***Supplementary Tables and Figures***

**Supplementary Table 1. Four-way decomposition analysis assessing the effect of contaminated beds (exposure) on a contaminated room (potential mediator/ effect modifier) on *Clostridioides difficile* infection (CDI)\***

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Estimate** | **95% CI** | **P-Value** |
| Total Effect Risk Ratio | 1.45 | 1.05 | 1.85 | <.0001 |
| Total Excess Relative Risk | 0.45 | 0.05 | 0.85 | 0.03 |
| Excess Relative Risk due to CDE | 0.05 | -0.61 | 0.70 | 0.89 |
| Excess Relative Risk due to INTref | 0.05 | -0.63 | 0.73 | 0.89 |
| Excess Relative Risk due to INTmed | 0.28 | -0.03 | 0.59 | 0.07 |
| Excess Relative Risk due to PIE | 0.07 | -0.19 | 0.34 | 0.59 |
| Proportion CDE *(Neither Mediation/ Interaction)* | 0.11 | -1.29 | 1.50 | 0.88 |
| Proportion INTref *(Interaction Only)* | 0.11 | -1.44 | 1.66 | 0.89 |
| Proportion INTmed *(Mediation and Interaction)* | 0.62 | 0.24 | 1.00 | <0.01 |
| Proportion PIE *(Mediation Only)* | 0.16 | -0.39 | 0.72 | 0.56 |
| Overall Proportion Mediated | 0.78 | 0.59 | 0.98 | <.0001 |
| Overall Proportion Attributable to Interaction | 0.73 | -0.98 | 2.44 | 0.40 |
| Overall Proportion Eliminated | 0.89 | -0.50 | 2.29 | 0.21 |

*\** Adjusted for ICU admission and time at risk prior to HO-CDI or discharge, whichever occurred first

Abbreviations: CDE, controlled direct effect; INTref, reference due to interaction effect; INTmed, part of the total effect due to both mediation and interaction; PIE, pure indirect effect

We conducted a four-way decomposition analysis[16] to assess the extent to which contaminated rooms mediate and/or modify the association between contaminated beds and hospital-onset *C. difficile* infection (HO-CDI). The four-way decomposition divides the total effect of a contaminated bed on HO-CDI (RR: 1.45, 95% CI: 1.05, 1.85 or excess relative risk [ERR]: 0.45, 95% CI: 0.05, 0.85) into four components. First, the Controlled Direct Effect (CDE): the effect of a contaminated bed on HO-CDI without exposure to a contaminated room (i.e. the effect that is neither due to interaction or mediation from a contaminated room [proportion CDE: 11%, 95% CI: -29% to 50%]). Second, the Reference Interaction (INTRef): the additive interaction which represents the effect on HO-CDI of having exposure to both contaminated bed and a contaminated room, such that it differs from the sum of the effect of exposure only to a contaminated bed plus the effect of exposure only to a contaminated room. An additional 11% of the total effect was due to this interaction (95% CI:-44% to 66%). Third, the Mediated Interaction (INTmed): the proportion of the total effect that is due to both mediation and interaction. This is an additive interaction that describes how much effect the exposure (contaminated bed) has on the mediator (contaminated room). 62% of the total effect was due to this mediated interaction (95% CI: 24% to 100%). Lastly, the Pure Indirect Effect (PIE): the proportion of the total effect from the mediator (contaminated room) in the absence of the exposure (contaminated bed). The proportion attributable to the contaminated room (mediator) alone is 16% (95% CI: -39% to 72%). Of the four components, mediated interaction (component 3) accounted for majority of the total effect between contaminated beds and HO-CDI. The overall proportion of the effect mediated by a contaminated room is 78% (sum of components 3 and 4, Supplementary Figure 1).

**Supplementary Figure 1. Graphical display showing the amount of the relationship between a contaminated bed and hospital-onset *C. difficile* caused by mediation from a contaminated room or interaction with a contaminated room.**

