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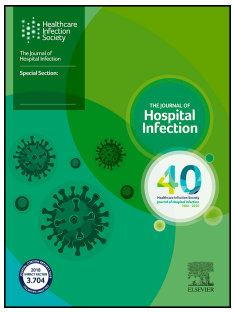

Healthcare-associated infections and the prescribing of antibiotics in hospitalized patients of the Caribbean Community (CARICOM) States: a mixed-methods systematic review

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Healthcare-associated infections and the prescribing of antibiotics in hospitalized patients of the Caribbean Community (CARICOM) States: a mixed-methods systematic review.

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Background
Healthcare-associated infections (HAI) and variation in antibiotic prescribing pose a significant public health challenge in hospitals of low-resource countries.
Aim
To critically appraise and synthesize the evidence on HAI and the prescribing of antibiotics in CARICOM States.
Methods
We included all primary qualitative and quantitative studies that addressed HAI, and the prescribing of antibiotics in hospitalized patients of CARICOM States. We searched Ovid MEDLINE, EMBASE, Global Health and regional databases. Risk of bias was assessed using the Mixed-methods Appraisal Tool. Findings were presented in narrative and table formats.
Results
Twenty-one studies met the inclusion criteria for this mixed-methods systematic review (MMSR). Studies were from four different CARICOM States: Trinidad and Tobago, Jamaica, Haiti and Antigua and Barbuda. The ICU had the highest rate of Infections, 67% over four years. Surgical site infections were discussed by seven studies and ranged from 1.5 to 7.3%. For inpatients with contaminated or infected wounds, rates ranged from 29% to 83%. Empiric and prophylactic therapies were common and inappropriately prescribed. Resources, and training for healthcare workers in infection control and antimicrobial stewardship were insufficient. Few qualitative studies existed, so we were unable to integrate evidence from qualitative and quantitative paradigms.
Conclusions
Evidence from CARICOM States show high rates of healthcare-associated infections, and inappropriately prescribed antibiotics primarily in the ICU. Disease surveillance, infection control and antimicrobial stewardship programs require urgent evidence-based improvements.

Keywords: Healthcare-associated infections, antibiotic prescribing, systematic review, mixed-methods, evidence synthesis, Caribbean

Date of registration in PROSPERO 1st April 2019

Introduction

Healthcare-associated infections (HAI) can be acquired by patients seeking care in healthcare facilities.[1] Factors such as the improper and extended use of invasive medical devices and non-compliance with infection control measures can increase HAI risk. [1] Furthermore, the irrational prescribing and ill-timed administration of antibiotics in hospitals is significant in the emergence of antibiotic-resistant bacteria repeatedly implicated in HAI. [2] Information on HAI and the prescribing of antibiotics in hospitalised patients is limited in low-resource countries. [1] A preliminary literature search of Google Scholar revealed few studies in hospitals of CARICOM States. Antibiotic resistance was the chief focus; however, outpatient antibiotic prescribing, and perceptions of use have also been evaluated [3-9]. Coverage for studies on HAI was higher, albeit the number retrieved was small. These studies focused on overall rates with few studies reporting on device-associated HAI (DA-HAI). [10, 11] Given the importance of antimicrobial resistance and its impact on patient safety when drug-resistant organisms are responsible for HAI, it was crucial to have an in-depth look at available regional evidence. This review aimed to critically appraise and synthesize the evidence on HAI and the prescribing of antibiotics in CARICOM States, using a mixed-method systematic review (MMSR), a "*comprehensive syntheses of two or more types of data… aggregated into a final, combined synthesis." [12]* The integration of qualitative and quantitative evidence would be valuable since healthcare is dynamic and complex. [12]

Methods

The protocol for this systematic review was registered at PROSPERO on 1st April 2019 (ID CRD42019128747). This review is reported according to the Preferred Reporting Items for

Systematic Reviews and Meta-analyses (PRISMA) statement [13] and the Synthesis without meta-analysis (SWiM) in systematic reviews: reporting guidelines.[14]

Eligibility Criteria

We included primary qualitative and quantitative studies in our search. Case studies, letters and editorials were excluded. Both published and unpublished literature with no date or language restrictions were considered. See Appendix A for details of the eligibility criteria.

Search Methods

Search terms for the prescribing of antibiotics differed from those on HAI. Therefore, two search strategies were developed and initially piloted on Ovid Medline (See Appendix B). We searched major databases, MEDLINE®(OvidSP)[1946-present], Global Health (OvidSP)[1973-present], and EMBASE(OvidSP)[1974-present]. Reference lists of included studies were also screened. The last search was completed on the 30th of September 2020. See Appendix C for the complete list of databases and websites searched.

Study selection

Titles and abstracts of retrieved articles were screened using a modified, piloted version of Cochrane's Data Collection Form for intervention reviews. [15] Two reviewers (TW and DC) independently examined full-text articles for compliance with the inclusion criteria. A PRISMA flow diagram [13] of the process has been included (**Figure 1**).

Data extraction

Two reviewers (TW and DC) independently applied the inclusion criteria and extracted data from both paradigms concurrently. We extracted information on study design, settings, patient/participant characteristics, outcome measures, findings, and barriers and limitations. Disagreements were resolved through discussion with a third reviewer (IO).

Risk of bias assessment in individual studies

The Mixed Methods Appraisal Tool [16] (MMAT) was used to assess the included studies' methodological quality. Two reviewers (TW and DC) independently evaluated the risk of bias and IO cross-checked the completed assessments. Discrepancies were resolved via discussion. Figures 2 and 3 show the risk of bias assessments for quantitative studies.

Data analysis and presentation

For the analysis and synthesis of extracted data, we had planned to use an approach similar to the one described by Thomas and Harden [17] followed by a nested analysis of the limitations and barriers. See **Figure 4** for the flow of the MMSR.[18] The investigation of statistical heterogeneity was not planned. However, we visually examined the tabulated data for clinical and methodological heterogeneity.

Findings from the quantitative studies were narratively synthesized, and tables were used for added information. For the nested analysis, we generated descriptive themes using the textual data and presented a descriptive account of the limitations and barriers. We created a codebook of descriptive themes to guide application **(Appendix D).** [19] TW piloted and applied QSR International's NVIVO software (Version 12) to extract and group textual data,

which was defined as the authors' accounts of the factors that may have hindered HAI reduction and affected the rational prescribing of antibiotics. Extracted information was synthesized as described by Thomas and Harden. [20] Our secondary objective was addressed in the discussion section using the products of this synthesis.

2.5 Results

Description of studies

Of 401 retrieved citations, 124 abstracts were screened. Forty-nine articles were eligible for full-text screening; however, eight were excluded since full-text articles were unavailable. [21-28] Nineteen of the 41 remaining articles, were excluded for various reasons. See **Appendix E** for the list of excluded studies. Twenty-one studies comprising 22 articles were included, with two reports from the same study linked since the unit of interest was each study.[29-31] For a description of the studies' characteristics, see **Appendix F**.

Quality of included studies

The methodological quality of included studies was examined according to 7 domains defined by the MMAT Tool. The reporting for quantitative studies related to HAI (n=14) was low to moderate, and the overall risk of bias for studies related to prescribing of antibiotics (n=7) was moderate.

Narrative synthesis

Healthcare-Associated Infections (HAI)

It was not possible to provide summary estimates or in-depth comparisons due to the diversity of measurement tools and sampled populations, as this would have provided misleading results.

Table 1 summarizes the HAI. Rate of HAI was used as an outcome variable in five studies with DA-HAI reported by three.[10, 11, 29, 32, 33] Device use and longer durations of use were associated with higher infection rates.[10, 11] HAI rates ranged from 10 to 63% across included studies. Three studies revealed high overall rates of HAI in inpatients admitted to intensive care units (ICU).[11, 32, 33] One study reported that the ICU had the highest infection rate, 67% over four years. [29]

Seven studies discussed surgical site infections (SSI).[10, 11, 29, 32-35] SSI rates following surgeries on clean wounds ranged from 1.5 to 7.3%.[10, 34, 35] For inpatients with contaminated or infected wounds, rates ranged from 29% to 82.2%.[10, 34] In ICU inpatients, rates ranged from 5 to 31%.[11, 29, 32, 33]

Five studies included data on respiratory infections with one reporting on device-associated pneumonia.[10, 11, 29, 32, 33] Infections of the respiratory tract were highest in the ICU.[11, 32, 33] Bloodstream infections (BSI) were reported by six studies, but central line-associated BSI was not well covered.[10, 11, 29, 32, 33, 36] Of the five studies that reported urinary tract infections, four cited indwelling catheters as contributors to higher infection rates.[10, 11, 29, 32, 33]

Evaluation of infection control guidelines

Sixty-four to 81% of Health Care Workers (HCW) noted that they knew infection control precautions.[37, 38] Knowledge varied among the categories of HCW with porters (8%) having the least amount of knowledge.[38] Compliance with standard precautions, including the use of personal protective equipment also varied among HCW. [37, 39] One study reported a compliance rate of 40% for established infection control guidelines. [37] Two studies reported compliance rates of 38.9% and 48.7% for hand hygiene compliance, and improvements were seen post-intervention in Deshommes and others' research.[40, 41]

Prescribing of antibiotics

Table II encompasses information on prescribing patterns. The duration of antibiotic use ranged from stat doses to 42 days, [2, 34, 42] and intravenous administration ranged from 71.1-96.6%.[2, 34, 43] Rates of antibiotic use for more than one antibiotic ranged from 22-100%, [34, 43-45] sometimes with no clinical or lab-confirmed evidence of infection or consideration for surgical wound classification.[2, 34, 45] Rates of empiric use were as high as 85.8%. According to two studies, empiric antibiotics were continued in the presence of sensitivity results or given in conjunction with culture-directed therapy. [2, 43] The appropriateness of antibiotic treatment varied across units, ranging from 11% in an ICU to 89% in a neonatal ICU.[2, 42] Compared to general wards, adherence to hospital protocol was the lowest, 44%, in one ICU.[43] Regarding knowledge of antibiotic use and resistance, 91% of respondents in one study acknowledged that extensive use of antibiotics contributed to resistance, but 35% of them did not perceive it as a local threat. [46]

Nested analysis

Education, training, knowledge and perceptions

The gap between theory and practice, and the non-standardization of academic programmes were highlighted.[47] Nurse respondents believed that staff were insufficiently trained in infection prevention and control (IPC) and the need for training in IPC and antibiotic use was expressed.[32, 37, 42, 46, 47]

Resources

Human resources

A general shortage of human resources was identified as a common challenge across the CARICOM States. [29, 41, 43, 44, 47] Respondents in one study spoke of substantial workloads, "…*one nurse cannot have all these responsibilities*".[47] For some hospitals, the absence of microbiologists, and clinical pharmacists were cited as problematic for monitoring antimicrobial use. [29, 43, 44] The mismanagement of task distribution, unclear roles, and collaboration within the healthcare setting were other described challenges.[47] Complacency among staff in healthcare institutions, vis-à-vis showing up for duties, and completing tasks was stressed. [44, 47] Noted also was the resistance or reluctance to comply with guidelines.[33, 36, 44, 46]

Hygiene and HAI

Poor hand hygiene infrastructure, coupled with inadequate hand hygiene supplies, was documented in several settings.[29, 41, 47] Functioning handwashing stations were located

away from the point of care, single-use hand drying towels were unavailable, and bed linens were used to dry hands.[29] Workspace cleanliness and the spread of HAI was concerning for staff, "*We do dressings in a room that is not sterile…The patient can contract an infection*." [47] Respondents spoke of clinical specimen on floors, dirty beds and open or unemptied bins in their surroundings "…*the bed is not disinfected, and the garbage is not taken out*". [29, 47] Overcrowded wards and inappropriate isolation areas were also highlighted as contributors to HAI burden. [11, 29, 40]

Hospital Practices

The prescribing of antibiotics for inpatients was based on coverage and the clinical impression of the physician/physician experience with extended use based on physician instruction.[42, 44] Authors hypothesized that; poor communication, inattentiveness of hospital management, delayed reporting of susceptibility results, unavailability of antibiograms, physician negligence in following up, and poorly implemented interventions could explain unjustified antibiotic use.[33, 37, 42-44]

Data integrity

Documentation within the hospital setting was substandard.[29, 34, 45, 47] Inpatient records lacked information on the use of medical devices, wound assessments, and specifics on antibiotic therapy.[30, 45, 47] Researchers noted that there might have been inaccuracies in reported HAI rates due to premature patient discharge, poor surveillance, and the untimely dissemination and collection of diagnostic results.[29, 35, 37, 44]

Discussion

Summary of main findings

Twenty-one studies were selected based on the eligibility criteria. We observed some flaws in the reporting quality of the studies. The areas frequently ill-addressed included using appropriate measurement tools, describing the recruitment strategies for surveys, and using appropriate statistical measures to address the research question.

The burden of HAI was reported by 38% (n=8) of included studies. It was clear that overall and site-specific HAI rates were high, particularly in patients using medical devices. SSI rates were generally high but varied depending on surgical wound classification. The frequency of respiratory tract infections was notable in the ICU. Evidence shows that the rates of all site-specific infections were highest in the ICU and contributed substantially to overall rates. Regarding IPC measures, non-clinical HCW have been shown to have the least amount of knowledge, and compliance rates were low.

Thirty-three per cent (n=7) of the studies reported on the prescribing of antibiotics. It was noted that they are often prescribed inappropriately in comparison to standard guidelines. Of concern were high prescription rates and extended use in all inpatient areas, especially the ICU.

Findings of the descriptive synthesis suggest two overarching challenges in hospitals that may have inadvertently impacted HAI's burden and the prescribing of antibiotics; limited resources and inadequate education and training. Concerning human resources, it was evident that a shortage of qualified personnel plagued hospitals. Poor human resource management may result in negative impacts, such as resistance to change, consequently affecting productivity and compliance with guidelines. With inadequate hygiene infrastructure, HCW have developed

coping mechanisms to deal with resource constraints. However, emphasis needs to be placed on improving infrastructure as its unavailability will inevitably lead to an increase in HAI. Further, the provision of guidelines and training would be useless if the appropriate hygiene tools are not provided.

The need for education and training was made known by many of the authors. Within hospital settings, it was evident that although some staff had a theoretical understanding of the subjects being investigated, it was not applied to real-world settings. The dissemination of contradictory information by academic and healthcare institutions can confuse, and in the absence of evidence-based guidelines, HCW may be forced to make opinionated or 'expert' decisions. Additionally, inadequate documentation of clinical practices was routine, an undesirable occurrence for surveillance and clinical auditing teams. The findings of the investigated phenomena may have also been affected by research methods. With flawed methods, we can expect biased results.

Comparison with the existing literature

We identified two systematic reviews (SR) which looked at prevalence rates of HAI. Unlike our study which examined various study designs, both reviews narrowly focused on point prevalence surveys that applied standardized definitions peculiar to the studies' geographical region. [48, 49] Both studies reported that the HAI rate was higher in ICU compared to other inpatient units while noting the need for standardized surveillance methods.[48, 49] These findings corroborate the findings of our study. Regarding antibiotic prescribing, there were some similarities among results from two identified studies and our study. One SR that examined observational and experimental studies concluded that physicians' knowledge of

antibiotic prescribing was insufficient, signalling the need for training.[50] A hospital-based global (53 countries) point prevalence survey on antimicrobial consumption reported that an average of 71.4% of antibiotics was administered parenterally,[51] similar to our range of 71 to 96.6%. Guidelines were few in approximately 25% of hospitals with compliance rates ranging from 66.3 to 85.8%, [51] values better than those reported in our study.

Strengths and limitations

To our knowledge, this is the first MMSR that assessed HAI and the prescribing of antibiotics in hospitalized patients of CARICOM States. We conducted comprehensive literature searches on various databases and websites, allowing for the retrieval of an unbiased collection of articles. We explored two interrelated phenomena that are subject areas on their own and allowed for a comprehensive understanding of the difficulties in planning for the assessment of two different areas in one review. For practical reasons, the number of objectives was reduced and refined due to time and resource constraints, challenges inherent in mixed-methods approaches.[52] However, we recognize several limitations. We may not have identified all primary studies during our comprehensive literature search, mainly unpublished research. Guidelines for reporting systematic reviews of prevalence have not yet been developed, [53] therefore, those generated for systematic reviews of interventions were used.

The current situation with the prescribing of antibiotics and HAI could not be determined since 81% (n=17) of the included studies were over five years old. The lack of qualitative studies limited this MMSR to the extent where an integrated synthesis of paradigms was unattainable. The variation in study designs prevented us from making meaningful comparisons of prevalence

rates across studies. However, the synthesis of the barriers and limitations described by the studies' authors provided invaluable information on the challenges encountered in the region. Because 48% of included studies were conducted in specific hospitals of two CARICOM States, the findings from the narrative synthesis of our quantitative results cannot be generalized to all CARICOM States.

Implications for practice and research

There is a need to improve surveillance methods, IPC education and training for HCW, and undertake clinical audits with feedback to manage challenges better. Given the evidence on the high rates of infections, and antibiotic prescribing in the ICU, the next step would be to replicate studies addressing HAI and antibiotic use in these critical care units. Considering the difficulties with the inadequacy of documentation, it would be worthwhile to conduct prospective studies to ensure accurate accrual of data. Qualitative research evidence would also contribute to the development of IPC and AMS interventions in the ICU.

Conclusion

Limited evidence from CARICOM states shows that HAI rates and the inappropriate prescribing of antibiotics are high, particularly in the ICU. Our findings also indicate that current surveillance practices fail to identify HAI's actual burden in hospitals. IPC and AMS measures are unsatisfactory, and the adverse effects are exaggerated by non-compliant HCW. Greater emphasis needs to be placed on HCW education and training. Still, there is insufficient evidence to determine what measures need to be adopted to reduce HAI's burden and the irrational prescribing of antibiotics in the region. Findings from high-quality research will provide the

ammunition for evidence syntheses which can be used to inform the development of targeted interventions for CARICOM States.

Declaration of interests

TW is currently employed at the Mount St. John's Medical Centre, Antigua in the Infectious Disease/ Employee Health Division which is responsible for infection prevention and control, and antimicrobial stewardship.

CH holds grant funding from the NIHR School of Primary Care Research Evidence Synthesis Working Group [PROJECT 390], and the NIHR BRC Oxford. He receives expenses for teaching EBM and is also paid for his GP work in NHS out of hours (contract Oxford Health NHS Foundation Trust). He is the Director of CEBM and Editor in Chief of BMJ Evidence-Based Medicine and an NIHR Senior Investigator.
IO, NR, DC and VW have no interests to disclose.

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Tables

Table I Healthcare-associated infections

							Device-associated infections		
Study ID	**Study Design**	**Target Population**	**Sample size**	**Measurement Tool**	**Prevalence rate of Healthcare Associated Infection (%)**	**Surgical Site Infection (%)**	**Catheter- Associated Urinary Tract Infection (%)**	**Central Line-Associated Blood Stream Infection (%)**	**Ventilator Associated Pneumonia (assisted respiration) (%)**
Guerrier 2016	Prospective	Caesarean section patients	523	A case definition of SSI included infection which had occurred within 30 days after surgical procedure and had restricted to skin and subcutaneous tissue, in addition to at least one of the following criteria: 1. Purulent drainage from the incision; 2. Organism isolated from an aseptically obtained culture of fluid or tissue from the incision; and 3. At least one of the following signs or symptoms of infections at the surgical site: pain, tenderness, swelling, redness or heat.	-	1.5*	-	-	-
Macfarlane 1985	Chart review	Patients with positive blood cultures	222	Bacteraemias which developed within 3 days after admission, or before admission to hospital were designated as community-acquired; those with later onset were considered to be hospital-acquired.	-	-	-	-	-
Martin 2006	Retrospective review	Appendicectomy patients	143	Postoperative infection was defined as a fever persisting more than three days after surgery or a wound infection	-	6.3 (1.7*)	-	-	-
O'Shea 2004	Retrospective review	ICU-admitted neurosurgical patients	73	Garner, J. S., Jarvis, W. R., Emori, T. G., Horan, T. C., & Hughes, J. M. (1988). CDC definitions for nosocomial infections, 1988. American journal of infection control,	28.8	5		-	-

				16(3), 128-140.					
Orrett 1998	Retrospective review	All hospitalized patients with nosocomial infections	72,532	Wenzel et al (1976). Hospital-Acquired infections I. Surveillance in A university hospital. American Journal of Epidemiology, 103(3), 251-260	10 (67**)	26.8 (31**)	31 (4.58[0])	-	-
Orrett 2002	Retrospective review	ICU patients	629	Wenzel et al (1976). Hospital-Acquired infections I. Surveillance in A university hospital. American Journal of Epidemiology, 103(3), 251-260	22.1	25.2	-	-	-
Prabhakar 1983	Prospective	Surgical patients from general and paediatric wards.	829	1. A nosocomial infection was defined as one that became clinically related to a surgical or a hospital procedure. 2. A wound was considered infected, with or without bacterial confirmation, by the following criteria: (1) a wound discharging purulent or serosanguinous material; (2) a wound that was tender, red, and edematous. 3. Urinary tract infection A definite diagnosis of urinary tract infection with temperature 99.6" F, dysuria, a colony count of > 100,000 organisms/ml of urine, and isolation of one pathogen. 4.Septicaemia/Bacteraemia A definite diagnosis of septicemia with temperature >99.6" F, hypotension (systolic blood pressure ~90 mm), oliguria, and with or without a positive blood culture. 5. Respiratory tract infection -A definite physician diagnosis of a lower respiratory infection with temperature >99.6" F, cough, purulent sputum, and positive evidence of an infiltrate, consolidation, or pneumonia in a chest x-ray.	27	22.8 (7.3*)	23	43	-

Prabhakar 1985	Retrospective chart review	ICU patients	1352	1. An ICU-acquired infection was defined as any infection which clinically manifested 48 hours after admission into the ICU. 2. Wound Infection A wound was considered infected when there was a purulent or sero-sanguinous discharge with or without bacteriological confirmation. 3. Urinary tract infection A definite diagnosis of urinary tract infection with a temperature > 99.6F, a colony count of 10-5 organism/ml of urine and isolation of one species of pathogen. 4.Septicaemia/Bacteraemia Septicaemia was diagnosed when there was fever (>99.6F), hypotension (systolic B.P. <90 mm Hg) and shock, with or without positive blood culture. 5. Respiratory tract infection -A definite diagnosis of lower respiratory tract infection with a temperature >99.6 F, positive evidence of an infiltrate, consolidation, or pneumonia in a chest X-ray, and purulent secretions with or without positive growth of potentially pathogenic organisms	63	17	5.6 (17.8□)	9 (33.7□)	16 (46.7□)

*Clean surgical wound
** Infection rate in Intensive Care Unit
□ Device in situ > 7 Days
ª Paediatric population

Abbreviation:
ICU: Intensive Care Unit

Table II Prescribing patterns

Study ID	Study design	Target Population	Sample size	Measurement tools-Appropriateness	Inappropriate use (%)	Prophylactic (%)	Empiric (%)	Intravenous Administration (%)	> 1 antibiotics (%)
Chin 2010.	Cross-sectional analytical study	Patients admitted to the ICU with complete chart information.	109	American Thoracic Society and the Infectious Diseases of America Guidelines +	88.9*, 29 □	41	67.9	-	-
Hariharan 2009	Prospective observational study	Inpatients of the adult and paediatric medical and surgical wards and the ICU.	889	Hospital Antimicrobial Policy	36.3	-	-	89	100
Hariharan 2013	Prospective observational study	All patients receiving antimicrobials in the NICU.	353	1.CDC-Prevention of perinatal Group B Streptococcal Disease 2002 2. World Health Organisation. Explore Simplified Antimicrobial Regimens for The Treatment of Neonatal Sepsis. 2002	14.2	-	85.8	71.1	-
Macfarlane 1985	Chart review	All patients with positive blood cultures.	222	Garrod LP, Lambert HP, O'Grady F. Antibiotic and chemotherapy, 5th ed. Edinburgh:Churchill Livingstone, 198l.	43	-	-	-	-
Martin 2006	Retrospective review	All cases of appendicectomy	73	Surgical Infection Society Guidelines	73	96.6	-	96.6	88.6
Orrett 2001	Survey	Discharged inpatients	527	-	-	-	-	-	22
Pereira 2004	Cross-sectional	Adult in- patients (over 13 years) who had received 3GC	192	Sanford Antibiotic Guide	64.6	29.7	68.2	-	49.6

□ Empiric

*Prophylactic

Abbreviations

ICU: Intensive care unit

NICU: Neonatal intensive care unit

CDC: Centers for Disease Control

3GC: Third-generation cephalosporin

Figures

Figure 1 Flow diagram [13] of article selection process

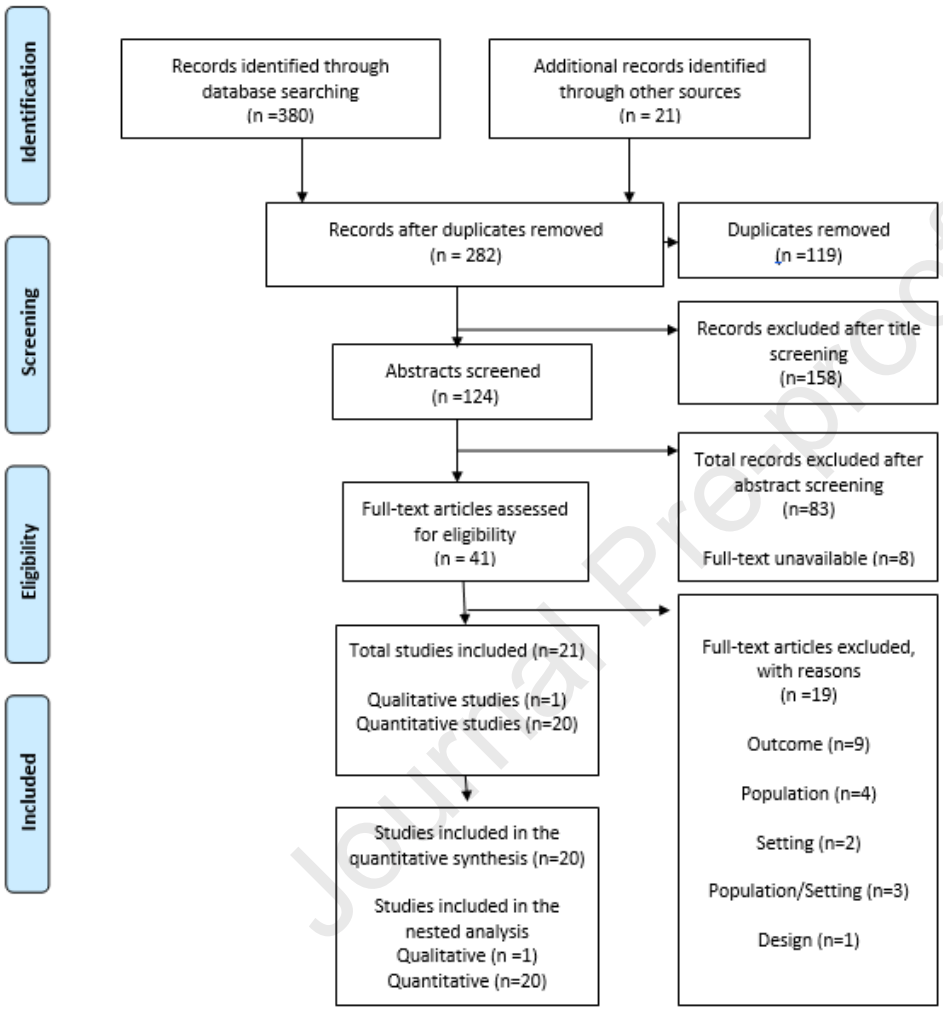
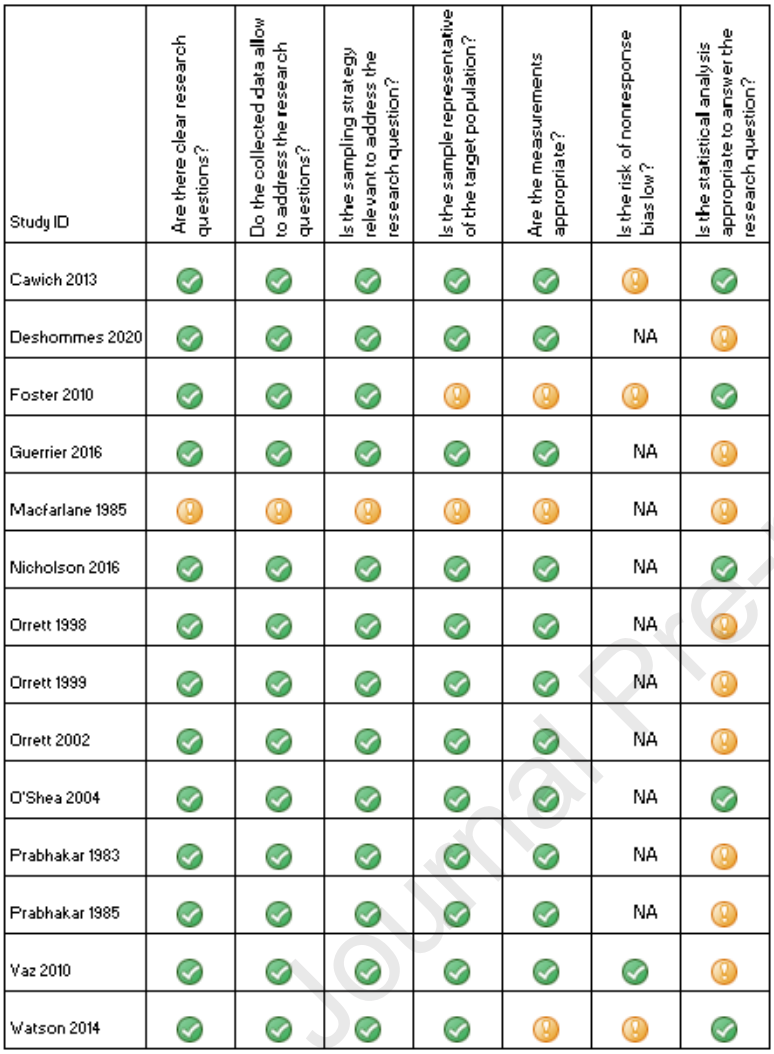
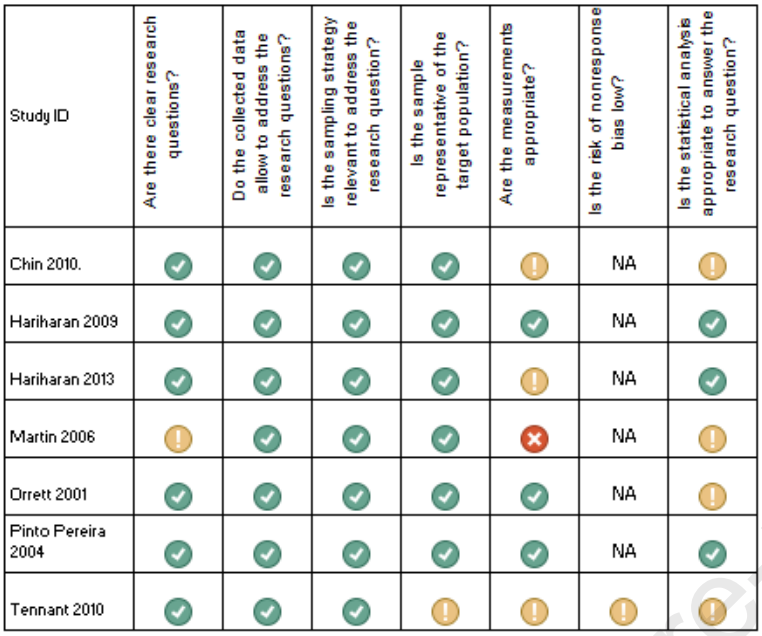


Figure 2 Risk of bias table for included quantitative studies related to HAI



Study ID	Are there clear research questions?	Do the collected data allow to address the research questions?	Is the sampling strategy relevant to address the research question?	Is the sample representative of the target population?	Are the measurements appropriate?	Is the risk of nonresponse bias low?	Is the statistical analysis appropriate to answer the research question?
Cawich 2013	✓	✓	✓	✓	✓	!	✓
Deshommes 2020	✓	✓	✓	✓	✓	NA	!
Foster 2010	✓	✓	✓	!	!	!	✓
Guerrier 2016	✓	✓	✓	✓	✓	NA	!
Macfarlane 1985	!	!	!	!	!	NA	!
Nicholson 2016	✓	✓	✓	✓	✓	NA	✓
Orrett 1998	✓	✓	✓	✓	✓	NA	!
Orrett 1999	✓	✓	✓	✓	✓	NA	!
Orrett 2002	✓	✓	✓	✓	✓	NA	!
O'Shea 2004	✓	✓	✓	✓	✓	NA	✓
Prabhakar 1983	✓	✓	✓	✓	✓	NA	!
Prabhakar 1985	✓	✓	✓	✓	✓	NA	!
Vaz 2010	✓	✓	✓	✓	✓	✓	!
Watson 2014	✓	✓	✓	✓	!	!	✓

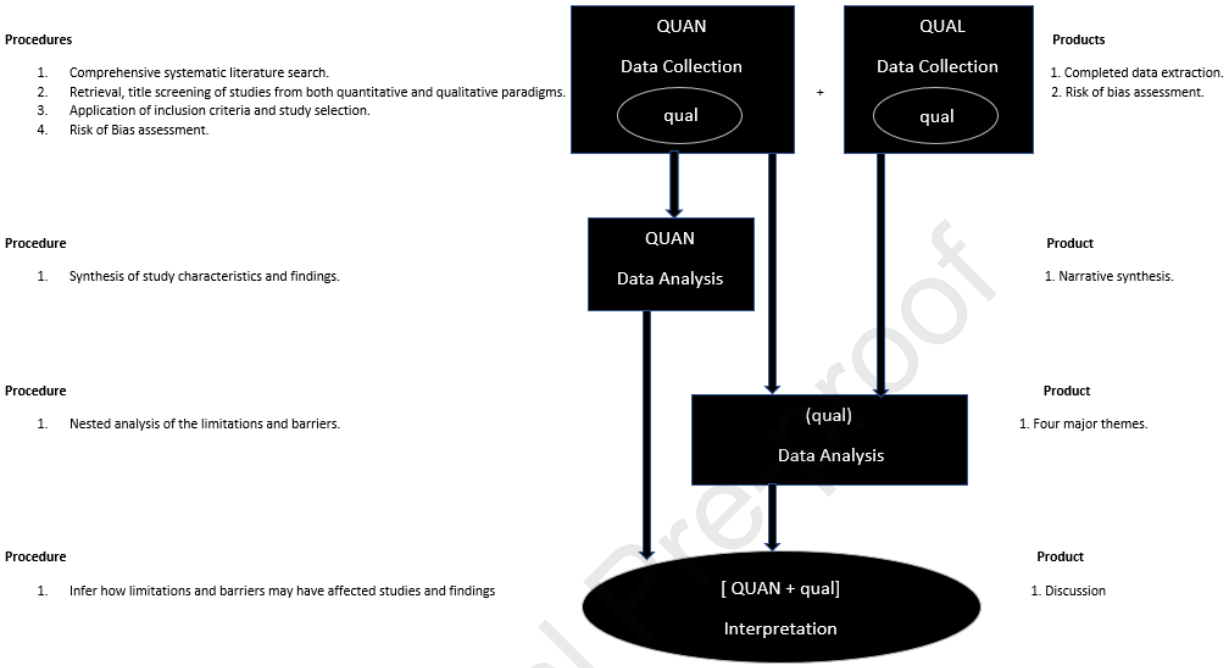
Figure 3 Risk of bias for included quantitative studies related to the prescribing of antibiotics



Study ID	Are there clear research questions?	Do the collected data allow to address the research questions?	Is the sampling strategy relevant to address the research question?	Is the sample representative of the target population?	Are the measurements appropriate?	Is the risk of nonresponse bias low?	Is the statistical analysis appropriate to answer the research question?
Chin 2010.	✓	✓	✓	✓	!	NA	!
Hariharan 2009	✓	✓	✓	✓	✓	NA	✓
Hariharan 2013	✓	✓	✓	✓	!	NA	✓
Martin 2006	!	✓	✓	✓	✗	NA	!
Orrett 2001	✓	✓	✓	✓	✓	NA	!
Pinto Pereira 2004	✓	✓	✓	✓	✓	NA	✓
Tennant 2010	✓	✓	✓	!	!	!	!

Figure Legend

Figure 4 Flow of the mixed-methods systematic review



Appendix A Table A.1 Eligibility Criteria

Table 1: Table showing eligibility criteria for studies.

	Inclusion criteria		***Exclusion criteria***
	Quantitative component	*Qualitative component*	
Population/participants	Inpatients of all ages who were identified as having HAI or nosocomial infections, CAUTI, VAP, SSI, CLABSI and NS. Inpatients who were prescribed antibiotics. Clinicians who prescribed antibiotics for inpatients. HCW exposed to IPC/AMS interventions in hospital settings.	HCW	Studies were excluded if they; evaluated fungal, viral or protozoal HAI, solely assessed antimicrobial susceptibility profiles, Solely assessed community-acquired infections, assessed Group B Streptococcus as the cause of neonatal sepsis.
Intervention/ phenomena of interest	Overall burden of HAI/nosocomial infections/ hospital-acquired infections -evaluated the burden of individual HAIs - CAUTI, CLABSI, VAP, SSI, and NS with or without bacteriological pathogen identification. -evaluated compliance with, knowledge of universal precautions and antimicrobial prescribing guidelines	Studies that explored, knowledge of, acceptability, and compliance with guidelines that focused on practices used for the reduction of HAI, and the appropriate prescribing of antibiotics	
Outcomes	primary and secondary: Incidence/prevalence of HAI including device-associated HAI. Antibiotic use/consumption including appropriateness of use Patient outcomes following a HAI, including mortality HCW knowledge, practices and/or compliance with IPC and AMS guidelines	primary and secondary: acceptability of, compliance with guidelines, knowledge of/attitudes towards guidelines.	
Setting	Within hospital Done in either of the 15 full member CARICOM* States	Within hospital Done in either of the 15 full member CARICOM States	

Types of studies to be included.	All quantitative study designs and mixed methods research.	All qualitative study designs and mixed methods research.

VAP: ventilator-associated pneumonia

CAUTI: catheter-associated urinary tract infections

CLABSI: central line-associated bloodstream infection

SSI: surgical site infections

NS: neonatal sepsis

HCW: healthcare workers

IPC: infection prevention and control

AMS: antimicrobial stewardship

*CARICOM States- a 20 member group of Caribbean nations whose integration ''rests on four main pillars: economic integration; foreign policy coordination; human and social development; and security.'' [27]

Full member states include Antigua & Barbuda, Belize, Dominica, Grenada, Haiti, Montserrat, St. Kitts & Nevis, St. Lucia, St. Vincent & the Grenadines, Bahamas, Barbados, Guyana, Jamaica, Suriname, Trinidad and Tobago.

Appendix B Table B.1 Search strategy (Ovid Medline)

Search terms -strategy one	Search terms -strategy two
1.catheter-related infections/ or cross infection/ or pneumonia, ventilator-associated/ or surgical wound infection/	1. Anti-Bacterial Agents/
2. healthcare-associated or catheter associated or nosocomial or hospital acquired or neonatal or ventilator related or catheter related or ventilator associated or central line associated) adj2 (infection or infections or pneumonia or sepsis)	2. antibiotic*.ti,ab.
3. 1 and 2.	3. 1 or 2
4. caribbean region/ or "antigua and barbuda"/ or bahamas/ or barbados/ or dominica/ or grenada/ or haiti/ or jamaica/ or "saint kitts and nevis"/ or saint lucia/ or "saint vincent and the grenadines"/ or "trinidad and tobago"/	4. "quality of health care"/ or guideline adherence/
5. (Montserrat or dominica or guyana or antigua or barbuda or st kitts or st vincent or bahamas or barbados or trinidad or grenada or jamaica or haiti)	5. Practice Patterns, Physicians'/
6. 4 or 5	6. Drug Prescriptions/
7. 3 and 6	7. 4 or 5 or 6
	8. 3 and 7
	9. (Montserrat or dominica or guyana or antigua or barbuda or st kitts or st vincent or bahamas or barbados or trinidad or grenada or suriname or belize or jamaica or haiti)
	10. 8 and 9

Appendix C Figure C.1 Databases and websites searched

- Medline (Ovid MEDLINE® Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE® Daily and Ovid MEDLINE®)[1946-present]
- EMBASE (OvidSP)[1974-present]
- Global Health (OvidSP)[1973-present]
- Applied Social Sciences Index and Abstracts (ASSIA)(Proquest)[1987-present]
- The Cumulative Index to Nursing and Allied Health Literature (CINAHL) [1997-2020]
- Proquest Dissertations and Theses Global [1973-present]
- Oxford Research Archives (ORA) [https://ora.ox.ac.uk/]
- Global Health Library-Global Index Medicus (LILACS) [http://lilacs.bvsalud.org/en/]
- Caribbean Public Health Agency (CARPHA) [http://carphaevidenceportal.bvsalud.org/]
- West Indian Medical Journal (WIMJ) [https://www.mona.uwi.edu/fms/wimj/]
- Pan American Health Organization (PAHO)-Virtual Health Library [https://www.who.int/library/databases/paho/en/]
- The Cochrane Database of Systematic Reviews (Cochrane Library, Wiley) [Issue 9 of 12, September 2020] [https://www.cochranelibrary.com/cdsr/reviews]
- The International Prospective Register of Systematic Reviews (PROSPERO) [https://www.crd.york.ac.uk/prospero/]

Appendix D Table D.1 Code book

Code	Definition	Purpose or meaning of code	Example
Data Integrity	Researcher describes their experience or findings with relation to data.	Identify instances where the quality, quantity and dissemination of data were substandard. Was anything affected by the data?	*Catheter use during surgical procedures may also be underreported in this review because of failure to document it in the patients records.*
Education, training, knowledge and perceptions	Researcher describes what was uncovered about people's knowledge and perception vis a vis HAI and the prescribing of antibiotics.	Identify instances where knowledge was lacking and perceptions were skewed. Identify instances where education and training may have had ramifications on preventing HAI and improving the prescribing of antibiotics.	*'However, it is important to note that due to insufficient information retention, knowledge and adherence to taught practice may still be deficient in spite of training and education.''*
Hospital practices	Researcher describes the different hospital practices they observed or those reported by respondents.	Identify situations where hospital practices may deviate from protocol.	*'Gloves were consistently used except when doing venepuncture or performing intravenous (IV) access insertion''*
Resources	Researcher describes different types of resources that are needed at the hospitals	Identify instances where the lack of resources could have negative impacts on improving the prescribing of antibiotics and the prevention of HAI.	*'Staff often are frustrated by inadequate supplies of paper towels, delays in obtaining handwashing soaps, and the common use of bed linens to dry hands. ''*

Appendix E Table E.1 Studies excluded following full article review (By order of study ID)

Study ID	Reason for exclusion
Ali 2004	Outcomes do not fit inclusion criteria
Allen 1992	Population does not fit inclusion criteria
Bell 2005	Outcomes do not fit inclusion criteria.
Boulos 2017	Outcomes do not fit inclusion criteria
Christie 1988	Outcomes do not fit inclusion criteria
Christie 1992	Outcomes do not fit inclusion criteria
Desinor 2004	Population do not fit inclusion criteria
Gossell-Williams 2007	Outcomes do not fit inclusion criteria
Kane 1992	Study type does not fit inclusion criteria
Kaseje 2018	Population does not fit inclusion criteria
Mohan 2004	Setting does not fit inclusion criteria
Mungrue 2009	Setting does not fit inclusion criteria
Nicholson 2009	Outcomes do not fit inclusion criteria
Orrett 2001	Outcome do not fit inclusion criteria
Orrett 2007	Outcomes do not fit inclusion criteria
Ostan 2017	Population/setting does not fit inclusion criteria
Tennant 2005	Outcomes do not fit inclusion criteria
Trotman 2006	Population does not fit inclusion criteria
Walsh 2015	Population/setting does not fit inclusion criteria

Appendix E Table E.2 Studies excluded prior to full article review (By order of study ID)

Study ID	Reason for exclusion
Bain 1994	Full text unavailable
Denny 1984	Full text unavailable
Francois 2019	Full text unavailable
Gardiner 1985	Full text unavailable
Hunt 2016	Full text unavailable
Nagassar 2017	Full text unavailable
St. John 1990	Full text unavailable
Riche 2016	Full text unavailable

Appendix F Table F.1 Characteristics of included studies (By order of study ID)

Study ID	Study year	Type of study	Duration	Sample size	Population	Outcome (pre-specified in protocol/methods of study)	Setting
Cawich	2013	Questionnaire	6 months	132	All medical staff stationed in the operating room for over 6 months.	Knowledge of existing infection control policies Adherence to existing infection control policies	University Hospital of the West Indies, Jamaica
Chin	2010	Cross-sectional analytical study	5 months	109	Patients admitted to general ICU with complete information.	Antibiotic usage patterns Comparison of practices with international standards	University Hospital of the West Indies, Jamaica
Deshommes	2020	Prospective	15 months	34	NICU Staff	Compliance with WHO"s "Five Hand Hygiene Moments	St. Damien Pediatric Hospital/Nos Petits-Fre`res et Sœurs, Tabarre, Haiti
Foster	2010	Cross-sectional	-	100	Physicians and nurses	Knowledge of infectious body fluids Knowledge of risk of HIV transmission following needle stick Compliance with infection control procedures	St Ann's Bay Hospital (SABH) and Mandeville Regional Hospital (MRH)
Guerrier	2016	Prospective	6 months	523	All patients attending the obstetrics department who underwent a Caesarean section	Incidence of surgical site infections Risk factors Pathogens	Maternity Ward, Medicine San Frontiers, Haiti
Hariharan	2009	Prospective observational study	12 weeks	889	All inpatients admitted to the 4 general wards	Appropriateness of antibiotic usage Antimicrobial consumption	Eric Williams Medical Sciences Complex, Trinidad and Tobago
Hariharan	2013	Prospective observational study	3 months	353	All patients receiving antimicrobials	Prescribing patterns of parenteral and oral antimicrobials	Neonatal Intensive Care units at the three major public hospitals

Macfarlane	1985	Chart review	12 months	222	All patients with positive blood cultures	Identification of community or nosocomial bacteraemia Antibiotic therapy	University Hospital of the West Indies, Jamaica
Martin	2006	Retrospective review	2 years	143	All cases of appendicectomy	Post-operative wound infection rate Antibiotic use Length of hospital stay. Mortality	Holberton Hospital, Antigua and Barbuda
Nicholson	2016	Prospective observational study /survey	2 weeks	87	HCWs - physicians and nurses at all levels, nursing aides, physiotherapists, technicians, medical students, ancillary workers	Compliance with WHO's Five Hand Hygiene Moments Physical factors (infrastructure) affecting compliance	University Hospital of the West Indies, Jamaica
Orrett	1998	Retrospective review	5 years	72,532	All patients with nosocomial infections	Nosocomial infection rates Cost analysis	San Fernando General Hospital, Trinidad and Tobago
Orrett	2002	Retrospective review	18 months	629	ICU patients	Nosocomial ICU infection rates Major pathogens and antimicrobial resistance	Eric Williams Medical Sciences Complex, Trinidad and Tobago
Orrett	2001	Survey	2 months	527	Discharged patients	Total antimicrobials used	San Fernando General Hospital, Trinidad and Tobago
O'Shea	2004	Retrospective review	39 months	73	Neurosurgical patients admitted to ICU	Rates of infection Patient outcome	University Hospital of the West Indies, Jamaica
Pereira	2004	Cross-sectional	6 months	192	Inpatients over 13 years who had received one or more courses of treatment with one of the 3GCs (cefotaxime, ceftriaxone, ceftazidime)	Appropriate antibiotic prescriptions Cost of antibiotic treatment	General Hospital, Port of Spain

Prabhakar	1985	Retrospective chart review	5 years	1352	Patients admitted to general ICU	Infection rate Risk factors Mortality rate	University Hospital of the West Indies, Jamaica
Prabhakar	1983	Prospective	12 months	829	Surgical patients (adult and paediatric) with wounds. All operations on patients with diabetic gangrene were included in this group.	Incidence of Post-operative wound infection Incidence of other nosocomial infections	University Hospital of the West Indies, Jamaica
Tennant	2010	Cross-sectional survey	7 months	240	Physicians	Physicians' perceptions on the magnitude of antibiotic resistance Prescribing practices Physicians' opinion of their scope of knowledge and interest in further education	University Hospital of the West Indies, Jamaica
Timmins	2018	Qualitative descriptive design	2 months	16(interviewed) 15 (observed)	Nursing staff on the general surgery, orthopaedics and maternity units	Wound care practices Facilitators and barriers for nurses performing wound care	Port Au Prince-tertiary hospital, Haiti
Vaz	2010	Cross-sectional survey	2 months	200	Physicians, medical technologists, nurses and porters	Knowledge and awareness of universal precautions Compliance with universal precautions	University Hospital of the West Indies, Jamaica
Watson	2014	Descriptive cross-sectional study	12 months	62	Physicians, nurses, emergency room technicians	Compliance rates with universal precautions in ER Knowledge of staff members of universal precautions in ER Practices of staff members of universal precautions in ER Perceptions of staff members on universal precautions in ER	University Hospital of the West Indies, Jamaica

Abbreviations: ICU: Intensive care unit

HCW: Health Care Worker

NICU: Neonatal intensive care unit

WHO: World Health Organization

3GC: Third-generation cephalosporin

ER: Emergency room

Appendix G Table G.1 Criteria used for identifying healthcare-associated infections (as documented in included studies)

				Definitions used for Healthcare associated infections		
Study ID	**Setting**	**Healthcare-associated infection/ Nosocomial infection**	**Surgical site infection/ Post-operative wound infection**	**Catheter-associated urinary tract infection/ Urinary tract infections**	**Central line-associated urinary tract infection /Bacteraemia/Septicaemia**	**Ventilator-associated pneumonia/ Respiratory tract infection**
Guerrier 2016	Maternity Ward, Medecin sans frontier, Haiti	Not reported	A case definition of SSI included infection which had occurred within 30 days after surgical procedure and had restricted to skin and subcutaneous tissue, in addition to at least one of the following criteria: 1. Purulent drainage from the incision; 2. Organism isolated from an aseptically obtained culture of fluid or tissue from the incision; and 3. At least one of the following signs or symptoms of infections at the surgical site: pain, tenderness, swelling, redness or heat.	Not reported	Not reported	Not reported
Macfarlane 1985	University Hospital of the West Indies, Jamaica	Not reported	Not reported	Not reported	Bacteraemias which developed within 3 days after admission, or before admission to hospital were designated as community-acquired; those with later onset were considered to be hospital-acquired.	Not reported
Martin 2006	Holberton Hospital, Antigua	Not reported	Postoperative infection was defined as a fever persisting more than three days after surgery or a wound infection.	Not reported	Not reported	Not reported
Orrett 1998	San Fernando General Hospital, Trinidad	Any infection that became clinically evident during hospitalisation (at least 72 hours after admission) not present or incubating prior to admission. Infections acquired by neonates during delivery.	Guided by Wenzel et al (1976). Hospital-Acquired infections I. Surveillance in A university hospital. American Journal of Epidemiology, 103(3), 251-260	Guided by Wenzel et al (1976). Hospital-Acquired infections I. Surveillance in A university hospital. American Journal of Epidemiology, 103(3), 251-260.	Guided by Wenzel et al (1976). Hospital-Acquired infections I. Surveillance in A university hospital. American Journal of Epidemiology, 103(3), 251-260	Guided by Wenzel et al (1976). Hospital-Acquired infections I. Surveillance in A university hospital. American Journal of Epidemiology, 103(3), 251-260.
O'Shea 2004	University Hospital of the West Indies, Jamaica	Nosocomial infections defined according to CDC criteria (1988)	Guided by CDC Criteria, 1988	Guided by CDC Criteria, 1988	Guided by CDC Criteria, 1988	Guided by CDC Criteria, 1988
Orrett 2002	Eric Williams Medical Sciences Complex, Trinidad	Nosocomial infection-any infection that became clinically evident during hospitalisation (at least 72 hours after admission) not present or incubating prior to admission.	Guided by Wenzel et al (1976). Hospital-Acquired infections I. Surveillance in A university hospital. American Journal of Epidemiology, 103(3), 251-260	Guided by Wenzel et al (1976). Hospital-Acquired infections I. Surveillance in A university hospital. American Journal of Epidemiology, 103(3), 251-260.	Guided by Wenzel et al (1976). Hospital-Acquired infections I. Surveillance in A university hospital. American Journal of Epidemiology, 103(3), 251-260	Guided by Wenzel et al (1976). Hospital-Acquired infections I. Surveillance in A university hospital. American Journal of Epidemiology, 103(3), 251-260.
Prabhakar 1985	University Hospital of the West Indies, Jamaica	An ICU-acquired infection was defined as any infection which clinically manifested 48 hours after	Wound Infection A wound was considered infected when there was a purulent or sero-sanguinous	Urinary tract infection A definite diagnosis of urinary tract infection with a temperature > 99.6F, a	Septicaemia/Bacteraemia Septicaemia was diagnosed when there was fever (>99.6F), hypotension (systolic B.P. <90 mm Hg) and	Respiratory tract infection -A definite diagnosis of lower respiratory tract infection with a temperature >99.6 F,

		admission into the ICU	discharge with or without bacteriological confirmation	colony count of 10-5 organism/ml of urine and isolation of one species of pathogen.	shock, with or without positive blood culture.	positive evidence of an infiltrate, consolidation, or pneumonia in a chest X-ray, and purulent secretions with or without positive growth of potentially pathogenic organisms
Prabhakar 1983	University Hospital of the West Indies, Jamaica	A nosocomial infection was defined as one that became clinically related to a surgical or a hospital procedure.	A wound was considered infected, with or without bacterial confirmation, by the following criteria: (1) a wound discharging purulent or serosanguinous material; (2) a wound that was tender, red, and edematous.	A definite diagnosis of urinary tract infection with temperature 99.6” F, dysuria, a colony count of > 100,000 organisms/ml of urine, and isolation of one pathogen.	A definite diagnosis of septicemia with temperature >99.6” F, hypotension (systolic blood pressure ~90 mm), oliguria, and with or without a positive blood culture.	A definite physician diagnosis of a lower respiratory infection with temperature >99.6” F, cough, purulent sputum, and positive evidence of an infiltrate, consolidation, or pneumonia in a chest x-ray.

Abbreviations:

SSI: Surgical site infection

CDC: Center for Disease Control

ICU: Intensive Care Unit

B.P.: Blood Pressure