Supplement 1

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**Space-time K-function analysis**

The approach is described in details in Diggle et al. 1995. Briefly, the space-time K-function \( K(s,t) \) measures the number of cases expected within a distance \( s \) and a time \( t \) from a randomly-selected case, divided by the intensity \( \lambda \) (the mean number of cases per unit of space and time). When there is no space-time interaction, the space-time K-function corresponds to the product of the spatial and temporal K-functions, \( K(s) \) and \( K(t) \), respectively, such as \( K(s,t) = K(s)*K(t) \). \( D(s,t) \) is defined as the difference \( K(s,t) - K(s)*K(t) \). Consequently, values of \( D(s,t) > 0 \) are indicative of space-time interaction at distance \( s \) and time \( t \), with higher \( D(s,t) \) values associated with stronger evidence. To facilitate comparisons across space and time, we calculate \( D_0(s,t) \) defined as \( D(s,t) / [K(s)*K(t)] \), which corresponds to the number of cases that are due to the space-time interaction divided by the number of cases that would have been observed in the absence of space-time interaction. Therefore, \( D_0(s,t) \) represents the proportional increase (or excess risk) in cases attributable to space-time interaction. Accordingly, values of \( D_0(s,t) > 0 \) indicates the presence of space-time interaction and values of \( D_0(s,t) > 1 \) indicates that the number of observed cases in the space-time window defined by \( s \) and \( t \) around a case is greater than at least twice the number of cases that would have been observed in the absence of space-time interaction. To test the null hypothesis
of no space-time interaction, the dates of the cases are randomly permuted on the fixed set of
the locations of the cases using Monte-Carlo simulation, generating a distribution of D(s,t)
under the null hypothesis. This distribution is compared with the calculated D(s,t) from the
observed cases. If it exceeds 95% of the simulated D(s,t) values, then the interpretation is that
there is less than 5% probability that the observed space-time interaction occurred by chance
and so the null hypothesis is rejected and it is concluded that there was a significant space-
time interaction.

**Space-time permutation scan statistic**

The approach is described in details in Kulldorf et al. 2005. Briefly, the approach is
based on creating series of hypothetical spatio-temporal cylinders centred at the coordinates
of each case. The base and the height of the cylinder represents the spatial and temporal
dimensions of each potential cluster, respectively. To test the null hypothesis of no space-time
interaction, random permutations of the spatial and temporal attributes of each case are
performed using Monte-Carlo simulation. For each cylinder, the model computes the Poisson
generalized likelihood ratio (GLR), defined as \((c/\mu)c (C-c/C- \mu)(C-c)\), with C the total number
of observed cases, c the number of observed cases in the cylinder and \(\mu\) the expected cases in
the cylinder. Among all cylinders evaluated, the one with the largest GLR is identified as the
cluster that is least likely to occur by chance.

**References**
