

Table S1- Characteristics of included studies addressing risk factors for recurrence

Study Year of diagnosis* Country	Design	Diagnostic test	Follow- up period	Time between episodes (days)	Population	Comparison group	Quality variables	Mean/median age $\pm$ SD Dispersion	N	% Recurrence (n)	Method	Nv	EPV
Choi 2011 [95] 2008-2010 Korea	RC	NS toxin essay	NA	<60	Inpatients >15years with CDI, pseudomembranous colitis or diarrhoea	Non recurrent	SI, IS, RS, AB, AU	62.5 ^y 15-84	84	13.1 (11)	MLR	11	1
Do 1998 [39] 1993-1994 Canada	RCC	Toxigenic culture	NA	45	Adult inpatients with ≥ 2 CDI episodes	Patients with 1 CDI episode	SI, PE, IS, AB, AU	77 ^y 28-92	59	22 (13)	MLR	4	3.3
Drekonja 2011 [34] 2004-2006 USA	RC	Culture or NS toxin essay	NA	90	New CDI case in Veterans Affairs	Users/non- users of non-CDI antimicrobials > 30 days after CDI	SI, IS, RS, AB, AU	71 $\pm$ 13 ^s	246	30 (74)	MLR	8	9.2
Eyre 2012 [25] 2006-2010 UK	PC	Toxin A and B EIA	≥ 90	≥ 14	Adult inpatients with 1 st CDI	Non recurrent	SI, PE, IS, RS	77 ^y IQR=64- 85	1678	22 (393)	Cox hazards model	12	32.7
Fekety 1997 [71] NR USA	RCT	Culture or NS toxin essay	60	< 60	Patients with CDI assigned to placebo in double-blind trial	Patients with a history of recurrent CDI	PE, IS, RS, AB	59.2 ^s $\pm$ 21.1	67	51 (34)	MLR	13	1.9
Freedberg 2013 [27] 2009- 2012 USA	RC	PCR (toxin B)	90	15 to 90	Inpatients with primary CDI	Non recurrent	SI, PE, IS, AB, AU	64 ^s $\pm$ 19	894	18.7 (167)	Cox hazards model	10	16.7
Garey 2010 [40] 2007-2008 USA	PC	Direct CTA	90	< 48h of Abx completion	Inpatients with primary CDI	Non recurrent	RS, AB, AU	61 ^s $\pm$ 16	96	24 (23)	MLR	NR	-
Kim 2010 [30] 2006-2007 Korea	RC	Toxin A and B EIA	90	90	Inpatients with primary CDI	Non recurrent	SI, AB, AU	67.6 ^s $\pm$ 13.9	125	21.6 (27)	MLR	4	6.8
Kim 2012 [35] 2004-2008 Korea	RCC	Toxin A and B EIA	NA	30	Patients with primary CDI	Non recurrent	SI, PE, IS, RS, AB, AU	66.8 ^s $\pm$ 2.7	42	14.1 (28)	Propensity score MLR	7	3.1
Kyne 2001 [32] 1998 USA	PC	Toxin A EIA or direct CTA	60	> 48h	Inpatients with CDI	Patients with one CDI episode	IS, AU	70 $\pm$ 20 ^s 34-95	63	35 (22)	MLR	10	2.2
Lavergne 2013 [29] 2009-2010 Canada	PC	2-step approach: glutamate dehydrogenase (GDH) EIA, and direct CTA	60	< 60 of treatment completion	Adult inpatients with primary CDI	Non recurrent	SI, PE, AB, AU	77 ^y 65-84	121	33.1 (40)	Cox hazards model	4	10

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Linsky 2010 [20] 2004-2008 USA	RC	Toxin A and B EIA	NA	15-90	Patients from VA with CDI exposed to PPIs	Patients not exposed to PPIs	SI, IS, AB, AU	74 [¥] 63-82	1166	21.5 (251)	Cox hazards model	10	25.1
Louie 2013 [36] 2006- 2009 Multicentre	RCT	Toxin A or B EIA	40	28	CDI patients randomly receiving oral vancomycin or fidaxomicin	Non recurrent	PE, AB	NR	567	NR	MLR	4	-
Marsh 2012 [38] 2001- 2009 USA	RC	Direct CTA	NA	14	Patients with recurrent CDI	Patients with reinfection	PE, IS, AB, AU	64 [¥]	82	62.2 (51)	MLR	13	4
McFarland 1999 [28] 1993-1996 USA	RCT	Culture, toxin A EIA or direct cytotoxin assay	60	60	Patients with recurrent CDI treated with Abx and placebo in a clinical trial	Non recurrent	PE, AB	62.1 $\pm$ 18.5 [§]	103	41.7 (43)	MLR	15	2.9
Pepin 2005 [31] 1991-2004 Canada	RC	Direct CTA	NA	60	Inpatients with CDI	Non recurrent	SI, PE, IS, RS, AB	All ages	2042	11.9 (243)	Cox hazards model	9	27
Petrella 2012 [33] 2006- 2009 Multicentre			Same as Louie 2013 [36]				PE, AB	NR	999	18.9 (150/794)	MLR	9	16.7
Shakov 2011[96] 2003-2008 USA	RC	NS toxin A and B assay	NA	< 180	Inpatients with CDI	Patients without readmission for CDI	AB, AU	74 [¥] 59.8- 82.0	247	30.7 (76)	MLR	7	10.9
Stewart 2013[37] NR USA	RC	PCR on positive culture	NR	21	Inpatients and outpatients with <i>C. difficile</i> positive stool	Non recurrent	RS, AU	64 $\pm$ 13 [§]	69	41 (28)	MLR	NR	-

Nv= number of variables in the final model. EPV=events per variable. MLR=multivariate logistic regression. NA=not applicable. NR=not reported.

*Year of diagnosis=year(s) of cases diagnosis. § Mean age; ¥ Median age.

Design= RC=retrospective cohort; PC=prospective cohort; RCC=retrospective case-control; PCC=prospective case-control.

NS=Not specified. EIA=Enzyme immunoassay. CTA=cytotoxin assay. PCR=Polymerase chain reaction;

Quality variables: SI= site of acquisition of the infection (nosocomial vs. community-acquired), PE= previous episode(s) of CDI, IS= immunosuppression, RS= recent surgeries and procedures, AB= recent antibiotherapy, AU= use of anti-ulcer medication.