Supplementary material

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Supplementary Figure S1. Organisms detected by the BioFire FilmArray GI Panel assay.

Samples were positive or negative for *C. difficile* toxin (Cell-cytotoxin neutralisation assay; CCNA).

None = None detected. ADENOVLDS=Adenovirus. ASTROVLDS=Astrovirus. CAMPYLDS=Campylobacter. CRYPOS=Cryptosporidium. CYCCAYLDS=Cyclospora cayetanensis. EAECLDS=E. coli Enteroaggregative (EAEC). EIECLDS= Shigella/Enteroinvasive E. coli (EIEC). ENTHISLDS=Entamoeba histolytica. EPECLDS=E. coli Enteropathogenic (EPEC). ETECLDS=E. coli Enterotoxigenic (ETEC). GIRLAMLDS=Giardia lamblia. NOVOVLDS=Norovirus. O157LDS=E. coli O157. PLESHILDS=Plesiomonas Shigelloides. ROTAVLDS=Rotavirus. SALMLALDS=Salmonella. SAPOVLDS=Sapovirus. STECLDS=E. coli Shiga - Like Toxin - Producing (STEC). VIBCHLLDS=Vibrio Cholerae. VICRIOLDS=Vibrio. YERENTLDS=Yersinia Enterocolitica.

### Co-infections detected by BioFire GI panel assay in *C. difficile* toxin positive samples (CCNA positive)

- **Hospital (n=83)**: 85.5% None, 0.0% ADENOVLDS, 1.2% ASTROVLDS, 0.0% CAMPYLDS, 0.0% CRYPOS=, 1.2% CYCCAYLDS, 0.0% EAECLDS, 0.0% EIECLDS, 0.0% ENTHISLDS, 7.2% EPECLDS, 0.0% ETECLDS, 0.0% GIRLAMLDS, 0.0% NOVOVLDS, 7.2% O157LDS, 0.0% PLESHILDS, 0.0% ROTAVLDS, 0.0% SALMLALDS, 0.0% SAPOVLDS, 0.0% STECLDS, 0.0% VIBCHLLDS, 0.0% VICRIOLDS, 0.0% YERENTLDS
- **Community (n=19)**: 73.7% None, 0.0% ADENOVLDS, 0.0% ASTROVLDS, 5.3% CAMPYLDS, 0.0% CRYPOS=, 0.0% CYCCAYLDS, 5.3% EAECLDS, 0.0% EIECLDS, 0.0% ENTHISLDS, 0.0% EPECLDS, 0.0% ETECLDS, 0.0% GIRLAMLDS, 0.0% NOVOVLDS, 0.0% O157LDS, 0.0% PLESHILDS, 5.3% ROTAVLDS, 0.0% SALMLALDS, 0.0% SAPOVLDS, 0.0% STECLDS, 0.0% VIBCHLLDS, 0.0% VICRIOLDS, 0.0% YERENTLDS

### Other organisms detected by BioFire GI panel assay in *C. difficile* toxin negative samples (CCNA negative)

- **Hospital (n=214)**: 72.4% None, 2.8% ADENOVLDS, 0.5% ASTROVLDS, 3.3% CAMPYLDS, 0.5% CRYPOS=, 0.9% CYCCAYLDS, 2.8% EAECLDS, 0.9% EIECLDS, 0.5% ENTHISLDS, 8.9% EPECLDS, 0.5% ETECLDS, 1.9% GIRLAMLDS, 0.0% NOVOVLDS, 0.5% O157LDS, 0.0% PLESHILDS, 0.5% ROTAVLDS, 0.0% SALMLALDS, 0.0% SAPOVLDS, 0.0% STECLDS, 0.0% VIBCHLLDS, 0.0% VICRIOLDS, 0.0% YERENTLDS
- **Community (n=106)**: 70.8% None, 2.8% ADENOVLDS, 0.0% ASTROVLDS, 7.5% CAMPYLDS, 0.0% CRYPOS=, 0.9% CYCCAYLDS, 1.9% EAECLDS, 1.9% EIECLDS, 0.0% ENTHISLDS, 5.7% EPECLDS, 2.8% ETECLDS, 1.9% GIRLAMLDS, 0.0% NOVOVLDS, 0.9% O157LDS, 0.0% PLESHILDS, 0.0% ROTAVLDS, 0.0% SALMLALDS, 0.0% SAPOVLDS, 0.0% STECLDS, 0.0% VIBCHLLDS, 0.0% VICRIOLDS, 2.8% YERENTLDS
### Supplementary Table S1. Metadata of undiagnosed CDI cases.

Metadata was as reported in medical records, Europe, 2018.  
CDI = *Clostridioides difficile* infection  
n/a = Data not available

| Missed cases # | Age groups in years | CDI test previous 6 months | Other enteropathogens positive result if tested | Diagnosis other than CDI | Outcome CDI tested following 6 months | Outcome Admitted to hospital within 30 days | Outcome Admitted to hospital 30 days - 6 months | Outcome Died | Summary finding: Reason for not being tested |
|----------------|---------------------|---------------------------|-----------------------------------------------|--------------------------|--------------------------------------|---------------------------------------------|-----------------------------------------------|-------------|-----------------------------------------------|
| #1             | <5                  | No                        | none detected                                 | Feeding difficulties     | n/a                                  | No                                         | No                                            | No          | Paediatric                                    |
| #2             | <5                  | No                        | none detected                                 | Dehydration              | n/a                                  | No                                         | No                                            | No          | Paediatric                                    |
| #3             | <5                  | No                        | Rotavirus                                     | Rotavirus infection      | No                                   | Yes (5 days) for diarrhoea and rotavirus  | Yes (57, 77, 113 days) for diarrhoea and renal failure | No          | Paediatric and other infection detected      |
| #4             | <5                  | No                        | Adenovirus, Metapneumovirus                   | Viral pneumonia          | No                                   | No                                         | No                                            | No          | Paediatric and other infection detected      |
| #5             | <5                  | No                        | Rotavirus                                     | Enterocolitis            | n/a                                  | No                                         | No                                            | No          | Paediatric and other infection detected      |
| #6             | <5                  | No                        | Respiratory Enterovirus                       | Acute gastroenteritis    | No                                   | No                                         | No                                            | No          | Paediatric and other infection detected      |
| #7             | 65-84               | No                        | none detected                                 | Lymphoma, Chronic obstructive pulmonary disease | No                                   | No                                         | No                                            | No          | Missed case; no report of CDI testing but was treated with antibiotic for CDI |
| #8             | 65-84               | Yes                       | Adenovirus, Norovirus, Rotavirus              | Steatohepatitis non alcoholic | n/a                                  | No                                         | n/a                                           | No          | Another sample tested positive, not true missed case |
| #9             | 65-84               | Yes                       | No other test done                            | Data not available       | No                                   | Yes (date unknown)                         | Yes (118, 135 days) for abdominal pain        | Yes (139 days) | Missed case; recurrent CDI (positive 53 days before, but negative 30 days before sample) |
| #10            | 65-84               | No                        | none detected                                 | Pneumonia                | Yes positive (40,80 days)             | No                                         | Yes (33, 78 days,) for pneumonia               | Yes (84 days) | Missed case; lack clinical suspicion         |
| #   | Age  | Test   | Diagnosis                        | Symptoms | CDI | Other Infections | Other Infections | Notes                                                                 |
|-----|------|--------|----------------------------------|----------|-----|------------------|------------------|----------------------------------------------------------------------|
| #1  | <5   | No     | none detected                    | Dehydration | n/a | n/a              | n/a              | Paediatric                                                          |
| #2  | <5   | No     | No other test done               | Data not available | No | No               | No               | Paediatric                                                          |
| #3  | 18-49| No     | Enterohaemorrhagic E. coli       | Gastroenteritis | No | No               | No               | Missed case; CDI not suspected as other infection detected          |
| #4  | 18-49| No     | No other test done               | Gastroenteritis | No | No               | No               | Missed case; lack clinical suspicion                                 |
| #5  | 18-49| No     | Campylobacter                    | Data not available | No | Data not available | Data not available | Missed case; lack clinical suspicion                                 |
| #6  | 18-49| No     | none detected                    | Complications of surgical and medical care | No | No               | No               | Missed case; lack clinical suspicion                                 |
| #7  | 50-64| No     | No other test done               | Data not available | Yes positive (25, 57, 79, 125, 163 days) | Yes (25 days) for diarrhoea | Yes (58, 80 days) for CDI | Missed case; lack clinical suspicion                                 |
| #8  | 50-64| No     | No other test done               | Data not available | Yes positive (102 days) | Yes positive (2 days) | No               | Missed case; lack clinical suspicion                                 |
| #9  | 50-64| No     | No other test done               | Diarrhoea      | Yes (3 days) | Yes positive (3 days) | No               | Missed case; lack clinical suspicion                                 |
| #10 | 50-64| Yes negative (102 days)         | none detected     | Data not available | Yes positive (2 days) | Yes positive (3 days) | No               | Missed case; test for CDI was negative 102 days before sample       |
| #11 | 65-84| No     | none detected                    | Data not available | Yes positive (2 days) | Yes positive (3 days) | No               | Missed case; lack clinical suspicion                                 |
**Supplementary Table S2. Features, previous exposure, and co-morbidities of undiagnosed adult CDI cases.**

Features, previous exposure, and co-morbidities, as reported in medical records, Europe, 2018.

CDI = *Clostridioides difficile* infection

n/a = Data not available

| Missed cases # | Age groups in years | Days of diarrhoea before the sample | Contact HCF (6 months prior) | Contact infant (3 months prior) | Antibiotic use (12 weeks prior) | Co-morbidities | Charlson Index | White cell count 10⁹/Liter | Has the patient ever had CDI? | Treated with antibiotic for CDI |
|----------------|---------------------|-----------------------------------|-----------------------------|--------------------------------|-------------------------------|----------------|----------------|------------------------|-------------------------------|-------------------------------|
| **Hospital**   |                     |                                   |                             |                                |                               |                |                |                        |                               |                               |
| #7             | 65-84               | 40                                | Yes                         | n/a                            | Cephalosporins, Clindamycin, Fluoroquinolones | Chronic obstructive pulmonary disease, Pneumonia, Solid tumour within last 5 years | 7              | 21.00                  | Yes                    | Yes                           |                               |
| #9             | 65-84               | 1                                 | Yes                         | n/a                            | Cephalosporins                  | Diabetes without organ damage | 6              | 13.20                  | Yes                    | No                            |                               |
| #10            | 65-84               | n/a                               | No                          | n/a                            |                                | Congestive heart failure, Cerebrovascular disease, Diabetes without organ damage | 8              | 8.00                   | No                     | No                            |                               |
| **Community**  |                     |                                   |                             |                                |                               |                |                |                        |                               |                               |
| #3             | 18-49               | 5                                 | No                          | n/a                            | No                            |                | n/a            | 16.10                  | No                            | No                            |
| #4             | 18-49               | 14                                | No                          | n/a                            | n/a                           |                | n/a            | n/a                    | No                            | No                            |
| #5             | 18-49               | n/a                               | n/a                         | n/a                            | n/a                           |                | n/a            | n/a                    | No                            | n/a                           |
| #6             | 18-49               | 28                                | Yes                         | Yes                            | Broad-spectrum Penicillins      | None           | 0              | n/a                    | No                            | n/a                           |
| #7             | 50-64               | n/a                               | Yes                         | n/a                            | n/a                           | Other          | 2              | n/a                    | No                            | No                            |
| #8             | 50-64               | n/a                               | No                          | n/a                            | Yes: n/a                      | n/a            | n/a            | n/a                    | No                            | No                            |
| #9             | 50-64               | 6                                 | No                          | n/a                            | No                            | n/a            | n/a            | n/a                    | No                            | Yes                           |
| #10            | 50-64               | n/a                               | Yes                         | n/a                            | Broad-spectrum Penicillins, Aminoglycosides, Fluoroquinolones | Chronic kidney disease, Liver disease | 5              | 12.90                  | No                     | No                            |
| #11            | 65-84               | n/a                               | No                          | n/a                            | No                            | Peripheral vascular disease | 5              | n/a                    | No                     | No                            |
Supplementary Figure S2. Number of PCR ribotypes isolated from samples submitted.

Numbers are shown in the Venn diagram. The five most common PCR ribotypes isolated from samples submitted across Europe are shown below the Venn diagram (left: isolated from hospital samples; middle: isolated from both hospital and community samples; right: isolated from community samples). PCR ribotypes found in both hospital and community samples are also listed.

| Most common          | HOSPITAL | COMMUNITY |
|----------------------|----------|-----------|
| 1. 181               | 181      | 078       |
| 2. 027               | 014      | 039       |
| 3. 014               | 078      | 001       |
| 4. 010               | 010      | 020       |
| 5. 002               | 039      | 009, 010  |

PCR ribotypes found in both hospital and community samples

181, 014, 078, 010, 039, 002, 020, 001, 003, 005, 106, 009, 015, 018, 046, 026, 035, 126, 023, 031, 013, 070, 154, 430, 815, 902.
### Supervised Table S3. Location of the participants.

Location of the participants at the time of sampling as reported in medical records. Cases were participants group CCNA positive (presence of *C. difficile* toxin using reference test). CD term was chosen to describe participants group CTC positive/CCNA negative/SIMOA negative (presence of *C. difficile* without toxin). SIMOApos term was chosen to describe participants group SIMOA positive/CCNA negative (presence of *C. difficile* toxin using novel test).

CCNA: cell-cytotoxin neutralisation assay; CTC: cell cytotoxigenic culture; SIMOA: ultra-sensitive toxin single molecule array.

|                  | Cases       | CD           | SIMOApos     | Controls     |
|------------------|-------------|--------------|--------------|--------------|
| **Number of patients (%)** | Hospital | Community | Hospital | Community | Hospital | Community | Hospital | Community | Hospital | Community |
| **Admitting speciality** |           |             |           |             |           |             |           |             |           |             |
| Elderly medicine | 13 (17%)   | ..          | 2 (11%)   | ..          | 3 (9%)    | ..          | 25 (8%)   | ..          | ..         |             |
| Emergency medicine | 11 (15%)  | ..          | 2 (11%)   | ..          | 2 (6%)    | ..          | 42 (14%)  | ..          | ..         |             |
| Gastroenterology | 6 (8%)     | ..          | 2 (11%)   | ..          | 3 (9%)    | ..          | 22 (7%)   | ..          | ..         |             |
| Haematology/Oncology | 5 (7%)    | ..          | 1 (6%)    | ..          | 4 (11%)   | ..          | 35 (12%)  | ..          | ..         |             |
| Intensive care unit | 1 (1%)    | ..          | 0         | ..         | 1 (3%)    | ..          | 17 (6%)   | ..          | ..         |             |
| Infectious diseases | 16 (21%) | ..          | 1 (6%)    | ..          | 4 (11%)   | ..          | 50 (17%)  | ..          | ..         |             |
| Surgery          | 6 (8%)     | ..          | 2 (11%)   | ..          | 2 (6%)    | ..          | 13 (4%)   | ..          | ..         |             |
| General/Acute Medicine | 3 (4%)    | ..          | 2 (11%)   | ..          | 6 (17%)   | ..          | 65 (22%)  | ..          | ..         |             |
| Paediatric       | 4 (5%)     | ..          | 1 (6%)    | ..          | 1 (3%)    | ..          | 22 (7%)   | ..          | ..         |             |
| Other            | 10 (13%)   | ..          | 5 (28%)   | ..          | 8 (23%)   | ..          | 5 (2%)    | ..          | ..         |             |
| Unknown          | 1 (1%)     | ..          | 0         | ..          | 1 (3%)    | ..          | 5 (2%)    | ..          | ..         |             |
| **Community**    |           |             |           |             |           |             |           |             |           |             |
| Intermediate care | ..        | ..          | 2 (13%)   | ..          | ..        | ..          | ..        | 13 (9%)    |             |             |
| Other outpatient | ..        | ..          | 1 (6%)    | ..          | ..        | ..          | ..        | 8 (6%)     |             |             |
| Own home         | ..        | 18 (100%)  | ..        | 13 (81%)   | ..        | 8 (100%)   | ..        | 118 (82%)  |             |             |
| Residential home | ..        | ..          | ..        | ..          | ..        | ..          | ..        | 4 (3%)     |             |             |
### Supplementary Table S4. Categorical variables (previous exposure) of cases and CD participants groups.

Cases were participants group CCNA positive (presence of *C. difficile* toxin using reference test).

CD term was chosen to describe participants group CTC positive/CCNA negative/SIMOA negative (presence of *C. difficile* without toxin).

Data are number of patients (%) in hospital or community setting with previous exposure prior to the sample being taken, and calculated odds ratio, 95% CI, Chi-squared p values or Fischers exact test p values (when the cell count was less than 5) of cases versus controls and CD versus controls. Antibiotic use and class of antibiotics refers to antibiotics prescribed for treatment or prophylaxis of an infection other than CDI in the preceding 12 weeks. Significant variables are highlighted in bold (p values <0.05 and 95% CI that do not include 1.0).

CCNA: cell-cytotoxin neutralisation assay; CDI: *Clostridiodes difficile* infection; CI: confidence intervals; CTC: cell cytotoxigenic culture; n= number of participants exposed to indicated variable.; N= total number of participants in analysis (with data); na=not able to compute odds ratio due to a value of 0 in one of the groups; p: p values; SIMOA: ultra-sensitive toxin single molecule array.

| Variable/Exposure | Cases | CD | Controls | Cases vs. Controls | CD vs. Controls |
|------------------|-------|----|----------|--------------------|----------------|
|                  | % (n/N) | % (n/N) | % (n/N) | Odds ratio [95% CI] | p | Odds ratio [95% CI] | p |
| Contact with healthcare facility (previous 6 months) | | | | | | | |
| Hospital | 81.0% (51/63) | 62.5% (10/16) | 53.9% (138/256) | 3.63 [1.80-5.35] | <0.0001 | 1.43 [0.50-4.04] | 0.50 |
| Community | 53.0% (9/17) | 42.9% (6/14) | 38.8% (45/116) | 1.78 [0.64-4.94] | 0.27 | 1.18 [0.39-3.64] | 0.77 |
| Contact with CDI (previous 3 months) | | | | | | | |
| Hospital | 2.9% (1/35) | 0% (0/7) | 0.8% (1/118) | 3.44 [0.21-56.5] | 0.41 | na [na] | 1.00 |
| Community | 0% (0/4) | 0% (0/8) | 2.0% (1/49) | na [na] | 1.00 | na [na] | 1.00 |
| Contact with infant (previous 3 months) | | | | | | | |
| Hospital | 3.7% (1/27) | 0% (0/5) | 7.8% (7/90) | 0.46 [0.05-3.88] | 0.68 | na [na] | 1.00 |
| Community | 33.3% (1/3) | 0% (0/4) | 10.7% (3/28) | 4.17 [0.29-60.9] | 0.35 | na [na] | 1.00 |
| Antibiotic use (previous 12 weeks) | | | | | | | |
| ≥ one antibiotic | | | | | | | |
| Hospital | 76.1% (51/67) | 75.0% (12/16) | 60.9% (157/258) | 2.05 [1.11-3.79] | 0.02 | 1.93 [0.61-6.15] | 0.26 |
| Community | 46.2% (6/13) | 9.1% (1/11) | 17.7% (17/96) | 3.98 [1.19-13.4] | 0.03 | 0.47 [0.06-3.88] | 0.69 |
| > one antibiotic | | | | | | | |
| Hospital | 43.3% (29/67) | 43.8% (7/16) | 38.0% (98/258) | 1.25 [0.72-2.15] | 0.43 | 1.27 [0.46-3.52] | 0.65 |
| Community | 23.1% (3/13) | 0% (0/11) | 2.1% (2/96) | 14.10 [2.10-94.7] | 0.01 | na [na] | 1.00 |
| > two antibiotics | | | | | | | |
| Hospital | 23.9% (16/67) | 18.8% (3/16) | 23.6% (61/258) | 1.01 [0.54-1.90] | 0.97 | 0.75 [0.21-2.70] | 0.77 |
| Community | 23.1% (3/13) | 0% (0/11) | 2.1% (2/96) | 14.10 [2.10-94.7] | 0.01 | na [na] | 1.00 |
| > three antibiotics | | | | | | | |
| Hospital | 11.9% (8/67) | 6.3% (1/16) | 15.1% (39/258) | 0.76 [0.34-1.72] | 0.51 | 0.37 [0.05-2.92] | 0.48 |
| Community | 15.4% (2/13) | 0% (0/11) | 0% (0/96) | na [na] | 0.01 | na [na] | 1.00 |
| Class of antibiotic (previous 12 weeks) | | | | | | | |
| Narrow spectrum penicillins | | | | | | | |
| Hospital | 6.0% (4/67) | 6.3% (1/16) | 10.9% (28/258) | 0.52 [0.18-1.54] | 0.23 | 0.55 [0.07-4.31] | 1.00 |
| Community | 0% (0/13) | 9.1% (1/11) | 2.1% (2/96) | na [na] | 1.00 | 4.70 [0.39-56.5] | 0.28 |
| Broad spectrum penicillins | | | | | | | |
| Hospital | 20.9% (14/67) | 37.5% (6/16) | 30.2% (78/258) | 0.61 [0.32-1.16] | 0.13 | 1.39 [0.49-3.94] | 0.58 |
| Community | 30.8% (4/13) | 0% (0/11) | 5.2% (5/96) | 8.09 [1.84-35.6] | 0.01 | na [na] | 1.00 |
| Class                   | Community | Hospital | Community | Hospital | Community | Hospital | Community | Hospital | Community | Hospital | Community | Hospital | Community |
|-------------------------|-----------|----------|-----------|----------|-----------|----------|-----------|----------|-----------|----------|-----------|----------|-----------|
| Cephalosporins          |           |          |           |          |           |          |           |          |           |          |           |          |           |
|                         | 7.7% (1/13) | 0% (0/11) | 0% (0/96) | na [na]  | 0.12     | na [na]  | 1.00     |           |           |          |           |          |           |
| Other betalactams       |           |          |           |          |           |          |           |          |           |          |           |          |           |
|                         | 7.7% (1/13) | 0% (0/11) | 1.0% (1/96)| 7.92 [0.46-135.0]| 0.23     | na [na]  | 1.00     |           |           |          |           |          |           |
| Tetracyclines           |           |          |           |          |           |          |           |          |           |          |           |          |           |
|                         | 4.5% (3/67) | 0% (0/16) | 2.1% (2/96)| 3.98 [0.79-20.2] | 0.11     | na [na]  | 1.00     |           |           |          |           |          |           |
| Aminoglycosides         |           |          |           |          |           |          |           |          |           |          |           |          |           |
|                         | 6.0% (4/67) | 6.3% (1/16) | 4.3% (11/258)| 1.43 [0.44-4.63] | 0.52     | 1.50 [0.18-12.4]| 0.52     |           |           |          |           |          |           |
| Macrolides              |           |          |           |          |           |          |           |          |           |          |           |          |           |
|                         | 7.5% (5/67) | 0% (0/16) | 7.8% (20/258)| 0.96 [0.35-2.66] | 0.94     | na [na]  | 0.62     |           |           |          |           |          |           |
| Clindamycin             |           |          |           |          |           |          |           |          |           |          |           |          |           |
|                         | 3.0% (2/67) | 0% (0/16) | 3.9% (10/258)| 0.76 [0.16-3.57] | 1.00     | na [na]  | 1.00     |           |           |          |           |          |           |
| Sulphonamides           |           |          |           |          |           |          |           |          |           |          |           |          |           |
|                         | 3.0% (2/67) | 0% (0/16) | 1.9% (5/258)| 1.56 [0.30-8.21] | 0.64     | na [na]  | 1.00     |           |           |          |           |          |           |
| Trimethoprim            |           |          |           |          |           |          |           |          |           |          |           |          |           |
|                         | 3.0% (2/67) | 12.5% (2/16)| 3.5% (9/258)| 0.85 [0.18-4.04] | 1.00     | 3.95 [0.78-20.1]| 0.13     |           |           |          |           |          |           |
| Antituberculous drugs   |           |          |           |          |           |          |           |          |           |          |           |          |           |
|                         | 1.5% (1/67) | 0% (0/11) | 0.8% (2/258)| 1.94 [0.17-21.7] | 0.50     | na [na]  | 1.00     |           |           |          |           |          |           |
| Nitroimidazoles         |           |          |           |          |           |          |           |          |           |          |           |          |           |
|                         | 6.0% (4/67) | 6.3% (1/16) | 5.0% (13/258)| 1.20 [0.38-3.80] | 0.76     | 1.26 [0.15-10.3]| 0.58     |           |           |          |           |          |           |
| Glycopeptides           |           |          |           |          |           |          |           |          |           |          |           |          |           |
|                         | 6.0% (4/67) | 12.5% (2/16)| 7.0% (18/258)| 0.85 [0.28-2.59] | 0.23     | 1.91 [0.40-9.04]| 0.33     |           |           |          |           |          |           |
| Fluoroquinolones, Other quinolones | | | | | | | | | | | | | |
|                         | 25.4% (17/67) | 18.8% (3/16)| 13.2% (34/258)| 2.24 [1.16-4.33] | 0.01     | 1.52 [0.41-5.61]| 0.46     |           |           |          |           |          |           |
| Other antibiotics       |           |          |           |          |           |          |           |          |           |          |           |          |           |
|                         | 17.9% (12/67) | 6.3% (1/16) | 13.6% (35/258)| 1.39 [0.68-2.85] | 0.37     | 0.43 [0.05-3.32]| 0.70     |           |           |          |           |          |           |
### Supplementary Table S5. Categorical variables (number and type of co-morbidities) of cases and CD participants groups.

Cases were participants group CCNA positive (presence of *C. difficile* toxin using reference test).

CD term was chosen to describe participants group CTC positive/CCNA negative/SIMOA negative (presence of *C. difficile* without toxin).

Data are number of patients (%) in hospital or community setting with reported co-morbidities, and calculated odds ratio, 95% CI, Chi-squared p values or Fischers exact test p values (when the cell count was less than 5) of cases versus controls and CD versus controls. Significant variables are highlighted in bold (p values <0.05 and 95% CI that do not include 1.0).

CCNA: cell-cytotoxic neutralisation assay; CDI: *Clostridioides difficile* infection; CI: confidence intervals; CTC: cell cytotoxicogenic culture; n= number of participants exposed to indicated variable. ; N= total number of participants in analysis (with data); na= not able to compute odds ratio due to a value of 0 in one of the groups; p: p values; SIMOA: ultra-sensitive toxin single molecule array.

| Co-morbidities | Cases | CD | Controls | Cases vs. Controls | CD vs. Controls |
|----------------|-------|----|----------|--------------------|-----------------|
|                | % (n/N) | % (n/N) | % (n/N) | Odds ratio [95% CI] | p |
| **With ≥ 2 co-morbidities** | | | | | |
| Hospital       | 59.5% (44/74) | 52.9% (9/17) | 43.0% (122/284) | 1.95 [1.16-3.28] | 0.01 |
| Community      | 33.3% (4/12)  | 21.4% (3/14)  | 15.1% (16/106) | 2.81 [0.76-10.5] | 0.12 |
| **Charlson index score** | | | | | |
| 0              | 10.8% (8/74) | 11.8% (2/17) | 25.4% (72/284) | 0.36 [0.16-0.78] | 0.01 |
|                 | 25.0% (3/12) | 64.3% (9/14) | 48.1% (51/106) | 0.36 [0.09-1.40] | 0.13 |
| 1              | 2.7% (2/74)  | 11.8% (2/17) | 4.2% (12/284) | 0.63 [0.14-2.88] | 0.74 |
|                 | 0% (0/12)    | 7.1% (1/14)  | 6.6% (7/106)  | na [na]          | 1.00 |
| 2              | 5.4% (4/74)  | 11.8% (1/17) | 8.5% (24/284) | 0.62 [0.21-1.84] | 0.47 |
|                 | 8.3% (1/12)  | 0% (0/14)    | 13.2% (14/106) | 0.60 [0.07-4.99] | 1.00 |
| 3              | 5.4% (4/74)  | 5.9% (1/17)  | 9.5% (27/284) | 0.54 [0.18-1.61] | 0.26 |
|                 | 8.3% (1/12)  | 7.1% (1/14)  | 6.6% (7/106)  | 1.29 [0.14-11.4] | 0.59 |
| 3+             | 81.1% (60/74) | 64.7% (11/17) | 62.0% (176/284) | 2.63 [1.40-4.93] | <0.01 |
| Hospital       | 66.7% (8/12) | 28.6% (4/14) | 32.1% (34/106) | 4.24 [1.19-15.0] | 0.03 |
| Community      | na [na]      | 6.6% (7/106) | na [na]       | 1.09 [0.12-9.56] | 1.00 |
| 4+             | 75.7% (56/74) | 58.8% (10/17) | 52.5% (149/284) | 2.82 [1.58-5.03] | <0.0001 |
| Hospital       | 58.3% (7/12) | 21.4% (3/14) | 25.5% (27/106) | 4.10 [1.20-14.0] | 0.04 |
| Community      | na [na]      | 6.6% (7/106) | na [na]       | 0.80 [0.21-3.08] | 1.00 |

**Co-morbidities**

| Cerebrovascular Disease | Cases | CD | Controls | Cases vs. Controls | CD vs. Controls |
|------------------------|-------|----|----------|--------------------|-----------------|
| Hospital               | 23.0% (17/74) | 5.9% (1/17) | 6.7% (19/284) | 4.16 [2.04-8.50] | <0.0001 |
| Community              | 8.3% (1/12)   | 0% (0/14)    | 0% (0/106)   | na [na]          | na |
| Chronic kidney disease | Hospital     | 17.6% (13/74) | 23.5% (4/17) | 10.6% (30/284) | 1.80 [0.89-3.66] | 0.10 |
| Community              | 16.7% (2/12)  | 0% (0/14)    | 6.6% (7/106) | 2.83 [0.52-15.5] | 0.23 |
| Solid tumour within last 5 years | | | | | |

0.05
| Condition                                      | Hospital % | Community % | Pneumonia |
|-----------------------------------------------|------------|-------------|-----------|
| Renal failure                                 | 20.3% (15/74) | 8.3% (1/12) | 17.6% (13/74) |
| COPD                                          | 5.9% (1/17) | 7.1% (1/14) | 0% (0/17) |
| Myocardial Infarction                         | 12.7% (36/284) | 4.7% (5/106) | 5.3% (15/284) |
| Congestive Heart Failure                      | 1.75 [0.90-3.41] | 1.84 [0.20-17.2] | 3.82 [1.73-8.45] |
| Metastatic diabetes                           | 0.10 [0.06-3.35] | 0.48 [0.17-14.4] | <0.0001 |
| Mental Disorientation                         | 0.43 [0.06-3.35] | 1.55 [0.17-14.4] | na [na] |
| Diabetes without organ damage                 | 7.1% (1/14) | 1.9% (0/106) | 1.89 [0.88-4.06] |
| Pneumonia                                     | 6.6% (7/106) | 0.23 [0.12-9.56] | 2.83 [0.52-15.5] |
| UTI                                           | 0.10 [0.10-5.33] | na [na] | 0.68 [0.10-5.33] |
| Mental Disorientation                         | 0.12 [0.10-5.33] | na [na] | na |
| Peripheral Vascular Disease                  | 0% (0/17) | 0.0% (0/106) | 0% (0/17) |
| Congestive Heart Failure                      | 0.0% (0/106) | 0.0% (0/106) | 0.0% (0/106) |
| Dementia                                      | 0.0% (0/17) | 0.0% (0/106) | 0.0% (0/17) |
| Myocardial Infarction                         | 0.0% (0/17) | 0.0% (0/106) | 0.0% (0/17) |
| COPD                                          | 0.0% (0/17) | 0.0% (0/106) | 0.0% (0/17) |
| Moderate or severe liver disease              | 0.0% (0/17) | 0.0% (0/106) | 0.0% (0/17) |
| Diabetes with organ damage                    | 0.0% (0/17) | 0.0% (0/106) | 0.0% (0/17) |
| Chemotherapy previous 12 weeks               | 0.0% (0/17) | 0.0% (0/106) | 0.0% (0/17) |
| Leukaemia within last 5 years                 | 0.0% (0/17) | 0.0% (0/106) | 0.0% (0/17) |
| Renal RT within 7 days of sample             | 0.0% (0/17) | 0.0% (0/106) | 0.0% (0/17) |
| Transplant                                    | 0.0% (0/17) | 0.0% (0/106) | 0.0% (0/17) |
| Condition                                      | Hospital | Community |
|-----------------------------------------------|----------|-----------|
| Cystic Fibrosis                               | 3.8% (4/106) | na [na] |
| HIV positive                                  | 0.42 [0.05-3.36] | 0.69 |
| Radiotherapy                                  | 2.60 [0.43-15.9] | 0.28 |
| Connective Tissue Disease                     | 2.1 [0.58-59.5] | na |
| Lymphoma within last 5 years                  | 2.5% (7/284) | 1.10 [0.22-5.41] |
| Hemiplegia                                    | 1.4% (4/284) | 0.96 [0.11-8.71] |
| Mild liver disease                            | 1.4% (4/284) | 1.28 [0.13-12.5] |
| Radiotherapy previous 12 weeks                | 0.7% (5/12) | na [na] |
| Cardiac Arrest previous 7 days                | 0.4% (1/284) | 3.88 [0.24-62.7] |
| AIDS not just HIV positive                    | 1.4% (4/106) | 0.37 |
| Peptic Ulcer Disease                          | 3.8% (4/106) | 1.00 |
| Cystic Fibrosis                               | 30.6% (87/284) | 1.02 [0.59-1.78] |
| Other comorbidities listed                    | 14.3% (2/14) | 0.92 [0.19-4.52] |
| None                                          | 0.51 [0.15-1.70] | 0.27 |

The table above summarizes the prevalence of various conditions among patients in hospital and community settings. The values represent the percentage of patients with the condition, with 95% confidence intervals in parentheses. The p-values indicate the statistical significance of differences between hospital and community settings, with p-values less than 0.05 considered significant.

For example, in the last row, the prevalence of None in hospital is 9.5% (7/74) with a p-value less than 0.0001, indicating a significant difference from the community setting.
Supplementary Table S6. Categorical variables (exposure) of SIMOApos participants group.

Categorical variables of patients negative for \textit{C. difficile} infection at the European Coordinating Laboratory but positive for novel SIMOA technology at bioMérieux. SIMOApos term was chosen to describe participants group SIMOA positive/CCNA negative (presence of \textit{C. difficile} toxin using novel test). Data are number of patients (%) in hospital or community setting with previous exposure prior to the sample being taken, and calculated odds ratio, 95% CI, Chi-squared p values or Fischers exact test \( p \) values (when the cell count was less than 5) of SIMOApos versus controls. Antibiotic use and class of antibiotics refers to antibiotics prescribed for treatment or prophylaxis of an infection other than CDI in the preceding 12 weeks. Significant variables are highlighted in bold (\( p \) values <0.05 and 95% CI that do not include 1.0).

CCNA: cell-cytotoxin neutralisation assay; CDI: Clostridioides difficile infection; CI: confidence intervals; \( n \)= number of participants exposed to indicated variable. \( N \)= total number of participants in analysis (with data); na=not able to compute odds ratio due to a value of 0 in one of the groups; \( p \): \( p \) values; SIMOA: ultra-sensitive toxin single molecule array.

| Variable/Exposure                                      | SIMOApos % (n/N) | Controls % (n/N) | Odds ratio [95% CI] | \( p \) |
|--------------------------------------------------------|-------------------|------------------|---------------------|------|
| Contact with healthcare facility (previous 6 months)   |                   |                  |                     |      |
| Hospital                                               | 56.7% (17/30)     | 53.9% (138/256)  | 1.12 [0.52-2.40]    | 0.77 |
| Community                                              | 83.3% (5/6)       | 38.8% (45/116)   | 7.89 [0.89-69.7]    | 0.04 |
| Contact with CDI (previous 3 months)                   |                   |                  |                     |      |
| Hospital                                               | 8.3% (1/12)       | 0.8% (1/118)     | 10.64 [0.62-182.0]  | 0.18 |
| Community                                              | 33.3% (1/3)       | 2.0% (1/49)      | 24.0 [1.07-539.1]   | 0.11 |
| Contact with infant (previous 3 months)                |                   |                  |                     |      |
| Hospital                                               | 0% (0/10)         | 7.8% (7/90)      | na [na]             | 1.00 |
| Community                                              | 50.0% (1/2)       | 10.7% (3/28)     | 8.33 [0.41-170.7]   | 0.25 |
| Antibiotic use (previous 12 weeks)                     |                   |                  |                     |      |
| ≥  one antibiotic                                      |                   |                  |                     |      |
| Hospital                                               | 76.7% (23/30)     | 60.9% (157/258)  | 2.11 [0.88-5.11]    | 0.09 |
| Community                                              | \textbf{71.4%} (5/7) | \textbf{17.7%} (17/96) | \textbf{11.62 [2.08-65.0]} | 0.01 |
| > one antibiotic                                       |                   |                  |                     |      |
| Hospital                                               | 43.3% (13/30)     | 38.0% (98/258)   | 1.25 [0.58-2.68]    | 0.57 |
| Community                                              | \textbf{28.6%} (2/7) | \textbf{2.1%} (2/96) | \textbf{18.80 [2.18-162.5]} | 0.02 |
| > two antibiotics                                      |                   |                  |                     |      |
| Hospital                                               | 33.3% (10/30)     | 23.6% (61/258)   | 1.62 [0.72-3.64]    | 0.24 |
| Community                                              | 0% (0/7)          | 2.1% (2/96)      | na [na]             | 1.00 |
| > three antibiotics                                    |                   |                  |                     |      |
| Hospital                                               | 23.3% (7/30)      | 15.1% (39/258)   | 1.71 [0.69-4.26]    | 0.29 |
| Community                                              | 0% (0/7)          | 0% (0/96)        | na [na]             | na   |
| Class of antibiotic (previous 12 weeks)                |                   |                  |                     |      |
| Narrow spectrum penicillins                            |                   |                  |                     |      |
| Hospital                                               | 6.7% (2/30)       | 10.9% (28/258)   | 0.59 [0.13-2.60]    | 0.75 |
| Community                                              | 0% (0/7)          | 2.1% (2/96)      | na [na]             | 1.00 |
| Broad spectrum penicillins                             |                   |                  |                     |      |
| Hospital                                               | 30.0% (9/30)      | 30.2% (78/258)   | 0.99 [0.43-2.26]    | 0.98 |
| Community                                              | 28.6% (2/7)       | 5.2% (5/96)      | 7.28 [1.12-47.3]    | 0.07 |
| Drug Class                  | Hospital          | Community       | p value | OR (95% CI) | p value |
|-----------------------------|-------------------|-----------------|---------|-------------|---------|
| Cephalosporins              | 33.3% (10/30)     | 14.3% (1/7)     | 0.06    | 2.19 [0.96-4.97] | 0.07 |
| Other beta-lactams          | 16.7% (5/30)      | 14.3% (1/7)     | 0.22    | 1.86 [0.66-5.30] | 0.13 |
| Tetracyclines               | 3.3% (1/30)       | 0% (0/7)        | 0.36    | 2.93 [0.30-29.1] | na |
| Aminoglycosides             | 6.7% (2/30)       | 0% (0/7)        | 0.63    | 1.60 [0.34-7.61] | na |
| Macrolides                  | 6.7% (2/30)       | 0% (0/7)        | 1.00    | 7.8% [0.19-3.83]  | na |
| Clindamycin                 | 0% (0/30)         | 0% (0/7)        | 0.61    | 3.9% [0.10-258]  | na |
| Sulphonamides               | 0% (0/30)         | 0% (0/7)        | na      | na          | na |
| Trimethoprim                | 3.3% (1/30)       | 0% (0/7)        | 1.00    | 3.5% [0.12-7.80]  | na |
| Antituberculous drugs       | 0% (0/30)         | 0% (0/7)        | 1.00    | 0.8% [0.19-3.83]  | na |
| Nitroimidazole              | 6.7% (2/30)       | 0% (0/7)        | 0.66    | 5.0% [0.29-6.72]  | 0.13 |
| Glycopeptides               | 10.0% (3/30)      | 0% (0/7)        | 0.47    | 7.0% [0.41-5.36]  | na |
| Fluoroquinolones, Other quinolones | 26.7% (8/30) | 0% (0/7) | 0.06    | 13.2% [0.99-5.81] | na |
| Other antibiotics           | 20.0% (6/30)      | 0% (0/7)        | 0.41    | 13.6% [0.61-4.17]  | 0.25 |
### Supplementary Table S7. Categorical variables (number and type of co-morbidities) of SIMOApos participants group.

Categorical variables of patients negative for *C. difficile* infection at the European Coordinating Laboratory but positive for novel SIMOA technology at bioMérieux. SIMOApos term was chosen to describe participants group SIMOA positive/CCNA negative (presence of *C. difficile* toxin using novel test).

Data are number of patients (%) in hospital or community setting with reported co-morbidities, and calculated odds ratio, 95% CI, Chi-squared p values or Fischers exact test p values (when the cell count was less than 5) of SIMOApos versus controls. Significant variables are highlighted in bold (p values <0.05 and 95% CI that do not include 1.0).

CCNA: cell-cytotoxin neutralisation assay; CDI: *Clostridiodes difficile* infection; CI: confidence intervals; n= number of participants exposed to indicated variable.; N= total number of participants in analysis (with data); na=not able to compute odds ratio due to a value of 0 in one of the groups; p: p values; SIMOA: ultra-sensitive toxin single molecule array.

| Co-morbidities                  | SIMOApos | Controls | SIMOApos vs. Controls |
|---------------------------------|----------|----------|-----------------------|
|                                 | % (n/N)  | % (n/N)  | OR [95% CI] | p       |
| With ≥ 2 co-morbidities         |          |          |            |         |
| Hospital                        | 60.0% (21/35) | 43.0% (122/284) | 1.99 [0.97-4.08] | 0.06 |
| Community                        | 66.7% (4/6) | 15.1% (16/106) | 11.25 [1.90-66.6] | 0.01 |
| Charlson index score             |          |          |            |         |
| 0                               |          |          |            |         |
| Hospital                        | 11.4% (4/35) | 25.4% (72/284) | 0.38 [0.13-1.11] | 0.07 |
| Community                        | 16.7% (1/6) | 48.1% (51/106) | 0.22 [0.02-1.91] | 0.21 |
| 1                               |          |          |            |         |
| Hospital                        | 8.6% (3/35) | 4.2% (12/284) | 2.13 [0.57-7.93] | 0.22 |
| Community                        | 0% (0/6) | 6.6% (7/106) | na [na] | 1.00 |
| 2                               |          |          |            |         |
| Hospital                        | 5.7% (2/35) | 8.5% (24/284) | 0.66 [0.15-2.91] | 0.75 |
| Community                        | 16.7% (1/6) | 13.2% (14/106) | 1.31 [0.14-12.1] | 0.58 |
| 3                               |          |          |            |         |
| Hospital                        | 0% (0/35) | 9.5% (27/284) | na [na] | 0.06 |
| Community                        | 16.7% (1/6) | 6.6% (7/106) | 2.83 [0.29-27.7] | 0.37 |
| 3+                              |          |          |            |         |
| Hospital                        | 74.3% (26/35) | 62.0% (176/284) | 1.77 [0.80-3.93] | 0.15 |
| Community                        | 66.7% (4/6) | 32.1% (34/106) | 4.24 [0.74-24.3] | 0.18 |
| 4+                              |          |          |            |         |
| Hospital                        | 74.3% (26/35) | 52.5% (149/284) | 2.62 [1.18-5.78] | 0.01 |
| Community                        | 50.0% (3/6) | 25.5% (27/106) | 2.93 [0.56-15.4] | 0.34 |
| Co-morbidities                   |          |          |            |         |
| Cerebrovascular Disease          |          |          |            |         |
| Hospital                        | 14.3% (5/35) | 6.7% (19/284) | 2.33 [0.81-6.68] | 0.16 |
| Community                        | 0% (0/6) | 0% (0/106) | na [na] | na |
| Chronic kidney disease           |          |          |            |         |
| Hospital                        | 17.1% (6/35) | 10.6% (30/284) | 1.75 [0.67-4.56] | 0.26 |
| Community                        | 33.3% (2/6) | 6.6% (7/106) | 7.07 [1.10-45.5] | 0.07 |
| Solid tumour within last 5 years |          |          |            |         |
| Hospital                        | 5.7% (2/35) | 12.7% (36/284) | 0.42 [0.10-1.82] | 0.40 |
| Condition                                      | Community | Hospital | Pneumonia | Community | Hospital | Diabetes without organ damage | Community | Hospital | COPD | Community | Hospital | UTI | Community | Hospital | Community | Community |
|-----------------------------------------------|-----------|----------|-----------|-----------|----------|--------------------------------|-----------|----------|------|-----------|----------|-----|-----------|----------|-----------|-----------|
| Community                                     | 16.7% (1/6) | 4.7% (5/106) | 4.04 [0.39-41.4] | 0.29     | 0% (0/6) | 0% (0/106) | na [na] | na | na | na | na | na | na | na | na | na |
| Hospital                                      | 11.4% (4/35) | 5.3% (15/284) | 2.31 [0.72-7.41] | 0.14     | 0% (0/6) | 0% (0/106) | na [na] | na | na | na | na | na | na | na | na | na |
| Diabetes without organ damage                 | 14.3% (5/35) | 8.5% (24/284) | 1.81 [0.64-5.08] | 0.34     | 0% (0/6) | 6.6% (7/106) | na [na] | na | na | na | na | na | na | na | na | na |
| UTI                                           | 11.4% (4/35) | 6.3% (18/284) | 1.91 [0.61-6.00] | 0.28     | 16.7% (1/6) | 0% (0/106) | na [na] | na | na | na | na | na | na | na | na | na |
| Mental Disorientation                          | 17.1% (6/35) | 4.6% (13/284) | 4.31 [1.52-12.2] | 0.01     | 0% (0/6) | 0.9% (1/106) | 21.00 [1.14-386.8] | 0.11 | 16.7% (1/6) | 1.9% (2/106) | 10.40 [0.80-134.9] | 0.15 |
| Peripheral Vascular Disease                   | 11.4% (4/35) | 7.7% (22/284) | 1.54 [0.50-4.75] | 0.51     | 0% (0/6) | 2.8% (3/106) | na [na] | na | na | na | na | na | na | na | na | na |
| Congestive Heart Failure                       | 8.6% (3/35) | 9.5% (27/284) | 0.89 [0.26-3.11] | 1.00     | 0% (0/6) | 5.3% (15/284) | 2.31 [0.72-7.41] | 0.14 | 16.7% (1/6) | 0.9% (1/106) | 21.00 [1.14-386.8] | 0.11 |
| Dementia                                       | 11.4% (4/35) | 5.3% (15/284) | 2.31 [0.72-7.41] | 0.14     | 0% (0/6) | 2.8% (3/106) | na [na] | na | na | na | na | na | na | na | na | na |
| Myocardial Infarction                          | 2.9% (1/35) | 7.0% (20/284) | 0.39 [0.05-2.99] | 0.49     | 0% (0/6) | 1.9% (2/106) | na [na] | na | na | na | na | na | na | na | na | na |
| COPD                                           | 8.6% (3/35) | 7.7% (22/284) | 1.12 [0.32-3.94] | 0.75     | 0% (0/6) | 0.9% (1/106) | na [na] | na | na | na | na | na | na | na | na | na |
| Moderate or severe liver disease               | 5.7% (2/35) | 6.7% (19/284) | 0.85 [0.19-3.79] | 1.00     | 0% (0/6) | 0.9% (1/106) | na [na] | na | na | na | na | na | na | na | na | na |
| Diabetes with organ damage                     | 2.9% (1/35) | 5.6% (16/284) | 0.49 [0.06-3.83] | 0.71     | 0% (0/6) | 5.7% (6/106) | na [na] | na | na | na | na | na | na | na | na | na |
| Chemotherapy previous 12 weeks                 | 8.6% (3/35) | 7.7% (22/284) | 1.12 [0.32-3.94] | 0.75     | 16.7% (1/6) | 3.8% (4/106) | 5.10 [0.48-54.5] | 0.25 | 0% (0/6) | 2.8% (8/284) | 3.23 [0.82-12.8] | 0.11 |
| Leukaemia within last 5 years                  | 8.6% (3/35) | 2.8% (8/284) | 3.23 [0.82-12.8] | 0.11     | 0% (0/6) | 0% (0/106) | na [na] | na | na | na | na | na | na | na | na | na |
| Renal RT within 7 days of sample               | 2.9% (1/35) | 2.1% (6/284) | 1.36 [0.16-11.70] | 0.56     | 0% (0/6) | 0% (0/106) | na [na] | na | na | na | na | na | na | na | na | na |
| Transplant                                     | 2.9% (1/35) | 4.2% (12/284) | 0.67 [0.08-5.29] | 1.00     | 0% (0/6) | 3.8% (4/106) | na [na] | na | na | na | na | na | na | na | na | na |
| Condition                                      | Hospital                  | Community                | p-value |
|------------------------------------------------|---------------------------|--------------------------|---------|
| Other malignancy within last 5 years           |                           |                          |         |
| Other malignancy within last 5 years Hospital  | 5.7% (2/35)               | 3.2% (9/284)             | 1.85 [0.38-8.94] | 0.35    |
| Other malignancy within last 5 years Community | 0% (0/6)                  | 1.9% (2/106)             | na [na]  | 1.00    |
| Connective Tissue Disease                      |                           |                          |         |
| Connective Tissue Disease Hospital              | 2.9% (1/35)               | 1.1% (3/284)             | 2.76 [0.28-27.2] | 0.37    |
| Connective Tissue Disease Community            | 0% (0/6)                  | 0% (0/106)               | na [na]  | na      |
| Lymphoma within last 5 years                   |                           |                          |         |
| Lymphoma within last 5 years Hospital          | 0% (0/35)                 | 2.5% (7/284)             | na [na]  | 1.00    |
| Lymphoma within last 5 years Community         | 0% (0/6)                  | 0.9% (1/106)             | na [na]  | 1.00    |
| Hemiplegia                                     |                           |                          |         |
| Hemiplegia Hospital                            | 2.9% (1/35)               | 1.4% (4/284)             | 2.06 [0.22-19.0] | 0.44    |
| Hemiplegia Community                           | 0% (0/6)                  | 0% (0/106)               | na [na]  | na      |
| Mild liver disease                             |                           |                          |         |
| Mild liver disease Hospital                    | 0% (0/35)                 | 1.4% (4/284)             | na [na]  | 1.00    |
| Mild liver disease Community                   | 0% (0/6)                  | 1.9% (2/106)             | na [na]  | 1.00    |
| Radiotherapy previous 12 weeks                 |                           |                          |         |
| Radiotherapy previous 12 weeks Hospital         | 0% (0/35)                 | 1.1% (3/284)             | na [na]  | 1.00    |
| Radiotherapy previous 12 weeks Community       | 0% (0/6)                  | 3.8% (4/106)             | na [na]  | na      |
| Cardiac Arrest previous 7 days                 |                           |                          |         |
| Cardiac Arrest previous 7 days Hospital         | 0% (0/35)                 | 0.4% (1/284)             | na [na]  | 1.00    |
| Cardiac Arrest previous 7 days Community       | 0% (0/6)                  | 0% (0/106)               | na [na]  | na      |
| AIDS not just HIV positive                     |                           |                          |         |
| AIDS not just HIV positive Hospital            | 2.9% (1/35)               | 0% (0/106)               | na [na]  | 0.11    |
| AIDS not just HIV positive Community           | 0% (0/6)                  | 0% (0/106)               | na [na]  | na      |
| HIV positive                                   |                           |                          |         |
| HIV positive Hospital                          | 0% (0/35)                 | 0% (0/106)               | na [na]  | na      |
| HIV positive Community                         | 0% (0/6)                  | 3.8% (4/106)             | na [na]  | 1.00    |
| Peptic Ulcer Disease                           |                           |                          |         |
| Peptic Ulcer Disease Hospital                  | 0% (0/35)                 | 0% (0/106)               | na [na]  | na      |
| Peptic Ulcer Disease Community                 | 0% (0/6)                  | 0% (0/106)               | na [na]  | na      |
| Cystic Fibrosis                                |                           |                          |         |
| Cystic Fibrosis Hospital                       | 0% (0/35)                 | 0% (0/106)               | na [na]  | na      |
| Cystic Fibrosis Community                      | 0% (0/6)                  | 0% (0/106)               | na [na]  | na      |
| Other comorbidities listed                     |                           |                          |         |
| Other comorbidities listed Hospital            | 48.6% (17/35)             | 30.6% (87/284)           | 2.14 [1.05-4.35] | 0.03    |
| Other comorbidities listed Community           | 16.7% (1/6)               | 17.9% (19/106)           | 0.92 [0.10-8.30] | 1.00    |
| None                                           |                           |                          |         |
| None Hospital                                  | 20.0% (7/35)              | 29.2% (83/284)           | 0.61 [0.25-1.44] | 0.25    |
| None Community                                 | 33.3% (2/6)               | 58.5% (62/106)           | 0.36 [0.06-2.02] | 0.40    |