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# Multivariate analysis of factors affecting Clostridium difficile infection rates; the more you look, the more you find, but should you believe what you see?

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**Background:** *C. difficile* infection (CDI) rates are increasing in many settings. It is suggested in the literature that reported rates can be impacted by factors including testing frequency and diagnostic

methods; albeit based on univariate analyses. We aimed to describe the impact of multiple factors on CDI rates using a multivariate model.

**Material/methods:** Up to 40 institutions/hospitals in each of five countries (France, Germany, Italy, Spain & UK) (total = 189) provided data on the size and type of institution, *C. difficile* testing methodology, monthly numbers of tests performed and monthly patient bed days (pbds). Incidence rates were compared between countries, different sized institutions, types of institutions (acute/primary, secondary, tertiary, Long-term healthcare facilities) and testing method (recommended testing algorithms (GDH/toxin or NAAT/toxin) versus non-recommended methods (including, but not limited to, not detecting toxin e.g. NAAT alone, or only detecting toxin (EIA alone)). Multivariate logistic regression included these variables: testing rate/10,000pbds, institution size, institution type, country, testing method and test month.

**Results:** Univariate analysis demonstrated that the highest rates of CDI/10,000pbds were observed in Italian institutions (average 11.8/10,000pbds/ institution/month), acute/primary hospitals (12.3/10,000pbds/hospital/month), small institutions (16.7/10,000pbds/ institution/month), and those institutions using methods that do not detect toxin (10.7/10,000pbds/ institution/month).

After testing density was taken into consideration, the highest incidence rates were still seen in Italian institutions, and in those institutions using methods that do not detect toxin. There was a large shift in rates according to institution type however; long-term healthcare facilities now had a similar CDI/test rate as acute/primary hospitals (13.9 and 12.5 CDI cases/10,000pbds per tests/10,000pbds/hospital/month, respectively), although these were still higher than the rates at other institution types. Size of institution no longer influenced the CDI rate.

Once testing density had been taken into account, winter peaks in CDI rates were only seen in those institutions using standalone toxin detection methods, with an annual average of 10.1/10,000pbds, but 5.5/10,000pbds vs 18.3/10,000pbds in summer vs winter, respectively.

Following multivariate analysis testing method ($p = 0.045$), type of institution ($p = 0.003$) and the testing density ($p = <0.001$) remained significant predictors of CDI rate. The sizes of the effects indicated that testing density has the biggest impact on CDI rates.

**Conclusions:** Testing density has the largest effect on reported CDI rates. Use of standalone NAAT testing still results in higher CDI rates even when testing density is taken into account; this is consistent with a test that 'overcalls' true CDI. Low testing density can mask the true burden of CDI, such as in long-term healthcare facilities, highlighting the importance of good quality surveillance. Lastly, month of testing was not significant in the multivariate model, demonstrating the non-seasonal nature of CDI.