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Outbreak prediction methods and measures to control the spread of camelpox in Kazakhstan

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Abstract

Background and Aim. *Camelpox* is a highly contagious orthopoxviral disease of camelids causing fever, lymphadenopathy, skin lesions, abortions, and high mortality in young animals. It is endemic across Africa, the Middle East, and Asia and has been repeatedly reported in Kazakhstan, most recently in 2019-2020 in Mangystau and Atyrau oblasts. With the camel population on the rise, the risk of rapid disease spread from new foci is rising. This study aimed to summarize current evidence on *camelpox* in Kazakhstan and to propose practical approaches for assessing the epizootiological situation, forecasting outbreaks, and implementing veterinary control measures based on surveillance data and a risk analysis conducted in 2021-2022.

Materials and Methods. A targeted review of publications indexed in PubMed/Medline and Google Scholar, WOAH resources, national statistics, and selected media reports was performed (coverage up to November 22, 2025). Evidence was synthesized to define key risk indicators for introduction and spread, establish principles for surveillance design (including minimum sample size estimation and sampling across epizootiological units), and formulate recommendations for diagnostics and interventions. Findings from the authors' 2021-2022 cross-sectional survey in western and southern Kazakhstan were incorporated.

Results. Historical outbreak data indicate periodic recurrence in western regions. In the 2021-2022 survey (486 camels from 63 herds across seven regions), antibodies to CMLV were detected in 10.9% of unvaccinated and 73.6% of vaccinated animals; all unvaccinated seropositive cases were confined to Atyrau oblast. Viral nucleic acid was detected in 1.1% of unvaccinated seropositive animals, and phylogenetic analysis confirmed CMLV. A three-zone framework for Kazakhstan was proposed to guide risk-based surveillance and vaccination strategies.

Conclusion. Continuous risk-based surveillance integrating serology and molecular testing, coupled with targeted vaccination and strengthened movement control in high-risk areas, is essential to prevent introduction, limit spread, and support potential regional eradication of *camelpox* in Kazakhstan.

Keywords: *Camelpox virus*; Kazakhstan; outbreak forecasting; veterinary measures.

Introduction

Camelpox is a highly contagious disease of tylopods caused by the camelpox virus (*Camelpox* virus, CMLV; genus *Orthopoxvirus*, family *Poxviridae*). Clinically, camelpox presents with systemic and dermatological signs, including fever, lymph node enlargement, and progressive skin lesions that may appear as nodules, papules, or generalized rash. Reproductive disorders such as abortion can occur, and mortality is particularly high among juvenile animals [1].

CMLV is a member of the genus *Orthopoxvirus* and possesses a large linear double-stranded DNA genome characterized by terminal hairpin loop structures. The viral genome is approximately 205.7 kb in length and encodes more than 200 predicted genes. Structurally, the virion consists of a nucleoprotein core surrounded by a complex, multilayered envelope composed of lipoproteins with embedded surface projections. Replication of CMLV occurs entirely within the cytoplasm of infected cells, where virus-specific inclusion bodies are formed. Despite their environmental stability, virions are susceptible to commonly used disinfectants and detergent-based agents.

A distinguishing biological property of *orthopoxviruses* is their capacity to induce hemagglutination. Besides CMLV, this genus comprises several other species of medical and veterinary relevance, including cowpox virus (CPXV), variola virus (VARV), vaccinia virus (VACV), monkeypox virus (MPXV), raccoonpox virus (RCNPV), vole poxvirus (VPXV), skunkpox virus (SKPXV), and ectromelia virus (ECTV) [2]. From a phylogenetic perspective, CMLV exhibits the closest genetic relationship to variola virus, the etiological agent of smallpox [2]. In addition to genomic similarity, these viruses share comparable biological properties and aspects of pathogenesis, which has attracted particular scientific interest. Therefore, the mutational processes affecting the CMLV warrant close attention from the scientific community, as it is considered a potential zoonotic infectious agent. Although traditionally regarded as a disease of camelids, accumulating evidence indicates that CMLV possesses zoonotic potential. Human infections have been documented in recent years, typically presenting with mild to moderate clinical symptoms such as febrile episodes, cutaneous lesions, and gastrointestinal disturbances [3, 4]. In view of this capacity to infect humans, CMLV is categorized as a Group 2 biological risk agent. From a veterinary standpoint, *camelpox* is recognized internationally as a disease of regulatory importance and is listed among notifiable animal diseases maintained by the World Organisation for Animal Health (WOAH). Due to reduced productivity in infected adult animals, high mortality rates among young stock, and abortions in female camels, *camelpox* causes significant economic losses in countries and regions with developed camel husbandry. Large outbreaks of *camelpox* typically exhibit a cyclical pattern, recurring in the same territories at intervals of 10-25 years [1, 5].

Camelpox remains enzootic across large parts of the Middle East, Africa, and Asia. In Kazakhstan, the infection has historically been concentrated in the western regions of the country. Recurrent outbreaks were documented in Mangystau and Atyrau oblasts in the 1930s, again during 1942-1943, and later between 1965 and 1969 [6], with another episode reported in 1996 [5]. In 2012, increased mortality among camels was recorded in the Mangystau region, with clinical manifestations resembling *camelpox*; however, laboratory investigations did not confirm the presence of CMLV [7]. More recently, during 2019-2020, confirmed cases of camelpox were registered in the rural districts of Tazhen and Syngyrlau (Mangystau region), affecting at least 75 animals [5]. Camels in Kazakhstan are mainly imported from Turkmenistan [8], where outbreaks of *camelpox* occur regularly. The most recent outbreak in Turkmenistan was reported in 2018, during which, in addition to infected camels, at least five cases of human infection were documented [9].

Since the most recent outbreak in 2020, the camel population in Kazakhstan has been increasing annually, thereby elevating the risk of rapid disease spread in the event of a new outbreak. Unfortunately, studies on the prevalence of *camelpox* in Kazakhstan are largely lacking, with the exception of the Mangystau and Atyrau regions, despite the widespread distribution of camel breeding in other parts of the country [10].

As a result of a cross-sectional study conducted by us in 2021-2022, the circulation of CMLV in the Atyrau region was demonstrated. Serological surveillance, which analyzed serum samples from 486 camels originating from 63 herds across seven regions of western and southern Kazakhstan, revealed the presence of antibodies against CMLV in 10.9% of unvaccinated camels and 73.6% of vaccinated camels. All seropositive unvaccinated animals were identified exclusively in the Atyrau region. In

addition, CMLV RNA was detected in three (1.1%) unvaccinated seropositive animals from the Atyrau region. Phylogenetic analysis of one sequenced PCR-positive sample confirmed that the detected strain belonged to CMLV [11]. These findings highlight the importance of continuous surveillance of this infection and the implementation of effective control measures in regions at increased risk.

However, the lack of a clear understanding of the epizootiological situation regarding *camelpox* in the country limits the effective application of control measures, such as mass vaccination of camels in regions at high risk of infection. In the absence of a unified national disease control system, vaccination is carried out privately by farmers, often resulting in only partial herd coverage. The effectiveness of such privately administered vaccination remains unknown. Incomplete and ineffective vaccination facilitates the spread of infection within herds in the event of virus introduction from neighboring countries. Eradication of the infection under such conditions would require substantial financial and labor resources.

Materials and Methods

To prepare the literature review and to develop approaches for assessing the epizootiological situation and forecasting outbreaks, as well as to formulate recommendations for veterinary interventions and the camelpox control in Kazakhstan, we analyzed scientific publications indexed in the Medline (PubMed) and Google Scholar databases, data from official sources of the World Organisation for Animal Health (WOAH) and the Bureau of National Statistics of the Republic of Kazakhstan, as well as reports from news agencies. The literature search was conducted using the following keywords: *"camelpox"* and/or "camelpox transmission routes" and/or "risks of camelpox spread." In total, 42 data sources were identified from scientific databases and 3 from other sources. Following a thematic analysis of the literature across three main research areas and after the exclusion of sources containing duplicate data, the final review included 17 publications from scientific databases, 2 sources containing statistical data, 2 reports from news agencies, and 2 publications authored by the present study's authors addressing the distribution and risk assessment of *camelpox* spread in the Republic of Kazakhstan. The literature search was limited to publications available up to November 22, 2025.

Results and Discussion

Transmission mechanisms, clinical signs, and disease course

The primary route of virus transmission is direct contact. Virus dissemination occurs primarily through direct contact with infected animals. Pathogen shedding into the environment takes place via mucosal secretions and lesion exudates containing high viral loads. In addition, tissues and fluids associated with abortion represent a significant source of infection. Transmission typically follows the penetration of the virus through damaged skin or mucous membranes, with increased susceptibility observed in animals experiencing epithelial injury or nutritional deficiencies [2]. The presence of CMLV genetic material has also been reported in *Hyalomma dromedarii*, a principal ectoparasite of camels, suggesting a potential auxiliary role of arthropods in virus maintenance and mechanical spread [12]. The involvement of other competent arthropod vectors, such as blood-feeding flies, cannot be excluded. However, if vector-borne transmission occurs, it does not appear to play a primary role in virus spread [2].

The incubation period ranges from three to fifteen days and is shorter in young animals than in adults. The disease may present in acute (most commonly in newborn and young animals), subacute, or chronic forms and is often latent, with the latter being more frequently observed in pregnant camels. The most characteristic manifestation of *camelpox* is the cutaneous form with a subacute disease course, characterized by mucous discharge, edema, and rash, which subsequently progresses to gray-colored papules and pustules. In some animals, corneal opacity (leukoma) develops. Infected newborn camel calves often die. In cases of systemic infection, diarrhea and anorexia may be observed. Although *camelpox* rarely results in fatal outcomes in adult animals (mortality rates in adults range from 5% to 28%, whereas in young animals they range from 25% to 100%), death may occur due to secondary infections arising from post-infection immunosuppression, as well as sepsis [13].

At present, there is no approved specific antiviral therapy for camelpox. Although experimental studies have demonstrated that certain antiviral compounds can inhibit viral replication under laboratory conditions, these approaches have not translated into routine clinical application [14]. Consequently,

prevention remains the cornerstone of disease control. Immunization is the principal strategy used to reduce morbidity and limit virus circulation. Both live attenuated and inactivated camelpox vaccines are available and have been implemented in different countries. In addition, vaccinia virus–based preparations have demonstrated cross-protective efficacy against CMLV infection [13]. In terms of protective efficacy, attenuated vaccines generally induce stronger and more durable immunity than inactivated formulations. Protection following administration of inactivated vaccines is typically short-term and requires annual revaccination, whereas live attenuated vaccines may provide immunity lasting several years. Nevertheless, their use in areas officially free of *camelpox* should be approached cautiously. Circulation of vaccine-derived strains within naïve camel populations may occur and can be associated with undesirable effects, including temporary reductions in productivity such as decreased milk yield and slower weight gain.

Methods, principles, and procedures for forecasting camelpox outbreaks

To analyze the risks of introduction and spread of camelpox, as well as to assess the level of potential economic damage associated with the dissemination of this pathogen among tylopods, it is essential to evaluate the following factors:

1) the history of *camelpox* outbreaks in the target territory;
2) the density and total population size of animals susceptible to CMLV (camels) in the given region;
3) the mode of pathogen transmission and, where vectors are involved, an assessment of their distribution within the region;
4) the availability of preventive measures aimed at minimizing the risks associated with disease spread (e.g., vaccines), the extent of their implementation in practice (including vaccine accessibility for farms), and the availability of therapeutic options;
5) the genotype of the pathogen, which determines the severity of clinical manifestations, mortality rates, and the level of infectivity;
6) the current status of the epizootiological process of *camelpox* in the given region (or country), including the average level of seroprevalence in herds;
7) the risk of disease introduction from endemic regions or neighboring countries and an assessment of the potential rate of spread, taking into account the geographical characteristics of regions (i.e., suitability or unsuitability for camel breeding);
8) the capacity for disease eradication in endemic areas, including the presence or absence of legislative frameworks for disease control and eradication.

Analysis of the history of *camelpox* outbreaks. A thorough analysis of data on previous *camelpox* outbreaks within the country is of critical importance, as well as an examination of media reports describing outbreaks of infectious diseases of unspecified etiology with clinical manifestations similar to camelpox. If a *camelpox* outbreak has previously occurred in a given region of the country, there is a high probability that a new outbreak will occur in the same region.

Animals susceptible to infection. All tylopods (camels, llamas, guanacos, and vicunas) are susceptible to CMLV infection. At the same time, only in the Old World does this infection, affecting dromedary and Bactrian camels (and their hybrids), remain widespread and exert a significant economic impact. The virus infects both dromedary and Bactrian camels with equal efficiency.

Mode of pathogen transmission. The primary route of virus transmission is direct contact. Infected animals shed the virus into the environment by producing and dispersing virus-containing exudates (gray mucus). Aborted materials are also infectious. Camels most commonly become infected when the virus enters the body through the skin and mucous membranes, particularly when their integrity is compromised or in cases of vitamin deficiency [2]. It should be noted that CMLV has been detected in the main ectoparasites of camels, the ticks *Hyalomma dromedarii* [12]. The presence of other competent arthropod vectors, such as blood-feeding flies, also cannot be excluded. However, even if vector-borne transmission exists, it does not play a primary role in virus spread [2].

Preventive control measures. Currently, therapeutic options for *camelpox* remain limited, as no specific antiviral treatment has been approved for routine veterinary use. Although experimental studies have demonstrated inhibition of viral replication by certain antiviral compounds, these findings have not led to standardized treatment protocols in field conditions [14]. Therefore, disease management relies

predominantly on preventive measures. Vaccination constitutes the main tool for controlling *camelpox*. Both live attenuated and inactivated vaccines have been developed and applied in various endemic settings. In addition, vaccinia virus–based preparations have shown cross-protective capacity against CMLV infection [13]. Comparative data indicate that live attenuated vaccines generally induce a more robust and durable immune response than inactivated formulations. Protection following inactivated vaccination is relatively short-term and typically necessitates repeated annual administration, whereas attenuated vaccines may confer immunity lasting for more than a year. However, the implementation of live vaccines in regions officially free from camelpox requires careful risk assessment. The unintended circulation of vaccine-derived strains in naïve camel populations may occur and has been associated with adverse production outcomes, including transient reductions in milk yield and slower weight gain.

Genotype of the infectious agent. Poxviruses are characterized by a very high degree of genomic stability (their genome consists of double-stranded DNA with covalently closed ends forming looped structures, and complex DNA repair systems operate within viral particles). Consequently, genetic diversity within this group is relatively limited. At the same time, certain loci allow differentiation between different poxvirus species. During prolonged virus passaging, the nucleotide loci of the ATI, L1R, and ORF-185 genes undergo changes that make them resemble the corresponding loci of vaccinia virus (VACV) [15, 16]. Thus, sequencing of amplicons derived from these CMLV gene loci enables discrimination between vaccine strains used for animal vaccination in a given region and field (non-vaccine) virus strains. Moreover, some CMLV strains may differ substantially in the severity of clinical manifestations and mortality rates.

Actual status of the epizootiological process. Regardless of the results of modeling the risk of introduction and spread of infection in a given territory, without consideration of actual data on the epizootшological process, the level of confidence in risk assessment outcomes cannot be regarded as high.

Among the key factual indicators used to assess the risk of *camelpox* is the level of seroprevalence of antibodies to CMLV in herds where vaccination has not been carried out. An overall seroprevalence of antibodies to *camelpox* exceeding 25%, together with the detection of viral DNA in the blood of at least one animal within a herd, indicates a high risk of an outbreak.

Risk of infection introduction. If a region is non-endemic for the infection, one of the most important indicators in risk assessment is the likelihood of virus introduction from regions of the country that are endemic for the disease or from other countries. To assess these risks, it is necessary, first, to analyze the epizootiological situation of *camelpox* in neighboring regions and to evaluate the proportion of livestock imported into the region from countries or areas endemic for the infection, as well as to determine the actual number of camels imported into the region. To assess the rate of infection spread in non-endemic territories, knowledge of the density of animals susceptible to CMLV alone is insufficient. It is essential to consider geographical barriers to virus dissemination, including the presence of mountain ranges, large rivers and lakes, and deserts. With regard to camelpox, climatic characteristics of the studied regions are of particular importance. Areas occupied by deserts and semi-deserts are the most suitable for camel distribution and, consequently, for the spread of the disease.

Assessment of the potential for eradication of the infection in regions endemic for the disease. If a region is determined to be endemic for *camelpox*, spontaneous elimination of the infection is highly unlikely. The disease tends to have a protracted course and persist for long periods within affected territories. Poxviruses in general are characterized by exceptionally high stability; in a dried state, they can remain viable for many years. Eradication of poxvirus infections from a given region requires the implementation of stringent national and transboundary disease control programs. An important indicator in this context is the degree of concentration of camel populations within production systems. If the majority of camels are kept by private owners in small-scale farms and household holdings, programs aimed at the control and eradication of camelpox cannot be considered effective.

Principles for conducting surveillance studies in regions of the country with a high level of risk

Surveillance is usually conducted in regions at the highest risk of infection. The minimum (critical) sample size required for annual surveillance studies of *camelpox* is determined using the following formula [17]:

$$\text{Sample size } (n) = N * [Z2 * p * (1-p)/e2] / [N - 1 + Z2 * p * (1-p)/e2] \quad (1)$$

where: N – camel population size in the surveillance area;
Z – critical value of the normal distribution at the required confidence level;
p – expected prevalence level, %;
e – acceptable margin of error.

As of November 13, 2025, according to official data from the Bureau of National Statistics of the Republic of Kazakhstan [18], the country's camel population totaled 297,569 animals. Since large-scale camelpox surveillance studies have not previously been conducted nationwide, the level of antibody seroprevalence was assumed to be 50%, as recommended in [17]. For epidemiological studies, a confidence interval of 95% is used in the vast majority of cases; therefore, this value is recommended for calculations, corresponding to a Z value of 1.96 [1, 17]. The acceptable margin of error is typically set at 5% in such calculations [13, 14]. Thus, for groups ranging from five to forty animals, the minimum required sample size was calculated to be 385 animals per year. As a rule, the number of animals included in surveillance exceeds the critical sample size by at least 10%, since a proportion of samples may be unsuitable for analysis (e.g., due to hemolysis of serum or coagulation of blood).

The established number of samples collected for surveillance purposes should be distributed across sampling sites, with sample collection carried out in at least ten different locations or epizootiological units (EUs). It is desirable that several districts within each region covered by the surveillance program be included. Within a given location (or EU), the selection of animals for surveillance should be random, provided that animals do not exhibit clinical signs attributable to camelpox. It is important that animals of both sexes and different age groups be included among those selected for monitoring. If animals displaying clinical signs suggestive of camelpox are identified, these animals should be additionally sampled for laboratory analysis.

Samples collected from live animals for laboratory testing include whole peripheral blood, serum, nasal swabs, and, if skin papules are present, swabs from papular lesions.

Methods for detecting indicators of CMLV circulation

Accurate diagnosis of *camelpox* requires careful differentiation from other infectious and non-infectious conditions presenting with similar clinical signs. Differential diagnosis should include necrobacillosis, foot-and-mouth disease, dermatophytosis and other fungal dermatoses, mange, contagious ecthyma, papillomatosis, brucellosis, as well as inflammatory skin reactions caused by arthropod bites.

A combination of serological and molecular approaches is employed for laboratory confirmation. Commonly applied serological assays include hemagglutination inhibition tests, virus neutralization assays, and enzyme-linked immunosorbent assays (ELISA). These are complemented by direct detection techniques, such as virus isolation in cell culture and polymerase chain reaction (PCR)-based methods targeting specific viral genes [13].

Serological interpretation, however, requires consideration of cross-reactivity within the genus *Orthopoxvirus*, as antibodies generated against one *orthopoxvirus* species may react with others. Despite this serological overlap, only CMLV is known to produce typical clinical disease in camels [14]. In contrast, *parapoxviruse*s and papillomaviruses infecting camelids do not exhibit serological cross-reactivity with CMLV, allowing reliable differentiation using antibody-based assays.

Additional molecular confirmation may be necessary in regions where other *orthopoxviruses* could be encountered. Although CPXV does not usually cause clinical disease in tylopods, experimental data indicate that replication in camels is possible; therefore, differentiation between CPXV and CMLV should be performed using PCR amplification and sequencing of specific genomic loci. Furthermore, in areas where vaccinia virus–based vaccines may have been used, diagnostic protocols must also exclude VACV to avoid misinterpretation of laboratory findings.

Serological assays, particularly ELISA and virus neutralization tests, are generally reliable tools for assessing exposure in unvaccinated camel populations. However, their interpretative value declines substantially in settings where vaccination has been implemented. This limitation is especially

pronounced following the use of live attenuated vaccines, as vaccine-induced antibodies are serologically indistinguishable from those generated after natural infection. Consequently, in vaccinated herds, serology alone cannot be considered a definitive indicator of active virus circulation within a region.

In the case of conventional PCR, the World Organisation for Animal Health (WOAH) recommends the use of the ATIP (A-type inclusion protein) locus for the detection of CMLV [14]. For virus detection by quantitative real-time PCR, primers targeting the HA gene developed by Pfeffer et al. [19] or the C18L gene locus [20] are recommended.

If vaccination of camels with a live attenuated vaccine is carried out in areas included in the surveillance zone, it is necessary to be able to differentiate mesogenic vaccine strains of CMLV from field virus strains at the molecular level.

Camelpox control measures

According to the WOAH requirements for *camelpox* [13], in the event that circulation of CMLV strains is detected in territories officially free from camelpox, it is necessary to strengthen surveillance programs in regions at risk. Such programs should include visual detection of clinical signs of the disease in camels as indicator animals, serological testing of serum samples, PCR-based analysis of nucleic acids isolated from skin swabs and peripheral blood, as well as vaccination.

Vaccination remains the principal measure for both prevention and control of camelpox. Two vaccine categories are currently in use: live attenuated and inactivated formulations. Attenuated vaccines are generally associated with prolonged immunity; however, animals immunized at an early age (before 6-9 months) require subsequent revaccination to ensure sustained protection. In contrast, inactivated vaccines induce shorter-term immunity and therefore necessitate annual administration.

Effective disease management also depends on timely laboratory confirmation. The implementation of rapid molecular diagnostic tools to verify suspected clinical cases is essential for early detection, containment, and interruption of virus transmission. Importantly, camelpox is host-specific and affects only camelids, with no known wildlife reservoir. Combined with the availability of reliable diagnostic assays and effective vaccines, this biological characteristic supports the view that *camelpox* fulfills the principal criteria for potential eradication.

From a sanitary perspective, CMLV demonstrates susceptibility to commonly used disinfectants. It can be readily inactivated by standard physical methods, including autoclaving, brief ultraviolet exposure, and boiling for at least 10 minutes. These measures may be practically implemented at the farm level to reduce environmental contamination. Control strategies should additionally include prompt isolation of clinically affected animals and immunization of susceptible stock using either established cowpox-based vaccines or specifically developed camelpox vaccines.

In order to prevent the occurrence of *camelpox* outbreaks and to ensure effective implementation of preventive measures, it is proposed to conditionally divide the territory of the Republic of Kazakhstan into three zones. These zones were defined based on our previously conducted cross-sectional study [11] and an analysis of the risks of *camelpox* emergence and spread in Kazakhstan [21]:

Zone 1 – *camelpox-affected* zone, where the infection is present in a latent form (Atyrau and Mangystau regions). In this zone, mass vaccination of camels is recommended, mandatory livestock surveillance should be implemented, and stricter control should be applied to animals that may enter the country from neighboring Turkmenistan.

Zone 2 – *camelpox-free* zone with a high risk of disease emergence and spread (West Kazakhstan, Kyzylorda, Turkestan, Zhambyl, and Almaty regions). In Zone 2, continuous serological as well as molecular genetic surveillance for camelpox is recommended. Vaccination of livestock should be carried out using inactivated rather than live attenuated vaccines until animals with clinical signs of infection are detected in these territories or until the virus or its nucleic acids are identified (by virus neutralization assay or PCR followed by DNA sequencing).

Zone 3 – *camelpox-free* zone with a low risk of infection emergence (North Kazakhstan, East Kazakhstan, Akmola, Kostanay, Pavlodar, and Karaganda regions). In this zone, animals transported from the other two zones should be carefully examined for clinical signs of camelpox. At present, an increasing number of farms in the central and northern regions of the country are purchasing camels; therefore, it is crucial to prevent the introduction of infection into these areas (Figure 1).

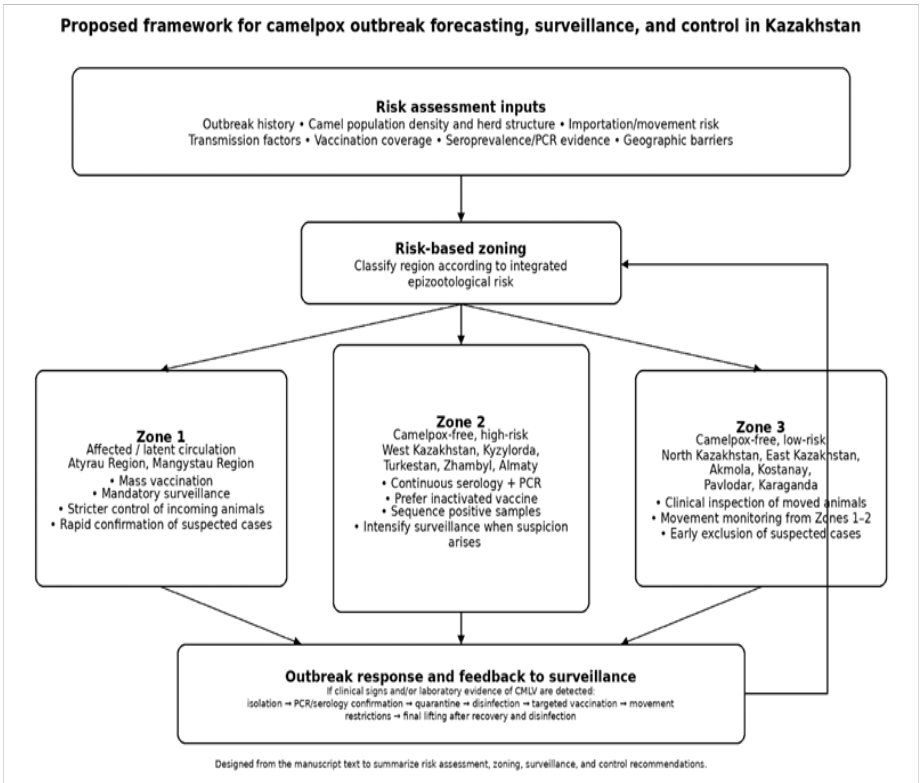

Figure 1. Proposed framework for *camelpox* outbreak forecasting, surveillance, and control in Kazakhstan. The scheme summarizes the key components of the proposed approach, including risk assessment inputs, risk-based zoning of the country, surveillance priorities for each zone, and the sequence of response measures to be implemented when clinical suspicion or laboratory evidence of *camelpox* virus circulation is detected

Procedure for implementing veterinary measures in cases of camelpox

This section outlines measures aimed at preventing the introduction and spread of the CMLV.

General recommendations:

- regular vaccination of camels, particularly young animals;
- in endemic areas, public awareness of risk factors is necessary to reduce the impact of the disease;
- camel herders should be informed about the zoonotic significance of *camelpox*. Routine epidemiological surveillance of the disease is required;
- validation of a simple, rapid, inexpensive, and accurate diagnostic method suitable for field use is necessary;
- further investigation of the zoonotic aspects of this disease is strongly recommended.

Measures for the prevention of *camelpox*:

To prevent the occurrence of *camelpox* and limit its spread, farm managers, organizations and institutions, veterinary specialists, as well as camel owners are required to:

- prevent the introduction (importation) into farms, holdings, subdivisions, and settlements of camels, as well as feed and equipment, from premises affected by *camelpox*;
- keep all newly introduced animals in isolation for a period of 30 days;
- maintain pastures, watering sites, and livestock facilities in proper veterinary and sanitary condition at all times;
- carry out systematic veterinary monitoring of animal health status;
- prohibit individuals from handling animals for a period of 14 days after vaccination against smallpox;

- vaccinate the entire camel population in farms and settlements located in zones threatened by *camelpox* using vaccines available on the market, in accordance with the manufacturer's instructions for camel immunization.

Camelpox can be controlled or prevented through vaccination. To date, four *camelpox* vaccines have been developed and evaluated (in addition to the domestic vaccine based on strain KM-40). All of them are derived from CMLV and include the Jouf-78 strain, the VD47/25 strain, Ducapox 298/89, and the CMLV-T8 strain. The Jouf-78 strain is an attenuated CMLV strain obtained through 80 serial passages in cell culture and has been shown to confer complete protection against CMLV infection. . According to field studies, a single vaccine dose in the range of 103 to 104 $TCID_{50}$ provides full protection. The attenuated VD47/25 strain, also passaged 80 times in cell culture, was evaluated in experiments conducted in Mauritania. This strain was found to be harmless to camels when administered subcutaneously at a dose of 104.7 $TCID_{50}$ and to fully protect camels against lethal CMLV infection. In the United Arab Emirates, a modified live CMLV vaccine obtained by passaging the CaPV298-2 strain in Vero cells has been used.

The vaccine known as Ducapox (DUbai CAmelPOX) is produced by Highveld Biological in South Africa. It was used for field vaccination shortly before the onset of a major *camelpox* outbreak in Dubai in 1993-1994. Among 2,000 vaccinated camels, disease developed in seven animals; however, it is unknown whether these animals had been infected prior to vaccination or whether these cases represented true vaccine failures. In addition, protection was shown to last for six years in two animals. Vaccine efficacy was also demonstrated in New World camelids against lethal CMLV infection. In Morocco, a vaccine containing inactivated CMLV (strain T8) combined with an adjuvant is produced and distributed by Biopharma. The T8 strain was isolated from scab material during an outbreak in Morocco in 1984. The vaccine has been shown to be safe for both young and adult camels and to induce neutralizing antibodies; however, effective protection requires a second injection administered one month later.

Due to the immaturity of the immune system, vaccination is generally recommended for camels aged at least 6 months, and booster vaccination may be required for young calves. In animals younger than 6 months, antiviral agents are used to prevent the spread of the disease.

Measures for detecting camelpox in animals. Although a presumptive diagnosis of camelpox may be established based on characteristic clinical manifestations, reliance on clinical presentation alone is insufficient. Cutaneous lesions caused by CMLV may resemble those observed in other viral infections of camelids, including contagious ecthyma (parapoxvirus infection) and papillomatosis, and may even be confused with non-infectious dermatological reactions such as insect bites. For this reason, laboratory confirmation is strongly recommended. For etiological verification, samples obtained directly from lesions such as skin crusts, nodules, or biopsy material are considered the most informative. A range of complementary laboratory techniques is available for specific identification of CMLV, including transmission electron microscopy (TEM), virus isolation in embryonated eggs or cell culture, polymerase chain reaction (PCR), immunohistochemical detection of viral antigens, and serological assays targeting neutralizing antibodies.

Among these methods, TEM provides rapid confirmation through visualization of the characteristic brick-shaped morphology typical of *orthopoxviruses* in lesion material. This morphological feature allows differentiation from *parapoxviruses*, which display an ovoid structure and represent the principal differential diagnosis (camel orf). However, mixed infections cannot be excluded, as both viral particles may be observed concurrently in the same specimen.

Immunohistochemistry represents an accessible alternative for laboratories without electron microscopy facilities. Detection of *camelpox* antigens in scabs or tissue sections enables confirmation of infection, and the use of paraffin-embedded material allows long-term storage and retrospective epidemiological analysis.

Biological isolation methods further support diagnosis. CMLV is capable of replicating on the chorioallantoic membrane of embryonated chicken eggs, producing characteristic lesions within several days. In cell culture systems, the virus induces a typical cytopathic effect, and infected cells demonstrate intracytoplasmic eosinophilic inclusion bodies consistent with poxvirus replication following hematoxylin and eosin staining.

The presence of viral nucleic acid can be confirmed by PCR, and different CMLV strains can be identified using restriction fragment length polymorphism (RFLP) analysis of viral DNA.

A wide range of serological tests is also available for the detection of *camelpox*, including virus neutralization assays and ELISA. However, given that all *orthopoxviruses* exhibit immunological cross-reactivity to varying degrees, immunodiagnostic methods are of limited value, with the possible exception of demonstrating neutralizing antibodies.

Measures for disease eradication.

Rapid molecular confirmation of suspected cases is a key prerequisite for timely containment of *camelpox* outbreaks. The availability of sensitive PCR-based assays enables early detection of virus circulation and supports targeted response measures, which are essential for effective control and long-term elimination strategies.

From an epidemiological perspective, *camelpox* possesses characteristics that favor eradication. The virus is host-specific and infects only camelids, with no recognized wildlife reservoir contributing to its maintenance in nature. When combined with the existence of reliable diagnostic tools and effective vaccines capable of interrupting transmission, these biological features position *camelpox* among diseases that meet the fundamental criteria for potential eradication. Environmental control measures further strengthen this prospect. CMLV is susceptible to a range of standard disinfectants and can be readily inactivated by conventional physical methods, including autoclaving, brief ultraviolet irradiation, and boiling for at least 10 minutes. Such procedures can be implemented at the farm level to reduce viral persistence in contaminated environments. In practice, outbreak management relies on rapid isolation of affected animals coupled with ring or mass vaccination, an approach conceptually similar to strategies successfully employed during smallpox eradication in humans.

The biological similarity between CMLV and variola virus, particularly their dependence on a single host species, further supports the theoretical feasibility of elimination through coordinated surveillance, vaccination, and quarantine measures. Historical evidence underscores this possibility: in the early 1990s, Higgins and co-workers reported successful interruption of an outbreak following immunization of camels with a human smallpox vaccine. However, due to concerns that smallpox virus might be inadvertently transmitted from recently vaccinated camels to unvaccinated humans, domestic animals, or wildlife, research efforts have focused on the development of attenuated *camelpox* vaccines that are capable of infecting camels only.

Significant progress has been achieved in the development of attenuated *camelpox* vaccines through serial passaging in cell culture systems. In the United Arab Emirates, repeated passaging of a field isolate in camel skin–derived cell lines (approximately 80 passages) resulted in a markedly attenuated strain subsequently commercialized as Ducapox®, which demonstrated high safety in young animals. In Saudi Arabia, a tissue culture adapted strain led to the development of Orthovac®, a vaccine that has shown both safety and protective efficacy under field conditions. Additional national products have been generated in Mauritania using attenuation approaches and in Morocco through formalin inactivation of the virus. An important practical advantage of these poxvirus vaccines is their relative thermostability compared with products requiring strict cold-chain maintenance, which facilitates deployment in desert and semi-desert regions where *camelpox* is endemic.

Global blanket vaccination is not a prerequisite for elimination of the disease. Instead, a targeted containment strategy may be more appropriate. The "ring vaccination" model – successfully applied during the final stages of smallpox eradication relies on rapid case identification, followed by immunization of all epidemiologically linked animals and intensified surveillance to interrupt transmission chains. In the context of *camelpox*, implementation of such an approach would require robust laboratory confirmation of suspected cases, ideally using multiple complementary diagnostic techniques to distinguish CMLV infection from clinically similar conditions, particularly contagious ecthyma caused by *parapoxvirus*. When *camelpox* occurs on a farm, quarantine restrictions are imposed, prohibiting the introduction and removal of animals from the quarantine area, the export of wool and products of animal slaughter, and requiring treatment of animals as well as the implementation of comprehensive sanitary and hygienic measures aimed at preventing disease spread. Restrictions are lifted no earlier than 20 days after recovery of the last affected camel and completion of final disinfection of the farm premises.

The diagnosis of *camelpox* is established on the basis of analysis of clinical and epizootiological data, pathological (post-mortem) findings, and the results of laboratory investigations. The initial stage of *camelpox* must be differentiated from contagious pustular dermatitis of camels (ecthyma) and foot-and-mouth disease.

1. Upon confirmation of *camelpox* in camels, the veterinary specialist responsible for the farm (settlement) shall immediately notify the district chief veterinary officer and, jointly with the farm management and authorized authorities:

- immediately isolate diseased and suspected camels;
- prohibit any movement of animal groups, restrict access by unauthorized persons, and ban the introduction or removal of working livestock, dogs, and other animals that may act as mechanical carriers of the CMLV;
- take measures to identify, localize, and eliminate the source of infection.

2. Upon receipt of notification of *camelpox* occurrence, the district chief veterinary officer shall urgently organize an epizootiological investigation of the affected area to identify the infection focus and implement measures for its rapid containment; the necessary documentation shall be submitted to the authorized authorities for the imposition of quarantine.

3. The executive body of the authorized authority, based on the submission of the district chief veterinary officer, shall issue a decision to impose quarantine on *camelpox*-affected territories. The boundaries of the affected area and the threatened zone shall be defined, key disease eradication measures specified, timelines for their implementation established, and responsible persons designated.

Under quarantine conditions, the following activities are prohibited:

a) introduction and importation of camels into affected settlements, as well as removal and exportation of camels from them;

b) collection of camel hides, wool, and down in affected settlements and exportation of previously collected hides, wool, and down from these areas;

c) regrouping of camels within a farm (with the exception of removing diseased animals to isolation facilities), as well as grazing, watering, and housing of diseased camels together with healthy animals of any species;

d) access of persons not involved in the care of animals from affected groups to premises and other locations where these animals are kept;

e) trade in animals and animal products, as well as the organization of exhibitions, fairs, markets, and other events involving the gathering of animals within the quarantined area;

f) removal of feed (hay, straw, etc.) that has come into contact with camels affected by *camelpox.* Such feed shall be used on-site (within the farm) for animals not susceptible to *camelpox* or for camels that have recovered from the disease and have been immunized against this infection;

g) use of camel milk and products derived from it in an untreated form. Milk obtained from camels on quarantined farms must be disinfected on-site by pasteurization at 85 °C for 30 minutes or by boiling for 5 minutes, followed by use within the farm;

h) passage of private, passenger, freight, and other vehicles through the *camelpox* outbreak area. In such cases, alternative routes to the destination must be designated.

5. In the affected settlement, a veterinary inspection and inventory of all camels are carried out, and owners are informed of the rules for animal management during the quarantine period.

6. Camels affected by *camelpox* are isolated and treated, while clinically healthy animals are vaccinated with available vaccines in accordance with the instructions for their use against *camelpox*. In addition to symptomatic treatment, young animals are administered serum or blood from convalescent camels obtained from clinically healthy animals 20-40 days after recovery.

7. Sanitary assessment and use of meat and other products obtained from the slaughter of camels affected by or suspected of *camelpox* are carried out in accordance with the current regulations for veterinary inspection of slaughter animals and veterinary and sanitary examination of meat and meat products.

8. Wool and hides obtained from camels during the period when the farm is affected by *camelpox* are disinfected in accordance with the current guidelines for disinfection of raw materials of animal origin.

9. Carcasses of camels that have died with clinical signs of *camelpox* are destroyed. Removal of hides and use of wool from such carcasses are prohibited.

10. In the outbreak area, livestock premises, equipment, harness items, and other locations associated with the presence of camels affected by *camelpox* are disinfected every five days throughout the quarantine period until final disinfection is carried out. Manure is disinfected using the biothermal method.

11. Quarantine restrictions are lifted 20 days after the complete recovery, death, or slaughter of the last camel affected by *camelpox* in the given settlement.

Conditions for lifting quarantine measures and exit strategy

Before lifting quarantine restrictions:

- final disinfection is carried out in accordance with the current instructions for veterinary disinfection, disinvasion, disinsection, and deratization;

- the district chief veterinary officer, together with the head of the farm (enterprise), verifies the implementation of veterinary and sanitary measures and prepares an official report authorizing the lifting of quarantine. This report specifies: when and in which territory *camelpox* was established, the source of infection, the number of camels affected, dead, and culled, the dates of vaccination and the number of vaccinated animals, the nature of the disease course, the date of slaughter, death, or recovery of the last affected animal, the date on which final measures for CMLV elimination were carried out in the affected area, as well as the measures to be implemented after quarantine removal.

Conclusion

Based on the research conducted by us, the results of the assessment of the epizootiological situation, and the analysis of the risks of *camelpox* spread in Kazakhstan during 2021-2022 [11, 22], we developed approaches for evaluating the epizootiological situation and forecasting outbreaks, as well as recommendations for implementing veterinary measures and controlling *camelpox* in Kazakhstan. Application of the recommendations described in this article will ensure the effective implementation of veterinary and control measures aimed at preventing the introduction of CMLV into the country, limiting the spread of infection to non-endemic territories, and eradicating the disease from endemic regions.

Author contributions

YO: original draft; AZ, YP: investigation, methodology, original draft; AN: investigation; AA: funding acquisition; SM: reviewing and editing.

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