**Appendix A: Maximum component size test**

To test for period prevalence of a large hospital-borne epidemic, we implement the *maximum component size* test.29 In this test we compare the maximum size of components in $CPG\_{(T,D)}^{CDI,obs}$ to the expected maximum size of components of $CPG\_{(T,D)}^{CDI,rand}$ conditioned on the absence of spatiotemporal interactions. As in the case of the other tests, we use Monte Carlo simulations with the time stamps randomly permuted 20,000 to obtain an empirical distribution and calculate the expectation.

**Results.** The observed maximum component sizes in $CPG\_{(T,D)}^{CDI,obs}$ are 6, 7, 11, and 11 respectively for *D* = 2, 3, 4, and 5, with *T* = 14. These observed maximum component sizes trend larger than the corresponding expected maximum component sizes in a $CPG\_{(T,D)}^{CDI,rand}$ derived from20,000 time stamp permutations (see Figure 6, left; p = 0.05, 0.11, 0.02 and 0.14 for D = 2, 3, 4 and 5, respectively). In contrast, the observed maximum component sizes in$CPG\_{(T,D)}^{AP,obs}$ (Figure 4, bottom right) appear right in the middle of the corresponding distributions of the maximum component sizes in random$CPG\_{(T,D)}^{AP,rand}$.



Figure 6. The maximum component size test results are shown for CDI (left) and for aspiration pneumonia (right) for *T* = 14 and *D* = 2, 3, 4, and 5.

**Appendix B: Test results for all *T*, *D* threshold values**

|  |  |  |
| --- | --- | --- |
| **Knox Test**  |  **CDI**  |  **Aspiration pneumonia**  |
| **obs** | **rand mean** | **rand std dev** | **p-value** | **obs** | **rand mean** | **rand std dev** | **p-value** |
| **T=7 D=2**  | 162 | 79.291 | 8.94969 | <0.001 | 8 | 12.0105 | 3.45254 | 0.14975 |
|  **T=7 D=3**  | 244 | 138.326 | 11.7732 | <0.001 | 18 | 21.2897 | 4.60206 | 0.2829 |
|  **T=7 D=4**  | 304 | 189.04 | 13.7238 | <0.001 | 34 | 34.6517 | 5.77531 | 0.5009 |
|  **T=7 D=5**  | 356 | 241.101 | 15.4666 | <0.001 | 44 | 45.114 | 6.57694 | 0.47485 |
|  **T=14 D=2**  | 287 | 157.902 | 12.5193 | <0.001 | 8 | 12.0042 | 3.44786 | 0.153158 |
|  **T=14 D=3**  | 438 | 275.084 | 16.5161 | <0.001 | 18 | 21.2742 | 4.56785 | 0.278364 |
|  **T=14 D=4**  | 554 | 376.153 | 19.3214 | <0.001 | 34 | 34.6859 | 5.79514 | 0.50195 |
|  **T=14 D=5**  | 682 | 478.904 | 21.8199 | <0.001 | 44 | 45.0712 | 6.64006 | 0.479324 |
|  **T=21 D=2**  | 375 | 236.627 | 15.3831 | <0.001 | 8 | 12.0142 | 3.42795 | 0.151 |
|  **T=21 D=3**  | 594 | 411.851 | 20.3613 | <0.001 | 18 | 21.2675 | 4.54421 | 0.27895 |
|  **T=21 D=4**  | 762 | 562.99 | 23.8534 | <0.001 | 34 | 34.6207 | 5.85542 | 0.50765 |
|  **T=21 D=5**  | 963 | 717.283 | 27.2592 | <0.001 | 44 | 45.0423 | 6.70619 | 0.47885 |

|  |  |  |
| --- | --- | --- |
| **Mean Component Size Test**  |  **CDI**  |  **Aspiration pneumonia**  |
| **obs** | **rand mean** | **rand std dev** | **p-value** | **obs** | **rand mean** | **rand std dev** | **p-value** |
| **T=7 D=2**  | 1.06569 | 1.03253 | 0.004062 | <0.001 | 1.00564 | 1.01125 | 0.004589 | 0.93725 |
| **T=7 D=3**  | 1.09849 | 1.05726 | 0.005426 | <0.001 | 1.01711 | 1.02003 | 0.006123 | 0.72695 |
| **T=7 D=4**  | 1.12043 | 1.07899 | 0.006448 | <0.001 | 1.02885 | 1.0327 | 0.007824 | 0.7217 |
| **T=7 D=5**  | 1.14128 | 1.10183 | 0.007371 | <0.001 | 1.03883 | 1.04276 | 0.008885 | 0.702 |
| **T=14 D=2**  | 1.11661 | 1.06513 | 0.00571 | <0.001 | 1.02294 | 1.02253 | 0.006435 | 0.5126 |
| **T=14 D=3**  | 1.1861 | 1.11551 | 0.007719 | <0.001 | 1.04288 | 1.04054 | 0.008661 | 0.4228 |
| **T=14 D=4**  | 1.23304 | 1.16094 | 0.009316 | <0.001 | 1.06362 | 1.06619 | 0.011163 | 0.61925 |
| **T=14 D=5**  | 1.2923 | 1.21006 | 0.011061 | <0.001 | 1.06151 | 1.08688 | 0.012749 | 0.9873 |
| **T=21 D=2**  | 1.15607 | 1.09806 | 0.00703 | <0.001 | 1.02687 | 1.03392 | 0.007953 | 0.8453 |
| **T=21 D=3**  | 1.25995 | 1.17529 | 0.00974 | <0.001 | 1.05315 | 1.0608 | 0.010637 | 0.7897 |
| **T=21 D=4**  | 1.3381 | 1.24616 | 0.011808 | <0.001 | 1.09407 | 1.10044 | 0.013798 | 0.69835 |
| **T=21 D=5**  | 1.44444 | 1.32519 | 0.014336 | <0.001 | 1.11691 | 1.13237 | 0.015965 | 0.8504 |

|  |  |  |
| --- | --- | --- |
| **Largest Component Size Test**  |  **CDI**  |  **Aspiration pneumonia**  |
| **obs** | **rand mean** | **rand std** | **p-value** | **obs** | **rand mean** | **rand std** | **p-value** |
|  **T=7 D=2**  | 4 | 3.2112 | 0.530574 | 0.22155 | 2 | 2.0893 | 0.297372 | 0.998 |
|  **T=7 D=3**  | 4 | 3.81125 | 0.726533 | 0.65175 | 2 | 2.2952 | 0.485972 | 0.99995 |
|  **T=7 D=4**  | 6 | 4.48415 | 0.86746 | 0.1086 | 2 | 2.6305 | 0.598905 | 1 |
|  **T=7 D=5**  | 9 | 5.19175 | 1.05496 | 0.0104 | 3 | 2.9103 | 0.629741 | 0.7697 |
|  **T=14 D=2**  | 6 | 4.11324 | 0.789826 | 0.050098 | 2 | 2.3134 | 0.490107 | 1 |
|  **T=14 D=3**  | 7 | 5.27204 | 1.06011 | 0.111844 | 3 | 2.8001 | 0.60496 | 0.707 |
|  **T=14 D=4**  | 11 | 6.751 | 1.49439 | 0.0221 | 3 | 3.2993 | 0.644702 | 0.9547 |
|  **T=14 D=5**  | 11 | 8.51727 | 1.97993 | 0.139143 | 3 | 3.728 | 0.796793 | 0.9949 |
|  **T=21 D=2**  | 6 | 4.9766 | 0.996445 | 0.23345 | 3 | 2.5828 | 0.575553 | 0.54115 |
|  **T=21 D=3**  | 10 | 6.77875 | 1.4954 | 0.0522 | 3 | 3.18615 | 0.622991 | 0.92045 |
|  **T=21 D=4**  | 11 | 9.363 | 2.28873 | 0.24515 | 4 | 3.83135 | 0.795072 | 0.63485 |
|  **T=21 D=5**  | 13 | 12.9491 | 3.41988 | 0.47215 | 5 | 4.46695 | 0.983949 | 0.4066 |

|  |  |  |
| --- | --- | --- |
| **Mantel Test** |  **CDI**  |  **aspration pneumonia**  |
| **obs** | **rand mean** | **rand std** | **p-value** | **obs** | **rand mean** | **rand std** | **p-value** |
|   | 0.019242 | 0.00158532 | 0.004685 | 0.000267 | 0.007236 | 0.00623183 | 0.009303 | 0.451191 |

**Table 2:** Summary of our results for the four different spatiotemporal interaction and clustering tests on the CDI and aspiration pneumonia cases using different values of *T* and *D*, namely values *T* = 7,14,21 and *D* = 2,3,4,5. We show four values for each test: (1) the observed statistic, (2) the mean and (3) standard deviation of the statistic over the distributions generated by the Monte Carlo simulation, and (4) the *p*-value of the tests.

**Appendix C: Interpretation of results**

In the Knox test, the measure of spatiotemporal interaction is simply the *number* of case pairs that are within the threshold *T* in temporal distance and within the distance *D* in spatial distance. In our formulation, this is represented by the number of edges of the case proximity graph. The results of the Knox test for thresholds *T* = 7, 14, 21 days and *D* = 2, 3, 4, 5 are shown in Table 2 and these are visually depicted for *T* = 14 in Figure 3. The Mantel test measures spatiotemporal interaction by computing the Pearson correlation between the spatial and temporal distance matrices of the cases. There are no time and distance thresholds associated with the Mantel test; distances at all scales matter. The results of the Mantel test are shown in Table 2 and Figure 5. Both tests confirm the presence of spatiotemporal interaction for CDI in different ways and the null hypothesis of no spatiotemporal interaction is rejected with p-value < 0.001 – in the case of the Knox test, for all threshold value (*T*, *D*) pairs. In the case of aspiration pneumonia, the results are strikingly different and our tests do not reveal any significant spatiotemporal interaction. These results implicate the environment, in a broad sense, for CDI spread. While surfaces (e.g., beds, toilets, sinks) or shared healthcare workers could be playing a role, it could also be other latent factors. As mentioned in the “Discussion” section more work is needed to tease out these different environmental factors in CDI spread.

The other two tests we performed, the mean and maximum component size tests, can be viewed as extensions of the Knox test in which we are interested not just in the presence of spatiotemporal interaction, but its *structure*. One way of measuring spatiotemporal interaction is by the size of components, i.e., clusters of cases that are all reachable from each other via paths in the case proximity graph. The results for the mean component size test are shown in Table 2 and visually depicted in Figure 4. In the case of CDI, the observed mean component sizes are significantly larger than the mean component sizes obtained from the Monte Carlo simulations, rejecting the null hypothesis of no spatiotemporal clustering with *p*-value < 0.0001, for all threshold value (*T*, *D*) pairs. Again, the results are strikingly different for aspiration pneumonia, revealing no spatiotemporal clustering. This result suggests that there is spatiotemporal clustering of CDI cases that can be ascribed to the environment. However, the results from the maximum component size test for CDI are not consistently significant as can be seen from Table 2 and Figure 6. This difference between the results of the mean and maximum component size tests may be suggesting that while there is spatiotemporal clustering of CDI cases attributable to the environment, we do not see large outbreaks. This also means that our results implicating the environment in CDI spread are not inconsistent the presence of many genetically-unrelated cases.

**Appendix D: Results for CDI cases at least 48 hours after admission**

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| --- | --- | --- |
| **Knox Test**  |  **CDI**  |  **Aspiration pneumonia**  |
| **obs** | **rand mean** | **rand std dev** | **p-value** | **obs** | **rand mean** | **rand std dev** | **p-value** |
| **T=14 D=2** | 182 | 93.7831 | 9.58397 | <0.001 | 8 | 10.6758 | 3.51282 | 0.282675 |
| **T=14 D=3** | 277 | 161.697 | 12.6708 | <0.001 | 18 | 18.7497 | 4.98123 | 0.501475 |
| **T=14 D=4** | 341 | 218.066 | 14.7143 | <0.001 | 34 | 31.0695 | 6.57061 | 0.345216 |
| **T=14 D=5** | 682 | 379.956 | 100.832 | <0.001 | 34 | 35.3685 | 5.91634 | 0.45555 |

|  |  |  |
| --- | --- | --- |
| **Mean Component Size Test**  |  **CDI**  |  **Aspiration pneumonia**  |
| **obs** | **rand mean** | **rand std dev** | **p-value** | **obs** | **rand mean** | **rand std dev** | **p-value** |
| **T=14 D=2** | 1.09015 | 1.04653 | 0.0054 | <0.001 | 1.010 | 1.01996 | 0.0065005 | 0.9564 |
| **T=14 D=3** | 1.14537 | 1.08136 | 0.0073 | <0.001 | 1.023 | 1.03499 | 0.00860298 | 0.92725 |
| **T=14 D=4** | 1.17293 | 1.11146 | 0.0086 | <0.001 | 1.056 | 1.05967 | 0.0113032 | 0.6499 |
| **T=14 D=5** | 1.21685 | 1.14589 | 0.0101683 | <0.001 | 1.073 | 1.07748 | 0.0128672 | 0.65885 |

|  |  |  |
| --- | --- | --- |
| **Largest Component Size Test**  |  **CDI**  |  **Aspiration pneumonia**  |
| **obs** | **rand mean** | **rand std dev** | **p-value** | **obs** | **rand mean** | **rand std dev** | **p-value** |
| **T=14 D=2** | 5 | 3.4621 | 0.635361 | 0.05455 | 2 | 2.23675 | 0.447448 | 1 |
| **T=14 D=3** | 5 | 4.23195 | 0.809433 | 0.2902 | 2 | 2.6201 | 0.601244 | 1 |
| **T=14 D=4** | 5 | 5.1121 | 1.0774 | 0.6956 | 3 | 3.1422 | 0.633087 | 0.89645 |
| **T=14 D=5** | 9 | 6.11365 | 1.31656 | 0.05295 | 3 | 3.50705 | 0.749185 | 0.97795 |

|  |  |  |
| --- | --- | --- |
| **Mantel Test** |  **CDI**  |  **Aspiration pneumonia**  |
| **obs** | **rand mean** | **rand std** | **p-value** | **obs** | **rand mean** | **rand std** | **p-value** |
|   | 0.0087135 | 0.0020752 | 0.00461187 | 0.07295 | 0.00645761 | 0.00705979 | 0.0101998 | 0.484163 |