Development of a Simple Clostridium Difficile Infection Clinical Risk Prediction Tool for Medical Inpatients

Winnie Ma, B.Sc.(Pharm), ACPR; Torey Lau B.Sc.(Pharm), ACPR; Vivian WY Leung B.Sc.(Pharm), Pharm.D, PhD, ACPR
Victoria Su B.Sc.(Pharm), Pharm.D, ACPR; Joseph Puyat, PhD, M.Sc, MA (Psych); Stephen Shalansky B.Sc.(Pharm), ACPR, Pharm.D

Background

- *Clostridium difficile* infection (CDI) remains a significant cause of hospital-acquired infectious diarrhea
- Risk prediction tools could potentially identify high-risk patients to reduce the risk of primary infection
- Various tools have been studied but none have been widely adopted, likely due to the complexities of existing tools and the need for clinical factors that are not readily accessible at the point-of-care.

Objectives

- To develop a simple risk prediction tool identifying medicine inpatients at high-risk of developing primary CDI

Methods

Design

- Single-centre case-control study

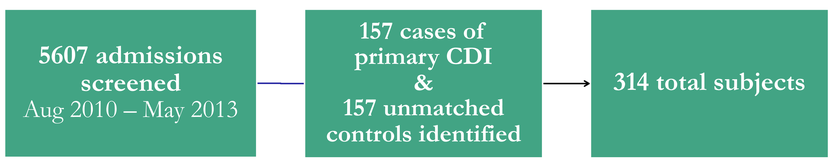
Patients

- Inclusion: Adults admitted to acute medicine service for ≥ 48 hours between Aug 2010 & May 2013
  - Cases: Positive *C. difficile* polymerase chain reaction (PCR) assay in loose stool
  - Controls: No positive *C. difficile* PCR assay, meeting inclusion criteria
- Exclusion: History of CDI in previous 60 days, active malignancy, inflammatory owel disease, hematologic stem cell transplant, solid organ transplant

Statistics

- Multivariable logistic regression analyses to identify most parsimonious variables that predict CDI – based on clinical relevance and availability at admission.
- Model fit evaluated by receiver operating characteristics (ROC) area under the curve (AUC), higher indicates better fit.
- Model parsimony assessed using Akaike Information Criterion (AIC) – lower AIC values preferred.
- Final prediction tool developed according to Framingham study risk score functions.
- Risk cut-points selected based on sensitivity and specificity associated with various thresholds of predicted risk.
- Strength of prediction tool evaluated using statistical measures of model discrimination (C statistic) and calibration (Brier score)

Figure 1. Subject Flow Chart



Results

Table 1. Patient Characteristics

	Case (N=157) n (%)	Controls (N=157) n (%)
Age, years		
Median (range)	72 (22 - 98)	61 (19 - 96)
Age ≤ 70	74 (47.1)	107 (68.2)
Age > 70	83 (52.9)	50 (31.8)
Sex		
Female	73 (46.5)	67 (42.7)
CDI>60 days prior to admission	11 (7.0)	3 (1.9)
Abdominal surgery	14 (8.9)	12 (7.6)
Antibiotic use within 3 months of admission	83 (52.9)	53 (33.8)
Medication use		
Immunosuppressants	7 (4.5)	4 (2.5)
Corticosteroids	19 (12.1)	23 (14.6)
H_2RA	20 (12.7)	9 (5.7)
PPI	70 (44.6)	49 (31.2)
Modified Horn's Disease Index		
Low	18 (11.5)	71 (45.2)
Moderate	51 (32.5)	56 (35.7)
Severe	56 (35.7)	24 (15.3)
Extreme	32 (20.4)	6 (3.8)

Table 2. Variables in final logistic regression for the CDI Clinical Risk Prediction Tool

	Case (N=157) n(%)	Control (N=157) n(%)	Regression Coefficients	Odds Ratio (95% CI) Adjusted/weighted
Age, years				
≤ 70	74 (47.1)	107 (68.2)		1 (ref. group)
> 70	83 (52.9)	50 (31.8)	1.0452	2.84 (1.52-5.31)
Modified Horn's Severity Index				
Low	18 (11.5)	71 (45.2)		1 (ref. group)
Moderate	51 (32.5)	56 (35.7)	1.1905	3.29 (1.67-6.47)
Severe	56 (35.7)	24 (15.3)	2.2362	9.36 (4.32-20.26)
Extreme	32 (20.4)	6 (3.8)	2.9152	18.45 (5.98-56.96)
Recent antibiotic use*				
No	74 (47.1)	104 (66.2)		1 (ref group)
Yes	83 (52.9)	53 (33.8)	0.5543	1.74 (0.95-3.19)

*Within 3 months of admission

Table 3. 5-Point CDI Clinical Risk Tool

	Points
Age group	
70 and under (reference)	0
Over 70	1
Modified Horn's Index	
Low (reference)	0
Moderate	1
Major	2
Extreme	3
Antibiotic within previous 3 months	
No (reference)	0
Yes	1
Total	/5

Table 4. Predicted CDI Risk based on 5-point Tool

Total Points	Model-Predicted Risk	True Positive (%)	False Positive (%)
0	0.0038	100.0	100.0
1	0.0109	100.0	100.0
2	0.0303	91.7	57.9
3	0.0816	74.5	31.8
4	0.2016	36.7	5.7
5	0.4180	5.7	0.6

Figure 2. ROC Curve for CDI Risk Prediction Model

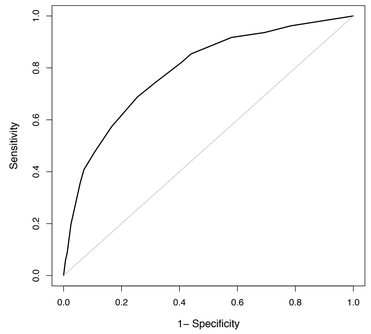


Figure 3. CDI Risk Prediction Model Calibration Plot

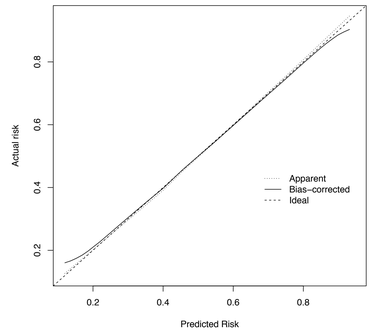
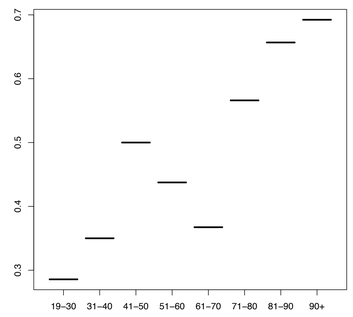


Figure 4. CDI risk by age



Discussion

- The C statistic of 0.79 indicates our model successfully discriminates between patients who developed CDI from those without CDI.
- Our model demonstrated reasonable calibration with Brier score of 0.188 and optimism of 0.04.
- We recommend using a score of 2 as an indication to implement CDI risk mitigating strategies. A score of 2 corresponds with a model-predicted risk of 3% which approximates the background incidence of 2.8%.
- Using higher cut-offs would result in a lower false positive rate, but also lower true positive detection rates.
- Limitations to our study include small sample size which may be the reason why in-patient antibiotic exposure was not found to significantly increase the risk of CDI. Inter-observer agreement was not assessed in our data collection process.

Conclusion

- We developed a simple, 3-vairable risk prediction tool based on age, disease severity and recent antibiotic use. Our 5-point risk tool allows for rapid assessment at the bedside
- Identification of high risk individuals allows for proactive interventions to mitigate the risk of primary CDI

Acknowledgements & Conflicts of Interest

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