Middle East Respiratory Syndrome-Coronavirus in Camels: An Overview for Sub-Saharan and North Africa

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List of abbreviations

ELISA	Enzyme-Linked Immunosorbent Assay
MERS	Middle East Respiratory Syndrome
MERS-CoV	Middle East Respiratory Syndrome Coronavirus
PCR	Polymerase Chain Reaction
RT-PCT	eal Time Polymerase Chain Reaction

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SECTION 1

Introduction to Middle East Respiratory Syndrome Coronavirus (MERS-CoV)

More than 60 percent of the world population of one-humped dromedary camels (*Camelus dromedarius*) lives in the Greater Horn of Africa. Their role as one of the most important livestock species for nutrition in arid and semi-arid areas of Eastern Africa is likely to increase since the predicted climate change is in favour of this drought resilient species.

Camel milk, for domestic consumption or sale, is often the most important product for female and male pastoralists alike (K. Marshall et al. 2014). In 2012, a novel coronavirus called Middle East Respiratory Syndrome Coronavirus (MERS-CoV) emerged on the Arabian Peninsula. Human cases have been reported from 25 countries with the most recent outbreak in the Republic of Korea (which itself originated in the Middle East). MERS-CoV has caused at least 1,200 laboratory confirmed cases of severe respiratory infection, including more than 400 deaths.

Several studies have demonstrated that dromedary camels can act as a source of human MERS-CoV infection (Reusken et al. 2015). However, although the animal reservoir has been identified, the route of infection and types of exposures remains largely unknown.

MERS-CoV is an important zoonotic pathogen that might pose a risk to pastoral communities and other consumers of raw camel products such as milk. Furthermore, other potential sources of infection e.g. faeces and nasal discharge need to be characterised. So far no human cases of MERS-CoV infection have been reported in Africa. However, infections with MERS-CoV may go undetected in many African countries since routine surveillance systems are simply not in place due to the lack of diagnostic capacity and diagnostic networks of laboratories and courier services in most countries.

The objective of this report is to summarise the current knowledge on camel systems and MERS-CoV focusing on Africa and to highlight research gaps that need to be addressed in order to make rational decisions on disease mitigation in the African context.

1.1 Recommendations

To elucidate and mitigate the risk of MERS-CoV infections of humans and camels the following research questions need to be tackled:

- Diagnostic capacity needs to be established in many African laboratories
- The African camel population needs to be systematically screened in different countries regarding the presence of MERS-CoV
- MERS-CoV from African camels need to be characterized and compared to MERS-CoV in the Middle East

- The infection rate of camels (seroprevalence) in different regions of Africa needs to be elucidated to identify if possible disease free camel populations exist
- Tailor made diagnostic assays that can be applied in the field need to be developed together with African stakeholders
- The African camel populations and their trade routes need to be mapped

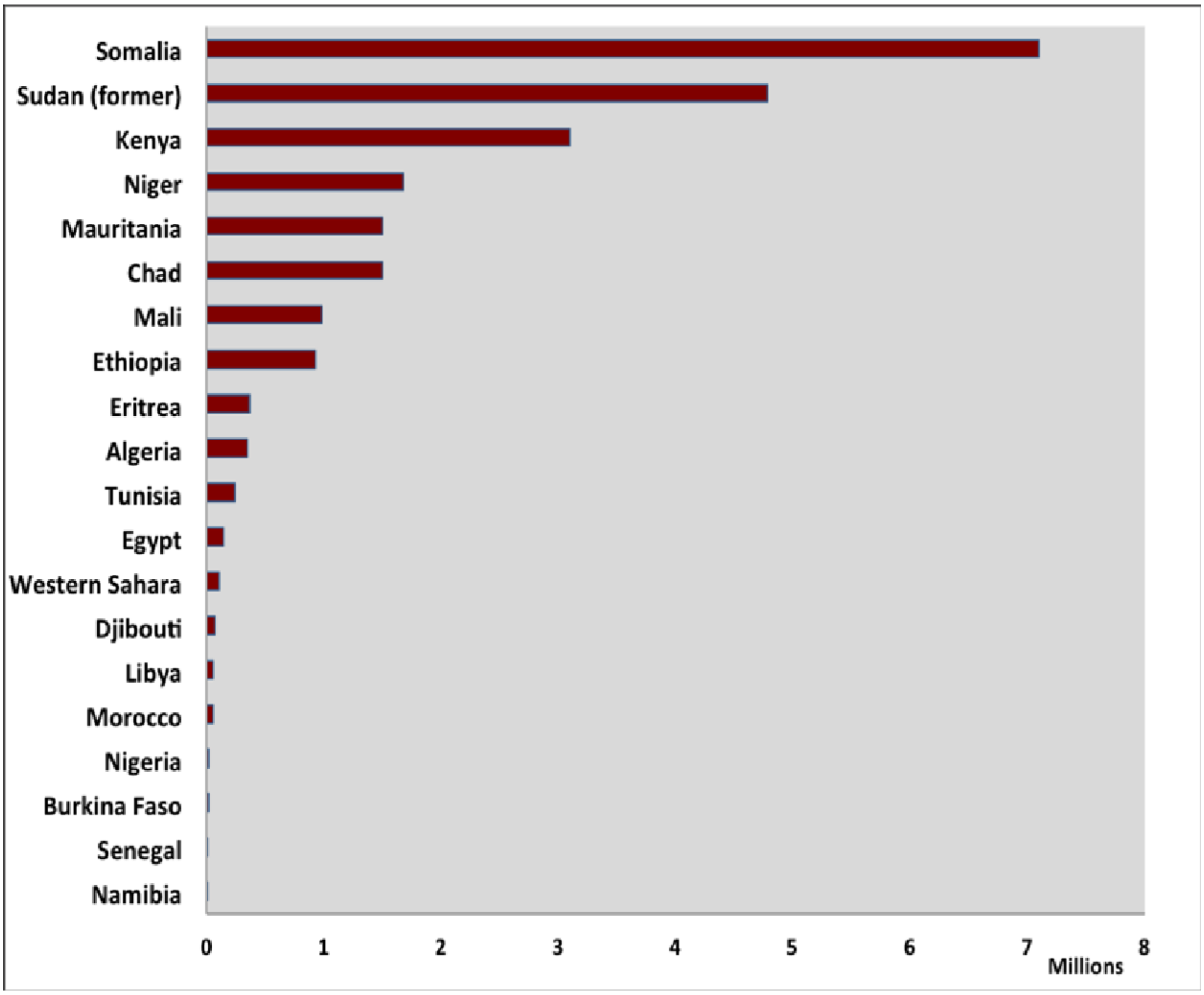
SECTION 2

Existing camel populations in Africa and the trade of camels within and from Africa: what we know

2.1 Camel populations in Africa

Camels have been a largely neglected group of livestock in the discourse relating to livestock and development. This is despite the fact that Africa hosts many million animals (Figure 1), with individual countries, such as Kenya, having substantial and growing camel populations.

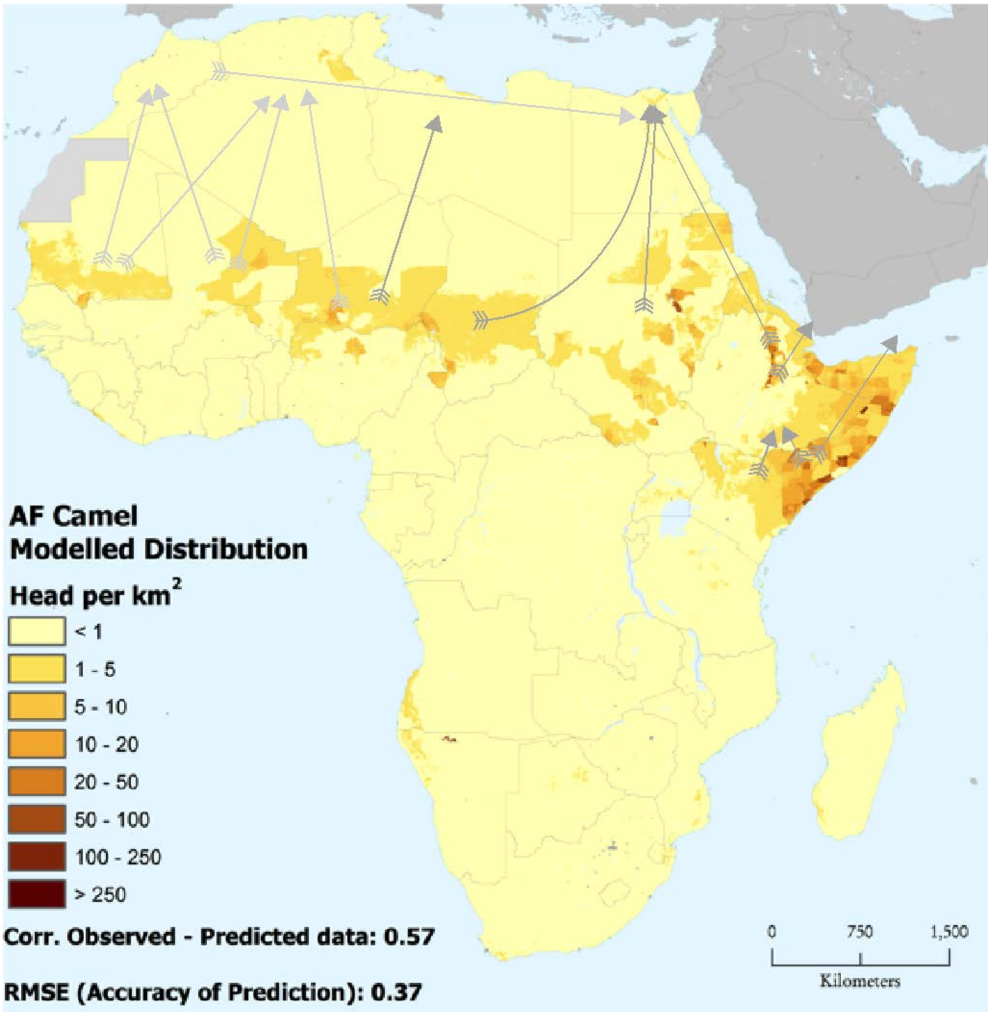
Figure 1 African camel populations (Source: FAO STATS)



Dromedaries play a vital role in the livelihoods and survival of majority of the nomadic pastoralists in Africa. They generate income for their owners' through provision of milk, meat, draught power, and transport. Camels not only act as social security to pastoralists but also provide transport for the nomadic communities. The unique adaptability of camels to the arid and marginalised areas and the significant contribution to the food security of the nomadic pastoral households cannot be ignored (Schwartz 1992). As the impact of climate change takes hold, it is likely that camels will gain in importance due to their adaptability to arid areas. The African continent harbours the vast majority of dromedary camels world-wide.

The Food and Agriculture Organization (FAO) of the United Nations estimates the world camel population to be 26,989,193 of which 89% are single-humped dromedary and 11 % are Bactrian (two-humped) (FAOSTAT 2015). Africa has 85% (estimated to be 24 million) of the world's camel population. More than 60% of the world's camel population is found in the Horn of Africa region (see Figure 2).

Figure 2 Map displaying African dromedary camel densities, Source: (Sebastian 2014) with added major camel trade routes shown as grey arrows (the light grey arrows correspond to expected lower numbers of animals traded)



2.2 Economic contribution of camels

Pastoralism is the main production system for camels in Africa but, to a low extent, large camel ranches do exist..

The economic contribution of camels in comparison to other domestic livestock is rather marginal on a global perspective. Nonetheless, in the Greater Horn of Africa, camel production contributes significantly to national economies. For instance, camel milk production in Kenya was valued at $ 21 million USD (Musinga et al. 2008).

2.2.1 The African camel trade

Egypt has a high demand for camel meat and has dominated camel trade in Africa accounting for 60% of imports from the Horn of Africa (Muthee 2006). It has the largest live camel market in the continent, Birqash Camel Market located 60 kilometres from Cairo. Camels traded in Birqash market are imported from numerous countries including: Ethiopia, Somalia, Sudan and Eritrea. Camels shipped from Somalia and Ethiopia are transported to Djibouti then moved to Egypt via the Red Sea from the port of Safaga for the Upper Egypt or from the port of Suez for the Lower Egypt markets respectively (Sayour et al. 2015). Camels from West Sudan are walked in convoys from El-Fasher, North Darfur state through the “Forty-Road” along the River Nile to Daraw camel market in Aswan. Likewise, camels from the east are trekked from Kassala State to Haleyeb and Shalateen areas in Egypt. Figure 2 above displays the camel density in Africa as well as major trade directions.

Considering the porous nature of most borders in the Horn of Africa and the North African region generally, it can be concluded that informal trade of live animals is substantial. For instance, there is minimal or no border control between Kenya and Ethiopia and Somalia. The unaccounted movement of camels from Kenya to its neighbours is sizeable. Moyale market, at the border of Kenya and Ethiopia acts as the catchment area for camels from Kenya and Somalia, before being trucked to Ethiopia for export to Egypt either through Nazareth to the prominent Djibouti route or through Nazareth to the Sudan route. Customarily, the Djibouti route is preferential as it is less perilous and the reported camel deaths are fewer (Mahmoud 2010).

The situation is similar in North Africa. According to (Kadim 2012) camels from Chad are exported to Egypt through Sudan (see Figure 2). In Niger camels are exported to Libya and Algeria while in Mali and Mauritania traders have an organised trade of live camels to markets in Morocco and Algeria (see Figure 2). The convergence of camels from the Horn of Africa and other northern nations to Egypt emphasise the fact that Egypt is a major camel market for Africa.

Equally important is the domestic trade of camels within respective nation. For example, camel trade within the precincts of Somalia is exemplified by the fact that livestock (including camels) contributes up to 40% of the national GDP. Hargeisa, the capital of Somaliland, is the main domestic camel market, receiving camels from various places within its borders.

Export of camels from Somalia to the Middle East has increased steadily over the last decade. According to a study in 2012 approximately 120,962 camels worth more than US$ 30 million were exported to Middle Eastern countries particularly: Saudi Arabia, the UAE, Oman, Yemen, Libya, Kuwait, Qatar and Bahrain. This well-coordinated trade takes place from four key export ports, namely: Berbera, Bosasso, Mogadishu and Kismayo and other minor ports of Merka and El Ma’an (Massimo et al. 2012).

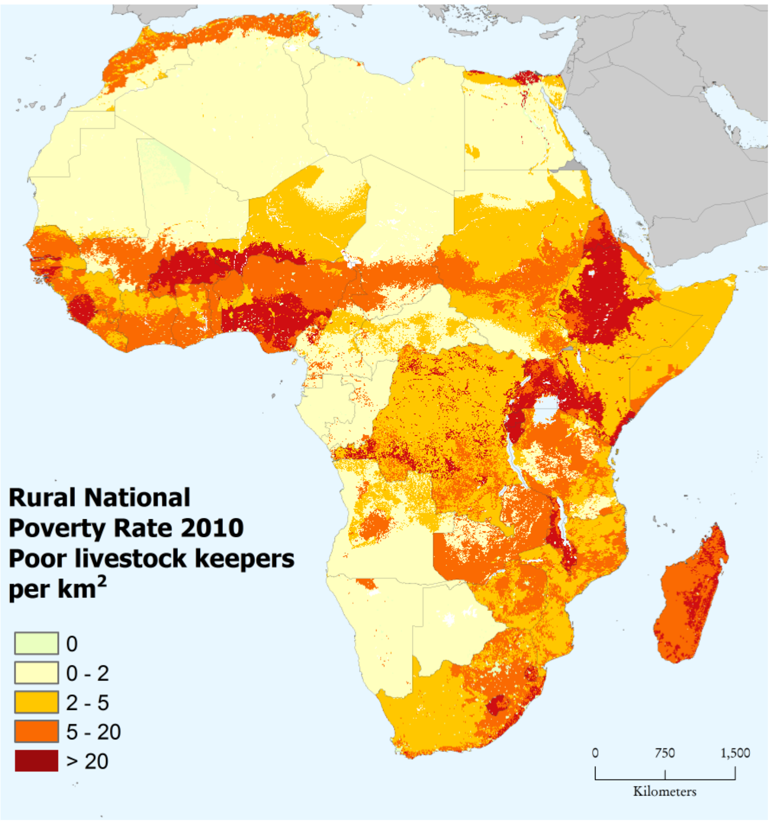
The camel trade both for domestic and export markets has a huge potential in Africa. The main enigma has been lack of satisfactory economic data to quantify the export flow and the impact of the trade in both national and regional economies.

2.2.2 Likely implications of a trade ban

Trade bans are imposed on countries that have infectious diseases in their livestock, which do not occur in countries that are free of these pathogens. They are imposed in order to prevent the spread of a disease and to protect the livestock in the importing country. A ban on camel trade within Africa is unlikely to be useful in current circumstances for the following reasons:

- A ban would only be effective with respect to disease control if MERS-CoV free camel populations exist in importing countries. Since the current status of MERS-CoV prevalence in many parts of Africa is unknown, a trade ban is likely to be more costly than efficient in MERS-CoV control.
- Imposing a ban on camel trade is difficult to justify on ethical grounds because MERS-CoV infections in humans have not been reported from Africa. It will be difficult to justify because it will affect the livelihoods of many poor people (see Figure 3).
- Last but not least, it is likely to be very difficult to impose a ban on informal camel trade, which is very common in Africa.

Figure 3 Map displaying African poor livestock keepers, Source: (Sebastian 2014)



SECTION 3

Review of existing published literature and any on-going research (where identified) to assess the prevalence of MERS-CoV in dromedary camel populations and the epidemiology of the disease

3.1 Assessing the prevalence of MERS-CoV

MERS-CoV infections in dromedary camels are often asymptomatic or associated with short periods of nasal discharge (rhinitis). To assess the prevalence of MERS-CoV infections two types of diagnostic methods have been used, one is the indirect detection method i.e. detection of host antibodies towards viral molecules using serological methods e.g. enzyme-linked immunosorbent assay (ELISA). The other one is the direct detection of viral nucleic acids (through quantification of the presence of nucleic acids via real-time polymerase chain reaction (RT-PCR) or conventional polymerase chain reaction (PCR) or alternatively the viral antigen through a capture ELISA targeting the nucleocapsid protein (NP). Using the indirect diagnostic methods, previous infections with MERS-CoV resulting in specific antibody responses to the pathogen, can be monitored. Since different coronaviruses circulating in camelids are antigenically sufficiently related, cross-reactivity in unspecific test formats, such as ELISA can result. Additional tests such as immunofluorescence assays or virus neutralisation assays require time-consuming analyses in expert laboratories or even live MERS-CoV within high containment facilities. Serological assays do however allow for studies regarding the epidemiological patterns, infection dynamics and whether the camels have had a previous infection or not. The timing of weaning of camel antibodies post infection adds substantial value when it comes to interpretation of the ELISA results.

Temporal patterns in viral detection have been described in the Arabian Peninsula but so far no longitudinal study has been published describing dynamics in pastoral herds in Africa. Thus, the prevalence and epidemiology of MERS-CoV in African camel populations remains largely unknown.

Several cross sectional studies based on indirect detection methods report a wide spread seropositivity in camels all over Africa (Corman et al. 2014b, Deem et al. 2015, Muller et al. 2014, Reusken et al. 2014b). However, the total number of African camels tested is low compared to the number of camels tested from the Arabian Peninsula.

Until now MERS-CoV isolation and characterisation in Africa has only been reported from a camel in Egypt likely imported from Ethiopia/Sudan (Chu et al. 2014). The virus isolated is genetically closely related to the human virus isolates, which may imply identical or very similar infection properties. The seroprevalence of camels in the Arabian Peninsula has been reported high, while the few data on African camels showed marked differences in seroprevalence (Corman et al. 2014b, Reusken et al. 2014b), which might be associated with different farming systems and smaller herd size.

A viral isolation rate of up to 30 % has been reported on the Arabian Peninsula while no data on isolation rates are available on African camels at the moment. The high recovery rate observed in many farms on the Arabian Peninsula might be attributed to the different farming systems, but this requires further investigation. Data obtained from camels in the Arabian Peninsula showed that especially camel calves get infected after the maternal antibodies weaned and are therefore the main pool of infected (Zumla et al. 2015).

Attempts to isolate MERS-CoV from a limited number of nasal swabs from Kenyan camels have not yet identified the virus (unpublished negative data based on only 450 nasal swabs investigated by ILRI researchers and its research partners). Whether the level of virus circulation is linked to different farming systems such as the predominant pastoralist systems in Africa compared to the intensive farming systems on the Arabian Peninsula is currently unknown. The time window of virus excretion is, according to experimental infections using a low number of animals (N=3), very short (up to one week) (Adney et al. 2014).

It has been shown that camel milk can contain MERS-CoV, but data supporting an active excretion of virus in milk in contrast to contamination of the teats via infected calves are not available at the moment (Reusken et al. 2014a). Experiments in which MERS-CoV has been added to camel milk have shown that the virus is relatively stable in milk and can survive for several days when stored at 4 degree Celsius (van Doremalen et al. 2014). Pasteurising milk kills the virus efficiently. Additionally it has been shown that virus can be excreted via the faecal route (Reusken et al. 2014a). Virus excreting and persistence have not been investigated on pastoral production systems.

In summary, the epidemiology of MERS-CoV in African dromedary camels is far from understood since very little research has been carried out on the continent and research gaps need to be addressed in the future.

SECTION 4

Review existing knowledge on the risk of transmission of MERS-CoV from camels to humans and vice versa

4.1 Transmission between infected and non-infected humans

Transmission of MERS-CoV has been reported via two routes, between infected and non-infected humans and between dromedary camels and humans. The existence of clusters of infected medical staff and families underpins the potential of the virus to spread between humans. The basic reproduction number (R_0), which is a measure to determine the contagious nature of the pathogen has been determined to be <1 (Cotten et al. 2014) and is relatively low compared to highly infectious diseases (such as Measles, which has an R0 >15). Therefore the current MERS-CoV has a very low potential to cause a pandemic. But since coronaviruses mutate constantly (albeit at a low rate compared to other viruses such as HIV), MERS-CoV has the potential to cause a pandemic if a mutation leads to a highly transmissible and virulent virus. A recent study calculated an evolutionary rate of 1.12×10^{-3} substitutions per site per year (Cotten et al. 2014) and a common ancestor of the current virus dating back to 2012, which underpins the potential of MERS-CoV to change within a short time window and demands further monitoring. While the transmission of the MERS-CoV has been shown between humans, many humans that have been infected were male above 50 years of age and had underlying diseases such as diabetes of liver disease (Zumla et al. 2015). The exact mechanisms of infection and the minimal infectious dose are not fully understood at the moment. However, MERS-CoV infections that lead to clinical signs have been shown to have a high rate of mortality (about 40 %).

4.2 Transmission from camels to humans

The epidemiology of many human MERS-CoV infections could not be correlated to the contact with diseased humans and therefore it was suspected that these humans might have been infected from other sources. Since many infectious diseases have their origin in animals (Woolhouse et al. 2012, Woolhouse and Gowtage-Sequeria 2005), several livestock species have been investigated for the presence of MERS-CoV via serological methods. In a first study the livestock species dromedary camel, goat, sheep and cattle have been investigated (Reusken et al. 2013a, Reusken et al. 2013b). Only the livestock species dromedary camel harboured neutralising antibodies against MERS-CoV.

It has been shown that a fraction of MERS index patients had previous contact with camels in one way or the other pointing towards the dromedary camel as a reservoir for infection with MERS-CoV (Zumla et al. 2015). Afterwards, research efforts have shown that MERS-CoV isolated from camels that had interactions with human patients before they developed MERS were identical with the MERS-CoV isolated from the humans (Alagaili et al. 2014, Haagmans et al. 2014). Several other studies confirmed the presence of MERS-CoV in dromedary camels all over the Arabian Peninsula (Hemida et al. 2014, Nowotny and Kolodziejek 2014, Raj et al. 2014, Yusof et al. 2015) and in Egypt (Chu et al. 2014). Additional screenings employing a high number of specimens collected from camels on the Arabian Peninsula concluded that dromedary camels harbour the pathogen all over the

Arabian Peninsula (Zumla et al. 2015). The isolation of identical virus from a camel and a MERS patient confirmed the transmission of MERS-CoV between camels and humans (Azhar et al. 2014a), but the 100% identity of the two MERS-CoV isolates has been challenged by others (Drosten et al. 2014). To answer the question of the direction of transmission from camels to humans or vice versa without performing laboratory experiments scientists employed an extensive phylogenetic analysis using full genome data of available MERS-CoV.

Many coronaviruses such as SARS-CoV have ancestors that can be found in bats (Drexler et al. 2014). Evidence about the direction of transmission from camels to humans was obtained from a phylogenetic study that incorporated a bat-derived coronavirus isolate from South Africa. The incorporation of this isolate enabled the rooting of the phylogenetic tree and confirmed more diverse and ancestral camel isolates compared to human isolates. Therefore, it can be assumed that camel MERS-CoV evolution preceded the human MERS-CoV evolution. As a result dromedary camel MERS-CoV represent donors of viruses for humans rather than the other way around (Corman et al. 2014a). A direct ancestor for MERS-CoV has not been identified yet and remains to be found. Humans that had interactions with camels developed a higher seroprevalence than humans without contact. They do not necessary have to develop disease but are likely to transmit the pathogen (Muller et al. 2015).

It can be assumed that humans infect themselves from infected droplets, derived from camels. It has been shown that camel barns can contain high numbers of infectious particles in the air (Azhar et al. 2014b), but whether the virus concentrations are sufficient to cause an active infection in humans remains to be elucidated. The vast majority of African dromedary camels are not kept in barns.

At the moment foodborne transmission of MERS-CoV via consumption of unpasteurised milk cannot be excluded and requires additional investigations (Reusken et al. 2014a, van Doremalen et al. 2014). Moreover, the absence of robust surveillance systems in many regions in Africa are likely to result in the non-detection of human MERS (Gossner et al. 2014). The implementation of robust surveillance systems and training courses for the diagnosis of MERS-CoV infections and other emerging pathogens are considered to be a necessity.

Up to now no clinical disease of people that have been infected in Africa has been reported. Only people that were infected on the Arabian peninsula and who returned to Tunisia (Africa) have been reported (Abroug et al. 2014).

SECTION 5

Researchable issues related to MERS in sub-Saharan and North Africa

Middle East Respiratory Syndrome is a zoonotic disease and research in Africa should follow a One Health approach. This means that the research should include: camels; people that have contact with camels; and people who consume camel products.

As part of this study we contacted a number of relevant development agencies and other research organisations to identify existing or planned initiatives to research the epidemiology of MERS in Sub-Saharan and North Africa. Their responses are provided in Annex 1. On the basis of this contact and our own undertaking of the issues we suggest that researchable issues include:

- the two topics of a) camels and b) humans at risk
- the development of diagnostic assays that are adapted for African field settings.

All research has to go hand in hand with capacity building in Africa to ensure its sustainable translation into policies and best practises to implement early warning systems for epidemics and this is also considered as part of our recommendations. Listed below are research questions that we consider important to be addressed, in order of priority.

A) Do dromedary camels in Africa harbour the same MERS-CoV as detected in the Arabian Peninsula?

MERS-CoV clearly has the potential to be zoonotic and infect humans. However, it is not clear to what extent this is a feature of MERS-CoV as a whole, or if it relates to some mutation that has occurred in a subset of virus populations in the Arabian Peninsula where human infections and outbreaks have been recorded. Thus, through collections of virus, it will be important to determine, at the genetic level, what MERS diversity is and what specific parts of its genome confer zoonotic potential. This activity will depend on close collaboration between field veterinarians and biologists and molecular systematics, linking cutting edge sequencing approaches to well characterised field isolates. This undertaking will include the more intricate task of sampling young animals in different geographical regions and different camel production systems, in an attempt to isolate MERS virus in a range of ecologies in sub-Saharan Africa. This will be essential to feed in to the global picture of MERS phylogenetics (Corman et al. 2014a, Cotten et al. 2014), understanding and quantifying viral diversity and evolutionary origins.

B) Why have human MERS-cases never been reported from Africa despite the high number of dromedary camels present?

It is difficult to imagine the presence of thousands of dromedary camels that are infected with MERS-CoV regularly infecting humans without observing clusters of infections in families or among medical staff. Therefore it is important to study the pathogen in Africa and to elucidate whether African MERS-CoV is less virulent and/or less (or even not) transmissible to humans? This can be addressed by comparing the African camel MERS-CoV (see above) with a focus on the main attachment protein (spike protein). It is important to also to determine the extent of human exposure to MERS-CoV in sub-Saharan Africa. A first obvious place to start is at risk populations, including camel slaughterhouse workers and camel herders. This surveillance should, in the first instance, be serological (in order to achieve rapid coverage), though such at risk groups should be closely monitored routinely for clinical signs of disease. Screening of at-risk populations would ideally be the subject of targeted surveillance operations with a few dedicated teams linked to local partnerships, with diagnostic activities concentrated in a small number of laboratories to retain consistency and quality.

Most of the current MERS cases in the Arabian Peninsula do not allow tracing back contact of the patients to camels before infection. Therefore it is important to investigate possible airborne routes of transmission and transmission via vectors such as insects that surround camels and humans constantly. In this regard it is most interesting to investigate the stability of MERS-CoV outside of mammalian hosts, attempting to address a hypothesis of MERS-CoV as an arboviral infection.

C) Development of tailor-made diagnostic assays for Africa

This research component should focus on the development of field-applicable diagnostic devices that can be used in rural settings without laboratory infrastructure to assist in addressing research questions A and B above. Tailor made diagnostic assays will foster the establishment of routine surveillance systems in Africa. The availability of field-applicable diagnostic tests would enable the diagnosis of ongoing MERS-CoV infections in camels and humans in the absence of infrastructure and laboratories.

D) Do dromedary camels in Africa have the same seroprevalence as in the Arabian Peninsula?

With respect to the role of camels as reservoirs of MERS, much of the work published to date confirms dromedary camels to be a component of the reservoir community (Viana et al. 2014). Further work to elucidate the role of camels as reservoirs of the virus, either with respect to other camels or indeed to humans is essential to quantify this putative reservoir role. Extensive serological surveys should be carried out across the range of camels in sub-Saharan Africa, in all ecologies in which they exist, in order to understand exposures. Work in Kenya has shown (Corman et al. 2014b) that camels have had a long history of exposure, with high prevalence in some areas (Deem et al., in press in PLOS ONE). Expanding such knowledge across the range of camels will be essential.

E) Research priorities relating to routine surveillance

Longer-term routine surveillance in humans, building on institutional partnerships in a number of countries, will be important in monitoring the potential emergence of MERS-CoV in sub-Saharan Africa. Routine random surveillance of at-risk humans, of camel herds and potentially of other reservoir hosts should be undertaken as a foresight activity. The recently DFID-funded ZELS-ZooLinK programme provides an excellent framework for this, collecting and analysing biological samples with a backbone of digital data entry shareable to stakeholders.

F) What is the exact geographic distribution of the dromedary camel and its genetic background in Africa?

Knowledge about African dromedary camels itself and the pathogens they carry is rather limited compared to other livestock species such as cattle, sheep and goats. This is rather surprising, since the camel population in Africa is constantly rising and the highest in the world. Many livestock dependent people in semi-arid and arid regions in Africa consume raw camel milk and this poses a risk of acquiring infections with zoonotic pathogens such as Brucella mellitensis, which have been reported to have a high prevalence in dromedary camels (Wernery 2014). In order to understand the epidemiology of many infectious diseases, knowledge on camel population itself, in terms of camel population genetics and distribution, is an important researchable area. While useful in its own right, this is of direct relevance to MERS, since a host-virus relationship is present. A key research priority is thus to map current and future expected camel populations and their density and trade routes, while understanding camel population genetics across sub-Saharan Africa.

G) Mathematical modelling of MERS transmission

Mathematical modelling to project disease spread scenarios and to identify entry points of disease control for disease policy interventions are needed in order to predict scenarios of epidemics. This knowledge will enable the stakeholders to develop strategies to contain outbreaks and the modelling will build on data on camel populations and trade routes in Africa (see above). Constructing robust modelling frameworks will be essential to better predict and understand the risks of MERS-CoV, but developing such models is dependent on the best quality data on viral diversity, camel movements and contact, levels of exposure etc. (see points above).

H) Are other ways of transmission than contact to infected camels or infected humans possible?

The current data from index patients in the Arabian Peninsula do not allow tracing back the sources of infection for most of the patients. Therefore it is necessary to investigate other ways of transmission between camels and between camels and humans. Possible transmissions via dried camel saliva, which can contain high numbers of virus, or via insect vectors that surround camels and humans in semiarid and arid regions should be investigated.

The expected costs of the above mentioned research packages to be carried out in four countries in the horn of Africa (Kenya, Ethiopia, Somalia and Northern Sudan) over two years would cost about £3.5 million. A break down of the required funds is shown in the annex 2.

Partnerships for all these activities are in place at ILRI and its partner academic institutes.

SECTION 6

The diagnostic capacity for camel MERS in Africa and key gaps in diagnostic tools and capacity

At the moment the diagnostic capacity of MERS-CoV and other coronavirus is rather sparse or non-existing within many countries on the African continent. This might be attributed to the costs associated with the commercial test kits available and the necessary infrastructure that supports the use of the current diagnostic tests. While most, if not all laboratories, in Africa can use serological methods such as ELISA to diagnose serological responses, the implementation of diagnostic methods based on real time PCR poses challenges to many African laboratories in the livestock sector that do not have the required equipment or capacity in terms of storage of valuable supplies nor constant electrical power. As for many other diagnostics developed for laboratories that adhere to high technical standards, tailor-made diagnostics that can be run in resource-poor environments would add substantial value to the African capacity to diagnose MERS-CoV.

To our best knowledge diagnostic techniques such as virus neutralisation assays and cultivation of the virus that do require high biosecurity containment facilities are not implemented nor possible in many African countries that have a substantial camel population at the moment. A MERS-CoV workshop held at the Fairview hotel in Nairobi, Kenya in July 2014 with various international and national stakeholders concluded that MERS-CoV diagnostic capacity should be built in East Africa.

In order to foster MERS-CoV diagnostics in African countries it would be most beneficial if medical and veterinary research laboratories work together and that staff are trained to be able to diagnose the pathogen or infections.

Diagnostic capacity in terms of basic infrastructure is available in many countries such as Kenya with the department of veterinary services and ILRI. The Kenya Medical Research Institute has also the capacity to diagnose MERS-CoV infections. Training courses and ring trials to establish and validate routine diagnostic procedures for diagnosis of MERS-CoV infections are highly demanded in all African countries and this should be, despite the presence of infrastructure. We contacted veterinary diagnostic laboratories of African countries that have a substantial camel population and got responses about their capacity to diagnose MERS-CoV infections in camels (see table 1). Most countries lack trained staff and funds to perform routine diagnosis (see table 1). All laboratories contacted expressed their wish to build capacity in MERS-CoV diagnosis.

Country	MERS-CoV diagnostic assays implemented with respect to serology and nucleic acid detection	ELISA equipment available	RNA isolation possible	PCR machines available	Real time PCR equipment available	Level III containment facilities available
Chad	No	Yes	Yes	Yes	Yes	No
Eritrea	No	Yes	Yes	Yes	□	No
Ethiopia	No	Yes	Yes	Yes	□	□
Kenya (ILRI, DVS)	Yes	Yes	Yes	Yes	Yes	Yes
Mali	No	Yes	Yes	Yes	Yes	No
Mauretania	No	Yes	Yes	Yes	Yes	No
Niger	No	Yes	Yes	Yes	Yes	No
Somalia/ Somaliland	No	Yes	□	No	No	No
Sudan	No	Yes	Yes	Yes	Yes	Yes

⦸ - No information provided

Table 1 MERS-CoV diagnostic assays in place and infrastructure available to conduct diagnosis of MERS-CoV infections

SECTION 7

Summary and Recommendations

Middle East Respiratory Syndrome was first reported in Saudi Arabia in 2012. The case fatality rate of the disease is about 40 %. So far, all human cases of the diseases have been linked to the Arabian Penisula. Camels have been confirmed to be a reservoir of the pathogen. Since the majority of the world dromedary camel population are residing in Africa and first studies on African camels confirmed their infection with a MERS-CoV it is important to shed light on the circulation of the virus in Africa to be prepared for potential outbreak scenarios and to be able to mitigate the risk of MERS-CoV infections on the African continent. Currently, limited data on camel populations and their associated pathogens are available. This might be mainly attributed to limited funds, fragmentary veterinary services, informal camel trade and a lack of diagnostic capacity in most African countries. Therefore it is of paramount importance to build diagnostic capacity and to get more insight about camels and their role as reservoir for zoonotic pathogens such as MERS-CoV. Another important aspect that requires attention is to elucidate the possible infection of humans with MERS-CoV on the African continent. Therefore, efforts should focus on humans that have a high risk of contracting infections due to their interactions with camels such as herders and abattoir workers. Below listed are development and research recommendations that will enable a better understanding of the epidemiology of MERS-CoV dynamics in Africa.

Recommendations:

Development recommendations

- The implementation of robust surveillance systems and training courses for the diagnosis of MERS-CoV infections and other emerging pathogens are necessary.

Research recommendations

- The African camel population needs to be systematically screened in different countries regarding the presence of MERS-CoV
- MERS-CoV from African dromedaries needs to be characterized and compared to MERS-CoV in the Middle East
- The infection rate of camels (seroprevalence) and their dynamics in different regions of Africa and related to different production systems needs to be elucidated to characterize the epidemiology of MERS-CoV in African camel populations
- Diagnostic assays that can be applied in the field need to be developed and established in cooperation with African stakeholders
- The African camel populations and their trade routes need to be mapped

Annex 1 Report on ongoing research activities related to MERS-CoV in Africa

The following funding agencies and research institutes have been contacted and ask whether they fund MERS-CoV related research in Africa or know of any research, respectively.

The results are displayed in Table S1.

Donor agency contacted	Designated Funding of MERS-related research in Africa
German Ministry of Economic Development	No current funding
CIDA	No answer
SIDA	No answer
German Research Foundation	No answer
European Union	No answer
Bill and Melinda Gates Foundation	No current funding
Wellcome Trust	No current funding
FAO	Yes (see below)
USAID	Yes (see below)
Swiss Development Cooperation	No current funding
CVL laboratoty in UAE	The staff is not aware of any MERS-CoV related research initiatives in Africa that are funded from donors on the Arabian Peninsula

Table S2 Current Funds available to conduct research on MERS in Africa

Dr Bouna Diop, the regional manager from FAO-ECTAD, Eastern Africa provided us with the following information.

USAID

MERS related research will be funded from USAID under the Emerging Pandemic Threats phase 2 (EPT2). The framework of implementation of this program, FAO and PREDICT2, in coordination with other organisations such as CDC, NAMRU-3, and WHO are expected to conduct activities aiming to:

Develop an evidence base for designing and targeting risk-mitigation interventions

- Better define boundaries of MERS-CoV epizone using a combination of viral detection and serology (by 2016/2017)
- Identify key points along value chains (e.g. farms, markets, households, etc.) where animal-to-animal and animal-to-human transmission may be occurring (by 2016/2017)
- Design/test/evaluate interventions (by 2019).

Minimise or interrupt animal-to-animal transmission and animal-to-human transmission of the MERS-CoV by targeting risk-mitigation interventions based on where the virus is present and when and how it spreads (long-term goal). During the initial stages of this research, EPT-2 will not focus on human-to-human transmission.

Short-term research questions to be answered by implementing partners under the EPT-2 program (2015-2017) include:

- What animals serve as hosts for the virus?
- In what geographic locations is the virus present in animal populations?

- Are all camels at high-risk for infection with MERS-CoV or only some sub-populations associated with specific practices?
- How is the virus spreading among animals and are there any seasonal patterns?
- How is the virus spilling over to human populations and are there any seasonal patterns?
- Is the virus being maintained in camels within the Middle East (and other locations) or is there serial reintroduction of the virus from other locations and species?

Target countries include Egypt, Ethiopia, Kenya, Jordan, Sudan, South Sudan, and Uganda. This list of countries is subject to change based on the findings of the desk review of information related to surveillance data and value chain analyses. The work already done in Kenya will be useful here.

Over the next 20 months, activities will focus on better defining:

- the range of affected geographic areas;
- affected animal species;
- dynamics associated with transmission, maintenance, and elimination of the virus in animal populations (to include wildlife, livestock, and domestic animals).

The Food and Agriculture Organization

In Egypt, FAO has started some work on camel value chain and to develop a risk-based surveillance plan. Initial coordination meetings have already taken with key partners that include the Veterinary Services, the National Research centre (NRC) under Ministry of Higher Education, and the Epidemiology and Surveillance Unit (ESU) of the Ministry of Health. FAO has hired or is in the process of hiring consultants exclusively working on MERS-CoV. Focal points from partner organizations who will participate in day-to-day activities of the project have also been identified. Procurements of inputs required to support MERS-CoV surveillance activities are underway.

ECTAD Egypt has been contacted recently by EcoHealth Alliance/PREDICT2. Egypt has been identified as a country where EcoHealth Alliance's expertise in MERS research could complement ongoing country efforts to address zoonotic diseases. In particular, they are interested in the interfaces where bats, camels and humans may be at highest risk of MERS transmission.

Discussions are still ongoing with USAID to finalise the FAO component but activities are expected to start in October 2015. A budget available has not been communicated yet.

Annex 2 Break down of the recommended budget to carry out suggested research and to develop diagnostic capacity in selected African countries that harbour high camel populations

	Figures in GBP		
	Year 1	Year 2	TOTAL
Personnel			
ILRI Principal Scientist 50%	73,565	77,244	150,809
ILRI Senior Scientist 100%	127,115	133,471	260,586
ILRI Post Doc-100%	99,836	104,828	204,664
ILRI Post Doc-100%	99,836	104,828	204,664
ILRI Technician 100%	34,237	35,949	70,185
ILRI Technician 100%	34,237	35,949	70,185
ILRI Program Management Officer 30%	9,908	10,403	20,311
Sub-total-Personnel	**478,735**	**502,671**	**981,406**
Other Direct Costs			
Equipment (for DVS laboratories in Africa	200000	0	200,000
Lab supplies	150000	150000	300,000
Travel	50000	50000	100,000
International workshops	100000	100000	200,000
Fieldwork	500000	500000	1,000,000
Consultancies	100000	100000	200,000
			-
Sub-total-Other Direct Costs	**1,100,000**	**900,000**	**2,000,000**
TOTAL DIRECT COSTS	**1,578,735**	**1,402,671**	**2,981,406**
Indirect cost 15%	236,810	210,401	447,211
TOTAL PROJECT COSTS	**1,815,545**	**1,613,072**	**3,428,617**

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