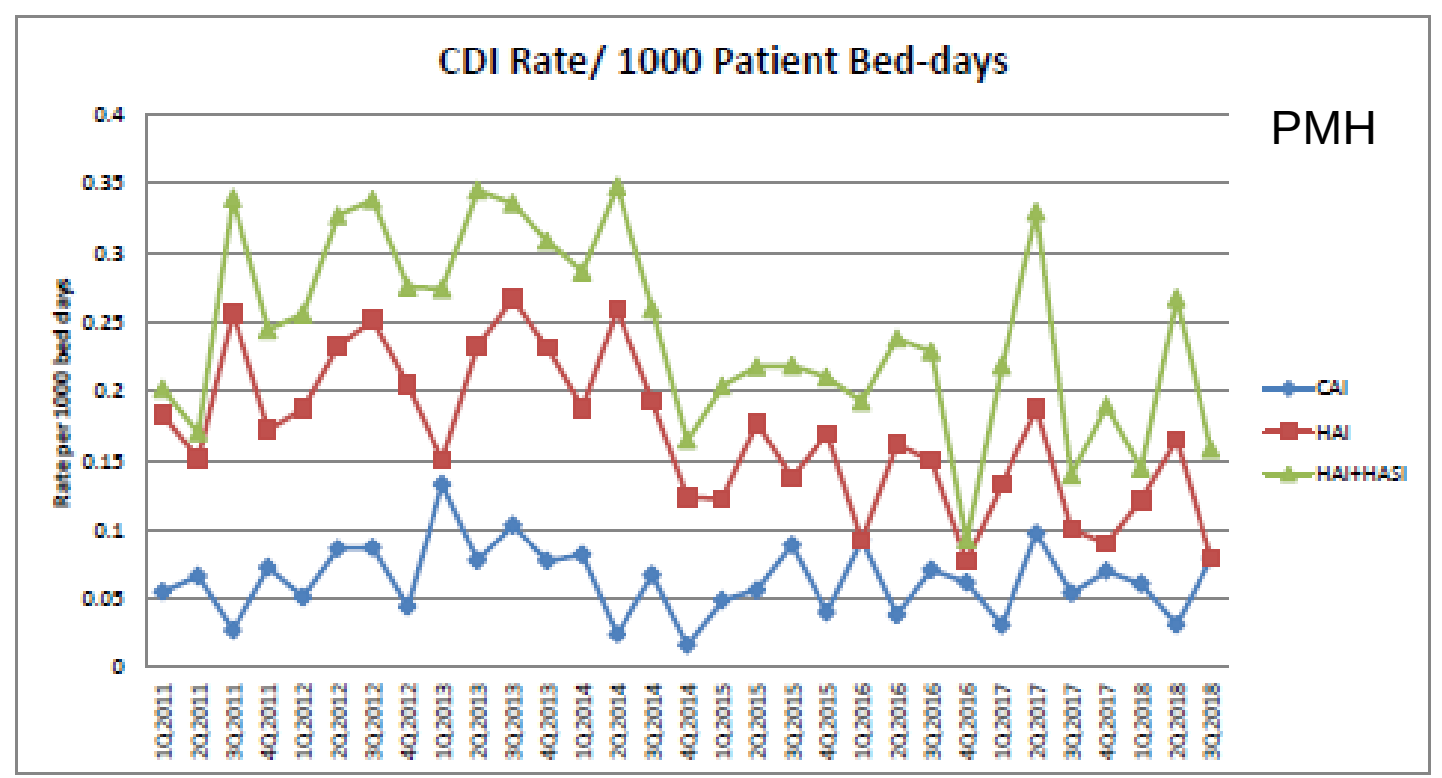
Dr Kristine Luk PMH

HIGH PREVALENCE AND FREQUENT ACQUISITION OF *CLOSTRIDIUM DIFFICILE* RIBOTYPE 002 AMONG NURSING HOME RESIDENTS IN HONG KONG

Local epidemiology



Remarks:
New surveillance definitions on "**HAI/ HAsI/ CAI/ Indeterminate/ Recurrent**" cases were adopted since 1Q 2015

HAI: CDI symptom onset more than 72 hrs after admission to hospital

HAsI : CDI symptom onset in the community or ≤ 72 hrs after admission, and symtom onset was < 4 wks after the last discharge from hospital

CAI: CDI symptom onset in the community or ≤ 72 hrs after admission to hospital and symptom onset was > 12 wks after the last discharge from hospital

Indeterminate: Symptom onset in the community > 4 wks but < 12 wks after the last discharge from hospital

Recurrent: Episode of CDI occurs < 8 wks after the onset of a previous episode, and CDI symptoms from the earlier episode resolved

Rates of CDAD for facilities where CDI is endemic range from 5-10 case / 10,000 patient-days

INFECTION CONTROL AND HOSPITAL EPIDEMIOLOGY FEBRUARY 2007, VOL. 28, NO. 2

Table 1 Estimated crude annual incidence of positive *C. difficile* tests in Hong Kong, calculated based on population data in the service region.

Year	Serving population (100,000)	Number of positive CDI tests	Crude incidence (per 100,000)	Positive CDI tests aged ≥65 years	Incidence (per 100,000)
2009	12.76	128	10.0	99	73.9
2010	12.94	193	14.9	130	93.9
2011	12.96	298	23.0	190	133.2
2012	13.21	441	33.4	314	206.6
2013	12.58	386	30.7	296	194.9

Journal of Infection (2016) **73**, 115–122

US >=65 567-687/100,000 population

N Engl J Med 2015;372:825-34

Table 1 Ribotype distribution of toxin-producing strains of *Clostridium difficile* among 307 patients in Hong Kong

	Total number of strains (%)	Total number of patients (%)
PCR ribotype 002[a]	35 (10.1%)	29 (9.4%)
PCR ribotype og39[b]	13 (3.8%)	11 (3.6%)
PCR ribotype 012	8 (2.3%)	7 (2.3%)
PCR ribotype 014	4 (1.2%)	4 (1.3%)
PCR ribotype 017	2 (0.6%)	2 (0.7%)
PCR ribotype 001	1 (0.3%)	1 (0.3%)
PCR ribotype 027	0	0
Other pattern	242 (70%)	221 (72%)[c]
Non-typable	40 (11.6%)	32 (10.4%)
Total	345	307

[a] PCR ribotype 002 constituted 55.6% (35/63) of strains and 53.7% (29/54) of patients with known ribotyping results

[b] This cluster of strains was identified by *slpA* typing

[c] Using 80% similarity in the dendrogram as the cutoff value, there were 106 distinct patterns with no more than eight isolates in each pattern

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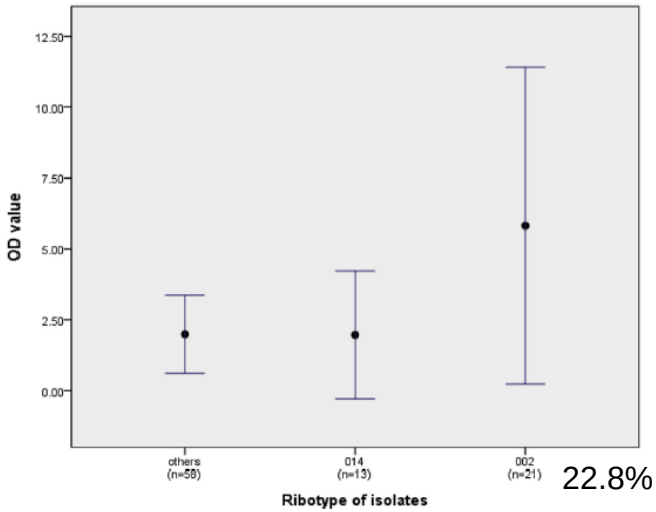
Sporulation frequency (spore/total cell ratio)
002 20.2% vs non-002 3.7% p<0.001



22.8%

Figure 1 The error bars (mean ± 2 S.E.) indicate the OD values of an ELISA toxin assay, shown according to bacterial ribotypes. Toxin levels tend to be higher with ribotype *002*, as suggested by the higher OD values (see text). S.E. = Standard Error.

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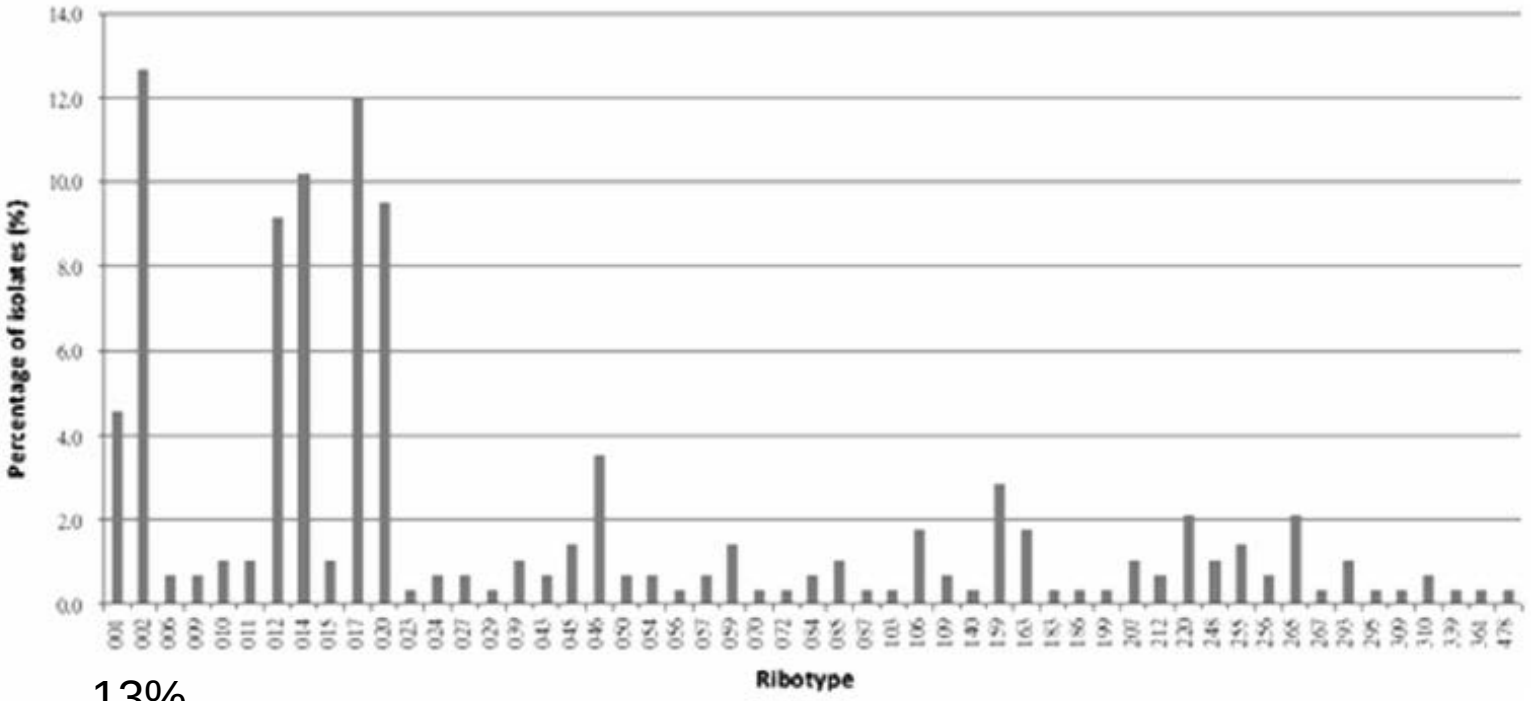
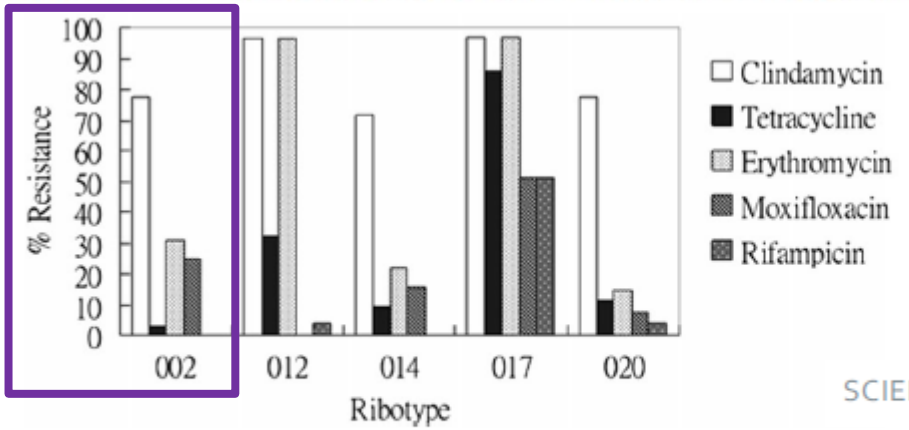


13%

Figure 1. Distribution of PCR ribotypes among the 284 toxigenic *C. difficile* strains isolated in Hong Kong.



SCIENTIFIC REPORTS | 7: 17218 | DOI:10.1038/s41598-017-17523-7

Figure 2. Rates of resistance to clindamycin, tetracycline, erythromycin, moxifloxacin, and rifampicin, of the five most prevalent ribotypes of toxigenic *C. difficile* clinical isolates in Hong Kong.

Table 2 Clinical characteristics, antibiotics exposure, clinical severity and outcomes of patients with confirmed *C. difficile* infections, as compared with the non-CDI, PCR-negative controls.

Variables	CDI cases n = 139 (%)	Non-CDI controls n = 114 (%)	Unadjusted OR (95% CI)	P-value
Age, year (mean ± S.D.)	71.5 ± 16.8	66.9 ± 16.3		0.02
Female	67 (48.2)	58 (50.8)		0.706
Nursing home resident	34 (24.5)	4 (3.5)	8.8 (3.0–35.5)	<0.001
Recent hospitalization	97 (69.8)	48 (42.1)	3.2 (1.8–5.5)	<0.001
Source of infection				
Healthcare-associated	107 (77.0)	–		
Community-associated	20 (14.4)	–		
Indeterminate	12 (8.6)	–		
Previous CDI episodes				
0	125 (90.0)	–		
1	12 (8.6)	–		
2	2 (1.4)	–		
Underlying comorbidities[a]	123 (88.5)	96 (84.2)		0.357
Chronic renal diseases	53 (38.1)	35 (28.1)		0.109
Diabetes mellitus	44 (31.7)	39 (34.2)		0.688
Active malignancy	29 (20.9)	12 (10.5)	2.2 (1.0–5.1)	0.039
Exposure to antibiotics[b]	130 (93.5)	96 (84.2)	2.7 (1.1–7.1)	0.023
Penicillins	103 (74.1)	71 (62.3)		0.056
Extended-spectrum penicillins	30 (21.6)	12 (10.5)	2.3 (1.1–5.3)	0.027
Cephalosporins	63 (45.3)	33 (28.9)	2.0 (1.2–3.6)	0.009
Carbapenems	27 (19.4)	2 (1.75)	13.4 (3.2–119.1)	<0.001
Macrolides	18 (12.9)	12 (10.5)		0.697
Fluoroquinolones	46 (33.1)	33 (28.9)		0.498
Aminoglycosides	11 (7.91)	4 (3.51)		0.184
Use of proton-pump inhibitors	50 (36.0)	25 (21.9)	2.0 (1.1–3.7)	0.019
Use of immunosuppressants[b]	12 (8.6)	13 (11.4)		0.528
SHEA/IDSA-defined severe disease[c]	58 (41.7)	–		
Max. WBC >15 × 10^9/L	32 (23.0)	–		
Creatinine rise >50%	37 (26.6)	–		
Complications, any	23 (16.5)	–		
Hypotension	17 (12.2)	–		
Paralytic ileus	6 (4.3)	–		
Toxic-megacolon	1 (0.7)	–		
Refractory disease[d]	29 (20.9)	–		
Recurrence within 60 days[d]	14 (10.1)			
Length-of-stay, days (mean ± S.D.)	20.4 ± 15.3	14.1 ± 14.0		<0.001
All-cause death within 30 days	23 (16.5)	7 (6.7)		0.029

(The results are presented as numbers and percentages unless otherwise specified).

[a] Other medical conditions including chronic cardiovascular, pulmonary and liver diseases, inflammatory bowel diseases (n = 4), and HIV/AIDS (n = 4) were compared, and showed no significant difference between groups.

[b] Received ≥1 antibiotics within 8 weeks prior to CDI onset. Extended-spectrum penicillins refer to anti-pseudomonal penicillins, such as ureidopenicillins. Use of immunosuppressants was defined as 15 mg/day of prednisone or equivalent for one month or longer, or any dose of anti-metabolites, alkylating agents, calcineurin inhibitors or biologic therapies.

[c] Severe CDI was defined according to SHEA/IDSA criteria as WBC >15 × 10^9/L or serum creatinine rise >1.5 time from baseline.

[d] Refractory disease was defined by persistent symptom despite treatment for >7 days. Recurrence was defined as symptom recurrence after initial resolution, and a positive CDI test.

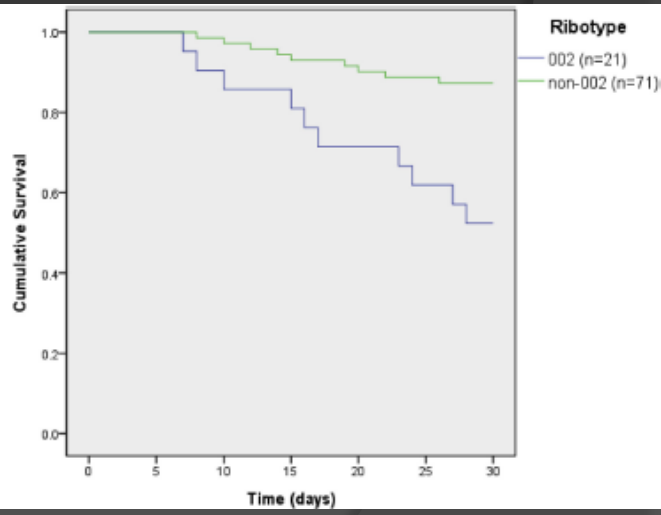


Table 3 Demographic characteristics of patients with culture isolation of *Clostridium difficile* ribotype 002 and non-ribotype 002 in Hong Kong

	Clostridium difficile ribotype 002 (n=29)	*Clostridium difficile* ribotype other than 002[b] (n=56)	p-value
Age (mean±SD)	68.1±25.5	58.3±26.2	0.97
Sex (M/F)	20/9	33/23	0.37
Residence in elderly home	11 (37.9%)	7 (12.5%)	0.01[a]
Patients with			
Malignancy	12 (41.4%)	20 (35.7%)	0.61
Organ transplant	2 (6.9%)	5 (8.9%)	1.0
Cardiopulmonary condition	9 (31.0%)	10 (17.9%)	0.18
Renal failure	5 (17.2%)	7 (12.5%)	0.55
Cerebrovascular accident	5 (17.2%)	6 (10.7%)	0.40
Diabetes mellitus	4 (13.8%)	9 (16.1%)	0.78
Patients with			
Asymptomatic colonization	12 (41.4%)	26 (46.4%)	0.66
Severe CDAD[c]	7/17 (41.2%)	13/30 (43.3%)	0.90
Number of hospitalizations in the past year, median (interquartile range)	6 (4–12)	5.5 (2–12.75)	0.52
Number of patients with isolation of toxigenic *C. difficile* in the past year	3 (10.3%)	8 (14.3%)	0.74
Antibiotic therapy in the week preceding the culture of *C. difficile*	21 (72.4%)	34 (60.7%)	0. 29
Days of antibiotics[d] received by patients in the past 3 months (mean±SD)			
β-lactams	23.7±17.9	16.2±14.6	0.04
Fluoroquinolones	2.6±5.1	5.6±10.0	0.14
Clindamycin	0	0.2±1.2	0.35
Number of patients using proton pump inhibitors			
Within 90 days	14 (48.3%)	19 (33.9%)	0.24
91–180 days	8 (27.6%)	12 (21.4%)	0.59
181–365 days	5 (17.2%)	10 (17.9%)	1
Mean (range) days between the identification of *C. difficile* and admission	35.2 (1–376)	31.4 (0–416)	0.99
30-day survival after the identification of *C.difficile* and admission	3 (10.3%)	6 (10.7%)	0.96

21.2%

[a] Odds ratio 1.89; 95% confidence interval 1.04–3.42

[b] Patients with *Clostridium difficile* ribotype 001 (n=1), 012 (n=6), 014 (n=3), 017 (n=2), og39 (n=8), and unrecognized ribotype (n=36) were randomly selected as the control

[c] Severe CDAD (*C. difficile*-associated diarrhea) is defined according to the disease score, as previously described [26]

[d] Penicillin group included ampicillin, amoxicillin–clavulanate, ampicillin–sulbactam, ticarcillin–clavulanate, piperacillin, and piperacillin–tazobactam; cephalosporin group included cefazolin, cefuroxime, cefotaxime, ceftriaxone, ceftazidime, cefoperazone, cefoperazone–sulbactam, cefepime; carbapenem group included imipenem–cilastatin, meropenem, and ertapenem; fluoroquinolones included ciprofloxacin, levofloxacin, and moxifloxacin

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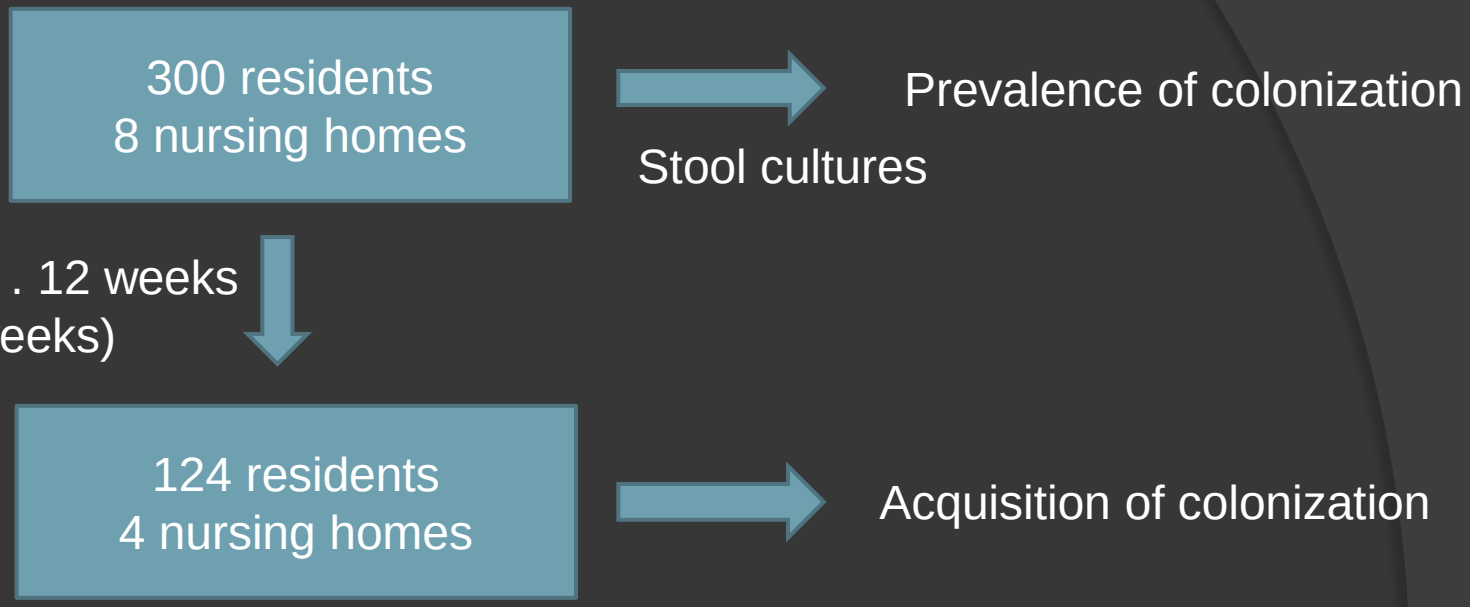


Definition of acquisition in nursing home

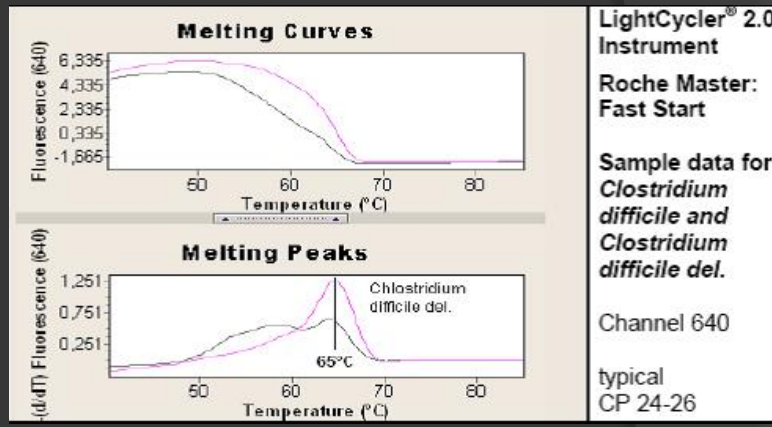
1) Past 90 days no history of hospitalization
   negative stool culture -> positive
2) Discharged from hospitals
   negative stool culture at baseline & after discharge
   -> positive

Laboratory protocol

Culture by chromogenic agar

(Consists of peptones, taurocholate that has superior ability to stimulate germination; β-glucosidate – chromogenic substrate grey to black)

Real-time PCR (target:176 bp fragment of the *tcdC* gene -> early identification of ribotype 027 -18 bp del, 078 - 39 bp del)



Ribotyping of 1st patient isolate

61% reduction in material cost

Additional 9% positive cases

TABLE 1 Comparison of real-time PCR results with those of toxigenic culture for the diagnosis of CDI[a]

	No. of specimens with toxigenic culture result	
PCR result	Positive	Negative
Positive	106	2
Negative	11	416

[a] Anaerobic culture was performed on the 538 test stools by plating the specimens onto CDIF medium. All *C. difficile* culture isolates were tested for the presence of toxin production (as evidenced by detection of the *tcdC* gene) by real-time PCR. Real-time PCR for the presence of *tcdC* was performed on 535 stool specimens. The quantities of three specimens were insufficient for real-time PCR, and one of these was found to be toxigenic culture positive. The sensitivity, specificity, positive predictive value, and negative predictive value were 90.6%, 99.5%, 98.1%, and 97.4%, respectively.

***J. Clin. Microbiol.* 2014, 52(2):671.**

TABLE 1. Characteristics of 8 Nursing Homes in Hong Kong

	Nursing Home								
	A	B	C	D	E	F	G	H	
Type	Nonprivate	Private	Private	Private	Private	Private	Private	Nonprivate	Total
Resident-to-staff ratio	38/16	41/11	72/13	190/90	96/23	45/11	214/69	149/48	845/281
	2.38:1	3.73:1	5.54:1	2.11:1	4:17:1	4.09:1	3.10:1	3.10:1	3.01:1
Infection control staff, no.									
Nurse	1	1	1	N/A	0	0	1	2	
Health assistant	1	1	1		2	1	1	0	
Staff training	Regular	Once	Regular	Regular	Regular	Regular	Regular	Regular	
Residents >75 y old, %	92.1	78	63.4	95.3	84.9	95.6	70.4	94	77.3
Environment cleansing agent	Chlorine	Chlorine	Chlorine	Chlorine	Chlorine	Chlorine	Chlorine	Chlorine	
No. of residents sharing 1 handwashing facility	4.8	20.5	36.0	14.6	32	15	26.8	5.5	
Provision of alcohol-based hand disinfectant	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	

TABLE 2. Prevalence of Toxigenic *Clostridium difficile* Colonization and Acquisition Among Nursing Home Residents in Hong Kong

	Nursing Home								
Variable	A	B	C	D	E	F	G	H	Total
No. of specimens, baseline	32	19	35	56	33	56	20	49	300
No. of patients in follow-up	…	…	…	…	185	299	58	135	677
Toxigenic *C. difficile* prevalence, no. (%)	1 (3.1)	6 (31.6)	1 (2.9)	8 (14.3)	4 (12.1)	4 (7.1)	4 (20.0)	2 (4.1)	30 (10.0)
95% confidence interval	0.6–15.8	15.4–54.0	0.6–14.6	10.0–29.9	4.9–27.4	2.9–17.0	8.1–41.7	1.2–13.8	7.1–14.0
Acquisition[a]/Residents at risk[b] (%)	…	…	…	…	2/26 (7.7)	5/44 (11.4)	1/13 (7.7)	1/41 (2.4)	9/124 (7.3)
Acquisition[a] per 1,000 resident days at risk[c]	…	…	…	…	0.256	0.396	0.524	0.163	0.316

Comparing to overseas LTCF

Table 1. Summary data of individual studies.

Study, year	Country	Setting	Preceding outbreak of CDI	Method of *C.dificile* detection	N	Mean Age (years)	Female gender(%)	n (%) colonized
All studies	**6/9 (67%) USA**	**21 LTCFs**	**4/9 (44%)**	**All used multi-step detection**	**1371**	**70 to 85**	**Range 0–81%**	**17014.8 (95% CI 7.6–24.0)†**
Arvand, 2012 [30]	Germany	11 LTCFs	No	Culture and toxigenicity confirmation with EIA and PCR	239	85 (38–100)	78%	9 (3.8%)
Ryan, 2010 [31]	Ireland	1 LTCF (2 wards)	No	Culture and PCR for detection of *C. difficile* and toxigenicity confirmation with EIA for toxin A/B and PCR	100	83	69%	7 (7.0%)
Riggs, 2007 [7]	USA, OH	1 LTCFs (2 wards)	Yes	Culture and toxigenicity confirmation with EIA for toxins A/ B	68	70±12	0%	35 (51.5%)
Rivera, 2003 [32]	USA, OH	1 LTCF (2 wards)	No	Culture and toxigenicity confirmation with EIA for toxins	42	NR	NR	2 (4.8%)
Simor, 1993 [34]	Canada	2 LTCF (9 wards)	No	Culture and toxigenicity confirmation with CCCA	489	NR	NR	57 (11.7%)
Walker, 1993 [33]	USA, MN	2 LTCFs	No	Culture and toxigenicity confirmation with CCCA	225	84.2±9.9	81%	9 (4.0%)
Bennett,1992 [35]	USA, MD	1 LTCF	Yes	Culture and toxigenicity confirmation with CCCA	59	75(28–99)	66%	23 (38.9%)
Larson, 1991 [36]	USA, MD	1 LTCF (5 wards)	Yes	Culture and toxigenicity confirmation with CCCA	100	NR	NR	23 (23%)
Kerr, 1990 [37]	USA, MT	1 LTCF	Yes	Culture and toxigenicity confirmation with CCCA	49	85(38–100)	71%	5 (10.2%)

CDI = *C.difficile* infection, CCCA = cell culture cytotoxicity assays, EIA = enzyme immunoassay, LTCF = long-term care facility, NR = not reported, †pooled random-effects estimate

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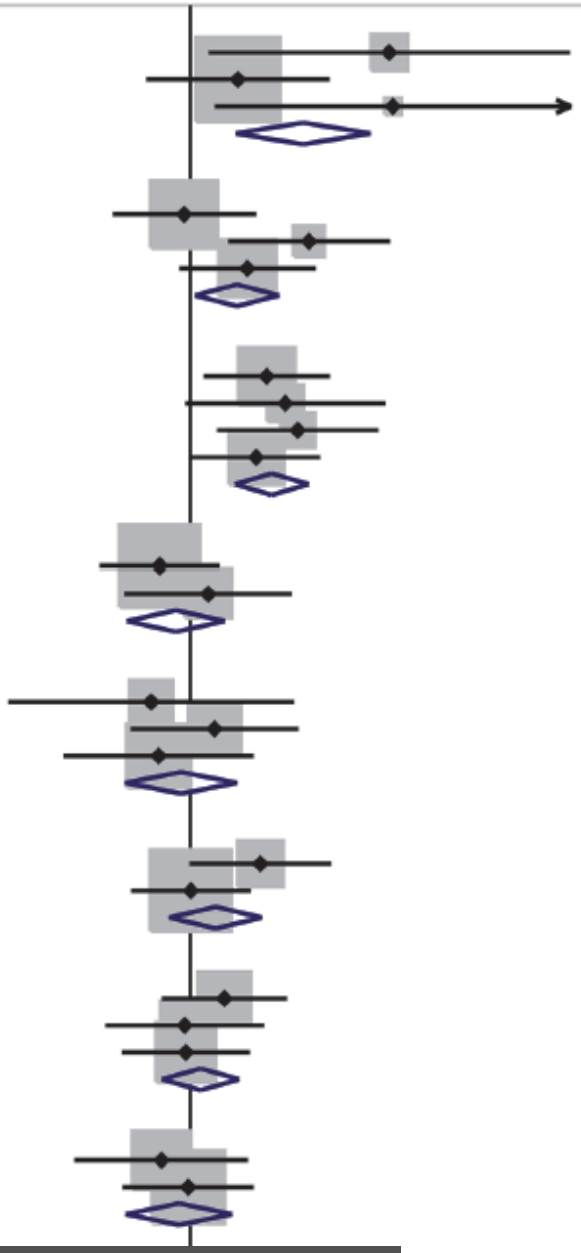
Risk factors for colonization, patient–level exposure



study	OR (95% CI)	Events, colonized	Events, non–colonized	% Weight
History of CDI				
Riggs,2007	24.02 (1.34, 431.79)	9/35	0/33	14.83
Ryan, 2010	2.14 (0.50, 9.24)	3/10	15/90	82.24
Arvand, 2012	25.44 (1.47, 440.19)	1/10	1/230	2.94
Subtotal (I–squared = 47.2%, p = 0.150)	6.07 (2.06, 17.88)	13/55	16/353	100.00
Previous Hospitalization				
Riggs, 2007	0.91 (0.29, 2.87)	27/35	26/33	52.18
Arvand, 2012	6.67 (1.82, 24.40)	5/10	30/230	10.66
Walker, 1993	2.49 (0.84, 7.42)	11/16	98/209	37.15
Subtotal (I–squared = 61.4%, p = 0.075)	2.11 (1.08, 4.13)	43/61	154/472	100.00
Prior antibiotic use				
Riggs, 2007	3.39 (1.24, 9.29)	25/35	14/33	37.11
Ryan, 2010	4.57 (0.92, 22.73)	8/10	42/90	15.14
Arvand, 2012	5.57 (1.53, 20.26)	5/10	35/230	13.14
Walker, 1993	2.87 (1.03, 8.02)	8/16	54/209	34.61
Subtotal (I–squared = 0.0%, p = 0.869)	3.68 (2.04, 6.62)	46/71	145/562	100.00
Proton pump inhibitor use				
Riggs, 2007	0.61 (0.23, 1.61)	17/35	20/33	74.63
Ryan, 2010	1.33 (0.35, 5.09)	4/10	30/90	25.37
Subtotal (I–squared = 0.0%, p = 0.357)	0.80 (0.36, 1.74)	21/45	50/123	100.00
male gender				
Kerr, 1990	0.54 (0.05, 5.24)	1/5	14/44	21.52
Ryan, 2010	1.48 (0.39, 5.65)	4/10	28/90	31.63
Walker, 1993	0.60 (0.13, 2.76)	2/16	40/209	46.86
Subtotal (I–squared = 0.0%, p = 0.608)	0.86 (0.35, 2.12)	7/31	82/343	100.00
Diabetes				
Walker, 1993	3.06 (0.99, 9.50)	5/16	27/209	23.95
Riggs, 2007	1.01 (0.39, 2.63)	16/35	15/33	76.05
Subtotal (I–squared = 54.3%, p = 0.139)	1.50 (0.71, 3.16)	21/51	42/242	100.00
Fecal incontinence				
Riggs, 2007	1.73 (0.63, 4.69)	15/35	10/33	31.83
Arvand, 2012	0.92 (0.26, 3.25)	5/10	120/230	27.05
Walker, 1993	0.93 (0.34, 2.60)	7/16	95/209	41.12
Subtotal (I–squared = 0.0%, p = 0.635)	1.18 (0.64, 2.19)	27/61	225/472	100.00
Urinary incontinence				
Arvand, 2012	0.63 (0.16, 2.53)	7/10	181/230	38.89
Walker, 1993	0.97 (0.34, 2.76)	6/16	80/209	61.11
Subtotal (I–squared = 0.0%, p = 0.631)	0.84 (0.36, 1.96)	13/26	261/439	100.00

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TABLE 3. Univariate Analysis and Multivariable Logistic-Regression of the Risk Factors Associated With *C. difficile* Colonization

Risk Factor	Colonized (N = 18)	Not colonized (N = 135)	Unadjusted OR (95% CI)	*P* Value	Adjusted OR (95% CI)	*P* Value
Age, mean y ± SD (median)	82.9 ± 7.2 (83.5)	82.1 ± 10.4 (83)	1.01 (0.96–1.06)	.814		
Sex, male	6 (33.3)	53 (39.3)	0.77 (0.27–2.19)	.628		
Duration of residence, mean mo ± SD (median)	29.2 ± 25.5 (25.7)	33.9 ± 39.6 (21.5)	0.10 (0.98–1.01)	.984		
Hepatic disease	2 (11.1)	1 (0.7)	16.75 (1.44–195.23)	**.037**	13.23 (0.90–194.75)	.06
History of hospitalization within 12 weeks	11 (61.1)	34 (25.2)	4.67 (1.68–13.00)	**.002**	2.10 (0.51–8.63)	.306
Penicillin group antibiotics within 12 weeks[a]	7 (38.9)	18 (13.3)	4.14 (1.42–12.06)	**.013**	2.33 (0.56–9.69)	.246
Proton pump inhibitor within 12 weeks	7 (38.9)	23 (17.0)	3.10 (1.09–8.84)	.051		
Bed-bound functional status	4 (22.2)	7 (5.3)	5.14 (1.34–19.78)	**.028**	0.84 (0.10–6.93)	.872
Barthel index, mean ± SD (median)	38.3 ± 42.8 (19)	47 ± 35.8 (45.5)	0.99 (0.98–1.01)	.243		
Presence of devices[b]	5 (27.8)	14 (10.4)	3.32 (1.03–10.72)	.051		
Urinary catheter	1 (5.6)	7 (5.2)	1.08 (0.13–9.29)	1		
Nasogastric tube	4 (22.2)	4 (3.0)	9.36 (2.11–41.58)	**.007**	8.59 (1.18–62.53)	**.034**

NOTE. *C. difficile*, *Clostridium difficile*; SD, standard deviation. Data are no. (%), unless otherwise indicated. Bold *P* values indicate statistical significance.

[a]Penicillin group antibiotics included penicillins, aminopenicillins, carboxypenicillins, ureidopenicillins and β-lactam/β-lactamase inhibitor combinations (ie, amoxicillin-clavulanate, ticarcillin-clavulanate, ampicillin-sulbactam, and piperacillin-tazobactam).

[b]Devices included urinary catheters, nasogastric tubes, percutaneous endoscopic gastrostomy tubes, tracheostomy tubes, and Tenckoff catheters for peritoneal dialysis.

Disruption in normal gut flora?
Dependence on nursing home staff for enteral feeding
Fecal-oral route acquisition?

Infect Control Hosp Epidemiol 2018;1–6

Nasogastric tube as a risk factor for colonization of MDROs as well

Table 1
Clinical characteristics of patients with *Klebsiella pneumoniae* bacteraemia.[a]

Characteristic	pAmpC group ($n=23$)	ESBL group ($n=37$)	pAmpC + ESBL group ($n=26$)	Controls ($n=23$)	Total ($N=109$)
Devices					
Urinary catheter	12 (52.2)	13 (35.1)	13 (50.0)	9 (39.1)	47 (43.1)
Nasogastric tube	12 (52.2)	8 (21.6)	13 (50.0)	3 (13.0)	36 (33.0)
Central venous catheter	1 (4.3)	7 (18.9)	3 (11.5)	3 (13.0)	14 (12.8)
Endotracheal tube	3 (13.0)	5 (13.5)	3 (11.5)	0 (0.0)	11 (10.1)

Table 2
Risk factors for bacteraemia caused by pAmpC-producing *K. pneumoniae*.

Risk factor	pAmpC group vs Controls					
	Unadjusted OR[a] (95% CI)	*p* value	Interim adjusted OR[b] (95% CI)	*p* value	Final adjusted OR[c] (95% CI)	*p* value
Age	1.07 (1.02,1.13)	**0.008**	1.01 (0.95,1.08)	0.711		
Nursing home residence	16.33 (3.06,87.18)	**<0.001**	34.17 (1.83,637.61)	**0.018**	41.47 (4.55,377.75)	**0.001**
Recent use of cephalosporins	0.55 (0.16,1.92)	0.530				
APACHE score	1.16 (1.05,1.28)	**0.001**	1.22 (1.05,1.42)	**0.011**	1.22 (1.06,1.41)	**0.006**
Nasogastric tube	7.27 (1.68,31.43)	**0.011**	0.94 (0.06,13.79)	0.0966		
Chest infection as source of bacteraemia	3.56 (0.80,15.72)	0.165				
Biliary tract infection as source of bacteraemia	0.13 (0.01,1.17)	0.096				

Risk factors	pAmpC group vs ESBL group					
	Unadjusted OR[a] (95% CI)	*p* value	Interim adjusted OR[b] (95% CI)	*p* value	Final adjusted OR[c] (95% CI)	*p* value
Age	1.05 (1.01,1.10)	**0.036**	1.09 (1.00,1.19)	0.056	1.09 (1.00,1.18)	**0.046**
Nursing home residence	9.96 (2.82,35.12)	**<0.001**	6.22 (1.05,36.83)	**0.044**	7.13 (1.36,37.54)	**0.02**
Recent use of cephalosporins	0.11 (0.03,0.38)	**<0.001**	0.06 (0.01,0.49)	**0.007**	0.07 (0.01,0.40)	**0.003**
APACHE score	1.07 (1.01,1.14)	**0.015**	1.02 (0.92,1.12)	0.748		
Nasogastric tube	3.95 (1.27,12.27)	**0.024**	3.28 (0.41,26.56)	0.265		
Chest infection as source of bacteraemia	6.04 (1.40,26.01)	**0.015**	66.64 (1.71,2595.66)	**0.025**	51.54 (2.50,1060.71)	**0.011**
Biliary tract infection as source of bacteraemia	0.09 (0.01,0.79)	**0.011**	0.76 (0.06,9.91)	0.831		

APACHE, Acute Physiology and Chronic Health Evaluation; CI, Confidence interval; ESBL, Extended-spectrum beta-lactamase; OR, Odds ratio; pAmpC, plasmid-mediated AmpC beta-lactamase.

[a] Unadjusted OR, univariate analysis performed between single risk factor and bacteraemia caused by pAmpC producing *K. pneumoniae*.

[b] Interim Adjusted OR, multivariate logistic regression performed on all risk factors and bacteraemia caused by pAmpC producing *K. pneumoniae*.

[c] Final Adjusted OR, multivariate logistic regression performed on all risk factors and bacteraemia caused by pAmpC producing K. pneumonia after a backward selection model with likelihood ratio for selection criteria.

Journal of Global Antimicrobial Resistance 7 (2016) 37–42

Nasogastric tube as a risk factor for colonization of MDROs as well

TABLE 1. Univariate Analysis and Multivariable Logistic Regression of the Risk Factors Associated with Methicillin-Resistant *Staphylococcus aureus* (MRSA) Colonization at Admission

Risk factor	MRSA carriers (n = 1,095)	Non-MRSA carriers (n = 6,566)	Unadjusted OR (95% CI)	P	Adjusted OR (95% CI)	P
Demographic data						
Age, mean ± SD (median), years	79.2 ± 12.9 (81)	69.7 ± 17.2 (74)	1.04 (1.04–1.05)	<.001	1.01 (1.00–1.02)	.008
Sex, male	575 (52.5)	3,368 (51.3)	1.05 (0.92–1.19)	.046	1.32 (1.13–1.54)	<.001
Old age home residence	631 (57.6)	949 (14.5)	8.05 (7.01–9.24)	<.001	3.32 (2.78–3.98)	<.001
Underlying diseases						
Chronic skin lesions	56 (5.1)	95 (1.4)	3.67 (2.62–5.14)	<.001	1.51 (0.99–2.30)	.006
Cardiovascular diseases	617 (56.3)	2,575 (39.2)	2.00 (1.76–2.28)	<.001	1.07 (0.90–1.28)	.045
Renal failure	176 (16.1)	717 (10.9)	1.56 (1.31–1.87)	<.001	1.28 (1.03–1.60)	.026
Chronic lung diseases	261 (23.8)	1,158 (17.6)	1.46 (1.25–1.70)	<.001	1.25 (1.04–1.52)	.021
Diabetes mellitus	373 (34.1)	1,784 (27.2)	1.39 (1.21–1.59)	<.001	1.23 (1.04–1.46)	.015
Devices						
Nasogastric tube	193 (17.6)	183 (2.8)	7.46 (6.03–9.24)	<.001	1.63 (1.25–2.13)	<.001
Urinary catheter	163 (14.9)	303 (4.6)	3.62 (2.95–4.43)	<.001	1.38 (1.08–1.75)	.009
Dependency						
Bedbound	356 (32.5)	510 (7.8)	7.88 (6.69–9.29)	<.001	2.19 (1.75–2.74)	<.001
Chairbound	258 (23.6)	623 (9.5)	4.67 (3.93–5.55)	<.001	1.80 (1.46–2.22)	<.001
Other risk factors						
History of MRSA	129 (11.8)	76 (1.2)	11.40 (8.52–15.26)	<.001	4.60 (3.28–6.44)	<.001
Hospitalization within past 12 mo	978 (89.3)	3,981 (60.6)	5.43 (4.45–6.62)	<.001	2.52 (2.02–3.14)	<.001
Operation within past 12 mo	188 (17.2)	773 (11.8)	1.55 (1.31–1.85)	<.001	1.03 (0.84–1.27)	.754
Active skin lesion	172 (15.7)	284 (4.3)	4.12 (3.37–5.04)	<.001	1.44 (1.12–1.85)	.004
Infection-related admission diagnosis	430 (39.3)	1,536 (23.4)	2.12 (1.85–2.42)	<.001	1.16 (0.98–1.36)	.008

NOTE. Data are no. (%), unless otherwise indicated. Unadjusted odds ratio (OR), univariate analysis performed between single risk factor and MRSA carriage. Adjusted OR, multivariable logistic regression performed on all risk factors and MRSA carriage. CI, confidence interval.

Infect Control Hosp Epidemiol 2014;35(1):42-48

Nasogastric tube as a risk factor for colonization of MDROs as well

TABLE 3. Risk Factors in Residents With Colonization by Carbapenem-Resistant *Acinetobacter baumannii* (CRAB) and Methicillin-Resistant *Staphylococcus aureus* (MRSA) Using Multiple Logistic Regression[a]

	Colonization by CRAB		Colonization by MRSA	
Characteristic	Odds Ratio (95% CI)	*P* Value	Odds Ratio (95% CI)	*P* Value
Dependency: bed-bound	2.70 (1.52–4.79)	.001	2.50 (1.66–3.77)	<.001
Incontinence with adult diapers	5.01 (2.30–10.92)	<.001	1.78 (1.26–2.52)	.001
Presence of nasogastric tube	2.98 (1.25–7.09)	.014	2.64 (1.45–4.77)	.001
Presence of chronic cerebral conditions	NS	NS	1.55 (1.13–2.11)	.006
Use of beta-lactam/beta-lactamase inhibitors in preceding 6 months	NS	NS	2.34 (1.44–3.82)	.001

NOTE. CI, confident interval.

[a]All epidemiological characteristics listed were used as independent variables. Final model was selected using a forward selection procedure. For the analysis of CRAB colonization, the Hosmer-Lemeshow goodness-of-fit statistic was 4.17, and $P = .841$. For the analysis of MRSA colonization, the Hosmer-Lemeshow goodness-of-fit statistic was 3.23, and $P = .780$.

Infect Control Hosp Epidemiol 2016;37:983–986

High Prevalence of *C. difficile* colonization – does it matter?

- Skin & environmental contamination of carriers

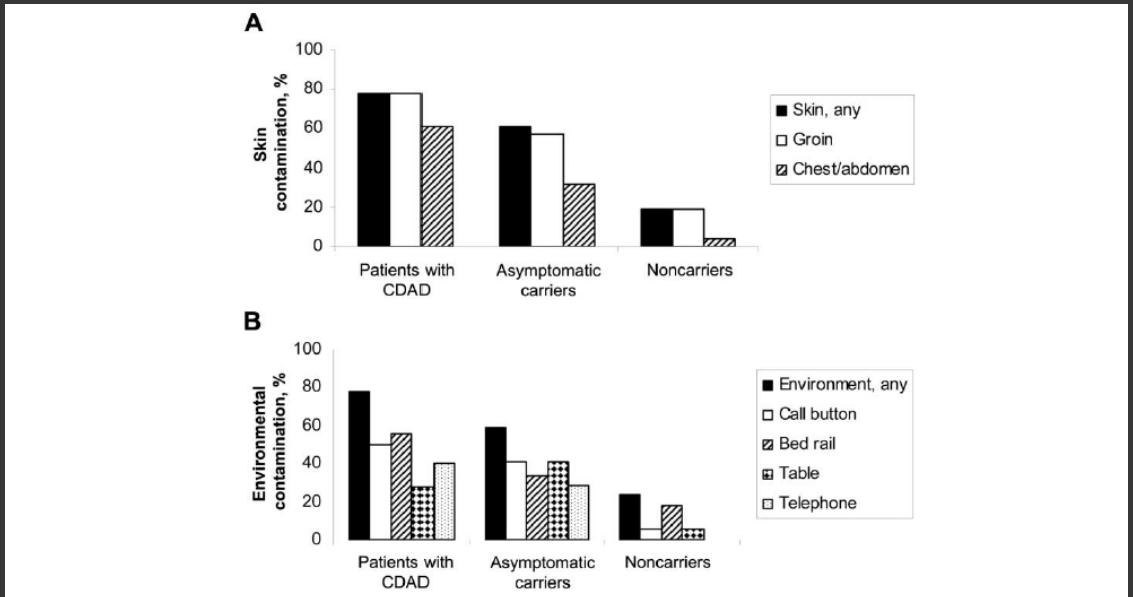
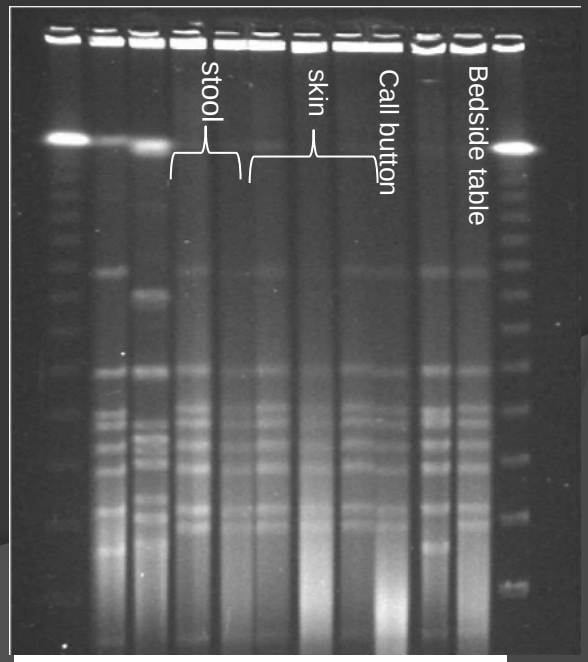


Figure 1. Percentages of *Clostridium difficile* skin *(A)* and environmental *(B)* contamination among study groups. Samples from skin and environmental surfaces were collected for culture concurrently with stool samples from patients with *C. difficile*–associated disease (CDAD; $n = 18$), asymptomatic fecal carriers ($n = 35$), and noncarriers (i.e., patients with negative stool culture results; $n = 33$). Patients with missing skin ($n = 13$) or environmental ($n = 3$) culture samples were excluded.



Clinical Infectious Diseases 2007; 45:992–8

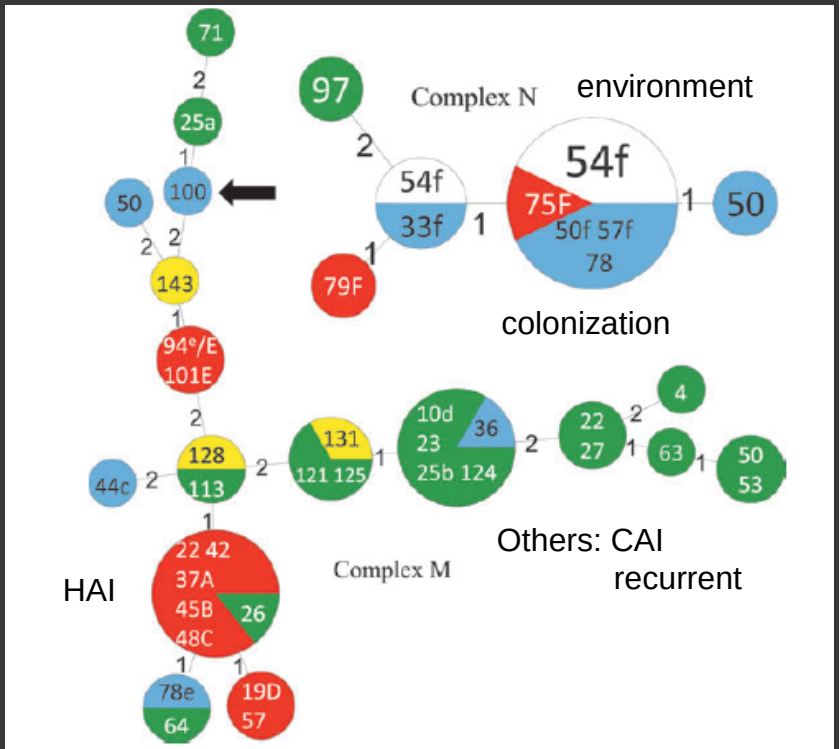
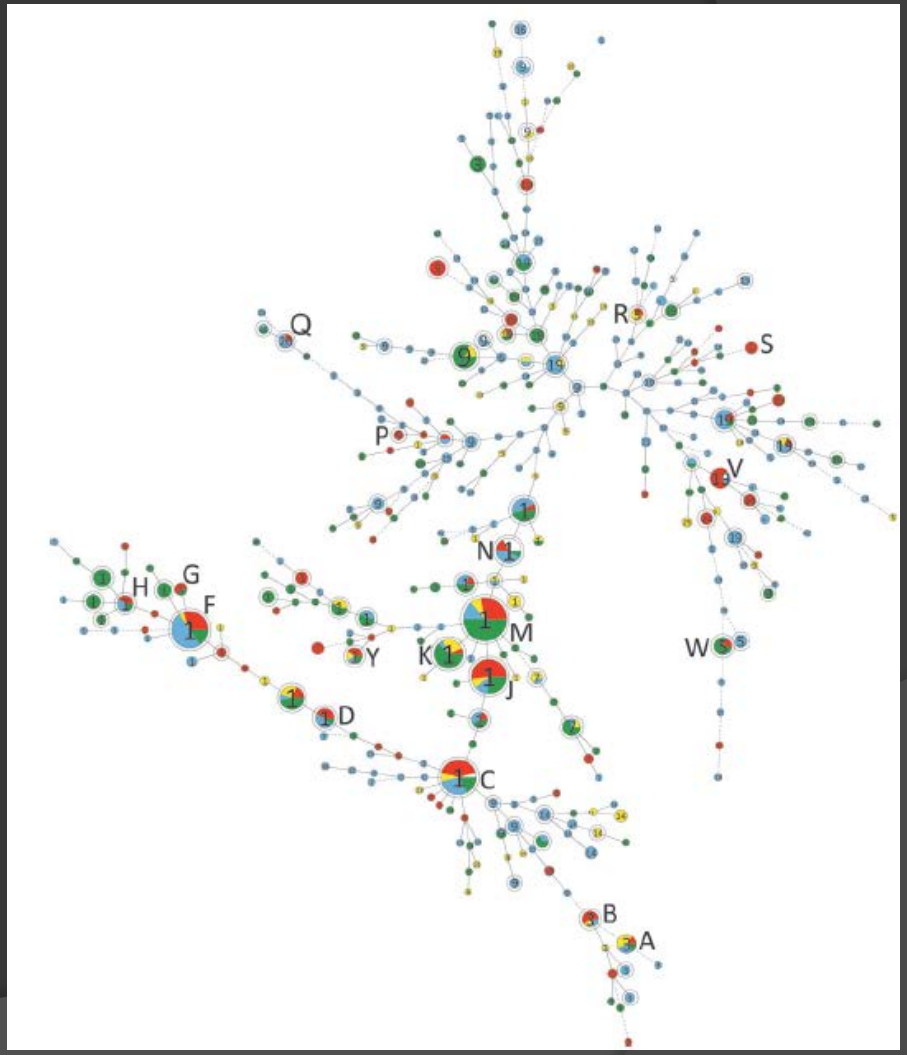


Figure 2. Minimum spanning tree depicting the detailed relationships between multilocus variable number of tandem repeats analysis (MLVA) genotypes in complexes M and N (Figure 1). Each circle represents 1 MLVA genotype scaled in size to the number of isolates comprising it. Numbers between genotypes indicate the summed tandem-repeat difference between them. The color coding of MLVA genotypes conforms to that in Figure 1. Numbers within genotypes represent the study day(s) on which each isolate within the genotype was collected. Isolates with capital letters (A–F) indicate isolates from patients with HA *C. difficile* infection (HA-CDI) listed in Table 1; the source isolates for these cases based on epidemiological analysis are labeled by corresponding lower-case letters (a–f). One isolate labeled e/E is both a hospital-associated CDI case isolate as well as a source for a subsequent case. The MLVA genotype indicated by the arrow shows an example of a *C. difficile* genotype recovered by screening tests only that was essential to the formation of a complex.

30% (17/56) HAI cases with associated with CDI patients

29% (16/56) HAI cases associated with carriers

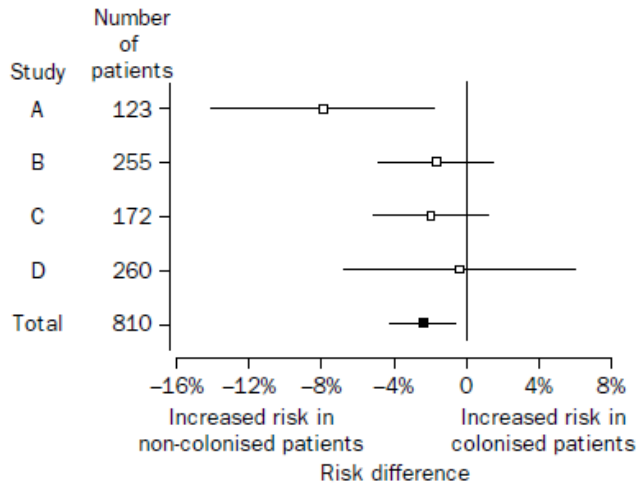


Clinical Infectious Diseases 2013;57(8):1094–102

Decrease risk of infection?

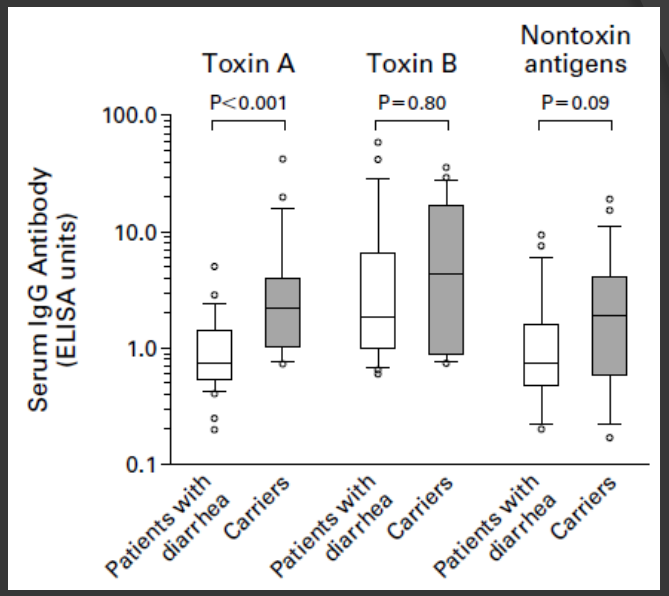
	Prospective study				Total
	A	B	C	D	
Non-colonised					
Number of patients	88	172	149	209	618
Weeks of observation (mean [SD])	148·5 (1·7 [1·2])	292·5 (1·7 [1·3])	236·5 (1·6 [0·8])	388·5 (1·9 [1·5])	1066·0 (1·7 [1·3])
Number of CDAD cases	7 (8·0%)	3 (1·7%)	3 (2·0%)	9 (4·3%)	22
Colonised					
Number of patients	35	83	23	51	192
Weeks of observation (mean [SD])	35 ·5 (1·0 [1·0])	110 (1·3 [1·8])	33·4 (1·5 [1·1])	103·5 (2·0 [1·4])	282·4 (1·5 [1·5])
Number of CDAD cases	0	0	0	2 (3·9%)	2

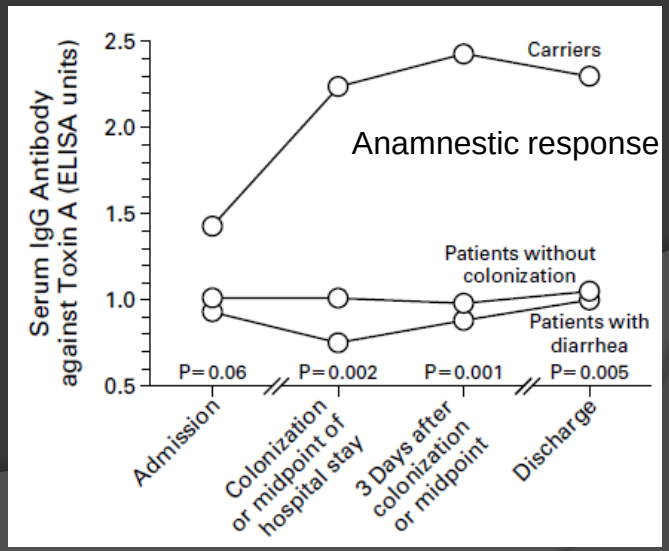
Table 1: **Rate of CDAD and weeks of observation for all patients initially colonised and non-colonised with *C difficile***



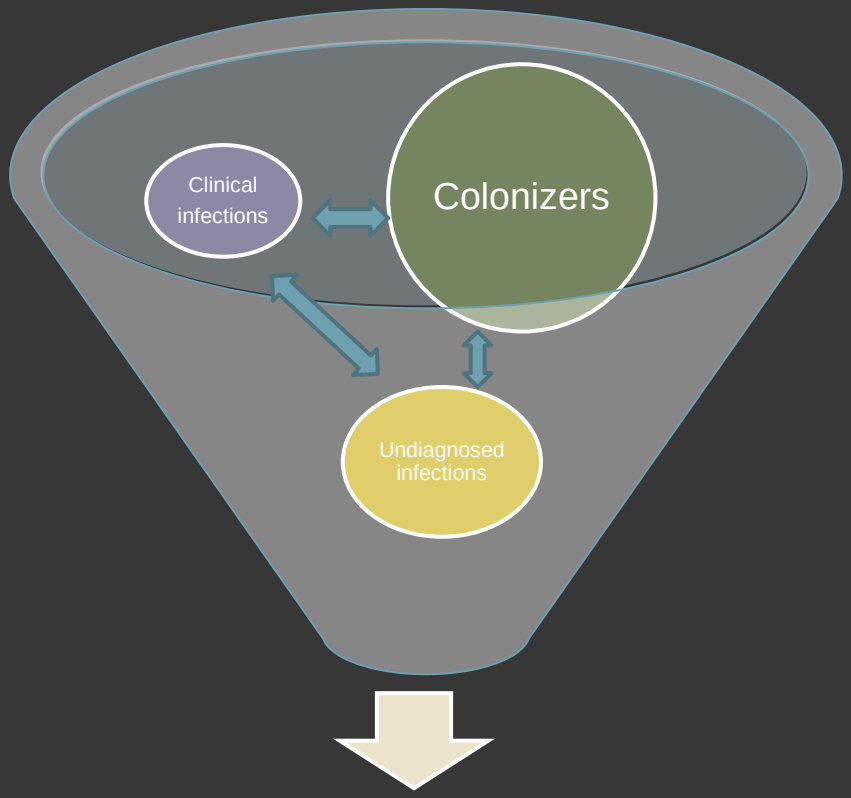
Risk difference (95% CI) for CDAD among patients initially colonised and non-colonised with *C difficile* in four studies

Risk difference pooled across studies with a random effects model[14] is shown in bottom row (total).





Dynamics of transmission, colonization & infection



20% patients admitted to Medical Department are Nursing home residents

Moderate increase in CDI

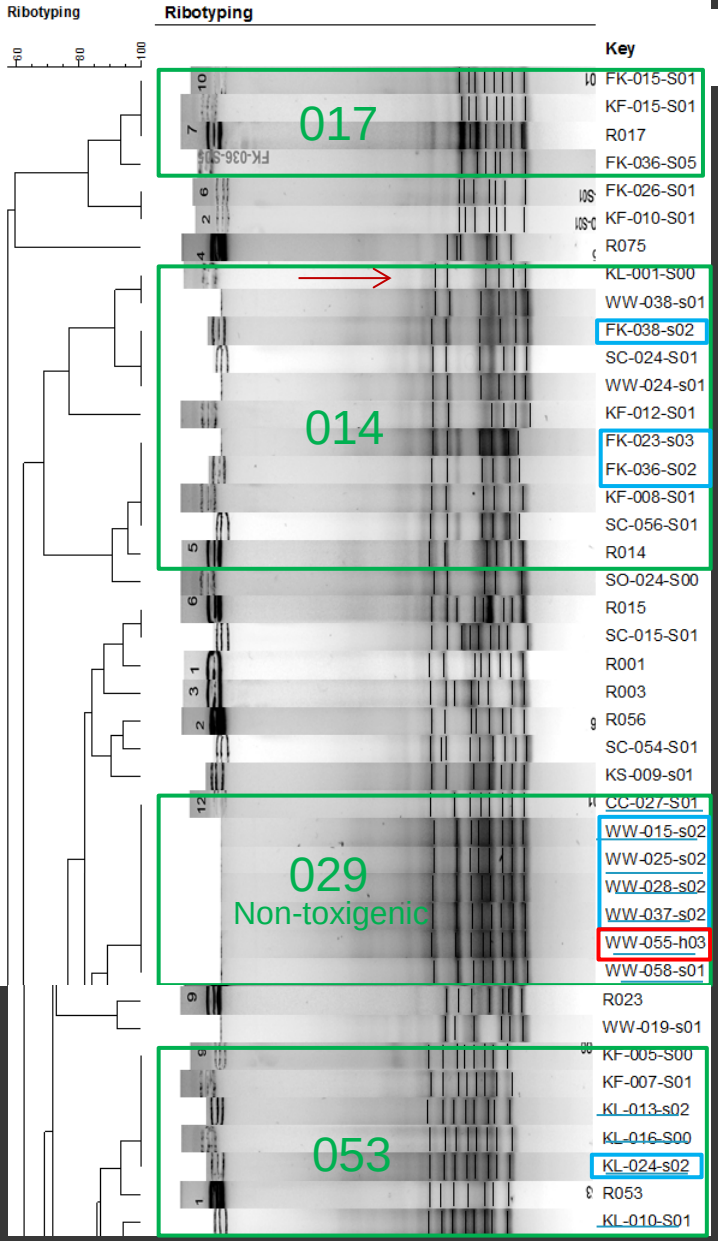
Table 3 MLVA profile of the isolates obtained from each nursing home resident

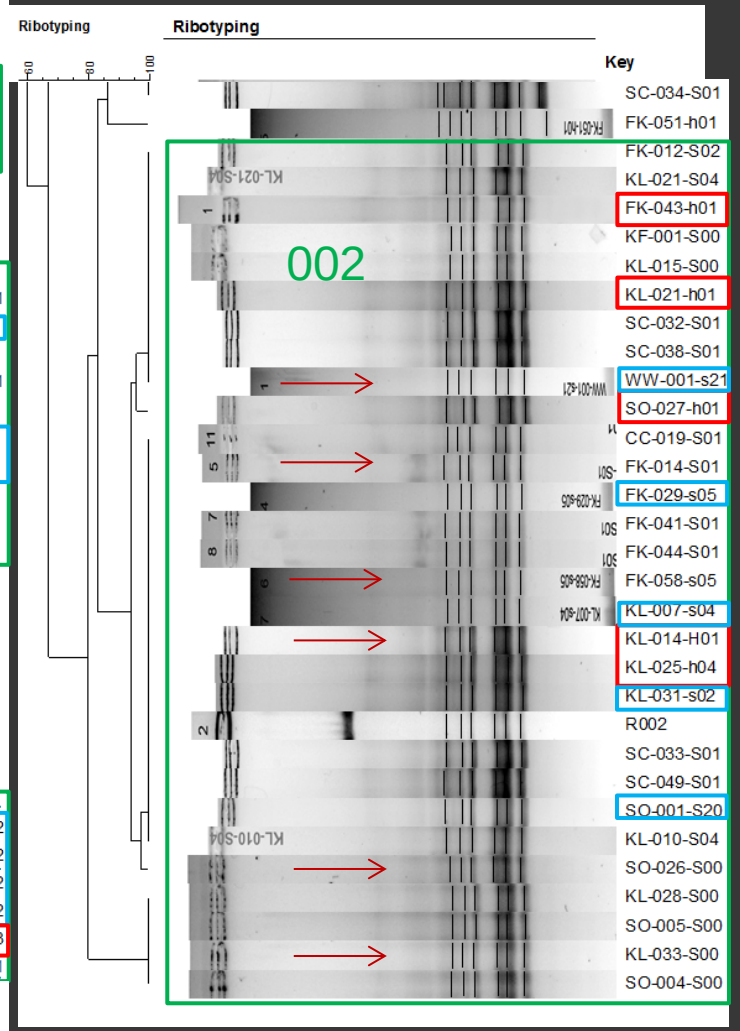
PCR-Ribotype	MLVA profile								Resident number	No. of isolates	Week
	A6	B7	C6	E7	G8	CDR5	CDR60	Total			
027	22	9	38	10	17.5	3.9	7.2	107.6	15	4	1[E] 2[E] 6[E] 7[E]
									18	1	5[E]
	23	9	38	10	17.5	3.9	7.2	108.6	15	1	3[E]
	22	9	39	10	17.5	3.9	7.2	108.6	15	1	7[D]
	22.2	9	37.8	10	17.5	3.9	7.2	107.6	15	3	9[D] 10[E] 14[E]
									18	1	15[E]
									19	1	12[D]
	22.2	9	37.8	10	17.5	3.8	7.2	107.5	15	1	8[E]
	22	9	37.8	10	17.5	3.8	7.2	107.3	15	1	9[E]
	23	9	37.8	10	17.5	3.8	7.2	108.3	15	1	12[D]
	22.2	9	26.5	10	18.5	3.9	7.2	97.3	15	1	12[E]
	23	9	40	10	17.5	3.9	7.1	110.5	18	1	2[E]
	22	9	36.8	10	17.5	3.9	7.2	106.4	18	1	7[D]
	22.2	9	37.8	10	17.6	3.9	7.2	107.7	18	1	7 [E]
	23	9	36.8	10	17.5	3.8	7.2	107.3	18	1	9 [E]
	22	9	37	10	17.5	3.9	7.2	106.6	19	1	3 [E]
	22.2	9	36.8	10	17.5	3.8	7.2	106.5	19	2	7 [E] 11[E]
UCL16a	30.8	14.1	23.5[a]	5	10.8	6.8	3.2	94.2	1	1	1[E]
	30.8	14	23.5	5	10.8	6.8	3.2	94.1	1	2	2[E] 16[E]
	30.8	14	24.5	5	10.8	6.8	3.2	95.1	1	1	10[E]
	30.7[b]	14[c]	11.3	5	10.8	6.8	3.2	81.8	1	1	11[E]
	29.8	14	23.5	5	10.8	6.8	3.2	93.1	1	2	12[E] 16[D]
	31.8[d]	14	23.5	5	10.8	6.8	3.2	95.1	1	1	14[D]
UCL46	28.8	21.1	22.3	14	8	8.8	2.2	105.2	19	1	1[E]
	28.8	21.1	22.5	14	8	8.8	2.3	105.5	19	1	2[E]
UCL36	19.2	17	42.8	8	9.9	4.9	10.2	112	13	1	1[D]
	18.3	16	42.8	8	9.9	4.9	10.2	110[e]	13	1	1[E]
	18.3	16	36.8	8	9.9	4.9	10.2	104.1	13	1	2[D]
	19.2	16.1[f]	41.8	8	9.9	4.9	10.2	110.1	13	1	2[E]
	30.8	17	34.7	8	10.8	4.9	10.2	117.4	17	1	8[E]
	31.8	17.1	34.7	8	10.8	4.9	10.2	118.5	19	1	7[D]
	31.8	17	34.8	8	10.8	4.9	10.2	118.5	24	1	3[D]
	31.8	17	34.7	8	10.8	4.9	10.2	118.4	24	1	5[E]
	31.8	18.1[g]	35.8	8	10.8	4.9	10.2	120.6	24	1	8[E]

Differences found in the results after one or more repetitions: [a]24.5; [b]30.8; [c]17.3; [d]26.9; [e]10.3; [f]16; [g]18

[E] Strain isolated after 3 days of feces enrichment

[D] Strain isolated after direct culture of the feces

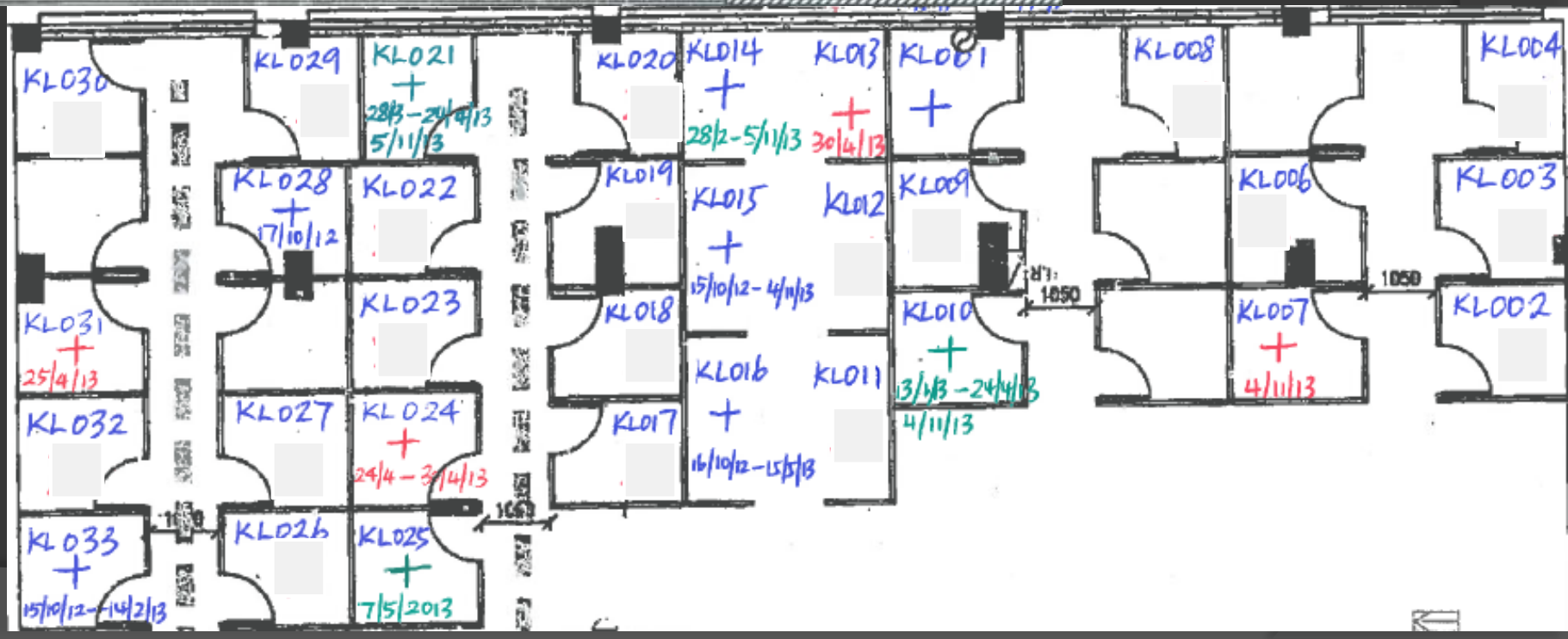




Hospital acquired
N=8 (5 isolates r002)

Nursing home
acquired N=16
(5 isolates r002)


ISOLATION ROOM
A11
Store Room
A10
A9
Store Room
Living Room
A12
ISOLATION ROOM
A13
A17
A18
A15
A16
A8
A7
A6
A5
A3
A2
A1
B9
B10
B11
B12
B13
B15
B16
B17
MEDICAL ROOM
STORE ROOM
FEMALE TOILET
ISOLATION ROOM
Not covered
+ RCHE Acquired C. Diff
+ Hospital Acquired C. Diff
+ Baseline +ve


KL030
KL029
KL021
+
28/3 - 24/4/13
5/11/13
KL020
KL014
+
28/2 - 5/11/13
KL013
+
30/4/13
KL001
+
KL008
KL004
KL028
+
17/10/12
KL022
KL019
KL015
+
15/10/12 - 4/11/13
KL012
KL009
KL006
KL003
KL031
+
25/4/13
KL023
KL018
KL010
+
13/1/13 - 24/4/13
4/11/13
KL007
+
4/11/13
KL002
KL032
KL027
KL024
+
24/4 - 3/4/13
KL017
KL016
+
16/10/12 - 15/5/13
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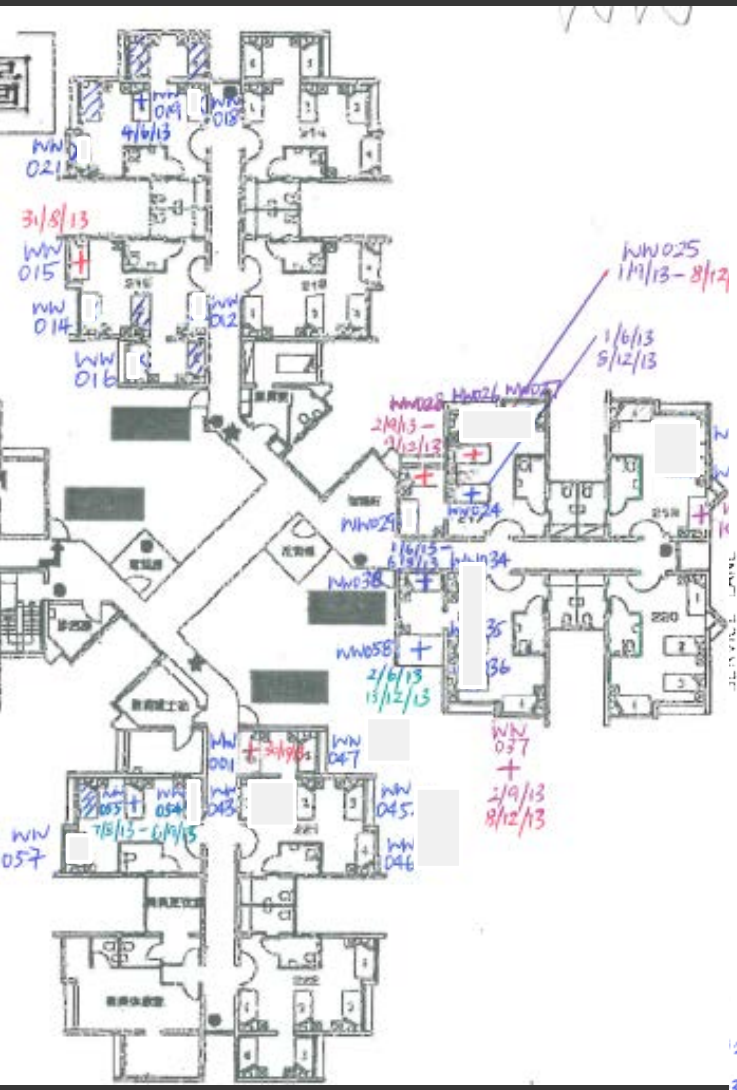
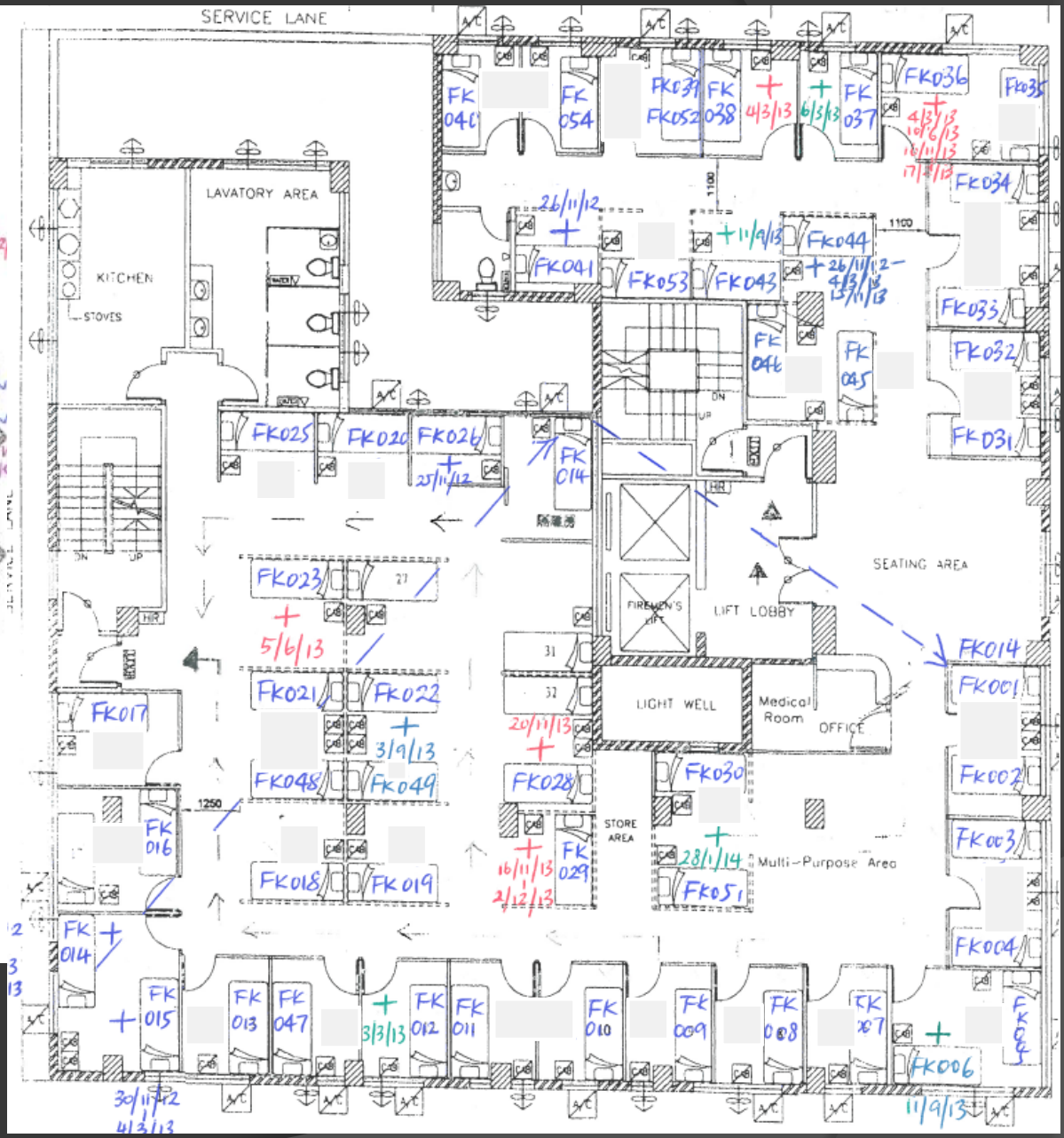
KL026
KL025
+
7/5/2013
1050
1050





+ RC+E Acquired C. Diff
+ Hospital Acquired C. Diff
+ Baseline +ve

Carriage of *C. difficile*

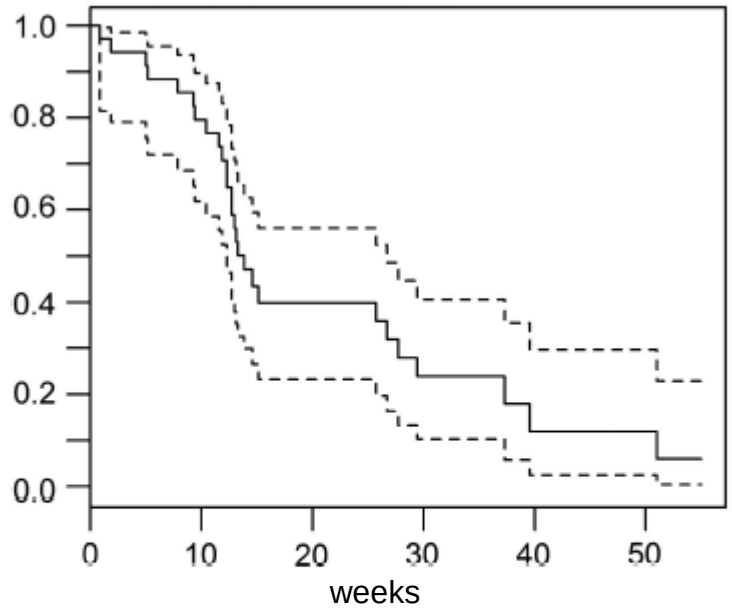


FIGURE 1. Kaplan-Meier estimate of the duration of *Clostridium difficile* carriage for the 35 nursing home residents with a follow-up duration ≥90 days with positive cultures at baseline sampling or sampling upon nursing home residence. The dotted lines show the 95% confidence interval of the curve.

Most spontaneously clear by 2 months

>=3 months 19%

Clin Infect Dis 1993;17:672-678.

K-M estimate of median carriage duration 13 weeks
Mark variation – 2 residents >10 months

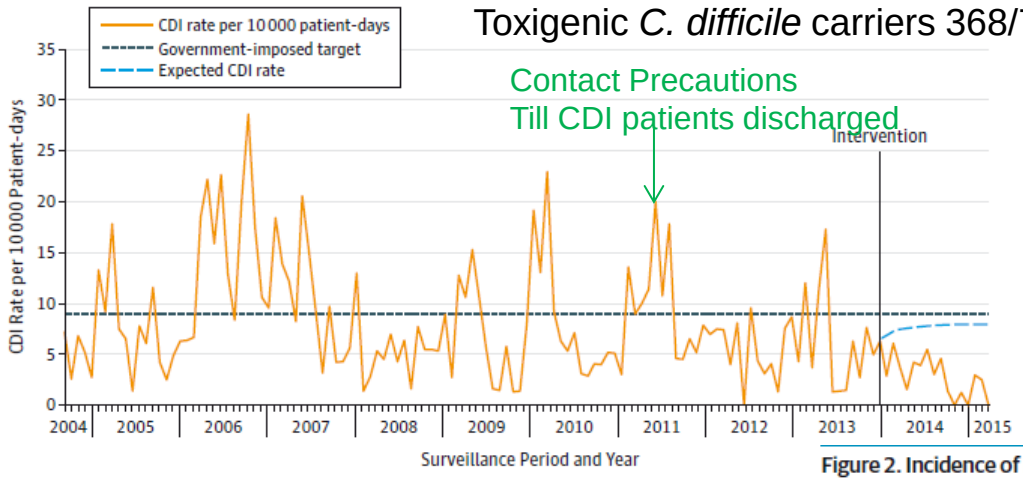
Take home messages

- For residents (N=36) who had toxigenic *C. difficile* isolated in this study, 8 (22%) had been admitted to hospitals with the presentation of acute diarrhea
- Stool specimens of only 2 patients were sent for toxigenic *C. difficile*
- There should be clinical suspicion for nursing-home-onset CDI.

Screening & contact precautions considered?

JAMA Intern Med. 2016;176(6):796-804. doi:10.1001/jamainternmed.2016.0177

Figure 1. Incidence of Health Care–Associated *Clostridium difficile* Infection (CDI) per 4-Week Period According to Standardized Surveillance Definitions, August 2004 to March 2015, Québec Heart and Lung Institute, Québec City, Canada



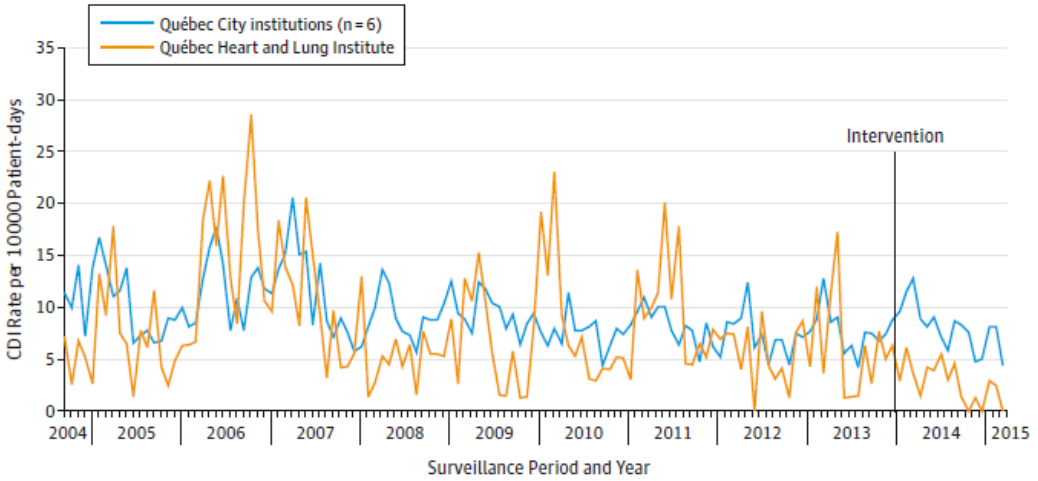
Toxigenic *C. difficile* carriers 368/7599 (4.8%)

Contact Precautions
Till CDI patients discharged

An intervention consisting of screening and isolation of *C difficile* asymptomatic carriers was introduced on November 19, 2013. The institution is subjected to a government-imposed threshold of 9.0 per 10 000 patient-days (dashed black line). The expected CDI rate during the intervention using an autoregressive integrated moving

Number needed to screen: 121
Number of asymptomatic carriers needed to isolate: 6
US$130,000 versus $627,000 (Test/isolation costs vs 63 cases of CDI prevented)

Figure 2. Incidence of Health Care–Associated *Clostridium difficile* Infection (CDI) per 4-Week Period at the Québec Heart and Lung Institute and in 2 Control Groups, August 2004 to March 2015



Summary

- Nursing home residents in Hong Kong were at substantial risk for *C. difficile* colonization and acquisition.
- Carriage could be prolonged for more than 3 months for the majority of the patients.
- Presence of nasogastric tube was an independent risk factor associated for carriage.
- Underscored the importance of adherence to hand hygiene in procedures such as diaper change and feeding via nasogastric tube.
- The predominance of *C. difficile ribotype 002* confirmed that nursing homes as epicenters in sustaining the transmission across the continuum of care