# Effect of a pharmacist-driven management protocol on the probiotic combination of *Lactobacillus* strains for prevention of *Clostridium difficile* infection (CDI) in hospitalized adult patients

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## Background

- In 2011, an estimate of 435,000 cases with CDI was reported and 29,000 deaths occurred as the result of the disease.
- The financial burden of U.S. health care relating to CDI was immense, costing about $4.8 billion.
- Probiotic has been a major debate in literature whether it should be recommended for primary prevention of CDI.
- The strain that was found to have the most prominent data in reducing CDI rate is *Lactobacillus casei* according to a meta-analysis.
- *Lactobacillus acidophilus, Lactobacillus casei, and Lactobacillus rhamnosus* have been used in conjunction to standard protective measures at a community hospital in the Quebec region to reduce the incidence of CDI.

## Purpose

- To determine if a pharmacist-driven protocol using combination strains of *Lactobacillus acidophilus, Lactobacillus casei, and Lactobacillus rhamnosus* would help to reduce the incidence of CDI

## Methods

Study design
- Single-center, observational, retrospective cohort pre-post study

Data collection period
- Pre-implementation data: October to February 2017
- Post-implementation data: October to February 2018

Inclusion criteria
- Hospitalist's patient
- Patients who received probiotics within 48 hours of administration of the following antibiotics: Piperacillin/tazobactam, ampicillin/sulbactam, ceftriaxone, levofloxacin, cefepime, ciprofloxacin, meropenem, imipenem, clindamycin, and ceftazidime

Pharmacist-driven protocol approved by Pharmacy & Therapeutics and Performance Improvement committee was implemented to automatically start probiotic if patient meets criteria and has no exclusion
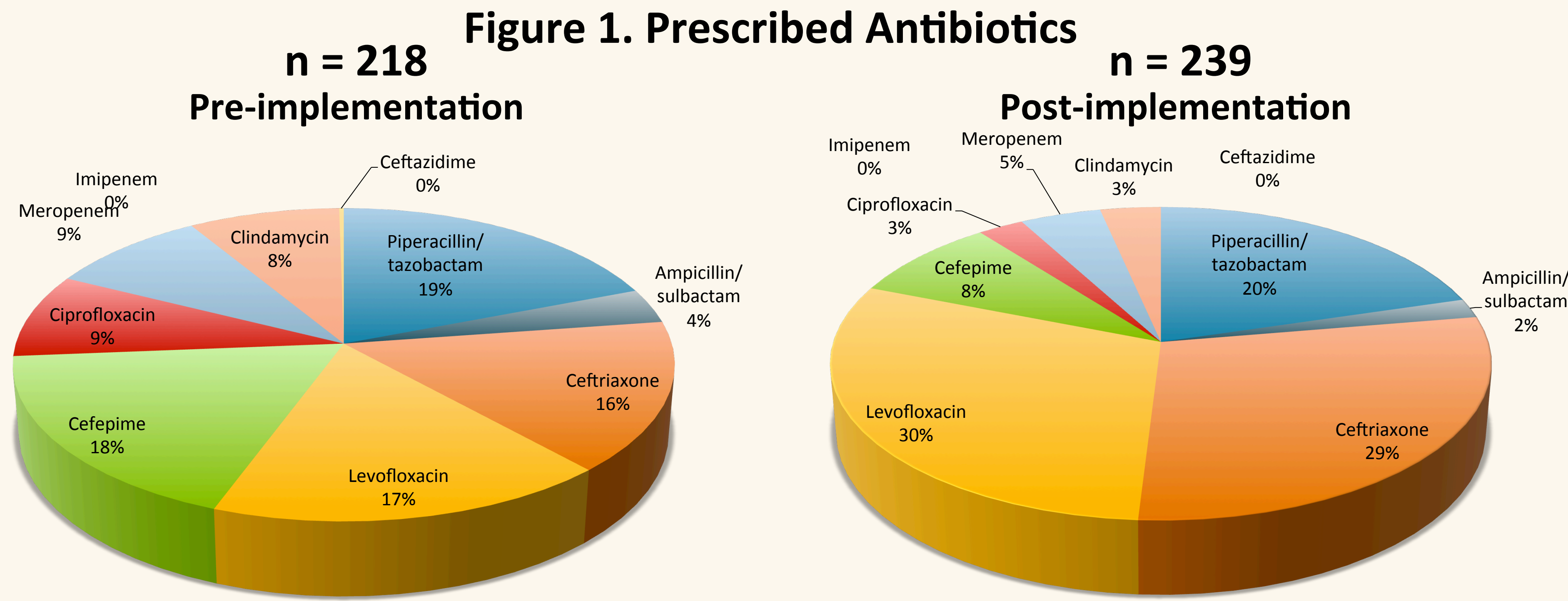
## Results

### Figure 1. Prescribed Antibiotics



n = 218
Pre-implementation

Imipenem 0%
Meropenem 9%
Clindamycin 8%
Ceftazidime 0%
Piperacillin/tazobactam 19%
Ampicillin/sulbactam 4%
Ceftriaxone 16%
Levofloxacin 17%
Cefepime 18%
Ciprofloxacin 9%

n = 239
Post-implementation

Imipenem 0%
Meropenem 5%
Clindamycin 3%
Ceftazidime 0%
Ciprofloxacin 3%
Cefepime 8%
Piperacillin/tazobactam 20%
Ampicillin/sulbactam 2%
Ceftriaxone 29%
Levofloxacin 30%

### Table 1. Baseline characteristics

| Characteristics | Pre-implementation (n = 218) | Post-implementation (n = 239) |
|---|---|---|
| Age (mean in years) | 60.0 | 61.7 |
| Weight (mean in kg) | 85.7 | 88.2 |
| BMI (%) | | |
| • <18.5 kg/m$^2$ | 5.1 | 5.4 |
| • 18.5 – 24.9 kg/m$^2$ | 23.9 | 28.9 |
| • 25 – 29.9 kg/m$^2$ | 30.7 | 25.5 |
| • ≥ 30 kg/m$^2$ | 40.0 | 40.2 |
| Gender (%) | | |
| • Male | 50.9 | 56.9 |
| • Female | 49.1 | 43.1 |
| Prior history of CDI (n) | 6 | 8 |
| Number of previous CDI (n) | 10 | 9 |
| Hospitalization or long-term care facility within 90 days (%) | 28.0 | 28.9 |
| Duration of antibiotics (mean in days) | 6.9 | 5.51 |
| Indications of antibiotic during hospitalization (%) | | |
| • Bone and joint infections | 2.3 | 5.9 |
| • Cardiovascular infections | 3.7 | 0.8 |
| • Central nervous system infections | 0.9 | 1.3 |
| • Intra-abdominal infections | 22.5 | 8.4 |
| • Skin and soft tissue infections | 21.6 | 22.6 |
| • Upper and lower respiratory tract infections | 30.7 | 45.6 |
| • Urinary tract infections | 23.9 | 23.0 |
| Acid-suppression therapy (AST) during hospitalization (%) | 64.7 | 49.4 |
| Laxative (s) used during hospitalization (%) | 53.7 | 47.7 |
| Narcotic(s) used during hospitalization (%) | 79.4 | 63.2 |

### Table 2. Outcomes

| 1º & 2º Outcomes and Safety results | Pre-implementation (n = 218) | Post-implementation (n = 239) |
|---|---|---|
| **Primary outcomes** | | |
| Incidence of CDI during hospitalization (n, %) | 6 (2.75) | 6 (2.51) |
| • Mild to moderate (n, %) | 3 (1.38) | 2 (0.84) |
| • Severe (n, %) | 2 (0.92) | 4 (1.67) |
| • Severe, complicated (n, %) | 1 (0.46) | 0 (0.0) |
| **Secondary outcomes** | | |
| • Antibiotic-associated diarrhea (AAD) during hospitalization (n, %) | 36 (15.5) | 22 (9.21) |
| • Hospital length of stay (mean in days) | 8.52 | 6.62 |
| **Safety** | | |
| • Lactobacillus bacteremia (n, %) | 0 (0.0) | 0 (0.0) |

## Discussion

- Since the p-value for primary outcome is 0.884, there is no significant reduction in the rate of CDI using *Lactobacillus* strains probiotic.
- For secondary outcomes, AAD rate is significantly less in the probiotic group as p-value = 0.021 and hospital length of stay is also shorter.
- Limitations include single center and retrospective study, extensive exclusion criteria, inclusion of only hospitalist's patients, and potential confounding factors.

## Conclusion

- The study with larger sample size is warranted in order to confirm this finding.
- Combination of *Lactobacillus* strains probiotic has the potential to reduce AAD and hospital length of stay in hospitalized adult patients.

## Disclosure

- The authors of this study do not have any conflicts of interest.

## References

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