



RAPID RISK ASSESSMENT

Middle East respiratory syndrome coronavirus (MERS-CoV)

17th update, 11 June 2015

Main conclusions and options for response

- The detection of a MERS-CoV case in South Korea with a travel history to the Arabian Peninsula is not an unexpected event. MERS-CoV cases with travel history to the Arabian Peninsula have been diagnosed outside of the Middle East in the past. Additional cases can be expected in the future, given the ongoing transmission in the Middle East and frequent international travel to and from this region. On several occasions, notably in France, the United Kingdom and Iran, such importations have resulted in secondary transmission to patients, healthcare workers and visitors who have been in contact with the primary imported cases and close relatives of cases.
- Although the MERS-CoV cluster in South Korea is the largest observed outside of the Arabian Peninsula, the cluster remains limited to patients, visitors to patients and healthcare workers in a few healthcare facilities, and close relatives of the cases who were visiting the health facilities where the cases were admitted. The pattern noticed in Korean hospitals corresponds to what had been observed in Saudi Arabian hospitals, notably in Jeddah in the first months of 2014, when extended nosocomial transmission occurred following the admission of one case. This resulted in 'super-spreader' situations, amplified by the absence of triage in emergency rooms.
- The event does not represent an increased risk of infection for travellers or visitors to South Korea. However, EU citizens travelling to the Middle East and South Korea need to be aware of the presence of MERS-CoV in these areas, especially in healthcare facilities. Member States may consider raising awareness in travellers of the areas most at risk. Currently, we cannot exclude a continued increased risk of exposure in affected healthcare facilities where cases of MERS-CoV have been recently reported.
- Travellers returning from the Middle East and South Korea who develop respiratory symptoms either during travel or up to 14 days after their return should seek medical attention and report their travel history. In addition, patients who present with severe acute respiratory disease in the EU and have recently been in contact with healthcare services in South Korea should be considered for MERS-CoV assessment, similar to patients who have been in contact with healthcare services in the Arabian Peninsula.
- The fact that the index case in the South Korean cluster does not have a documented history of exposure to camels or healthcare settings in the Arabian Peninsula is cause for concern. Continuous vigorous efforts are required to determine the likely source of infection in order to ensure that other undetected transmission chains are not ongoing. WHO has stated that there is currently no indication that the virus is behaving differently to how it has behaved in the past, and that there is no indication of sustained transmission from person to person in the community.

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- ECDC's assessment continues to be that the MERS-CoV outbreak poses a low risk to the EU. Because of the continued risk of case importation to Europe after exposure in the Middle East and South Korea, international surveillance for MERS-CoV cases among travellers remains essential. Moreover, rapid efforts to contain the nosocomial clusters in the affected countries are vital to prevent broader transmission. Although sustained human-to-human community transmission is unlikely, secondary transmission to unprotected close contacts, especially in healthcare settings, remains possible, as now documented in South Korea. Many of the cases detected in the Middle East continue to be caused by nosocomial exposure.
- The importance of eliciting a travel history from patients with severe respiratory disease cannot be overemphasised. The immediate, systematic and strict implementation of infection prevention and control measures in hospital settings is essential to interrupt transmission and prevent clusters of healthcare-associated infection. Furthermore, the challenges of detecting rare imported cases of respiratory infection early on highlight the need for adequate infection prevention and control measures for all patients showing symptoms of acute respiratory infection.
- WHO recommends that probable and confirmed cases should be admitted to adequately ventilated single rooms or airborne precaution rooms. Healthcare workers caring for probable or confirmed cases of MERS-CoV infection should use contact and droplet precautions (medical mask, eye protection such as goggles or face shield, gown, and gloves) in addition to standard precautions. Airborne precautions should be applied when performing aerosol-generating procedures [12].
- An overview of MERS-CoV infection is presented in an ECDC fact sheet [13] and a WHO factsheet updated in June 2015 [14] which also provides details on measures to be taken by health professionals for case management and treatment.
- Additional information on clinical presentation, further details on epidemiological features of the cluster, and knowledge of MERS-CoV genetic sequences will be required to confirm/refute these initial conclusions. In addition, more details on the potential exposure in the community of the index case would be useful in order to elucidate the potential source of the infection and the cause of the high number of secondary cases.
- The outbreak in South Korea highlights the continued risk of healthcare-associated transmission and the need for timely diagnosis and implementation of prevention and control measures.

Source and date of request

ECDC Internal Decision, 8 June 2015.

Public health issue

This update was prompted by the recent increase in the number of confirmed MERS-CoV cases in South Korea; the disease cluster was generated by a primary case imported from the Middle East.

Consulted experts

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Disease background information

Since it was first identified in Saudi Arabia in September 2012, more than 1 000 MERS-CoV cases have been detected in over 20 countries. In Europe, seven countries have reported confirmed cases, all with direct or indirect connection with the Middle East.

The clinical presentation of MERS-CoV infection ranges from asymptomatic to very severe pneumonia with acute respiratory distress syndrome, septic shock and multi-organ failure resulting in death. The clinical course is more severe in immunocompromised patients.

Although it is likely that a zoonotic transmission is the starting point of most clusters, human-to-human transmission is currently the dominant mode of transmission for MERS-CoV, and almost all new cases are generated in healthcare facilities or among family members. Nosocomial transmission has been a hallmark of MERS and the majority of cases have been reported from hospital outbreaks in Saudi Arabia and United Arab Emirates.

There is growing evidence that the dromedary camel is a host species for the virus and that camels play an important role in the direct or indirect transmission to humans.

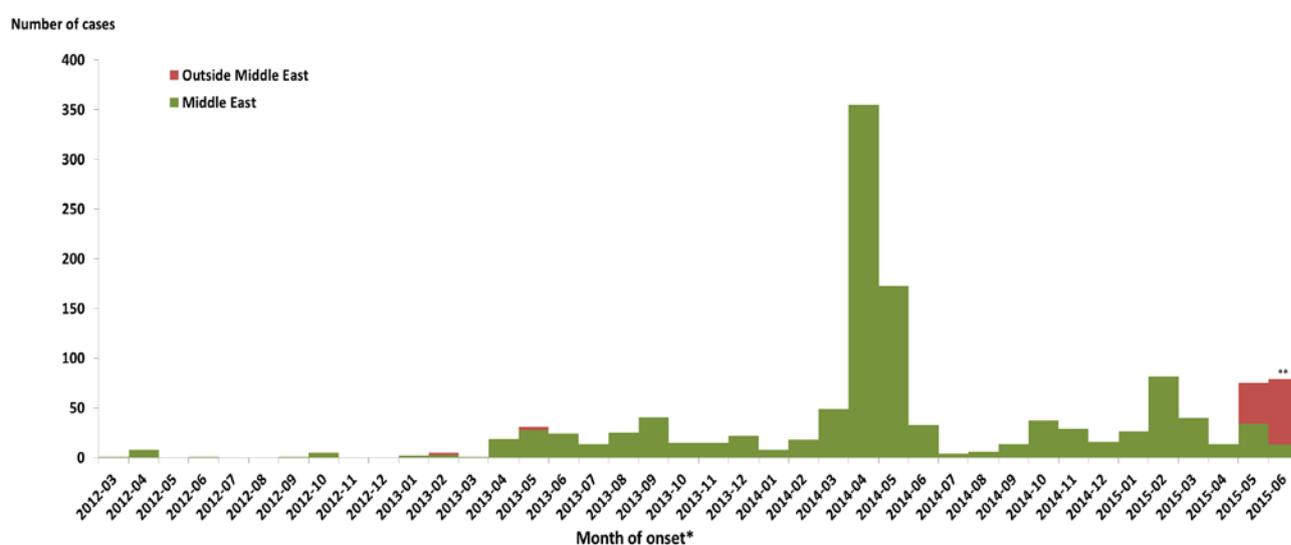
See more at: <http://ecdc.europa.eu/en/healthtopics/coronavirus-infections/mers-factsheet/Pages/default.aspx#sthash.tTUYgixK.dpuf>

Event background information

Worldwide situation

Since April 2012 and as of 10 June 2015, 1 288 cases of MERS-CoV (including 498 deaths) have been reported by health authorities worldwide (Figure 1, Table 1).

Figure 1. Distribution of confirmed cases of MERS-CoV by month and probable place of infection, March 2012 – 10 June 2015 (n=1 288)



* If the month of onset is unknown, month of reporting has been used.

** Data for June 2015 are incomplete.

Geographical distribution

Most of the cases have occurred in the Middle East: Saudi Arabia, United Arab Emirates, Qatar, Jordan, Oman, Kuwait, Egypt, Yemen, Lebanon and Iran (Table 1 and Figure 2).

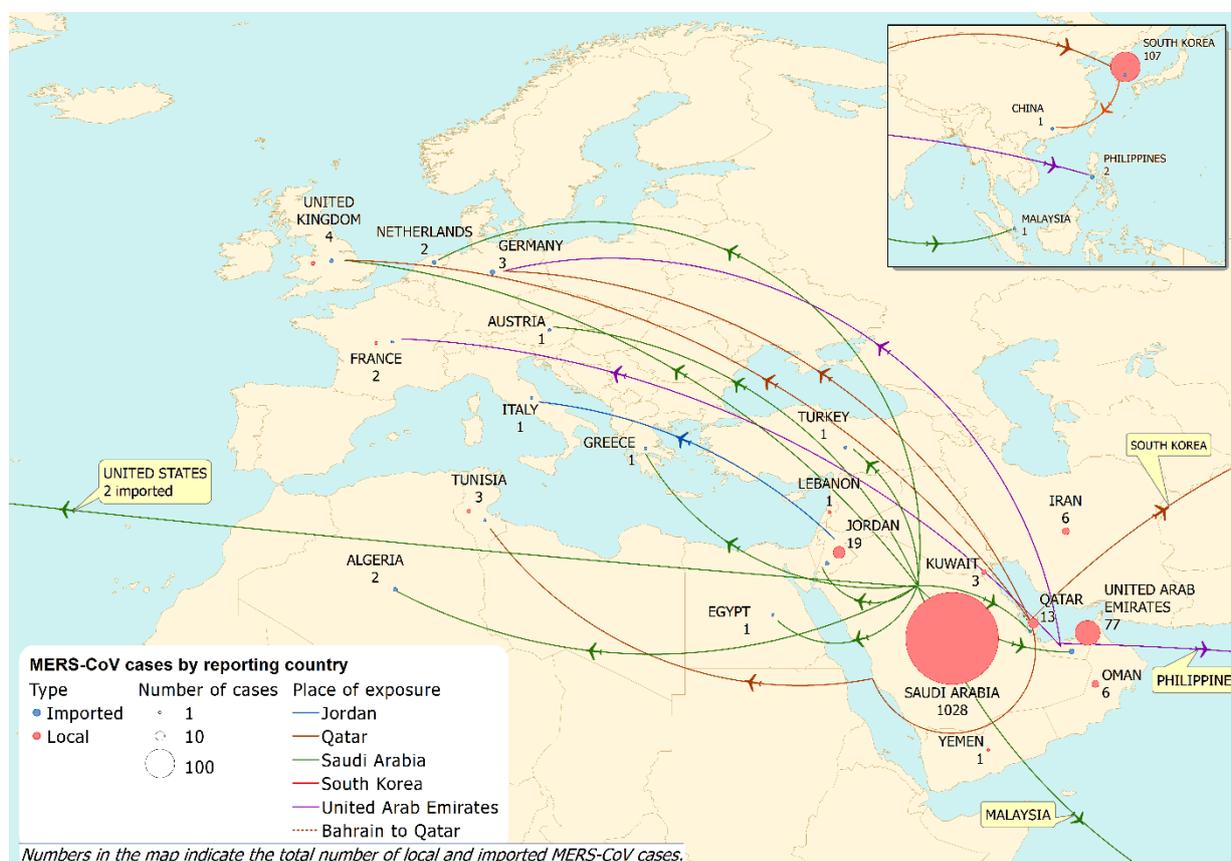
Table 1. Confirmed MERS-CoV cases and deaths, by country of reporting, March 2012– 10 June 2015

Reporting country	Cases	Deaths
Middle East	1 155	479
Saudi Arabia	1 028	451
United Arab Emirates	77	10
Qatar	13	5
Jordan	19	6
Oman	6	3
Kuwait	3	1
Egypt	1	0
Yemen	1	1
Lebanon	1	0
Iran	6	2
Europe	15	7
Turkey	1	1
Austria	1	0
United Kingdom	4	3
Germany	3	1
France	2	1
Italy	1	0

Reporting country	Cases	Deaths
Greece	1	1
Netherlands	2	0
Rest of the world	118	12
Tunisia	3	1
Algeria	2	1
Malaysia	1	1
Philippines	2	0
South Korea	107	9
China	1	0
United States of America	2	0
Total	1 288	498

All cases reported from outside the Middle East have a recent travel history to the Middle East or are linked to a case with a travel history to the Middle East (Figure 2).

Figure 2. Distribution of confirmed MERS-CoV cases by place of probable infection, as of 10 June 2015 (n=1 288)



Current epidemiological situation

Since the first case in South Korea was diagnosed on 20 May, 107 confirmed cases and nine deaths of MERS-CoV have been reported in that country as of 10 June 2015. Since the previous update of the ECDC Rapid Risk Assessment on MERS-CoV (5 June 2015), there have been 77 new cases and six additional deaths reported: Saudi Arabia (nine cases and one death), United Arab Emirates (one case) and South Korea (67 cases and five deaths).

South Korea and China

South Korea

On 20 May 2015, the Korea Centres for Disease Control and Prevention notified WHO of the first laboratory-confirmed case of MERS-CoV infection in a 68-year-old man with recent travel history to the Middle East.

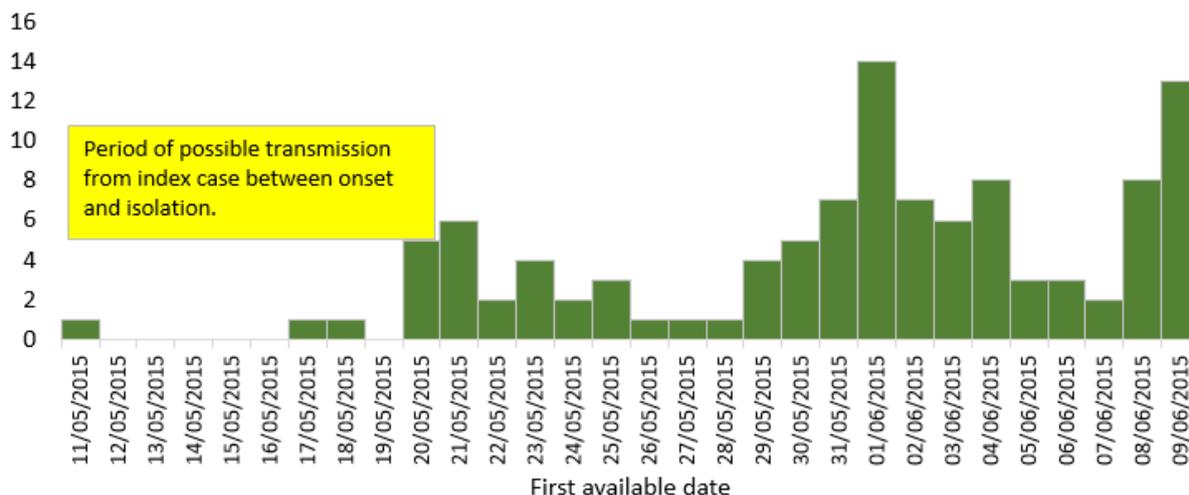
According to WHO, the man had travelled to Bahrain (18–29 April), the United Arab Emirates (29–30 April), Bahrain (30 April–1 May), Saudi Arabia (1–2 May), Bahrain (2 May) and Qatar (2–3 May). The case arrived at Korea’s Incheon International airport via Qatar on 4 May and was asymptomatic on arrival. The patient has no

history of exposure to camels or contacts with MERS-CoV patients, and he did not visit any healthcare facilities while travelling in the Middle East. Investigation of the source of infection is ongoing [1].

Since the diagnosis of the index case, 107 secondary and tertiary cases have been reported in South Korea. One case infected in South Korea travelled to Guangdong in China, where he was hospitalised. Nine cases have died in South Korea due to MERS-CoV.

Figure 3. Distribution of confirmed cases of MERS-CoV by first available date*, South Korea and China, 11 May–10 June 2015 (n=108)

Number of cases



* If the date of onset is unknown, date of reporting has been used.

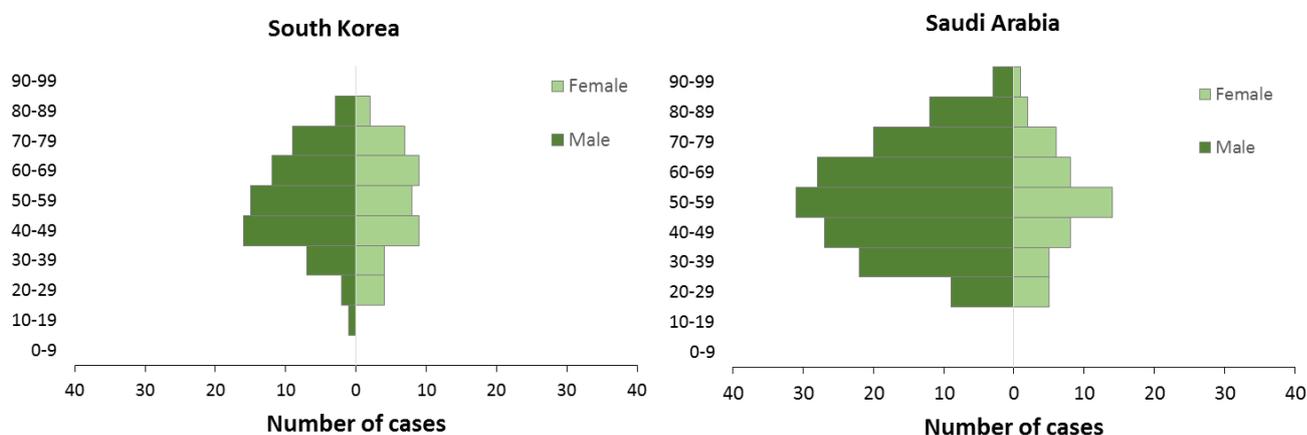
The index case had onset of symptoms on 11 May and was diagnosed and isolated on 20 May 2015. During the 10-day period (Figure 3, yellow box), he visited several healthcare facilities. The cases on 8 and 9 June are plotted by date of reporting. These cases may be reassigned to earlier dates once date-of-onset information is available.

Table 2. Distribution of confirmed MERS-CoV cases by reporting year and gender, as of 10 June 2015

	2012 Global	2013 Global	2014 Global	2015 Saudi Arabia	2015 South Korea	2015 Global
Male	14	100	381	152	65	229
Female	2	60	196	49	43	95
Number of cases	16	160	577	201	108	324
Male/female ratio	7.0	1.7	1.9	3.1	1.5	2.4

Since the beginning of the epidemic, males are consistently overrepresented compared with females. This overrepresentation of males is less marked among Korean cases (Table 2 and Figure 4).

Figure 4. Distribution of confirmed MERS-CoV cases by age and gender in 2015 in South Korea and Saudi as of 10 June 2015



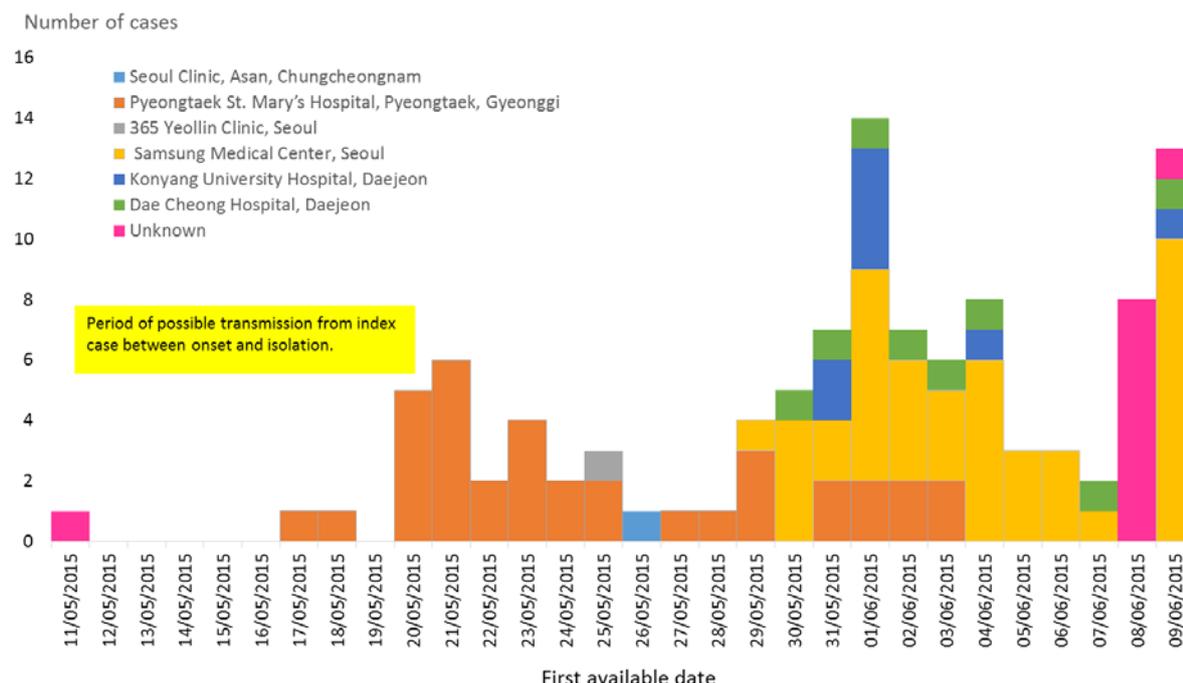
As of 10 June, 108 cases have been reported in South Korea (107) and China (one, exposed in Korea).

Breakdown of cases:

- One primary case in South Korea
- Thirty secondary cases exposed to the primary case before he was diagnosed with MERS-CoV and isolated:
 - thirteen were admitted to the same ward as the index case (or had contact with the index case as patients);
 - four are healthcare workers who provided care for him; and
 - thirteen were family contacts or visitors to patients admitted to the same ward (or sharing the same room) as the index case: the wife of the index case and twelve visitors, one of whom later travelled to China.
- Forty tertiary cases who had contact with a secondary case but no contact with the index case.
- One case had contact with the index case and also with secondary cases.
- Thirty-six cases with exposure not reported in publicly available reports.

Among the cases are nine healthcare workers.

Figure 5. Distribution of confirmed cases of MERS-CoV by place of presumed exposure and first available date*, South Korea and China, 11 May–10 June 2015 (n=108)



* If the date of onset is unknown, date of reporting has been used.

The yellow box represents the period between onset of symptoms and isolation of the index case.

China

On 30 May 2015, WHO notified of a case of MERS-CoV in China. The case is a 44 year-old male from South Korea. The patient is the son of the third MERS-CoV case in South Korea and the younger brother of the fourth MERS-CoV case. He visited his father who was hospitalised in the same room as the index case. He developed symptoms on 21 May and travelled to Hong Kong, China, on 26 May where he continued to Huizhou through an entry point in Shenzhen City, Guangdong Province. The local health authority found him on 27 May and immediately transferred him to a designated hospital for isolation. This patient was confirmed positive for MERS-CoV infection on 29 May [2].

Saudi Arabia

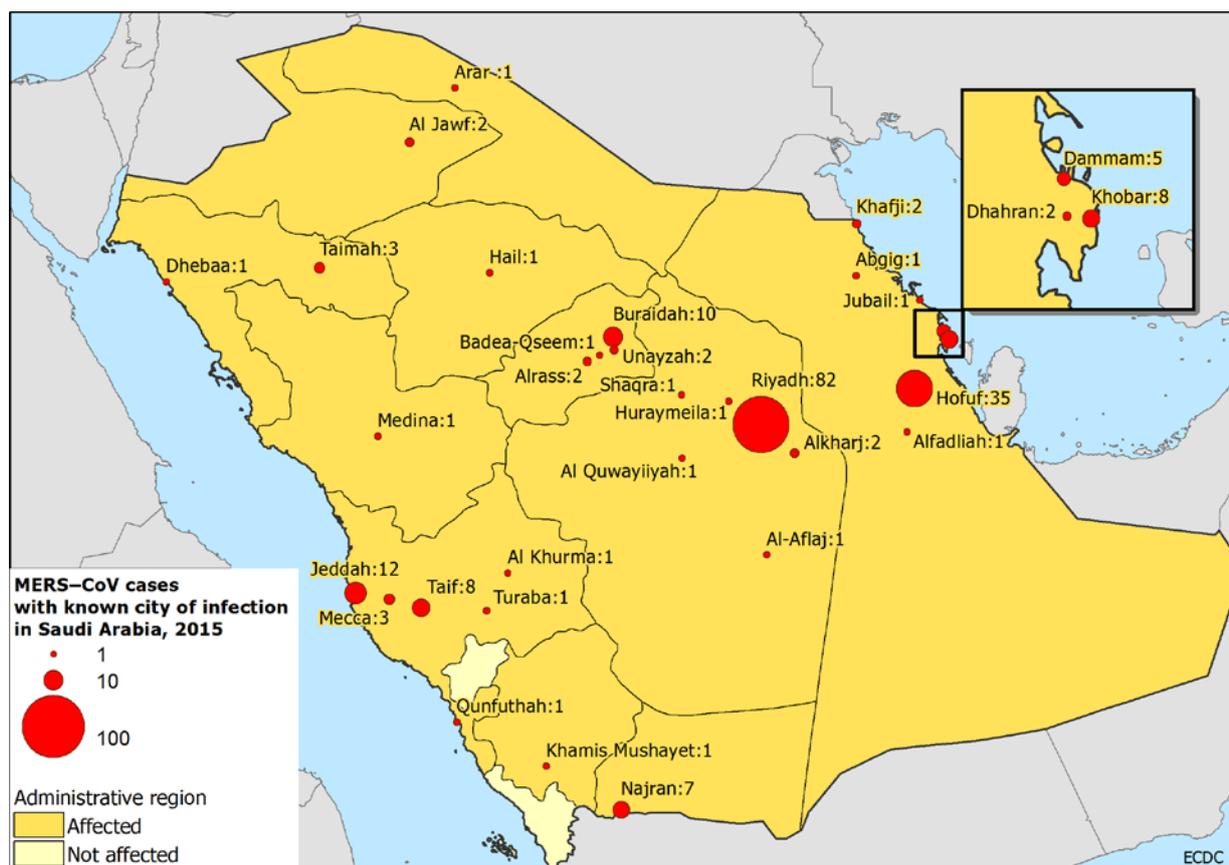
Since the beginning of 2015 and as of 10 June, Saudi Arabia has reported 201 cases of MERS-CoV (Figure 7).

Of these cases,

- sixty-seven (34%) were reported as resulting from secondary transmission; 42 of the 67 were classified as nosocomial transmission;
- twenty-three (11%) were identified as healthcare workers; for nineteen of the 23 healthcare workers there were indications of nosocomial transmission;
- twenty-six (18%) reported animal contact, 18 of the 26 cases reported direct contact with camels;
- eighteen (9%) reported to have drunk camel milk.

Since the last ECDC rapid risk assessment (published 5 June 2015), Saudi Arabia has reported eight additional cases. The [WHO Regional Office for the Eastern Mediterranean](#) has published an overview of two hospital outbreaks and one household cluster of community-acquired infections of MERS-CoV from Hofuf City in the Al-Ahsaa region in Saudi Arabia during the period from mid-April to the end of May 2015. This indicates that transmission of MERS-CoV is ongoing in the hospitals and in the community, involving most administrative regions.

Figure 7. MERS-CoV cases with known city of infection in Saudi Arabia, 1 January – 10 June 2015



Virological information

Two whole genome sequences have been produced from viruses isolated from cases linked to the nosocomial cluster in South Korea. One sequence originated from a virus isolated from a patient in Guangdong and was sequenced by the Chinese CDC (GenBank KT006149). The other sequence was generated by the Korea National Institute of Health and Seoul National University from a virus isolated from a patient in South Korea. There is a 22-nucleotide difference between the Korean and Chinese sequences, most likely due to technical issues of

sequencing and the fact that the Korean virus isolate was obtained from a cell culture-passaged virus, while the Chinese isolate was sequenced directly from a patient swab [3].

Sequence analysis suggests that there are no significant amino acid exchanges in the spike protein – the glycoprotein mediating MERS-CoV virus entry and an important determinant of virulence [4]. Preliminary analysis suggests that the viruses from China and Korea are unlikely to be phenotypically different from the MERS-CoV currently circulating in the Arabian Peninsula and are unlikely to present different virulence or transmission properties [3].

A phylogenetic analysis of the Korean and Chinese MERS-CoV sequences clustered them closest to a recent outbreak in Riyadh in February–March 2015. However, the level of diversity observed might be explained by a separate zoonotic event, and the originating country cannot be determined with certainty [3].

The performance of the laboratory assays for detection and confirmation of MERS-CoV widely used across the EU/EEA should not be affected by the genetic changes observed in the viruses sequenced in South Korea and China (Drosten C., personal communication and [5-7]).

ECDC threat assessment for the EU

Continuing transmission of MERS-CoV is being observed in the Arabian Peninsula. There is growing serological and molecular evidence that the dromedary camel (*Camelus dromedarius*) is a host species for the MERS-CoV.

Circulation of MERS-CoV or MERS-like CoV in dromedaries in Africa and the Arabian Peninsula was probably occurring long before 2012. It is to be expected that cases will be seen in the vicinity of the host species, notably in Africa and the Arabian Peninsula. The current transmission pattern of MERS-CoV is consistent with the one observed since 2013: sporadic primary zoonotic cases which lead to nosocomial clusters of variable size.

There is an ongoing risk of MERS-CoV infection being imported into the EU, especially during periods of increased disease activity in the Arabian Peninsula. Although sustained human-to-human transmission has not been observed in communities, transmission to unprotected close contacts, including healthcare workers and other patients in hospital settings, is frequently reported.

The evolving cluster in South Korea that originated from a single traveller returning from the Arabian Peninsula, is the largest cluster of cases outside the Middle East. The fact that no exposure to camels or healthcare settings in the Arabian Peninsula has been documented for this primary case raises the possibility of ongoing sources of transmission in the region other than those recognised thus far. Therefore, thorough investigations to identify the source are warranted.

Although the number of confirmed secondary cases is high, such clusters of healthcare-associated infections have previously been observed in Saudi Arabia [8]. Currently, there is no evidence of community transmission in South Korea. All secondary and tertiary cases are reported to be linked to transmission in healthcare settings. Further monitoring of chains of transmission is required in order to evaluate the sustainability of transmission. The number of reported tertiary cases is large compared with the previously documented outbreak, although not unexpected.

Taiwan CDC has issued a Level-2 travel notice ('Alert for MERS-CoV to Seoul, South Korea') and a Level-1 travel notice ('Watch for MERS-CoV to other areas in South Korea') [9]. In addition, the media reported that Hong Kong issued a 'red alert' advisory on 9 June against non-essential travel to South Korea [10].

A joint mission by the World Health Organization and the Republic of Korea's Ministry of Health and Welfare is conducted from 9 to 13 June 2015. The joint mission team consists of 16 experts, eight from WHO and eight from South Korea. Planned activities include epidemiological investigations, infection control, hospital visits, and an analysis of the characteristics of MERS-CoV in Korea in cooperation with KCDC [11].

Conclusions and options for response

The detection of a MERS-CoV case in South Korea with a travel history to the Arabian Peninsula is not an unexpected event. MERS-CoV cases with travel history to the Arabian Peninsula have been diagnosed outside of the Middle East in the past. Additional cases can be expected in the future, given the ongoing transmission in the Middle East and frequent international travel to and from this region. On several occasions, notably in France, the United Kingdom and Iran, such importations have resulted in secondary transmission to patients, healthcare workers and visitors who have been in contact with the primary imported cases and close relatives of cases.

Although the MERS-CoV cluster in South Korea is the largest observed outside of the Arabian Peninsula, the cluster remains limited to patients, visitors to patients and healthcare workers in a few healthcare facilities, and close relatives of the cases who were visiting the health facilities where the cases were admitted. The pattern noticed in Korean hospitals corresponds to what had been observed in Saudi Arabian hospitals, notably in Jeddah in the first months of 2014, when extended nosocomial transmission occurred following the admission of one case. This resulted in 'super-spreader' situations, amplified by the absence of triage in emergency rooms.

The event does not represent an increased risk of infection for travellers or visitors to South Korea. However, EU citizens travelling to the Middle East and South Korea need to be aware of the presence of MERS-CoV in these areas, especially in healthcare facilities. Member States may consider raising awareness in travellers of the areas most at risk. Currently, we cannot exclude a continued increased risk of exposure in affected healthcare facilities where cases of MERS-CoV have been recently reported.

Travellers returning from the Middle East and South Korea who develop respiratory symptoms either during travel or up to 14 days after their return should seek medical attention and report their travel history. In addition, patients who present with severe acute respiratory disease in the EU and have recently been in contact with healthcare services in South Korea should be considered for MERS-CoV assessment, similar to patients who have been in contact with healthcare services in the Arabian Peninsula.

The fact that the index case in the South Korean cluster does not have a documented history of exposure to camels or healthcare settings in the Arabian Peninsula is cause for concern. Continuous vigorous efforts are required to determine the likely source of infection in order to ensure that other undetected transmission chains are not ongoing. WHO has stated that there is currently no indication that the virus is behaving differently to how it has behaved in the past, and that there is no indication of sustained transmission from person to person in the community.

ECDC's assessment continues to be that the MERS-CoV outbreak poses a low risk to the EU. Because of the continued risk of case importation to Europe after exposure in the Middle East and South Korea, international surveillance for MERS-CoV cases among travellers remains essential. Moreover, rapid efforts to contain the nosocomial clusters in the affected countries are vital to prevent broader transmission. Although sustained human-to-human community transmission is unlikely, secondary transmission to unprotected close contacts, especially in healthcare settings, remains possible, as now documented in South Korea. Many of the cases detected in the Middle East continue to be caused by nosocomial exposure.

The importance of eliciting a travel history from patients with severe respiratory disease cannot be overemphasised. The immediate, systematic and strict implementation of infection prevention and control measures in hospital settings is essential to interrupt transmission and prevent clusters of healthcare-associated infection. Furthermore, the challenges of detecting rare imported cases of respiratory infection early on highlight the need for adequate infection prevention and control measures for all patients showing symptoms of acute respiratory infection.

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The outbreak in South Korea highlights the continued risk of healthcare-associated transmission and the need for timely diagnosis and implementation of prevention and control measures.

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