



LEIDEN UNIVERSITY MEDICAL CENTER

*Emergence of Clostridium difficile Infection  
due to a new Hypervirulent strain,  
Polymerase Chain Reaction ribotype 078*

*Abraham Goorhuis, Dennis Bakker, Jeroen Corver, Sylvia Debast,  
Celine Harmanus, Daan Notermans, Aldert Bergwerff, Friedo Dekker  
and Ed Kuijper*



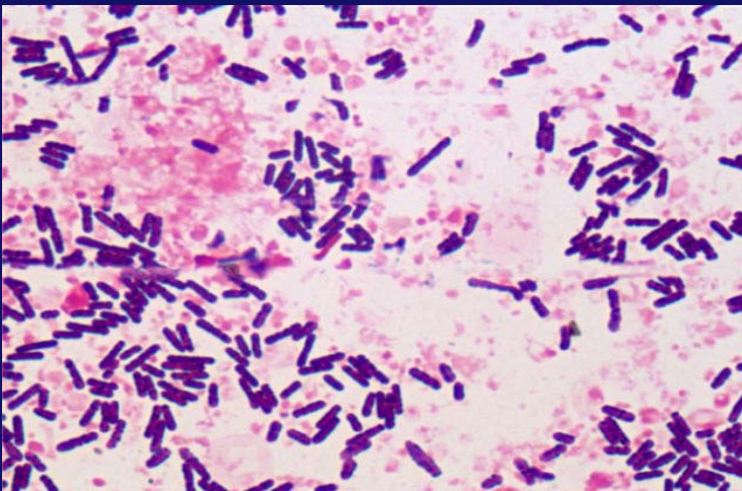
## Introduction

- A recent increase of CDI by the PCR-ribotype 078 strain was observed among patients in The Netherlands
- This strain is predominant in pigs and calves

(Keel K, Brazier JS, Post KW et al Prevalence of PCR ribotypes among *Clostridium difficile* isolates from pigs, calves, and other species. J Clin Microbiol 2007; 45:1963-4)

- Type 078 was found at pig farms in the Netherlands as a causative agent of diarrhea in piglets

(Goorhuis A, Debast SB, van Leengoed LA, et al. *Clostridium difficile* PCR ribotype 078: an emerging strain in humans and in pigs? J Clin Microbiol 2008; 46:1157).



## Methods and results

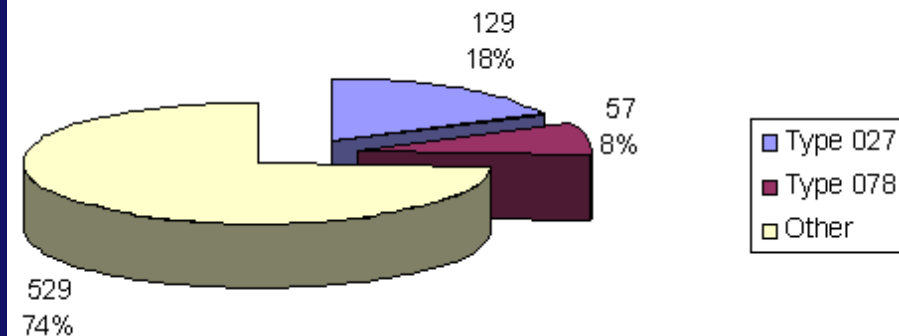
- Study period: February 2005 through February 2008
- 1687 isolates typed from 75 healthcare facilities

	Overall	Second half 2005	Second half 2007
<b>Type 027</b>	289 (17%)	62 (27%)	3 (1%)
<b>Type 078</b>	150 (9%)	7 (3%)	40 (13%)
<b>Total</b>	1687	232	308

To date: Type 078 most frequent type (14%)

- Other frequent types:
  - Type 014 (n = 173; 10%)
  - Type 001 (n = 129; 8%)
- Questionnaires
  - 714 (42%) of 1687 patients
- Equal percentages of questionnaires among different types

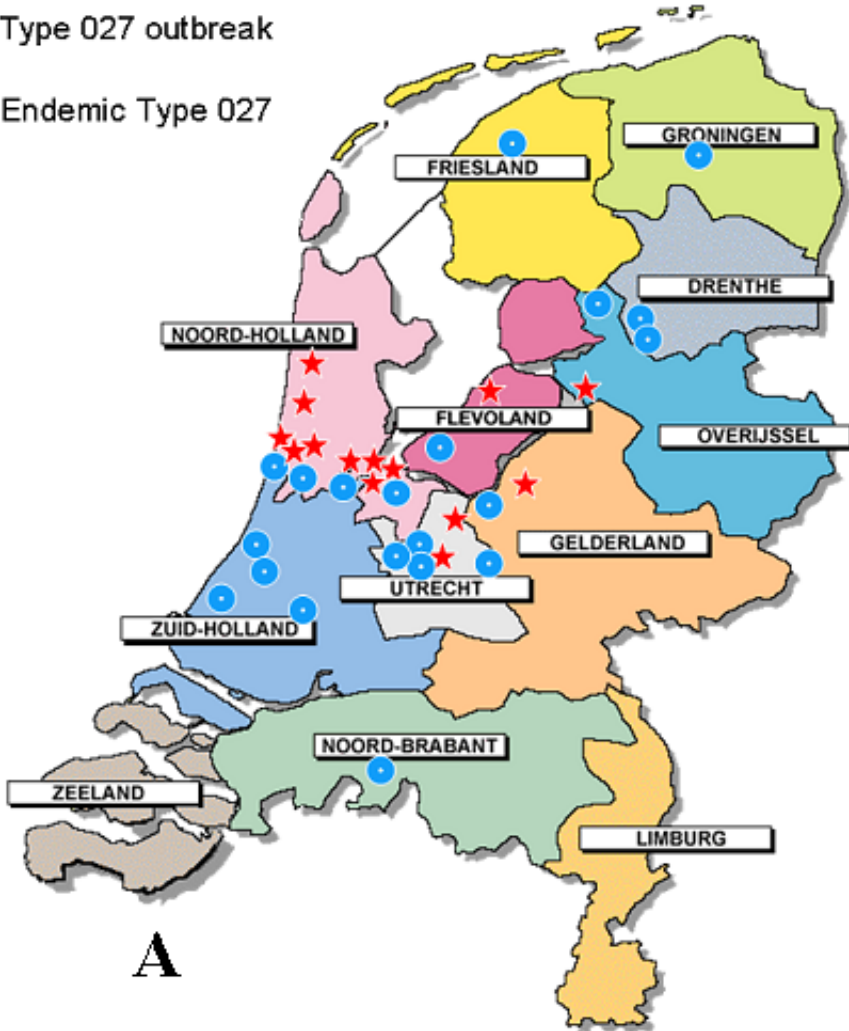
Distribution of ribotypes among patients with clinical information



# Methods and results (2)

★ Type 027 outbreak

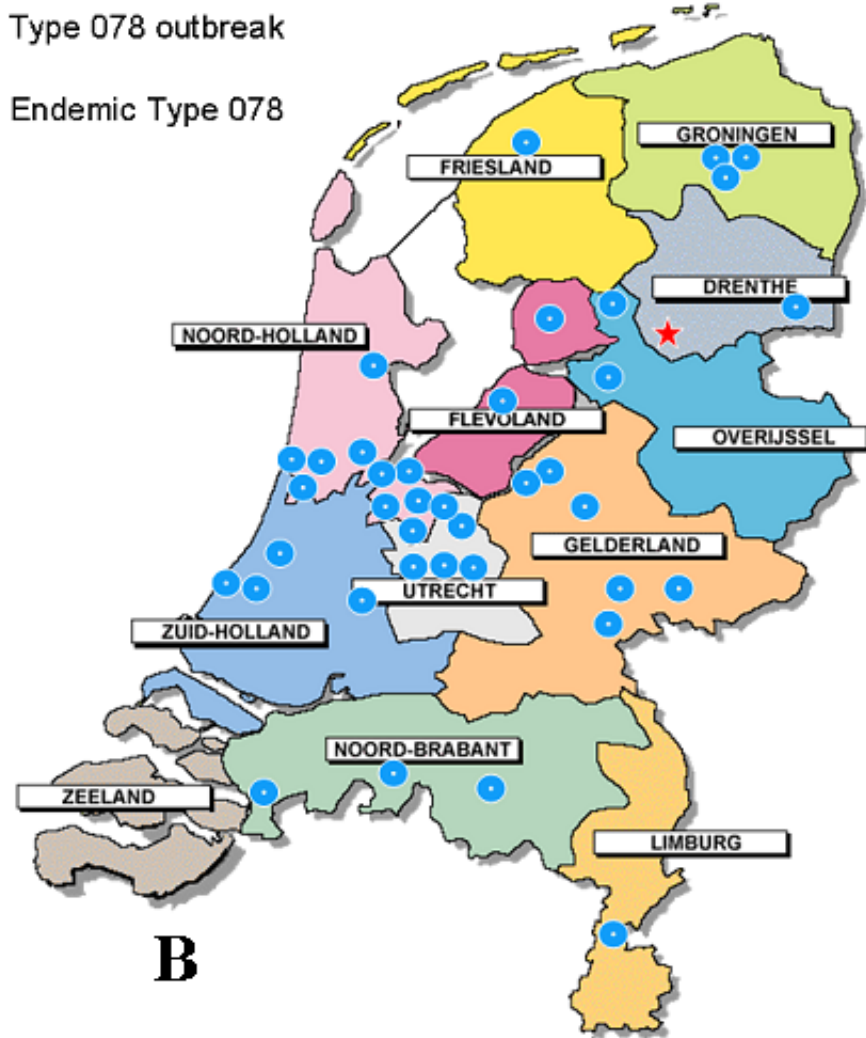
● Endemic Type 027



A

★ Type 078 outbreak

● Endemic Type 078



B

## • Severe diarrhoea

- Bloody diarrhoea and/or
- Diarrhoea with hypovolaemia or hypo albuminaemia (<20g/L) and/or
- Diarrhoea with fever ( $T > 38,0\text{ }^{\circ}\text{C}$ ) and leucocytosis (WBC count  $> 12 \times 10^9/\text{l}$ ) and/or
- Diarrhoea with pseudomembranous colitis.

## • Community associated CDI

- Development of CDI  $< 2$  days after admission or more than 12 weeks after discharge.

# Methods and results (3)

Risk factor	Proportion of patients with CDI (%)					
	Type 078		Type 027		Other types	
<b>Age</b>						
0-64	47/145	32,4	59/270	21,9	418/1148	36,4
65-79	55/145	37,9	111/270	41,1	391/1148	34,1
80+	43/145	29,7	100/270	37,0***	339/1148	29,5
<b>Male sex</b>	68/133	51,1	115/254	45,3	463/1052	44,0
<b>Healthcare association</b>	41/57	71,9	112/120	93,3***	385/491	78,4
<b>Community association</b>	10/57	17,5	8/120	6,7***	78/491	15,9
<b>Indeterminate association</b>	6/57	10,5	0/120	0,0***	28/491	5,7
<b>Underlying disease</b>	47/51	92,2	114/126	90,5	462/504	91,7
Solid tumor	6/47	12,8	16/120	13,3	71/486	14,6
Haematologic malignancy	8/49	16,3	12/121	9,9	46/488	9,4
Endocrine disease	8/48	16,7	13/119	10,9	81/480	16,9
Respiratory system diseases	16/48	33,3	51/121	42,1	129/478	27,0
Digestive system diseases	11/49	22,4	31/120	25,8	133/482	27,6
Cardiovascular system diseases	17/49	34,7	42/121	34,7	178/483	36,9
Genitourinary system diseases	13/49	26,5	37/120	30,8	135/477	28,3
Other diseases	11/46	23,9^	43/119	36,1	177/471	37,6
<b>Use of antibiotics</b>	44/52	84,6	110/123	89,4	425/501	84,8
Penicillins	23/51	45,1	55/122	45,1	236/478	49,4
Cephalosporins	22/51	43,1	68/121	56,2*	201/477	42,1
1st generation	1/48	2,08	8/121	7,14	34/456	7,46
2nd generation	9/48	18,8	36/112	32,1*	85/456	18,6
3rd generation	10/48	20,8	21/112	18,8	91/456	20,0
Fluoroquinolones	15/51	29,4^	37/122	30,3*	95/480	19,8
Macrolides and clindamycin	6/51	11,8	15/121	12,4^	94/480	19,6
Aminoglycosides	9/51	17,6	6/123	4,9***	52/481	10,8
Carbapenems	4/51	7,8	4/120	3,3	23/473	4,9
Vancomycin	4/51	7,8	18/123	14,6^	43/479	9,0
Metronidazol	6/51	11,8	16/121	13,2	41/480	8,5
Sulfonamides/thrimetoprim	7/51	13,7	11/121	9,1	68/478	14,2
<b>Outcome</b>						
<b>Severe diarrhoea</b>	21/54	38,9^	48/120	40,0*	134/476	28,2
<b>Complicated course</b>	5/52	9,6	22/124	17,7*	54/501	10,8
<b>Recurrent infections</b>	6/38	15,8	21/68	30,9^	62/333	18,6
<b>Overall mortality</b>	3/52	5,8	16/124	12,9*	35/501	7,0
<b>Attributable mortality</b>	2/52	3,8	5/124	4,0*	5/501	1,0
<b>Contributable mortality</b>	0/52	0,0	3/124	2,4	13/501	2,6

## Conclusions

- In a period of two-and-a-half years we experienced the emergence of CDI caused by Type 078, which has been reported as the predominant Type in pigs and calves.
- Higher prevalence of this type in areas with pig farms in the proximity
- To date, Type 078 is the most frequently encountered Type (14%).
- CDI due to type 078 causes severe diarrhoea in a younger population than 027-CDI with a high frequency of community-associated disease.
- Use of fluoroquinolones predisposes for acquisition of this type.