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Assessing appropriateness of inpatient rifaximin use in a community health system

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OBJECTIVE

- To evaluate the appropriateness of inpatient rifaximin use and healthcare resource utilization best-practices within a community health-system.

BACKGROUND

- Rifaximin is a non-systemic, gastrointestinal site-specific antibiotic, with a wide spectrum of antibacterial activity against aerobic and anaerobic gram-positive and gram-negative organisms. It acts by inhibiting bacterial ribonucleic acid (RNA) synthesis.¹
- Rifaximin is FDA approved for three indications: treatment of traveler’s diarrhea (TD) caused by noninvasive strains of *Escherichia coli*, the reduction in risk of hepatic encephalopathy (HE) recurrence, and treatment of irritable bowel syndrome with diarrhea (IBS-D).²
- Off-label uses, supported by literature, include the treatment of HE episodes, *Clostridioides difficile* infections (CDI), and small intestinal bacterial overgrowth (SIBO).^{3,4,5}
- As evidence-based indications for rifaximin have expanded since it first reached the market in 2010, so has its utilization within the organization.
- The goal of this study is to ensure the clinically appropriate and cost-effective use of rifaximin, while maintaining optimal therapeutic outcomes.

METHODS

- A retrospective chart review was conducted on inpatients for whom rifaximin was ordered between August 1, 2018 – July 31, 2019.
- Within this timeframe, rifaximin was ordered 487 times. Of these, 300 random orders were assessed and included in this study.
- Endpoints:
 - Primary – appropriate use of rifaximin, including indication, dose, and frequency
 - Secondary – cost, indications, and reasons associated with appropriate vs inappropriate use, and new starts versus continuations of home rifaximin
- Appropriate use was defined by evidence available for each indication, including FDA-approved indications or as recommended by current guidelines, or after failure of or contraindication to use of alternatives as noted in Table 1.¹⁻⁸

Table 1. Criteria for Appropriate Inpatient Rifaximin Use

Indication	Criteria	Dosing
HE Prevention	Continuation of home rifaximin as an add-on to lactulose, and ≥ 1 HE episode is charted; or Intolerance or contraindication to lactulose, and ≥ 1 HE episode is charted	550 mg BID
HE Treatment	<u>Lactulose, rifaximin, or both prior to admission:</u> As an add-on to lactulose <u>Neither lactulose or rifaximin prior to admission:</u> Add-on to lactulose, after 24h of lactulose monotherapy, or Intolerance or contraindication to lactulose	400 mg TID or 550 mg BID
TD	Treatment failure, allergies, or contraindications to first-line therapies (azithromycin, fluoroquinolones)	200 mg TID
IBS-D	Use alternative (which may include home supplied rifaximin)	---
CDI	Second or subsequent recurrence (or history unknown); and Previously tried: pulsed-tapered vancomycin, or fidoxamicin, or nitazoxanide, or fecal transplant	400 mg TID
SIBO	Treatment failure to ≥ 1 prior gastrointestinal-targeted antibiotic regimen	550 mg TID

RESULTS

Table 2. Baseline Characteristics

Characteristic	n = 300
Age (mean age in years ± SD)	56.7 ± 12.4
Male (n, %)	163 (54.3%)
Listed Indication (n, %)	
HE Treatment	149 (49.7%)
HE Prevention	139 (46.3%)
SIBO	6 (2.0%)
IBS-D	4 (1.3%)
TD	1 (0.3%)
CDI	1 (0.3%)
Rifaximin Use Prior to Admission (n, %)	162 (54.0%)
Lactulose Use Prior to Admission (n, %)	173 (57.7%)

Figure 1. Appropriateness of Rifaximin Orders

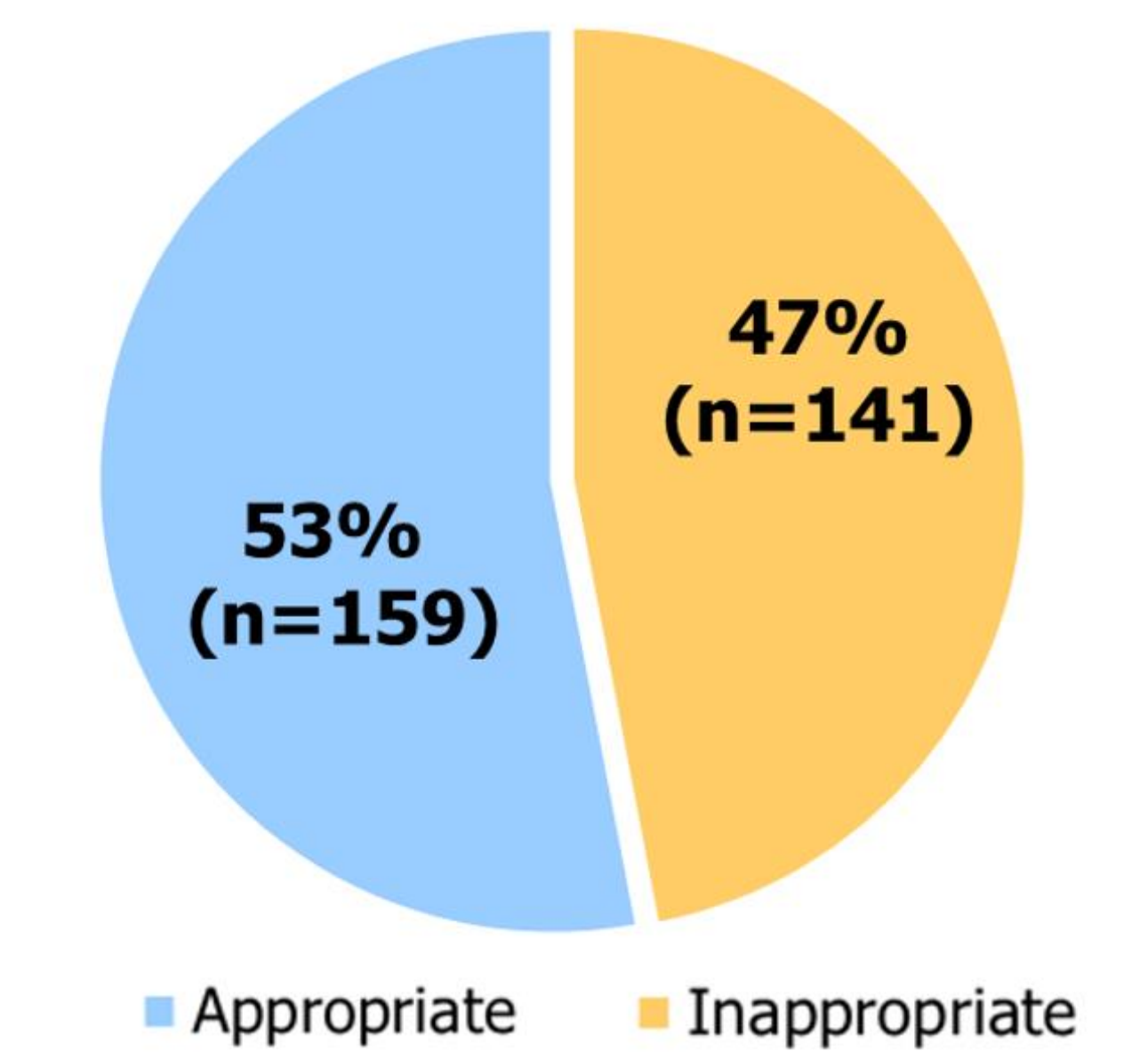


Figure 2. Number of Tablets Administered & Associated Costs Based on Average Wholesale Price

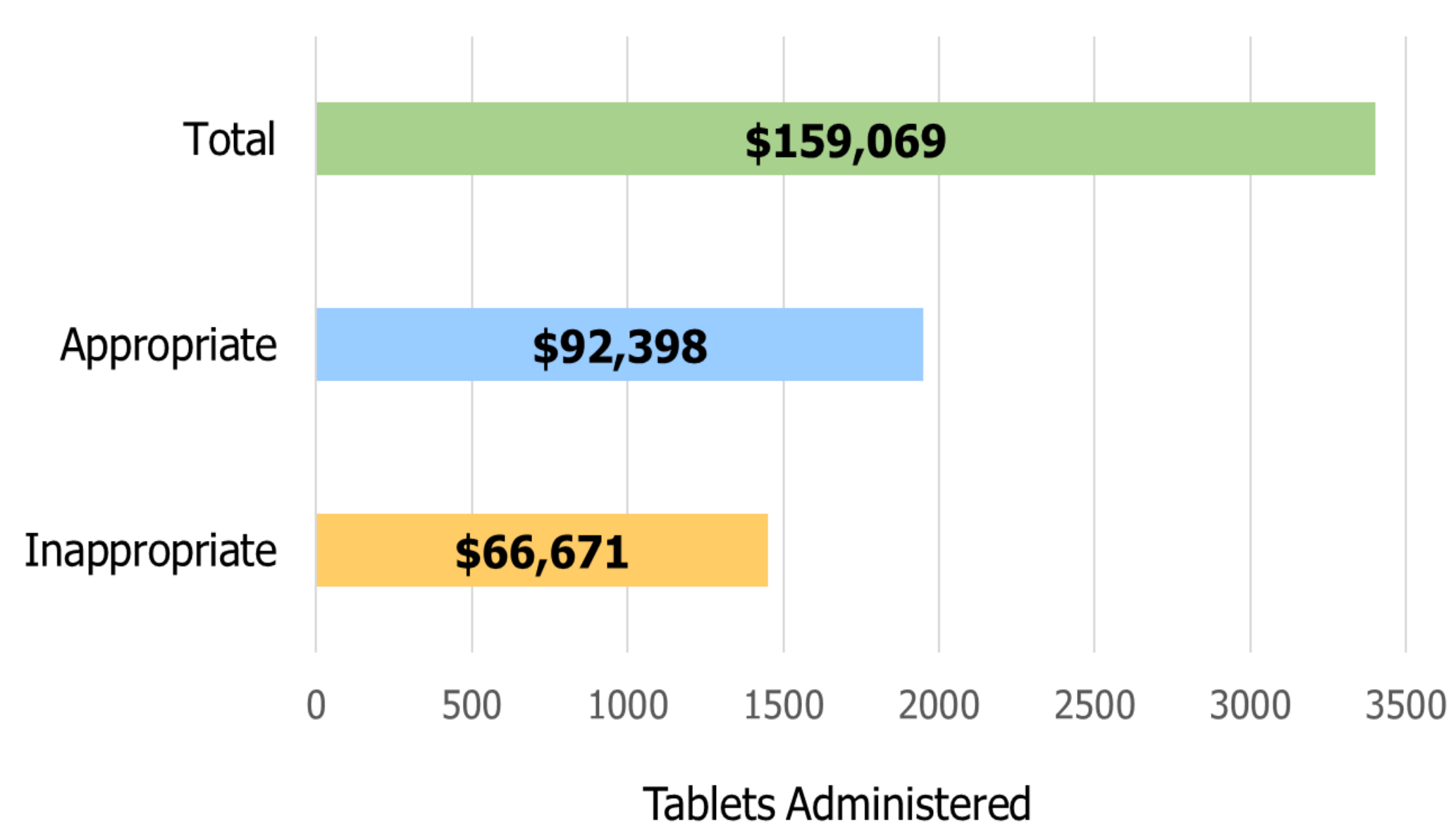


Figure 3. Appropriateness of Rifaximin Orders Based on Indication

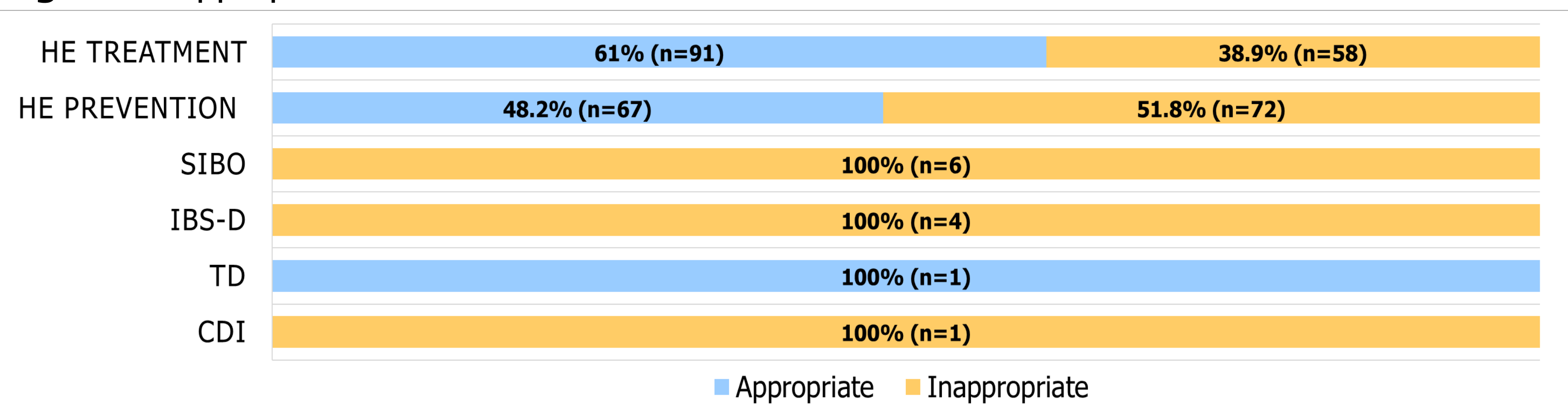


Figure 4. HE Treatment – Reasons for Inappropriate Use

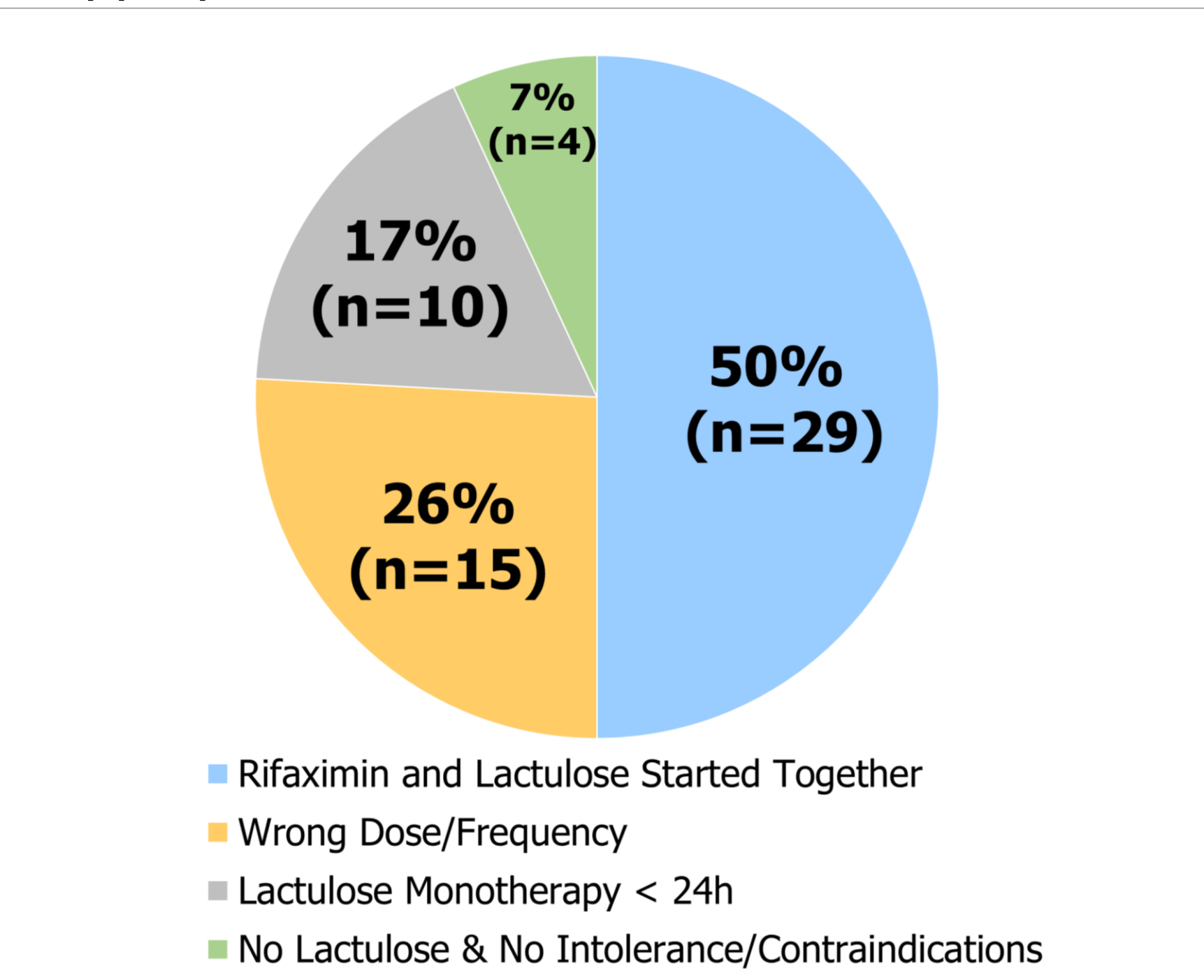
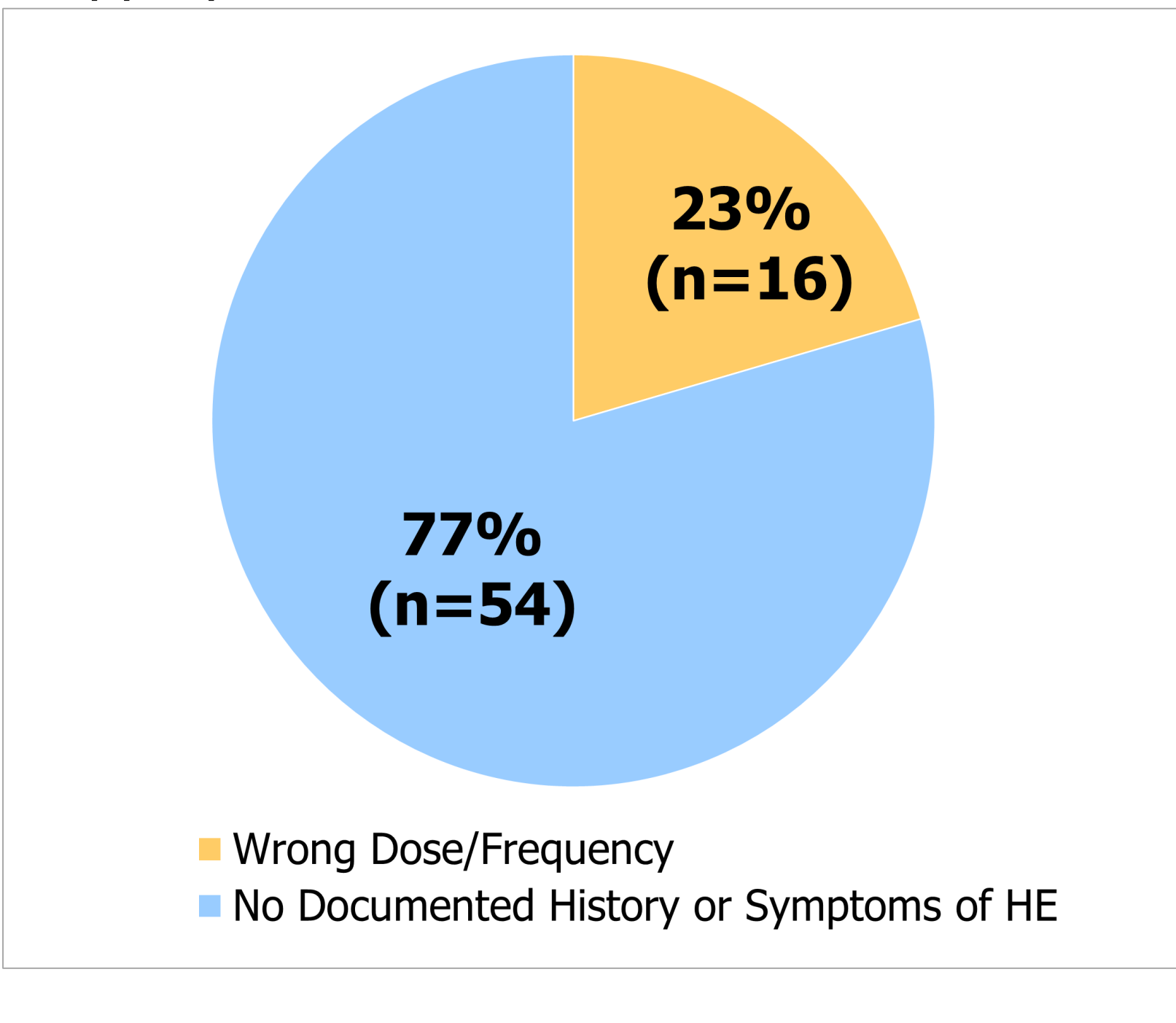
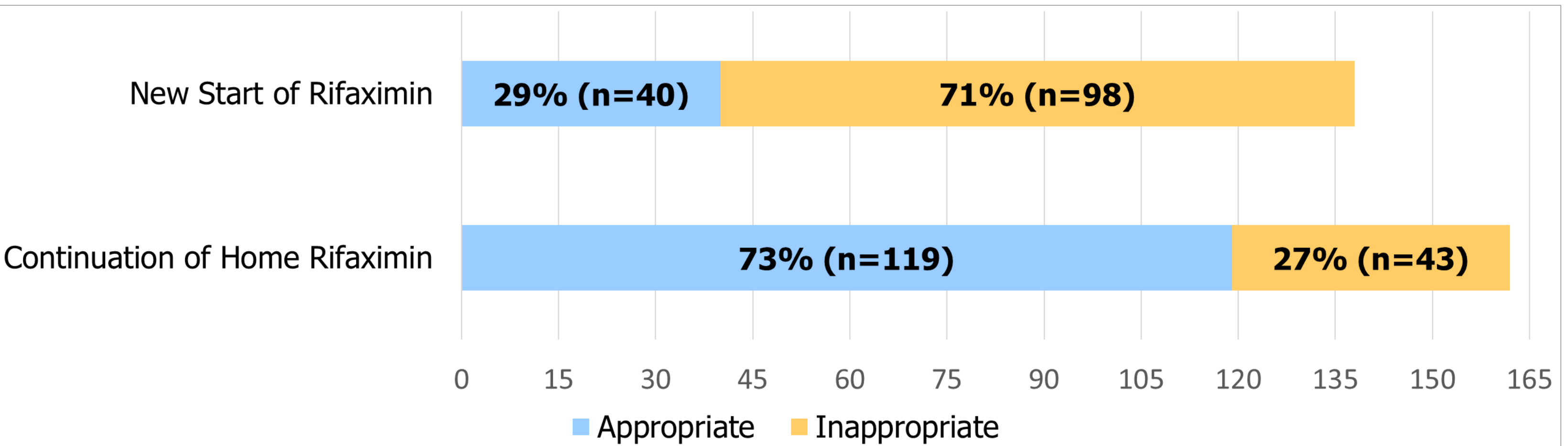


Figure 5. HE Prevention – Reasons for Inappropriate Use



RESULTS

Figure 6. Appropriateness of New Starts of Rifaximin vs Continuations of Home Rifaximin



DISCUSSION & CONCLUSIONS

- Of the 300 rifaximin orders placed within the study timeframe, 47% were considered inappropriate, indicating an opportunity for improvement regarding the practice of evidence-based, clinically appropriate, cost-effective inpatient rifaximin use.
 - Almost all orders for non-HE conditions, and nearly half of HE indications, were considered inappropriate.
 - The majority of inappropriate usage was seen in patients who were not on rifaximin prior to admission. However, a quarter of home rifaximin continuations were also inappropriate.
- Challenges involving appropriate inpatient use likely lie in its strict criteria for initiation, such as an adequate trial of first-line therapies, and the reliance on a robust documentation of a patient’s past-medical history.
- Future directions should involve leveraging the electronic medical record to improve ordering and follow-up for patients receiving rifaximin, such as prompting the provider for documentation of prior agent use or contraindication at the time of ordering.
- Pharmacists can play a key role in establishing the judicious use of inpatient rifaximin through the assessment of dosages and frequencies based on a stated indication, if available, and assessing appropriate trial of first-line therapies.
 - Currently, this health system has a clinical monitoring alert for pharmacists to assess all patients receiving rifaximin. Next steps will include evaluating alert saliency for inappropriate orders placed in this timeframe, and using this information to tailor strategies for increasing clinically appropriate use.

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