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Version: Accepted Version

Proceedings Paper:

Monaghan, TM, Jilani, T, Hamed, M et al. (11 more authors) (2017) A Protein Microarray Assay For Predicting Severe Outcomes in Clostridium Difficile Infection. In: Gut. British Society of Gastroenterology Annual General Meeting, 19-22 Jun 2017, Manchester, UK. BMJ Publishing Group , A31-A31.

<https://doi.org/10.1136/gutjnl-2017-314472.58>

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A PROTEIN MICROARRAY ASSAY FOR PREDICTING SEVERE OUTCOMES IN CLOSTRIDIUM DIFFICILE INFECTION

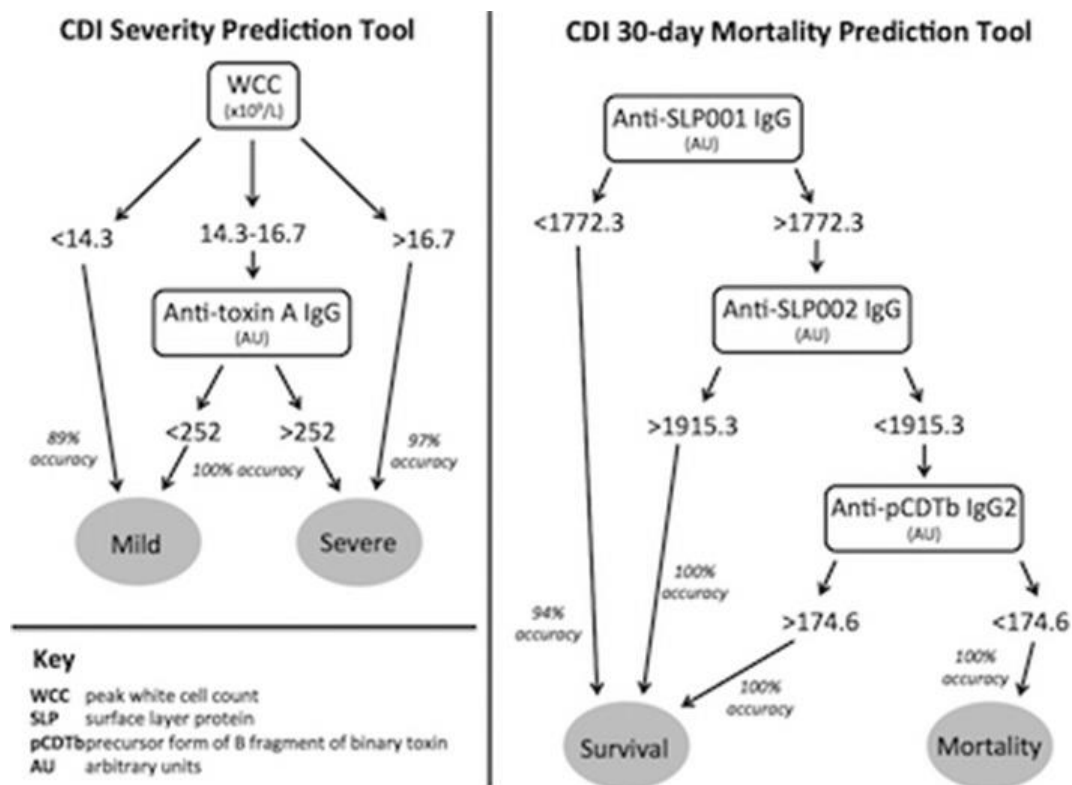
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Introduction The impact of host biomarkers on predicting clinical outcomes in *C. difficile* infection (CDI) has rarely been assessed using integrated clinical and immune data sets. We aimed to identify host systemic immune and clinical factors associated with severe CDI and mortality using microarray technology.

Method We analysed data from a prospective cohort of inpatients at Nottingham University Hospitals NHS Trust from 2009 to 2013. Co-morbidities, history, laboratory data, imaging and endoscopy data were recorded. Serum subclass and strain-specific anti-toxin and anti-surface layer protein (SLP) antibody responses were determined by an established and validated *C. difficile* antigen-specific protein microarray. Anti-toxin A and B neutralising antibodies (NAb) were assessed using a Caco-2 cellbased NAb assay. A reverse-phase protein microarray assay was used for the simultaneous quantification of serum interleukin-(IL-) 1-a, IL-1-b, IL-6, IL-8, IL-12/IL-23, IL-27, tumour necrosis factor-a, granulocyte-macrophage colony stimulating factor, interferon-g (IFN-g), transforming growth factor-b. Logistic regression models with univariate and multivariate analyses were used.

Results Of 151 study subjects (52.3% female, median age 72y, range 19-98y), severe CDI was present in 32%; 30 day mortality was 8.6%. For severity, peak white cell count (109/L) is partitioned into 3 categories. Anti-toxin A IgG is partitioned into 2 categories. Using these two factors alone a clinical prediction rule can be produced (figure) which correctly categorised 91.3% of the cohort into mild or severe. Accuracy can be further improved by examining IFN-g, anti-SLP001 IgA, anti-toxin B IgG2. For 30 day mortality, anti-SLP001 IgG, anti-SLP002 IgG and anti-pCDTb IgG2 were each partitioned into 2 categories. Using these 3 factors, a predictive tool for 30 day mortality was able to correctly categorise 94.7% of the cohort. Accuracy can be further improved by examining anti-toxin B IgG, anti-toxin B IgA and anti-SLP001 IgA.

Conclusion We present two novel microarray-based clinical risk stratification tools for patients with CDI who may benefit from receiving early, more aggressive and personalised treatment interventions. These models correctly categorise severity and 30 day all-cause mortality in 91.3% and 94.7% of this cohort respectively.



Abstract OC-058 Figure 1

Disclosure of Interest T. Monaghan: None Declared, T. Jilani: None Declared, M. Hamed: None Declared, O. Ahmad: None Declared, B. MacKenzie: None Declared, D. Humphreys Conflict with: Owns UCB stock options, C. Shone: None Declared, K. R. Acharya: None Declared, C. Loscher: None Declared, I. Marszalowska: None Declared, M. Lynch: None Declared, M. Wilcox Conflict with: Astellas, AstraZeneca, Abbott, Actelion, Alere, Bayer, bioMerieux, Cerexa, Cubist, Da Volterra, Durata, Merck, Nabriva, Pfizer, Qiagen, Roche, Seres, Synthetic Biologics, Conflict with: As per grant/research support, P. Quinlan: None Declared, O. Negm: None Declared