Middle East respiratory syndrome coronavirus (MERS-CoV)

WHO MERS Global Summary and Assessment of Risk

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Global summary

Between 2012 and 30 June 2018, 2229 laboratory-confirmed cases of Middle East respiratory syndrome-coronavirus (MERS-CoV) infection were reported to WHO, 83% of whom were reported by the Kingdom of Saudi Arabia (Figure 1). In total, cases have been reported from 27 countries in the Middle East, North Africa, Europe, the United States of America, and Asia (Table 1). Males above the age of 60 with an underlying medical conditions, such as diabetes, hypertension and renal failure, are at a higher risk of severe disease, including death. To date, 791 individuals have died (crude CFR 35.5%).

Since the last global update published on 21 July 2017, 189 laboratory-confirmed cases of MERS-CoV from four countries were reported to WHO (182 from Saudi Arabia, three from Oman, three from the United Arab Emirates, and one from Malaysia), of whom 60 (31.7%) have died. Among these cases, 75.5% were male and the median age was 54 years old (IQR 40-65.5; range 10-93 years old). The median age is similar to the median age of all cases reported to WHO since 2012 (52 years old, IQR 37-65).

At the time of writing, 19 of 189 (10.0%) patients were reported as asymptomatic or having mild. At least one underlying condition was reported in 137 cases (72%) since the last update, including chronic renal failure, heart disease, diabetes mellitus, and hypertension.

Overall, the epidemiology, transmission patterns, clinical presentation of MERS patients and viral characteristics reported since the last update are consistent with past patterns described in previous WHO risk assessments: MERS-CoV is a zoonotic virus that has repeatedly entered the human population via direct or indirect contact with infected dromedary camels in the Arabian Peninsula. Limited, non-sustained human-to-human transmission mainly in health care settings continues to occur, primarily in Saudi Arabia. The risk of exported cases to areas outside of the Middle East due to travel remains significant.

While there have been significant improvements in surveillance for MERS, especially in the Middle East, and in reacting to suspect clusters, early identification in the community and in health care systems, compliance with the infection prevention and control measures and contact follow up remain major challenges for MERS outbreak prevention and control.

The continued importance of MERS-CoV in health care settings

Since the last global update of 21 July 2017, 17 of the 45 secondary cases reported to WHO were associated with transmission in a health care facility. These cases included health care workers (12 cases), patients sharing rooms/wards with MERS patients, or family visitors.

Though not unexpected, these transmission events continue to be deeply concerning, given that MERS-CoV is still a relatively rare disease about which medical personnel in health care facilities have low awareness. Globally, awareness for MERS is low and, because symptoms of MERS-CoV infection are non-specific, initial cases are sometimes easily missed. With improved compliance in infection prevention and control, namely adherence to the standard precautions at all times, human-to-human transmission in health care facilities can be reduced and possibly eliminated with additional use of transmission-based precautions.

Since the last update of July 2017, several MERS clusters were reported, including the following:

- In July-August 2017, two clusters of MERS were reported from AL-Jawf Region, Saudi Arabia. These clusters were not epidemiologically linked.
 - The first health care associated cluster included 13 cases, 2 who died. Among the 12 secondary cases, 10 were asymptomatic, including 8 health care workers.
 - The second cluster included 7 cases, 6 of whom were household contacts. Of the 6 secondary cases, five were asymptomatic. None of the cases identified in this cluster were health care workers and there were no fatalities.
- In January-February 2018, a health care associated cluster was reported in Hafr Al Batin Region, Saudi Arabia. The cluster included 4 cases and 1 death, including 3 asymptomatic health care workers identified through contact tracing.
- In February-March 2018, a health care associated cluster of 6 cases occurred in a hospital in Riyadh, Saudi Arabia. Of the 6 cases, none were health care workers and three were fatal.
- In March 2018, there was a household cluster reported from Jeddah, Saudi Arabia. This cluster included 3 individuals, all of whom survived.

 In May-June 2018, a household cluster was reported from the Najran Region, Saudi Arabia. The index case reported regular contact with dromedary camels. Ten family contacts and one health care worker were identified as secondary cases. Out of the 12 cases identified in this cluster, none were fatal.

Since 2015, the increase in the number of asymptomatic contacts identified in health care settings is due to a policy change by the Ministry of Health of the Kingdom of Saudi Arabia, in which all high-risk contacts are tested for MERS-CoV regardless of the development of symptoms. This comprehensive contact identification, follow-up, testing and isolation of positive cases continues into 2018.

Drivers of transmission and the exact modes of transmission in health care settings still are unclear and are currently the focus of collaborative scientific research. From observational studies, transmission in health care settings is believed to have occurred before adequate infection prevention and control procedures were applied and cases were isolated. Investigations at the time of the outbreaks indicate that aerosolizing procedures conducted in crowded emergency departments or medical wards with sub-optimal infection prevention and control measures in place resulted in human-to-human transmission and environmental contamination.

Community-acquired cases and reported links to dromedary camels

Since the last update, 56 human cases are believed to have been infected in the community. Of these 56 reported cases, 37 (66.1%) reported direct or indirect contact with dromedaries in Saudi Arabia (33 cases), Oman (2 cases), the United Arab Emirates (one case) and Malaysia (one case; contact with dromedary was in Saudi Arabia).

Improvement in multi-sectoral investigation of community-acquired cases is evident, including testing of dromedary animals/herds in the vicinity of community-acquired laboratory-confirmed cases and follow-up of human contacts of laboratory-confirmed cases. The Ministries of Health in affected countries notify the Ministries of Agriculture when human cases report a link with animals. Investigations in animals are carried out by officials from the Ministries of Agriculture and results, if positive for MERS-CoV, are reported to OIE.

Exported cases identified outside the Middle East

Since the last update, one case was reported outside of the Middle East. The case, a 55 year old, had recently returned from Jeddah to Malaysia in December 2017. The patient was treated and recovered, contacts were identified and followed and no further cases were identified by authorities in Malaysia.

Summary – information available from 2012 to date

Thus far, no sustained human-to-human transmission has occurred anywhere in the world, however limited non-

sustained human-to-human transmission in health care facilities remains a prominent feature of this virus. WHO continues to work with health authorities in the affected countries to prevent and minimize health care-associated cases. WHO understands that health authorities in affected countries, especially those in the most affected countries, are aggressively investigating cases and contacts, including testing for MERS-CoV among asymptomatic contacts, and applying mitigation measures to stop human-to-human transmission in health care settings. These efforts are proving successful in mitigating the size of outbreaks.

Of all laboratory-confirmed cases reported to date (n=2228), the median age is 52 (IQR 37-65) and 67.2% are male.

At the time of reporting, 21% of the 2228 cases were reported to have no or mild symptoms, while 46% had severe disease or died. Overall, 18.6% of the cases reported to date are health care workers.

Since 2012, 27 countries have reported cases of MERS-CoV infection. In the Middle East: Bahrain, Egypt, Iran, Jordan, Kuwait, Lebanon, Oman, Qatar, Saudi Arabia, the United Arab Emirates and Yemen; in Africa: Algeria and Tunisia; in Europe: Austria, France, Germany, Greece, Italy, the Netherlands, Turkey and the United Kingdom; in Asia: China, the Republic of Korea, Malaysia, the Philippines and Thailand; and in the Americas: the United States of America (Table 1).

The majority of cases (approximately 83%) have been reported from Saudi Arabia (Figure 1).

Populations in close contact with dromedaries (e.g. farmers, abattoir workers, shepherds, dromedary owners) and health care workers caring for MERS-CoV patients are believed to be at higher risk of infection. Healthy adults infected with MERS-CoV tend to have mild subclinical or asymptomatic infections. To date, limited human-to-human transmission has occurred between close contacts of confirmed cases in household settings.

More efficient human-to-human transmission occurs in health care settings due to inadequate and/or incomplete compliance with the infection prevention and control measures and delay in triage or isolation of suspected MERS patients.

Health care-associated transmission has been documented in several countries between 2012-2016, including Saudi Arabia, Jordan, the United Arab Emirates, France, the United Kingdom, and the Republic of Korea with varying outbreak sizes (2-180 reported cases per outbreak).

The largest outbreak outside of the Middle East occurred in the Republic of Korea resulting in 186 cases (including one case who travelled to China) and 39 deaths.

Overall, the reproduction number (R_0) of MERS-CoV is <1 with significant heterogeneity in specific contexts. Specifically, outbreaks in health care settings can have R>1, but they can be brought under control (R<1) with proper application of infection prevention and control measures and early isolation of subsequent cases.

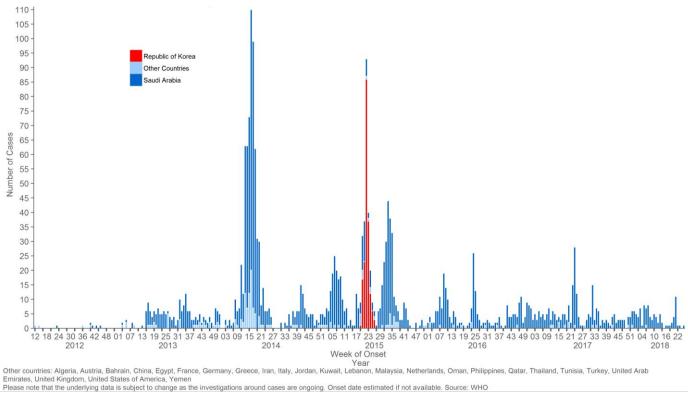


Figure 1. Epidemic curve of MERS-CoV human cases* as of 30 June 2018

Table 1. Number of laboratory-confirmed MERS cases reported by countries, by year, since 2012*

Country reporting	Number of laboratory-confirmed
	MERS-CoV cases reported
Algeria	2
Austria	2
Bahrain	1
China	1
Egypt	1
France	2
Germany	3
Greece	1
Iran	6
Italy	1
Jordan	28
Kuwait	4
Lebanon	2
Malaysia	2
Netherlands	2
Oman	11
Philippines	2
Qatar	19
Republic of Korea	185
Saudi Arabia	1,854
Thailand	3
Tunisia	3
Turkey	1
United Kingdom	4
United Arab Emirates	86
United States of America	2
Yemen	1
Total	2,229

^{*} Data as of 30 June 2018

^{*}Symptomatic cases are plotted by date of symptom onset; asymptomatic cases are plotted by date of notification to WHO.

^{**}Red = Republic of Korea; blue = Kingdom of Saudi Arabia; light blue = all other countries reporting MERS-CoV cases to date including Algeria, Austria, Bahrain, China, Egypt, France, Germany, Greece, Iran, Italy, Jordan, Kuwait, Lebanon, Malaysia, the Netherlands, Oman, the Philippines, Qatar, Thailand, Turisia, Turkey, United Arab Emirates, the United Kingdom, the United States, Yemen.

WHO MERS-CoV guidance and activities

- Since July 2017, WHO updated the following information products and guidance materials:
- Middle East respiratory syndrome coronavirus (MERS-CoV) Fact Sheet. Updated February 2018
- Frequently asked questions on Middle East respiratory syndrome coronavirus (MERS-CoV) Updated January 2018
- <u>Laboratory testing for Middle East Respiratory</u>
 <u>Syndrome Coronavirus</u>, Updated 30 January 2018
- Management of asymptomatic persons who are RTPCR positive for Middle East respiratory syndrome coronavirus (MERS-CoV), Updated 3 January 2018
- Considerations for mass gathering events and Middle
 East respiratory syndrome coronavirus (MERS CoV), Updated May 2018
- Update on MERS-CoV transmission from animals to humans, and interim recommendations for at-risk groups, Updated 26 January 2018
- Investigation of cases of human infection with <u>MERS-CoV</u>, Updated June 2018
- Surveillance for human infection with Middle East respiratory syndrome coronavirus (MERS - CoV), Updated June 2018
- Home care for patients with Middle East respiratory syndrome coronavirus (MERS-CoV) infection presenting with mild symptoms and management of contacts, Updated 26 June 2018
- WHO is in the process of updating the investigation tools aimed at assisting member states during outbreak investigations to evaluate risk factors for and extent of infection in specific human populations. The updates take into consideration recent scientific knowledge and experience from similar studies conducted by partners. An updated protocol, entitled Cross-sectional seroepidemiologic study of MERS-CoV infection in high risk populations in contact with dromedary camels, was published in July 2018. Accompanying this protocol are six questionnaires for study subjects with different dromedary occupations.
- In May 2017, WHO launched a new introductory course on MERS. The course is hosted on the new OpenWHO learning platform and consists of four interactive models featuring video lectures, presentations and self-tests. The free course aims to provide information about what is known about MERS-CoV, the disease it causes and the ways to prevent, respond to and control outbreaks of

MERS-CoV. Access to the training course is available here: https://openwho.org/courses/introduction-to-mers

In May 2018, the MOOC was published into French. From 31 January-1 February 2017, WHO EMRO held a technical consultation on health risk assessment tools for mass gathering events in Jeddah, Kingdom of Saudi Arabia.

- On 22-23 August 2017, WHO EMRO hosted a consultation on emerging pathogens for laboratories (EDPLN) within the WHO Eastern Mediterranean Region. The participants in this meeting discussed laboratory capacity in the region and defined key priorities for laboratory activities on emerging pathogens, including MERS-CoV.
- In August and September 2017, WHO EMRO supported the Ministry of Health of the Kingdom of Saudi Arabia to prepare and develop mitigation efforts for potential health threats related to Hajj pilgrimage.
- On 25-28 September 2017, WHO EMRO conducted a scenario-based training in Beirut, Lebanon for Rapid Response Teams (RRT) in the region. The training covered early detection, field investigation and rapid response to outbreaks caused by novel respiratory pathogens, pandemic influenza and MERS-CoV.
- On 25-27 September, 2017, WHO, the Food and Agriculture Organization of the United Nations (FAO), the World Organisation for Animal Health (OIE), together with leading stakeholders on MERS-CoV, convened in Geneva, Switzerland to review the latest scientific findings on MERS-CoV, and to identify and prioritize the global research activities necessary to prevent, manage and control MERS-CoV. The meeting was the latest in a series of technical meetings on MERS hosted by WHO since 2012. More than 130 experts from 33 countries, organizations and research institutions met to share what is known about the virus, identify priority research needs, improve crosscollaboration between animal and human health sectors and agree on a plan to address crucial gaps. A full meeting report is in press.
- On 1-3 October 2017, WHO EMRO conducted a training workshop for public health staff of the Ministry of Health of Lebanon on outbreak preparedness, detection, field investigation, development of a national RRT and emergency coordination during epidemics.
- On 18-21 November 2017, WHO officials met with the Ministry of Health of Saudi Arabia, including senior officials responsible for MERS-CoV surveillance, case management, infection prevention and control, data collection and analysis, data base management and training. The Ministry of Health also arranged for a joint informal meeting with Ministry of Agriculture officials to discuss their ongoing surveillance and research activities in dromedary camel population. The objectives of the meetings were to outline WHO support for national activities on MERS-CoV in Saudi Arabia.

- On 27 November 2017, WHO and FAO held a coordination meeting in Rome, Italy to plan coordinated MERS related activities at the animal human interface for 2017-2018.
- On 30 January-3 February 2018, the Ministry of Health of Saudi Arabia held a workshop to update their National Guidance Update on MERS, in which WHO participated.
- On 6-7 February 2018, WHO conducted their annual review of the WHO R&D Blueprint list of priority of diseases. For the purposes of the R&D Blueprint, WHO uses a special tool for determining which diseases and pathogens to prioritize for research and development in public health emergency contexts. This tool seeks to identify those diseases that pose a public health risk because of their epidemic potential and for which there are no, or insufficient, countermeasures. The diseases identified through this process are the focus of the work of R& D Blueprint. This is not an exhaustive list, nor does it indicate the most likely causes of the next epidemic. Experts consider that given their potential to cause a public health emergency and the absence of efficacious drugs and/or vaccines, there is an urgent need for accelerated research and development for*: Crimean-Congo haemorrhagic fever (CCHF), Ebola virus disease and Marburg virus disease, Lassa fever, Middle East respiratory syndrome coronavirus (MERS-CoV) and Severe Acute Respiratory Syndrome (SARS), Nipah and henipaviral diseases, Rift Valley fever (RVF), Zika, and "Disease X". Disease X represents the knowledge that a serious international epidemic could be caused by a pathogen currently unknown to cause human disease, and so the R&D Blueprint explicitly seeks to enable cross-cutting R&D preparedness that is also relevant for an unknown "Disease X" as far as possible.
- On 15-16 February, WHO HQ and AFRO held a planning meeting to discuss MERS-CoV and emerging respiratory disease-related activities for the African Region.
- Senior representatives from FAO, OIE and WHO met on 21-22 February 2018 at the OIE headquarters in Paris, France at the 24th Tripartite Annual Executive Meeting. Progress and plans for joint work on issues such as preparedness and response to emerging, re-emerging and neglected infectious diseases, antimicrobial resistance, and food safety were discussed.
- WHO EMRO and HQ participated in a mission in Doha, Qatar to discuss progress on MERS-related research conducted by the Qatar Ministry of Health, to plan future field studies and to update Qatar's National Preparedness Planning for respiratory diseases, including MERS. The Mission took place from 9 to 15 March 2018.
- WHO and IVI held a joint symposium for MERS-CoV Vaccine Development in Seoul Korea on 26-27 June.
 The meeting brought together more than 120 experts and professionals from industry, academia, international agencies and government. Progress on the development

- and trials of dromedary and human vaccines were presented.
- WHO EMRO conducted a training in Riyadh, Saudi Arabia on 1-5 July 2018 on building national and subnational rapid response capacity for detection and response to MERS suspect cases and outbreaks.

Risk assessment

WHO continues to work with ministries of health in all affected and at-risk countries and with international partners to better understand transmission patterns and risk factors of MERS-CoV infection in community and health care settings and to develop improved measures to prevent human infections. WHO's global risk assessment of MERS remains unchanged from the last publication, on 21 July 2017.

The continued occurrence of health care-associated outbreaks is deeply concerning and is the result of low awareness and early suspicion of MERS-CoV infections. The non-specificity of MERS symptoms complicates surveillance activities for the virus, often resulting in early missed cases, including the index case, in outbreaks and thereby providing the opportunity for human-to-human transmission in health care settings.

Investigations are ongoing to evaluate transmission within health care facilities and more comprehensive scientific studies are underway to better understand the drivers of transmission, including studies of surface and air survival and persistence. Secondary cases have reported varying levels of contact with confirmed patients, ranging from direct contact (e.g., health care workers providing direct care to infected patients before diagnosis with MERS) to no clear contact (e.g., patients sharing wards with infected patients, but without sharing health care workers or rooms). At present, it is unclear which exposures result in transmission of the virus in health care settings or what the role of environmental contamination may play in such transmissions. Several studies from the Republic of Korea have identified MERS-CoV virus on surfaces inside patient rooms and on equipment during patient stays and after discharge or death. These findings highlight the importance of adequate cleaning and disinfection of patient rooms.

During the March 2017 WHO-led meeting to further evaluate the role of environmental contamination in MERS-CoV transmission, participants outlined critical scientific experimental and observational studies that need to be conducted. Some of these collaborative studies are currently underway.

WHO has updated its surveillance guidance for MERS-CoV and has specifically stated that any individuals presenting with respiratory symptoms who have recently visited the Middle East must be asked whether they have visited any health care facility there or had any direct or indirect contact with dromedary camels.

WHO is currently in the process of reviewing and updating, as necessary, all WHO information products and guidance materials. Updates are done in collaboration with our

international partners and will be posted <u>online</u> as they become available. The latest updates are listed in the section above.

WHO stresses that it is a person's activities and exposures while in the Middle East that are relevant for MERS-CoV rather than the fact that he or she may have visited a particular country. The movement of patients between hospitals within countries and between countries for treatments and/or surgery (medical tourism) complicates the epidemiologic picture. Genetic sequencing of samples collected from confirmed patients should be a routine part of investigations into MERS-CoV clusters to better understand transmission patterns between patients and to help identify the source of the infection.

Since July 2015, WHO recommends that, in documented cases of human-to-human transmission in a health care setting, all health care contacts (e.g., health care workers and patients sharing space with a confirmed case), household contacts, and social contacts should be tested for MERS-CoV, regardless of whether they display symptoms. Among contacts who are at higher risk of infection are those who are in direct physical contact with the patient or the patient's biological fluids before MERS-CoV was diagnosed (e.g., treating physicians, health care professionals who performed intubation, cleaning staff). For these people, multiple specimens, including lower-respiratory specimens whenever possible, should be collected and tested for MERS-CoV within the 14-day incubation period.

In 2018, the epidemiologic patterns of MERS-CoV remain the same: multiple introductions from dromedary camels in the Middle East to humans and secondary transmission in health care settings. Transmission among close family members within households remains limited for unclear reasons. What is different, however, is that the health careassociated outbreaks in the Middle East are occurring more frequently and, often, though not always, are small in size and can affect several hospitals. The large outbreaks in Jeddah/Riyadh in 2014, in the Republic of Korea in June 2015 and in Riyadh in August 2015, remind us that MERS-CoV, if not adequately controlled, can cause explosive outbreaks with substantial socio-economic consequences.

Until zoonotic transfer of the virus from infected dromedary

human-to-human transmission, thorough investigation of all cases and rapid dissemination of knowledge gained during outbreak investigations and research on MERS-CoV. WHO is pleased that affected countries have improved their responses to MERS-CoV and is also encouraged by the sharing of information on individual cases and investigations of clusters.

Have MERS-CoV transmission patterns changed?

There is no evidence of sustained human-to-human transmission in the community nor is there evidence of airborne transmission as main routes of transmission from all information available from recent MERS-CoV cases.

Therefore, the overall transmission patterns previously observed remain unchanged. WHO bases this assessment on the evidence that:

- The clinical picture seen in recent outbreaks appears to be similar to that observed throughout previous outbreaks; secondary cases in the absence of comorbidities tend to present with milder disease than primary cases; and many of the recently reported secondary cases have been mild or were in patients whose tests were positive for MERS-CoV, but were reported to be asymptomatic;
- 2. The cases recently exported to countries outside of the Middle East have not resulted in sustained onward transmission to persons in close contact with these cases in the community;
- 3. Intensive screening of MERS-CoV contacts has revealed few instances of household transmission and no transmission has been identified thus far on airplanes or other forms of transportation;
- 4. There has been no increase in the size or number of observed household clusters; and
- 5. While there is variation of the R_0 number in different settings, the overall R_0 of MERS-CoV is < 1. The R_0 can be higher in health care settings, as has been seen in several health care associated outbreaks in Saudi Arabia and the Republic of Korea. Experiences in Austria, China. Saudi Arabia. Thailand, and the United Arab

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