# Exportations of Symptomatic Cases of MERS-CoV Infection to Countries outside the Middle East

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In 2012, an outbreak of infection with Middle East respiratory syndrome coronavirus (MERS-CoV), was detected in the Arabian Peninsula. Modeling can produce estimates of the expected annual number of symptomatic cases of MERS-CoV infection exported and the likelihood of exportation from source countries in the Middle East to countries outside the region.

In September 2012, the first confirmed case of Middle East respiratory syndrome coronavirus (MERS-CoV) infection was reported in the Kingdom of Saudi Arabia (KSA) (*1*). Approximately 900 laboratory-confirmed cases had been identified as of January 16, 2015; more than 300 (37%) have resulted in death. Although KSA has reported >80% of cases, infections have been confirmed in other Middle Eastern, European, North American, and, more recently, Asian countries (*2*). Multiple introductions from an animal reservoir have occurred (*3*), but human-to-human transmission of MERS-CoV has also been documented among family members of case-patients and healthcare personnel who cared for case-patients (*4–6*). More than a dozen cases have been identified among travelers returning from the Middle East to their home countries; onward transmission in destination countries also occurred (*7,8*).

## The Study

We calculated the expected annual number of exportations of symptomatic cases of infection with MERS-CoV and the likelihood of exportation from the Middle Eastern countries where additional cases have been detected (KSA, Jordan, Qatar, and the United Arab Emirates [UAE], which we refer to as source countries) to countries outside the Middle East. We defined exportation as the arrival of a person infected with MERS-CoV in a country other than KSA, Jordan, Qatar, and UAE as a result of MERS-CoV

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infection in those source countries and subsequent outbound travel (not including medical evacuation). Because it is unclear whether MERS-CoV cases in Middle Eastern countries other than the source countries resulted from importation or a local outbreak, those countries were excluded from the analysis. Exportations can occur by visitors returning to their home countries or source country residents traveling abroad. We produced example calculations for destination countries outside the Middle East where exportation of MERS-CoV infection cases has been confirmed (Algeria, Austria, France, Greece, Italy, Malaysia, Netherlands, Tunisia, United Kingdom, and the United States) as of January 16, 2015 (Table 1, http://wwwnc.cdc.gov/EID/article/22/4/15-0976-T1.htm).

To calculate exportations, we used a simple multiplier model whereby MERS-CoV incidence rates among source country residents were extrapolated to rates among visitors. In particular, for each source country, the expected number of cases among travelers was calculated by multiplying the infection rate among residents in the affected countries (total number of cases divided by number of residents) by the number of travelers and the days travelers spend, on average, in the affected countries (*9*). To calculate incidence rates in destination countries, the number of symptomatic cases was considered to be 10 times greater than the reported number of cases (*8*). Calculations were made by using Excel (Microsoft Corporation, Redmond, Washington, USA). The probability of exportation was calculated while assuming the number of exportations was Poisson distributed, with the mean equal to the expected exportations (online Technical Appendix 1, http://wwwnc.cdc.gov/eid/article/22/4/15-0976-Techapp1.pdf, and online Technical Appendix 2, http://wwwnc.cdc.gov/eid/article/22/4/15-0976-Techapp2.xlsx).

Expected annual exportations of symptomatic MERS-CoV infection cases among visitors to the Middle East source countries were highest among visitors to KSA (Table 2). For visitors returning from KSA, expected exportations were higher among visitors returning to Algeria, where the number of expected exportations was 1 (95% CI 0–5) and the likelihood of ≥1 exportation was 58%; and Malaysia, where the number of expected exportations was 1 (95% CI 0–5) and the likelihood of ≥1 exportation was 47%.

Expected exportations among residents from the Middle East source countries traveling abroad also were estimated to be higher for visitors from KSA (Table 3). Expected exportations among residents in KSA visiting abroad were highest for the United States, where the

**Table 2.** Estimated annual number of symptomatic cases of MERS-CoV infection exported and likelihood of >1 exportation for countries outside the Middle East among visitors to the source countries*

| Country of destination | Observed no. symptomatic cases exported | No. cases exported from source countries (95% CI); % likelihood for >1 exportation† | | |
|---|---|---|---|---|
| | | Jordan | KSA | UAE |
| Algeria | 2 from KSA | 0 (0–4); 0 | 1 (0–5); 58 | NA |
| Austria | 0 | 0 (0–4); 0 | 0 (0–4); 1 | NA |
| France | 1 from UAE | 0 (0–4); 0 | 0 (0–4); 11 | 0 (0–4); 9 |
| Italy | 1 from Jordan | 0 (0–4); 0 | 0 (0–4); 3 | 0 (0–4); 9 |
| Greece | 0 | 0 (0–4); 0 | 0 (0–4); 1 | NA |
| Netherlands | 2 from KSA | 0 (0–4); 0 | 0 (0–4); 5 | 0 (0–4); 4 |
| Malaysia | 1 from KSA | 0 (0–4); 0 | 1 (0–5); 47 | NA |
| Tunisia | 1 from Qatar | 0 (0–4); 0 | 0 (0–4); 19 | NA |
| United Kingdom | 1 from KSA | 0 (0–4); 0 | 0 (0–4); 24 | 0 (0–4); 35 |
| United States | 0 | 0 (0–4); 1 | 0 (0–4); 27 | 0 (0–4); 31 |

*The incubation period considered was 5.5 days (95% CI 3.6–10.2 days) (*8*). MERS-CoV, Middle Eastern respiratory syndrome coronavirus; KSA, Kingdom of Saudi Arabia; UAE, United Arab Emirates; NA, not available.
†Information on tourists to Qatar was not available.

number of expected exportations was 1 (95% CI 0–5) and the likelihood of >1 exportation was 51%.

## Conclusions

More complex models have been developed to characterize exportations of infectious disease cases via infectious travelers (*10,11*). The main advantage of our approach is its simplicity and reproducibility within short timeframes. This model also complements previous work on the risk for MERS-CoV exportation by global air travel, which attempted to quantify travel volume to the affected areas and calculate exportations among Hajj pilgrims in KSA (*12,13*). In our calculations, however, the visitor data included persons traveling by air, land, and sea and distinguished between visitors to the Middle East and persons from the Middle East traveling abroad over the period of 1 year. Unlike Khan et al. (*12*), we accounted for the rate of infection in the source countries by calculating source country–specific MERS-CoV incidence rates. Furthermore, by accounting for the different travel volume of visitors to the Middle East compared with Middle East residents traveling to non–Middle Eastern countries, we suggested the mode of exportation (visitor to the Middle East vs. Middle East resident visiting abroad). For Malaysia, estimated

expected exportations were higher among visitors to source countries than among source country residents visiting abroad, consistent with the number of exportations detected by surveillance. However, the opposite was true for the United States, where 2 source country residents were found to have MERS-CoV infection during their US visit (*7*).

Our findings have limitations. The estimates are based on historical incidence data. Thus, they are especially applicable for periods in which the incidence of the disease remains stable. For outbreaks characterized by a highly transmissible pathogen, the model might severely underestimate exportations if incidence rates are not projected to the period for which exportations are calculated. In addition, our small multiplier only took into account exportations of symptomatic cases. Given that most of the detected exportations resulted in hospitalization of the infected case-patient, the number of exportations calculated here likely refers to exportations of severe symptomatic cases. Recent results from a serologic survey performed during December 2012–December 2013 indicate that there might be as many as 44,951 (95% CI 26,971–71,922) persons infected with MERS-CoV in KSA (*14*). During that period, there were 125 reported confirmed cases; thus, the ratio of asymptomatic to reported cases might be much higher, possibly

**Table 3.** Estimated annual number of symptomatic cases of MERS-CoV infection exported and likelihood of >1 exportation for countries outside the Middle East among source country residents traveling outside the Middle East*

| Country of destination | Observed no. symptomatic cases exported | No. cases exported from source countries (95% CI); % likelihood for >1 exportation† | | | |
|---|---|---|---|---|---|
| | | Jordan | KSA | Qatar | UAE |
| Italy‡ | 0 | 0 (0–4); 1 | 0 (0–4); 18 | NA | 0 (0–4); 8 |
| Malaysia§ | 0 | 0 (0–4); 0 | 0 (0–4); 33 | 0 (0–4); 1 | 0 (0–4); 2 |
| Tunisia‡ | 0 | 0 (0–4); 0 | 0 (0–4); 2 | 0 (0–4); 0 | 0 (0–4); 0 |
| United Kingdom§ | 0 | 0 (0–4); 0 | 0 (0–4); 35 | 0 (0–4); 3 | 0 (0–4); 25 |
| United States§ | 2 from KSA | 0 (0–4); 0 | 1 (0–5); 51 | 0 (0–4); 2 | 0 (0–4); 8 |

*The incubation period considered was 5.5 days (95% CI 3.6–10.2 days) (*8*). *MERS-CoV, Middle Eastern respiratory syndrome coronavirus; KSA, Kingdom of Saudi Arabia; UAE, United Arab Emirates; NA, not available.
†Information on Middle Eastern visitors to France, Netherlands, and Greece was not available. Number of Middle Eastern residents visiting Algeria and Austria was not available by country of residence.
‡Number of Middle Eastern visitors traveling to Italy and Tunisia corresponds to persons whose nationality is that of Middle Eastern source countries.
§Number of Middle Eastern visitors traveling to Malaysia, the United Kingdom, and the United States corresponds to residents in the Middle East.

in the hundreds. This finding suggests that exportations of asymptomatic cases might be several orders of magnitude higher than those of severe symptomatic cases.

The upper bound of exportations for the countries least likely to receive symptomatic case importations was 4, suggesting that small numbers of importations are largely stochastic events. Although every country is at risk, as illustrated by the recent outbreak of MERS-CoV infections in South Korea that was triggered by just 1 importation (*15*), our model can be used to assess risk level. Combined with other indicators, our model can help determine the level of additional public health measures (e.g., border screenings) required for infectious diseases threats from abroad.

No exportations of symptomatic cases were detected in some of the top travel volume countries for trips originating in KSA, Jordan, UAE, and Qatar. Travel volume to Egypt, India, and Pakistan was several times higher than that for other countries where MERS-CoV has been detected. However, only 1 case of MERS-CoV infection has been detected in Egypt (in a KSA resident) (http://www.who.int/csr/don/2014_05_01_mers), and no MERS-CoV cases have been detected in India or Pakistan. This finding suggests that MERS-CoV introductions may have already occurred in these countries but have not been detected.

In summary, by adapting a simple model of disease spread, we estimated the expected number of MERS-CoV symptomatic case exportations during a 1-year period among visitors to the Middle East and visitors from KSA, Jordan, Qatar, and UAE to non–Middle Eastern countries where case exportations have occurred. Our estimations suggest that the risk for repeated exportations of severe symptomatic MERS-CoV cases is low, although the number of asymptomatic case exportations might be higher.

Dr. Carias is a modeler in the National Center for Emerging and Zoonotic Infectious Diseases at the Centers for Disease Control and Prevention. She is interested in using economic and infectious disease models to assist decision making in public health.

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# Exportations of Symptomatic Cases of MERS-CoV Infection to Countries outside the Middle East

**Technical Appendix 1**

## Methods

### Data

We used data on laboratory-confirmed cases in the source countries, census data, and travel volume. Data regarding the number of cases of infection Middle East respiratory syndrome coronavirus (MERS-CoV) were taken from the case list of the World Health Organization, updated as of January 16, 2015. To calculate the infection rate we divided the number of confirmed cases in each source country of origin with onset date of 2013 through 2015 (as of January 16, 2015) by the total population size of the country of origin and days between January 1, 2013 and January 16, 2015 (the exact date of outbreak onset for each country remains unknown and so a common period with end date close to the date of the last report date was chosen for all source countries). Population estimates were extracted from national publicly available sources (*1–4*).

Data on arrivals of visitors to and from the Middle East source countries, per nationality/ country of residence, were extracted from the United Nations World Tourism Organization (UNWTO) Yearbook of Tourism Statistics (*5*); for UAE official tourism statistics were used as well (*6,7*). Travel volumes extracted from UNWTO Yearbook include all modes of travel (air, road, sea) and refer to 2012.

For arrivals of visitors to the Middle East, data from UNWTO yearbook were extracted for Saudi Arabia and Jordan. For the United Arab Emirates (UAE), visitor data were only available for Dubai (for 2012) and Abu Dhabi (period: Jan–Apr 2013) for the United Kingdom, the United States, France, Italy, Netherlands; the travel volume for Abu Dhabi was scaled to a

year by multiplying by 3 (*6,7*). For Qatar, data on arrivals of nonresident visitors were not available.

Data on arrivals of visitors from the source countries on destination countries were extracted from UNWTO Yearbook of Tourism Statistics. Information on arrivals of Middle East source country visitors to Algeria, Austria, France, the Netherlands, and Greece was not available.

Information on the length of stay of visitors in the Middle Eastern source countries was taken from different sources. For visitors traveling to Jordan and Qatar, data were drawn from the UNWTO Compendium of Tourism Statistics (*8*). For Qatar, data were only available for 2008; for Jordan, 2012 data were used (*8*). For Saudi Arabia, length of stay was obtained per nationality for 2006 from official statistics (*9*). For each nationality, number of passengers per length of stay interval was available. The final length of stay was a weighted average between the midpoints for each interval, in which the weights were the share of travelers in that length of stay category. Lengths of stay larger than 10.2 days were limited to 10.2 days (the upper bound of the incubation period [*10*]), to restrict the estimated number of exportations to infectious cases. If using a longer time, exportations would include number of residents in the Middle East source countries that had MERS-CoV cases but were no longer infectious, less useful to understand risk of person-to-person transmission in the destination countries. For UAE, data were retrieved from Dubai (2012 data) and Abu Dhabi (Jan–Apr 2013) official websites (*6,7*). For UAE, length of stay data were not available per nationality and so an average across all international destination countries was used. For source countries residents visiting abroad, duration of exposure in the source countries was taken to be 10.2 days, the upper bound of the incubation period, again to restrict our estimations to arriving MERS-CoV infectious cases (*10*).

**Estimation**

Overview

For each destination country, we calculated the expected number of exportations, and the probability of exportation from each of the source countries (Saudi Arabia, Jordan, Qatar, UAE) among travelers to and from the source countries. For each source country, the expected number of cases among travelers was calculated by multiplying the infection rate among residents in the affected countries by the person-time at risk among travelers (*11*). The incidence rate of infection

among travelers was estimated by multiplying the travel volume by the average duration of stay of travelers in each source country. To calculate the expected number of symptomatic cases exported to the destination country we further adjusted for under-reporting: expected number of symptomatic cases exported to destination country = ratio of symptomatic to reported cases × [cases in source country)/(total population in source × outbreak duration)] × [(number of travelers) × (traveler's duration of stay)] (*1*).

For MERS-CoV, the ratio between reported and estimated total symptomatic MERS-CoV cases has been calculated to be 10 (*10*). We thus used the factors of 10 in expression (*1*) to calculate the total number of expected annual exportations of symptomatic cases.

In both calculations, we used Poisson confidence intervals to reflect stochastic variation in the expected number of exportations (*11*). CIs do not take into account uncertainty in the number of travelers, which is likely small if compared to uncertainty related to the outbreak size and so will be unlikely to bias the results.

We also calculated the likelihood of disease exportation to any of the countries considered. We assumed that the number of symptomatic cases exported to any destination country followed a Poisson distribution with a mean equal to expression 1. We then estimated the probability of the number of exportations being different and higher than 0, that is, the probability of having at least one exportation.

### Exportations among Visitors to Source Countries

To calculate the number of exportations among visitors to the source countries, the number of travelers to the source countries was taken to be the total number of persons traveling to the source countries. This includes groups traveling for different purposes such as tourists, professionals traveling for business, or pilgrims. Travelers' duration of stay in the source countries was taken to be the average length of stay of visitors in each country.

### Exportations among Source Country Residents Traveling outside Source Countries

To estimate exportations among travelers who are residents in the Middle Eastern source countries, the number of travelers was considered to be the number of Middle Eastern residents visiting the destination countries. Visitors from the source countries include source country residents (persons that live in the Middle East source countries) and/or persons whose nationality

is that of the source countries (for the United Kingdom, the United States, Malaysia, the number of Middle East residents visiting in these countries was available; for Italy and Tunisia, the number of visitors was available per nationality only). Length of stay in the Middle East was taken to be the upper bound of the incubation period (10.2 days [*10*]), to ensure exportations were restricted to infectious persons.

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