

Impact of Antimicrobial Stewardship Program on Hospital-wide Burden of Antibiotic Resistant Organisms: A Controlled Interrupted Time Series Analysis Over 14 years



A Controlled Interrupted Time Series Analysis Over 14 years

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BACKGROUND

Reducing antimicrobial resistance (AMR) is a major incentive for institutional antimicrobial stewardship programs (ASPs); however, there remains a paucity of high quality data evaluating the impact of these programs on nosocomial AMR.

The Sunnybrook Health Sciences Centre (SHSC) Bayview Campus is a shared site, home to a 627-bed acute care hospital and a 530-bed long-term-care facility (LTCF). A prospective audit-and-feedback (PAF) ASP was implemented in the acute care facility in October 2009.

No specific intervention was initiated in LTCF, but there was potential for antimicrobial prescribing in the LTCF to be influenced by policy and practice at the adjoining acute care facility.

OBJECTIVE

To evaluate the impact of the SHSC PAF-ASP on the burden of antibiotic-resistant organisms (ARO) and multidrug-resistant organisms (MDRO) and on inpatient antibiotic use in the 7 years following program implementation.

METHODS

Study Design
Retrospective controlled interrupted time series over 14 years (pre-intervention period October 2002 – September 2009; post-intervention period October 2009 – September 2016).

Study Setting
SHSC Bayview Campus, Toronto, Ontario, Canada
• 627-bed acute care teaching hospital & 530-bed long-term-care facility (LTCF)

Data Collection
Patient-level microbiologic data (clinical isolates gram positive and aerobic gram-negative bacteria) and antibiotic use data (days of therapy (DOT) for all systemic agents) were extracted from the SHSC Microbiology and Pharmacy Databases for all patients admitted during the study period.

Standard definitions of ARO and MDRO were applied. ARO and MDRO collected >48h after admission were classified as hospital-acquired (HA-ARO, HA-MDRO); isolates collected ≤48h of admission were classified as community-acquired (CA-ARO, CA-MDRO).

Primary Outcomes
Burden of AMR in the acute care facility, expressed as the monthly incidence of HA-AROs and HA-MDROs standardized to 10,000 patient days (HA-ARO/10000 PD; HA-MDRO/10000 PD)

Process Outcomes
Total antibiotic use (TTLA), targeted antibiotic use (TGDA), and non-targeted antibiotic use (NTGA) in the acute care facility, expressed as monthly DOT standardized to 10,000 patient days (DOT/10000 PD/month)

Control Outcomes
Burden of AMR in the community, expressed as the incidence of CA-AROs and CA-MDROs standardized to 10,000 patient days (CA-ARO/10000 PD; CA-MDRO/10000 PD)

Exploratory Outcomes
Burden of AMR in the geographically adjacent LTCF, expressed as the incidence of LTCF-acquired AROs and MDROs standardized to 10,000 patient days (LTCF-ARO/10000 PD; LTCF-MDRO/10000 PD)

Statistical Analyses
Changes in ARO, MDRO, and AMU trends (Δ in time series slopes) and relative incidences (Δ relative incidence/7 year period) from the pre- and post-intervention periods were determined using Poisson regression.

RESULTS

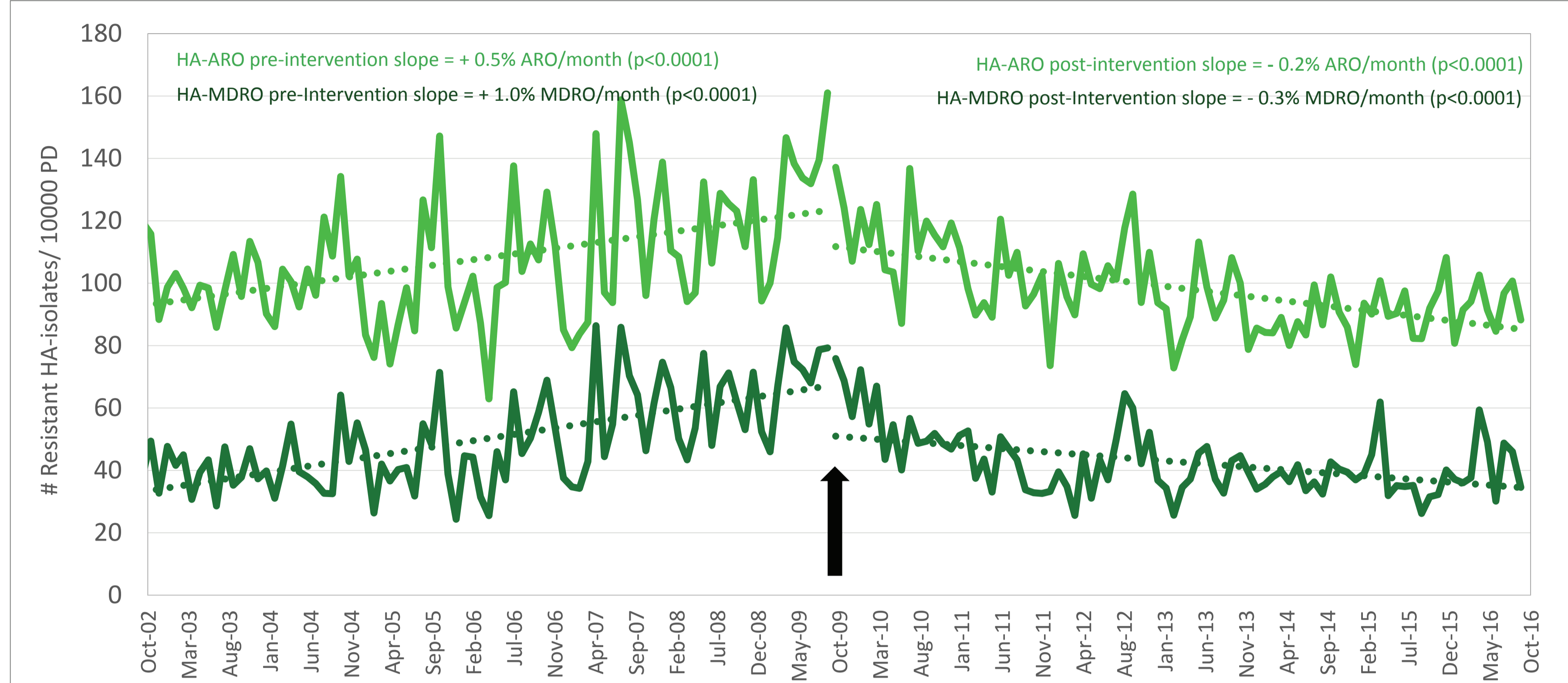


Figure 1. Trends in HA-ARO (LIGHT GREEN LINE) and HA-MDRO (DARK GREEN LINE) at the SHSC acute care facility over the 14 year (168 month) study period. The pivot in HA-ARO and HA-MDRO trend coinciding with implementation of the SHSC PAF-ASP (BLACK ARROW) suggest that PAF-ASP implementation was associated with improvements in nosocomial resistance rates.

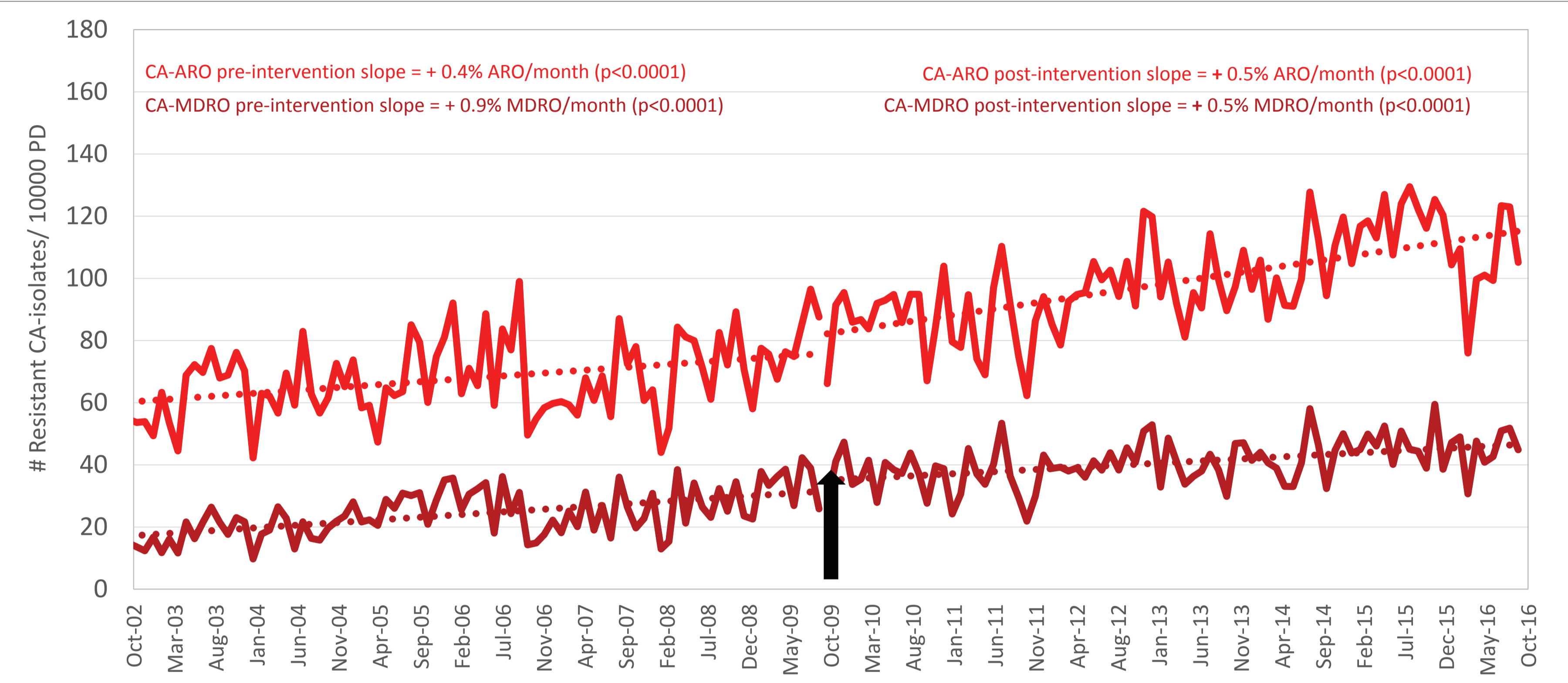


Figure 3. Trends in CA-ARO (LIGHT RED LINE) and CA-MDRO (DARK RED LINE) at the SHSC acute care facility over the 14 year (168 month) study period. The continued increase in CA-ARO and CA-MDRO seen post-PAF-ASP implementation suggests PAF-ASP implementation was not associated with improvements in community AMR; this is expected since outpatient AMR should be unaffected by an inpatient PAF-ASP.

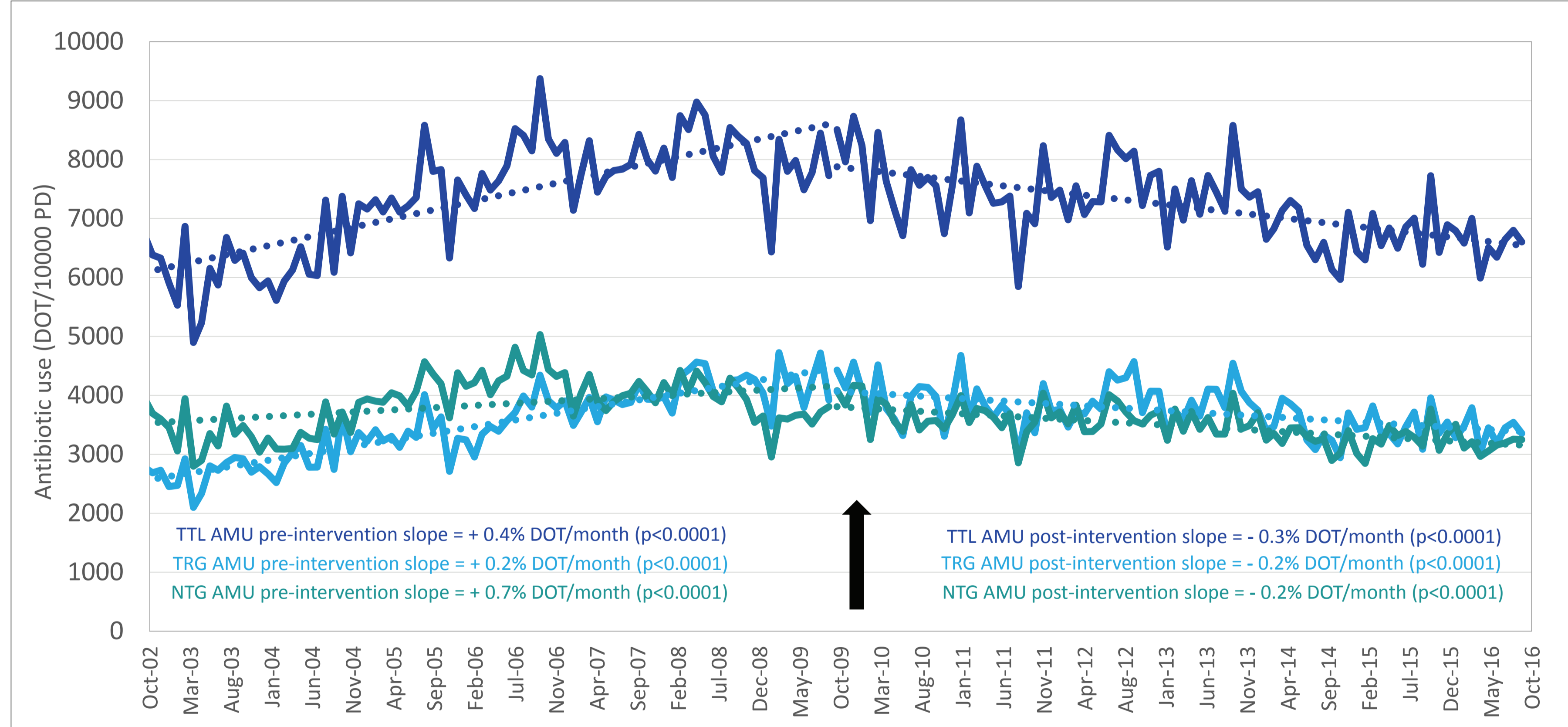


Figure 2. Trends in total antibiotic use (TTLA; DARK BLUE LINE), targeted antibiotic use (TGDA; LIGHT BLUE LINE), and non-targeted antibiotic use (NTGA; TEAL LINE) at the SHSC acute care facility over the 14 year (168 month) study period. The pivot in TTLA, TRGA, and NTGA trend coinciding with implementation of the ASP (BLACK ARROW) suggest that ASP implementation was associated with improvements in inpatient antibiotic use.

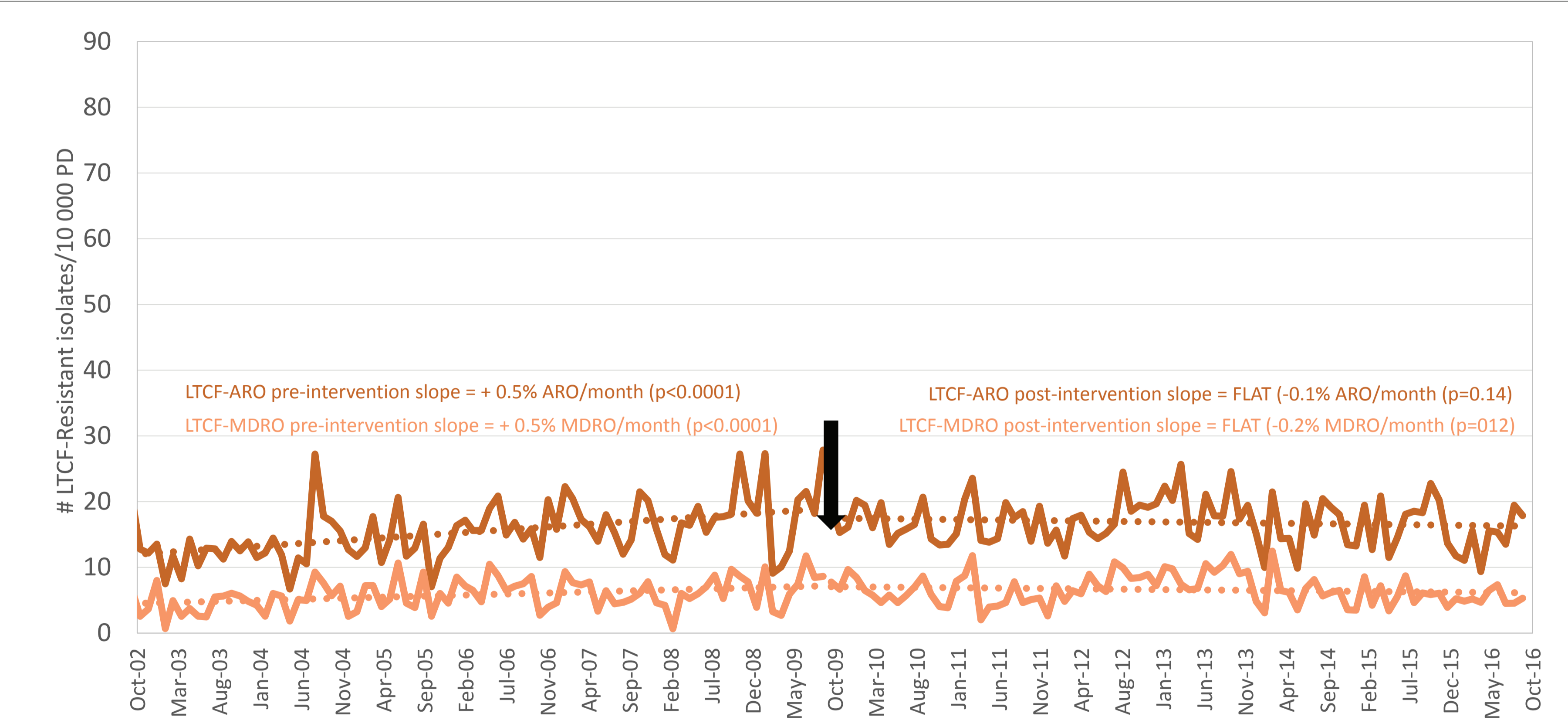


Figure 4. Trends in LTCF-ARO (BROWN LINE) and LTCF-MDRO (ORANGE LINE) at the SHSC LTCF over the 14 year (168 month) study period. The stabilization of the increasing pre-intervention period trends coinciding with implementation of the SHSC antimicrobial stewardship program (ASP) (BLACK ARROW) suggest that ASP implementation was associated with improvements in the trajectory of resistance.

DISCUSSION

Implementation of an acute care ASP was associated with a:

- significant improvement in HA-ARO and HA-MDRO trends (Figure 1);
- significant reduction in post-intervention HA-ARO incidence (-9% relative incidence/7yr period, $p = 0.023$); and
- reduction in post-intervention HA-MDRO incidence trending towards significance (-13% relative incidence/7yr period, $p=0.13$)
- significant improvements in TTLA, TGDA, NTGA trends (Figure 2), but relative reductions in antibiotic use across the entire post-intervention period did not reach statistical significance.
- stabilization of the pre-intervention period increasing LTCF-ARO and LTCF-MDRO trends (Figure 4). The transition from an increasing trend to the absence of a trend (i.e. flat trend) is consistent with an acute care facility ASP-associated improvement in the LTCF AMR and a possible indirect or “trickle-down” effect of the acute care program.

In the absence of a dedicated ASP:

- CA-ARO and CA-MDRO rates continued to rise in the post-intervention period (Figure 3); and
- significant increases in post-intervention CA-ARO burden (+40% relative incidence /7yr period, $p<0.001$) and CA-MDRO burden (+69% relative incidence/7yr period, $p<0.0001$) were detected

Strengths: First study examining the impact of PAF-ASP on collective nosocomial AMR using a high quality quasi-experimental design; inclusion of process outcomes and control groups strengthens causal inference
Limitations: Retrospective, single centre, observational design limits causal inference; exploratory LTCF analyses

CONCLUSION

Implementation of the acute care PAF-ASP was associated with improvements in acute care AMR and AMU
The absence of improvement in corresponding CA-AMR outcomes, and limited improvement in the corresponding LTCF AMR outcomes, strengthen the causal inference of the acute care PAF-ASP curbing development of acute care AMR

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Disclosure:
No author has any conflict of interest related to this study.