

Appendix 2: Data Extraction

Data charting

The researchers developed a form for abstracting data that captured the main study characteristics as well as the specific metrics relevant to the objectives of this scoping review. The form was subjected to preliminary calibration to ensure its accuracy, consistency, and reliability. The data items extracted (see below) included the reference, the study type, the study objectives, population or setting, country, the intervention, intervention duration, healthcare workers involved, outcome measures or findings, and the conclusions of the study. A second reviewer audited 20% the data extracted by the first reviewer for accuracy and completeness.

STUDIES ON INTERVENTIONS TARGETING CLOSTRIDIUM DIFFICILE IN HEALTHCARE SETTINGS							
Reference	Study type	Aims/ objectives	Population/ Setting	Intervention	Outcome/ key findings	Conclusions	Useful notes
[42]	Retrospective observational time-series.	To examine the effectiveness of an antimicrobial stewardship programme on utilization and cost of antimicrobials in leukemia patients in Canada	Leukemia patients. Canada Multi-site	Academic detailing (audits and feedback)	Utilization of antimicrobials reduced from 278DDD/100 PD to 247 DDD/100 PD CDI remained stable	AMS reduces antimicrobial use but has no effect on mortality	Immunosuppressed persons have neutropenia, mostly treated with broad spectrum antibiotics hence high risk for CDI
[43]	Quasi-experimental	To assess the impact of an ASP on antimicrobials use, CDIs, and AMR patterns	Rehabilitation hospital 150 beds Spinal injuries patients	Bedside ID consultation Revision of antibiotics prophylaxis protocols Staff education	Abiotics consumption reduced from 42 to 22 DDD/ 100 PDs (Carbapenems from 13 to 0.4 DDD/100PDs, Fluoroquinolones from 11.8 to 0.99 DDD/ 100 PDs) CDIs reduced from 3.6 to 1.2 cases per 10000 PDs Prevalence of KP reduced from 42% to 17% No effect on mortality or length of stay.		
[44]	Quasi-experimental	To optimize the use of antibiotics through trainee-led time outs	679 inpatients Montreal University tertiary care hospital (417 beds) Internal medicine.	Twice-weekly time-out audits using a structured electronic checklist and monthly feedback. AMS monthly education: 30 minutes to all rotating staff	A 46% reduction of antibiotics costs from \$149 743 to \$69 424 78% of the cost reduction linked with reduced use of carbapenems 80% adherence to the audit	An antibiotic self-stewardship bundle to implement the Centers for Disease Control and Prevention's suggested time-outs seems to have	About 50% use of antibiotics is not necessary or inappropriate

			2 units, 46 beds	Involved: Consultants (Infectious diseases expert, critical care, and general medicine)	CDI reduced from 24.2 to 19.6 per 10,000 PDs	reduced overall costs and targeted antibiotic use.	
[45]	Quasi-experimental	To implement an AMS program in a long-term care hospital using telemedicine Provide antimicrobial oversight To improve the quality of care by standardizing antimicrobial prescribing practices	212 bed-New England Sinai Hospital in Stoughton Massachusetts Oversight undertaken by staff from Tufts Medical Center	CDIs Offsite electronic medical record audit Program involved ID physicians and pharmacists	An overall decrease in antimicrobials use. Overall usage of antibiotics reduced by 6.58DDD/1,000 PDs A reduction in the incidence of HAIs and CDIs (from 1.4 to 0.57/1000PDs)	AMS using remote EMR audit is associated with a reduction in antimicrobials use.	
[46]	Quasi-experimental	To reduce the number of healthcare associated CDI cases	450-bed district general hospital Hairmyres Hospital (Glasgow, United Kingdom)	A restrictive policy on the use of ceftriaxone and ciprofloxacin Educational campaign	Overall reduction of targeted antimicrobials (ceftriaxone: 95% and ciprofloxacin: 72.5%) (Ceftriaxone from 46.213 to 2.129 DDD/1000PDs Ciprofloxacin from 109.804 to 30.205 DDDs/1000PDs) 77% reduction in hospital acquisition of CDIs Sustained reduction of CDIs up to 0.259 cases/ 1000 patient-beds 3 years post-intervention	Restricting the two antibiotics significantly reduced healthcare associated CDIs	
[47]	Prospective, controlled interrupted time series	To evaluate the impact of audit and feedback on the use of broad-spectrum antimicrobials in critical care patients	Single site Tertiary hospital Intensive care unit (3)	Review of all patients on day 3 and 10 after admission with suggestions for optimizing antimicrobial use given to responsible physicians. Then placing a computer-generated progress note on the patient chart, then feedback completed on same day Critical care team Targeted antimicrobials: ceftriaxone, ceftazidime, piperacillin-tazobactam,	Use of broad-spectrum antimicrobials reduced from 644 to 503 therapy days per 1,000 PDs Nosocomial CDIs incidence reduced from 11 to 6	Prospective audit and feedback appears to be an effective and safe means for reducing the use of broad-spectrum antimicrobials	Approximately half of antibiotics use in hospitals is inappropriate or not necessary

				meropenem, ertapenem, levofloxacin, ciprofloxacin, and vancomycin Personnel involved: Consultants (Pharmacists, ID physician)			
[48]	Quasi experimental	Assessing the impact of automated tracking and ordering precautions on multidrug resistant organisms (MDROs)	University of California, Irvine Medical center 410 beds Serves trauma, burns and cancer patients.	An automated system for identifying, tracking CDIs and other MDROs that involved monitoring microbiology results, triggering chart-based alerts, ordering for appropriate contact precautions on admission as well as inactivation of the precautions. The alert was in form of a visual header banner on the electronic health records	Time savings estimated at 43 hours per 1000 admissions Timely initiation of contact precautions	Automated systems integrated within the electronic health records have potential for protecting patients by ensuring precautions are ordered in a timely manner. The system also contributes to time savings for Infection prevention teams.	No report on CDI outcomes
[49]	Quasi-experimental	To assess the effect of biocidal copper oxide impregnated linen on HCAs CDIs	Multi-site (six hospitals). Sentara Albermarle Healthcare hospitals 1019 beds NC, USA	Replacement of linen with copper oxide impregnated linen	A reduction in C. diff associated HCAs by 41.1-61.2% per 10,000 PDs during the intervention period	The use of the biocidal impregnated copper-oxide linen significantly reduced C. diff associated HCAs as well as other MDROs	Copper has some biocidal activity against some drug resistant bacteria. Its use in hospital environments potentially reduces the bioburden of HCA pathogens
[50]	Quasi-experimental	To examine the effect of copper impregnated linens on MDROs and CDIs	Long-term acute care hospital (LTACH). 40-beds Charlottesville, Virginia	Copper-impregnated linens including bedsheets, pillowcases, towels, and washcloths	Copper linens were associated with a much higher rate of CDIs. (1.5 to 2.8 cases per 1000PDs) There was a reduction in the compliance with hand hygiene practices (-5.6%)	There was no beneficial effect of the copper impregnated linens	No blinding of staff members
[51]	Secondary analysis of a multicenter cluster RCT	To assess the effectiveness of disinfection strategies on C. diff incidence in hospital settings BETR (Benefits of enhanced terminal room) disinfection study	Multisite: 9 hospitals in southeastern USA	Four disinfection strategies post-discharge of MDRO or C. diff patients: Standard disinfection with quaternary ammonium solution or 10% hypochlorite (bleach) for C. diff cases. Standard disinfection and ultraviolet (UV) light or bleach and UV light for C. diff cases. Bleach strategy with 10% hypochlorite	No significant differences in the hospital-wide risk of the target organisms between standard disinfection and the other three enhanced disinfection strategies. The use of UV light as part of the disinfection strategy significantly reduced the risk of C. diff (from 18.1 to 17.2/1000PDs)	Enhanced terminal room disinfection using UV light contributed to a reduction in the risk of C. diff and VRE. Enhanced terminal room disinfection overcomes the challenges of standard	Contaminated healthcare environments act as sources of infectious pathogens hence the importance of enhanced terminal room disinfection.

				Bleach and UV light		disinfection and potentially reduces acquisition of <i>C. diff</i> and other MDROs.	
[52]	Quasi-experimental. Retrospective pre- and post-intervention	To assess the impact of an ASP intervention on HA-CDI	The Western Pennsylvania Hospital (WPH). 317-bed community teaching hospital. Approximately 6800 admissions yearly.	Education. Restriction of target antimicrobials requiring prior approval. Audit and feedback. Annual guidelines for antimicrobials use.	Significant reduction in HA-CDIs from 0.84 to 0.28 cases per 1000PDs (P=0.035). A cumulative reduction in the use of clindamycin, ceftriaxone, carbapenems, fluoroquinolones, linezolid, tigecycline (from 295.1 to 261.3 DDD/1000PDs)	Implementing an ASP program significantly reduced the incidence of HA-CDI as well as antibiotics use	Antibiotics associated with higher rates of CDI include fluoroquinolones, clindamycin, and ceftriaxone
[53]	Pre- and post-intervention	To assess the impact of intensive IPC activities on MRSA, drug resistant <i>P. aeruginosa</i> (DRP), and <i>C. diff</i> acquisition.	Tsukuba Medical Center Hospital (TMCH) Japan. 409 beds. Tertiary emergency medical center.	Screening and notification of new and previous MDROs. Daily review of new patients' medical records/ microbiological results. Contact precautions or standard precautions. Monitoring inappropriate use of carbapenems and promptly instructing responsible doctors.	Reduction of carbapenems' use from 28.5 to 17.8 DDD/1000PDs. Improved uptake of contact precautions. A reduction in the incidence of CDI (from 0.47 to 0.11 cases/1000PDs). Incidence of MRSA and DRP also reduced significantly	Proactive intensive ICT measures have the potential for reducing the hospital transmission of MDROs.	
[54]	Prospective observational study	To assess the impact of a technology-mediated pharmacy-directed ASP in a rural hospital	St. Mary Medical center. 141 beds. Community hospital. Washington	Weekly antimicrobial review teleconferences involving an ID pharmacist	Pharmacy-initiated AMS interventions increased from 2.1 to 6.8 interventions per week. Antimicrobial streamlining improved from 44% to 96%. There was enhanced interdisciplinary collaboration. A 51% reduction in the cost of targeted antimicrobials. Healthcare associated CDIs reduced from 5.5 to 1.6 cases per 10,000PDs		

[55]	Retrospective observational cross-sectional study	To assess the effect of intensive staff education on CDIs amongst hospitalized geriatrics	390-bed geriatric hospital 217 geriatric patients observed	Staff education on isolation precautions, handwashing, transporting patients within the hospital, and cleaning.	There were no significant differences in the incidence of CDIs pre- and post-intervention.	Intensive staff education did not reduce the nosocomial CDI rates but remains an important strategy	Toxin positive <i>C. diff</i> is the leading cause of diarrhea amongst geriatrics.
[56]	Retrospective cohort study	To assess the impact of real-time notification upon detecting toxigenic <i>C. difficile</i>	Single center. 433 bed tertiary care medical center. Lexington, Kentucky. Adult patients aged more than 18 years	Computer generated real-time notification of toxigenic <i>C. diff</i> results and Initiation of appropriate antimicrobial therapy (Vancomycin or Vancomycin and metronidazole). Contact precautions.	The time for initiating appropriate treatment reduced from 5.75 to 2.05 hours. The ASP intervention shortened the time from diagnosis to recording the appropriate antimicrobial in the electronic medical records	The real-time notification intervention reduced the time for entering and initiating the appropriate antimicrobial treatment as well as contact precautions.	
[57]	Quasi-experimental	To assess the impact of collaborative intervention on hospital onset <i>C. difficile</i>	35 acute hospitals New York	IP bundle and environmental cleaning protocol Standard IP precautions and environmental cleaning protocols were monitored using checklists. Monthly teleconferences to discuss challenges and successes also implemented. Incidence of CDIs monitored monthly Intervention overseen by interdisciplinary teams	Significant reduction in hospital onset CDIs was reported 95% compliance with IP precautions 96% compliance with environmental cleaning protocol 37% reduction in the absolute risk of CDIs		
STUDIES ON INTERVENTIONS TARGETING CRKP IN HEALTHCARE SETTINGS							
Reference	Study type	Aims/ objectives	Population/ Setting	Intervention	Outcome/ key findings	Conclusions	Useful notes
[58]	Retrospective observational Quasi-experimental Medical records	To devise a local strategy for eradication of a hospital-wide outbreak caused by carbapenem-resistant <i>Klebsiella pneumoniae</i> (CRKP)	Carbapenem-resistant <i>Klebsiella pneumoniae</i> CRKP patients 1000 bed tertiary care university hospital	Emergency department flagging system Cohorting Eradicating clusters Environmental and personnel hand cultures Carbapenem restriction policy	CRKP infections reduced from 5.26 to 0.18 per 10,000 patient days No nosocomial CRKP infections diagnosed Meropenem use reduced		
[59]	Quasi-experimental?	To examine the effect of active screening on the	Intensive care unit (ICU)	Active screening	Improved detection of MDROs (KP)	Active screening reduces the resistance rates of pathogenic bacteria	

		resistance rates of MDROs in ICUs				and useful in detecting MDRO	
[60]	Quasi-experimental	To reduce the prevalence of CRKP	Medical center Israel	Guidelines for isolation, cohorting, environmental cleaning, staff education, and computerized notification/ flagging	A decrease in the CRKP incidence rate sustained over 30 months from 6.6 to 0.5/10,000PDs Reduction in cross-infections from 6% to 2.7% Surveillance of asymptomatic carriers improved from 20% to 89%	A multidisciplinary IP programme is effective in controlling the prevalence of CRKP	
[61]	Quasi-experimental	To optimize the use of antimicrobials	510-bed Danish university hospital Copenhagen University Hospital-Denmark	Multi-disciplinary change project Kotter's stages of change Multi-level intervention: 1. Professional: Education, clinician leaflets, new drug container, yellow sticker for bed post, signboard for doors, hotline, notification on prescription of restricted antimicrobials 2. Social: Presentations for the quality board, prevalence studies, feedback, newsletter, and website. 3. Patient: Information leaflets for isolation precautions Organizational: Revising antimicrobial guidelines, cefuroxime restriction.	Overall antimicrobials consumption remained unaffected. Immediate and sustained reduction in cefuroxime use (74.5%) An increase in the use of ertapenem, piperacillin/ tazobactam, and beta-lactamase sensitive penicillin. Reduction in ESBL-KP diagnostic samples Reduced incidence of ESBL-KP infections from 39.5 to 22.5% Reduced need for isolation precautions	Changing antimicrobial consumption and reducing the incidence of ESBL-KP is possible through a multi-faceted intervention that does not require ongoing antibiotic stewardship	Restricting cephalosporins may reduce ESBL infection rates Carbapenems (beta-lactamase inhibitors) are recommended as first-lines for serious ESBL producing bacteria
[62]	Quasi-experimental	To evaluate the impact of an AMS program restricting carbapenems (imipenem and meropenem)	Hospital das Clinicas Institute of Orthopedics and Traumatology 200 beds tertiary care hospital	Ertapenem was made mandatory for treatment of ESBL-Enterobacteriaceae Restricting group 2 carbapenems for gram negative bacteria	A reduction of group 2 carbapenems use from 61.1 DDD to 48.7 DDD/1,000 patient days Susceptibility of <i>K. pneumoniae</i> and <i>P. aeruginosa</i> to trimethoprim-sulfamethoxazole	There was a significant reduction in the use of carbapenems following preferential use of ertapenem.	
[63]	Prospective Observational	To contain an outbreak of CRKP	27 Acute care hospitals Israel 14,000 beds	Screening Mandatory reporting of every CRKP patient to PH authorities Mandatory isolation of hospitalized new and previous carriers (single rooms or cohorting)	Increase in the incidence of KP was halted with a subsequent reduction of 11.7 cases per 100,000	An intervention coordinated centrally showed better outcomes for containment of a KP outbreak as compared to local measures. Strategic planning and	Outbreak control

				Dedicated staff Oversight taskforce that supervised adherence to isolation protocols, provided technical support, and feedback to management		national oversight are crucial in addressing AMR	
[64]	Quasi experimental	To curb the spread of KPC-3 producing KP	Italy 12-bed ICU hospital Cannizaro hospital, Catania	Screening Environmental cleaning Respiratory equipment disinfection Hand hygiene Single room isolation Weekly meetings between IP and ICU staff	Outbreak containment within 4 months Improved adherence to contact precautions		Outbreak control Ten recognized KPC types (KPC-2 to KPC 11). KPC-2 are the commonest
[65]	Prospective observational study	To curb CRKP and Acinetobacter baumannii	Greece Serres General Hospital 250-bed hospital	Prokroustes action plan: Surveillance and compulsory notification and IP measures: Isolation or cohorting, contact precautions, hand hygiene	Containment of CRKP three years post-intervention. An increase in CRKP resistant to Colistin, Tigecycline, and gentamycin	There exist challenges for addressing MDROs in regions with established carbapenem resistance.	
[66]	Observational	To identify and control CRKP originating from endoscopic equipment	206-beds cancer center + 988 beds tertiary hospital	Active surveillance using rectal swabs Source isolation Contact precautions Environmental cleaning Hand hygiene PPE: Gowns and gloves MDRO flags on electronic medical records and charts	Seven CRKP cases identified resistant to imipenem		Transmission of carbapenem resistant genes across microbial species within the same environment contributes to resistance. KP outbreaks have also been associated with contaminated sinks, intravenous saline solutions, bath soap, and ultrasonography gel
[67]	Quasi-experimental	To assess the impact of intensified IC measures on colonization and infections associated with CRKP, P.	Solid organ transplant department	Active surveillance + contact precautions + hand hygiene + education + environmental cleaning + monitoring adherence + audit and feedback	Reduction in incidence of colonization from 19 to 9%. Improved adherence to contact precautions.	In CR gram negative bacteria endemic regions, SOT patients have disproportionately higher infections rates of the	

		aeruginosa, and Actionbater baumannii			An increase in the monthly incidence of CRKP from 2.8 to 6.9/ 1000 PDs	organisms. Implementation of enhanced IP measures significantly reduces the colonization	
[68]	Prospective observational study	To control an outbreak of imipenem resistant K. pneumoniae (IR- KP)	France Abdominal surgery care center. 15-bed liver ICU	Screening all patients and Contact isolation and hand hygiene using alcohol-based hand sanitizer. Enhanced measures: Cohorting carriers, dedicated staff, restricting ward admissions, and strict control of patient transfers	Rapid containment of the outbreak		
[69]	Quasi- experimental	To establish if IPC interventions can reduce CRKP infection in ICU	ICU China 629 patients enrolled.	Screening of cultures, de-escalation interventions, contact precautions, isolation/ cohorting, sterilization and disinfection, and bundles (for IV catheter infections, ventilator associated pneumonia, catheter associated urinary tract infections, and skin or soft tissue infections).	CRKP incidence reduced from 10.08 to a low of 2.84 cases per 1000 PDs. ICU acquired CRKP bloodstream infections decreased from 2.54 to 0.41 cases per 1000PDs	Comprehensive IPC interventions significantly reduced ICU related CRKP infections	
[70]	Quasi- experimental	To assess the effect of IP on a CRKP outbreak	Neonatal ICU. 20-beds	Active surveillance using rectal swabs. IPC measures: hand hygiene, auditing compliance, environmental cleaning, and cohorting.	Outbreak containment after cohorting and IPC measures.	Physical isolation is important in preventing the spread of MDROs. ASP is useful in reducing the spread of MDROs	
[71]	Cohort. Prospective observational study	Assessing the effectiveness of multidisciplinary interventions on the transmission of ESBL-KP	Parkland Memorial Hospital, Dallas. Neonatal ICU. 61 infants	Re-educating staff. Auditing hand hygiene and environmental sanitation. Contact precautions. Cohorting Staff & infants. Reducing overcrowding. Screening Neonatal ICU cultures frequently.	Outbreak contained within three weeks	Multidisciplinary intervention using standard IPC measures halted the transmission of extended spectrum beta-lactamase (ESBL) producing KP in the Neonatal ICU.	
[72]	Retrospective observational study	To halt the spread of CRKP	Cà Granda Ospeda- le Maggiore Hospital.	Active surveillance. Isolation.	Outbreak containment		

			ICU. Milan, Italy	Hand hygiene			
[73]	Prospective observational study	To assess the effect of enhanced contact precautions on CRE/CRKP incidence and resistance rates	Tertiary care university hospital. 900 beds. South Korea	Staff education Contact precautions without active surveillance. Cohort isolation. Hand hygiene	An initial increase of the CRE cases (from 1.62 to 9.81/100,000PDs) after which the rates fell back to (0.882/100,000PDs) below baseline levels. A reduction in the resistance rates to imipenem and meropenem following enhanced contact precautions. Hand hygiene adherence improved from 35.2% to 70%	Enhanced infection control measures without active surveillance appear to be effective against the spread of CRE in low prevalence settings	
[74]	Retrospective & Prospective observational study	To stop the spread of ESBL-producing nosocomial bacteria in NICU	17-bed NICU. 355 patients observed. University of Szeged Pediatrics Department. Hungary	Introduction of the INSURE protocol. Antimicrobial regimens review. Microbiological screening. Bathing protocol. Hand hygiene. Continuous monitoring of cases	A significant reduction in the proportion of CRKP colonization or infections. Average number of PDs reduced from 343.72 to 292.44 PDs/ month. Hand hygiene compliance improved from 26.02 to 33.6 hand hygiene procedures per patient per hospital day.	A successful roll back of the CRE infections and colonization was achieved through an interdisciplinary approach.	ESBL-producing bacteria includes <i>E. coli</i> , <i>Enterobacter cloacae</i> , and <i>K. pneumoniae</i>
[75]	Quasi-experimental	To track an outbreak of ESBL-KP using whole genome sequencing	The University Medical Center Groningen (UMCG). 1300 bed tertiary care center. Netherlands	Screening patients and the environment using whole genome sequencing	There was no association between the sporadic case of KP and those that had been diagnosed prior to 2013	Tailor-made makers for identifying genomic signatures have potential for improving the efficiency of IP measures	

Abbreviation footnotes

CDI, *Clostridioides difficile* infections; CRKP, Carbapenem-resistant *Klebsiella pneumoniae* DDD, Daily defined dose; ESBL, Extended spectrum beta-lactamase; HAIs, Healthcare associated infections; ICU, Intensive care unit; ID, Infectious diseases; IP, Infection prevention; MDROs, Multidrug resistant organisms; PD, Patient days; PH, Public health