disease variability in different climates [33-35] suggested that the differences in the mortality of disease from influenza were caused by factors such as population density, the proportion of older adults, and access to healthcare rather than climate. A thorough examination of how the seasonal pattern of influenza impacts morbidity and related economic burden, on the other hand, is absent.

According to the information presented above, seasonal variation in infectious disease transmission plays a major part in deciding when epidemics occur; even though it is not the only determinant. For example, several infectious illnesses with documented seasonal transmission, such as pertussis and measles, can have multi-annual outbreaks, indicating that epidemics occur for two or four years rather than yearly. This is because the timing of these epidemics is regulated by a combination of

(a) seasonal transmission and

(b) various factors influencing the number of susceptible people in the population, a significant number of which is required for an outbreak to occur [36].

In the first decade of the 21st century, infectious diseases had a lower mortality rate compared to non-communicable diseases in the Republic of Kazakhstan. Despite considerable progress in vaccination, provided at no cost under the Republic of Kazakhstan's national schedule, vaccine-preventable diseases such as pertussis, measles, and influenza remain major medical and economic issues. Based on this observation, we aimed to study the long-term trends and attain information on the epidemiology of pertussis, measles, and influenza infections in Kazakhstan over a ten-year period.

METHODS

Study Population and Data Sources

This is a retrospective study of the Kazakhstani population diagnosed with vaccine-preventable diseases according to the international statistical classification of diseases and related health problems (ICD-10) from 2010 to 2020. The following ICD-10 codes were utilized to identify patients: A37-A37.9 for pertussis (whooping cough); B05-B05.9 for measles and J09-J10 for influenza. In order to avoid the risk of misclassification with non-influenza respiratory viruses, ICD-10 code J11 ("seasonal influenza, virus not identified") was excluded as a primary diagnosis in conjunction with "acute respiratory tract infection" as primary. Duplicate records with the same population registry number (RPN ID) from the UPS database were removed for measles and pertussis registries.

The official data of registered patients were retrieved from the statistical collections "The health of the population of the Republic of Kazakhstan and the activities of healthcare organizations" [37] for the period between 2010 and 2020 and the unified payment system (UPS) database from 2014 to 2020, which is part of the unified national electronic health system (UNEHS). The database included data on outpatient and inpatient registries, including admission dates, regions, RPN ID, ICD-10 codes, and incidence rates. Retrospective weather parameters including average temperature (°C), average atmospheric pressure (hPa), and average relative humidity (%) were obtained from the "reliable prognosis" website [38].

Outcome Assessment

The incidence rates and seasonality were assessed. The incidence rate was calculated by dividing the new cases of the disease by population size during the same period × 100,000. Seasonality was monitored by the number of new cases in each month over 2014-2020 and as an epidemiological week graph for final years due to a higher number of registered patients.

Study Area

Kazakhstan is the world's largest landlocked country with an area of 2.724 million square kilometers and a population of 19 million [39]. Its population density is low with seven persons per square kilometer (18 people per mile^2) [40]. The climate is diverse; temperature varies by latitude and is divided into different zones. The contrast of temperatures in the north and south may range from -40°C to 45°C in winter and summer, respectively. The average annual precipitation ranges from 196 to 310 mm, with the warm season accounting for around 80% of the total [41, 42]. The country is divided into 14 administrative regions - North Kazakhstan (Kostanay, Akmola, Pavlodar, and North Kazakhstan region); South Kazakhstan (Kyzylorda, Turkestan, Jambyl, and Almaty region); Central Kazakhstan (Karaganda region); East Kazakhstan (East Kazakhstan region); West Kazakhstan (Atyrau, Aktobe, Mangystau, and West Kazakhstan region); and three cities of republican significance a (Nur-Sultan, Almaty, and Shymkent cities) with a population of over one million [43].

Statistical Analysis

Data were represented as descriptive, where absolute values and percentages for categorical variables were calculated. Incidence rates within the population are presented as per 100,000 population.

Table 1. The number of cases and incidences of pertussis, measles, and influenza (/100,000 population) by year

Year	Pertussis		Measles		Influenza		Total	
	n	Inc.	n	Inc.	n	Inc.	n	%
2010	35	0.21	4	0.02	199	1.22	238	0.65
2011	66	0.4	127	0.77	722	4.36	915	2.50
2012	43	0.26	55	0.33	626	3.73	724	1.98
2013	14	0.08	73	0.43	896	5.26	983	2.69
2014	23	0.13	321	1.86	960	5.55	1,304	3.57
2015	74	0.42	2,341	13.3	1,206	6.87	3,621	9.91
2016	32	0.18	122	0.69	2,185	12.3	2,339	6.40
2017	44	0.24	2	0.01	1,810	10.03	1,856	5.08
2018	97	0.53	576	3.15	2,196	12.02	2,869	7.85
2019	147	0.79	13,326	71.97	2,214	11.96	15,687	42.93
2020	54	0.28	3,270	17.21	2,678	14.09	6,002	16.43
Total n (%)	629	3.35	20,217	107.79	15,692	83.67	36,538	100%

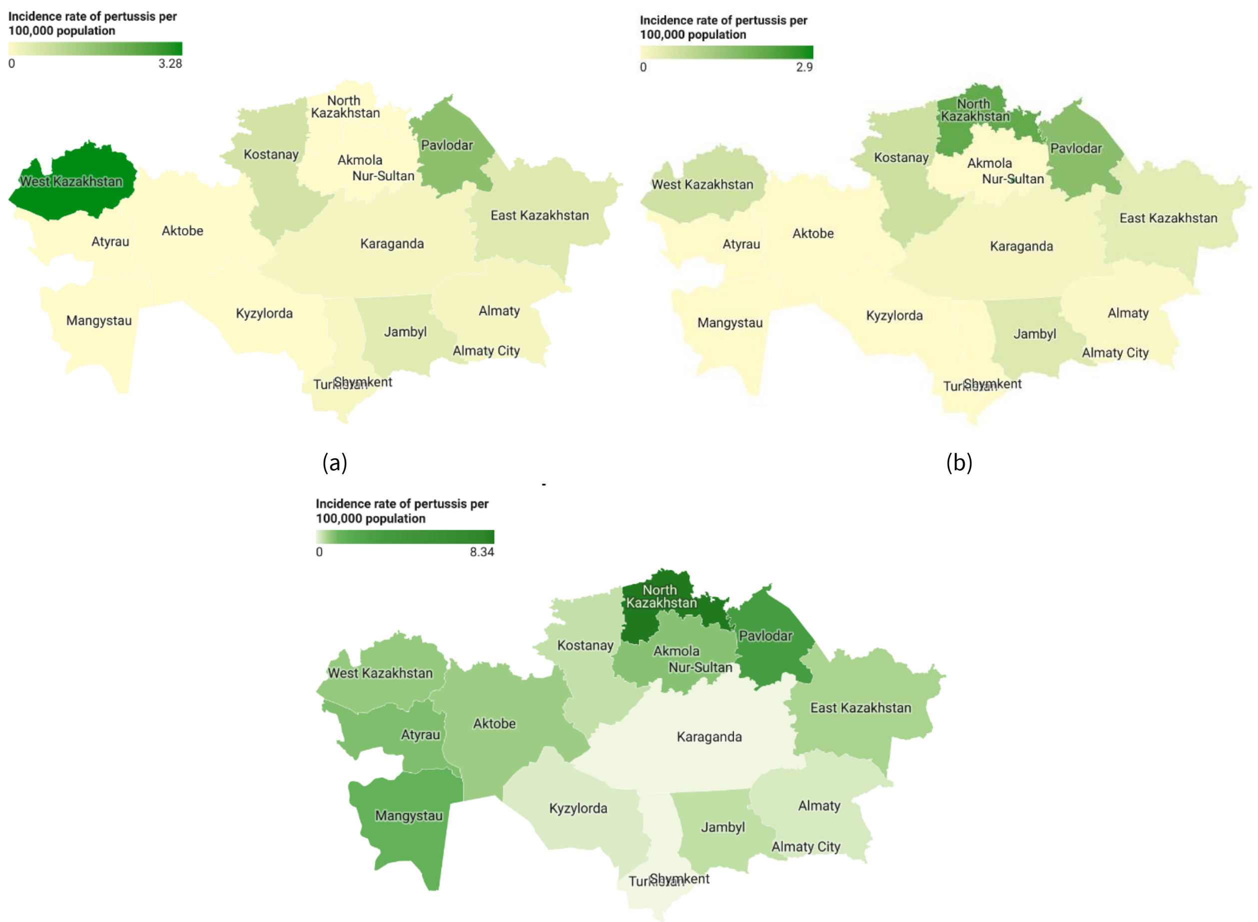
The corresponding maps were constructed using the QGIS 3.14.1-Pi version and the Datawrapper application by Datawrapper GmbH. Data management and statistical analysis were performed using STATA 16.1 MP2 Version (STATA Corporation, College Station, TX).

RESULTS

Pertussis

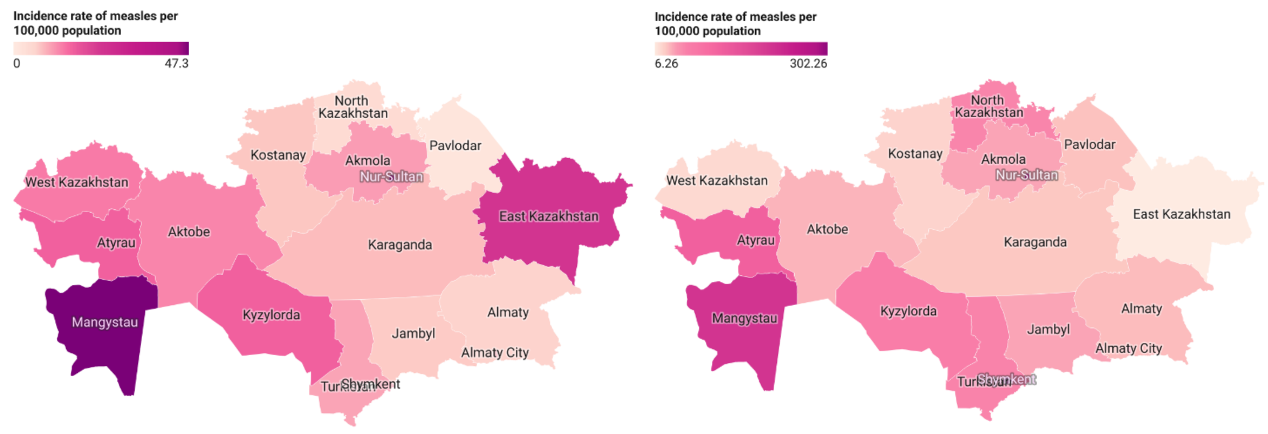
The incidence of pertussis in the country over the past 10 years has been fluctuating. The highest peaks were recorded in 2011, 2015, and 2019 and amounted to 0.4 (66 cases), 0.42 (74 cases), and 0.79 (147 cases) per 100,000 population, respectively (**Table 1**, **Figure 1**). Of these, the largest number was distributed in 2011 in the West Kazakhstan region and the city of Almaty, in 2015 and 2019 in the city of Nur-Sultan, Pavlodar and North Kazakhstan region (**Figure A1** in **Appendix A**).

The incidence rate decreased between 2012 and 2013, reaching the lowest rate of 0.08 (14 cases) per 100,000 population in 2013. Starting from 2016 to 2019, there was an increase in the incidence rate from 0.18 (32 cases) to 0.79 (147 cases). In 2020, the incidence rate was 0.28 per 100,000 population.



(a) (b) (c)

Figure 1. The incidence rates of pertussis in Kazakhstan regions in (a) 2011, (b) 2015, and (c) 2019 [37]



(a) (b)

Figure 2. The incidence rates of measles in Kazakhstan regions in (a) 2015 and (b) 2019 [37]

At the same time, there is an uneven distribution of cases on the territory of Kazakhstan. In Akmola, Aktobe, Karaganda, Kostanay and Kyzylorda regions there were no cases for more than half of the ten-year period. For the first time in many years, a single case of pertussis was reported in Kyzylorda in 2019. Morbidity rose over summer reaching a peak in the autumn of 2019 and declined during the winter and spring seasons the following year. Seasonal distribution revealed a distinct semi-annual epidemic in pertussis infections, with higher incidence from June to November (**Figure B1** in **Appendix B**).

Measles

The total number of people infected by measles was 18,937 during the measles epidemics of 2015, 2019, and 2020 years in the Republic. The incidence rate in 2015, 2019, and 2020 per 100,000 population was 13.3, 71.97, and 17.21, respectively (**Table 1**, **Figure 2**). In the period 2010-2020, the greatest distribution of morbidity was in the cities Shymkent, Nur-Sultan and Mangystau, Atyrau and Kyzylorda regions. The long-term incidence of measles is characterized by an increase in the frequency of the disease after four-five years and a decrease in the incidence after responding to the outbreak in the form of additional mass immunization of vulnerable groups of the population (**Figure 3** & **Figure A2** in **Appendix A**).

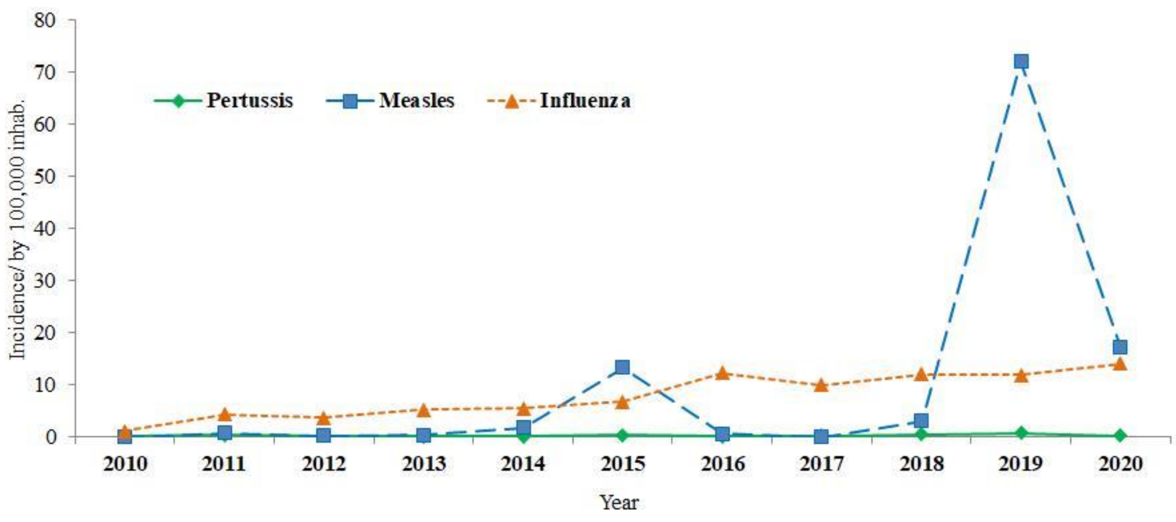
Morbidity varied from winter to spring. In most situations, the distribution occurred throughout the school season (**Figure B2** in **Appendix B**).

Influenza

Between 2010 and 2020, 15,692 cases of influenza with an incidence rate of 87.39 per 100,000 population were detected in the country. The incidence has continuously risen throughout this time, increasing from 1.22 (199 cases) to 14.09 (2,678 cases) (**Table 1**, **Figure 4**).

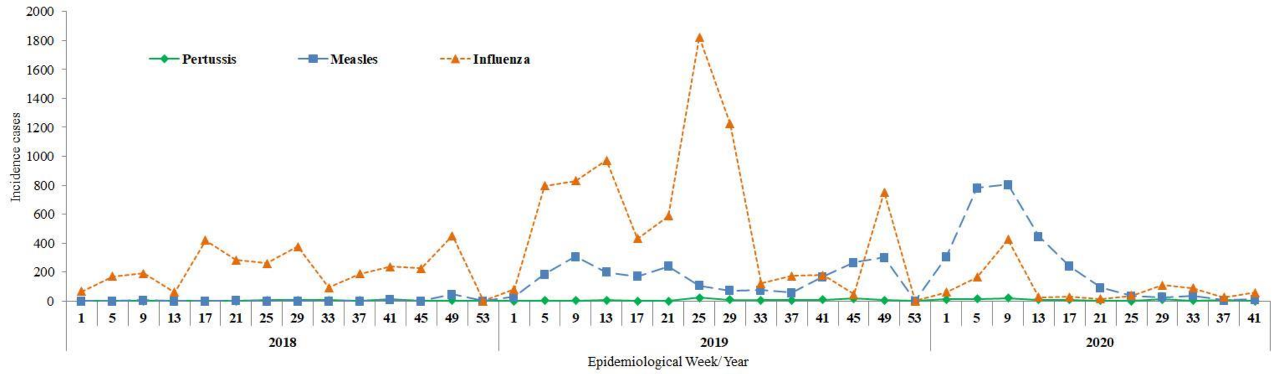
The distribution of cases in Kazakhstan was unequal during the observation period; nevertheless, the highest indicators were observed in the North Kazakhstan, Mangystau, Akmola regions, and Nur-Sultan city (**Figure A3** in **Appendix A**).

In the Akmola region and the city of Nur-Sultan, the number of incidents was 375 and 422, respectively, in 2020. The incidence occurred all year round, but it was higher in winter (**Figure 3** & **Figure B3** in **Appendix B**).



(a)

Figure 3. (a) Incidence of pertussis, measles, and influenza (cases/100,000 population) by year & (b) incidence of pertussis, measles, and influenza (number of cases) by Epidemiological Week [37]



(b)

Figure 3 (continued). (a) Incidence of pertussis, measles, and influenza (cases/100,000 population) by year & (b) incidence of pertussis, measles, and influenza (number of cases) by Epidemiological Week [37]

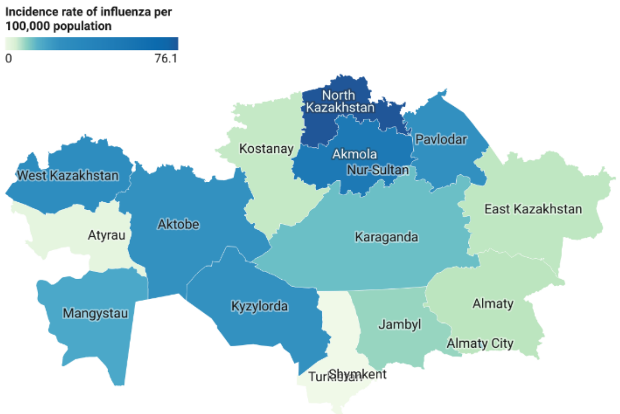


Figure 4. The incidence rates of influenza in Kazakhstan regions in 2020 [37]

DISCUSSION

According to the Branch "Scientific and Practical Center for Sanitary and Epidemiological Expertise and Monitoring" of the National Center of Public Health Care of the Ministry of Health of the Republic of Kazakhstan, the national epidemiological situation of infectious diseases is characterized as stable in the last year [37], which could be attributed to broad preventative measures implemented to battle the novel COVID-19 infection. However, vaccine-preventable infections have reemerged as a serious public health concern in Kazakhstan and around the world in recent years. Understanding the potential key determinants is the foundation for developing preventive and control strategies.

It was shown that a high epidemiological and immunological effect of vaccination has been observed since the first years of mass immunoprophylaxis, which is reflected in a sharp decrease in morbidity and mortality [44]. However, given the increasing proportion of the unvaccinated population, an epidemic rise in morbidity is periodically observed [45]. We also believe that the formation of a non-immune layer among the population as a result of medical contraindications and refusals of preventive vaccinations was the primary cause of infection growth and transmission. Our findings are consistent with the data from [46], which found a significant proportion of unvaccinated people against measles due to vaccine refusal in the following regions: Mangystau region-246 (39.3%), Atyrau region-129 (28.3%), Karaganda region-59 cases (26.4%), Aktobe region-38 (29.9%), Almaty-140 (27.3%), and Shymkent-512 (28.1%). There is also a substantial number of unvaccinated people due to medical contra indications in all regions, ranging from 24% to 40.4% [46].

According to our results, the climatic data and pertussis outbreaks over the research period showed strong seasonal correlations. During the summer and fall seasons, the incidences of pertussis cases were at their peak. These findings are comparable to a Dutch study, which revealed that the yearly peak of pertussis activity occurred during summer [47].

In addition, a prior laboratory study discovered that the effect of pertussis toxin increased with rising temperature [48]. However, the highest prevalence of pertussis was reported during the winter months when temperatures were low. Surprisingly, the peak season for pertussis differs in each country. Peaks in pertussis behavior were seen in Australia during the fall and winter [49], Canada during the spring season [50], and the southern and southeastern regions of Brazil, which match our findings in some locations but contradict in others. This could be attributed to the fact that, for unexplained reasons, seasonal characteristics of pertussis vary greatly among nations and locations; potentially climatic factors have a role. Average air pressure has an inverse effect on Bacillus spores, and the measles virus may have a similar relationship [51]. The measles virus is temperature sensitive and survives somewhat longer at 15°C than at 20°C [52], which is consistent with our findings on the influence of average temperature on measles incidence. According to studies, the survival of the measles virus is mostly dependent on relative humidity and the virus thrives at low relative humidity [52, 53]. Our result documented an unequal distribution of cases which confirms prior research by Tolegenova et al., which also reported that children aged 0-14 years constitute a susceptible section of the population [54].

According to the viral stability hypothesis [55], the start of influenza outbreaks in temperate regions is most closely associated with a decrease in absolute humidity (AH) during the winter season [56] which is consistent with our findings. In warmer climates, AH also signals the start of flu season as part of the monsoon or rainy season [57]. Overall, our study shows a continuously increasing trend of influenza incidences over the studied ten-year period, despite the high quarantine measures implemented in 2020. Although there is no published data on the compliance and coverage of influenza immunization in the country, the nation's awareness and acceptance of influenza vaccination is low. A systematic review of Asian countries revealed the average coverage rate among the general population as 14.9% and 37.3% among high-risk groups, which is far below the WHO target of 75% [58], indicating that more research is needed to understand the barriers that must be overcome to improve assimilation.

There are a few limitations that should be admitted. Firstly, we could not conduct an in-depth investigation to analyze their linkages and relevance due to the provision of only annual data and lack of information on demographic, geographic, socio-economic, and weather parameters. Secondly, we could not exclude the possibility of understatement or overstatement of reporting for various statements, for instance, indicators such as increased infant mortality rates and reduced vaccine coverage, hesitancy to seek treatment among patients with mild symptoms, especially during the COVID-19 pandemic, as well as discrepancies in the work of medical institutions. However, despite the above mentioned, our analysis gives primary information on the epidemiology and seasonality of the disease in Kazakhstan with overall visualization based on official data.

CONCLUSION

To conclude, the present study provides the incidence and distribution of common vaccine-preventable diseases in the Republic of Kazakhstan over a 10-year period. Our findings suggest a relationship between temperature and the seasonality of all three infectious diseases. The cause of frequent outbreaks of measles and influenza virus could be attributed to the low vaccination rate in the country. These findings can help forecast epidemics and reduce the burden of vaccine-preventable diseases by undertaking preventative public health measures including active immunization and campaigns that include press conferences and media events to endorse preventive measures.

Author contributions: All authors have sufficiently contributed to the study and agreed with the results and conclusions.

Funding: This work was supported by the Ministry of Education and Science of the Republic of Kazakhstan grant funding [Funder Project Reference: #AP09259016, Title: Epidemiology and Forecasting of Infectious Diseases in Kazakhstan Using Big Healthcare Data, Mathematical Modeling, and Machine Learning].

Acknowledgments: The authors would like to thank all staff from the Republican Center of Electronic Healthcare for providing data and consultancy. Preliminary versions of the manuscript were presented at the 24th Annual Conference of the European Society for Clinical Virology (ESCV-2022), September 7-10, 2022, Manchester, England.

Ethical statement: The study was approved by the Institutional Review and Ethics Committee (NU-IREC 315/21092020 on 23/09/2020) with an exemption from informed consent.

Declaration of interest: No conflict of interest is declared by authors.

Data availability statement: The part of supporting data of this study is available at the National Research Center for Health Development, http://www.rcrz.kz/index.php/ru/statistika-zdravookhraneniya-2. The other half of the data is available from the Republican Center for Electronic Health of the Ministry of Health of the Republic of Kazakhstan, but restrictions apply to accessing these data, which were used under the contract agreement for the current study, and so are not publicly available. Data are, however, available from the corresponding author upon reasonable request and with permission of the Ministry of Health of the Republic of Kazakhstan.

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APPENDIX A

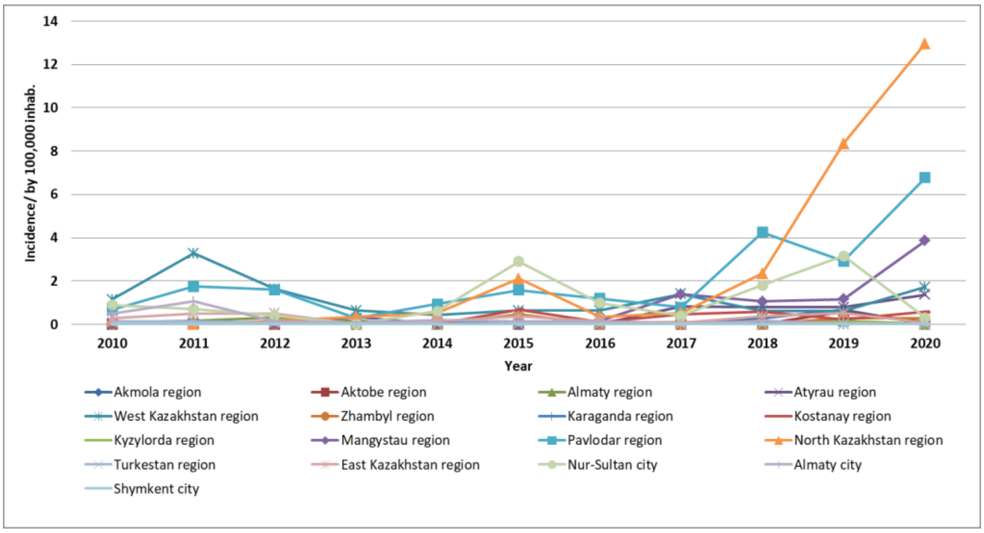

Figure A1. Incidence of pertussis (/100,000 population) by year [37]

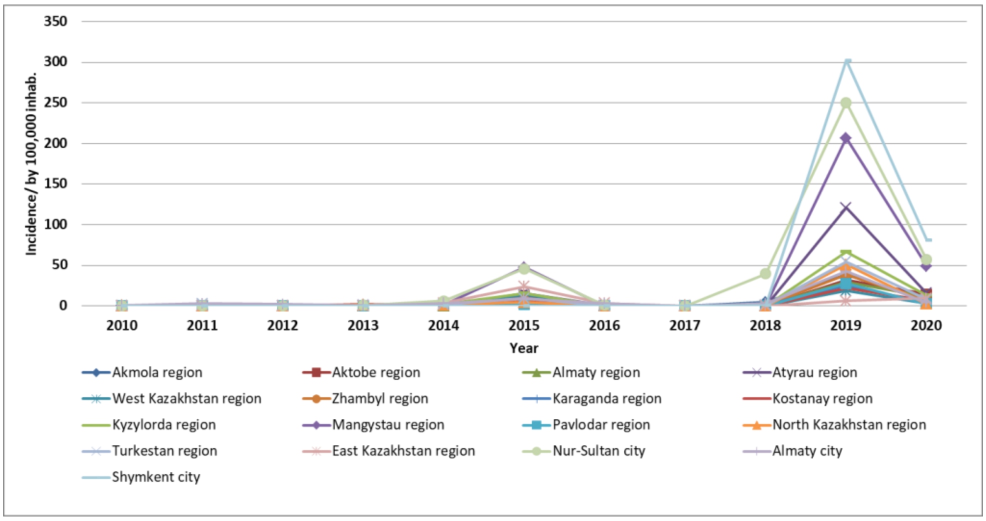

Figure A2. Incidence of measles (cases/100,000 population) by year [37]

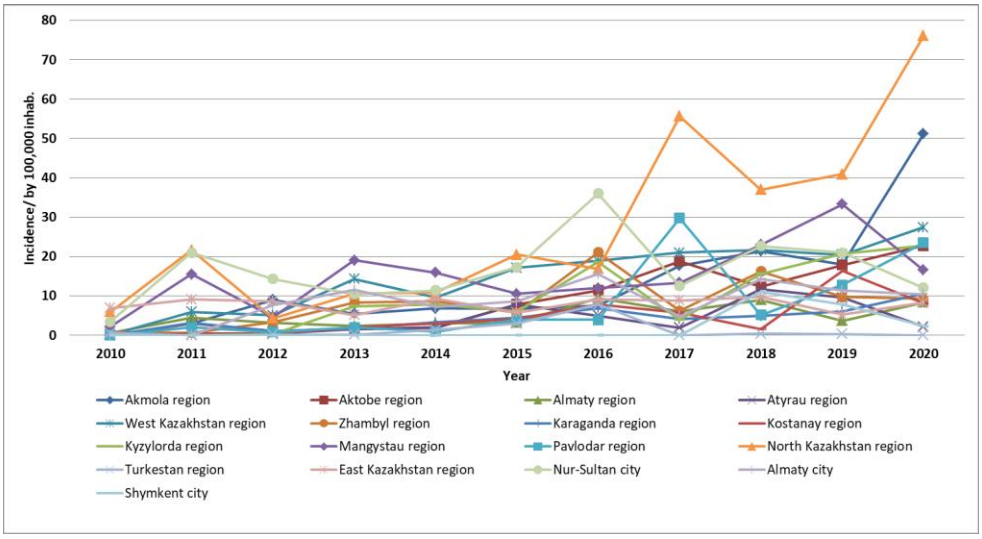

Figure A3. Incidence of influenza (cases/100,000 population) by year [37]

APPENDIX B

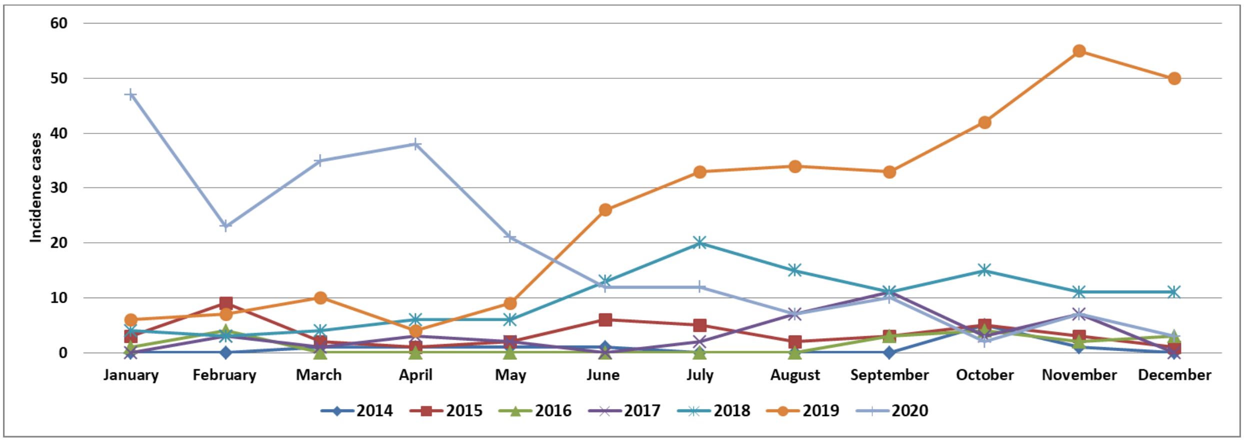

Figure B1. Incidence cases of pertussis by year [37]

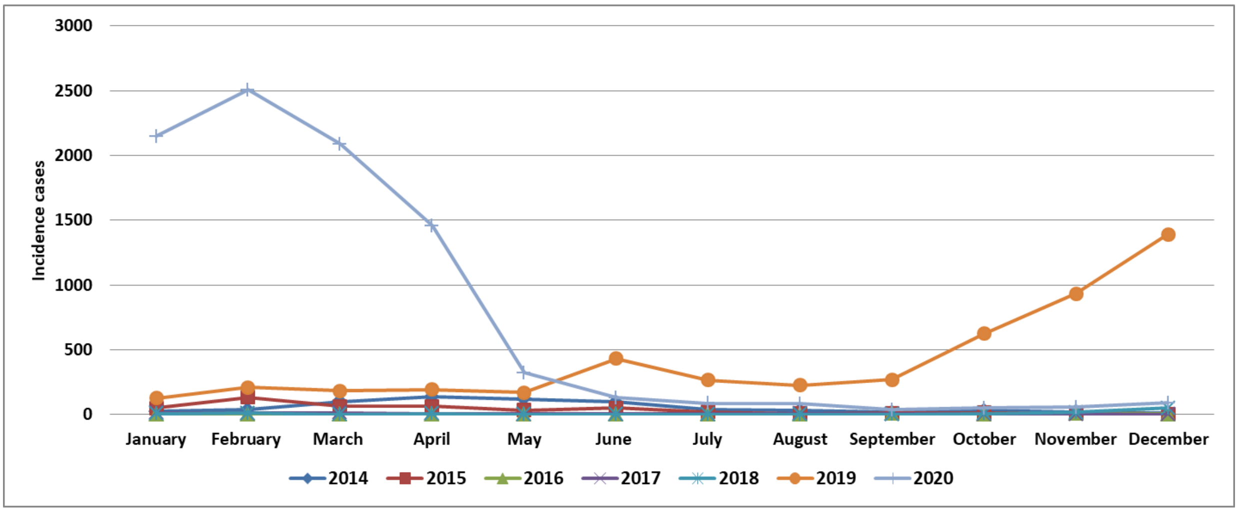

Figure B2. Incidence cases of measles by year [37]

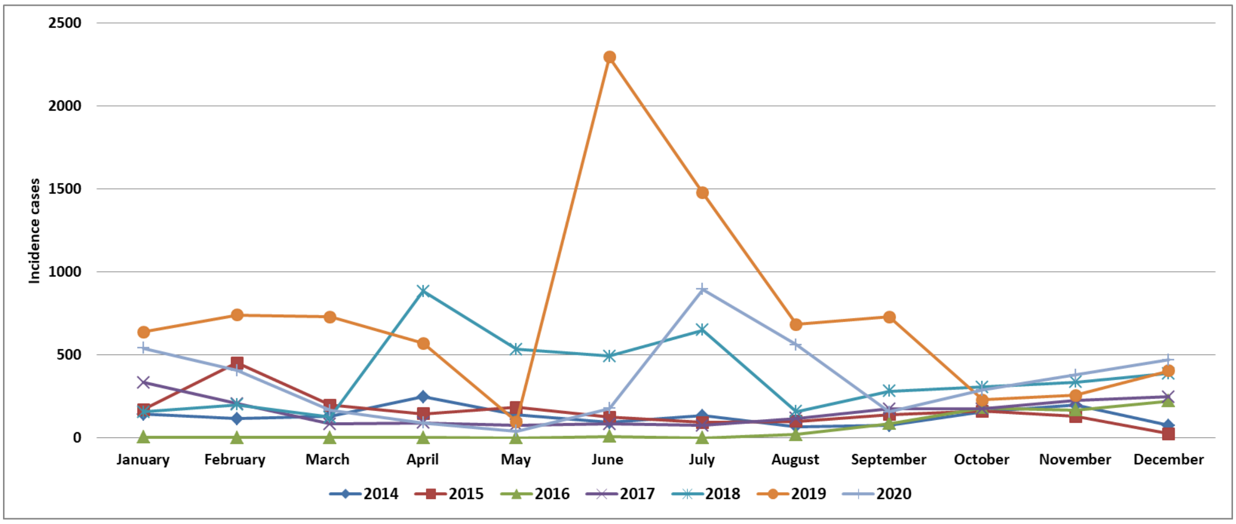

Figure B3. Incidence cases of influenza by year [37]