

## Resume: リアルタイムの感染症流行の分析

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*Resume of printed articles*

Original studies were printed elsewhere, and herewith a Resume of published studies is provided for this proceedings.

## Background

The Middle East respiratory syndrome (MERS) associated coronavirus has been imported via travelers into multiple countries around the world. In order to support risk assessment practice, the present study aimed to devise a novel statistical model to quantify the country-level risk of experiencing an importation of MERS case.

The outbreak was observed in the Republic of Korea, 2015. Korean outbreak was featured by the presence of superspreaders who generated extraordinary large number of secondary cases. We also aimed to investigate the heterogeneous transmission patterns of Middle East respiratory syndrome (MERS) in the Republic of Korea, with a particular focus on epidemiological characteristics of superspreaders.

## Method

In the first part, we analyzed the arrival time of each reported MERS importation around the world, i.e., the date on which imported cases entered a specific country, which was modeled as a dependent variable in our analysis. We also used openly accessible data including the airline transportation network to parameterize a hazard-based risk prediction model. The hazard was assumed to follow an inverse function of the effective distance (i.e., the minimum effective length of a path from origin to destination), which was calculated from the airline transportation data, from Saudi Arabia to each country. Both country-specific religion and the incidence data of MERS in Saudi Arabia were used to improve our model prediction.

The second part of the study, i.e., reconstruction of the transmission network, rested on retrospective epidemiological analysis. In the 2015 Korean outbreak, multiple healthcare facilities of secondary and tertiary care centres in an urban setting were involved. Study participants were the total of 185 laboratory-confirmed cases with

partially known dates of illness onset and most likely sources of infection. Superspreaders were identified using the transmission tree. The reproduction number, that is, the average number of secondary cases produced by a single primary case, was estimated as a function of time and according to different types of hosts.

## Results

Our estimates of the risk of MERS importation appeared to be right skewed, which facilitated the visual identification of countries at highest risk of MERS importations in the right tail of the distribution. The simplest model that relied solely on the effective distance yielded the best predictive performance (Area under the curve (AUC) = 0.943) with 100 % sensitivity and 79.6 % specificity. Out of the 30 countries estimated to be at highest risk of MERS case importation, 17 countries (56.7 %) have already reported at least one importation of MERS. Although model fit measured by Akaike Information Criterion (AIC) was improved by including country-specific religion (i.e. Muslim majority country), the predictive performance as measured by AUC was not improved after accounting for this covariate.

A total of five superspreaders were identified. The reproduction number throughout the course of the outbreak was estimated at 1.0 due to reconstruction of the transmission tree, while the variance of secondary cases generated by a primary case was 52.1. All of the superspreaders involved in this outbreak appeared to have generated a substantial number of contacts in multiple healthcare facilities (association:  $p < 0.01$ ), generating on average 4.0 (0.0-8.6) and 28.6 (0.0-63.9) secondary cases among patients who visited multiple healthcare facilities and others. The time-dependent reproduction numbers declined substantially below the value of 1 on and after 13 June 2015.

## Discussion

Our relatively simple statistical model based on the effective distance derived from the airline transportation network data was found to help predicting the risk of importing MERS at the country level. The successful application of the effective distance model to predict MERS importations, particularly when computationally intensive large-scale transmission models may not be immediately applicable could have been benefited from the particularly low transmissibility of the MERS coronavirus.

Superspreaders who visited multiple facilities drove the epidemic by generating a disproportionate number of secondary cases. Our findings underscore the need to limit

the contacts in healthcare settings. Contact tracing efforts could assist early laboratory testing and diagnosis of suspected cases.

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