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# ***Risk factors for Clostridium difficile infections in an endemic setting in The Netherlands.***

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## Methods and results

- Period: July 2006 through December 2007
- Prospective case-control study in 1 hospital
  - All patients diagnosed with CDI (39 CDI patients)
  - 2 control groups
    - 37 patients without diarrhoea (control patients)
    - 25 patients with diarrhoea who tested negative for *C. difficile* (non-CDI diarrhoea)
- Definitions
  - Severe diarrhoea
    - Bloody diarrhoea and/or diarrhoea with hypovolaemia or hypoalbuminaemia (<20g/L) and/or with fever ( $T > 38,0\text{ }^{\circ}\text{C}$ ) and leucocytosis ( $\text{WCC} > 12 \times 10^9/\text{l}$ ), and/or with pseudomembranous colitis.
  - Community associated CDI
    - Development of CDI < 2 days after admission or more than 12 weeks after discharge.

- Incidence of CDI 2.1 per 10.000 patient-days.
- Overall mortality at 6 months follow-up
  - 21% among patients with CDI
  - 8% among patients with non-CDI diarrhoea
  - 11% among control patients
- Among the 25 patients with non-CDI diarrhoea
  - None developed CDI
    - 16 of 25 (64%) repeatedly tested negative on consecutive stool samples
  - One patient was diagnosed with *Giardia Lamblia*; among the other 24 patients, no causal agent was found.

## Methods and results (2)

Risk factors	CDI	Non-CDI	Controls
<b>N</b>	39	25	37
<b>Charlson co-morbidity index</b>	2.41	2.32	2.19
<b>Male sex</b>	22/39 (56.4%)	16/25 (64.0%)	21/37 (56.8%)
<b>Age &gt; 65 years</b>	19/39 (48.7%)*	5/25 (20.0%)	7/37 (18.9%)
<b>Community associated diarrhoea</b>	5/39 (12.8%)	7/25 (28.0%)	...
<b>Any underlying disease</b>	38/39 (97.4%)	23/25 (92.0%)	34/37 (91.9%)
Solid tumor	2/39 (5.1%)	2/25 (8.0%)	4/37 (10.8%)
Hematologic malignancy	7/39 (17.9%)	8/25 (32.0%)	7/37 (18.9%)
Diabetes	9/39 (23.1%)	5/25 (20.0%)	8/37 (21.6%)
Respiratory tract diseases	6/39 (15.4%)	3/25 (12.0%)	5/37 (13.5%)
Gastro-intestinal tract diseases	18/39 (46.2%)*	6/25 (30.7%)	8/37 (21.6%)
Cardiovascular tract diseases	17/39 (43.6%)	9/25 (36.0%)	10/37 (27.0%)
Urogenital tract diseases	20/39 (51.3%)*	6/25 (24.0%)	10/37 (27.0%)
<b>Any antibiotic</b>	37/39 (94.9%)*	17/26 (68.0%)	29/37 (78.4%)
Cephalosporins	26/39 (66.7%)*	12/25 (48.0%)	13/36 (36.1%)
1st generation cephalosprins	5/39 (12.8%)	3/25 (12.0%)	5/36 (13.9%)
2nd generation cephalosporins	22/39 (56.4%)*	8/25 (32.0%)	7/36 (19.4%)
3rd generation cephalosporins	9/39 (23.1%)*	4/25 (16.0%)	2/36 (5.6%)
Penicillins	21/39 (53.8%)	9/25 (36.0%)	14/36 (38.9%)
Fluoroquinolones	13/39 (33.3%)	9/25 (36.0%)	10/36 (27.8%)
Clindamycin	2/39 (5.1%)	1/25 (4.0%)	1/36 (2.8%)
Gentamicin	11/39 (28.2%)	10/25 (40.0%)*	6/36 (16.7%)
Sulfonamides/trimethoprim	9/39 (23.1%)	4/25 (16.0%)	5/36 (13.9%)
Metronidazole	3/39 (7.7%)	7/25 (28.0%)*	2/36 (5.6%)
Vancomycin	8/39 (20.5%)	6/25 (24.0%)	4/36 (11.1%)
<b>Proton pump inhibitors</b>	30/39 (76.9%)*	13/25 (52.0%)	18/37 (48.6%)
<b>Antacids</b>	8/39 (20.5%)	5/25 (20.0%)	4/37 (10.8%)
<b>NSAIDs</b>	3/39 (7.7%)	2/25 (8.0%)	2/37 (5.4%)
<b>Immunosuppressive agents</b>	21/39 (53.8%)	14/25 (56.0%)	15/37 (40.5%)
<b>Cytostatic agents</b>	9/39 (23.1%)	7/25 (28.0%)	5/37 (13.5%)
<b>Nasogastric tube</b>	17/37 (45.9%)	8/25 (32.0%)	12/36 (33.3%)
<b>Abdominal surgery</b>	15/39 (38.5%)	10/25 (40.0%)	11/37 (29.7%)
<b>Endoscopy</b>	7/39 (17.9%)	5/25 (20.0%)	5/37 (13.5%)
<b>Previous admission</b>	29/39 (74.4%)*	10/25 (40.0%)	13/37 (35.1%)
<b>Previous admission to ICU</b>	12/39 (30.8%)*	6/25 (24.0%)	4/36 (11.1%)

## Methods and results (3)

Use of antibiotics expressed in Defined Daily Doses (DDD's)	CDI	Non CDI	Controls	CDI vs. controls	Non-CDI vs. Controls
				P-value	P-value
Total number of antibiotics	3.21	3.21	1.83	<0.01*	0.04*
Total number of antibiotic classes	2.72	2.75	1.81	0.02*	0.09**
Total number of DDD's	20.5	44.5	15.8	0.48	0.06**
Cephalosporins	4.21	4.83	3.87	0.86	0.56
1st generation	0.76	1.44	1.93	0.12	0.62
2nd generation	3.67	3.94	3.86	0.94	0.97
3rd generation	2.67	5.78	5.25	0.55	0.89
Penicillins	13.3	10.2	12.6	0.92	0.72
Fluoroquinolones	11.5	26.2	10.4	0.87	0.19
Gentamicin	2.20	6.99	6.53	0.05*	0.90
Co-trimoxazole	1.57	8.06	10.5	0.22	0.66
Metronidazole	2.33	4.92	4.50	0.41	0.92
Vancomycin	3.78	6.97	4.59	0.78	0.61

## *Conclusions*

- Independent risk factors for CDI
  - age above 65 years
  - intestinal and urogenital tract diseases
  - use of 2nd generation cephalosporins
- The total numbers of prescribed antibiotics and Defined Daily Doses (DDD's) were highest among patients with non-CDI diarrhoea.
- No association with fluoroquinolones
- Previous admissions and use of proton pump inhibitors were not significantly associated with CDI after adjustment for the major confounder, concomitant use of 2nd generation cephalosporins.