

Clostridium difficile Pseudo-outbreak: Effect of a Suboptimal Assay Lot on Perceived C. difficile Incidence

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Abstract

Background: Since 2000 there has been an increase in incidence and morbidity of *Clostridium difficile* - associated disease (CDAD) in North America. Most hospital laboratories use positive *C. difficile* toxin EIA assays to diagnose CDAD. We describe a five-week increase in CDAD corresponding to a specific EIA assay lot.

Objective: To determine the impact of a suboptimal assay lot on CDAD incidence and proportion of positive *C. difficile* toxin tests in hospitalized patients at a tertiary care center.

Methods: Barnes-Jewish Hospital, a 1250-bed hospital, has used the Remel ProSpecT *C. difficile* Toxin A/B Microplate Assay since 7/1/04. Hospital lab-based CDAD surveillance detected a large increase in the CDAD rate in 11/05. Initial investigation revealed the increase was associated with a change in toxin assay lot numbers. Run-control & chi square tests were done to determine if the identified toxin assay lot was associated with a significant change in the CDAD rate & proportion of positive toxin assays.

Results: From 7/04 until 10/05 the average monthly CDAD incidence rate was 1.5/1000 patient days (pt-days). In 11/05 the CDAD rate increased to 2.6/1000 pt-days ($p < .01$). The microbiology laboratory was contacted to determine if there were any changes in *C. difficile* testing. The increase in the number of positive toxin assays correlated with a change in the toxin assay lot number. The total proportion of positive assays from 7/04 to 10/05 was 13.6% (1490/10942). In 11/05, the proportion of positive assays increased to 22.1% (148/671) ($p < .01$). The CDAD rate and proportion positive toxin assays decreased to an average of 1.3/1000 pt-days ($p < .01$) and 11.8% (624/5284) ($p < .01$), respectively, over the next 7 months after the lot in question was no longer used. The increase in CDAD incidence and proportion of positive toxin assays in 11/05 was significant by run control analyses using >3 standard deviations above the mean as a cut off.

The manufacturer was contacted and verified that the lot in question was prone to degradation with storage, causing negative specimens to appear weakly positive. Our laboratory confirmed a high number of weakly positive assays associated with the lot in question.

Conclusions: The first step in outbreak investigation is to confirm a true increase in disease incidence. We identified a CDAD pseudo-outbreak that was due to a faulty lot of toxin assays. Early steps in finding a cause for the perceived increase in CDAD prior to enhancing CDAD containment measures likely saved resources. Our microbiology laboratory now uses the proportion of positive toxin assays to assess quality control.

Introduction

• Since 2000 there has been an increase in the incidence and morbidity of *Clostridium difficile*-associated disease (CDAD) in North America¹.

• Most hospital laboratories use positive *C. difficile* toxin EIA assays to diagnose CDAD.

• The purpose of this study was to describe a 5-week increase in CDAD corresponding to a specific EIA assay lot, to determine the impact of a suboptimal assay lot on CDAD incidence and proportion of positive *C. difficile* toxin tests in hospitalized patients at a tertiary care center, and to describe the steps taken to identify the increase as a pseudo-outbreak, before committing additional resources.

Methods

• **Design:** Outbreak investigation

• **Setting:** 1250-bed, academic, tertiary care hospital.

• **Definitions:**

• Case of CDAD was defined as a patient with a stool toxin assay positive for *Clostridium difficile*.

• CDAD rate was defined as the number of assays positive >48 hours from admission per 1,000 patient-days (pt-days).

• **Data collection:**

• The laboratory performed *C. difficile* toxin assays only on unformed stool samples, and did not test stool samples from patients whose stool tested positive for the toxin in the previous seven days.

• Our hospital microbiology laboratory has been using the Remel ProSpecT *C. difficile* Toxin A/B Microplate Assay for detection of *C. difficile* toxin since July 1st, 2004².

• In November of 2005, hospital lab-based surveillance detected a large increase in CDAD rate.

• Initial investigation revealed the increase was associated with a change in toxin assay lot numbers.

• **Data analysis:**

• Run-control chart & chi square tests were performed to determine if the increase in CDAD rate and proportion of positive toxin assays associated with the suspect toxin assay lot were significantly different from before and after the lot was used.

• Data was analyzed using SPSS 15.0.

References:

1. Kuijper EJ, Coignard B, Tüll P, ESCMID Study Group for Clostridium difficile; EU Member states; European Centre for Disease Prevention and Control. Emergence of Clostridium difficile-associate disease in North America and Europe. Clin Microbiol Infect. 2006 Oct; 12 Suppl 6:2. Review.
2. Remel ProSpecT *C. difficile* Toxin A/B Microplate Assay, 96 well/kit. Package Insert – English. January 7, 2005.

Figure 1. CDAD Incidence: 7/04 – 6/06

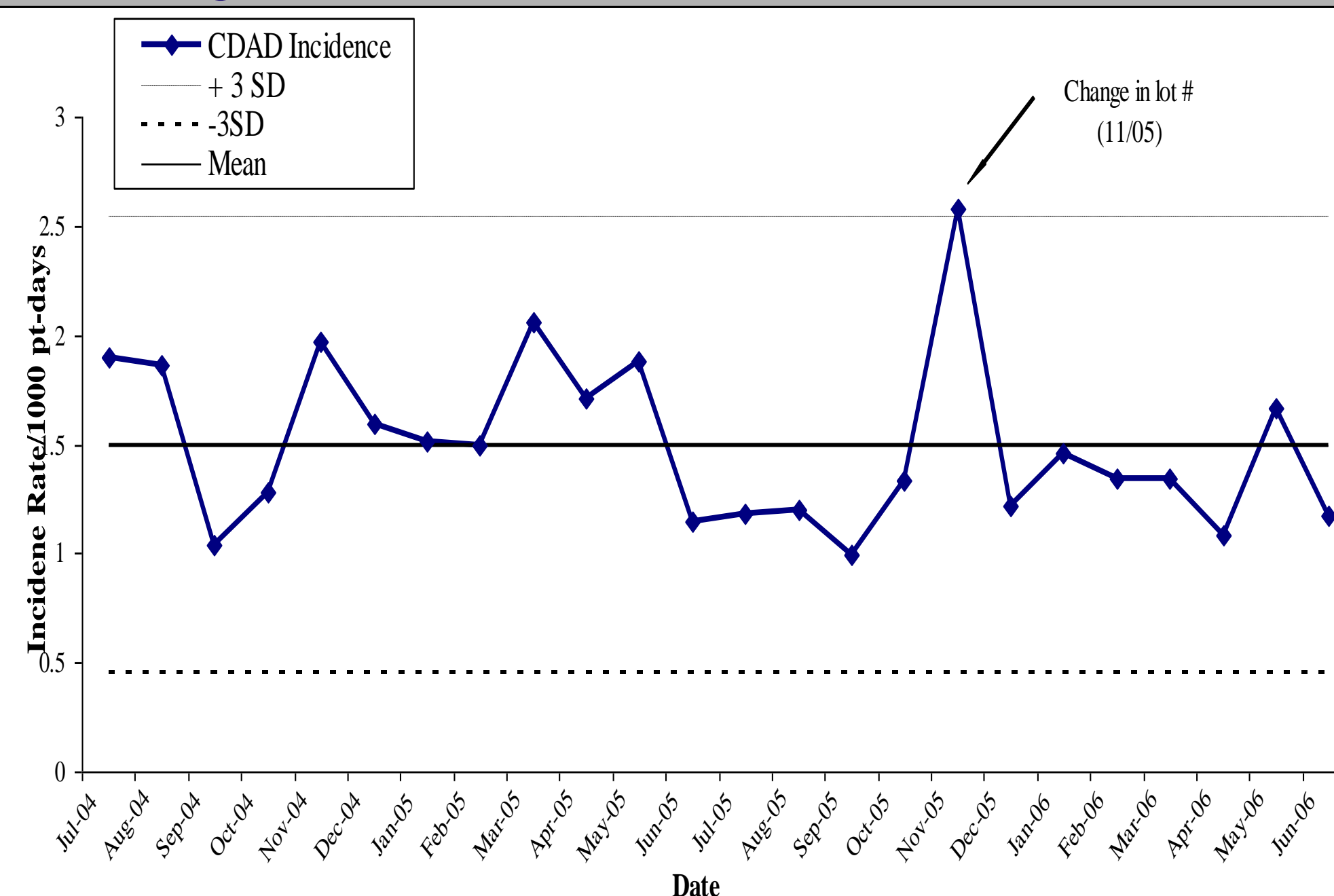
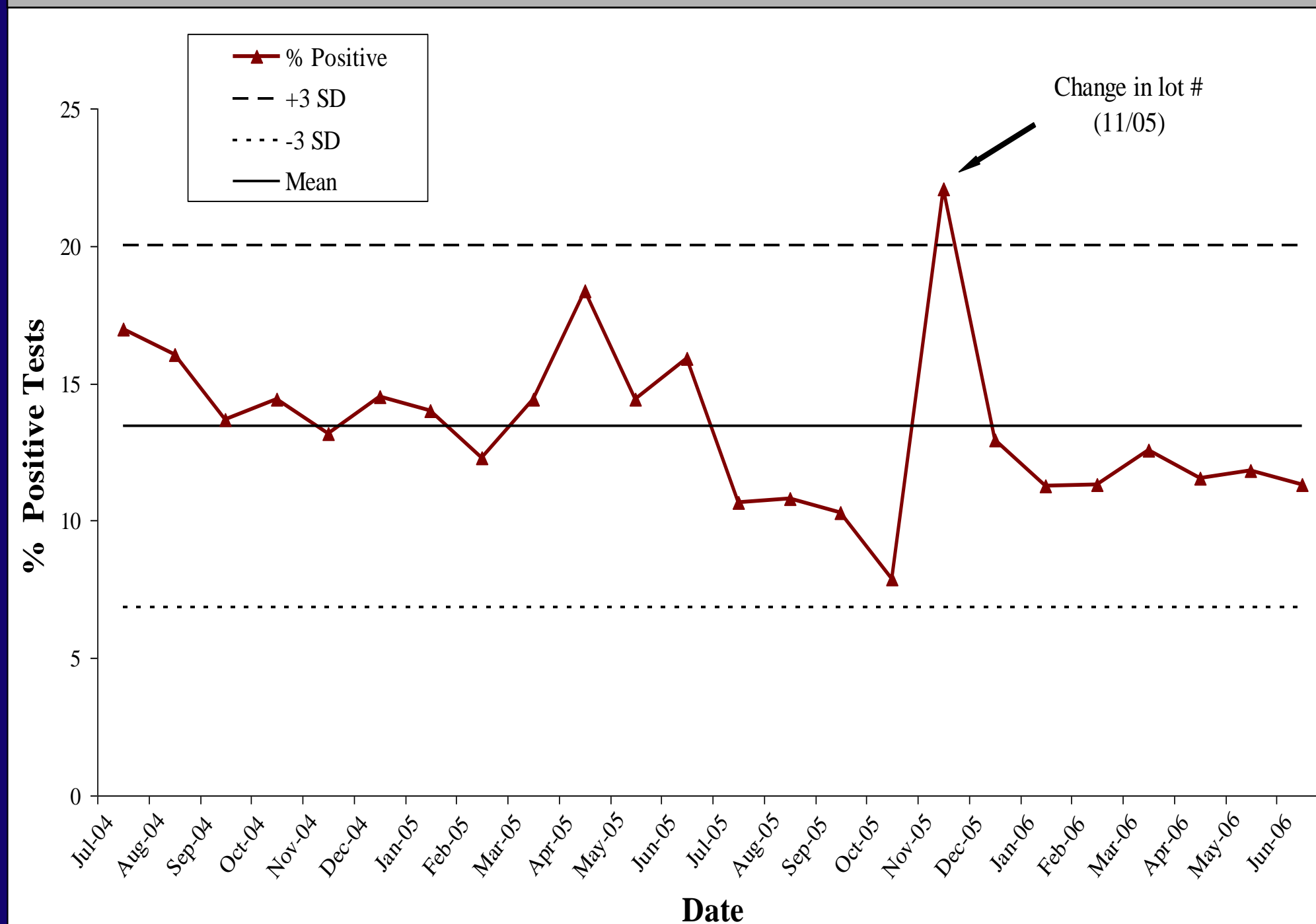


Figure 2. Percent Positive Tests: 7/04 – 6/06



Results

• From 7/04 to 10/05 the average monthly CDAD incidence rate was 1.5/1000 pt-days.

• In 11/05 CDAD rate increased to 2.6/1000 pt-days ($p < .01$) (Figure 1).

• The microbiology laboratory confirmed that increase in the number of positive toxin assays for *C. difficile* correlated with a change in the toxin assay lot number.

• The total proportion of positive assays 7/04 - 10/05 was 13.6% (1490/10942).

• In 11/05, the proportion of positive assays increased to 22.1% (148/671) ($p < .01$) (Figure 2).

• The CDAD rate and proportion positive toxin assays decreased to an average of 1.3/1000 pt-days ($p < .01$) and 11.8% (624/5284) ($p < .01$), respectively, over the next 7 months, after the lot in question was no longer used.

• The increase in CDAD incidence and proportion of positive toxin assays in 11/05 was significant by run control analyses using >3 standard deviations above the mean as a cut off (Figures 1 & 2).

• The manufacturer verified that the lot in question was prone to degradation with storage, causing negative specimens to appear weakly positive.

• Our laboratory confirmed a high number of weakly positive assays associated with the lot in question.

Conclusions

• The first step in outbreak investigation is to confirm a true increase in disease incidence.

• We identified a CDAD pseudo-outbreak that was due to a faulty lot of toxin assays.

• Early steps in finding a cause for the perceived increase in CDAD prior to enhancing containment measures likely saved resources.

• Our microbiology laboratory now uses the proportion of positive toxin assays for quality control.