Seroepidemiology of Crimean-Congo Haemorrhagic Fever among cattle in Cameroon: Implications from a One Health perspective

Lina González Gordon†, Paul R. Bessell†, Egbe F. Nkongho†, Victor N. Ngwa§, Vincent N. Tanya§, Melissa Sander$, Lucy Ndip$, Kenton L. Morgan†, Ian G. Handel†, Stella Mazeri†, Barend MdeC Bronsvoort†, Robert F. Kelly†

1 Royal (Dick) School of Veterinary Studies and the Roslin Institute, University of Edinburgh, Easter Bush, United Kingdom, 2 School of Life Sciences, University of Lincoln, Lincoln, United Kingdom, 3 School of Veterinary Sciences, University of Ngaoundere, Ngaoundere, Cameroon, 4 Cameroon Academy of Sciences, Yaoundé, Cameroon, 5 Tuberculosis Reference Laboratory Bamenda, Bamenda, Cameroon, 6 Laboratory of Emerging Infectious Diseases, University of Buea, Buea, Cameroon, 7 Institute of Ageing and Chronic Disease and School of Veterinary Science, University of Liverpool, Neston, United Kingdom

* lina.gonzalez@ed.ac.uk (LGG); mark.bronsvoort@roslin.ed.ac.uk (BMB); robert.kelly@roslin.ed.ac.uk (RFK)

Abstract

Background

Crimean-Congo Haemorrhagic Fever (CCHF) is a tick-borne viral zoonotic disease distributed across several continents and recognized as an ongoing health threat. In humans, the infection can progress to a severe disease with high fatality, raising public health concerns due to the limited prophylactic and therapeutic options available. Animal species, clinically unaffected by the virus, serve as viral reservoirs and amplifier hosts, and can be a valuable tool for surveillance. Little is known about the occurrence and prevalence of Crimean-Congo Haemorrhagic Fever Virus (CCHFV) in Cameroon. Knowledge on CCHFV exposure and the factors associated with its presence in sentinel species are a valuable resource to better understand transmission dynamics and assess local risks for zoonotic disease emergence.

Methods and findings

We conducted a CCHFV serological survey and risk factor analysis for animal level seropositivity in pastoral and dairy cattle in the North West Region (NWR) and the Vina Division (VD) of the Adamawa Region in Cameroon. Seroprevalence estimates were adjusted for sampling design-effects and test performance. In addition, explanatory multivariable logistic regression mixed-effects models were fit to estimate the effect of animal characteristics, husbandry practices, risk contacts and ecological features on the serological status of pastoral cattle. The overall seroprevalence was 56.0% (95% CI 53.5–58.6) and 6.7% (95% CI 2.6–16.1) among pastoral and dairy cattle, respectively. Animals going on transhumance had twice the odds of being seropositive (OR 2.0, 95% CI 1.1–3.8), indicating that animal movements could be implicated in disease expansion. From an ecological perspective,
absolute humidity (OR 0.6, 95% CI 0.4–0.9) and shrub density (OR 2.1, 95% CI 1.4–3.2) were associated with seropositivity, which suggests an underlying viral dynamic connecting vertebrate host and ticks in a complex transmission network.

Conclusions

This study demonstrated high seroprevalence levels of CCHFV antibodies in cattle in Cameroon indicating a potential risk to human populations. However, current understanding of the underlying dynamics of CCHFV locally and the real risk for human populations is incomplete. Further studies designed using a One Health approach are required to improve local knowledge of the disease, host interactions and environmental risk factors. This information is crucial to better project the risks for human populations located in CCHFV-suitable ecological niches.

Author summary

Crimean-Congo haemorrhagic fever poses an important threat for public health, particularly in endemic locations in Eurasia and parts of Africa. Despite its long-standing recognition, CCHF is considered a neglected disease, with sporadic official case reports and evidence of serological circulation in remote rural areas and less frequently, in peri-urban settings in sub-Saharan Africa. However, the drivers associated with its emergence and the spatial-temporal patterns linked to its circulation and spread are not well-understood. In this study, we identified a high proportion of cattle with CCHFV antibodies suggestive of high levels of viral circulation in the North West and the Adamawa Regions in Cameroon. In pastoral cattle, there was a positive relationship between going on transhumance, older age, higher shrub density and lower absolute humidity and CCHFV individual seropositivity. In contrast, non-indigenous breeds reported a lower risk of being seropositive. These results can be interpreted in connection to the underlying dynamics of CCHFV cycle and underline potential mechanisms linked to disease expansion. From a public health perspective, high levels of exposure to CCHFV in cattle highlight the possibility of unrecognized human infection and therefore, emphasize on the need to remain vigilant to possible disease risks for local groups involved in pastoralism and to dairy smallholders across the region.

Introduction

Crimean-Congo haemorrhagic fever is the most widespread tick-borne viral zoonosis of medical significance, whose pathogen, an Orthonairovirus, belongs to the Nairoviridae family [1,2]. Turkey, Iran, Pakistan, Russia, and Iraq have the highest burden of the disease with reports of sporadic human cases and outbreaks of different magnitude [2–4]. The rapid and growing incidence of the disease, as well as its recognized potential for emergence or re-emergence in previously naïve areas is a matter of public health concern given its infectious potential, the severity of the condition and the limited prophylactic and therapeutic options available [5,6]. As a result, in 2018, the WHO R&D Blueprint for action to prevent epidemics included CCHFV as one of the top infectious agents targeted for research and development [7].

Humans act as an incidental host and are the only known species to be clinically affected by CCHFV [8,9]. Most (~ 90%) human infections are asymptomatic or cause a non-specific mild fever with no further clinical impact [2]. Less frequently, patients develop a severe and often fatal
haemorrhagic disease after a brief incubation period (~ 1 week) characterized by high-fever, fatigue, myalgia, vomiting and diarrhoea that progress to a haemorrhagic period with reports of petechiae, hematomas, generalized bleeding and multi-organ insufficiency [1,9]. The overall case fatality rate (CFR) ranges from 4.7% to 11.7%, an estimate reflecting variation related to the infectious status (ongoing, recent or past infection) [10]. Primary infection occurs after an infected tick bite, by accidental crushing of infected ticks or through direct contact with tissues, fluids or blood of viraemic hosts (domestic or wildlife animals and humans)[1,2]. Outbreaks have been generally associated with nosocomial transmission from undiagnosed cases in settings where health assistance lacks the adequate conditions to identify and isolate patients [1,11]. Otherwise, CCHF remains an occupational disease predominantly restricted to rural areas [3]; primary cases often take place among animal handlers, veterinarians and abattoir and agricultural workers, hence, these groups are identified as high-risk populations for CCHFV infection [1–3].

The disease exists in a silent enzootic cycle, whose balance relies in a complex ‘animal-tick-environment’ interplay, ultimately involving humans as accidental hosts [8]. CCHFV has been detected in a wide range of Ixodidae (hard ticks) and some Argasidae ticks (soft ticks) [10,12,13]. Gargili et al. (2017), reviewed the species of ticks collected from different hosts in which CCHFV has been detected [13]; *Rhipicephalus* spp., *Ixodes* spp., *Dermacentor* spp., *Amblyomma* spp., *Hyalomma* spp. are among the species implicated. However, Ixodid ticks and especially the *Hyalomma* genus have a major role as the most important reservoir and vector of CCHFV and its presence closely approximates high-risk areas [13]. Landscape fragmentation, climate variations and shifts in the distribution or abundance of the main vectors and amplifying hosts affect the viral cycle; therefore, it has been proposed that CCHFV dynamics are strongly influenced by ecological variation [14,15]. Ultimately, these interactions have implications on viral seasonal patterns reported in endemic locations and can modify the likelihood of disease emergence and re-emergence in other settings [3,14–17].

Under this rationale, sero-surveys in domestic and wildlife species have been proposed as a powerful tool to estimate the potential risk that CCHFV poses to a region [18,19]. Livestock, in which CCHFV causes minor or no clinical disease, coexist closely with human populations and serve as a valuable species for surveillance purposes [12,19,20]. In addition, ecological analysis based on the presumed distribution of CCHFV in animals can provide insights on hidden disease dynamics, a resource worthwhile exploring in areas with scarce information on the disease distribution in human populations alongside reports of suitable vectors and ecological drivers that would facilitate disease emergence.

The *Hyalomma* genus of ticks is widely distributed across Africa [21]. However, despite the general lack of CCHF clinical case reports from Central Africa, with the exception of the Democratic Republic of the Congo [22], large geographical areas across the continent offer suitable tick habitats and the potential for CCHFV circulation and human outbreaks [4,23]. Most countries in Africa which have documented CCHFV serologically in livestock (including Sudan, Mauritania, South Africa, Egypt, Zimbabwe, Senegal and Uganda), have also documented CCHF cases in humans [4,24–35]. In contrast, other countries (including Niger and Guinea) have reported evidence of CCVFV circulation in animals, humans or tick vectors without official reports of clinical disease to date [36,37].

Cameroon, located in Central-Western sub-Saharan Africa, fulfils the requirements for a silent CCHFV cycle as already described in other settings: vector presence, availability and distribution of amplifying hosts, evidence of viral circulation and is adjacent to countries already identified to have endemic infection cycles [4,38,39]. In fact, recent estimations from global CCHFV ecological niche models suggest the possibility of CCHFV emergence in Cameroon based on viral and tick ecological suitability [23,39]. However, field-based epidemiological studies designed to assess local distribution in at-risk populations and reservoirs are scarce. On-site
studies have the potential to improve the understanding of viral patterns providing baseline information that can be later used for public health advocacy and to guide further epidemiological analysis aimed to accurately map the risk of CCHFV transmission in human populations.

In this study, we look to maximise the value of available epidemiological information and biobanked cattle serum samples (with associated metadata) to gain disease understanding preceding the report of human cases. We estimate CCHFV seroprevalence and present the results of an epidemiological risk factor analysis of CCHFV seropositivity in cattle in two of the major cattle keeping areas of Cameroon, the North West Region and the Vina Division of the Adamawa Region. Finally, we discuss the potential public health implications of our findings in Cameroon from a One Health perspective.

Materials and methods

Ethical statement

The Institute of Research and Development (Cameroon) and The University of Edinburgh Ethics Committee (UK) approved the study at the moment of data collection (VERC No: OS02-13). Verbal permission was obtained from all herdsmen in order to collect the biological samples from the animals and before administering the questionnaire. A brief explanation of the purpose and procedures of the study preceded the consent and herdsmen were informed of the possibility of opting out at any stage. The Roslin Institute, at the Royal (Dick) School of Veterinary Sciences, University of Edinburgh, UK, approved the serological assessment of CCHFV antibodies in the serum bank in 2019.

Background and study setting

Cameroon is an ecologically diverse country in Central Africa covering an area of 475,440 km$^2$. It borders Nigeria, the Republic of the Congo, Gabon, Equatorial Guinea, Central African Republic, and Chad as well as a coast on the Gulf of Guinea. Climate dynamics can be generally thought of in terms of a wet (May–October) and a dry period (November–April) with rainfall and temperature varying monthly according to the season [40,41]. The country is organized in 10 administrative Regions; these Regions are further split into Divisions and sub-Divisions [42]. Major cattle producing areas are the North West, North, Extreme North, northern parts of the East and Central, and the Adamawa Regions. Overall, the cattle population has increased over recent years and the country is a recognized livestock producer in the Central-West African region [40,43]. The current analysis is focused on data collected from animals reared in the North West Region (NWR) and Vina Division (VD) of the Adamawa Region (Fig 1).

The Adamawa Region occupies a 64,000 km$^2$ territory, generally located over 1,200 m and classified as Guinea savannah, characterized by woodland and grass savannah vegetation [41,44]. Rearing cattle is the main economic activity of the region and it is focused on pastoralist systems primarily managed by local ethnic groups; however, some residents are crop growers working under the principle of a collaborative agricultural economy [44]. Within the Adamawa Region, the VD has a land area of 17,196 km$^2$ with altitudes ranging between 500–2,500 m; the area is topographically characterized by a mountainous western border that softens as it reaches east into an undulating grassland savannah [40]. Similarly, the NWR occupies an area of 17,300 km$^2$ with distinctive rocky-mountains rising between 700 and 3,000 m, although subtropical forest and plateaux savannah are also present [40]. In terms of economy, the agricultural sector is strong and represents the main source of income in the rural areas (80%). Furthermore, it is estimated that 60% of the NWR is a viable terrain for livestock production leading to an active involvement in beef farming [45].
Fulbé, Mbororo, Niam Niam, Laka, Mboum and Baya ethnic groups populate the North West and Adamawa Regions. Some of them (e.g. Fulbé and Mbororo), are part of the Fulani ethnic group, widely extended across sub-Saharan West and Central Africa and recognized as the main pastoral community [40]. In 2013, the cattle populations of the NWR and VD were estimated to be 546,508 and 176,257 respectively, with herd sizes ranging from 50 to 150 cattle [40]. The predominant breed is the *Bos indicus* Fulani cattle but other improved breeds such as the Gudali and crossbreeds are also widespread particularly in the Adamawa Region. The latter breeds provide either better productivity or resilience against the harsh conditions of the territory [40]. Cattle are normally grazed in an extensive system on communal pastures close to the farm [40,45]. During the dry season, transhumance, a pastoral practice involving long-distance movement of animals takes place, with the aim of overcoming the seasonal shortages in

**Fig 1. Map of Cameroon depicting the study regions in the North West Region and the Adamawa Region.** The red area shows the North West Region and its Divisions. The blue area shows the Vina Division of the Adamawa Region and its sub-Divisions. Shapefile obtained from GADM database, freely available for academic uses with permission from Global Administrative Areas (https://gadm.org/maps/CMR.html). The figure was made with RStudio version 3.3.3.

https://doi.org/10.1371/journal.pntd.0010217.g001
pasture availability [46]. Intensive farming systems for cattle production are not a common practice. However, semi-intensive farming, primarily based on a cut-and-carry feeding system, is of growing importance for the dairy sector where imported Holstein-Friesian crosses are used. But this remains a very small proportion of the livestock industry in the country [45].

Study design
Pastoral herds located across the NWR and VD and dairy herds from the NWR were studied to estimate CCHFV antibody prevalence based on serum bank samples available from two previous cross-sectional studies investigating the epidemiology and phylogenetics of bovine tuberculosis and liver fluke infections in Cameroon [40]. Pastoral cattle located at the NWR and VD comprised the main sampling frame, which was built based on the official vaccination records for 2012 (Sampling frame: 5,053 pastoralists’ herds). Conversely, dairy herds from the NWR were retrieved and sampled based on data from the three largest dairy cooperatives registered for the area in 2012 (Sampling frame: 164 dairy herds). A herd was defined as an established group of animals managed collectively as a unit under a well-structured ownership model. In both cases, the Ministry of Livestock, Fisheries and Animal Industries (MINEPIA) provided the records as the closest representation of the true number of herds according to an official source. Sampling and data collection took place from January to May 2013 in the NWR and from September to November 2013 in the VD.

The list of pastoralist herds in each site was stratified by administrative area; seven Divisions in the NWR and eight sub-Divisions within the VD. A random sample of 50 herds was taken proportional to the total number of herds listed per study site in the NWR and the VD. In each herd, 14–15 animals were selected by quasi-random sampling, stratified to three age classes: 6 months–2 years-old, 2–5 years-old and >5 years-old, termed young, adult, and old groups, respectively. Likewise, a stratified random sample of 46 small-scale dairy herds was selected proportional to the number of dairy herds per cooperative in the NWR; all animals were sampled per herd (one to three animals per smallholder). Herd replacement by resampling was applied in both scenarios if herdsmen were unwilling to engage with the study or when unforeseen logistical situations prevented visiting one of the originally selected herds. In-depth information about study design, sample size calculations and sampling methods used in the original study has been reported by Kelly et al. (2016) [47].

Serum biobank and associated cattle metadata
Biobanked cattle serum samples were available for processing at the Roslin Institute at the Royal (Dick) School of Veterinary Medicine (University of Edinburgh), UK. Before transportation to UK, all samples underwent water-bath heat treatment for 120 minutes at 56°C. Serum samples were labelled to allow linking back to herd and animal level questionnaire data and stored at -20°C until processed. Individual and herd level data was available from a structured questionnaire administered to each herdsman in Fulfulde. The questionnaire covered aspects of cattle husbandry and management, dairy practices, individual animal features and GPS location of the farm. A copy of the questionnaire and further details on data collection are reported by Kelly et al. (2016, 2021) [47,48]. Age was estimated by dentition score according to the number of permanent incisor teeth present and classified from < 2 years (no permanent incisors) to ≥ 5 years (all incisors in wear/broken). Calves defined as less than 6 months old by the herdsman were excluded from the sampling to avoid potential issues of maternal antibodies. Breed was defined according to phenotypic traits as either mixed breed (mixed Bos indicus), exotic (any pure Bos taurus or crossbreeds Bos indicus x Bos taurus), Fulani and Gudali [40]. While Fulani and Gudali are considered local breeds,
the Gudali cattle has been systematically improved through a government-led programme over
the last 50 years [49]; therefore, Fulani was considered the indigenous breed for the study area.

**Laboratory testing**

Laboratory analysis was carried out in February and March 2019 at the facilities of the Roslin
Institute at the Royal (Dick) School of Veterinary Medicine (University of Edinburgh), UK.
Anti-CCHFV Immunoglobulin G screening (IgG) was performed by a commercial double-
antigen Enzyme Linked Immunoabsorbant Assay (ELISA) (ID.vet, Grabels, France) based on
the recombinant nucleoprotein antigen (NP), with a reported diagnostic sensitivity of 98.9%
(95% CI 96.8–99.8) and specificity of 100% (95% CI 99.8–100) [50]. The test was performed in
96-well microplates following the manufacturer’s instructions [51]. Duplicate kit positive and
negative controls were included per plate. Optical density (OD) values were determined
spectrophotometrically using an automated ELISA reader (Themocientific Multiskan Go) set at
450 nm. The validity of the test results was verified for every plate based on the manufacturers
recommendations of an OD for the positive controls > 0.35 and a ratio of the mean OD values
of the negative and positive controls > 3. The calculation of the S/P% as the ratio of the sample
OD and the mean OD of the positive controls of the plate was used as the output measure and
an S/P percentage >30% were recorded as positive. Quality control was performed for a total of
180 samples (2 plates), with 100% concordant results. Individual S/P% values were collected per
processed plate by using a standard report datasheet and combined into a final database.

**Data analysis and statistics**

All data analyses were performed using R packages and functions in RStudio version 3.5.3
[52,53]. Figures, graphs and maps were plotted using the ggplot2 package [54]. The shapefiles
of the country maps and its administrative divisions were obtained from the open access data-
base of Global Administrative Areas (GADM) [55].

**Prevalence estimation.** A design effect correction, accounting for the stratified popula-
tion structure of the pastoral cross-sectional study was implemented [56]. Clustering (herd
identification), strata information (Divisions and sub-Divisions) and animal and herd sam-
pling weights were combined into a nested complex survey object using the svydesign function
in the Survey package [56]. This survey object was then used within the package’s summary
functions to obtain CCHFV survey design-adjusted seroprevalence estimates. Thereafter, sero-
prevalence values in pastoralist and dairy herds were corrected for test performance using the
Wilson’s method to provide appropriate confidence intervals for the adjusted seroprevalence,
while accounting for the imperfect test sensitivity and specificity [57].

**Individual risk model and ecological analysis.** Within the pastoralist subset, two separate
explanatory multivariable mixed-effect logistic regression models were used to estimate the
effect of individual animal features, risk contacts, animal husbandry practices and environ-
mental variables on CCHFV serological status of cattle. Both herd and administrative Division
or sub-Division were included as random terms to account for the clustering effect of the sam-
pling design. Global models were built using all the selected fixed effects through the glmer
function in the lme4 package [58].

The first model explored the effect of individual traits, risk contacts and animal husbandry
practices ("Individual risk-factor model"). Preliminary variable selection considered central
biological or epidemiological attributes related to disease risk as per its potential causal depen-
dency network. Statistically significant variables based on univariable analysis with a cut-off
value of p≤0.2 were also included [59]. A multi-correlation matrix was used to check for the
presence of highly correlated explanatory variables. Multi-model inference was performed in
order to reduce variable selection bias, achieve a better precision and approach model selection uncertainty. Model averaging was used to estimate the final coefficients using the MuMIN package [60]. A subset of models was generated based on all the potential combinations of the fixed effects considered at the global model; each candidate model was assessed by the delta Akaike’s Information Criterion (AIC). Candidate models with a delta AIC ($\Delta_i \leq 2$) were averaged, as they are considered to be as good as the best model [61].

The second model focused on the role of ecological covariates (“Ecological model”) on CCHFV seropositivity by means of a standard logistic regression model adjusting for the influence of significant features identified through the Individual risk-factor model. Animals that went on transhumance were purposively removed from the analysis to reduce the possibility of bias introduced by animal movement on the inference of ecological features for past disease exposure.

Elevation at the georeferenced point was extracted from an SRTM30 digital elevation model (DEM). Modelled climate data was downloaded from the UEA Climate Research Unit (version 4.03)[62]. The mean of the mean, minimum, maximum temperature, vapour pressure (used to calculate absolute and relative humidity), and precipitation for the years 2011–2014 were extracted at the location of each georeferenced point. To test the immediate weather impacts on seropositivity, we compared the climate average of these to the mean values during a 90-day window prior to sampling. Landcover variables were downloaded from the European Space Agency (ESA) climate change initiative (CCI) landcover classification [63]. To describe the landcover in the area surrounding the farm, the number of pixels of grassland, shrubland and trees within 5 km of each point were extracted. Climate and spatial variables were rescaled to aid model fitting as required. Model selection was performed through the AIC criterion.

Final model estimates were converted from the log scale to OR and presented in conjunction with its 95% CI. Model diagnosis was conducted through visual inspection of plots and goodness-of-fit measures for hierarchical regression models with a binary outcome; residual diagnosis, coefficient of determination (D) and ROC curves were assessed [64–66]. In addition, the Intraclass Correlation Coefficient (ICC) was calculated to indicate the proportion of variance explained by the clustered study population [67]. Details on the procedures used for model selection and assessment of model performance and fit are documented in S1 Appendix (“Individual risk-factor model”) and S2 Appendix (“Ecological model”).

Results

Study population characteristics

A detailed description of cattle features and herd husbandry practices has been previously reported by Kelly et al. (2016)[47]. A brief overview of the population characteristics is included here as relevant background information and to support the interpretation of the results. In total, 1,498 cattle were analysed as part of the pastoral population with 71.2% (95% CI 68.9–73.5) of the sample comprised by females. There was a difference in the breeds identified per study location; in the NWR, 64.6% (95% CI 61.2–68.2) of cattle were mixed breed, whereas Gudali was the predominant breed reared in VD (82.4%, 95% CI 79.9–85.2). No difference in age distribution was identified across study locations ($\chi^2$-test, $p > 0.05$). The majority of herds reared animals in an open grazing system with access to natural pasture (90.9%, 95% CI 89.5–92.4); thus, contact with domestic and wildlife species, as well as with other herds was commonly documented. Almost a quarter of the cattle population went on transhumance (24.9%, 95% CI 22.7–27.1). However, 44.0% (95% CI 40.4–47.5) of animals from the NWR were involved with the practice, much more often than the animals reared in the VD (5.8%, 95% CI 4.1–7.5). In comparison, the 60 animals sampled within the dairy herds represented...
a mature (Adult: 49.1%, 95% CI 35.1–63.2 and Old: 43.4%, 95% CI 29.8–57.7), non-indigenous Holstein-Friesian (98.3%, 95% CI 91.1–99.9) and non-transhumant population. Around 95% (95% CI 86.1–98.9) of the animals were kept housed most of the time and 8.3% (95% CI 2.8–18.4) were allowed to graze in open pastures. Contact with domestic animals, especially birds, dogs, sheep and goats was frequent; in contrast, contact with wildlife species was not reported.

Pastoral cattle

CCHFV prevalence and spatial distribution of seropositive animals. Serological analysis revealed that 807 out of the 1,498 pastoral animals had been exposed to CCHFV, with an adjusted seroprevalence of 56.0% (95% CI 53.5–58.6) for the entire population. A slightly higher seroprevalence was estimated in the North West Region (57.9%, 95% CI 54.4–61.5) in comparison to the Vina Division (48.9%, 95% CI 45.3–52.6). The Divisional and sub-Divisional seroprevalence values were heterogeneous (Fig 2; seroprevalence calculations per location shown in S1 Table).

Analysis of the seroprevalence by herd identified a widespread distribution of the cases with 98.0% (95% CI 92.9–99.7) of the herds with at least one seropositive animal. Within the NWR, 22/50 herds (44%) reported 10 or more seropositive animals, whereas, for the VD this proportion was 17/50 sampled herds (34%).

Risk factors for animal-level seropositivity to CCHFV. Final results for the averaged “Individual risk-factor model” for the pastoral sub-population revealed that age, breed and going on transhumance were associated with past exposure to CCHFV (Table 1). Contact with other species including dogs, sheep, goats, hogs, buffaloes and antelopes did not influence the probability of individual exposure in our sample as indicated through herdsmen reports of cattle contacts. Adult animals had a higher risk of exposure when compared to young stock, with the oldest animals showing the highest likelihood of being seropositive (OR: 29.0, 95% CI 19.3–43.7). In addition, non-indigenous breeds (Gudali or cross-breeds) were less likely to have circulating antibodies against CCHFV compared to Fulani cattle (OR 0.6, 95% CI 0.4–0.9). Lastly, we identified that animals with a history of going on transhumance had twice the odds of being seropositive (OR: 2.0, 95% CI: 1.1–3.8) when compared to those not involved in the practice. Cattle purchase report was not identified as a risk factor for seropositivity. The AUC for the averaged model was 0.872, which indicates that the model discriminates well between seropositive and seronegative animals. Furthermore, around 28% of the variation in the results is explained by the hierarchical structure of the studied population, as shown by the adjusted ICC (ICC_adj) across the candidate models (See S1 Appendix). The latter measure explores the importance of the contextual background of cattle when modelling CCHFV seropositivity. ICC_adj accounts for the relatedness (non-independence) of animals within herds located in the same area as similarities in geographical conditions, husbandry practices and vector distribution have the potential to alter the probability of infection within a cluster. Additional information on model performance is available in S1 Appendix.

Absolute humidity and shrub density were the only two examined factors strongly associated with CCHFV antibody seropositivity in pastoral cattle that did not go on transhumance. These results were obtained after adjusting for the effect of age and breed, features already linked to seroprevalence through the individual risk-factor model (Table 2). The proportion of shrubland within a 5 km radius increased the odds of seropositivity (OR 2.1, 95% CI 1.4–3.2), whereas animals located in areas of higher absolute humidity had decreased odds of CCHFV exposure (OR 0.6, 95% CI 0.4–0.9). The grouping structure of the population explained
Fig 2. Crimean-Congo Haemorrhagic Fever Virus seroprevalence at the Division level within the North West Region and at the sub-Division level within the Vina Division of the Adamawa Region. The increasing gradient in the coloured areas indicates a higher seroprevalence according to the total of animals analysed for the location. Sized bubbles indicate the number of seropositive animals within each sampled herd. Total sample size: 750 animals (50 herds) at the NWR (a) and 748 animals (50 herds) at the VD (b). Shapefile obtained from GADM database, freely
approximately 20% of the variation in the exposure to CCHFV, as indicated by the ICC\textsubscript{adj}. The model performed well; its discriminatory power (as quantified by the AUC) was 0.862. Additional information on model performance is available in S2 Appendix.

Table 1. Multivariable averaged-mixed effects logistic regression model for Crimean–Congo Haemorrhagic Fever Virus seropositivity in pastoral cattle.

| Variable          | OR (95% CI)         | Sum of weights\textsuperscript{1} |
|-------------------|---------------------|----------------------------------|
| Sex               |                     |                                  |
| Female            | Reference (Reference) | 0.08                             |
| Male              | 0.99 (0.89–1.10)     |                                  |
| Breed             |                     |                                  |
| Fulani            | Reference (Reference) | 1                                |
| Gudali/Crossbreed | 0.59 (0.37–0.95)     |                                  |
| Age               |                     |                                  |
| Young             | Reference (Reference) | 3.29 (2.42–4.48)                 |
| Adult             | 29.06 (19.31–43.73)  |                                  |
| Old               | 1                   |                                  |
| Buying cattle     |                     |                                  |
| No                | Reference (Reference) | 1.47 (0.80–2.67)                 |
| Yes               | 2.01 (1.07–3.81)     |                                  |
| Going on transhumance |                 | 1                                |
| No                | Reference (Reference) | 1.01 (0.94–1.21)                 |
| Yes               | 2.01 (1.07–3.81)     |                                  |
| Contact with dogs |                     |                                  |
| No                | Reference (Reference) | 1.01 (0.73–1.55)                 |
| Yes               | 0.99 (0.86–1.15)     |                                  |
| Contact with sheep|                     |                                  |
| No                | Reference (Reference) | 1.01 (0.73–1.55)                 |
| Yes               | 1.07 (0.73–1.55)     |                                  |
| Contact with goats|                     |                                  |
| No                | Reference (Reference) | 0.99 (0.86–1.15)                 |
| Yes               | 0.99 (0.86–1.15)     |                                  |
| Contact with buffaloes |               |                                  |
| No                | Reference (Reference) | 1.03 (0.68–1.56)                 |
| Yes               | 1.03 (0.68–1.56)     |                                  |
| Contact with hogs |                     |                                  |
| No                | Reference (Reference) | 0.98 (0.82–1.18)                 |
| Yes               | 0.98 (0.82–1.18)     |                                  |
| Contact with antelopes |               |                                  |
| No                | Reference (Reference) | 1.01 (0.85–1.19)                 |
| Yes               | 1.01 (0.85–1.19)     |                                  |
| Study location    |                     |                                  |
| North West Region | Reference (Reference) | 1.01 (0.81–1.24)                 |
| Vina Division     | 1.01 (0.81–1.24)     |                                  |

\textsuperscript{1} Measure of the relative importance of each variable in the final averaged model, calculated as the sum of model weights over all models (n = 11) containing each explanatory variable.
Dairy cattle

**CCHF prevalence and spatial distribution of seropositive animals.** The seroprevalence of antibodies against CCHFV in dairy cattle was 6.7% (95% CI 2.6–16.1), equivalent to 4 animals, each from a different herd (herd location and serological status shown in S1 Fig). No statistically significant difference was found between animal features (demography, husbandry, and risk contacts) and CCHFV serological status of dairy cattle (Fisher’s test, \( p > 0.05 \)). Multivariable modelling was not conducted due to the low number of positive animals.

**Discussion**

Livestock species have a recognized role in CCHFV epidemiology; besides harbouring ticks with the potential to maintain and transmit CCFHV, they also serve as efficient amplifier hosts [19,68]. As a result, livestock are often included as part of surveillance initiatives and outbreak investigations in endemic and non-endemic areas [18,19]. In this survey, we found a high seroprevalence (~56.0%) of antibodies in pastoral cattle, which contrasts to the lower seroprevalence detected among the dairy population (~6.7%). A prior report documented the circulation of CCHFV in the country (2013–2014) using cattle samples collected in the Extreme North, North, Adamawa, Central and South Regions; this study showed an overall seroprevalence of 74% [69], a much higher estimate in comparison to the overall findings of our survey. The variation in IgG levels may be due to differences in the population, study design and analysis including discrepancies in the age structure and tick infestation of animals, sampling methods and locations, diagnostic test performance or data processing.

In Cameroon, pastoral and dairy cattle are managed very differently, which is likely to greatly alter their baseline risk of exposure to tick-borne pathogens such as CCHFV. Not many studies have focused on analysing viral circulation in dairy herds; however, our results were comparable to previous analyses that observed low CCHFV seroprevalence in dairy animals. For instance, in high-disease burden scenarios in Iran, serological assessments among dairy cattle have revealed less than 10% CCFHV reactivity [70,71]. In the NWR, smallholder dairy keeping is characterized by regular and closer contact with cattle. Dairy cattle were largely housed compared to the extensive rearing system in the traditional pastoralist herds. As a result, this semi-intensive production system allows fewer opportunities to graze and little

---

Table 2. Multivariable logistic regression model for Crimean-Congo Haemorrhagic Fever Virus seropositivity in non-transhumant pastoral cattle.

| Variable                  | OR (95% CI)   |
|---------------------------|---------------|
| Age                       |               |
| Young                     | Reference     |
| Adult                     | 3.13 (2.19–4.45) |
| Old                       | 25.3 (16.1–39.6) |
| Breed                     |               |
| Fulani                    | Reference     |
| Gudali/Crossbreed         | 0.48 (0.28–0.83) |
| Study location            |               |
| North West Region         | Reference     |
| Vina Division             | 1.13 (0.49–2.66) |
| Shrubland                 | 2.12 (1.42–3.18) |
| Absolute humidity         | 0.58 (0.38–0.90) |

https://doi.org/10.1371/journal.pntd.0010217.t002
contact with other domestic and wildlife species, which could act as a protective factor for tick infestation. Despite a presumed low risk of tick infestation under these conditions, ticks can still be a problem in ‘zero-grazed’ systems [72]. For example, ticks can be carried in on cut grass or may be introduced by new stock. Moreover, in zero-grazed systems, tick infestation rates vary, among others, according to the location, season, breed, sex, age group and other features linked to individual fitness [72–74]. The interaction between a large number of factors relating to both the tick vector and host may be important for viral maintenance and, although we have shed some light on these here, further work from longitudinal studies is needed to understand how and when animals are getting infected.

CCHFV endemicity is linked to the distribution and population dynamics of ticks which have the potential to act as competent vectors. While *Hyalomma marginatum* is the main vector and reservoir for CCHFV, many other tick species are known to be involved in its epidemiology [10,13]. In Cameroon, cattle-associated tick populations include *Amblyomma* spp, *Rhipicephalus* spp. and *Hyalomma* spp. ticks which are established in different agro-ecological zones across the country [75,76]. Although *Hyalomma* spp. ticks are not the most prevalent tick genera; *Hyalomma impeltatum*, *Hyalomma impressum*, *Hyalomma rufipes* and *Hyalomma truncatum* are all encountered by cattle in Cameroon [75,76]. CCHFV RNA has been detected in *H. truncatum* ticks in Cameroon [69], illustrating local viral circulation at the vector-level. Therefore, it is possible that other tick species currently act as CCHFV vectors and reservoirs and are capable of maintaining viral circulation in Cameroon [10,13]. However, this study was based on biobanked sera from a tuberculosis-related study and detailed tick infestation data was not available. Information on tick abundance, species diversity and its CCHFV status would have contributed to understanding the disease ecology in the studied area. Despite this limitation, the models revealed several individual and ecological factors that are associated with CCHFV seropositivity in cattle which suggest ongoing processes at the tick-virus-host interface. These include the role of transhumance on CCHFV infection, possibly facilitated by tick exposure in the transhumance routes and, the effect of climatic and land-cover variables on CCHFV past exposure in cattle.

As it is the case for many vector-borne pathogens, host factors are important when analysing the evidence of serological exposure to CCHFV. The occurrence of antibodies against CCHFV in cattle in African countries has shown to be heterogeneous and context-dependent. The effect of age, sex, tick infestation rates, animal purpose, grazing system, herd size, vector control strategies, and presence of comorbidities on CCHFV reactivity has been discussed in earlier studies [27,77,78]. Less frequently, studies have documented the association of landscape and climatic features on CCHFV antibody presence in livestock [79]. In our study, breed was connected to variations in seropositivity. Breed susceptibility to ticks, natural tick infestation rates and husbandry practices might be a contributing factor for this difference. Fulani cattle have a higher tick infestation burden, harbouring several tick species in comparison to the low tick burdens reported in Gudali cattle [80,81]. Herdsmen in Cameroon generally practice hand-removal of ticks as few areas have functioning dip tanks or access to acaricides. As a result, smaller ticks, nymphal stages, and ticks in inaccessible body locations (e.g. groins, hooves, mammary gland, tail) are usually left unattended [82]. In practice, this means that several tick species including *Rhipicephalus* spp., *Amblyomma variegatum* and *Hyalomma* spp., all potential CCHFV vectors with known presence in Cameroon [75,76], can easily remain attached long-enough to increase the probability of transmission [13].

Furthermore, animal’s age (being older) was strongly associated with an increased likelihood of the animal being seropositive in pastoral cattle. Age is a recognized risk factor for many vector-borne diseases in animals and in humans and consistent results are also available for CCHFV infection in livestock [26,27,35,83]. Higher tick infestation rates, typical of adult
cattle in African settings and therefore, an increased likelihood of coming into contact with an infected tick over time might translate into an increased probability of CCHFV infection, seroconversion and thus, antibody seropositivity [82].

Importantly, our analysis highlights the potential role of the seasonal transhumant movements on CCHFV increasing infection risk. Transhumance is a socio-cultural husbandry practice of pastoralist communities where herds move to river valleys during the dry season in search of better pasture. In Cameroon, transhumant herds can travel over 600 km across regions or international borders potentially passing through areas diversely suited for several tick species and directly connecting populations that would otherwise be spatially separated [46]. CCHFV naïve cattle can get infected along the way through the uptake of ticks from remote areas, but equally likely ticks can also spread to transhumance sites, a phenomenon already documented in Africa [3,84]. Similar mechanisms have been linked to the transboundary expansion of CCHFV through small ruminants and birds [85], and are known to contribute to the transmission of other tick-borne diseases in livestock [86].

The patterns and distribution of CCHFV can also be influenced by climatic, environmental and landscape differences due to their effect on the tick vector. The ecological model suggested that CCHFV seropositivity increased among cattle using areas of increased shrub-density, whereas locations with higher absolute humidity were associated with a decreased odds of CCHFV seropositivity. Water vapor uptake is fundamental to maintain water balance in ticks and directly influences their survival rates [87], and so, water vapour deficit (WVD) is thought to impact tick developmental rates [14]. As a result, it has been used to model environmental restrictions for H. marginatum and other hard-bodied ticks [14]. The inverse relationship between absolute humidity and CCHFV seropositivity that is indicated here, challenges the results of previous reports in which ticks tend to thrive preferentially in humid areas [21]. But it should be noted that there was no association with relative humidity in our analysis. Several studies document a positive association between high humidity and CCHF incidence in humans through the retrospective analysis of cases in endemic settings [88,89]. However, it is important to emphasize that in Cameroon the understanding of CCHFV is limited, particularly in the microhabitats in which the ticks exist rather than the 0.5˚ resolution of the climate data. Furthermore, a great deal of uncertainty surrounds the hosts and tick vectors involved in the viral epidemiological cycle at the local level. Some explanations for the inverse relation between absolute humidity and antibody presence in cattle are possible. From a biological perspective, several tick species display a great degree of environmental and climatic adaptation which is formally recognized as ‘ecological plasticity’ [90]. Consequently, it is possible that a lower absolute humidity is not an impediment for tick establishment in the studied setting. Further knowledge on the tick species inhabiting this area is necessary to clarify how well ticks adapt to the local conditions and if they indeed act as competent vectors for CCHFV. In contrast, from a methodological perspective, the lag time between the ecological exposure (humid climate) and the serological outcome might have played a role in this relationship. The exact time of CCFHV infection cannot be inferred based on serological evidence of past exposure to CCHFV, hence, the association might not be reflecting the ecological conditions at the time of exposure to the virus. This misclassification, common when inferring cross-sectional associations, cannot be ruled out as a plausible explanation for the unexpected link between absolute humidity and serological evidence of CCHFV in pastoral cattle [91].

Furthermore, tick abundance seems to be strongly related to tree species composition and shrub cover [92,93]. Some prior geo-spatial analyses on CCHFV occurrence have indicated a connection between land fragmentation, shrubby/grassy vegetation, and tick distribution in highly affected locations [94,95]. A higher proportion of grass and shrub land cover account for almost 62% of CCHFV predicted emergence or re-emergence in humans according to an
estimates obtained from a global CCHFV distribution model; land surface temperature, vegetation index and annual precipitation also contributed to the overall effect [39]. Vegetation structure might be an indicator of wildlife ecological niches supporting tick populations. Shrubby areas tend to be rich and diverse in small mammals. Therefore, the increased risk of CCHFV exposure in cattle could be better explained based on the wildlife-livestock interface enabled by open grazing systems adopted by pastoralists in the two study sites.

Contact between cattle and other domestic and wildlife species is usual in pastoralist systems. However, despite reports of different wildlife ungulates commonly grazing together with cattle in the North West and Adamawa Regions, we did not find an association of cattle contact history and CCHFV antibody presence. Yet, contact with wildlife and domestic species remains a possible source of CCHFV, especially in open-grazing, transhumant systems enabling a diverse configuration of host-vector-host interactions. Evidence collected from serological studies across Asia, Africa and Eastern Europe suggests that several domestic and wildlife species are involved in CCHFV ecology and can modulate local transmission patterns [19]. For instance, prior exposure to CCHFV has been reported in African warthogs (*Phacochoerus aethiopicus*), a species observed on the transhumance routes of the Adamawa Region [19,41]. Given the rich faunal inventories in Cameroon, the involvement of a number of endemic small mammals, birds and larger ungulates in the infection cycle, if any, is yet to be elucidated. Similarly, the participation and pathways in which other domestic animals and tick species contribute to CCHFV epidemiology merits further attention.

Our research, based on CCHFV antibody identification in cattle, highlights a potential public health risk to livestock-rearing communities and slaughterhouse workers in Cameroon. Nonetheless, further studies are required to explore the significance of CCHFV circulation in cattle for humans co-existing in this environment. To the best of our knowledge, there are no reports of CCHF clinical cases in human populations in Cameroon [4,10,31–33]. However, the infection is known to circulate at a low prevalence in rural and peri-urban areas [38,96]. Traditional communities might be at greater risk of infection. For instance, CCHFV exposure has been identified among pygmies located at the rain forest in Eastern Cameroon [38]. These communities are hunter-gatherer groups whose high-risk practices and close proximity to CCHFV-suitable ecological niches probably contributes to viral transmission. In parallel, pastoralist communities at the North West and the Adamawa Regions might engage in high-risk practices leading to contact with tissues, fluids, and blood from viraemic livestock or virus-carrying ticks. Manual-tick removal is one example of possible infection routes. Similar risks are transferable to dairy farmers; in the past, CCHFV circulation in dairy cattle has been linked to human outbreaks [97]. Thus, the potential risk of infection for herdsmen, dairy farmers and slaughterhouse workers should not be ignored.

A high CCHFV seroprevalence in cattle in the absence of clinical cases, as we report here, raises several questions as to the underlying eco-epidemiological dynamics of CCHFV in Cameroon and the drivers of disease emergence and clinical infection in the associated human populations. It is likely that clinical cases are being missed due to a milder course of infection or misdiagnosis in the health care setting [10,11,16]. In the studied areas, health care facilities are distant, and people face many difficulties to receive medical care, therefore underreporting is possible. Anecdotal evidence from discussion with clinicians suggest that fever is a common presenting symptom but, like in many areas in Africa, a lack of diagnostic resources means these cases are treated symptomatically and the causes are never identified. However, it is also possible that human cases are truly absent or occur quite rarely. CCHFV re-emergence after prolonged silent periods has been documented. In Central and East Africa, phylogenetic analysis and serological surveys in human populations have suggested ongoing viral circulation with only a few sporadic cases detected [22,98,99]. While close contact with livestock is one of
the strongest risk factors for CCHFV infection in humans, research in endemic and non-endemic locations has introduced contrasting evidence on the relationship between CCHFV exposure rates in livestock and human levels of infection. A multi-causal system involving ecological, environmental, climatic, social, and anthropogenic factors could be responsible of variations on the local viral cycle determining infection trends and human exposure events. A systemic, ‘One health’ view is necessary to unravel the epidemiology of CCHFV at the Cameroonian context.

This study illustrates how serological surveys in cattle can be informative and can contribute to the understanding of CCHFV circulation in settings with scarce epidemiological data. A large representative random sample accounting for the highly hierarchical population structure and a careful analytical approach is one of the main strengths of this study. However, the cross-sectional nature of our data is limited at determining cause-effect relationships, in particular when it comes to environmental and climatic features involved in disease occurrence. CCHFV can induce a strong, long-lasting immune response with an uncertain antibody decline rate. Hence, the possibility of differentiating CCHFV active exposure from passively acquired maternal antibodies or old viral exposures is limited.

Our findings provide baseline data on CCHFV circulation at the North West and Adamawa Regions in Cameroon and its associated factors. The extent to which the local epidemiological picture has changed since data collection remains an open question. In spite of this uncertainty, our results have the potential to create awareness among public health authorities and guide future epidemiological studies under a multi-disciplinary ‘One Health’ approach. An increased risk associated with occupational exposure for pastoralists and dairy keepers is not negligible. Livestock handlers, slaughterhouse workers, veterinarians and other personnel in frequent contact with CCHFV exposed animals should be informed about the risk so that adequate protective measures to avoid transmission are implemented. Upcoming studies should emphasize on quantifying the real impact of the CCHFV circulation for the local population through the combined assessment of viral evidence in ticks, animal hosts and humans. Identifying CCHFV incidence in hospital settings and estimating the prevalence of infection across high-risk populations is a priority. In addition, a deeper understanding of tick-mediated transmission including a better characterization of tick species involved with CCHFV and their distribution is required to clarify local viral dynamics and the risk of infection for human and animal populations. Lastly, molecular characterization of viral strains followed by phylogenetic and phylogeographic analysis are the next step towards a better understanding of viral genetic diversity and dispersion patterns across the country.

Supporting information

S1 Checklist. STROBE Statement—Checklist of items that should be included in reports of cross-sectional studies.

(S DOC)

S1 Appendix. Individual risk-factor model details, performance and fit.

(DOCX)

S2 Appendix. Ecological model details, performance and fit.

(DOCX)

S1 Table. Seroprevalence of Crimean-Congo Haemorrhagic fever in pastoral cattle stratified at the Divisional/sub-Divisional level.

(DOCX)
S1 Fig. Distribution of the seropositive herds in the dairy sample from the North West Region. The map shows the location of sampled herds and its serological status. Each herd is symbolized by a dot and the colour associated to it represents the classification according to the serological status of the herd. Shapefile obtained from GADM database, freely available for academic uses with permission from Global Administrative Areas (https://gadm.org/maps/CMR.html). The figure was made with RStudio version 3.5.3.

Acknowledgments
We would like to thank all the cattle keepers in the North West Region and the Vina Division of the Adamawa Region, whom collaborated in good will with their time and herd access to make data collection possible; also, we would like to acknowledge the support from the Ministry of Livestock, Fisheries and Industrial Agriculture -MINEPIA- during the planning and execution stages of the project. Many thanks to Saidou Hamman who facilitated many of the contacts with the herdmens, conducted the questionnaire in Fulfulde, English or French and supported the sampling process. To Rebecca Callaby for her coding advice.

Author Contributions
Conceptualization: Lina González Gordon, Paul R. Bessell, Barend MdeC Bronsvoort, Robert F. Kelly.
Data curation: Paul R. Bessell, Ian G. Handel, Barend MdeC Bronsvoort, Robert F. Kelly.
Formal analysis: Lina González Gordon, Paul R. Bessell.
Funding acquisition: Vincent N. Tanya, Lucy Ndip, Barend MdeC Bronsvoort.
Investigation: Lina González Gordon, Egbe F. Nkongho, Robert F. Kelly.
Methodology: Lina González Gordon, Paul R. Bessell, Egbe F. Nkongho, Victor N. Ngwa, Vincent N. Tanya, Melissa Sander, Lucy Ndip, Kenton L. Morgan, Ian G. Handel, Stella Mazeri, Barend MdeC Bronsvoort, Robert F. Kelly.
Project administration: Lina González Gordon, Barend MdeC Bronsvoort, Robert F. Kelly.
Resources: Lina González Gordon, Melissa Sander, Kenton L. Morgan, Ian G. Handel, Stella Mazeri, Barend MdeC Bronsvoort, Robert F. Kelly.
Software: Lina González Gordon, Paul R. Bessell.
Supervision: Barend MdeC Bronsvoort, Robert F. Kelly.
Visualization: Lina González Gordon.
Writing – original draft: Lina González Gordon, Paul R. Bessell, Barend MdeC Bronsvoort, Robert F. Kelly.
Writing – review & editing: Lina González Gordon, Paul R. Bessell, Egbe F. Nkongho, Victor N. Ngwa, Vincent N. Tanya, Melissa Sander, Lucy Ndip, Kenton L. Morgan, Ian G. Handel, Stella Mazeri, Barend MdeC Bronsvoort, Robert F. Kelly.

References
1. Ergınül Ö. Crimean-Congo haemorrhagic fever. Lancet Infect Dis. 2006; 6: 203–214. https://doi.org/10.1016/S1473-3099(06)70435-2 PMID: 16554245
2. Spengler JR, Bente DA, Bray M, Burt F, Hewson R, Korukluoglu G, et al. Second International Conference on Crimean-Congo Hemorrhagic Fever. Antiviral Res. 2018; 150: 137–147. https://doi.org/10.1016/j.antiviral.2017.11.019 PMID: 29190036

3. Spengler JR, Bergeron E, Spiropoulou CF. Crimean-Congo hemorrhagic fever and expansion from endemic regions. Curr Opin Virol. 2019; 34: 70–78. https://doi.org/10.1016/j.coviro.2018.12.002 PMID: 30660091

4. World Health Organization (WHO). Geographic distribution of Crimean-Congo Haemorrhagic Fever. 2017. Available: https://www.who.int/ emergencies/diseases/crimean-congo-haemorrhagic-fever/

5. Tipih T, Burt FJ. Crimean-Congo Hemorrhagic Fever Virus: Advances in Vaccine Development. Bioresearch Open Access. 2020; 9: 137–150. https://doi.org/10.1089/biores.2019.0057 PMID: 32461819

6. Spengler JR, Bente DA. Therapeutic intervention in Crimean-Congo hemorrhagic fever: where are we now? Future Virol. 2015; 10: 203–206. https://doi.org/10.2217/fvl.14.115 PMID: 26379760

7. Mehand MS, Al-Shorbaji F, Millett P, Murgue B. The WHO R&D Blueprint: 2018 review of emerging infectious diseases requiring urgent research and development efforts. Antiviral Res. 2018; 159: 63–67. https://doi.org/10.1016/j.antiviral.2018.09.009 PMID: 30261226

8. Hoogstraal H. The Epidemiology of Tick-Borne Crimean-Congo Hemorrhagic Fever in Asia, Europe, and Africa. J Med Entomol. 1979; 15: 307–417. https://doi.org/10.1093/jmedent/15.4.307 PMID: 113533

9. Cevik MA, Erbay A, Bodur H, Gülderen E, Baştuğ A, Kubar A, et al. Clinical and laboratory features of Crimean-congo hemorrhagic fever: predictors of mortality. Int J Infect Dis IS JD Off Publ Int Soc Infect Dis. 2008; 12: 374–379. https://doi.org/10.1016/j.ijid.2007.09.016 PMID: 18063402

10. Belobo JTE, Kenmoe S, Kengne-Nde C, Emoh CPD, Bowo-Ngandji A, Tchatchouang S, et al. Worldwide epidemiology of Crimean-Congo Hemorrhagic Fever Virus in humans, ticks and other animal species, a systematic review and meta-analysis. PLoS Negl Trop Dis. 2021; 15: e0009299. https://doi.org/10.1371/journal.pntd.0009299 PMID: 33886556

11. Fletcher TE, Guizhian A, Ahmeti S, Al-Abri SS, Asik Z, Atilla A, et al. Infection prevention and control practice for Crimean-Congo hemorrhagic fever-A multi-center cross-sectional survey in Eariasia. PLoS One. 2017; 12: e0182315–e0182315. https://doi.org/10.1371/journal.pone.0182315 PMID: 28886039

12. Spengler JR, Estrada-Peña A, Garrison AR, Schmaljohn C, Spiropoulou CF, Bergeron É, et al. A chronological review of experimental infection studies of the role of wild animals and livestock in the maintenance and transmission of Crimean-Congo hemorrhagic fever virus. Antiviral Res. 2016/10/03. 2016; 135: 31–47. https://doi.org/10.1016/j.antiviral.2016.09.013 PMID: 27713073

13. Gargili A, Estrada-Peña A, Spengler JR, Lukashev A, Nutall PA, Bente DA. The role of ticks in the maintenance and transmission of Crimean-Congo hemorrhagic fever virus: A review of published field and laboratory studies. Antivir Res. 2017; 144: 93–119. https://doi.org/10.1016/j.antiviral.2017.05.010 PMID: 28579441

14. Estrada-Peña A, De La Fuente J, Latapia T, Ortega C. The impact of climate trends on a tick affecting public health: A retrospective modeling approach for Hylomorpha marginata (ixodidae). PLoS One. 2015; 10: 1-16. https://doi.org/10.1371/journal.pone.0125760 PMID: 25956315

15. Gale P, Estrada-Peña A, Martinez M, Ulrich RG, Wilson A, Capelli G, et al. The feasibility of developing a risk assessment for the impact of climate change on the emergence of Crimean-Congo haemorrhagic fever in livestock in Europe: A Review. J Appl Microbiol. 2010; 108: 1859–1870. https://doi.org/10.1111/j.1365-2672.2009.04638.x PMID: 20015209

16. Estrada-Pena A, Jameson L, Medlock J, Vatansever Z, Tishkova F, Estrada-Peña A, et al. Unraveling the ecological complexities of tick-associated Crimean-congo hemorrhagic fever virus transmission: A gap analysis for the western palearctic. Vector-Borne Zoonotic Dis. 2012; 12: 743–752. https://doi.org/10.1089/zbv.2011.0767 PMID: 22448676

17. Gray JS, Dautel H, Estrada-Peña A, Kahl O, Lindgren E. Effects of Climate Change on Ticks and Tick-Borne Diseases in Europe. Interdiscip Perspect Infect Dis. 2009; 2009: 1–12. https://doi.org/10.1155/2009/593322 PMID: 19277106

18. Schuster I, Mertens M, Mrenoshi K, Staubach C, Mertens C, Brüning F, et al. Sheep and goats as indicator animals for the circulation of CCHFV in the environment. Hartemink N, editor. Exp Appl Acarol. 2016; 68: 337–346. https://doi.org/10.1007/s10493-015-9996-y PMID: 26704262

19. Spengler JR, Bergeron E, Rollin PE. Seroprevalence studies of Crimean-Congo hemorrhagic fever virus in domestic and wild animals. PLoS Negl Trop Dis. 2016; 10: e0004210. https://doi.org/10.1371/journal.pntd.0004210 PMID: 26741652

20. Gonzalez JP, Camicas JL, Cornet JP, Wilson ML. Biological and clinical responses of west African sheep to Crimean-Congo haemorrhagic fever virus experimental infection. Res Virol. 1998; 149: 445–455. https://doi.org/10.1016/s0923-2516(99)80013-2 PMID: 9923021
21. Walker AR, Bouattour A, Camicas J-L, Estrada-Peña A, Horak IG, Latif AA, et al. Ticks of Domestic Animals in Africa: a Guide to Identification of Species. Edinburgh: Biosciences Reports; 2003.

22. Grard G, Drexler JF, Fair J, Muyembe-J-J, Wolfe ND, Drosten C, et al. Re-emergence of Crimean-Congo hemorrhagic fever virus in Central Africa. PLoS Negl Trop Dis. 2011; 5: e1350–e1350. https://doi.org/10.1371/journal.pntd.0001350 PMID: 22022629

23. Okely M, Anan R, Gad-Allah S, Samy AM. Mapping the environmental suitability of etiological agent and tick vectors of Crimean-Congo hemorrhagic fever. Acta Trop. 2020; 203: 105319. https://doi.org/10.1016/j.actatropica.2019.105319 PMID: 31874130

24. Mangombi JB, Roqueplo C, Sambou M, Dahmani M, Medianikov O, Comtet L, et al. Seroprevalence of Crimean-Congo Hemorrhagic Fever in Domesticated Animals in Northwestern Senegal. Vector Borne Zoonotic Dis. 2020; 20: 797–799. https://doi.org/10.1089/vbz.2019.2592 PMID: 32429789

25. Balinandi S, von Brömssen C, Tumusime A, Kyondo J, Kwon H, Monteil VM, et al. Serological and molecular study of Crimean-Congo hemorrhagic fever virus in cattle from selected districts in Uganda. J Virol Methods. 2021; 114075. https://doi.org/10.1016/j.jviromet.2021.114075 PMID: 33515661

26. Adam IA, Mahmoud MAM, Aradaib IE. A seroepidemiological survey of Crimean Congo hemorrhagic fever among Cattle in North Kordufan State, Sudan. Virol J. 2013; 10: 178. https://doi.org/10.1186/1743-422X-10-178 PMID: 23738961

27. Adam IA, Mahmoud MA, Aradaib IE. Epidemiological survey of Crimean Congo hemorrhagic fever virus in cattle in East Darfur State, Sudan. TICKS Tick Borne Dis. 2015; 6: 439–444. https://doi.org/10.1016/j. tbbdis.2015.03.002 PMID: 25899893

28. Sas MA, Mertens M, Isselmu E, Reimer N, El Mamy BO, Doumbia M, et al. Crimean-Congo Hemorrhagic Fever Virus-Specific Antibody Detection in Cattle in Mauritania. Vector Borne Zoonotic Dis. 2017; 17: 582–587. https://doi.org/10.1089/vbz.2016.2084 PMID: 28605299

29. Burt FJ, Spencer DC, Leman PA, Patterson B, Swanepoel R. Investigation of tick-borne viruses as pathogens of humans in South Africa and evidence of Dugbe virus infection in a patient with prolonged thrombocytopenia. Epidemiol Infect. 1996; 116: 353–361. https://doi.org/10.1017/s0950268800052687 PMID: 866081

30. Swanepoel R, Shepherd AJ, Leman PA, McGillivray GM, Erasmus MJ, Searle LA, et al. Epidemiologic and clinical features of Crimean-Congo hemorrhagic fever in southern Africa. Am J Trop Med Hyg. 1987; 36: 120–132. https://doi.org/10.4269/ajtmh.1987.36.120 PMID: 310525

31. CDC. Crimean-Congo Hemorrhagic Fever (CCHF) Distribution Map. Available: https://www.cdc.gov/vhf/crimean-congo/outbreaks/distribution-map.html

32. Messina JP, Pigott DM, Duda KA, Brownstein JS, Myers MF, George DB, et al. A global compendium of human Crimean-Congo haemorrhagic fever virus occurrence. Sci data. 2015; 2: 150016. https://doi.org/10.1038/sdata.2015.03.002 PMID: 25977820

33. ProMED—International Society for Infectious Diseases. ProMED-mail. Available: https://promedmail.org

34. Horton KC, Wasyf M, Samaha H, Abdel-Rahman B, Safwat S, Fadl MA, et al. Serosurvey for Zoonotic Viral and Bacterial Pathogens Among Slaughtered Livestock in Egypt. Vector Borne Zoonotic Dis. 2014; 14: 633–639. https://doi.org/10.1089/vbz.2013.1525 PMID: 25198525

35. Schulz A, Barry Y, Stoek F, Ba A, Schulz J, Haki ML, et al. Crimean-Congo hemorrhagic fever virus antibody prevalence in Mauritanian livestock (cattle, goats, sheep and camels) is stratified by the animal’s age. J Virol Methods. 2021; 203: 105319. https://doi.org/10.1016/j.jviromet.2021.105319 PMID: 32684469

36. Naidenova V E, Zakharov KS, Kartashov MY, Agafonov DA, Senichkina AM, Magassouba NF, et al. Prevalence of Crimean-Congo hemorrhagic fever virus in rural areas of Guinea. TICKS Tick Borne Dis. 2020; 11: 101475. https://doi.org/10.1016/j.tbbdis.2020.101475 PMID: 32723661

37. Mariner JC, Morrill J, Ksiazek TG, J.C. M, J. M. Antibodies to hemorrhagic fever viruses in domestic liv- stock in Niger: Rift Valley fever and Crimean-Congo hemorrhagic fever. Am J Trop Med Hyg. 1995; 53: 217–221. https://doi.org/10.4269/ajtmh.1995.53.217 PMID: 7573699

38. Sadeuh-Mba SA, Yonga Wansi GM, Demanou M, Gessain A, Njouom R. Serological evidence of rift valley fever Phlebovirus and Crimean-Congo hemorrhagic fever orthonairovirus infections among pygmies in the east region of Cameroon. Virol J. 2018; 15: 63. https://doi.org/10.1186/s12985-018-0977-8 PMID: 29625611

39. Messina JP, Pigott DM, Golding N, Duda KA, Brownstein JS, Weiss DJ, et al. The global distribution of Crimean-Congo hemorrhagic fever. Trans R Soc Trop Med Hyg. 2015; 109: 503–513. https://doi.org/10.1093/trstmh/trv050 PMID: 26142451

40. Kelly RF. The epidemiology of bovine tuberculosis and influence of liver flu co-infection in Camerooon, Central Africa. University of Edinburgh. 2017.
41. Bronsvoo rt BMDC, Tanya VN, Kitching RP, Nfon C, Hamman SM, Morgan KL. Foot and Mouth Disease and Livestock Husbandry Practices in the Adamawa Province of Cameroon. Trop Anim Health Prod. 2003; 35: 491–507. https://doi.org/10.1023/a:102730252301 PMID: 14690088

42. Central Intelligence Agency (CIA). The World Factbook 2016. Skyhorse; 2015.

43. United Nations World Food Programme. Comprehensive Food Security and Vulnerability Analysis (CFSVA): Cameroon. 2017.

44. Epee Misse PT. Climate Change Adaptation Options for Maize Growers in the Adamawa Region of Cameroon. SSRN Electron J. 2019; 13. https://doi.org/10.2139/ssrn.3328092

45. Ngalim AN, Fern B. Cattle Rearing Systems in the North West Region of Cameroon: Historical Trends on Changing Techniques and Strategies. 2015; 2: 175–189.

46. Motta P, Porphyre T, Hamman SM, Morgan KL, Ngwa VN, Tanya VN, et al. Cattle transhumance and agropastoral nomadic herding practices in Central Cameroon. BMC Vet Res. 2018; 14. https://doi.org/10.1186/s12917-018-1515-z PMID: 29970084

47. Kelly RF, Hamman SM, Morgan KL, Nikongho EF, Ngwa VN, Tanya V, et al. Knowledge of Bovine Tuberculosis, Cattle Husbandry and Dairy Practices amongst Pastoralists and Small-Scale Dairy Farmers in Cameroon. PLoS One. 2016; 11: e0146538. https://doi.org/10.1371/journal.pone.0146538 PMID: 26745871

48. Kelly RF, Jennings A, Hunt J, Hamman SM, Mazeri S, Nikongho EF, et al. The epidemiology of bacterial zoonoses in pastoral and dairy cattle in Cameroon, Central Africa. Zoonoses Public Health. 2021; n/a. https://doi.org/10.1111/zph.12865 PMID: 34129288

49. Ebangi AL, Erasmus GJ, Neser FWC, Tawah CL. Genetic trends for growth in the Gudali and Wakwa cattle breeds of Cameroon. S Afr J Anim Sci. 2000; 30: 28–30. https://doi.org/10.4314/sajas.v30i4.3899

50. Sas MA, Comtet L, Donnet F, Mertens M, Vatansesev Z, Tordo N, et al. A novel double-antigen sandwich ELISA for the species-independent detection of Crimean-Congo hemorrhagic fever virus-specific antibodies. Antiviral Res. 2018; 151: 24–26. https://doi.org/10.1016/j.antiviral.2018.01.006 PMID: 29330092

51. IDvet Innovative Diagnostics. ID Screen CCHF Double Antigen Multi-species®. Grabels; 2019. p. 4.

52. R Core Team. R: a language and environment for statistical computing. Vienna (Austria): R Foundation for Statistical Computing; 2013.

53. Team Rs. RStudio: Integrated Development Environment for R. Boston, MA: RStudio, PBC.; 2020.

54. Wickham H. ggplot2: Elegant Graphics for Data Analysis. Springer-Verlag New York; 2016.

55. GADM. Database of Global Administrative Areas. Available: https://gadm.org

56. Lumley T. Analysis of complex survey samples. J Stat Softw. 2004; 9: 1–19.

57. Reiczigel J, Foldi J, Ozsvari L. Exact confidence limits for prevalence of a disease with an imperfect diagnostic test. Epidemiol Infect. 2010; 138: 1674–1678. https://doi.org/10.1017/S0950268810000385 PMID: 20196903

58. Bates D, Mächler M, Bolker B, Walker S. Fitting Linear Mixed-Effects Models Using [lme4]. J Stat Softw. 2015; 67: 1–48. https://doi.org/10.18637/jss.v067.i01

59. Heinze G, Wallisch C, Dunkler D. Variable selection—A review and recommendations for the practicing statistician. Biom J. 2018/01/02. 2018; 60: 431–449. https://doi.org/10.1002/bimj.201700067 PMID: 29292533

60. Bartoń K. MuMIn: Multi-Model Inference. 2019.

61. Fabozzi FJ, Focardi SM, Rachev ST, Selection M. Model Selection Criterion: AIC and BIC. 2014; 41: 399–403.

62. Harris I, Osborn TJ, Jones P, Lister D. Version 4 of the CRU TS monthly high-resolution gridded multivariate climate dataset. Sci Data. 2020; 7: 109. https://doi.org/10.1038/s41597-020-0453-3 PMID: 32246091

63. ESA. Land Cover CCI Product User Guide Version 2. Tech. Rep. 2017.

64. Hartig F. DHARMa: residual diagnostics for hierarchical (multi-level/mixed) regression models. 2021 [cited 23 Jun 2021]. Available: https://cran.r-project.org/web/packages/DHARMa/vignettes/DHARMa.html#calculating-scaled-residuals

65. Sanchez J, Doering M, Multiclass T. Package ‘pROC.’ 2021. p. 96.

66. Tjur T. Coefficients of determination in logistic regression models—A new proposal: The coefficient of discrimination. Am Stat. 2009; 63: 366–372. https://doi.org/10.1198/last.2009.08210

67. Nakagawa S, Johnson PCD, Schielzeth H. The coefficient of determination R2 and intra-class correlation coefficient from generalized linear mixed-effects models revisited and expanded. J R Soc Interface. 2017; 14. https://doi.org/10.1098/rsif.2017.0213 PMID: 28904005
Fisher-Hoch SP, McCormick JB, Swanepoel R, Van Middelkoop A, Harvey S, Kustner HG V, et al. Risk
83.
82.
81.
80.
79.
78.
77.
76.
75.
74.
73.
72.
71.
70.
69.
68.
67.
66.
65.
64.
63.
62.
61.
60.
59.
58.
57.
56.
55.
54.
53.
52.
51.
50.
49.
48.
47.
46.
45.
44.
43.
42.
41.
40.
39.
38.
37.
36.
35.
34.
33.
32.
31.
30.
29.
28.
27.
26.
25.
24.
23.
22.
21.
20.
19.
18.
17.
16.
15.
14.
13.
12.
11.
10.
9.
8.
7.
6.
5.
4.
3.
2.
1.

Lorusso V, Picozzi K, Bronsvoort BMC De, Majekodunmi A, Dongkum C. Ixodid ticks of traditionally
Eyo J, Felicia E, Ikechukwu O. Survey of Tick Infestation of Cattle at Four Selected Grazing Sites in the
Parasit Vectors. 2013; 6: 1. https://doi.org/10.1186/1756-3305-6-1 PMID: 23281838

Tawah CL. Comparative study of tick burdens in Gudali and Wakwa cattle under natural infestation in
the subhumid highlands of Wakwa, Cameroon. Preliminary observations. Rev Elev Med Vet Pays Trop.
1992; 45: 310–313. PMID: 1339999

Rehman A, Nijhof AM, Sauter-Louis C, Schaue r B, Staubach C, Conraths FJ. Distribution of ticks infest-
ing ruminants and risk factors associated with high tick prevalence in livestock farms in the semi-arid
and arid agro-ecological zones of Pakistan. Parasites and Vectors. 2017; 10: 1–15. https://doi.org/10.
1186/s13071-016-1943-1 PMID: 28049510

Awa DN, Adakal H, Luogbou NDD, Wachong KH, Leinyuy I, Achukwi MD. Cattle ticks in Cameroon: is
Rhipicephalus (Boophilus) microplus absent in Cameroon and the Central African region? Ticks Tick
Borne Dis. 2015; 6: 117–122. https://doi.org/10.1016/j.ttbdis.2014.10.005 PMID: 25575435

Silatsa BA, Simo G, Githaka N, Mwaura S, Kamga RM, Oumarou F, et al. A comprehensive survey of
the prevalence and spatial distribution of ticks infesting cattle in different agro-ecological zones of Cam-
eroon. Parasites and Vectors. 2019; 12: 1–14. https://doi.org/10.1186/s13071-018-3256-z PMID:
30606222

Mohamed M, Said AR, Murad A, Graham R. A serological survey of Crimean-Congo haemorrhagic
fever in animals in the Sharkia Governorate of Egypt. Vet Ital. 2008; 44: 513–517. PMID: 20405447

Sas MA, Mertens M, Kadiat JG, Schuster I, Pongombo CPS, Maloba AGK, et al. Serosurvey for Cri-
mean-Congo hemorrhagic fever virus infections in ruminants in Katanga province, Democratic Republic
of the Congo. Ticks Tick Borne Dis. 2017; 8: 858–861. https://doi.org/10.1016/j.ttbdis.2017.07.001
PMID: 28715556

Gonzalez J-P, LeGuennon B, Guillaud M, Wilson ML, J.-P. G, B. L, et al. A fatal case of Crimean-Congo
haemorrhagic fever in Mauritania: virological and serological evidence suggesting epidemic transmis-
sion. Trans R Soc Trop Med Hyg. 1990; 84: 573–576. https://doi.org/10.1016/0035-9203(90)90045-g
PMID: 2128671

Tawah CL. Comparative study of tick burdens in Gudali and Wakwa cattle under natural infestation in
the subhumid highlands of Wakwa, Cameroon. Preliminary observations. Rev Elev Med Vet Pays Trop.
1992; 45: 310–313. PMID: 1339999

Eyo J, Felicia E, Ikechukwu O. Survey of Tick Infestation of Cattle at Four Selected Grazing Sites in the
Tropics Four Selected Grazing Sites in the Tropics. 2014. https://doi.org/10.5829/idosi.gv.2014.12.04.
8325

Lorusso V, Piccozzi K, Bronsvoort BMC De, Majekodunmi A, Dongkum C. Ixodid ticks of traditionally
managed cattle in central Nigeria: where Rhipicephalus (Boophilus) microplus does not dare (yet?).
Parasit Vectors. 2013; 6: 1. https://doi.org/10.1186/1756-3305-6-1 PMID: 23281838

Fisher-Hoch SP, McCormick JB, Swanepoel R, Van Middelkoop A, Harvey S, Kustner HG V, et al. Risk
of human infections with Crimean-Congo hemorrhagic fever virus in a South African rural community.
Am J Trop Med Hyg. 1992; 47: 337–345. https://doi.org/10.4269/ajtmh.1992.47.337 PMID: 1524147

Adinci KJ, Akpo Y, Sessou P, Yessinou RE, Adehan SB, Issaka AK, et al. Influence of transhumance
on the spread of Rhipicephalus microplus (Canestrini, 1888) in Benin. 2018; 7710: 226–232.

De Liberato C, Frontoso R, Magliano A, Montemaggi ori A, Autorino GL, Sala M, et al. Monitoring for the
possible introduction of Crimean-Congo haemorrhagic fever virus in Italy based on tick sampling on
migratory birds and serological survey of sheep flocks. Prev Vet Med. 2018; 149: 47–52. https://doi.org/
10.1016/j.prevetmed.2017.10.014 PMID: 29290300

Sumner T, Orton RJ, Green DM, Kao RR, Gubbins S. Quantifying the roles of host movement and vec-
tor dispersal in the transmission of vector-borne diseases of livestock. PLoS Comput Biol. 2017; 13:
e1005470–e1005470. https://doi.org/10.1371/journal.pcbi.1005470 PMID: 28369082
87. Maldonado-Ruiz LP, Park Y, Zurek L. Liquid water intake of the lone star tick, Amblyomma americanum: Implications for tick survival and management. Sci Rep. 2020; 10: 6000. https://doi.org/10.1038/s41598-020-6304-9 PMID: 32265527

88. Duygu F, Sari T, Kaya T, Tavsan O, Naci M. The relationship between crimean-congo hemorrhagic fever and climate: Does climate affect the number of patients?. Acta Clin Croat. 2018; 57: 443–448. https://doi.org/10.20471/acc.2018.57.03.06 PMID: 31168176

89. Mostafavi E, Chinkar S, Bokaei S, Haghdoost A. Temporal modeling of Crimean-Congo hemorrhagic fever in eastern Iran. Int J Infect Dis. 2013; 17: e524–e528. https://doi.org/10.1016/j.ijid.2013.01.010 PMID: 23474177

90. Estrada-Peña A, Salman M. Current limitations in the control and spread of ticks that affect livestock: A review. Agric. 2013; 3: 221–235. https://doi.org/10.3390/agriculture3020221

91. Blakely TA, Woodward AJ. Ecological effects in multi-level studies. J Epidemiol Community Health. 2000; 54: 367 LP–374. https://doi.org/10.1136/jech.54.5.367 PMID: 10814658

92. Tack W, Madder M, Baeten L, De Frenne P, Verheyen K. The abundance of Ixodes ricinus ticks depends on tree species composition and shrub cover. Parasitology. 2012; 139: 1273–1281. https://doi.org/10.1017/S0031182012000625 PMID: 22717041

93. Tack W, Madder M, Baeten L, Vanhellemont M, Verheyen K. Shrub clearing adversely affects the abundance of Ixodes ricinus ticks. Exp Appl Acarol. 2013; 60: 411–420. https://doi.org/10.1007/s10493-013-9655-0 PMID: 23344639

94. Vescio FM, Busani L, Mughini-Gras L, Khoury C, Avellis L, Taseva E, et al. Environmental correlates of Crimean-Congo haemorrhagic fever incidence in Bulgaria. BMC Public Health. 2012; 12: 1116. https://doi.org/10.1186/1471-2458-12-1116 PMID: 23270399

95. Estrada-Peña A, Zatansever Z, Gargili A, Aktas M, Uzun R, Ergonul O, et al. Modeling the spatial distribution of Crimean-Congo Hemorrhagic Fever outbreaks in Turkey. Vector-Borne Zoonotic Dis. 2007; 7: 667–679. https://doi.org/10.1089/vbz.2007.0134 PMID: 18047397

96. Gonzalez JP, Josse R, Johnson ED, Merlin M, Georges AJ, Abandja J, et al. Antibody prevalence against haemorrhagic fever viruses in randomized representative central African populations. Res Virol. 1989; 140: 319–331. https://doi.org/10.1016/s0923-2516(89)80112-8 PMID: 2505350

97. Swanepoel R, Shepherd AJ, Leman PA, Shepherd SP, Miller GB. A common-source outbreak of Crimean-Congo haemorrhagic fever on a dairy farm. S Afr Med J. 1985; 68: 635–637. PMID: 3933131

98. Balinandi S, Patel K, Ojwang J, Kyondo J, Mulei S, Tumusiime A, et al. Investigation of an isolated case of human Crimean–Congo hemorrhagic fever in Central Uganda, 2015. Int J Infect Dis. 2018; 68: 88–93. https://doi.org/10.1016/j.ijid.2018.01.013 PMID: 29382607

99. Bukbuk DN, Dowall SD, Lewandowski K, Bosworth A, Baba SS, Varghese A, et al. Serological and Virological Evidence of Crimean-Congo Haemorrhagic Fever Virus Circulation in the Human Population of Borno State, Northeastern Nigeria. PLoS Negl Trop Dis. 2016; 10: 1–12. https://doi.org/10.1371/journal.pntd.0005126 PMID: 27926935