RISK FACTORS ASSOCIATED WITH ANTIMICROBIAL RESISTANT ORGANISM CARRIAGE

IN RESIDENTS OF RESIDENTIAL AGED CARE FACILITIES: A SYSTEMATIC REVIEW


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A thesis submitted in total requirements for the degree of Master of Clinical Science

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# Declaration

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Christine D Hunt

# Acknowledgement

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I would also like to acknowledge my employer, Eldercare Incorporated, for the support and encouragement they have given me during the last two and a half years.

# Dedication

This work is dedicated to my family:

In particular, to my partner Karen, without whom I would not have been able to complete this work. I will be forever grateful for her endless love, support and encouragement.

And also to my children and their families, including my two darling grandchildren who both arrived while I was working on this review, and a new little one who will be joining the family soon. I hope one day I will be an inspiration to them to pursue lifelong learning.

# Abstract

## Aim

The thesis reports the outcomes of a systematic review conducted to identify the risk factors associated with antimicrobial resistant organism (ARO) carriage in residents of residential aged care facilities (RACF).

## Background

The World Health Organization (WHO) recognises antimicrobial resistance as a critical world health issue and acknowledges that with the reduction in the development of new antibiotics there is an urgent need to take action to slow the spread of antimicrobial resistant organisms (AROs).

Residential Aged Care Facilities (RACFs) aim to provide nursing and personal care to the elderly who can no longer remain in their own home; in an environment that is safe and home-like. AROs are commonly found in aged care settings. A resident who is infected or colonised with an ARO may be a temporary or longer-term carrier of an ARO, and may act as a reservoir for the organism and a potential source of transmission to others. A risk-management approach is required in order to implement effective infection prevention strategies for dealing with residents with AROs. All facilities need to be able to identify the risks in their own context and select the appropriate course of action; however, little is known about the risk factors for ARO acquisition in this population.

## Method

A comprehensive literature search was conducted of Medline, Cumulative Index to Nursing and Allied Health Literature (CINHAL), Embase and Cochrane databases for quantitative studies that

examined the risk factors for carriage of AROs in residents of RACFs. All risk factors associated with carriage of any antibiotic resistant organism in the target population were considered in this review. The review followed the Johanna Briggs Institute (JBI) methodology for conducting systematic reviews of quantitative studies.

## Results

This review considered 32 quantitative studies that met the inclusion criteria and identified risk factors associated with ARO carriage in residents of residential aged care facilities. In all, over seventy potential risk factors were examined in the included studies. Data extracted from these studies were analysed with Comprehensive Meta Analysis (CMA) software. As a result of the meta-analysis a total of 10 statistically significant risk factors that influence the colonisation or infection of residents of RACFs with AROs were identified;

- Comorbidities
- Immobility
- Dependency
- Wounds
- Incontinence
- History of an ARO
- Male Sex
- Invasive devices
- Previous antibiotic therapy
- Hospitalisation

The results will be presented in detail in the thesis.

## Conclusions

Of the 10 risk factors identified not all were generalisable to the population as a whole; however some were, and this generalisability will be discussed further in the thesis. This information will inform risk identification and mitigation protocols for use in this setting. It may potentially lead to the development of a reliable risk assessment tool that staff can use to identify those residents most at risk. This review has provided an evidence base on which to build a planned approach to risk management and the implementation of transmission prevention strategies to prevent AROs in residents of RACFs.

**CHAPTER 1: INTRODUCTION**

## Background

AROs are defined as microorganisms that are able to survive and multiply in the presence of antibiotic concentrations higher than the concentrations in humans receiving therapeutic doses.[1] AROs are a worldwide problem and infections with these organisms can cause considerable morbidity and mortality. Some organisms become resistant to several classes of antibiotics; this phenomenon is referred to as multi-resistance.[2]

RACFs are facilities that provide long term residential care for the elderly and infirm, and they are staffed by people of varying qualifications who provide all the care needs of the individual. Their aim is to provide nursing and personal care to those who can no longer remain in their own home; in an environment that is safe and home-like.[3] RACFs can also be known as nursing or care homes, old folk's homes or geriatric homes. For the purposes of this review facilities that care for residents with a mental disability (regardless of age), short-term rehabilitation facilities, or residents in aged care wards in acute care hospitals were not included in the definition of RACFs. Unlike acute healthcare facilities, RACFs are places where residents reside for many months or even years.

It has long been recognized that residents of RACFs are more susceptible to infections than the elderly living in the general community.[4, 5] This is primarily due to factors that challenge their already diminishing immune system, such as multiple chronic diseases, polypharmacy, and functional impairment (which affects their hygiene practices), and communal living.[6, 7] Unlike the elderly living in their own homes, the RACF environment can be conducive for infection transmission by the nature of its shared living arrangements and frequent hands-on care, where many people interact directly with residents on a daily basis. Each one of these interactions increases the chance of the transference of pathogenic organisms. Some infections affecting residents of RACFs are caused by AROs.[8]

AROs are commonly found in aged care settings[9] and include: Methicillin Resistant *Staphylococcus aureus* (MRSA), Vancomycin Resistant *Enterococcus faecalis* (VRE), and Multi-Resistant Gram-Negative Organisms (MRGNs) such as *Escherichia coli* (*E. coli*) and *Pseudomonas aeruginosa,* and include extended spectrum beta lactamase (ESBL) producers.[8] A recent study by Adam et al[10] concluded that these organisms, when found in older people, are more likely to be resistant to antibiotics when compared to children and adults under 64 years of age with the same organisms.

Residents of RACFs can "carry" AROs on or in their body. This carriage can manifest as either colonisation or infection. Colonisation occurs when a resident has an ARO in or on a body site, but has no clinical signs or symptoms of disease. A colonised resident may be a temporary or a longer term carrier of an ARO, and may act as a reservoir for the organism and a potential source of transmission. Infection with an ARO occurs when the organism enters a body site and multiplies in the tissues, causing disease. Residents who are either infected or colonised with an organism can act as reservoirs for that organism. Human 'reservoirs' are defined as people who have the ability to pass on a pathogenic organism to others, while not necessarily being affected by that organism themselves.[2] While infections with AROs are uncommon in RACFs, when they do occur they are associated with both increased morbidity and mortality.[11-13] Additionally, if residents need to enter the health system, they may act as reservoirs for these organisms and introduce them into the acute care setting.[14]

This systematic review examines the evidence that identifies specific risk factors for the colonisation or infection of residents with AROs in RACFs. It provides an evidence base on which to build a planned approach to risk management, and infection prevention and control strategies to prevent ARO carriage in residents of RACFs.

## Overview of the aim and objectives

The aim of this review was to identify the risk factors associated with ARO carriage in residents of residential aged care facilities.

The objective of the review was to synthesize the best available evidence of the risk factors associated with ARO carriage in residents of residential aged care facilities, in order to determine the factors that make some residents more at risk than others to either colonisation or infection with an antimicrobial resistant organism.

The review question was what are the risk factors associated with antimicrobial resistant organism carriage in residents of RACFs? Specific risk factors were categorised into 3 main areas and this review was designed to answer the following questions:

1. What are the resident risk factors associated with antimicrobial resistant organism carriage in the residential aged care setting?
2. What are the institutional risk factors associated with antimicrobial resistant organism carriage in the residential aged care setting?
3. What are the environmental risk factors associated with antimicrobial resistant organism carriage in the residential aged care setting?

*Resident factors* include any endogenous factors that are related to the resident themselves, and are independent of any medical intervention or environmental influence. Examples of resident factors are: age, sex, predisposing medical conditions, immune status, functional capacity, mobility, wounds and ulcers.

*Institutional factors* include any iatrogenic factors that are related to the risks the institution may pose to the resident, including medical interventions. Examples of institutional factors are: presence of indwelling invasive devices, antibiotic use, hospital stay, length of stay in the RACF, staffing ratios, and clinical policies and procedures.

*Environmental factors* include any factors that are related to the risks the environment may pose to the resident. Examples of environmental factors are: facility size, share room, cleaning of environment, cleaning of equipment, ward layout, and hand hygiene facilities.

## Description of antibiotic resistance

Antimicrobial resistance is not new; bacteria have been developing resistance to antibiotics for almost as long as antibiotics have been available.[1] There is no doubt that the introduction of antibiotics to modern medicine has had a major positive impact on the mortality rate caused by bacterial infections. However, it was observed that within a relatively short time of these antibiotics being introduced, resistance to them developed.[1, 15] Common pathogenic bacteria have developed resistance to each new antibiotic and have become increasingly more difficult to treat. The number of new antibiotics being developed is slowing, making the issue of antimicrobial resistance more urgent.[16] A major cause of antibiotic resistance is the exposure of vulnerable populations (especially those accessing healthcare) to extensive antibiotic use, exacerbated by the frequent contact with healthcare providers who increase the risk of cross infection.[2]

Organisms may be become resistant to antimicrobials in a variety of ways: they may be intrinsically resistant to certain antimicrobial agents, or they may acquire resistance by mutation, or via the acquisition of resistance genes from other organisms. The latter occurs when new genetic material from resistant strains of bacteria is transferred to previously antimicrobial-susceptible bacteria. The use of antibiotics creates selective pressure for the emergence of such resistant strains.[17] Bacteria

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that are resistant have an advantage over those that are susceptible and survive to multiply and continue to pass on that resistance.[15] For the development and proliferation of antibiotic resistance the bacteria must be at first capable of developing resistance, and then may even be able to transfer resistance genes to another bacterial species.[18]

In 2001, recognising the importance of emerging antimicrobial resistance to the future of human health, WHO published a global strategy for the containment of antimicrobial resistance.[1] This stance was strengthened in 2012 when the WHO Patient Safety Programme published their document "The Evolving Threat of Antimicrobial Resistance: Options for Action".[16] This document clearly states infection prevention and control is one of five important areas for the control of antibiotic resistance. It sees infection prevention and control measures as suitable for not only hospitals but also for different types of health-care facilities, including RACFs. They believe the development, implementation and monitoring of Clinical Practice Guidelines that are based on evidence-based principles will be crucial in addressing the issue of AROs.

## Types of antibiotic resistant organisms

Methicillin Resistant *Staphylococcal aureus*

*Staphylococcus aureus* (*S. aureus)* is a gram-positive bacteria found on the skin and/or in the nose of most people. At any given time, 20% to 40% of adults are nasal carriers of *S. aureus*, and up to 70% of the population carries *S. aureus* in their nose at some time during their lifetime.[19, 20] Penicillin is an antibiotic that was developed in the early 1940s, however bacterial resistance to penicillin appeared very soon after its introduction.[21] It is estimated that more than 90% of *S. aureus* isolates are now penicillin resistant.[22] Penicillin resistance is due to the production of penicillinase, an extracellular enzyme that hydrolyzes penicillin. Methicillin, a specific type of penicillin, was designed to resist the action of penicillinase, but *S. aureus* also rapidly developed a resistance to methicillin, giving rise to the organism referred to as MRSA. *S. aureus* resistance can

be mediated via horizontal DNA transfer from one bacteria to another, or through the process of random mutation and selection under antibiotic pressure.[21]

MRSA was first identified in the US in the late 70s. It appears to be no more or less virulent than sensitive strains of Staphylococcus *aureus.*[19, 20] MRSA causes a range of illnesses, from skin and wound infections to pneumonia and bloodstream infections. MRSA bacteria are typical nosocomial pathogens and are often multi-drug resistant, that is, also resistant to other classes of antibiotics, not just methicillin. Multidrug-resistant strains of MRSA can be resistant to a range of other antibiotics such as oxacillin and nafcillin, cephalosporins, and imipenem. In addition, resistance to the fluoroquinolone antibiotics is widespread among MRSA isolates. *S. aureus* has demonstrated great ability to become rapidly resistant to multiple classes of antibiotics through a variety of mechanisms. This leads to the use of the term 'multidrug-resistant *Staphylococcus aureus*', which is often used interchangeably with methicillin resistant *Staphylococcus aureus*. More recently a new stain of MRSA has been identified: Community-acquired MRSA (CA-MRSA). CA-MRSA is generally not multi-drug resistant, and often carries a toxin that contributes to the severity of CA-MRSA infections. Infections with CA-MRSA, especially bloodstream infections, while more likely to be sensitive to antibiotics other than penicillin derivatives, are probably more virulent.[21]

In the United States it was estimated that 80,461 invasive MRSA infections and 11,285 related deaths occurred in 2011.[22] In determining the impact of MRSA on residents in RACFs other studies have estimated that 4 to 10% of residents become MRSA carriers per year, and 5-15% of these residents will develop a MRSA infection.[23, 24] Currently, the antibiotic vancomycin represents the cornerstone of therapy for MRSA. However, at the end of last decade, strains appeared that are intermediately resistant (VISA) or fully resistant (VRSA) to vancomycin.[16, 21]

Vancomycin Resistant Enterococci

Vancomycin Resistant Enterococci (VRE) are gram-positive organisms commonly found in the gut of animals and humans and are under normal circumstances relatively harmless; however they can become pathogenic in immunocompromised patients.[25-27] Developed in 1955, Vancomycin is a glycopeptide antibiotic designed to treat serious infections with gram-positive organisms. This class of drug inhibits the synthesis of bacterial cell walls, by binding to the amino acids within the cell wall of the bacteria and preventing the addition of new components.[28] In 1986, after more than 30 years of successful use, significant resistance to Vancomycin was noted in *Enterococcus faecium.*[28] Today, infections with VRE have become a worldwide problem.[22] Of particular concern is that VRE are often also resistant to other classes of antibiotics, such as penicillin and aminoglycosides, which significantly reduces the antibiotic choices available to prescribers.[29] In addition, there is the threat of transference of vancomycin resistance to bacteria such as *S. aureus.* Of concern is the increased risk for residents in aged care acquiring and carrying VRE.[30-32]

Multi-Resistant Gram-Negative Organisms

Gram-negative bacteria are widespread in humans, animals and the environment. They pose a different kind of threat than gram-positive organisms such as *S. aureus* and Enterococci. MRGNs have diverse mechanisms of resistance which result in a resistance to three or more different classes of antibiotics.[33]

Studies in RACFs show Multi-resistant Gram-Negative organisms (MRGNs) are more frequently isolated than gram-positive multi-resistant organisms.[12, 33-35] Gram-negative bacteria have now emerged that are resistant to most types of antibiotics, including carbapenems, which are considered key "last resort" class of antibiotics for gram-negative bacteria. MRGN organisms include the family of Enterobacteriaceae that includes commonly occurring organisms such as Escherichia, Enterobacter, Klebsiella, Proteus, Salmonella, Serratia and Shigella species.

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MRGN bacteria can cause potentially untreatable infection, and therefore death. The most serious gram-negative infections are healthcare-associated, and the most common pathogens are *Enterobacteriaceae, Pseudomonas aeruginosa*, and *Acinetobacter*. The presence of extended spectrum beta-lacatmases (ESBLs) within this group of organisms has meant that they contain enzymes capable of conferring resistance to a wide variety of antibiotics.[1]

Infections with carbapenem-resistant gram-negative bacteria are associated with high morbidity and mortality.[12] The mechanism of resistance for carbapenem-resistant Enterobacteriaceae (CRE) is usually through production of an enzyme (carbapenemase) that breaks down the antibiotic before it can have an effect of the bacteria. Carbapenemases can affect a range of antibiotics, including penicillin, cephalosporins, as well as carbapenems, thus bacteria producing this enzyme become resistant to a broad range of antibiotics by just this single mechanism of resistance.[16]

MRGNs are an emerging threat worldwide.[16] Their spread is increasing and is encouraged by indiscriminate antibiotic use, poor hygiene and sanitation and international travel.[1] Among all of the bacterial resistance problems, gram-negative pathogens are particularly worrisome, because they are becoming resistant to nearly all drugs that would be considered for treatment.[22] Patients in RACF may also be at increased risk.[34]

## Relevance to the profession

Many infection control guidelines, for example the Australian Guidelines for the Prevention and Control of Infection in Healthcare 2010,[2] Guidelines for the Control of Multidrug-resistant organisms in New Zealand 2007,[36] UK MRSA Guidelines,[37] and the Public Health Ontario Infection Control Guidelines[38] are designed primarily for use by acute healthcare facilities. They provide detailed and rigorous infection prevention strategies and additional infection control precautions for use with patients in acute healthcare facilities who are colonised or infected with AROs. They all also briefly

mention how these strategies can be modified to suit residents colonised or infected with AROs in the RACF setting. In recognizing that this setting is fundamentally different, they recommend a risk management approach be employed to decide the approach to implementing appropriate infection prevention strategies for dealing with residents with AROs.[2]

In practice, utilising risk management strategies as outlined in these types of guidelines is difficult for staff in RACFs because it presumes an awareness of the ARO burden in a facility, and that the at-risk population has been fully identified. Furthermore, the risk factors associated with carriage of AROs in this setting are not well understood. Where specific guidelines applicable to RACFs are available, such as in the US[39], they concentrate mainly on interventions designed to prevent transmission of AROs, and where resident risk factors are discussed, these guidelines describe resident, institutional and, to a lesser extent, environmental risk factors. On examination of the references provided in these guidelines to support the information around risk factors, it appears they are not based on systematic reviews of the literature.[39] Lack of suitable aged care specific guidelines for the management of AROs often sees acute care guidelines being used by staff in RACFs with minimal modification. This can result in the introduction of rigorous infection prevention strategies that, while appropriate for the acute care setting, are often inappropriate in the aged care setting. Such strategies often result in limiting a resident's activity and engagement with the residential care community.[6] In addition they impose potentially unnecessary financial burdens on facilities. Kim et al[40] determined the costs associated with isolation and management of colonised patients in the acute care setting was $1,363 per admission. Information on similar costing in the RACF setting, where length of stay would be much longer, is not readily available.

The results of this review will have significant relevance to the profession in that it will support the identification of relevant risk factors, and enable targeted and appropriate infection prevention and control interventions to be implemented in RACFs, which will reduce transmission of AROs within that setting.

## Certainties or uncertainties in the extant literature

A preliminary review of the literature revealed several cross-sectional studies that determined potential risk factors for colonisation with AROs in residential aged care settings. Raab et al[41] found risk factors associated with MRSA in residents of a German nursing home were: low body mass index ($p$ = 0.005), presence of cerebral circulatory disorder ($p$ = 0.07), and non-mobility status ($p$ = 0.09). Pop-Vicas et al[33] looked at factors associated with colonisation with multidrug-resistant gram-negative bacteria in residents of a RACF in Boston and found a diagnosis of advanced dementia (adjusted OR = 2.9, 95% CI: 1.2–7.35, $p$ = 0.02) and non-mobility status (adjusted OR = 5.7, 95% CI: 1.1–28.9, $p$ = 0.04) were significant risk factors for colonisation. A study by Mody et al[42] concluded that the use of indwelling devices (e.g. urinary catheters and feeding tubes) was associated with colonisation with MRSA at any site (OR = 2.0, $p$ = 0.04). A retrospective cohort study conducted by Nuorti et al[43] concluded that an outbreak of multidrug-resistant Pneumococcal pneumonia in residents was associated with antibiotic use, previous hospitalization, previous pneumonia, and the need for assistance to take oral medication.

A systematic review conducted in 2012 by Xue and Gyi[14] assessed risk factors for MRSA colonisation among adults in acute care settings. Notably, this review found that previous admission to a long-term care facility (such as a RACF) within the last 18 months was associated with MRSA colonisation. As previously discussed guidelines for the prevention of ARO transmission in acute care hospitals are well established but there is a lack of these recommendations for RACFs.[44]

## How this research proposes to address the uncertainties in the extant literature

Xue and Gyi[14] suggested that systematic reviews on risk factors in geriatric patients were a potential area for further research and their findings support the need for this review. While Xue and Gyi looked at a specific type of ARO (MRSA) in the acute setting, no systematic review has been conducted on risk factors for carriage of MRSA in the residential aged care setting. The paucity of systematic review evidence also extends to other types of AROs in the aged care setting. Consequently, this review considers a previously unexamined area of the literature. As such it will contribute to the evidence base for risk management strategies to reduce risk of ARO transmission in the RACF sector.

## Discussion on Methodology Chosen

A systematic review does not seek to create new knowledge but rather to evaluate, synthesize and summarize existing knowledge, and assumes that relevant research already exists on the topic.[45] The systematic review process is considered the highest level of evidence[46] and allows the results of two or more single studies to be reviewed together, providing an overview of the extent of the available literature on a topic. When several sufficiently similar primary research studies are found to have been conducted in an area, the results of these can be combined, thereby increasing the power and reliability of just a single study alone.[47] The value of utilising this methodology over yet another primary research study, is that it provides a greater reliability of results on which to base clinical decision making. It also provides direction to where the gaps in knowledge exist and can indicate further research opportunities.

As several primary research studies looking at risk factors for ARO carriage in residents had been identified, the JBI systematic review methodology for quantitative studies[48] was chosen for this research in order to identify the best available evidence on the topic. Unlike Cochrane,[46] the JBI methodology allows for the inclusion of studies that are drawn from various levels of evidence; from Randomised Control Trials (RCT) through to cross-sectional studies, case reports and expert opinion.[48] The JBI process includes a systematic critical appraisal of all studies and exclusion of those that do not meet the minimum criteria.[48]

In the case of this systematic review no RCTs were likely to be identified. RCTs are experimental studies that aim to interpret the impact of a specific intervention in a specific group, and compare the effect on that group with another (control) group who were not exposed to the intervention; where allocation to the two groups is random. While it is recognised that RCTs are one of the highest level of evidence available because the risk of bias is well controlled, studies of risk factors cannot be conducted via RCTs. RCTs are not appropriate for studies of risk factors as they require the application of an 'intervention' rather than the establishment of a causal link between a 'risk factor' and a disease outcome. By their very nature, the participants cannot be randomised because of the presence of risk factors and/or disease. Nevertheless, other levels of studies can be included in the review if they are appraised for risk of bias, and the controls applied to such biases are identified. The JBI has developed five levels of evidence; with observational studies of analytic designs being rated as level 3, and observational studies of descriptive studies being rated as level 4.[49] In Australia, the National Health and Medical Research Council (NHMRC) provide guidance on levels of evidence according to the type of research question. They classify prognostic studies, such as prospective cohort studies that assess risk, at evidence level II.[50]

## The Evidence Based Health Care movement: the Science of Evidence Synthesis

The Evidence Based Health Care (EBHC) movement came into popularity in the 1990s. In 1996 Sackett et al[51] described evidence based medicine as:

> '.....the conscientious, explicit, and judicious use of current best evidence in making decisions about the care of individual patients. The practice of evidence based medicine means integrating individual clinical expertise with the best available external clinical evidence from systematic research. By individual clinical expertise we mean the proficiency and judgment that individual clinicians acquire through clinical experience and clinical practice.'

EBHC purports that clinical care should be based on the best available scientific evidence, while at the same time recognising the preferences of the person receiving the care, the setting in which care is delivered, and the experience and judgment of the healthcare clinician.[47] The EBHC movement considers the randomised trial for interventions, and in particular the systematic review of several randomised trials, as the "gold standard" for deciding what is best practice. At the same time it recognises that such a level of research may not be necessary, appropriate or available. In these cases the next best available evidence needs to be explored. Evidence-based healthcare has gained increasing acceptance over time and contemporary approaches aim to consider a variety of sources of evidence in order to provide health professionals with the most up-to-date evidence available.[47] This systematic review has been conducted according to JBI methodology and commenced with the development of a review question and describing the population of interest, types of interventions, defining a comparator and detailing types of outcomes (PICO).[48] Unlike narrative literature reviews this methodology requires a rigorous, prescribed, step-wise approach that includes: defining objectives, developing inclusion and exclusion criteria, a planned

search to identify all relevant studies, critical appraisal of those studies by two reviewers independently, data extraction conducted in duplicate, analysis of the data and finally synthesising and presenting the findings.[45]

## Assumptions & Limitations

This systematic review has assumed that the identification of an ARO in a resident was valid, and wherever possible this was verified by information provided in the studies.

Specific limitations and areas for further research will be discussed in Chapter 4.

## Summary

AROs may pose a significant problem in the residential aged care setting; some residents may have factors that make them at risk of ARO carriage. A systematic review of available evidence was conducted. The aim of this thesis is to present:

- the methodology used to conduct the review

- the identified risk factors associated with ARO carriage in residents of residential aged care facilities

- the data on the risk factors associated with ARO carriage in residents of residential aged care facilities

- the factors identified that make some residents more at risk than others to either colonisation or infection with an ARO

- the classification of identified risk factors as either resident, institution, or environment related

- a discussion of the results and their implications

**CHAPTER 2: METHODS**

## Review question/objective

The aim of this review was to identify the risk factors associated with ARO carriage in residents of residential aged care facilities. This review was designed to answer three questions relating to risks in 3 areas (residents institution, environment) as outlined in Chapter 1, page 4.

The objective of the review was to synthesize the best available evidence of the risk factors associated with ARO carriage in residents of residential aged care facilities. More specifically, the objective was to identify the factors that make some residents more at risk than others to either colonisation or infection with an antimicrobial resistant organism.

While the individual risk factors were not pre-determined, the types of risk factors to be included were:

- patient/resident factors (e.g. predisposing medical conditions, immune status, functional capacity);

- institutional factors (e.g. staffing ratios, clinical policies and procedures, antibiotic use, presence of indwelling devices);

- environmental factors (e.g. facility size, cleaning of environment, cleaning of equipment, ward layout, hand hygiene facilities, shared and community living).

**Inclusion criteria**

## Types of Participants

This review considered studies that include permanent residents of residential aged care facilities, both male and female. Carriage of an ARO was defined as the presence of such an organism confirmed via a culture positive result from any site on the body. The carrier status had to be clearly defined in included studies. Studies that reported either ARO colonisation or infection were included. Studies that only looked at a specific disease sub-population of residents under 65 years of age were excluded. Studies that focussed exclusively on residents under the age of 65 were also excluded. Residents under the age of 65 included within studies that were not stratified by age were included.

## Phenomena of Interest

All risk factors associated with carriage of any ARO in residents of residential aged care facilities were considered in this review. A risk factor was defined as a condition that is associated with the presence of an ARO in a resident. Examples of risk factors include, but are not limited to predisposing medical conditions, immune status, functional capacity (resident factors); staffing ratios, clinical policies and procedures, antibiotic use, indwelling devices (institutional factors); and cleaning of environment, cleaning of equipment, ward layout, hand hygiene facilities, shared and community living (environmental factors).

## Types of outcomes

Outcomes of interest included the characteristics of residents with ARO carriage. These were associated with the resident, the facility, and/or the environment (e.g. immune status, clinical policies, ward layout etc.). The measurement of these outcomes included a risk ratio (RR) and/or odds ratio (OR) of risk factors in comparison to residents who do not have an ARO. Where

available, raw data was utilised as this allowed for both OR and RR to be calculated. Where studies did not provide the raw data but rather presented their results as OR and/or RR each set of data was analysed separately.

## Types of studies

This review considered quantitative studies that identified risk factors associated with ARO carriage in residents of residential aged care facilities. Both experimental and epidemiological study designs were considered for inclusion, including randomized controlled trials, non-randomized controlled trials, quasi-experimental, before and after studies, prospective and retrospective cohort studies, case control studies and analytical cross sectional studies. This review also considered descriptive epidemiological study designs including case series, individual case reports and descriptive cross sectional studies for inclusion. As the first ARO was confirmed in the late 1940's,[18] studies from 1950 onwards were included.

## **Search strategy**

The search strategy used aimed to find both published and unpublished studies. A three-step search strategy was utilized in this review. An initial limited search of MEDLINE and CINAHL was undertaken, followed by analysis of the text words contained in the title and abstract, and of the index terms used to describe the article. A second search using all identified keywords and index terms was then undertaken across all included databases. Thirdly, the reference lists of all included reports and articles were searched for additional studies. Studies published in English were considered for inclusion in this review.

The development of a search logic grid and MeSH terms (Appendix I) assisted with the identification of any relevant literature, and contained the following keywords:

- Residential aged care
- Infection control
- Drug resistance
- Risk factors

Where appropriate, alternative terms and spellings were included to allow for variations across countries and ensure all relevant articles were sourced. Search terms were combined with the appropriate Boolean logic. Initial keywords and MeSH terms were identified and included:

- Nursing home/homes for the aged/old age home/residential care

- Geriatric care/geriatric/aged/

- Cross infection/nosocomial infection

- Staphylococcal infection/gram-positive bacterial infection

- Bacterial infection

- *Streptococcus pneumoniae/* pneumococcal infection

- Urinary infection

- *E coli/Pseudomonas aeruginosa*

- Beta-lactamases/extended spectrum/ESBL

- Infection control/prevention and control

- Drug resistance bacterial/microbial

- Risk factor

The following databases were searched for published studies:

- Cochrane (CENTRAL)
- CINHAL
- MEDLINE/ PubMed
- Embase

The search for unpublished studies (Grey Literature), such as government reports, guidelines, conference papers, theses, etc., was conducted using the following search engines and databases:

- Mednar
- ProQuest (PQDT)
- Scirus
- Australian Group on Antimicrobial Resistance (AGAR)

## Assessment of methodological quality

Assessment of methodological quality of 36 studies was undertaken by two independent reviewers (D. Tivey & C Hunt), using standardized critical appraisal instruments from the JBI Meta-Analysis of Statistics Assessment and Review Instrument (JBI-MAStARI) (Appendix II). Inclusion of a study was based an overall score of 50% or more in the affirmative. Where assessment from the two reviewers were not in agreement this was resolved through discussion and subsequent agreement. A third reviewer was available to settle irreconcilable disputes, but was not required.

The inclusion criteria, search strategy and assessment of methodological quality were not changed from those pre-specified in the *a priori* published protocol.[52]

## Data collection

The data collection method deviated from the *a priori* published protocol[52] in that the standardized data extraction tool from JBI-MAStARI was not used. Instead, data were extracted into an Excel spreadsheet (Appendix III) and double checked. Data on populations, study methods and outcomes of significance to the review question were also recorded.

## Data synthesis

The data synthesis method deviated from the *a priori* published protocol[52] in that the JBI-MAStARI was not used to conduct statistical meta-analysis. The Comprehensive Meta Analysis (CMA) software[53] was used because it was necessary to analyse a mix of data formats. Selected studies presented data in variety of ways; raw data, odds ratio and risk ratio results. CMA has flexible functionality which allows for data from multiple formats to be combined for analysis.

Where appropriate, quantitative data was pooled and a statistical meta-analysis conducted using CMA. All results were subject to double data checking on extraction to Excel. Data was copied and pasted from Excel to CMA. Risk factors that were deemed to be of clinical significance were selected for meta-analysis. This determination was made on the basis of those risk factors that had been previously identified in association with ARO carriage in the acute care setting.[2, 14, 20, 35, 54]

Borenstein[55] suggests that the selection of a computational model should be based on the nature of the studies and the objective of the analysis. Fixed affects and random effects models are designed to answer different questions; the fixed effects model looks at determining what is the best estimate of the intervention effect, while the random effects model looks at determining what is the average estimate of the intervention effect and whether the result is generalisable.[56] For this meta-analysis, results were investigated using a random effects model. A random effects model

was preferred over a fixed effects model as it assumes that not all the studies have been conducted in the same way, or on the same type of subjects. This influences the results, and it is not possible to assume a common effect size. If results are to be used to generalise to a range of populations, the random effects model is the most appropriate. It predicts and draws inferences from the studies, rather than describes them. A random effects model assumes there is heterogeneity within and between the studies and we aim to estimate the inconsistencies across the studies. Heterogeneity within a random effects model informs the generalisability of the average effect.

In this analysis, variance between studies was assessed using $Tau^2$. The purpose of $Tau^2$ is to allow an estimate of between-study variance as well as within-study variance. The objective is to assess generalisability of data; i.e. can the next study value be predicted with a degree of certainty. Combined results were reported with 95% confidence interval (CI) and between-study variance was estimated using $Tau^2$. Where there was statistical significance of the meta-analysis results based on the CI, then the predictive interval (PI) was calculated to assess the full degree of heterogeneity. Overall variance, i.e. the combination of within and between-study variance, allows the additional parameter of PI to be calculated and the predictability of the effect assessed. The PI facilitates the full description of the results.[57]

Effect sizes of categorical data have been expressed as odds and/or risk ratio with 95% CI. Where PI has been calculated, this was done because of the expected heterogeneity of the studies and the usefulness of PI as an addition to CI in understanding the effect size. If using CI alone the effect of the heterogeneity may not be fully realised. The use of PI will represent the degree with which we can be 95% certain that the effect will be similar if the study were to be repeated.[57] Where both CI and PI are significant there is a 95 per cent chance that significant results will be achieved for the next observation. Thereby allowing a generalisation that the observed effect

reported for the meta-analysis is likely to generalisable to a broader setting than those reported in the included studies.

Heterogeneity was also explored using sub-group analyses where possible, based on the different study designs included in this review. Sensitivity was assessed using the 'one study removed' facility of CMA. Publication bias was assessed using the funnel plot and the Egger's regression coefficient. In order to minimise the likelihood of false results this assessment was only applied to risk factors that were examined in more than 10 studies. This is in accordance with the Cochrane handbook which states that "tests for funnel plot asymmetry should be used only when there are at least 10 studies included in the meta-analysis, because when there are fewer studies the power of the tests is too low to distinguish chance from real asymmetry".[46]

Some studies had data that did not lend itself to meta-analysis, and where this was the case, a narrative analysis is presented.

**CHAPTER 3: RESULTS**

## Description of Studies

The study selection process is detailed in Figure 1. A total of 1129 articles were identified using the online database search strategy as outlined in the search logic grid (Appendix I). Following the removal of 20 duplicates, the titles and abstracts of 1109 studies were reviewed, with 1046 excluded at this stage as they did not meet the inclusion criteria. The full text of the remaining 63 studies were then reviewed, along with a further 14 studies that were identified by hand-searching the reference lists of the selected studies. Of these 77 studies 41 were excluded as they did not meet the inclusion criteria. The reasons for exclusion are documented in Appendix IV. In one instance the study (Hoogendoorn[58]) combined risk factor data from 2 distinct settings, where only one was a RACF; separate data for each setting were not presented. After contacting the corresponding author and requesting the separate data, no response was received; therefore the study was excluded.

The remaining 36 studies were subjected to critical appraisal. Of these, a total of 4 were excluded (Table 1 & 2) due to not meeting the minimum criteria of 50% positive answers. A total of 32 studies were selected for quantitative analysis and data extraction.[13, 33, 34, 41-43, 59-84]

The 32 included studies were conducted in the United States of America (12), the United Kingdom (5), Germany (3), Italy (2), Belgium (2), Israel (1), China (1), Turkey (1), Australia (1), Slovenia (1), France (1), Spain (1), and Canada (1). Publication dates ranged from 1986 to 2013.

Antibiotic resistant organisms studied included; MRSA (18)[41, 59, 61-69, 71, 73, 77, 80-83], VRE (2)[60, 76] MDR GNB (7)[13, 33, 34, 74, 78, 79, 84] a combination of MRSA/VRE/MDR GNB (3)[42, 70, 72], Fluoroquinolone resistant Salmonella (1)[75] and MDR Streptococcus pneumoniae (1)[43]. The designs of included studies consisted of 25 Descriptive observational studies (13 Prevalence[61, 64, 66, 67, 69, 70, 72, 73, 76, 77, 79, 82, 84] and 12 Cross sectional [33, 41, 42, 59, 60, 62, 65, 68, 71, 78, 81, 84]) and 7 Analytic

observational studies (4 Case Control[34, 63, 75, 83] and 3 Cohort[43, 74, 80]). There were no experimental studies. A total of 72 different risk factors were identified that were examined by the authors of the included studies; 41 of these were resident-related, 25 were institution-related and 6 were environment-related. Sample sizes ranged from 11 participants[75] to 9,156 participants.[70] Overall a total of 29,957 residents were represented in the included studies. A summary of included studies is detailed in Table 3.

**Figure 1: Study Selection Flowchart**

Based on PRISMA Flow Diagram[85]

```
┌─────────────────────────────────┐        ┌─────────────────────────────────┐
│ Potentially relevant studies     │───────▶│ Duplicate studies excluded       │
│ identified by literature search  │        │ (n = 20)                         │
│ (n = 1,129)                      │        │                                  │
└─────────────────────────────────┘        └─────────────────────────────────┘
              │
              ▼
┌─────────────────────────────────┐        ┌─────────────────────────────────┐
│ Review of  Title & Abstract      │───────▶│ Studies excluded at Title and    │
│ (n = 1,109)                      │        │ Abstract review                  │
│                                  │        │ (n = 1,046)                      │
└─────────────────────────────────┘        └─────────────────────────────────┘
              │
              ▼
┌─────────────────────────────────┐        ┌─────────────────────────────────┐
│ Full-text studies retrieved      │◀───────│ Additional studies identifies    │
│ (n = 63)                         │        │ through other sources            │
│                                  │        │ (hand-searching)                 │
│                                  │        │ (n = 14)                         │
└─────────────────────────────────┘        └─────────────────────────────────┘
              │
              ▼
┌─────────────────────────────────┐        ┌─────────────────────────────────┐
│ Full-text articles reviewed      │───────▶│ Studies excluded at full-text    │
│ (n = 77)                         │        │ review                           │
│                                  │        │ (n = 41)                         │
└─────────────────────────────────┘        └─────────────────────────────────┘
              │
              ▼
┌─────────────────────────────────┐        ┌─────────────────────────────────┐
│ Full-text Studies critically     │───────▶│ Full-text articles excluded      │
│ appraised for methodological     │        │ after critical appraisal         │
│ quality                          │        │ (n = 4)                          │
│ (n = 36)                         │        │                                  │
└─────────────────────────────────┘        └─────────────────────────────────┘
              │
              ▼
┌─────────────────────────────────┐
│ Studies included in systematic   │
│ review                           │
│ (n = 32)                         │
└─────────────────────────────────┘
```

## Methodological Quality

The quality of 36 studies was assessed by critical appraisal. The results of this process are presented in Tables 1 and 2.

### Table 1: RESULTS OF CRITICAL APPRAISAL OF DESCRIPTIVE STUDIES

| First Author | MRO type | Q1 | Q2 | Q3 | Q4 | Q5 | Q6 | Q7 | Q8 | Q9 | *Total YES(%) |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Barr[59] | MRSA | N/A | Y | U | Y | Y | N/A | U | Y | Y | 5(71) |
| Brugnaro[61] | MRSA | N/A | Y | U | Y | Y | N/A | Y | Y | Y | 6(86) |
| Cheng[62] | MRSA | N/A | Y | U | Y | Y | N/A | N/A | Y | Y | 5(83) |
| Cox[64] | MRSA | N/A | Y | U | Y | U | N/A | Y | Y | Y | 5(71) |
| Denis[65] | MRSA | Y | Y | Y | Y | Y | N/A | N/A | Y | Y | 7(100) |
| Eveillard[66] | MRSA | Y | Y | Y | Y | Y | N/A | N/A | Y | Y | 7(100) |
| Fraise[67] | MRSA | Y | Y | U | Y | Y | N/A | Y | Y | Y | 7(87) |
| Karabay[68] | MRSA | N | Y | Y | Y | Y | U | Y | Y | Y | 7(78) |
| Lasseter[69] | MRSA | Y | Y | Y | Y | Y | N/A | N/A | Y | Y | 7(100) |
| Manzur[71] | MRSA | Y | Y | Y | Y | Y | N/A | N/A | Y | Y | 7(100) |
| Murphy[73] | MRSA | N | Y | Y | Y | Y | N/A | N/A | Y | Y | 6(86) |
| Pfingsten-W[77] | MRSA | N/A | U | U | Y | Y | U | N/A | Y | Y | 4(57) |
| Seutens[81] | MRSA | Y | Y | Y | Y | Y | N/A | N/A | Y | Y | 7(100) |
| Von Baum[82] | MRSA | Y | Y | U | Y | Y | N/A | N/A | Y | Y | 6(86) |
| Loeb[70] | MRSA/ Resistant Enterobacter/ Pseudomonas a | Y | Y | Y | Y | Y | Y | N/A | U | Y | 7(87) |
| March[72] | MRSA/VRE Enterobacter(ESBL) Other | N/A | Y | Y | Y | Y | N/A | U | Y | Y | 6(86) |
| Mody[42] | MRSA/VRE CTZ-R GNB | U | Y | Y | Y | Y | N/A | N/A | Y | Y | 6(86) |
| Benenson[60] | VRE | U | Y | Y | Y | Y | N/A | U | Y | Y | 6(75) |
| Padiglione[76] | VRE | N/A | Y | U | Y | N/A | N/A | Y | N | N | 3(50) |
| †Stuart[86] | VRE/ESBL | N/A | N | Y | U | U | Y | N/A | Y | U | 3(43) |
| †Bird[87] | MDR GNB: Klebsiella | U | U | U | N | N | U | Y | N | Y | 2(22) |
| Pop-Vicas[33] | MDR GNB | N/A | Y | Y | Y | Y | U | N/A | Y | Y | 6(86) |
| Raab[41] | MDR GNB | N/A | N | N | Y | Y | Y | U | Y | Y | 5(62) |
| Rooney[78] | MDR GNB: ESBL/ E Coli | U | Y | Y | Y | Y | Y | N/A | Y | Y | 7(87) |
| Shlaes[79] | MDR GNB | Y | Y | Y | Y | Y | Y | N/A | Y | Y | 8(100) |
| Wiener[13] | MDR GNB: Klebsiella/ E coli | Y | Y | Y | Y | Y | N/A | N/A | Y | Y | 7(100) |
| Wingard[84] | MDR GNB | N | Y | U | Y | Y | Y | Y | U | U | 5(56) |
| *Total YES(%) | | 10(37) | 23(85) | 16(59) | 25(93) | 23(85) | 6(22) | 7(26) | 23(85) | 24(89) | |

Q1 Was study based on random or pseudo-random sample? Deemed Not Applicable (N/A) if study included all residents within the facility.

Q2: Were the criteria for inclusion in the sample clearly defined?

Q3: Were confounding factors identified and strategies to deal with them stated?

Q4: Were outcomes assessed using objective criteria?

Q5: If comparisons are being made, were there sufficient descriptions of the groups? Deemed N/A if no comparisons made

Q6: Was follow-up carried out over sufficient time? Deemed N/A if study provided point estimates

Q7: Were the outcomes of people who withdrew described and included in the analysis? Deemed N/A if no withdrawals

Q8: Were outcomes measured in a reliable way?

Q9: Was appropriate statistical analysis used?

*% calculated as number of 'YES' answers divided by number of applicable answers x100      † Excluded at critical appraisal

## Table 2: RESULTS OF CRITICAL APPRAISAL OF ANALYTIC STUDIES

| First Author | MRO Type | Q1 | Q2 | Q3 | Q4 | Q5 | Q6 | Q7 | Q8 | Q9 | Total YES (%)* |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Coll[63] | MRSA | Y | Y | Y | Y | Y | Y | N/A | Y | Y | 8(100) |
| Stone[80] | MRSA | N/A | Y | Y | Y | Y | Y | Y | Y | Y | 8(100) |
| Vovko[83] | MRSA | Y | Y | N/A | Y | Y | N/A | N/A | Y | Y | 6(100) |
| †Washio (1996)[88] | MRSA | U | U | N | U | Y | N/A | N/A | Y | U | 2(29) |
| †Washio (2006)[89] | MRSA | N/A | N | Y | U | U | Y | N/A | Y | U | 3(43) |
| Muder[34] | MDR GNB: Enterobacter Pseudomonas a | Y | Y | Y | Y | Y | Y | N/A | Y | Y | 8(100) |
| O'Fallon[74] | MDR GNB | U | Y | Y | U | Y | Y | N/A | Y | Y | 6(75) |
| Olsen[75] | Fluoroquinolone resistant Salmonella | N | Y | U | Y | Y | Y | N/A | Y | Y | 6(75) |
| Nuorti[43] | MDR Streptococcus pneumoniae | U | Y | Y | U | Y | Y | U | Y | Y | 6(67) |
| Total YES(%)[1] | | 3(43) | 7(78) | 6(75) | 5(55) | 8(89) | 7(100) | 1(50) | 9(100) | 7(78) | |

Q1: Is the sample representative of patients in the population as a whole? Deemed Not Applicable (N/A) if study included all residents within the facility.

Q2: Are the patients at a similar point in the course of their condition/illness?

Q3: Has biased been minimised in relation to selection of cases and of controls? Deemed N/A if study was not a case control study.

Q4: Are confounding factors identified and strategies to deal with them stated?

Q5: Are outcomes assessed using objective criteria?

Q6: Was follow-up carried out over sufficient time period? Deemed N/A if study provided point estimates.

Q7: Were the outcomes of people who withdrew described and included in the analysis? Deemed N/A if no withdrawals.

Q8: Were outcomes measured in a reliable way?

Q9: Was appropriate statistical analysis used?

*% calculated as number of 'YES' answers divided by number of applicable answers x100     † Excluded at critical appraisal

If the overall score for a study was 50% or more in the affirmative they were considered for inclusion. Overall the general quality of the included studies was fair (50-74% affirmative) to good (>75% affirmative). There were 4 studies that scored less than 50%; Bird[87], Stuart[86], Washio (2006)[89] and Washio (1996).[88] These studies were excluded based on the results of the critical appraisal.

Ten of the 25 included descriptive studies clearly defined the inclusion criteria, and all but 2 studies (Pfingsten-W[77], Raab[41]) identified and dealt with confounding factors. Most of the included descriptive studies measured outcomes in a reliable way and used appropriate statistical analysis. However, in three descriptive studies (Karabay,[68] Murphy,[73] Wingard[84]) a random sample was not

used. In the Padligione[76] study outcomes were not measured in a reliable way and appropriate statistical analysis was not used (Table 3.2). All seven analytic studies looked at patients at a similar point in the course of their disease and assessed outcomes using objective criteria measured in a reliable way, with appropriate statistical analysis. All but three included analytic studies (O'Fallon[74], Olsen[75], Nuorti[43]) used a sample representative of the population as a whole. (Table 3)

## Table 3: SUMMARY OF INCLUDED STUDIES

| First Author | Year | Country | MRO type | Study Design | Number of participants | Resident Risk Factors Examined | Institutional Risk Factors Examined | Environmental Risk Factors Examined | Key findings (Statistically significant) | Comments |
|---|---|---|---|---|---|---|---|---|---|---|
| Barr[59] | 2007 | UK | MRSA | Cross sectional | 715 | Diabetes; history of colonisation; sex; wound | Hospital stay; IC Guidelines; invasive device; number of beds; previous AB; staff per bed; type of owner | N/A | **Resident Risk factors associated with MRSA:** Male sex **Institutional Risk factors associated with MRSA:** Hospital stay, invasive device; low staff to beds ratio | |
| Brugnaro[61] | 2008 | Italy | MRSA | Point Prevalence | 551 | Cognition; diabetes; decubitus ulcer; history of colonisation; malignancy; mobility; provenance; sex | Duration of stay in facility; gastrostomy; hospital stay; IDC; previous AB | N/A | **Resident Risk factors associated with MRSA:** Malignancy **Institutional Risk factors associated with MRSA:** Hospital stay | |
| Cheng[62] | 2013 | China | MRSA | Cross sectional | 2020 | Chronic cerebral condition; sex | IDC; nasogastric tube; previous AB | Size of living area | **Resident Risk factors associated with MRSA:** Nil **Institutional Risk factors associated with MRSA:** Nil **Environmental risk factors associated with MRSA:** Size of living area; larger area reduces risk | 436 MRSA |
| Coll[63] | 1994 | USA | MRSA | Case Control | 55 | Dependency; sex | Hospital stay; IDC; previous AB | N/A | **Resident Risk factors associated with MRSA:** Dependency **Institutional Risk factors associated with MRSA:** IDC; previous AB | 15 MRSA 40 Controls; Looking at bacteriuria |
| Cox[64] | 1999 | UK | MRSA | Prevelance | 275 | Immobility, sex; skin lesion | N/A | N/A | **Resident Risk factors associated with MRSA:** Male sex; skin lesion | 13 MRSA |
| Denis[65] | 2009 | Belgium | MRSA | Cross sectional | 2953 | Decubitus ulcer; dependency; history of MRSA; immobility; wound | Formulary; hospital stay; medical devices; previous AB; surveillance | N/A | **Resident Risk factors associated with MRSA:** Dependency; history of MRSA; immobility; wound (decubitus ulcer); **Institutional Risk factors associated with MRSA:** Hospital stay; medical devices; previous AB | |

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| First Author | Year | Country | MRO type | Study Design | Number of participants | Resident Risk Factors Examined | Institutional Risk Factors Examined | Environmental Risk Factors Examined | Key findings (Statistically significant) | Comments |
|---|---|---|---|---|---|---|---|---|---|---|
| Eveillard[66] | 2008 | France | MRSA | Point Prevalence | 109 | Age; decubitus; GIR score; sex; skin lesions; wound | Hospital stay; IDC; invasive device; medical imaging; nasogastric; physical therapy; previous AB; sub-cut catheter | N/A | **Resident Risk factors associated with MRSA:** Nil **Institutional Risk factors associated with MRSA:** Medical imaging, previous AB; sub-cut catheter | |
| Fraise[67] | 1996 | UK | MRSA | Point Prevalence | 191 | Wound | Hospital stay; previous AB; surgery | Share room | **Resident Risk factors associated with MRSA:** Nil **Institutional Risk factors associated with MRSA:** Hospital stay; surgery **Environmental Risk factors associated with MRSA:** Nil | |
| Karabay[68] | 2006 | Turkey | MRSA | Cross sectional | 79 | Cardiac disease; diabetes; renal failure; sex; skin lesion | Hospital stay; previous AB | N/A | **Resident Risk factors associated with MRSA:** Skin lesion **Institutional Risk factors associated with MRSA:** Hospital stay; previous AB | 4 MRSA History of infection & recent (last 15 days) ABs excluded |
| Lasseter[69] | 2010 | UK | MRSA | Point Prevalence | 748 | Age; dementia; dependency; history of colonisation; mobility; sex; wound | Hospital stay; invasive device; IV; nasogastric/PEG; surgery; tracheotomy | Share room | **Resident Risk factors associated with MRSA:** Dependency **Institutional Risk factors associated with MRSA:** Hospital stay **Environmental risk factors associated with MRSA:** Nil | |
| Manzur[71] | 2008 | Spain | MRSA | Cross sectional | 1377 | Age; comorbidities; decubitus ulcer; dependency; sex | Duration in facility; hospital stay; medical devices, number of beds; previous AB | N/A | **Resident Risk factors associated with MRSA:** Comorbidities; decubitus ulcer **Institutional Risk factors associated with MRSA:** Hospital Stay; medical devices; number of beds; previous AB | |

| First Author | Year | Country | MRO type | Study Design | Number of participants | Resident Risk Factors Examined | Institutional Risk Factors Examined | Environmental Risk Factors Examined | Key findings (Statistically significant) | Comments |
|---|---|---|---|---|---|---|---|---|---|---|
| Murphy[73] | 2012 | USA | MRSA | Point Prevalence | Unclear | Age; diabetes; education level; faecal incontinence; race; sex; skin lesions | Hospital stay; prevalence of MRSA on admission | N/A | **Resident Risk factors associated with MRSA:** Nil **Institutional Risk factors associated with MRSA:** High MRSA admission prevalence; medical devices | 1;649 admission swabs; 2;111 point prevalence swabs from 26 NH. Number of residents varied according to turnover. |
| Pfingsten-Wurzburg[77] | 2011 | Germany | MRSA | Point Prevalence | 1827 | Dependency; diabetes; sex; wound | Hospital stay; IDC | N/A | **Resident Risk factors associated with MRSA:** Dependency; wounds **Institutional Risk factors associated with MRSA:** Hospital stay; IDC | 139 residents Pos for MRSA |
| Raab[41] | 2006 | Germany | MRSA (PVL) | Cross sectional | 191 Res 104 Staff | Body mass; chronic cerebral condition; dependency; diabetes; eczema; immobility; infection; malignancy; PVD; prosthesis; renal dialysis; sex; smoker; urinary/faecal incontinence; wound | Gastrostomy; hospital stay; IDC; steroids; surgery | Share room/toilet/dining | **Resident Risk factors associated with MRSA:** Chronic cerebral condition; dependency; immobility; underweight; urinary/faecal incontinence **Institutional Risk factors associated with MRSA:** Hospital stay **Environmental Risk factors associated with MRSA:** Nil | No risk factors identified in staff |
| Seutens[81] | 2007 | Belgium | MRSA | Cross sectional | 2908 | Comorbidities; decubitus ulcer; hemiplegia; immobility; systemic disease; urinary continence; UTI | Duration of stay in facility; hospital stay; IDC; previous AB | Number of beds in room | **Resident Risk factors associated with MRSA:** Decubitus ulcer; immobility; systemic disease **Institutional Risk factors associated with MRSA:** Duration of stay in facility; hospital stay; IDC; previous AB **Environmental Risk factors associated with MRSA:** Number of beds in room | |

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| First Author | Year | Country | MRO type | Study Design | Number of participants | Resident Risk Factors Examined | Institutional Risk Factors Examined | Environmental Risk Factors Examined | Key findings (Statistically significant) | Comments |
|---|---|---|---|---|---|---|---|---|---|---|
| Stone[80] | 2012 | USA | MRSA | Cohort study | 412 | Comorbidities; history MRSA; wound | Hospital stay; invasive device; previous AB | N/A | **Resident Risk factors associated with MRSA**: History MRSA<br>**Institutional Risk factors for MRSA**: Invasive Device, previous AB | Prospective study |
| von Baum[82] | 2002 | Germany | MRSA | Point Prevalence | 3236 | Decubitus ulcer; immobility; wound | Duration of stay in facility; facility size; gastrostomy; hospital stay; IDC; previous AB | N/A | **Resident Risk factors associated with MRSA**: Immobility; wound<br>**Institutional Risk factors associated with MRSA**: Facility size; hospital stay; IDC | |
| Vovko[83] | 2005 | Slovenia | MRSA | Case Control | 102 | Age; atherosclerosis; comorbidities; dependency; diabetes; eating assistance; sex; wound | Duration in facility; gastrostomy; hospital stay; previous AB | N/A | **Resident Risk factors associated with MRSA**: Nil<br>**Institutional Risk factors associated with MRSA**: Hospital stay; previous AB | |
| Loeb[70] | 2003 | Canada | MRSA Resistant Enterobacter Pseudomonas a | Point Prevalence | 9156 | N/A | Bed occupancy;  IV therapy; previous AB; staffing ratios | Number of sinks; type of soap | **Institutional Risk factors associated with MRSA:** IV; staffing ratios<br>**Institutional Risk factors associated with Enterobacteriaceae**: IV; previous AB<br>**Institutional Risk factors associated with Pseudomonas a**: Previous AB<br>**Environmental Risk factors associated with MRSA**: Type of soap<br>**Environmental Risk factors associated with Enterobacteriaceae**: Number of sinks<br>**Environmental Risk factors associated with Pseudomonas a**: Nil | Did not look at individual risk factors - institutional and environmental RF only. Looked at only cultures sent for signs of clinical infection |

| First Author | Year | Country | MRO type | Study Design | Number of participants | Resident Risk Factors Examined | Institutional Risk Factors Examined | Environmental Risk Factors Examined | Key findings (Statistically significant) | Comments |
|---|---|---|---|---|---|---|---|---|---|---|
| March[72] | 2009 | Italy | MRSA VRE Enterobacter (ESBL) Other | Point Prevalence | 111 | Age; chronic pulmonary condition; decubitus ulcer; dementia; dependency; diabetes; malignancy; PVD; sex; | Gastrostomy; IDC; nasogastric; previous AB; tracheostomy | N/A | **Resident Risk factors associated with MRSA**: Chronic pulmonary condition; dependency **Institutional Risk factors associated with MRSA**: Nil **Resident Risk factors associated with ESBL**: Nil **Institutional Risk factors associated with ESBL**: Previous AB **Resident Risk factors associated with both MRSA and ESBL:** Nil In**stitutional Risk factors associated with both MRSA and ESBL**: Invasive medical devices | Also looked at staff for carriage |
| Mody[42] | 2007 | USA | MRSA VRE CTZ-R GNB | Cross sectional | 213 | N/A | Gastrostomy; invasive device | N/A | **Institutional Risk factors associated with MRSA**: Indwelling devices (Use of enteral feeding tubes was associated with MRSA colonization in the oropharynx) | Specifically looking at risk of Indwelling Devices. 105 Residents had an Indwelling Device; 108 did not |
| Benenson[60] | 2009 | Israel | VRE | Cross sectional | 1215 | Diabetes; dependency; renal failure; sex; | Duration of stay in facility; ET Tube; gastrostomy; hospital stay; IDC; previous AB | N/A | **Resident Risk factors associated with VRE**: Nil **Institutional Risk factors associated with VRE**: Hospital stay; previous AB | |
| Padiglione[76] | 2001 | Australia | VRE | Point Prevalence | 292 | Decubitus ulcer; sex | Hospital stay; previous AB | N/A | **Resident Risk factors associated with VRE**: Nil **Institutional Risk factors associated with VRE**: Hospital stay | |

| First Author | Year | Country | MRO type | Study Design | Number of participants | Resident Risk Factors Examined | Institutional Risk Factors Examined | Environmental Risk Factors Examined | Key findings (Statistically significant) | Comments |
|---|---|---|---|---|---|---|---|---|---|---|
| Muder[34] | 1997 | USA | MDR GNB: Enterobacter Pseudomonas a | Case Control | 390 | Cardiac disease; chronic cerebral condition; chronic pulmonary condition; chronic renal disease; decubitus ulcer, dementia; diabetes; immobility; malignancy; PVD; | Gastrostomy; hospital stay; IDC; previous AB | N/A | **Resident Risk factors associated with resistant Enterobacteriaceae:** Decubitus ulcer **Institutional Risk factors associated with resistant Enterobacteriaceae:** Previous AB **Resident Risk factors associated with resistant Pseudomonas a:** Nil **Institutional Risk factors associated with resistant Pseudomonas a:** Previous AB | 162 intermediate residents (not defined); 228 NH residents screened for MR GNB. Same number of cases & controls |
| O'Fallon[74] | 2010 | USA | MDR GNB | Cohort study | 172 | Age; decubitus ulcer; dementia; dependency; diabetes; comorbidities; race; sex; urinary/faecal incontinence | Hospital stay; previous AB | N/A | **Resident Risk factors associated with MDR GNB:** Nil **Institutional Risk factors associated with MDR GNB:** Previous AB | Nested matched case control study |
| Pop-Vicas[33] | 2008 | USA | MDR GNB | Cross sectional | 84 | Age; sex; comorbidities; decubitus ulcer; dementia, dependency; faecal incontinence; immobility; sex; wound | Hospital stay; previous AB | N/A | **Resident Risk factors associated with MDR GNB:** Dementia; immobility **Institutional Risk factors associated with MDR GNB:** Nil | |
| Rooney[78] | 2009 | UK | MDR GNB: ESBL E Coli | Cross sectional | 294 | Age; sex; history colonisation; UTI | Hospital stay; IDC; previous AB | N/A | **Resident Risk factors associated with MDR GNB:** History colonisation; UTI **Institutional Risk factors associated with MDR GNB:** Hospital stay; IDC; previous AB | |
| Shlaes[79] | 1986 | USA | MDR GNB | Point Prevalence | 86 | Diabetes; comorbidities; History of colonisation; immobility; UTI | IDC; previous AB | N/A | **Resident Risk factors associated with MDR GNB:** History of colonisation **Institutional Risk factors associated with MDR GNB:** IDC | Looked at Gentamycin resistance specifically; but all isolates had multi-resistance |

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| First Author | Year | Country | MRO type | Study Design | Number of participants | Resident Risk Factors Examined | Institutional Risk Factors Examined | Environmental Risk Factors Examined | Key findings (Statistically significant) | Comments |
|---|---|---|---|---|---|---|---|---|---|---|
| Wiener[13] | 1999 | USA | MDR GNB: Klebsiella E coli | Point Prevalence | 39 | Decubitus ulcer, dependency; sex | Gastrostomy; IDC; previous AB | N/A | **Resident Risk factors associated with MDR GNB**: Dependency **Institutional Risk factors associated with MDR GNB:** Gastrostomy; previous AB | NH Point Prevalence (also did Hospital case-controlled study) |
| Wingard[84] | 1993 | USA | MDR GNB | Cross sectional | 67 | Dependency; immobility; incontinence; marital status | CUD; duration in facility | N/A | **Resident Risk factors associated with MDR GNB**: Dependency **Institutional Risk factors associated with MDR GNB**: Nil | Looked specifically at Trimethoprim resistance but most isolates were also resistant to 3 or more AB classes |
| Olsen[75] | 2001 | USA | Fluoroquinolone resistant Salmonella | Case Control | 11 | Race; sex | Invasive device; previous AB | N/A | **Resident Risk factors associated with FR Salmonella:** Nil **Institutional Risk factors associated with FR Salmonella**: Previous AB (fluoroquinolones) | Facility Outbreak |
| Nuorti[43] | 1998 | USA | MDR Streptococcus pneumoniae | Cohort study | 78 | Age; assistance with medication; comorbidities, previous pneumonia; previous vaccination; sex | Hospital stay; previous AB | Child visitors; share room | **Resident Risk factors associated with MDR Strep p**: Assistance with medication; lack of vaccination; pneumonia in previous 12 months **Institutional Risk factors associated with MDR Strep p**: Hospital stay in previous 12 months; previous AB use at time of illness | 11 residents affected (13% attack rate). Staff screened; 2 colonised. |

## Review Findings

A total of 72 risk factors were examined in the included studies. In order to aid detailed analysis, similar risk factors were aggregated into groups, with a total of 16 risk factor groups being identified (Table 4). For the purpose of this study the creation of the risk factor group identified as 'Comorbidities' included those studies that used this label and either did not define a specific disease or disorder, and/or included the risk factors of Peripheral Vascular Disease (PVD), renal disease, cardiac disease (including atherosclerosis), and chronic pulmonary conditions. Where studies specifically identified factors such as diabetes, dementia and incontinence, these were assigned to their own separate groups because of the particular clinical significance these conditions represent in the aged care setting.

## Table 4: SUMMARY OF RISK FACTORS INCLUDED IN META-ANALYSIS

| Aggregated Risk Factor Group (Resident) | Risk Factors Included in Group | Studies Reporting Risk Factor as Odds Ratio | Studies Reporting Risk Factor as Risk Ratio |
|---|---|---|---|
| Comorbidities | All Comorbidities | Unspecified[71, 74, 79, 81, 83], renal failure/dialysis[34, 41, 60, 68], chronic cerebral condition[34, 41, 62], cardiac disease[34, 68], chronic pulmonary condition[34, 72], Peripheral vascular disease (PVD)[34, 41, 72], systemic disease (unspecified)[81], atherosclerosis[83] | Unspecified[79], renal failure/dialysis[41, 68, 34] chronic cerebral condition[62], cardiac disease[68], |
| | PVD | Unspecified[41, 72], ESBL[72], enterobacter, pseudomonas[34] | Enterobacter, pseudomonas[34] |
| | Cardiac Disease | Unspecified[68], enterobacter, pseudomonas[34] | Enterobacter, pseudomonas[34] |
| | Pulmonary Disease | MRSA, ESBL[72], enterobacter, pseudomonas[34] | Enterobacter, pseudomonas[34] |
| | Cerebral Disease | Enterobacter, pseudomonas[34] | Enterobacter, pseudomonas[34] |
| Age | Any Age | 33, 71, 72, 74, 78, 83 | 33, 69, 78 |
| | Under 80 | 78, 83 | 78 |
| | 80 and over | 71, 72, 74, 78 | 69, 78 |
| Sex | Male and Female | 13, 33, 41, 59-63, 66, 68, 71, 72, 74, 75, 77, 78, 83 | 33, 59, 61-64, 66, 68, 69, 75-78 |
| Dementia | All combined | 33, 34, 72, 74 | 33, 34, 69 |
| Diabetes | All combined | 34, 41, 59-61, 68, 72, 74, 79, 83 | 34, 61, 68, 79 |
| Limited mobility | All combined | 33, 34, 41, 61, 65, 79, 81-84 | 33, 34, 61, 64, 79, 84 |
| Dependency | All combined | 13, 33, 41, 60, 63, 65, 71, 72, 77, 83, 84 | 13, 33, 63, 69, 77, 84 |
| Wounds | All combined | 13, 33, 34, 42, 59, 61, 62, 65-67, 71, 72, 74, 76, 80-83 | 33, 34, 61, 66, 67, 69, 76, 77 |
| Incontinence | All combined | 41, 74, 81, 84 | 84 |
| History of ARO | All combined | 59, 61, 65, 78-80 | 61, 69, 78, 79 |

| Aggregated Risk Factor Group (Institutional) | Risk Factors Included in Group | Studies Reporting Risk Factor as Odds Ratio | Studies Reporting Risk Factor as Risk Ratio |
|---|---|---|---|
| Invasive devices | All combined | All Invasive devices (unspecified) [59, 66, 69, 71, 75, 80], indwelling urinary catheter (IDC)/continuous urinary drainage (CUD)[13, 34, 41, 60-63, 66, 69, 72, 77-79, 82, 84], gastrostomy/nasogastric tube[13, 34, 41, 61, 62, 66, 72, 82], tracheostomy[69, 72], sub-cut catheter[66], IV line[69] | All Invasive devices (unspecified)[66, 69] indwelling urinary catheter (IDC)/continuous urinary drainage (CUD)[34, 61-63, 66, 69, 77, 79, 84], gastrostomy/nasogastric tube[34, 61, 62, 66, 69], tracheostomy[69], sub-cut catheter[66], IV line[69] |
| Antibiotic (AB) use | All ABs/ Timeframes combined | 13, 33, 59-63, 65-68, 70-72, 74, 75, 78-83 | 33, 43, 61-63, 66-68, 76, 78, 79 |
| | In past 3 months | AB unspecified[33, 60, 62, 71, 72, 80-83], fluoroquinolone[65, 70, 81], cephalosporin, nitrofuran[81], amoxyl/clav[65], penicillin[70], TMP-SMX[70] | AB unspecified[33, 43, 62, 76] |
| | Fluoroquinolone/ Ciprofloxacin use | 13, 61, 65, 70, 75, 78, 81 | 61 |
| | Cephalosporin use | 61, 78, 81 | 61, 78 |
| | Penicillin use | 61, 65, 70, 78 | 61, 78 |
| | MRSA | 70, 72 | Nil |
| Hospital Stay in last 12 months | All combined | Hospital stay[33, 34, 41, 59-61, 63, 65, 68, 74, 77, 78, 80-83], surgery[41] | Hospital Stay[33, 34, 41, 43, 61, 63, 68, 69, 76, 77], surgery[41, 69] |
| Length of stay in RACF | Less than 12 months | 60, 61, 82, 83, | 61 |
| | 12 months and over | 61, 81, 84 | 61, 84 |

| Aggregated Risk Factor Group (Environmental) | Risk Factors Included in Group | Studies Reporting Risk Factor as Odds Ratio | Studies Reporting Risk Factor as Risk Ratio |
|---|---|---|---|
| Facility size | All combined | 71, 82 | Nil |
| Share room | All combined | 41, 67, 81 | 67, 69 |

## Meta-Analysis of Risk Factors

Meta-analysis was conducted on 15 of the aggregated risk factor groups. These were; 10 resident factors groups, 4 institutional risk factor group and 1 environmental risk factor group. A random effects model was used, and sub-group analyses were conducted for the following risk factors: co-morbidities, wounds, invasive devices, and antibiotic (AB) use.

Due to the volume of risk factors examined in the studies included in this review, not all were included in the meta-analysis (Appendix V). Factors such as child visitors, geographical region of RACF, previous vaccinations etc were not considered to be clinically significant in determining ARO carriage and were therefore not included in the meta-analysis. In addition, studies that did not provide data in a suitable format were not included in the meta-analysis. Additionally, there were several studies where the risk factors examined were unique to one study only; therefore these risk factors could not be included in the meta-analysis. Discussion of the findings from these studies will be provided separately later in this chapter.

Of the 15 risk factors subjected to meta-analysis, 7 resident-associated risk factors (comorbidities, limited mobility, dependency, wounds, incontinence, history of ARO and male sex), and 3 institution-associated risk factors (invasive device, AB use, hospital stay) showed significant association with the carriage of an ARO (Table 5). Forest plots of this data are provided in Appendix VI. The only environment-associated risk factor that could be meta-analysed (accommodation in a share room) was not found to be statistically significant. Sensitivity analysis to assess the impact of any one study on the outcome of the meta-analysis was conducted using the 'one study removed' facility of CMA across all risk factors undergoing meta-analysis. This process had no impact on the results, showing that no individual study was strongly influencing the result.

## Comorbidities

There were 11 studies that looked at comorbidities as a risk factor[34, 41, 60, 62, 68, 71, 72, 74, 79, 81, 83] (Table 4). Meta-analysis of these studies, with a total of 8,651 participants, demonstrated that residents with comorbidity have a statistically significantly increased odds and risk of carrying an ARO (OR $p$ = <0.01, RR $p$ = 0.04). Overall effect heterogeneity was assessed through PI. Based on the odds ratio data the PI was significant; however, PI for risk ratio results did not reach significance. These differences are a reflection of the number of studies included in each meta-analysis. (Table 5)

Sub group analysis revealed that effect sizes varied with the type of comorbidity; with chronic cerebral condition being the only comorbidity significantly associated with increased odds of ARO carriage (OR $p$ = 0.02). [34, 41, 62] In contrast, PVD, renal disease, cardiac and chronic pulmonary conditions showed no effect. The calculated PI for the risk factor of chronic cerebral condition returned a lower limit that was less than one and non-significant. This indicates that there is significant heterogeneity and that the result of the meta-analysis may not be reproducible. (Table 6)

## Limited Mobility

The assessment of limited mobility ranged from those residents who were totally bed-bound to those that had some limited ability to mobilise. There were 11 studies that looked at limited mobility as a risk factor.[33, 34, 41, 61, 64, 65, 79, 81-84] Meta-analysis of the results from these studies, with a total of 10,843 participants, showed that residents with limited mobility have an increased odds and risk of carrying an ARO ($p$ = <0.01). However, the calculated PI returned a lower limit that was less than one and non-significant. This indicates that there is significant heterogeneity and that the result of the meta-analysis may not be reproducible. (Table 5)

## Dependency

Residents are considered dependent when they require assistance with activities of daily living (ie feeding, bathing, dressing, toileting). There were12 studies [13, 33, 41, 60, 63, 65, 69, 71, 72, 77, 83, 84] that looked at dependency as a risk factor. Meta-analysis of the results from these studies with a total of 8,769 participants showed that residents who are dependent on others for assistance have a significantly increased odds and risk of carrying an ARO ($p$ = <0.01). However, there was a wide PI interval and therefore was non-significant. This indicates that there is significant heterogeneity and that the result of the meta-analysis may not be reproducible. (Table 5)

## Wounds

Residents with skin tears, surgical wounds, pressure (decubitus) ulcers and other breaks in the skin were identified as having a wound. There were 20 studies [13, 33, 34, 42, 59, 61, 62, 65-67, 69, 71, 72, 74, 76, 77, 80-83] that looked at the presence of a wound as a risk factor. Meta-analysis of the results from these studies with a total of 18,450 participants demonstrated that a resident who had a wound has a significantly increased risk and chance of carrying an ARO ($p$ = <0.01). The calculated PI was significant. There appeared to be minimal heterogeneity among the included studies making the results reproducible. (Table 5)

Sub group analysis on decubitus ulcers alone compared with all other wound types revealed that effect sizes varied slightly, but that both types of wounds remained associated with increased odds and risk of ARO carriage ($p$ = <0.01). PI data demonstrated that the odds data results for both wounds and decubitus ulcer would be reproducible, however the risk data results for decubitus ulcers were of borderline significance. More studies would need to be included in the analysis in order to mirror the reproducibility of the odds data for this risk factor. (Table 7)

## Incontinence

Incontinence of urine and/or faeces was examined as a risk factor in 4 studies.[41, 74, 81, 84] Meta-analysis of the results from these studies with a total of 3,338 participants demonstrated that residents who are incontinent have a significantly increased odds and risk of carrying an ARO ($p$ = <0.01). The calculated PI of odds ratio data was extremely large and crossed unity, and therefore was not significant. The risk ratio data was from 1 study only therefore the PI was not calculable. This indicates that there was heterogeneity among the included studies; therefore results are not reproducible. (Table 5)

## Male Sex

A total of 20 studies looked at sex as a potential risk factor.[13, 33, 41, 59-64, 66, 68, 69, 71, 72, 74-78, 83] Meta-analysis of the results from these studies with a total of 10,267 participants revealed that male residents were at higher risk of carrying an ARO than females, however the significance of this result was borderline as the lower confidence limit was approaching 1. In addition, the calculated PI was non-significant, indicating that there is significant heterogeneity and that the result of the meta-analysis may not be reproducible. (Table 5)

## History of an ARO

History of either colonisation or infection with an ARO was examined as a risk factor in 7 studies.[59, 61, 65, 69, 78-80] Meta-analysis of the results from these studies with a total of 5,759 participants demonstrated that residents who had a history of an ARO have a significantly increased odds and risk of carrying an ARO ($p$ = <0.01). Based on the $Tau^2$ value there is a large between-study variance, and given the small number of studies the PI is greatly affected. From these results is not possible to predict whether a history of an ARO would be significant if the study was repeated. (Table 5)

## Invasive devices

Studies looking at invasive devices included residents with urinary drainage devices, gastrostomy/nasogastric tubes, tracheostomy, and sub-cutaneous and intravenous catheters. There were 19 studies [13, 34, 41, 59-63, 66, 69, 71, 72, 75, 77-80, 82, 84] that looked at the presence of an invasive device as a risk factor. Meta-analysis of the results from these studies with a total of 13,454 participants demonstrated that residents who have an invasive device in situ have a significantly increased odds and risk of carrying an ARO ($p$ = <0.01). Based on the odds ratio data there is an apparent large between-study variance, with the lower PI being above 1. Based on $Tau^2$ however, within-study variation was small resulting in a significant predictive interval. (Table 5)

A sub group analysis of invasive devices showed a significant association between the carriage of an ARO in residents with a Gastrostomy/Nasogastric tube ($p$ = <0.01), and an indwelling urinary catheter/continuous urinary drainage (IDUC/CUD) ($p$ = <0.01). Of these results, the PI for the risk of carrying an ARO in residents with Gastrostomy/Nasogastric tube indicated that it was the only risk factor in which this result would be reproducible. (Table 8)

## Antibiotic Use

There were 24 studies that looked at previous antibiotic use as a risk factor. [13, 33, 43, 59-63, 65-68, 70-72, 74-76, 78-83] Meta-analysis of these studies with a total of 26,246 participants demonstrated that residents who have had previous antibiotic therapy have a significantly increased odds and risk of carrying an ARO ($p$ = <0.01).  However, the calculated PI was non-significant, indicating heterogeneity within the studies, and that the result of the meta-analysis may not be reproducible. (Table 5)

Sub group analysis showed a significant association between ARO carriage and with the use of antibiotics specifically within the last 12 weeks ($p$ = <0.01). With regards to type of antibiotic used, the

use of fluoroquinolone/ciprofloxacin and cephalosporins resulted in statistically significantly increased odds and risk of carriage ($p$ = <0.01), while the effect size for penicillin did not reach significance ($p$ = 0.34 and 0.911 for OR and RR respectively). The calculated PI for these sub-groups indicated that these results may not be reproducible. (Table 9)

## Hospital stay

Residents who had been admitted to hospital (including for surgery) were examined in 19 studies.[33, 34, 41, 43, 59-61, 63, 65, 68, 69, 74, 76-78, 80-83] Meta-analysis of the results from these studies with a total of 16,302 participants demonstrated that residents who had been in hospital have a significantly increased odds and risk of carrying an ARO ($p$ = <0.01). However, the calculated PI was non-significant, indicating heterogeneity within the studies, and that the result of the meta-analysis may not be reproducible. (Table 5)

## Length of stay

A meta-analysis of the 6 studies[60, 61, 81-84] examining the length of stay in the RACF of 8,097 participants showed no association with an increased odds and risk of carriage of an ARO with those residents whose length of stay was greater than 12 months ($p$ = 0.70 and 0.85 for OR and RR, respectively). For residents who had been in the facility for up to 12 months no significant effect was seen for odds of ARO carriage ($p$ = 0.75); however, in one study the risk of carriage was found to be significantly increased ($p$ = 0.04). (Table 5)

## Other risk factors

Following meta-analysis some risk factors did not show any correlation with the carriage of an ARO.

Age: a total of 7 studies[33, 69, 71, 72, 74, 78, 83] looked at age as a potential risk factor. There was no statistical significance for either residents who were under 80 years of age (OR $p$ = 0.77, RR $p$ = 0.98) or over 80

(OR $p$ = 0.09, RR $p$ = 0.11). Dementia: a meta-analysis of the 5 studies[33, 34, 69, 72, 74] that examined dementia did not demonstrate significance as a risk factor (OR $p$ = 0.93, RR $p$ = 0.10). Diabetes: a meta-analysis of the 10 studies [34, 41, 59-61, 68, 72, 74, 79, 83] that examined diabetes did not demonstrate significance as a risk factor (OR $p$ = 0.89, RR $p$ = 0.55). Share room: A meta-analysis of 4 studies[41, 67, 69, 81] showed no association with an increased odds and risk of carriage of an ARO in those residents who resided in a share room (OR $p$ = 0.37, RR $p$ = 0.98). (Table 5)

## Facility size

A total of 2 studies looked at facility size as a risk factor for ARO carriage[71, 82] but this data was not suitable for meta-analysis as the definition of size was not comparable, with one study classifying size as either 'small' or 'medium', and the other expressed size in terms of bed numbers (<150 beds).

## Publication Bias

Publication bias was assessed using the funnel plot and the Eggar's regression coefficient. The associated funnel plots with regression data for the meta-analysis are provided in Appendix VII The funnel plots and the Eggar regression data indicate presence of no, or minimal, publication bias for all risk factors except Antibiotic Use. The risk factors of all antibiotic use, and all antibiotic use within the previous 12 weeks showed significant publication bias. This may be due to the under-reporting of results that do not demonstrate an association between antibiotic use and ARO carriage. These results also did not look at individual classes of antibiotics, but rather grouped them all together, and this may have influenced the bias.

# Table 5: OVERALL RESULTS OF META-ANALYSIS OF RISK FACTORS

| Risk factor | Number of studies† | Odds ratio | Lower confidence limit* | Upper confidence limit* | p-Value | Lower predictive interval* | Upper predictive interval* | Tau² | Number of studies† | Risk ratio | Lower confidence limit* | Upper Confidence limit* | p-Value | Lower predictive interval* | Upper predictive interval* | Tau² |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Resident** | | | | | | | | | | | | | | | | |
| Comorbidities | 11 | **1.64** | **1.34** | **2.02** | **<0.01** | **0.01** | **2.66** | 0.034 | 5 | **1.43** | **1.02** | **1.99** | **0.04** | **0.49** | **4.13** | 0.082 |
| Limited Mobility | 10 | **2.20** | **1.53** | **3.16** | **<0.01** | **0.81** | **5.95** | 0.152 | 6 | **1.42** | **1.14** | **1.80** | **<0.01** | **0.77** | **2.62** | 0.036 |
| Dependency | 11 | **2.66** | **1.69** | **4.19** | **<0.01** | **0.58** | **12.09** | 0.394 | 6 | **1.90** | **1.40** | **2.57** | **<0.01** | **0.77** | **4.70** | 0.083 |
| Wounds | 17 | **2.35** | **1.90** | **2.91** | **<0.01** | **1.38** | **4.05** | 0.058 | 8 | **1.99** | **1.55** | **2.56** | **<0.01** | **1.47** | **2.67** | 0.000 |
| Incontinence | 4 | **4.05** | **1.51** | **10.86** | **<0.01** | **0.07** | **222.95** | 0.615 | 1 | **3.26** | **1.64** | **6.49** | **<0.01** | n/a | n/a | 0.000 |
| History of ARO | 6 | **2.70** | **1.69** | **4.32** | **<0.01** | **0.67** | **10.91** | 0.195 | 4 | **2.88** | **1.32** | **6.29** | **0.01** | **0.13** | **62.09** | 0.350 |
| Sex (male vs female) | 18 | **1.20** | **1.01** | **1.42** | 0.03 | **0.83** | **1.73** | 0.023 | 16 | **1.20** | **1.01** | **1.43** | 0.04 | **0.75** | **1.92** | 0.040 |
| Age: Under 80 | 2 | 1.08 | 0.66 | 1.76 | 0.77 | NR | NR | 0.000 | 1 | 0.99 | 0.63 | 1.56 | 0.98 | NR | NR | 0.000 |
| Age: 80 and over | 4 | 1.20 | 0.97 | 1.47 | 0.09 | NR | NR | 0.000 | 2 | 0.78 | 0.58 | 1.06 | 0.11 | NR | NR | 0.000 |
| Dementia | 4 | 0.96 | 0.39 | 2.35 | 0.93 | NR | NR | 0.629 | 3 | 1.17 | 0.97 | 1.40 | 0.10 | NR | NR | 0.000 |
| Diabetes | 10 | 0.98 | 0.75 | 1.28 | 0.89 | NR | NR | 0.016 | 4 | 0.84 | 0.49 | 1.47 | 0.55 | NR | NR | 0.063 |
| **Institutional** | | | | | | | | | | | | | | | | |
| Invasive Device | 19 | **2.61** | **2.02** | **3.38** | **<0.01** | **1.04** | **6.56** | 0.173 | 9 | **2.13** | **1.52** | **2.97** | **<0.01** | **0.71** | **6.41** | 0.188 |
| AB Use | 22 | **2.40** | **1.84** | **3.12** | **<0.01** | **0.84** | **6.82** | 0.233 | 11 | **1.73** | **1.39** | **2.14** | **<0.01** | **0.90** | **3.30** | 0.070 |
| Hospital stay (incl surgery) | 16 | **2.05** | **1.61** | **2.63** | **<0.01** | **0.91** | **4.64** | 0.129 | 10 | **1.73** | **1.34** | **2.24** | **<0.01** | **0.95** | **3.16** | 0.051 |
| Length of stay up to 12mo | 4 | 1.70 | 0.72 | 3.99 | 0.23 | NR | NR | 0.562 | 1 | 1.54 | 1.01 | 2.33 | 0.04 | NR | NR | 0.000 |
| Length of stay greater than 12mo | 3 | 0.90 | 0.55 | 1.50 | 0.70 | NR | NR | 0.261 | 2 | 1.05 | 0.62 | 1.78 | 0.85 | NR | NR | 0.192 |
| **Environmental** | | | | | | | | | | | | | | | | |
| Share room | 3 | 1.24 | 0.78 | 1.97 | 0.37 | NR | NR | 0.099 | 2 | 0.99 | 0.40 | 2.44 | 0.98 | NR | NR | 0.210 |

*95% confidence limit

† Refer to Table 1 for detail of included studies

NR = Not Reported: Predictive intervals not reported for factors not reaching statistical significance

## Table 6: SUB GROUP ANALYSIS OF CO-MORBIDITIES: BY TYPE

| Risk factor | Number of studies† | Odds ratio | Lower confidence limit* | Upper confidence limit* | p-Value | Lower predictive interval* | Upper predictive interval* | Tau² | Number of studies† | Risk ratio | Lower confidence limit* | Upper Confidence limit* | p-Value | Lower predictive interval* | Upper predictive interval* | Tau² |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Chronic cerebral condition | 3 | **1.70** | **1.10** | **2.64** | **0.02** | **0.67** | **4.35** | **0.037** | 2 | 1.30 | 0.87 | 1.92 | 0.20 | NR | NR | 0.058 |
| PVD§ | 3 | 1.04 | 0.39 | 2.73 | 0.94 | NR | NR | 0.052 | 1 | 0.50 | 0.24 | 1.04 | 0.06 | NR | NR | 0.000 |
| Cardiac condition | 2 | 1.74 | 0.37 | 8.12 | 0.48 | NR | NR | 0.747 | 2 | 1.46 | 0.68 | 3.10 | 0.33 | NR | NR | 0.227 |
| Chronic pulmonary condition | 2 | 2.52 | 0.58 | 10.83 | 0.21 | NR | NR | 0.771 | 1 | 1.27 | 0.70 | 2.28 | 0.43 | NR | NR | 0.000 |
| Renal disease/failure/ dialysis | 4 | 1.38 | 0.84 | 2.27 | 0.21 | NR | NR | 0.000 | 3 | 1.62 | 0.77 | 3.42 | 0.20 | NR | NR | 0.175 |

*95% confidence limit
†Refer to table 1 for detail of included studies
§Peripheral Vascular Disease
NR = Not Reported: Predictive intervals not reported for factors not reaching statistical significance

## Table 7: SUB GROUP ANALYSIS OF ALL WOUNDS

| Risk factor | Number of studies† | Odds ratio | Lower confidence limit* | Upper confidence limit* | p-Value | Lower predictive interval* | Upper predictive interval* | Tau² | Number of studies† | Risk ratio | Lower confidence limit* | Upper Confidence limit* | p-Value | Lower predictive interval* | Upper predictive interval* | Tau² |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Wounds | 8 | **2.35** | **1.75** | **3.14** | **<0.01** | **1.63** | **3.37** | **0.000** | 4 | **1.96** | **1.19** | **3.25** | **<0.01** | **0.36** | **10.83** | **0.091** |
| Decubitus ulcers | 9 | **2.90** | **2.20** | **3.84** | **<0.01** | **1.77** | **4.76** | **0.023** | 4 | **2.31** | **1.54** | **3.45** | **<0.01** | **0.96** | **5.58** | **0.000** |

*95% confidence limit
†Refer to table 1 for detail of included studies

## Table 8: SUB GROUP ANALYSIS OF INVASIVE DEVICE: BY TYPE

| Risk factor | Number of studies† | Odds ratio | Lower confidence limit* | Upper confidence limit* | p-Value | Lower predictive interval* | Upper predictive interval* | Tau² | Number of studies† | Risk ratio | Lower confidence limit* | Upper Confidence limit* | p-Value | Lower predictive interval* | Upper predictive interval* | Tau² |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Gastrostomy/ Nasogastric | 8 | 2.09 | 1.55 | 2.82 | <0.01 | 1.43 | 3.05 | 0.000 | 5 | 1.55 | 1.04 | 2.31 | 0.03 | 0.71 | 3.41 | 0.020 |
| IDUC/CUD§ | 14 | 2.95 | 1.98 | 4.41 | <0.01 | 0.77 | 11.28 | 0.302 | 9 | 2.60 | 1.61 | 4.19 | <0.01 | 0.53 | 12.84 | 0.397 |
| Tracheostomy | 2 | 1.87 | 0.79 | 4.39 | 0.15 | NR | NR | 0.000 | 1 | 4.76 | 0.20 | 115.11 | 0.34 | NR | NR | 0.000 |

*95% confidence limit
†Refer to table 1 for detail of included studies
§Indwelling Urinary Catheter/Continuous Urinary Drainage
NR = Not Reported: Predictive intervals not reported for factors not reaching statistical significance

## Table 9: SUB GROUP ANALYSIS OF AB USE

| Risk factor | Number of studies† | Odds ratio | Lower confidence limit* | Upper confidence limit* | p-Value | Lower predictive interval* | Upper predictive interval* | Tau² | Number of studies† | Risk ratio | Lower confidence limit* | Upper Confidence limit* | p-Value | Lower predictive interval* | Upper predictive interval* | Tau² |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| ABs within last 12 weeks | 11 | 2.35 | 1.62 | 3.42 | <0.01 | 0.63 | 8.73 | 0.299 | 4 | 1.98 | 1.42 | 2.76 | <0.03 | 0.96 | 4.09 | 0.000 |
| AB FluoroCipro§ | 7 | 2.03 | 1.31 | 3.16 | <0.01 | 0.51 | 8.03 | 0.23 | 1 | 1.66 | 1.25 | 2.19 | <0.01 | NA | NA | NA |
| AB Cephalosporins | 3 | 2.15 | 1.41 | 3.27 | <0.01 | 0.14 | 32.63 | 0.000 | 2 | 1.71 | 1.26 | 2.34 | <0.01 | NA | NA | NA |
| AB Penicillin | 4 | 1.15 | 0.87 | 1.52 | 0.33 | NR | NR | 0.049 | 2 | 1.03 | 0.82 | 1.29 | 0.82 | NR | NR | 0.000 |

*95% confidence limit
†Refer to table 1 for detail of included studies
§Fluoroquinolone and/or Ciprofloxacin
NR = Not Reported: Predictive intervals not reported for factors not reaching statistical significance

## Risk Factors Unique to One Study Only

There were 25 risk factors that were unique to one study only (Table 10). As these factors were not examined by any more than one study they were not suitable for meta-analysis. Of the 25, 7 risk factors were deemed statistically significant.

Cheng[62] et al found that there was an inverse linear relationship between MRSA prevalence and the average living area per resident (Pearson correlation -0.443, $p$ = 0.004), with the odds of resident acquiring MRSA reduced by a factor of 0.09 for each 10 square feet increase in living area.

Higher prevalence of MRSA on admission was associated with higher MRSA point prevalence ($p$ = 0.005) in the Murphy[73] study.

Raab et al[41] reported that having a BMI less than or equal to 18.5 (i.e. being underweight) was a predictor of a resident's PVL-MRSA carrier status ($p$ = 0.005).

The Denis[65] study assessed and scored the level MRSA control activities in place at each of the RACFs and found that the higher the MRSA control score, the lower the MRSA prevalence ($p$ = 0.031).

The use of antibacterial soap was identified by Loeb[70] et al as being associated with a reduced risk of MRSA (adjusted OR = 0.40, 95% CI: 0.18-0.90). Loeb also found that the more hand washing sinks available within the RACF the lower the risk of colonisation with trimethoprim-sulfamethoxazole (TMP=SMX) resistant Enterobacteriaceae (adjusted OR = 0.94, 95% CI: 0.90-0.98).

Eveillard[66] et al found that at residents who had had at least 1 medical imaging session within the preceding 12 months were more likely to carry MRSA (OR = 5.08; 95% CI: 2.66-9.69, $p$ = 0.0136).

## Table 10: ONE STUDY ONLY

| Study main author* | Risk factor | Significant results |
|---|---|---|
| Cheng[62] | Area per person | Yes |
| Murphy[73] | Educational level | No |
| | High MRSA admission prevalence | Yes |
| Raab[41] | Smoker | No |
| | Low BMI | *Yes* |
| | Eczema | No |
| | Prosthesis | No |
| | Topical antibiotics | No |
| Denis[65] | MRSA control score | Yes |
| Loeb[70] | Access to IDP or ICP | No |
| | Number of sinks/location | Yes |
| | Type of soap | Yes |
| Eveillard[66] | Physical Therapy in last 12 months | No |
| | Medical imaging | Yes |
| Barr[59] | Time since last hospital admission | No |
| | Staff training | No |
| | Staff turnover | No |
| | Use of Agency Staff in last 3 months | No |
| | Isolation of resident with ARO | No |
| | Treatment of ARO | No |
| Brugnaro[61] | Colonized roommate | No |
| Lasseter[69] | No of times hospitalized in 6 months | No |
| | Geographical region of RACF | No |
| Wingard[84] | Marital status Leaves unit | No |
| *Refer to table 1 for detail of included studies* | | |

**CHAPTER 4:**

**DISCUSSION & CONCLUSIONS**

# General discussion

The results of the systematic review and meta-analysis indicate that the following 10 statistically significant risk factors are associated with ARO carriage in residents of residential aged care facilities;

- Comorbidities
- Limited Mobility
- Dependency
- Wounds
- Incontinence
- History of ARO
- Male Sex
- Presence of an Invasive Device
- Antibiotic
- Hospital stay

These risk factors are similar to risk factors identified in studies of acute care settings[14, 36] but not identical.

## Discussion of resident risk factors

Comorbidities

For the purpose of this review comorbidities included renal failure/renal dialysis, chronic cerebral conditions, cardiac disease, chronic pulmonary conditions, atherosclerosis, and PVD. Sub group analysis suggests that a chronic cerebral condition was the only individual factor that reached statistical significance (OR = 1.7 CI: 1.10-2.64, $p$ = 0.02).

In one study looking at chronic cerebral conditions[41], a diagnosis of dementia was included as comorbidity, but was not analysed separately. Dementia is a condition commonly seen in residents of

RACFs[16] and was reported as being a risk factor for carriage of an ARO in one study.[33] Dementia as a specific diagnosis was examined in 5 studies[33, 34, 69, 72, 74] however meta-analysis of these studies did not suggest a significant association with the carriage of an ARO. The condition of dementia can be associated with a decrease in mobility, an increase in dependency, and incontinence[16] and therefore may be a marker for these risk factors.

## Limited mobility

Results of the meta-analysis showed that the risk factor of limited mobility was statistically significant; with the odds of a resident with limited mobility having an ARO being over double those of a resident who was mobile. Residents identified with restricted mobility included those who needed assistance with mobilisation, through to those who were completely bed-bound. By its nature, limited mobility may infer more "hands-on" intervention, and direct physical contact with care providers, and this may explain the increased risk as AROs can be transmitted to residents on the hands of care workers.[6]

## Dependency

This study showed that resident dependency was a statistically significant risk factor; the odds of a dependant resident having an ARO were over twice that of residents who were not dependant. Dependency was characterised by the need to provide the resident with assistance to achieve basic activities of daily living such as washing, feeding and elimination. As with limited mobility, more contact with care providers is a feature of residents who have higher dependency needs,[6, 90-92] which may facilitate ARO transmission.

## Wounds

Results of the meta-analysis showed that residents who have any kind of wound are at twice the risk of ARO carriage, when compared to those that do not. This was supported by sub-group analysis of both pressure ulcers and other types of wounds. It is widely recognised that non-intact skin can act as a portal of entry for opportunistic microorganisms.[6, 93] The presence of open, broken skin is recognised as a risk factor for ARO colonisation and infection generally[6], and this data supports this with respect to the residential aged care setting.

## Incontinence

Incontinence of urine is extremely common in the elderly, whereas faecal incontinence is less common.[94, 95] Of the 4 studies that examined incontinence, one combined both urinary and faecal incontinence,[84] all others reported on urinary incontinence only. Incontinence impacts of toileting and hygiene requirements of the older person, and as such may again infer a significant hands-on care requirement. Meta-analysis results supported incontinence as a risk factor for ARO carriage, with three to four times the odds and risk for affected residents; however this result was based on a small number of studies and may not be generalisable to a wider population.

## History of ARO

History of previous colonisation or infection with an ARO is considered one of the strongest predictors for further carriage in acute care settings.[15] This is the basis for the various admission screening and targeted history-taking processes in place at many acute healthcare facilities. Screening swabs are often taken from any patient declaring a past history of ARO carriage, to ascertain if the ARO is still present. Even if not found during this screening process many facilities feel the patient is high-risk enough to be isolated in a single room and additional contact precautions applied.[37, 39] Once a history of an ARO is identified, it is often recommended that a notation is put on the patient's file to alert staff

should any further admissions be required.[2, 36-38] The Aged Care setting has not tended to take up this approach. This may be due to two factors; the first being that the risks between the two settings are considered to be different. The acute care setting has many other patients who are often acutely ill and therefore vulnerable to the acquisition of an ARO. Secondly, the aged care setting is reluctant to impose restrictive isolation practices on residents in an effort to maintain their commitment to providing a "home-like" setting, and to avoid the extra costs that such practices incur. The results of this meta-analysis show that, like the acute care setting, history of ARO can be a risk factor for ARO carriage, with nearly a three times increase in the odds or risk for ongoing carriage. This result is important for the residential aged care setting in that it reinforces the predictive value that history of an ARO has on ongoing carriage in residents of residential aged care facilities. While this may still not justify the same kind of response seen in the acute care setting, it may warrant some review of current admission processes.

## Male sex

Data analysis revealed that male residents were at higher risk of carrying an ARO than females, however the clinical significance of this result was borderline as the lower confidence limit was approaching 1. Because of this it may not be possible to recommend any difference in approach to male versus female residents based on this result.

## Discussion of institutional risk factors

## Presence of an invasive device

Existing literature suggests invasive devices put patients at increase risk of infection, as the device offers a portal of entry for pathogenic organisms.[2, 42]. The results of this meta-analysis show that residents with an invasive device will be over twice as susceptible to carriage of an ARO as those residents who do not have an invasive device *in situ*.

Of the 19 studies included in this risk factor analysis, 4 did not specify the type of device.[59, 71, 75, 80] Where data on specific invasive devices was provided, sub group analysis demonstrated that the presence of a gastrostomy or nasogastric tube and an indwelling urinary catheter and continuous urinary drainage (IDUC/CUD) were significant risk factors for carriage of an ARO. The presence of a gastrostomy or nasogastric tube doubles the odds of ARO carriage, and an IDUC/CUD presents almost three times the odds and twice the risk. Enteral feeding that is provided by either a gastrostomy or nasogastric tube is commonly an indicator of underlying deficits in residents' ability to tolerate food and fluids orally.[96, 97] One reason for this deficit is dysphagia caused by stroke. Residents with stroke will almost always have some degree of limited mobility and increased dependency. The presence of such feeding tubes also means that hands on manipulation by staff will be regular, frequent and ongoing. Both of these factors could influence the risk of carriage.

## Antibiotic use

Previous antibiotic use is one of the most recognised risk factors for ARO carriage.[15, 98-100] Not surprisingly, this meta-analysis supported this finding for residents of RACFs. Sub-group analysis to determine if the use of any specific class of antibiotics was a higher risk than others revealed that both fluoroquinolone/ciprofloxacin and cephalosporin use were associated with increased risk, whereas use of penicillin was not. The lack of association with penicillin is unusual and unexpected, particularly in association with carriage of MRSA, as a key aspect of this organism's resistance is to methicillin, a type of penicillin. On examination, three studies looked at the association between MRSA and the use of penicillin or its derivatives. The Denis study[65] found an association with penicillin use in previous 3 months, however Brugnaro et al[61] and Loeb et al[70] found no association. Neither study provided an explanation for this result.

As well as the type of antibiotic, subgroup analysis revealed that the use of any antibiotic specifically within the last 12 weeks was a significant risk factor. This also is in line with the available evidence from studies conducted in acute health care and community settings that demonstrate previous recent antibiotic use is a risk factor for ARO carriage.[15, 98-100]

## Hospital stay

From time-to-time residents of RACFs need to go to hospital; this is may be due to an acute illness or as a result of an injury that requires treatment best delivered in an acute care setting. Residents may undergo surgery during a hospital admission. Once in this setting these residents are exposed to a new range of potentially pathogenic organisms that are circulating in that environment and on the hands of health care workers. Because of this, residents who have a history of a previous hospital stay are thought to be a risk factor of carriage of an ARO.[6, 39, 65] The meta-analysis of this risk factor confirmed that residents are twice as likely carry an ARO if they have been to hospital.

## Length of stay

The length of time a resident stays in a RACF can vary from months to years. A total of 6 studies examined length of stay. In order to analyse the data the study results were divided into 2 time periods; 12 months or less, and over 12 months. Only 1 study looked at lengths of stay for both time periods.[61] In examining the impact length of stay in a facility has on the likelihood of ARO carriage the meta-analysis data revealed an interesting result. The risk was significant in those residents who had been in the facility for 12 months or less, whereas there was no significance in residents who had been in the facility for over 12 months. There may be an expectation the longer the resident is exposed to risk of transmission, and as the resident becomes more dependant over time, then the risk of carriage would be increased, but the data did not support this. The explanation for this result is not clear but may be related to the adaption of the resident to the new microbial environment over time.[101]

## Discussion of environmental risk factors

There were no environmental risk factors identified as a significant risk factor for ARO carriage in residents of RACFs.  Overall, there were limited studies looking at environmental risk factors for ARO carriage, making meta-analysis difficult.

## Discussion of generalisability of meta-analysis results

Although this meta-analysis revealed 10 significant risk factors associated with the carriage of an ARO in residents, specific statistical analysis, such as $Tau^2$ and effect size based on predictive intervals, revealed that only three of these factors (comorbidities, all wounds, invasive devices) could confidently be generalised to the wider population of residents in residential aged care facilities. This means that for these three risk factors, if the study was to be repeated and the study was similar to the included studies, then the effect would have a 95% chance of being the same. With a significant PI, as with these three factors, the degree of confidence that similar results will appear again is increased. This generalisability also extends to two of the sub groups of wounds, decubitus ulcers (Table 7), gastrostomy and nasogastric tubes. (Table 8) These specific risk factors can also be generalised to the wider population.

As for the remaining factors whose PI was not significant, and where there was within and between-study variance; they are not statistically generalisable. In saying that, it is worth noting that the study selection process, based on the specific inclusion criteria, resulted in the study population being very closely aligned with the general population of residents in RACFs. This means that, although not statistically generalisable, these results may be used to draw assumptions and conclusions about the significant risk factors in the wider population of interest.

## Discussion of other risk factors

Studies that examined unique risk factors (and were therefore not suitable for meta-analysis) identified several risk factors as statistically significant. These present areas worth further discussion and may highlight areas for potential for further research topics.

The finding of Cheng et al[62] showed a correlation between size of living area and risk of carriage of an ARO, with the risk increasing where the living area was smaller. This may suggest that overcrowding in RACFs will increase the risk for residents. This may have important ramifications when designing facilities and estimating the numbers of residents that should be accommodated in any particular size facility.

The results demonstrated by Murphy et al[73] regarding MRSA prevalence on admission were not surprising. Given what we know about the persistence of ARO carriage [1, 2, 15, 37, 39] it is expected that higher MRSA admission prevalence would be associated with higher MRSA point prevalence. This information has been the basis for many admission sampling processes in acute care. It can be argued that the ability to microbiologically confirm who has an ARO on or shortly after admission will lead to the prompt implementation of more effective infection control strategies. However, as discussed the RACF approach to admission swabbing has been less rigorous than in acute care settings; most likely due to the reluctance to request invasive and expensive testing. In addition there is also a reluctance to introduce restrictive infection control measures into a residential-type environment, even if screening did reveal which residents were carrying an ARO.[24, 102] While this result confirms current thinking, this one study alone is unlikely to influence a change in ARO microbiological screening practices in RACF and further studies looking at this risk factor are warranted.

In the Raab[41] study the authors reported that having a Body Mass Index (BMI) less than or equal to 18.5 was a predictor of a resident's PVL-MRSA carrier status. The reason for this finding is unclear, although it may be that low BMI is a marker for poor overall health or underlying co-morbidities. The BMI is an internationally recognised assessment tool used to classify underweight, overweight and obesity in adults. It is defined as the weight in kilograms divided by the square of the height in metres ($kg/m^2$).[103] WHO define adults who have a BMI less than or equal to 18.5 as underweight.[104] Undernutrition is common in elderly people and can have ramifications for their general overall health and well being. Undernutrition may influence clinical outcomes, although it can be difficult to distinguish signs of poor nutrition from those due to disease or the processes of ageing.[96, 97,103]

The result from the study by Denis et al[65] study found that RACFs with a high level MRSA control activities in place (e.g. infection surveillance, infection control programs, antibiotic formulary) had a lower MRSA prevalence ($p = 0.03$). This result supports the belief that MRSA control activities, when correctly and diligently applied, are effective in controlling the spread of MRSA in a RACF setting.

Hand hygiene has long been cited as one of the single most important infection prevention strategies[105] and has been the cornerstone of infection control since Semmelweis[106] and Florence Nightingale[107]. There has been much work done on the most effective hand hygiene technique, and the most effective type of product to use while performing hand hygiene. It is now widely accepted that an alcohol based hand rub is the most appropriate product for decontaminating hands that are not visibly soiled.[105] Other products for hand hygiene are available, and these range from plain soap to a variety of antibacterial soaps, liquids and foams. Antibacterial products have long been used in the acute healthcare environment, especially before conducting identified high risk procedures such as insertion of invasive devices, or prior to performing surgical procedures. More recently antibacterial products have gained popularity with the general public of developed countries. The take up of antibacterial soap in RACF

has been variable, with the introduction of waterless alcohol based hand rubs being more widespread.[108] That fact that the study by Loeb et al[70] identified antimicrobial soap as being associated with a reduced risk of MRSA is supportive of their use within the RACF environment but further studies would be required to see if this effect is generalisable, and if the use of alcohol based hand rubs would be as effective. The Loeb study also found that more hand washing sinks available within the RACF the lower risk of colonisation with an ARO. This supports contemporary thinking and advice regarding the provision of accessible hand washing facilities, and where these are not readily available, access to the more portable waterless alcohol based hand rubs.[105] Any device, product or arrangement that makes it easier for staff to decontaminate their hands while moving between one resident and another will enhance compliance with this essential infection control strategy.

The study by Eveillard et al[66] found a correlation between residents who had had at least 1 medical imaging session within the preceding 12 months conducted outside the facility, and carriage of MRSA. The authors offer the hypothesis that staff knowledge of MRSA prevention strategies would be less in a medical imaging department, and therefore the risk of cross transmission would be greater. This lack of knowledge may lead to poor practice in decontamination of radiological equipment, which could then act as a fomite for transmission. The authors also cited poor communication of MRSA status between the RACF and the medical imaging department, which may have also resulted in increased risk of transmission due to the lack of implementation of the appropriate additional precautions. A final hypothesis was presented whereby residents requiring medical imaging may carry more comorbidity, thus increasing their risk of ARO carriage. Further research would be required to ascertain the significance of this finding.

## Important studies not included in the review

In a recently published paper (July 2015) Hogardt et al[109] conducted a point prevalence study in 26 RACFs in Germany and screened 690 and 455 residents for MRSA and ESBL/MRGN respectively. This study was not included in the systematic review as it was published after the selection of studies had been completed. This more recent study looked at sex, urinary and vascular catheters, pressure sores, impaired mobility, incontinence and disorientation, hospital stay in the past three months, surgery in the past 30 days, and current infection or antibiotic therapy. Most of their results support the findings of this meta-analysis. This study showed that MRSA carriage was significantly associated with MRSA history (OR = v9.9 CI: 1.6–61.1, *p* value not reported (NR) ), the presence of urinary catheters (OR = 4.2 CI: 2.1–8.7, *p* = NR), gastrostomy tube (OR = 2.7 CI: 1.2–6.2, *p* = NR) and previous antibiotic therapy. (OR = 2.6 CI: 1.3–5.1, *p* = NR). ESBL/MRGN carriage was associated with urinary catheters (OR = 1.9 CI: 1.0–3.8, *p* = NR).

An Australian study by Mitchell et al[110] (2014) examined the risk associated occupying a room that had previously housed an MRSA positive patient and MRSA carriage. This study was conducted in an acute healthcare facility and therefore was excluded from this review. The authors concluded that *"admission to a room previously occupied by a person with MRSA increased the odds for the subsequent patient, independent of other risk factors."* (OR = 2.7 95%CI 2.0-3.6, *p* = <0.01). While none of the studies included in this review looked at this specific risk factor, four looked at share rooms as a risk,[41, 67, 69, 81] and one study looked specifically at the risk of sharing a room with another ARO colonised resident. In this review, results of the meta-analysis of the four studies looking at share rooms did not show any increased chance of ARO carriage (OR = 1.24 CI: 0.78-1.97, *p* = 0.37, RR = 0.99 CI: 0.40-2.44, *p* = 0.98). Similarly, in the one study looking at sharing a room with a resident with an ARO,[61] there was no statistical significance shown (*p* = 0.80).

## Implications for practice

The identification of risk factors for ARO carriage in residents of RACFs means that staff working in those facilities will be able to identify, assess and manage the risk in a manner that is systematic, accurate, and informed by best available evidence.

Unsurprisingly, the current admission process used in RACFs around the world is not standardised, and is influenced by local legislative requirements, funding sources, and medical requirements. However, there are common elements across most RACFs with regards to the information collected at admission, and one of these includes medical diagnoses. In the light of the results of this review a revision of how medical diagnoses, and information regarding medical conditions are collected, would be useful. Collecting information regarding ARO carriage history and identifying the presence of any risk factors found to be significant in this review, would improve the identification of those residents most at risk.

Staff working in the sector should assess all residents for these identified risk factors on admission to the RACF. If any risk factors for ARO carriage are present then microbiological screening for an ARO may be justified. Regardless of the presence or absence of screening, if a risk factor was identified any required infection control interventions could be implemented promptly and proactively. This would be in line with current management guidelines where a risk management approach is advocated.[2, 36-38] The development of a risk assessment tool could assist in the identification of risk factors found to be significant in this review. To be effective, such a tool should be simple and provide a "tick-box" approach for staff to complete; if one or more of the risk factors are identified the form could provide instructions as to the next steps required. The development of such a tool would require careful development to ensure its validity and specificity.

As well as new residents being assessed on admission, existing residents within the RACF should also be monitored for the identified risk factors on an ongoing basis. This should include an ongoing regular assessment and reporting process and subsequent action if residents develop any of the risk factors found to be significant in this review.

Regardless of whether a resident is new to a facility or has lived there for some time, the presence of one or more risk factors should trigger a staged application of infection control precautions commensurate with the risk. Residents deemed at high risk should then be screened to determine ARO carriage status.

This review allows for a more informed risk assessment to be performed and will allow for appropriate and targeted infection control strategies to be applied. The information will provide surety that the risk will be minimised in an effective and timely fashion.

## Implications for research

This review relates to studies that are available currently. It has highlighted certain areas of potential further research which are worth considering. The effect of cerebral conditions, specifically dementia, on the risks of ARO carriage, needs more exploration. Many studies did not differentiate between types of cerebral conditions, while a few looked at dementia specifically. In this review dementia was not statistically significant as a risk factor, whereas chronic cerebral conditions were. Given that in 2010 the number of cases of dementia worldwide were estimated at 35.6 million, and this number is projected to nearly double every 20 years,[111] this could be an important area to gain further knowledge.

The equivocal results regarding the risk associated with male residents would suggest a closer investigation is warranted, and further research may useful in this area.

This study did not look at the risk associated with specific types of ARO. This is a potential area for further work. It would be useful to know if the risk factors vary between carriage of MRSA, VRE or MRGN, or are they all the same.

The results related to length of stay would suggest more work is needed to explore the impact of this risk factor. As this review indicated that residents who have been in the facility for longer are less at risk of ARO carriage it would be worthwhile exploring why this might be so.

The fact that there were limited studies examining environmental risk factors influencing ARO carriage in residents would suggest more work is required in this area. Those single studies looking at size of living area, share rooms and hand hygiene products, and other environmental influences (Table 10) provide an opportunity for further research to be conducted in order to add to the data.

In light of the work by Mitchell et al[110] on the risk of prior-room occupancy with someone who was MRSA positive, and the frequent reference in many Infection Control Guidelines to avoiding placement of vulnerable residents in share rooms with known ARO residents,[2, 36-38, 112] both these risk factors warrant further exploration.

Finally, all other studies that examined unique risk factors presented areas worth further discussion and may highlight areas for potential research topics.

## Limitations of this review

This review only included studies published in English, and therefore data provided in studies published in other languages will have been missed.

For the purpose of this review the risk factor group of comorbidities (Table 4) was created to include those studies that did not specify comorbidity types, and studies that looked at specific comorbidities such as renal dialysis, chronic cerebral conditions (which may have included dementia), cardiac disease/atherosclerosis, chronic pulmonary conditions, PVD, and unspecified systemic disease. Where a study specifically looked at dementia as a risk factor, this data was analysed separately. The sub group analyses were only conducted on those studies that clearly specified the condition being examined, and the result should be interpreted with caution as it may not represent the true risk.

Although an overall total of nearly 30,000 residents were represented in the studies included in this review, the sample size for some of the studies was relatively small, and therefore may reduce the significance of any results.

## Conclusions

AROs present a real and present danger to not only the wider healthcare population, but also to residents of RACFs. The objective of this review was to synthesize the best available evidence to determine the factors that make some residents more at risk than others to either colonisation or infection with an antimicrobial resistant organism.

In order to answer the review question the JBI quantitative systematic review methodology was utilised to identify the risk factors associated with ARO carriage in residents of RACFs.

Over 30 relevant studies were identified and included in the review. Following a meta-analysis of the data collected by these studies, 10 risk factors associated with ARO carriage in residential aged care setting have been identified. Seven of these are resident risk factors, and 3 are institutional risk factors. There were no environmental risk factors associated with antimicrobial resistant organism carriage in the residential aged care setting.

The identification of these risk factors will add to the body of knowledge clinicians can use to plan and implement infection prevention and control strategies. These results have clear implications for practice that will support the development of guidelines and risk assessment tools based on best-available evidence.

## Appendix I: Search Logic Grid: PubMed/Medline Example

| Aged Care[2] | Infection | Control | Drug Resistant | Risk Factors |
|---|---|---|---|---|
| Homes for the aged[mh] OR homes for the aged[tw] OR nursing home*[tw] OR nursing homes[mh] OR aged care [tw] OR old age home*[tw] OR geriatric care[tw]  OR (residential[ti] AND (aged[ti] OR aged[mh]  OR geriatric[ti] OR older[ti] OR elderly[ti])) OR (long term care[tw] AND (aged[mh] OR geriatric[tw] OR older[tw] OR elderly[tw])) | Cross infection[mh]  OR nosocomial infection*[tw] OR cross infection*[tw] OR Staphylococcal infections[mh] OR Staphylococcal infection*[tw] OR Gram-Positive Bacterial Infections[mh] OR Bacterial Infection*[tw] OR Streptococcus pneumoniae[mh] OR Streptococcus pneumonia*[tw] OR Pneumococcal infection*[tw] OR Urinary tract infections[mh] OR Urinary tract infection*[tw] OR E coli[mh]  OR E coli*[tw] OR Pseudomonas aeruginosa[mh] OR Pseudomonas aeruginosa[tw] OR beta-lactamases[mh] OR beta-lactamase*[tw] OR Extended Spectrum [tw] OR ESBL*[tw] | Infection control[mh:noexp] OR prevention and control[sh] OR control[tw] OR prevent*[tw] | Drug resistance, bacterial[mh] OR drug resistance, microbial [mh:noexp] OR resist*[tw] | Risk Factor[mh] OR Risk Factors[mh] OR Risk Factor*[tw] |

[1]This logic grid was modified as required to suit Embase, CINHAL and Cochrane databases. Filters applied for searches:1950 onwards, English language

[2]Within columns the OR operator is applied; between rows the AND operator is applied

## Appendix II: Appraisal instruments

Standardized critical appraisal instruments from the Joanna Briggs Institute Meta-Analysis of Statistics

Assessment and Review Instrument (JBI-MAStARI)

### JBI Critical Appraisal Checklist for Randomised Control / Pseudo-randomised Trial

Reviewer _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ Date _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _

Author _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ Year _ _ _ _ _ _ _ Record Number _ _ _ _ _ _ _

| | Yes | No | Unclear | Not Applicable |
|---|---|---|---|---|
| 1. Was the assignment to treatment groups truly random? | ☐ | ☐ | ☐ | ☐ |
| 2. Were participants blinded to treatment allocation? | ☐ | ☐ | ☐ | ☐ |
| 3. Was allocation to treatment groups concealed from the allocator? | ☐ | ☐ | ☐ | ☐ |
| 4. Were the outcomes of people who withdrew described and included in the analysis? | ☐ | ☐ | ☐ | ☐ |
| 5. Were those assessing outcomes blind to the treatment allocation? | ☐ | ☐ | ☐ | ☐ |
| 6. Were the control and treatment groups comparable at entry? | ☐ | ☐ | ☐ | ☐ |
| 7. Were groups treated identically other than for the named interventions | ☐ | ☐ | ☐ | ☐ |
| 8. Were outcomes measured in the same way for all groups? | ☐ | ☐ | ☐ | ☐ |
| 9. Were outcomes measured in a reliable way? | ☐ | ☐ | ☐ | ☐ |
| 10. Was appropriate statistical analysis used? | ☐ | ☐ | ☐ | ☐ |
| | ☐ | ☐ | ☐ | ☐ |

Overall appraisal:     Include ☐     Exclude ☐     Seek further info. ☐

Comments (Including reason for exclusion)

_____

_____

_____

# JBI Critical Appraisal Checklist for Descriptive / Case Series

Reviewer _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ Date _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _

Author _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ Year _ _ _ _ _ _ _ Record Number _ _ _ _ _ _ _

| | | Yes | No | Unclear | Not Applicable |
|---|---|---|---|---|---|
| 1. | Was study based on a random or pseudo-random sample? | ☐ | ☐ | ☐ | ☐ |
| 2. | Were the criteria for inclusion in the sample clearly defined? | ☐ | ☐ | ☐ | ☐ |
| 3. | Were confounding factors identified and strategies to deal with them stated? | ☐ | ☐ | ☐ | ☐ |
| 4. | Were outcomes assessed using objective criteria? | ☐ | ☐ | ☐ | ☐ |
| 5. | If comparisons are being made, was there sufficient descriptions of the groups? | ☐ | ☐ | ☐ | ☐ |
| 6. | Was follow up carried out over a sufficient time period? | ☐ | ☐ | ☐ | ☐ |
| 7. | Were the outcomes of people who withdrew described and included in the analysis? | ☐ | ☐ | ☐ | ☐ |
| 8. | Were outcomes measured in a reliable way? | ☐ | ☐ | ☐ | ☐ |
| 9. | Was appropriate statistical analysis used? | ☐ | ☐ | ☐ | ☐ |

Overall appraisal:     Include ☐          Exclude ☐          Seek further info ☐

Comments (Including reason for exclusion)

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## JBI Critical Appraisal Checklist for Comparable Cohort/ Case Control

Reviewer _____ Date _____

Author _____ Year _____ Record Number _____

|  |  | Yes | No | Unclear | Not Applicable |
|---|---|:---:|:---:|:---:|:---:|
| 1. | Is sample representative of patients in the population as a whole? | ☐ | ☐ | ☐ | ☐ |
| 2. | Are the patients at a similar point in the course of their condition/illness? | ☐ | ☐ | ☐ | ☐ |
| 3. | Has bias been minimised in relation to selection of cases and of controls? | ☐ | ☐ | ☐ | ☐ |
| 4. | Are confounding factors identified and strategies to deal with them stated? | ☐ | ☐ | ☐ | ☐ |
| 5. | Are outcomes assessed using objective criteria? | ☐ | ☐ | ☐ | ☐ |
| 6. | Was follow up carried out over a sufficient time period? | ☐ | ☐ | ☐ | ☐ |
| 7. | Were the outcomes of people who withdrew described and included in the analysis? | ☐ | ☐ | ☐ | ☐ |
| 8. | Were outcomes measured in a reliable way? | ☐ | ☐ | ☐ | ☐ |
| 9. | Was appropriate statistical analysis used? | ☐ | ☐ | ☐ | ☐ |

Overall appraisal:　　Include ☐　　　　Exclude ☐　　　　Seek further info. ☐

Comments (Including reason for exclusion)

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## Appendix III: Example of Data Extraction Tool

| STUDY AUTHOR | DATE | RISK FACTOR | RISK FACTOR SUB-GROUP | WITH ARO YES | WITH ARO NO | RELATIVE RISK | ODDS RATIO | CI LOWER | CI UPPER | WITHOUT ARO YES | WITHOUT ARO NO |
|---|---|---|---|---|---|---|---|---|---|---|---|
| BARR1 | 2007 | MALE SEX | yes | 43 | 116 | | | | | 98 | 458 |
| BARR2 | 2007 | Hx OF COLONISATION | yes | | | | 6.37 | 1.45 | 27.89 | | |
| BARR3 | 2007 | WOUND | yes | | | | 1.92 | 0.82 | 4.48 | | |
| BARR4 | 2007 | INVASIVE DEVICE | yes | | | | 3.15 | 1.5 | 6.62 | | |
| BARR5 | 2007 | AB IN PAST 6 MONTHS | yes | | | | 1.69 | 0.85 | 3.35 | | |
| BARR6 | 2007 | DIABETES | yes | | | | 0.58 | 0.25 | 1.33 | | |
| BARR7 | 2007 | WRITTEN IC G/LINES: Isolation | yes | | | | 1.51 | 0.84 | 2.71 | | |
| BARR8 | 2007 | WRITTEN IC G/LINES: Treatment | yes | | | | 3.15 | 0.64 | 19.6 | | |
| BARR9 | 2007 | DURATION OF HOSPITAL STAY IN PAST 2 YEARS 1-9 days | yes | | | | 1.2 | 0.69 | 2.11 | | |
| BARR10 | 2007 | DURATION OF HOSPITAL STAY IN PAST 2 YEARS 10-29 days | yes | | | | 1.93 | 1.1 | 3.37 | | |
| BARR11 | 2007 | DURATION OF HOSPITAL STAY IN PAST 2 YEARS ≥30days | yes | | | | 2.86 | 1.74 | 4.27 | | |
| BARR12 | 2007 | TYPE OF OWNER: Local authority | yes | 56 | 103 | | 1 | | | 244 | 312 |
| BARR13 | 2007 | TYPE OF OWNER: Private | yes | | | | 1.64 | 0.58 | 4.6 | | |
| BARR14 | 2007 | TYPE OF OWNER: Other | yes | | | | 1.44 | 0.8 | 2.56 | | |
| BARR15 | 2007 | >35 Beds | yes | | | | 1.62 | 0.94 | 2.8 | | |
| BARR16 | 2007 | ≥95 Single rooms | yes | | | | 1.01 | 0.5 | 2.05 | | |
| BARR17 | 2007 | <6 FTE NURSING STAFF per bed | yes | | | | 2.62 | 1.52 | 4.52 | | |
| BARR18 | 2007 | ≥6 FTE NURSING STAFF per bed | yes | | | | 0.93 | 0.47 | 1.84 | | |

EXAMPLE OF 1 STUDY ONLY (EXCEL)

## Appendix IV: Studies Excluded At Full Text Review

Aliberti LC. Enterococcal nosocomial infection: epidemiology and practice. Gastroenterology nursing : the official journal of the Society of Gastroenterology Nurses and Associates. 1995;18(5):177-81. *Reason for exclusion: did not meet inclusion criteria of a permanent resident of a RACF.*

Banerjee R, Johnston B, Lohse C, Porter SB, Clabots C, Johnson JR. Escherichia coli sequence type 131 is a dominant, antimicrobial- resistant clonal group associated with healthcare and elderly hosts. Infection Control and Hospital Epidemiology. 2013;34(4):361-9. *Reason for exclusion: did not meet inclusion criteria of a permanent resident of a RACF.*

Ben Othman A, Zribi M, Masmoudi A, Abdellatif S, Ben Lakhal S, Fendri C. Phenotypic and molecular epidemiology of Acinetobacter baumannii strains isolated in Rabta Hospital, Tunisia. Archives de l'Institut Pasteur de Tunis. 2007;84(1-4):11-9. *Reason for exclusion: did not meet inclusion criteria of a permanent resident of a RACF.*

Boyce JM. Methicillin-resistant Staphylococcus aureus in hospitals and long-term care facilities: microbiology, epidemiology, and preventive measures. Infection Control & Hospital Epidemiology. 1992;13(12):725-37. *Reason for exclusion: did not meet inclusion criteria for type of study.*

Bucher A, Sorknes N, Lundqvist K, Ronning K. [Infections and use of antibiotics in nursing homes]. Tidsskrift for den Norske laegeforening : tidsskrift for praktisk medicin, ny raekke. 2001;121(7):827-30. *Reasons for exclusion: carrier status not defined, did not meet inclusion criteria of presence of an ARO, did not examine risk factors.*

Butler JC, Schuchat A. Epidemiology of pneumococcal infections in the elderly. Drugs & aging. 1999;15 Suppl 1:11-9. *Reasons for exclusion: carrier status not defined, did not meet inclusion criteria of presence of an ARO, did not examine risk factors.*

Capitano B, Leshem OA, Nightingale CH, Nicolau DP. Cost effect of managing methicillin-resistant Staphylococcus aureus in a long-term care facility. Journal of the American Geriatrics Society. 2003;51(1):10-6. *Reason for exclusion: did not examine risk factors.*

Carter RJ, Sorenson G, Heffernan R et al. Failure to control an outbreak of multidrug-resistant Streptococcus pneumoniae in a long-term-care facility: emergence and ongoing transmission of a fluoroquinolone-resistant strain. Infection Control & Hospital Epidemiology. 2005;26(3):248-55. *Reason for exclusion: did not meet inclusion criteria of a permanent resident of a RACF.*

Cohen AE, Lautenbach E, Morales KH, Linkin DR. Fluoroquinolone-resistant Escherichia coli in the long-term care setting. The American journal of medicine. 2006;119(11):958-63. *Reason for exclusion: did not meet inclusion criteria of a permanent resident of a RACF.*

Coia JE, Duckworth GJ, Edwards DI et al. Guidelines for the control and prevention of meticillin-resistant Staphylococcus aureus (MRSA) in healthcare facilities. The Journal of hospital infection. 2006;63 Suppl 1:S1-44. *Reason for exclusion: did not meet inclusion criteria for type of study*.

Coll PP, Nurse BA. Implications of methicillin-resistant Staphylococcus aureus on nursing home practice. The Journal of the American Board of Family Practice / American Board of Family Practice. 1992;5(2):193-200. *Reasons for exclusion: carrier status not defined, did not meet inclusion criteria for type of study.*

Crossley K. SHEA position paper. Vancomycin-resistant enterococci in long-term-care facilities. Infection Control & Hospital Epidemiology. 1998;19(7):521-5. *Reason for exclusion: did not meet inclusion criteria for type of study*

Drinka P, Niederman MS, El-Solh AA, Crnich CJ. Assessment of Risk Factors for Multi-Drug Resistant Organisms to Guide Empiric Antibiotic Selection in Long Term Care: A Dilemma. Journal of the American Medical Directors Association. 2011;12(5):321-5. *Reason for exclusion: did not meet inclusion criteria for type of study.*

Drinka PJ, Crnich CJ. An approach to endemic multi-drug-resistant bacteria in nursing homes. Journal of the American Medical Directors Association. 2005;6(2):132-6. R*eason for exclusion: did not meet inclusion criteria for type of study.*

Drinka PJ, Stemper ME, Gauerke CD, Miller JE, Reed KD. Screening for methicillin-resistant Staphylococcus aureus in a nursing home... Muto CA, Jernigan JA, Ostrowsky BE et al. SHEA guideline for preventing nosocomial transmission of multidrug-resistant strains of Staphylococcus aureus and Enterococcus. Infect Control Hosp Epidemiol 2003;24:362-86. Infection Control & Hospital Epidemiology. 2004;25(2):95-6. *Reason for exclusion: did not meet inclusion criteria for type of study.*

Dy ME, Nord JA, LaBombardi VJ, Kislak JW. The emergence of resistant strains of Acinetobacter baumannii: clinical and infection control implications. Infection control and hospital epidemiology : the official journal of the Society of Hospital Epidemiologists of America. 1999;20(8):565-7. *Reason for exclusion: did not meet inclusion criteria of a permanent resident of a RACF.*

Harris AD, Karchmer TB, Carmeli Y, Samore MH. Methodological principles of case-control studies that analyzed risk factors for antibiotic resistance: a systematic review. Clinical infectious diseases : an official publication of the Infectious Diseases Society of America. 2001;32(7):1055-61. *Reason for exclusion: did not meet inclusion criteria for type of study.*

Hoogendoorn M, Smalbrugge M, Stobberingh EE, van Rossum SV, Vlaminckx BJ, Thijsen SF. Prevalence of antibiotic resistance of the commensal flora in Dutch nursing homes. Journal of the American Medical Directors Association. 2013;14(5):336-9. *Reason for exclusion: did not meet inclusion criteria of a permanent resident of a RACF.*

John Jr JF, Ribner BS. Antibiotic resistance in long-term care facilities. Infection control and hospital epidemiology : the official journal of the Society of Hospital Epidemiologists of America. 1991;12(4):245-50. *Reason for exclusion: did not meet inclusion criteria for type of study.*

Kauffman CA, Bradley SF, Terpenning MS. Methicillin-resistant Staphylococcus aureus in long-term care facilities. Infection Control & Hospital Epidemiology. 1990;11(11):600-3. *Reason for exclusion: did not meet inclusion criteria for type of study.*

Lescure F, Locher G, Eveillard M et al. Community-acquired infection with healthcare-associated methicillin-resistant Staphylococcus aureus: the role of home nursing care. Infection Control & Hospital

Epidemiology. 2006;27(11):1213-8. *Reason for exclusion: did not meet inclusion criteria of a permanent resident of a RACF.*

Manzur A, Gudiol F. Methicillin-resistant Staphylococcus aureus in long-term-care facilities. Clinical Microbiology & Infection. 2009;15:26-30. *Reason for exclusion: did not examine risk factors.*

Mendelson G, Hait V, Ben-Israel J, Gronich D, Granot E, Raz R. Prevalence and risk factors of extended-spectrum beta-lactamase-producing Escherichia coli and Klebsiella pneumoniae in an Israeli long-term care facility. European journal of clinical microbiology & infectious diseases : official publication of the European Society of Clinical Microbiology. 2005;24(1):17-22. *Reason for exclusion: did not meet inclusion criteria of a permanent resident of a RACF.*

Mody L, Bradley SF, Galecki A et al. Conceptual model for reducing infections and antimicrobial resistance in skilled nursing facilities: focusing on residents with indwelling devices. Clinical infectious diseases : an official publication of the Infectious Diseases Society of America. 2011;52(5):654-61. *Reason for exclusion: did not meet inclusion criteria for type of study.*

Monaco M, Bombana E, Trezzi L et al. Meticillin-resistant Staphylococcus aureus colonising residents and staff members in a nursing home in Northern Italy. Journal of Hospital Infection. 2009;73(2):182-4. *Reason for exclusion: did not meet inclusion criteria for type of study.*

Mylotte JM, Karuza J, Bentley DW. Methicillin-resistant Staphylococcus aureus: a questionnaire survey of 75 long-term care facilities in Western New York. Infection Control & Hospital Epidemiology. 1992;13(12):711-8. *Reason for exclusion: did not examine risk factors.*

O'Sullivan NR, Keane CT. The prevalence of methicillin-resistant staphylococcus aureus among the residents of six nursing homes for the elderly. The Journal of hospital infection. 2000;45(4):322-9. *Reason for exclusion: did not examine risk factors.*

Piagnerelli M, Kennes B, Brogniez Y, Deplano A, Govaerts D. Concise communications. Outbreak of nosocomial multidrug-resistant Enterobacter aerogenes in a geriatric unit: failure of isolation contact, analysis of risk factors, and use of pulsed-field gel electrophoresis. Infection Control & Hospital Epidemiology. 2000;21(10):651-3. *Reason for exclusion: did not meet inclusion criteria of a permanent resident of a RACF.*

Quagliarello V, Ginter S, Han L, Van Ness P, Allore H, Tinetti M. Modifiable risk factors for nursing home-acquired pneumonia. Clinical infectious diseases : an official publication of the Infectious Diseases Society of America. 2005;40(1):1-6. *Reasons for exclusion: carrier status not defined, did not meet inclusion criteria of presence of an ARO.*

Ray A, Perez F, Beltramini AM et al. Use of vaporized hydrogen peroxide decontamination during an outbreak of multidrug-resistant Acinetobacter baumannii infection at a long-term acute care hospital. Infection Control & Hospital Epidemiology. 2010;31(12):1236-41. *Reason for exclusion: did not meet inclusion criteria of a permanent resident of a RACF.*

Raz R. The clinical impact of multiresistant gram-positive microorganisms in long-term care facilities. Journal of the American Medical Directors Association. 2003;4(3 Suppl):S100-4.
Taylor ME, Oppenheim BA. Hospital-acquired infection in elderly patients. Journal of Hospital Infection. 1998;38(4):245-60. *Reason for exclusion: did not meet inclusion criteria for type of study.*

Stone ND, Lewis DR, Lowery HK et al. Importance of bacterial burden among methicillin-resistant Staphylococcus aureus carriers in a long-term care facility. Infection control and hospital epidemiology : the official journal of the Society of Hospital Epidemiologists of America. 2008;29(2):143-8. *Reason for exclusion: did not meet inclusion criteria of a permanent resident of a RACF.*

Tada A, Watanabe T, Yokoe H, Hanada N, Tanzawa H. Oral bacteria influenced by the functional status of the elderly people and the type and quality of facilities for the bedridden. Journal of applied microbiology. 2002;93(3):487-91. *Reason for exclusion: did not meet inclusion criteria of a permanent resident of a RACF.*

Taylor ME, Oppenheim BA. Hospital-acquired infection in elderly patients. Journal of Hospital Infection. 1998;38(4):245-60. *Reason for exclusion: did not meet inclusion criteria for type of study.*

Terpenning MS, Bradley SF, Wan JY, Chenoweth CE, Jorgensen KA, Kauffman CA. Colonization and infection with antibiotic-resistant bacteria in a long-term care facility. Journal of the American Geriatrics Society. 1994;42(10):1062-9. *Reason for exclusion: did not meet inclusion criteria of a permanent resident of a RACF.*

Trick, William E. Weinstein Robert A. DeMarais Patricia L. Kuehnert Matthew J. Tomaska WandaNathan CatherineRice Thomas W. McAllister Sigrid K. Carson Loretta A. Jarvis William R. Colonization of Skilled-Care Facility Residents with Antimicrobial-Resistant Pathogens. Journal of the American Geriatrics Society. 2001;49(3):270-6. *Reason for exclusion: did not meet inclusion criteria of a permanent resident of a RACF.*

van Buul LW, van der Steen JT, Veenhuizen RB et al. Antibiotic use and resistance in long term care facilities. Journal of the American Medical Directors Association. 2012;13(6):568 e1-13. *Reason for exclusion: did not meet inclusion criteria for type of study.*

Vanderkooi OG, Low DE, Green K, Powis JE, McGeer A, Toronto Invasive Bacterial Disease N. Predicting antimicrobial resistance in invasive pneumococcal infections. Clinical infectious diseases : an official publication of the Infectious Diseases Society of America. 2005;40(9):1288-97. *Reason for exclusion: did not meet inclusion criteria of a permanent resident of a RACF.*

Washio M. Risk factors for methicillin-resistant Staphylococcus aureus (MRSA) infection in a Japanese elderly care nursing home. Epidemiology and infection. 1997;119(2):285. *Reason for exclusion: did not meet inclusion criteria for type of study.*

Wendt C, Krause C, Xander LU, Loffler D, Floss H. Prevalence of colonization with vancomycin-resistant enterococci in various population groups in Berlin, Germany. The Journal of hospital infection. 1999;42(3):193-200. *Reason for exclusion: did not meet inclusion criteria of a permanent resident of a RACF.*

Westerman M, Bennett RG. Colonization of skilled-care facility residents with antimicrobial-resistant pathogens. Journal of the American Geriatrics Society. 2001;49(12):1735-7. *Reason for exclusion: did not meet inclusion criteria for type of study.*

# Appendix V: Risk Factors that were not included in meta-analysis

| RISK FACTOR |
| --- |
| Access to IDP or ICP |
| Assistance with medication |
| Body mass |
| Child visitors |
| Colonized roommate |
| Eating assistance |
| Eczema |
| Educational level |
| Formulary |
| Geographical region of RACF |
| Hemiplegia |
| High MRSA admission prevalence |
| IC Guidelines |
| Isolation of resident with ARO |
| Leaves unit |
| Malignancy |
| Marital status |
| Medical imaging |
| MRSA control score |
| No of times hospitalized in 6 months |
| Number of sinks |
| Number of sinks/location |
| Physical therapy |
| Previous pneumonia |
| Previous vaccination |
| Prosthesis |
| Provenance |
| Race |
| Size of living area/ area per person |
| Smoker |
| Staff per bed/staffing ratios |
| Staff training |
| Staff turnover |
| Steroid use |
| Surveillance |
| Time since last hospital admission |
| Topical antibiotics |
| Treatment of ARO |
| Type of owner |
| Type of soap available |
| Use of Agency Staff in last 3 months |

# Appendix VI: Forest Plots

Forest plots are shown for all risk factors that showed statistical significance of >0.05 as a result of both overall study and subgroup analysis. Where the subgroup within study is labelled "combined" this indicates that more than 1 subgroup was reported for each study.

**Figure 2: Forest Plot: Meta-Analysis of all Comorbidities Combined - Odds Ratio**

| Study name | Subgroup within study | Odds ratio | Lower limit | Upper limit | p-Value | Odds ratio and 95% CI |
|---|---|---|---|---|---|---|
| | | **Statistics for each study** | | | | |
| BENENSON 2009 | RENAL FAILURE | 1.200 | 0.557 | 2.585 | 0.642 | |
| CHENG 2013 | CHRONIC CEREBRAL CONDITION | 2.012 | 1.226 | 3.302 | 0.006 | |
| KARABAY 2006 | Combined | 5.278 | 1.202 | 23.175 | 0.028 | |
| MANZUR 2008 | COMORBIDITIES | 1.790 | 1.330 | 2.410 | 0.000 | |
| MARCH 2009 | Combined | 2.053 | 1.245 | 3.386 | 0.005 | |
| MUDER 1997 | Combined | 1.013 | 0.739 | 1.388 | 0.936 | |
| O'FALLON 2010 | COMORBIDITIES | 1.000 | 0.290 | 3.449 | 1.000 | |
| RAAB 2006 | Combined | 2.205 | 0.989 | 4.916 | 0.053 | |
| SHLAES 1986 | COMORBIDITIES | 2.121 | 0.549 | 8.187 | 0.275 | |
| SUETENS 2007 | Combined | 1.730 | 1.285 | 2.329 | 0.000 | |
| VOVKO 2005 | Combined | 1.761 | 0.590 | 5.255 | 0.310 | |
| | | 1.642 | 1.336 | 2.018 | 0.000 | |



0.01   0.1   1   10   100

Non-carriage          Carriage

**Figure 3: Forest Plot: Meta-Analysis of all Comorbidities Combined - Risk Ratio**

| Study name | Subgroup within study | Statistics for each study | | | | Risk ratio and 95% CI |
| --- | --- | --- | --- | --- | --- | --- |
| | | Risk ratio | Lower limit | Upper limit | p-Value | |
| CHENG 2013 | CHRONIC CEREBRAL CONDITION | 1.803 | 1.205 | 2.698 | 0.004 | |
| KARABAY 2006 | Combined | 2.604 | 1.418 | 4.781 | 0.002 | |
| SHLAES 1986 | COMORBIDITIES | 1.210 | 0.908 | 1.612 | 0.192 | |
| MUDER 1997 | Combined | 1.009 | 0.817 | 1.246 | 0.936 | |
| RAAB 2006 | RENAL DIALYSIS | 1.580 | 0.085 | 29.263 | 0.759 | |
| | | 1.428 | 1.022 | 1.995 | 0.037 | |



0.01    0.1    1    10    100

Non-carriage          Carriage

**Figure 4: Forest Plot: Sub-group analysis of Cerebral Comorbidities - Odds Ratio**

| Study name | Subgroup within study | Odds ratio | Lower limit | Upper limit | p-Value | Odds ratio and 95% CI |
|---|---|---|---|---|---|---|
| CHENG 2013 | CHRONIC CEREBRAL CONDITION | 2.012 | 1.226 | 3.302 | 0.006 | |
| MUDER 1997 | CHRONIC CEREBRAL CONDITION ENTEROBACTER | 1.122 | 0.439 | 2.868 | 0.811 | |
| MUDER 1997 | CHRONIC CEREBRAL CONDITION PSEUDOMONAS | 1.000 | 0.379 | 2.637 | 1.000 | |
| RAAB 2006 | CHRONIC CEREBRAL CONDITION | 3.200 | 1.072 | 9.551 | 0.037 | |
| | | 1.704 | 1.100 | 2.638 | 0.017 | |

0.01    0.1    1    10    100

Non-carriage            Carriage

# Figure 5: Forest Plot: Meta-Analysis of Limited Mobility - Odds Ratio



| Study name | Subgroup within study | Odds ratio | Lower limit | Upper limit | p-Value | Odds ratio and 95% CI |
|---|---|---|---|---|---|---|
| BRUGNARO 2008 | Combined | 1.226 | 0.788 | 1.909 | 0.366 | |
| SHLAES 1986 | IMMOBILITY | 3.250 | 0.850 | 12.433 | 0.085 | |
| MUDER 1997 | Combined | 1.605 | 0.777 | 3.315 | 0.201 | |
| POP 2008 | IMMOBILITY | 6.613 | 1.351 | 32.371 | 0.020 | |
| RAAB 2006 | IMMOBILITY | 4.400 | 1.412 | 13.714 | 0.011 | |
| DENIS 2009 | IMMOBILITY | 1.410 | 1.141 | 1.742 | 0.001 | |
| vonBAUM 2002 | Combined | 3.183 | 1.265 | 8.006 | 0.014 | |
| SUETENS 2007 | Combined | 1.992 | 1.453 | 2.732 | 0.000 | |
| VOVKO 2005 | IMMOBILITY | 4.230 | 0.352 | 50.840 | 0.256 | |
| WINGARD1993 | IMMOBILITY | 56.667 | 6.847 | 469.012 | 0.000 | |
| | | 2.199 | 1.529 | 3.164 | 0.000 | |

0.01    0.1    1    10    100

Non-carriage          Carriage

**Figure 6: Forest Plot: Meta-Analysis of Limited Mobility - Risk Ratio**

| Study name | Subgroup within study | Statistics for each study | | | | Risk ratio and 95% CI |
|---|---|---|---|---|---|---|
| | | Risk ratio | Lower limit | Upper limit | p-Value | |
| BRUGNARO 2008 | Combined | 1.124 | 0.881 | 1.434 | 0.348 | |
| COX 1999 | IMMOBILITY | 2.900 | 0.396 | 21.261 | 0.295 | |
| MUDER 1997 | Combined | 1.389 | 0.836 | 2.307 | 0.204 | |
| POP 2008 | IMMOBILITY | 1.261 | 1.047 | 1.519 | 0.014 | |
| SHLAES 1986 | IMMOBILITY | 1.422 | 1.042 | 1.940 | 0.026 | |
| WINGARD1993 | IMMOBILITY | 2.590 | 1.650 | 4.066 | 0.000 | |
| | | 1.421 | 1.141 | 1.770 | 0.002 | |

0.01    0.1    1    10    100

Non-carriage          Carriage

**Figure 7: Forest Plot: Meta-Analysis of Dependency - Odds Ratio**

| Study name | Subgroup within study | Odds ratio | Lower limit | Upper limit | p-Value | Odds ratio and 95% CI |
|---|---|---|---|---|---|---|
| BENENSON | Combined | 0.572 | 0.220 | 1.485 | 0.251 | |
| COLL | DEPENDANT | 5.881 | 1.172 | 29.506 | 0.031 | |
| DENIS | DEPENDANT | 1.630 | 1.191 | 2.231 | 0.002 | |
| MANZUR | DEPENDANT | 1.650 | 1.231 | 2.212 | 0.001 | |
| MARCH | Combined | 11.647 | 5.971 | 22.715 | 0.000 | |
| PFINGSTEN | DEPENDANT | 2.143 | 1.477 | 3.107 | 0.000 | |
| POP-VICAS | DEPENDANT | 1.862 | 0.735 | 4.714 | 0.190 | |
| RAAB | DEPENDANT | 3.300 | 1.004 | 10.845 | 0.049 | |
| VOVKO | DEPENDANT | 1.400 | 0.368 | 5.329 | 0.622 | |
| WIENER | Combined | 2.616 | 1.301 | 5.259 | 0.007 | |
| WINGARD | DEPENDANT | 49.500 | 9.638 | 254.231 | 0.000 | |
| | | 2.658 | 1.686 | 4.192 | 0.000 | |

0.01    0.1    1    10    100

Non-carriage          Carriage

# Figure 8: Forest Plot: Meta-Analysis of Dependency - Risk Ratio



| Study name | Subgroup within study | Statistics for each study | | | | Risk ratio and 95% CI |
|---|---|---|---|---|---|---|
| | | Risk ratio | Lower limit | Upper limit | p-Value | |
| COLL | DEPENDANT | 1.651 | 1.157 | 2.355 | 0.006 | |
| LASSETER | DEPENDANT | 4.160 | 1.529 | 11.320 | 0.005 | |
| PFINGSTEN | DEPENDANT | 1.756 | 1.365 | 2.260 | 0.000 | |
| POP-VICAS | DEPENDANT | 1.220 | 0.903 | 1.649 | 0.195 | |
| WIENER | DEPENDANT | 1.896 | 1.024 | 3.510 | 0.042 | |
| WINGARD | DEPENDANT | 3.771 | 2.058 | 6.911 | 0.000 | |
| | | 1.898 | 1.403 | 2.566 | 0.000 | |

0.01    0.1    1    10    100

Non-carriage            Carriage

# Figure 9: Forest Plot: Meta-Analysis of all Wounds - Odds Ratio

| Study name | Subgroup within study | Statistics for each study | | | | Odds ratio and 95% CI |
|---|---|---|---|---|---|---|
| | | Odds ratio | Lower limit | Upper limit | p-Value | |
| BARR 2007 | WOUND | 1.920 | 0.821 | 4.488 | 0.132 | |
| BRUGNARO 2008 | DECUBITUS ULCER | 2.068 | 0.683 | 6.261 | 0.198 | |
| MARCH 2009 | Combined | 1.482 | 0.664 | 3.309 | 0.337 | |
| MUDER 1997 | Combined | 3.625 | 1.660 | 7.918 | 0.001 | |
| O'FALLON 2010 | DECUBITUS ULCER | 3.100 | 0.501 | 19.169 | 0.224 | |
| PFINGSTEN 2011 | WOUND | 3.288 | 1.655 | 6.530 | 0.001 | |
| POP 2008 | Combined | 2.704 | 1.138 | 6.424 | 0.024 | |
| RAAB 2006 | WOUND | 1.500 | 0.302 | 7.450 | 0.620 | |
| STONE 2012 | WOUND | 2.200 | 1.391 | 3.479 | 0.001 | |
| DENIS 2009 | WOUND/DECUBITUS ULCER | 1.570 | 1.180 | 2.089 | 0.002 | |
| vonBAUM 2002 | Combined | 2.708 | 1.365 | 5.373 | 0.004 | |
| SUETENS 2007 | DECUBITUS ULCER | 3.500 | 1.922 | 6.373 | 0.000 | |
| WIENER 1999 | DECUBITUS ULCER | 1.500 | 0.622 | 3.614 | 0.366 | |
| FRAISE 1997 | WOUND | 1.473 | 0.642 | 3.380 | 0.360 | |
| VOVKO 2005 | WOUND | 4.300 | 0.580 | 31.860 | 0.153 | |
| EVEILLARD 2008 | WOUNDS/DECUBITUS/ SKIN LESIONS | 1.841 | 0.803 | 4.220 | 0.149 | |
| MANZUR 2008 | DECUBITUS ULCER | 4.170 | 2.769 | 6.279 | 0.000 | |
| | | 2.353 | 1.902 | 2.911 | 0.000 | |



0.01    0.1    1    10    100

Non-carriage          Carriage

**Figure 10: Forest Plot: Meta-Analysis of all Wounds - Risk Ratio**

| Study name | Subgroup within study | Risk ratio | Lower limit | Upper limit | p-Value |
|---|---|---|---|---|---|
| BRUGNARO 2008 | DECUBITUS ULCER | 1.969 | 0.716 | 5.415 | 0.189 |
| EVEILLARD 2008 | WOUNDS/DECUBITUS/ SKIN LESIONS | 1.595 | 0.859 | 2.962 | 0.139 |
| FRAISE 1997 | WOUND | 1.330 | 0.736 | 2.403 | 0.345 |
| LASSETER 2010 | WOUND | 1.550 | 0.681 | 3.527 | 0.296 |
| MUDER 1997 | Combined | 2.500 | 1.397 | 4.473 | 0.002 |
| PADIGLIONE 2001 | DECUBITUS ULCER | 2.480 | 0.540 | 11.395 | 0.243 |
| PFINGSTEN 2011 | WOUND | 3.107 | 1.639 | 5.887 | 0.001 |
| POP 2008 | Combined | 2.278 | 1.099 | 4.722 | 0.027 |
| | | 1.991 | 1.546 | 2.563 | 0.000 |



Risk ratio and 95% CI

0.01    0.1    1    10    100

Non-carriage          Carriage

# Figure 11: Forest Plot: Sub-group analysis of Wounds Only (excl Decubitus Ulcer) - Odds Ratio

| Study name | Subgroup within study | Statistics for each study | | | | Odds ratio and 95% CI |
| --- | --- | --- | --- | --- | --- | --- |
| | | Odds ratio | Lower limit | Upper limit | p-Value | |
| BARR 2007 | WOUND | 1.920 | 0.821 | 4.488 | 0.132 | |
| PFINGSTEN 2011 | WOUND | 3.288 | 1.655 | 6.530 | 0.001 | |
| POP 2008 | WOUND | 5.263 | 0.588 | 47.143 | 0.138 | |
| RAAB 2006 | WOUND | 1.500 | 0.302 | 7.450 | 0.620 | |
| STONE 2012 | WOUND | 2.200 | 1.391 | 3.479 | 0.001 | |
| vonBAUM 2002 | WOUND | 3.250 | 1.310 | 8.061 | 0.011 | |
| FRAISE 1997 | WOUND | 1.473 | 0.642 | 3.380 | 0.360 | |
| VOVKO 2005 | WOUND | 4.300 | 0.580 | 31.860 | 0.153 | |
| | | 2.346 | 1.753 | 3.139 | 0.000 | |



0.01    0.1    1    10    100

Non-carriage          Carriage

**Figure 12: Forest Plot: Sub-group analysis of Wounds Only (excl Decubitus Ulcer) - Risk Ratio**

| Study name | Subgroup within study | Statistics for each study | | | | Risk ratio and 95% CI |
|---|---|---|---|---|---|---|
| | | Risk ratio | Lower limit | Upper limit | p-Value | |
| FRAISE 1997 | WOUND | 1.330 | 0.736 | 2.403 | 0.345 | |
| LASSETER 2010 | WOUND | 1.550 | 0.681 | 3.527 | 0.296 | |
| PFINGSTEN 2011 | WOUND | 3.107 | 1.639 | 5.887 | 0.001 | |
| POP 2008 | WOUND | 4.767 | 0.581 | 39.087 | 0.146 | |
| | | 1.965 | 1.187 | 3.254 | 0.009 | |

0.01    0.1    1    10    100

Non-carriage          Carriage

**Figure 13: Forest Plot: Sub-group analysis of Decubitus Ulcers only - Odds Ratio**

| Study name | Subgroup within study | Odds ratio | Lower limit | Upper limit | p-Value | Odds ratio and 95% CI |
|---|---|---|---|---|---|---|
| BRUGNARO 2008 | DECUBITUS ULCER | 2.068 | 0.683 | 6.261 | 0.198 | |
| MARCH 2009 | Combined | 1.482 | 0.664 | 3.309 | 0.337 | |
| MUDER 1997 | Combined | 3.625 | 1.660 | 7.918 | 0.001 | |
| O'FALLON 2010 | DECUBITUS ULCER | 3.100 | 0.501 | 19.169 | 0.224 | |
| POP 2008 | DECUBITUS ULCER | 3.039 | 1.079 | 8.564 | 0.035 | |
| vonBAUM 2002 | DECUBITUS ULCER | 2.130 | 0.751 | 6.045 | 0.155 | |
| SUETENS 2007 | DECUBITUS ULCER | 3.500 | 1.922 | 6.373 | 0.000 | |
| WIENER 1999 | DECUBITUS ULCER | 1.500 | 0.622 | 3.614 | 0.366 | |
| MANZUR 2008 | DECUBITUS ULCER | 4.170 | 2.769 | 6.279 | 0.000 | |
| | | 2.903 | 2.196 | 3.838 | 0.000 | |

0.01    0.1    1    10    100

Non-carriage          Carriage

**Figure 14: Forest Plot: Sub-group analysis of Decubitus Ulcers only - Risk Ratio**

| Study name | Subgroup within study | Risk ratio | Lower limit | Upper limit | p-Value |
|---|---|---|---|---|---|
| BRUGNARO 2008 | DECUBITUS ULCER | 1.969 | 0.716 | 5.415 | 0.189 |
| MUDER 1997 | Combined | 2.500 | 1.397 | 4.473 | 0.002 |
| PADIGLIONE 2001 | DECUBITUS ULCER | 2.480 | 0.540 | 11.395 | 0.243 |
| POP 2008 | DECUBITUS ULCER | 2.174 | 1.040 | 4.547 | 0.039 |
| | | 2.309 | 1.545 | 3.450 | 0.000 |

Risk ratio and 95% CI

0.01    0.1    1    10    100

Non-carriage        Carriage
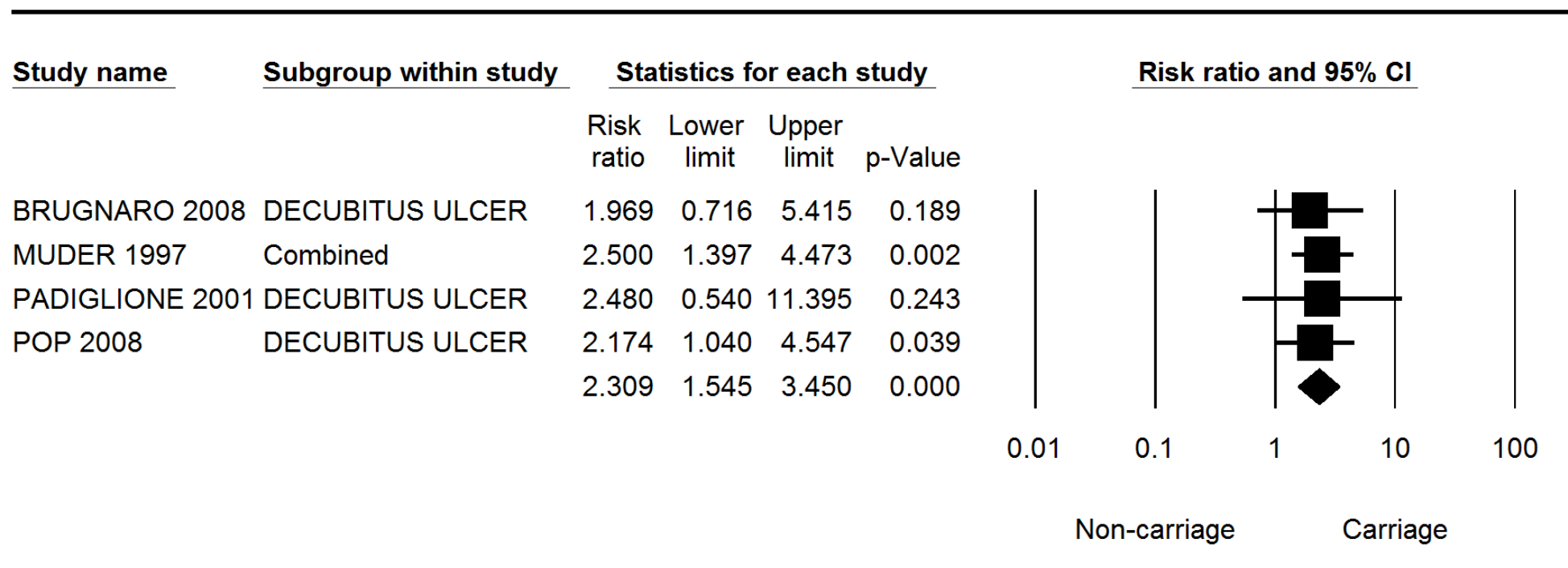
**Figure 15: Forest Plot: Meta-Analysis of Incontinence - Odds Ratio**

| Study name | Statistics for each study | | | | Odds ratio and 95% CI |
|---|---|---|---|---|---|
| | Odds ratio | Lower limit | Upper limit | p-Value | |
| O'FALLON 2010 | 7.000 | 0.861 | 56.938 | 0.069 | |
| RAAB 2006 | 4.500 | 0.943 | 21.477 | 0.059 | |
| SUETENS 2007 | 1.800 | 1.200 | 2.700 | 0.004 | |
| WINGARD 1993 | 8.929 | 2.932 | 27.192 | 0.000 | |
| | 4.055 | 1.514 | 10.860 | 0.005 | |

0.01    0.1    1    10    100

Non-carriage        Carriage

**Figure 16: Forest Plot: Meta-Analysis of Incontinence - Risk Ratio**

| Study name | Risk ratio | Lower limit | Upper limit | p-Value | Risk ratio and 95% CI |
|---|---|---|---|---|---|
| WINGARD 1993 | 3.265 | 1.642 | 6.494 | 0.001 | |
| | 3.265 | 1.642 | 6.494 | 0.001 | |

0.01   0.1   1   10   100

Non-carriage          Carriage

**Figure 17: Forest Plot: Meta-Analysis of History of ARO - Odds Ratio**



| Study name | Subgroup within study | Odds ratio | Lower limit | Upper limit | p-Value |
|---|---|---|---|---|---|
| BARR 2007 | Hx OF COLONISATION | 6.370 | 1.452 | 27.937 | 0.014 |
| BRUGNARO 2008 | Hx OF MRSA infection | 1.635 | 0.694 | 3.853 | 0.261 |
| SHLAES 1986 | Hx OF COLONISATION | 7.714 | 2.339 | 25.439 | 0.001 |
| ROONEY 2009 | Combined | 2.112 | 1.210 | 3.686 | 0.008 |
| STONE 2012 | Hx OF MRSA | 3.900 | 2.388 | 6.369 | 0.000 |
| DENIS 2009 | Combined | 1.629 | 1.125 | 2.358 | 0.010 |
| | | 2.704 | 1.693 | 4.320 | 0.000 |

**Figure 18: Forest Plot: Meta-Analysis of History of ARO - Risk Ratio**

| Study name | | Risk ratio | Lower limit | Upper limit | p-Value | Risk ratio and 95% CI |
|---|---|---|---|---|---|---|
| | | | | | | **Statistics for each study** → **Risk ratio and 95% CI** |
| BRUGNARO 2008 | Hx OF MRSA infection | 1.531 | 0.743 | 3.156 | 0.248 | |
| LASSETER 2010 | Combined | 2.156 | 0.872 | 5.333 | 0.096 | |
| SHLAES 1986 | Hx OF COLONISATION | 3.937 | 1.920 | 8.076 | 0.000 | |
| ROONEY 2009 | Hx OF COLONISATION | 48.400 | 2.932 | 799.037 | 0.007 | |
| | | 2.885 | 1.322 | 6.293 | 0.008 | |

0.01    0.1    1    10    100

Non-carriage          Carriage

**Figure 19: Forest Plot: Meta-Analysis of Sex (Male vs Female) - Odds Ratio**

| Study name | Subgroup within study | Odds ratio | Lower limit | Upper limit | p-Value | Odds ratio and 95% CI |
|---|---|---|---|---|---|---|
| BARR 2007 | Blank | 1.732 | 1.147 | 2.617 | 0.009 | |
| BENENSON 2009 | Blank | 1.000 | 0.582 | 1.718 | 1.000 | |
| BRUGNARO 2008 | Blank | 0.710 | 0.332 | 1.518 | 0.377 | |
| CHENG 2013 | Blank | 0.806 | 0.528 | 1.228 | 0.315 | |
| COLL 1994 | Blank | 2.211 | 0.640 | 7.639 | 0.210 | |
| EVEILLARD 2008 | Blank | 1.298 | 0.617 | 2.730 | 0.492 | |
| KARABAY 2006 | Blank | 1.327 | 0.131 | 13.445 | 0.811 | |
| LASSETER 2010 | Blank | 1.905 | 1.095 | 3.312 | 0.022 | |
| MANZUR 2008 | Blank | 1.150 | 0.846 | 1.563 | 0.372 | |
| MARCH 2009 | Combined | 1.019 | 0.642 | 1.617 | 0.937 | |
| O'FALLON 2010 | Blank | 2.813 | 0.499 | 15.857 | 0.241 | |
| OLSEN 2001 | Blank | 0.292 | 0.025 | 3.372 | 0.324 | |
| PFINGSTEN 2011 | Blank | 1.465 | 0.990 | 2.166 | 0.056 | |
| POP 2008 | Blank | 0.543 | 0.162 | 1.822 | 0.323 | |
| RAAB 2006 | Blank | 1.700 | 0.595 | 4.858 | 0.322 | |
| ROONEY 2009 | Blank | 0.916 | 0.532 | 1.578 | 0.752 | |
| VOVKO 2005 | Blank | 2.962 | 0.778 | 11.269 | 0.111 | |
| WIENER 1999 | Blank | 1.214 | 0.256 | 5.755 | 0.807 | |
| | | 1.200 | 1.014 | 1.420 | 0.034 | |

0.01    0.1    1    10    100

Non-carriage                    Carriage

**Figure 20: Forest Plot: Meta-Analysis of Sex (Male vs Female) - Risk Ratio**

| Study name | Subgroup within study | Statistics for each study | | | | Risk ratio and 95% CI |
| --- | --- | --- | --- | --- | --- | --- |
| | | Risk ratio | Lower limit | Upper limit | p-Value | |
| BARR 2007 | Blank | 1.534 | 1.123 | 2.097 | 0.007 | |
| BRUGNARO 2008 | Blank | 0.770 | 0.424 | 1.401 | 0.393 | |
| COLL 1994 | Blank | 1.404 | 0.865 | 2.277 | 0.170 | |
| COX 1999 | Blank | 3.300 | 1.135 | 9.595 | 0.028 | |
| CHENG 2013 | Blank | 0.862 | 0.640 | 1.160 | 0.327 | |
| KARABAY 2006 | Blank | 1.082 | 0.602 | 1.943 | 0.793 | |
| OLSEN 2001 | Blank | 0.433 | 0.068 | 2.753 | 0.375 | |
| PADIGLIONE 2001 | Blank | 0.390 | 0.046 | 3.309 | 0.388 | |
| PFINGSTEN 2011 | Blank | 1.338 | 1.004 | 1.782 | 0.047 | |
| POP 2008 | Blank | 0.596 | 0.212 | 1.673 | 0.326 | |
| ROONEY 2009 | Blank | 0.936 | 0.619 | 1.414 | 0.753 | |
| EVEILLARD 2008 | Blank | 1.182 | 0.741 | 1.884 | 0.484 | |
| LASSETER 2010 | Blank | 1.546 | 1.098 | 2.176 | 0.013 | |
| O'FALLON 2010 | Blank | 2.500 | 0.527 | 11.861 | 0.249 | |
| WIENER 1999 | Blank | 1.167 | 0.339 | 4.010 | 0.807 | |
| VOVKO 2005 | Blank | 2.308 | 0.897 | 5.937 | 0.083 | |
| | | 1.204 | 1.011 | 1.434 | 0.038 | |

0.01    0.1    1    10    100

Non-carriage        Carriage

**Figure 21: Forest Plot: Meta-Analysis of All Invasive Devices - Odds Ratio**

| Study name | Subgroup within study | Odds ratio | Lower limit | Upper limit | p-Value | Odds ratio and 95% CI |
|---|---|---|---|---|---|---|
| BARR 2007 | INVASIVE DEVICE | 3.150 | 1.499 | 6.617 | 0.002 | |
| BENENSON 2009 | IDC | 1.710 | 0.982 | 2.977 | 0.058 | |
| BRUGNARO 2008 | Combined | 0.946 | 0.424 | 2.113 | 0.893 | |
| CHENG 2013 | Combined | 2.597 | 1.474 | 4.575 | 0.001 | |
| COLL 1994 | IDC | 36.000 | 7.030 | 184.347 | 0.000 | |
| EVEILLARD 2008 | Combined | 1.800 | 1.166 | 2.778 | 0.008 | |
| LASSETER 2010 | Combined | 0.852 | 0.049 | 14.897 | 0.913 | |
| MANZUR 2008 | INVASIVE DEVICE | 4.670 | 2.829 | 7.708 | 0.000 | |
| MARCH 2009 | Combined | 2.649 | 1.794 | 3.912 | 0.000 | |
| MUDER 1997 | Combined | 1.372 | 0.856 | 2.200 | 0.189 | |
| OLSEN 2001 | INVASIVE DEVICE | 2.400 | 0.182 | 31.629 | 0.506 | |
| PFINGSTEN 2011 | IDC | 2.937 | 1.832 | 4.708 | 0.000 | |
| RAAB 2006 | Combined | 2.038 | 0.785 | 5.290 | 0.143 | |
| ROONEY 2009 | IDC | 4.350 | 1.350 | 14.018 | 0.014 | |
| SHLAES 1986 | IDC | 4.000 | 1.311 | 12.203 | 0.015 | |
| STONE 2012 | INVASIVE DEVICE | 2.800 | 1.883 | 4.163 | 0.000 | |
| vonBAUM 2002 | Combined | 2.116 | 1.113 | 4.024 | 0.022 | |
| WIENER 1999 | Combined | 1.880 | 1.109 | 3.187 | 0.019 | |
| WINGARD 1993 | CUD | 26.786 | 7.026 | 102.115 | 0.000 | |
| | | 2.614 | 2.023 | 3.379 | 0.000 | |

0.01    0.1    1    10    100

Non-carriage                Carriage

**Figure 22: Forest Plot: Meta-Analysis of All Invasive Devices - Risk Ratio**

| Study name | Subgroup within study | Statistics for each study | | | | Risk ratio and 95% CI |
|---|---|---|---|---|---|---|
| | | Risk ratio | Lower limit | Upper limit | p-Value | |
| BRUGNARO 2008 | Combined | 0.951 | 0.454 | 1.988 | 0.893 | |
| COLL 1994 | IDC | 8.000 | 3.052 | 20.967 | 0.000 | |
| CHENG 2013 | Combined | 2.478 | 1.457 | 4.216 | 0.001 | |
| LASSETER 2010 | Combined | 2.269 | 1.397 | 3.685 | 0.001 | |
| SHLAES 1986 | IDC | 2.059 | 1.258 | 3.371 | 0.004 | |
| MUDER 1997 | Combined | 1.165 | 0.927 | 1.464 | 0.190 | |
| PFINGSTEN 2011 | IDC | 2.589 | 1.743 | 3.845 | 0.000 | |
| EVEILLARD 2008 | Combined | 1.595 | 1.138 | 2.236 | 0.007 | |
| WINGARD 1993 | CUD | 4.034 | 2.072 | 7.853 | 0.000 | |
| | | 2.128 | 1.523 | 2.974 | 0.000 | |



0.01    0.1    1    10    100

Non-carriage          Carriage

**Figure 23: Forest Plot: Sub-group analysis of Gastrostomy/Nasogastric Devices - Odds Ratio**

| Study name | Subgroup within study | Odds ratio | Lower limit | Upper limit | p-Value | Odds ratio and 95% CI |
|---|---|---|---|---|---|---|
| BRUGNARO 2008 | GASTROSTOMY | 0.394 | 0.093 | 1.672 | 0.207 | |
| CHENG 2013 | NASOGASTRIC TUBE | 2.142 | 1.108 | 4.143 | 0.024 | |
| MARCH 2009 | Combined | 2.938 | 1.458 | 5.921 | 0.003 | |
| MUDER 1997 | Combined | 1.875 | 0.893 | 3.937 | 0.097 | |
| RAAB 2006 | GASTROSTOMY | 2.700 | 0.801 | 9.106 | 0.109 | |
| vonBAUM 2002 | GASTROSTOMY | 1.490 | 0.548 | 4.048 | 0.434 | |
| WIENER 1999 | GASTROSTOMY | 2.500 | 1.301 | 4.804 | 0.006 | |
| EVEILLARD 2008 | NASOGASTRIC TUBE | 2.072 | 0.443 | 9.688 | 0.354 | |
| | | 2.091 | 1.547 | 2.825 | 0.000 | |



0.01    0.1    1    10    100

Non-carriage          Carriage

**Figure 24: Forest Plot: Sub-group analysis of Gastrostomy/Nasogastric Devices - Risk Ratio**

| Study name | Subgroup within study | Risk ratio | Lower limit | Upper limit | p-Value | Risk ratio and 95% CI |
|---|---|---|---|---|---|---|
| BRUGNARO 2008 | GASTROSTOMY | 0.422 | 0.107 | 1.670 | 0.219 | |
| CHENG 2013 | NASOGASTRIC TUBE | 2.019 | 1.111 | 3.670 | 0.021 | |
| EVEILLARD 2008 | NASOGASTRIC TUBE | 1.994 | 0.466 | 8.528 | 0.352 | |
| LASSETER 2010 | NASOGASTRIC TUBE/ PEG | 1.200 | 0.190 | 7.559 | 0.846 | |
| MUDER 1997 | Combined | 1.563 | 0.917 | 2.662 | 0.101 | |
| | | 1.553 | 1.044 | 2.311 | 0.030 | |



0.01    0.1    1    10    100

Non-carriage          Carriage

**Figure 25: Forest Plot: Sub-group analysis of IDUC/CUD Devices - Odds Ratio**

| Study name | Subgroup within study | Odds ratio | Lower limit | Upper limit | p-Value | Odds ratio and 95% CI |
|---|---|---|---|---|---|---|
| BENENSON 2009 | IDC | 1.710 | 0.982 | 2.977 | 0.058 | |
| BRUGNARO 2008 | IDC | 2.025 | 0.744 | 5.507 | 0.167 | |
| COLL 1994 | IDC | 36.000 | 7.030 | 184.347 | 0.000 | |
| CHENG 2013 | IDC | 6.276 | 1.789 | 22.014 | 0.004 | |
| SHLAES 1986 | IDC | 4.000 | 1.311 | 12.203 | 0.015 | |
| MARCH 2009 | Combined | 2.925 | 1.684 | 5.082 | 0.000 | |
| MUDER 1997 | Combined | 1.122 | 0.521 | 2.417 | 0.768 | |
| PFINGSTEN 2011 | IDC | 2.937 | 1.832 | 4.708 | 0.000 | |
| RAAB 2006 | IDC | 1.300 | 0.279 | 6.051 | 0.738 | |
| ROONEY 2009 | IDC | 4.350 | 1.350 | 14.018 | 0.014 | |
| vonBAUM 2002 | IDC | 2.710 | 1.171 | 6.274 | 0.020 | |
| WIENER 1999 | IDC | 1.100 | 0.449 | 2.694 | 0.835 | |
| EVEILLARD 2008 | IDC | 2.288 | 0.791 | 6.613 | 0.127 | |
| WINGARD 1993 | CUD | 26.786 | 7.026 | 102.115 | 0.000 | |
| | | 2.954 | 1.979 | 4.409 | 0.000 | |



Non-carriage          Carriage

**Figure 26: Forest Plot: Sub-group analysis of IDUC/CUD Devices - Risk Ratio**

| Study name | Subgroup within study | Statistics for each study | | | | Risk ratio and 95% CI |
|---|---|---|---|---|---|---|
| | | Risk ratio | Lower limit | Upper limit | p-Value | |
| BRUGNARO 2008 | IDC | 1.905 | 0.781 | 4.648 | 0.156 | |
| CHENG 2013 | IDC | 6.058 | 1.780 | 20.613 | 0.004 | |
| COLL 1994 | IDC | 8.000 | 3.052 | 20.967 | 0.000 | |
| EVEILLARD 2008 | IDC | 2.068 | 0.824 | 5.189 | 0.122 | |
| LASSETER 2010 | IDC | 2.580 | 1.218 | 5.463 | 0.013 | |
| MUDER 1997 | Combined | 1.030 | 0.847 | 1.251 | 0.768 | |
| PFINGSTEN 2011 | IDC | 2.589 | 1.743 | 3.845 | 0.000 | |
| SHLAES 1986 | IDC | 2.059 | 1.258 | 3.371 | 0.004 | |
| WINGARD 1993 | CUD | 4.034 | 2.072 | 7.853 | 0.000 | |
| | | 2.600 | 1.612 | 4.193 | 0.000 | |



0.01    0.1    1    10    100

Non-carriage          Carriage

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## Figure 27: Forest Plot: Meta-Analysis of Antibiotic Use - Odds Ratio

| Study name | Subgroup within study | Statistics for each study | | | | Odds ratio and 95% CI |
|---|---|---|---|---|---|---|
| | | Odds ratio | Lower limit | Upper limit | p-Value | |
| BARR 2007 | AB PAST 6 MONTHS | 1.690 | 0.851 | 3.355 | 0.134 | |
| BENENSON 2009 | AB PAST 3 MONTHS | 5.210 | 2.615 | 10.382 | 0.000 | |
| BRUGNARO 2008 | Combined | 1.393 | 1.090 | 1.779 | 0.008 | |
| CHENG 2013 | AB PAST 3 MONTHS | 2.497 | 0.950 | 6.568 | 0.064 | |
| COLL 1994 | AB PAST 6 MONTHS | 16.962 | 0.945 | 304.603 | 0.055 | |
| DENIS 2009 | Combined | 1.590 | 1.288 | 1.963 | 0.000 | |
| EVEILLARD 2008 | AB PAST 12 MONTHS | 4.691 | 1.706 | 12.895 | 0.003 | |
| FRAISE 1996 | AB | 2.956 | 0.922 | 9.481 | 0.068 | |
| KARABAY 2006 | AB PAST 6 MONTHS | 38.172 | 1.944 | 749.461 | 0.017 | |
| LOEB 2003 | Combined | 1.042 | 1.024 | 1.060 | 0.000 | |
| MANZUR 2008 | AB PAST 3 MONTHS | 3.330 | 2.312 | 4.797 | 0.000 | |
| MARCH 2009 | Combined | 3.401 | 1.691 | 6.841 | 0.001 | |
| O'FALLON 2010 | AB PAST 12 MONTHS | 5.500 | 1.210 | 25.003 | 0.027 | |
| OLSEN 2001 | Combined | 5.881 | 0.937 | 36.914 | 0.059 | |
| POP-VICAS 2008 | AB PAST 2 WEEKS | 2.651 | 1.098 | 6.403 | 0.030 | |
| ROONEY 2009 | Combined | 1.547 | 1.228 | 1.949 | 0.000 | |
| SEUTENS 2007 | Combined | 2.294 | 1.733 | 3.037 | 0.000 | |
| SHLAES 1986 | AB PAST 6 MONTHS | 4.091 | 1.099 | 15.226 | 0.036 | |
| STONE 2012 | AB PAST 3 MONTHS | 2.100 | 1.404 | 3.141 | 0.000 | |
| vonBAUM 2002 | AB PAST MONTH | 1.620 | 0.691 | 3.797 | 0.267 | |
| VOVKO 2005 | AB PAST MONTH | 6.250 | 1.297 | 30.109 | 0.022 | |
| WIENER 1999 | Combined | 2.280 | 1.628 | 3.193 | 0.000 | |
| | | 2.398 | 1.845 | 3.117 | 0.000 | |



0.01  0.1  1  10  100

Non-carriage          Carriage

**Figure 28: Forest Plot: Meta-Analysis of Antibiotic Use - Risk Ratio**

| Study name | Subgroup within study | Statistics for each study | | | | Risk ratio and 95% CI |
|---|---|---|---|---|---|---|
| | | Risk ratio | Lower limit | Upper limit | p-Value | |
| BRUGNARO 2008 | Combined | 1.280 | 1.073 | 1.526 | 0.006 | |
| CHENG 2013 | AB PAST 3 MONTHS | 2.423 | 0.959 | 6.123 | 0.061 | |
| COLL 1994 | AB PAST 6 MONTHS | 1.499 | 1.176 | 1.911 | 0.001 | |
| EVEILLARD 2008 | AB PAST 12 MONTHS | 1.450 | 1.200 | 1.753 | 0.000 | |
| FRAISE 1996 | AB | 2.660 | 0.953 | 7.427 | 0.062 | |
| KARABAY 2006 | AB PAST 6 MONTHS | 4.717 | 2.728 | 8.156 | 0.000 | |
| NUORTI 1998 | AB AT ONSET OF ILLNESS/CULTURE | 2.300 | 1.280 | 4.134 | 0.005 | |
| PADIGLIONE 2001 | AB PAST 2 WEEKS | 2.630 | 0.682 | 10.136 | 0.160 | |
| POP-VICAS 2008 | AB PAST 2 WEEKS | 1.653 | 1.033 | 2.644 | 0.036 | |
| ROONEY 2009 | Combined | 1.108 | 0.897 | 1.368 | 0.342 | |
| SHLAES 1986 | AB PAST 6 MONTHS | 3.125 | 1.137 | 8.589 | 0.027 | |
| | | 1.727 | 1.390 | 2.145 | 0.000 | |

0.01    0.1    1    10    100

Non-carriage          Carriage

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**Figure 29: Forest Plot: Sub-group analysis of Antibiotic use within last 12 weeks - Odds Ratio**

| Study name | Subgroup within study | Odds ratio | Lower limit | Upper limit | p-Value | Odds ratio and 95% CI |
|---|---|---|---|---|---|---|
| BENENSON 2009 | AB PAST 3 MONTHS | 5.210 | 2.615 | 10.382 | 0.000 | |
| CHENG 2013 | AB PAST 3 MONTHS | 2.497 | 0.950 | 6.568 | 0.064 | |
| MARCH 2009 | Combined | 3.401 | 1.691 | 6.841 | 0.001 | |
| POP-VICAS 2008 | AB PAST 2 WEEKS | 2.651 | 1.098 | 6.403 | 0.030 | |
| STONE 2012 | AB PAST 3 MONTHS | 2.100 | 1.404 | 3.141 | 0.000 | |
| DENIS 2009 | Combined | 1.590 | 1.288 | 1.963 | 0.000 | |
| vonBAUM 2002 | AB PAST MONTH | 1.620 | 0.691 | 3.797 | 0.267 | |
| LOEB 2003 | Combined | 1.042 | 1.024 | 1.060 | 0.000 | |
| SEUTENS 2007 | Combined | 2.294 | 1.733 | 3.037 | 0.000 | |
| VOVKO 2005 | AB PAST MONTH | 6.250 | 1.297 | 30.109 | 0.022 | |
| MANZUR 2008 | AB PAST 3 MONTHS | 3.330 | 2.312 | 4.797 | 0.000 | |
| | | 2.353 | 1.617 | 3.425 | 0.000 | |



0.01    0.1    1    10    100

Non-carriage          Carriage

**Figure 30: Forest Plot: Sub-group analysis of Antibiotic use within last 12 weeks - Risk Ratio**

| Study name | Subgroup within study | Statistics for each study | | | | Risk ratio and 95% CI |
|---|---|---|---|---|---|---|
| | | Risk ratio | Lower limit | Upper limit | p-Value | |
| CHENG 2013 | AB PAST 3 MONTHS | 2.423 | 0.959 | 6.123 | 0.061 | |
| PADIGLIONE 2001 | AB PAST 2 WEEKS | 2.630 | 0.682 | 10.136 | 0.160 | |
| POP-VICAS 2008 | AB PAST 2 WEEKS | 1.653 | 1.033 | 2.644 | 0.036 | |
| NUORTI 1998 | AB AT ONSET OF ILLNESS/CULTURE | 2.300 | 1.280 | 4.134 | 0.005 | |
| | | 1.982 | 1.424 | 2.758 | 0.000 | |

0.01    0.1    1    10    100

Non-carriage            Carriage

108

**Figure 31: Forest Plot: Sub-group analysis of Fluoro/Cipro Antibiotic use - Odds Ratio**



| Study name | Subgroup within study | Odds ratio | Lower limit | Upper limit | p-Value |
|---|---|---|---|---|---|
| BRUGNARO 2008 | FLUOROQUINOLONES PAST 12 MONTHS | 2.575 | 1.368 | 4.848 | 0.003 |
| OLSEN 2001 | AB PAST 6 MONTHS Fluroquinolone | 22.000 | 0.660 | 733.091 | 0.084 |
| ROONEY 2009 | FLUORO USE | 2.790 | 1.586 | 4.908 | 0.000 |
| DENIS 2009 | AB PAST 3 MONTHS Fluoroquinolone | 1.590 | 1.168 | 2.165 | 0.003 |
| LOEB 2003 | Combined | 1.037 | 1.019 | 1.056 | 0.000 |
| SEUTENS 2007 | AB PAST 3 MONTHS Fluroquinolone | 2.400 | 1.420 | 4.057 | 0.001 |
| WIENER 1999 | Combined | 2.504 | 1.654 | 3.789 | 0.000 |
| | | 2.032 | 1.306 | 3.161 | 0.002 |

Non-carriage          Carriage

**Figure 32: Forest Plot: Sub-group analysis of Fluoro/Cipro Antibiotic use - Risk Ratio**

| Study name | Subgroup within study | Risk ratio | Lower limit | Upper limit | p-Value | Risk ratio and 95% CI |
|---|---|---|---|---|---|---|
| BRUGNARO 2008 | FLUOROQUINOLONES PAST 12 MONTHS | 1.659 | 1.254 | 2.195 | 0.000 | |
| | | 1.659 | 1.254 | 2.195 | 0.000 | |

0.01    0.1    1    10    100

Non-carriage                    Carriage

**Figure 33: Forest Plot: Sub-group analysis of Cephalosporin Antibiotic use - Odds Ratio**

| Study name | Subgroup within study | Odds ratio | Lower limit | Upper limit | p-Value | Odds ratio and 95% CI |
|---|---|---|---|---|---|---|
| BRUGNARO 2008 | CEPHALOSPORINS PAST 12 MONTHS | 2.478 | 1.313 | 4.677 | 0.005 | |
| ROONEY 2009 | CEPHALOSPORIN USE | 1.566 | 0.802 | 3.057 | 0.189 | |
| SEUTENS 2007 | AB PAST 3 MONTHS CEPHALOSPORINS | 3.100 | 1.122 | 8.567 | 0.029 | |
| | | 2.149 | 1.413 | 3.270 | 0.000 | |

0.01    0.1    1    10    100

Non-carriage                Carriage

# Figure 34: Forest Plot: Sub-group analysis of Cephalosporin Antibiotic use - Risk Ratio

| Study name | Subgroup within study | Statistics for each study | | | | Risk ratio and 95% CI |
|---|---|---|---|---|---|---|
| | | Risk ratio | Lower limit | Upper limit | p-Value | |
| BRUGNARO 2008 | CEPHALOSPORINS PAST 12 MONTHS | 1.825 | 1.261 | 2.641 | 0.001 | |
| ROONEY 2009 | CEPHALOSPORIN USE | 1.471 | 0.828 | 2.612 | 0.188 | |
| | | 1.713 | 1.256 | 2.338 | 0.001 | |



0.01     0.1     1     10     100

Non-carriage          Carriage

# Figure 35: Forest Plot: Meta-Analysis of Hospital Stay (including surgery) - Odds Ratio

| Study name | Subgroup within study | Odds ratio | Lower limit | Upper limit | p-Value | Odds ratio and 95% CI |
|---|---|---|---|---|---|---|
| BARR 2007 | Combined | 2.005 | 1.490 | 2.697 | 0.000 | |
| BENENSON 2009 | HOSPITAL STAY IN PAST 6 MONTHS | 6.750 | 3.859 | 11.806 | 0.000 | |
| BRUGNARO 2008 | HOSPITAL STAY IN PAST 12 MONTHS | 2.359 | 1.225 | 4.543 | 0.010 | |
| COLL 1994 | HOSPITAL STAY IN PAST 6 MONTHS | 2.042 | 0.603 | 6.909 | 0.251 | |
| KARABAY2006 | HOSPITAL STAY IN PAST 6 MONTHS | 15.750 | 1.508 | 164.465 | 0.021 | |
| MUDER 1997 | Combined | 1.065 | 0.532 | 2.133 | 0.859 | |
| O'FALLON 2010 | HOSPITAL STAY IN PAST 12 MONTHS | 2.000 | 0.190 | 21.024 | 0.564 | |
| PFINGSTEN 2001 | HOSPITAL STAY IN PAST 6 MONTHS | 2.247 | 1.582 | 3.192 | 0.000 | |
| POP-VICAS 2009 | HOSPITAL STAY IN PAST 12 MONTHS | 1.333 | 0.419 | 4.243 | 0.626 | |
| RAAB 2006 | Combined | 1.550 | 0.547 | 4.393 | 0.410 | |
| ROONEY 2009 | HOSPITAL STAY | 1.690 | 1.050 | 2.720 | 0.031 | |
| STONE 2012 | HOSPITAL STAY IN PAST 12 MONTHS | 1.500 | 0.989 | 2.275 | 0.056 | |
| DENIS 2009 | HOSPITAL STAY IN PAST 12 MONTHS | 1.310 | 1.068 | 1.607 | 0.010 | |
| vonBAUM 2002 | HOSPITAL STAY IN PAST 3 MONTHS | 2.210 | 1.028 | 4.751 | 0.042 | |
| SUETENS 2007 | HOSPITAL STAY IN PAST 12 MONTHS | 1.900 | 1.295 | 2.788 | 0.001 | |
| VOVKO 2005 | Combined | 5.667 | 2.036 | 15.771 | 0.001 | |
| | | 2.054 | 1.606 | 2.626 | 0.000 | |

0.01    0.1    1    10    100

Non-carriage          Carriage

113

**Figure 36: Forest Plot: Meta-Analysis of Hospital Stay (including surgery) - Risk Ratio**

| Study name | Subgroup within study | Statistics for each study | | | | Risk ratio and 95% CI |
|---|---|---|---|---|---|---|
| | | Risk ratio | Lower limit | Upper limit | p-Value | |
| BRUGNARO 2008 | HOSPITAL STAY IN PAST 12 MONTHS | 1.853 | 1.211 | 2.835 | 0.004 | |
| COLL 1994 | HOSPITAL STAY IN PAST 6 MONTHS | 1.556 | 0.758 | 3.192 | 0.228 | |
| KARABAY2006 | HOSPITAL STAY IN PAST 6 MONTHS | 4.688 | 2.176 | 10.098 | 0.000 | |
| LASSETER 2010 | SURGERY PAST 6 MONTHS | 1.510 | 0.607 | 3.759 | 0.376 | |
| MUDER 1997 | Combined | 1.042 | 0.663 | 1.636 | 0.859 | |
| NUORTI 1998 | HOSPITAL STAY IN PAST 12 MONTHS | 3.300 | 1.078 | 10.098 | 0.036 | |
| PADIGLIONE 2001 | HOSPITAL STAY IN PAST 3 MONTHS | 2.660 | 0.688 | 10.277 | 0.156 | |
| PFINGSTEN 2001 | HOSPITAL STAY IN PAST 6 MONTHS | 1.682 | 1.379 | 2.052 | 0.000 | |
| POP-VICAS 2009 | HOSPITAL STAY IN PAST 12 MONTHS | 1.271 | 0.483 | 3.348 | 0.627 | |
| RAAB 2006 | SURGERY IN PAST 6 MONTHS | 0.582 | 0.035 | 9.550 | 0.705 | |
| | | 1.733 | 1.343 | 2.238 | 0.000 | |

0.01　0.1　1　10　100

Non-carriage　　　Carriage

# Appendix VII: Funnel Plots

Funnel plots are shown for all risk factors that showed statistical significance of >0.05 and where the number of included studies was 11 or greater.

**Figure 37: Funnel Plot: Meta-Analysis of Comorbidities - Odds Ratio (11 studies)**
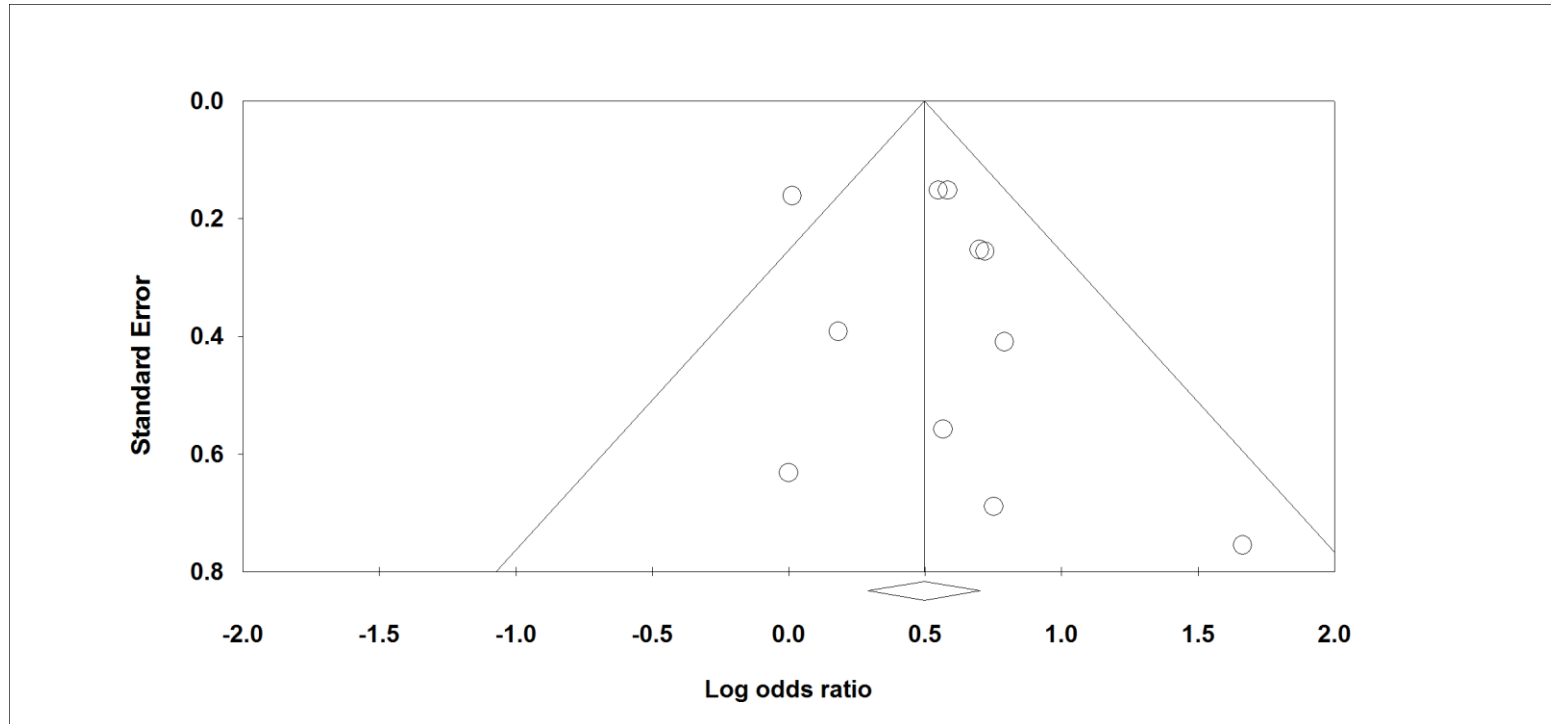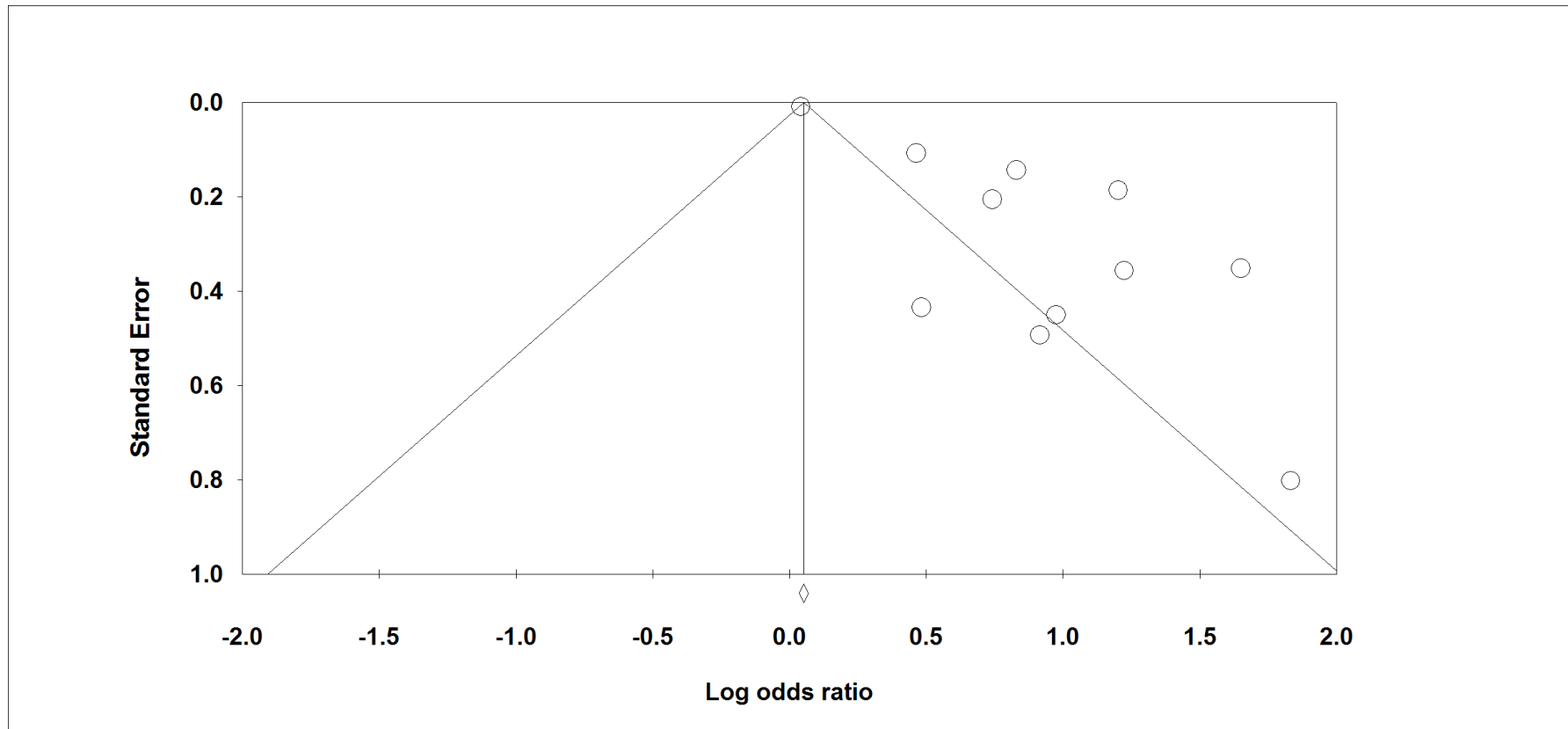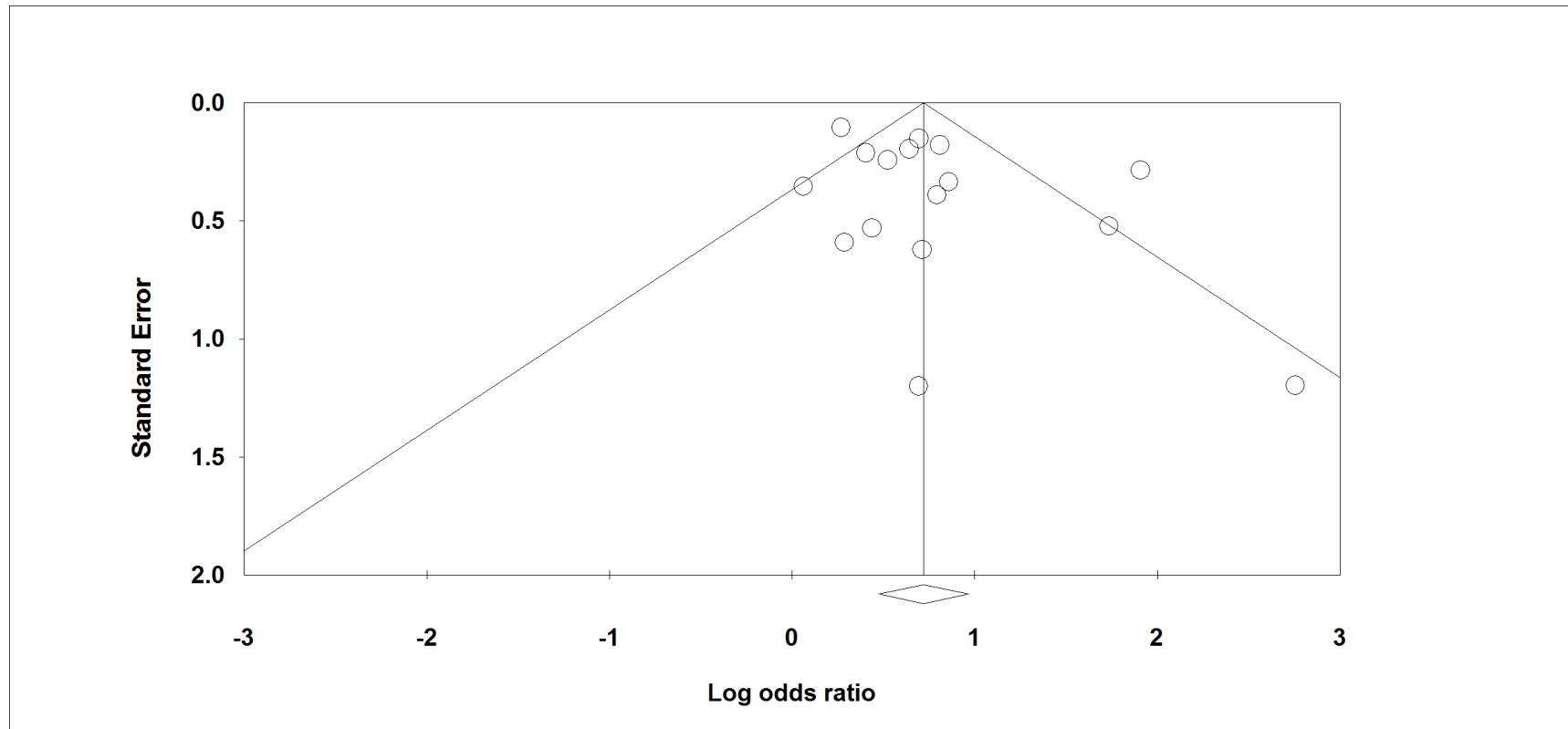


Egger's regression:
Intercept = 0.65
95% lower limit (2-tailed) = -1.04
95% upper limit (2-tailed) = 2.35
d/f = 9.00P-value (2 tailed) = 0.40

**Figure 38: Funnel Plot: Meta-Analysis of Dependency - Odds Ratio (11 studies)**
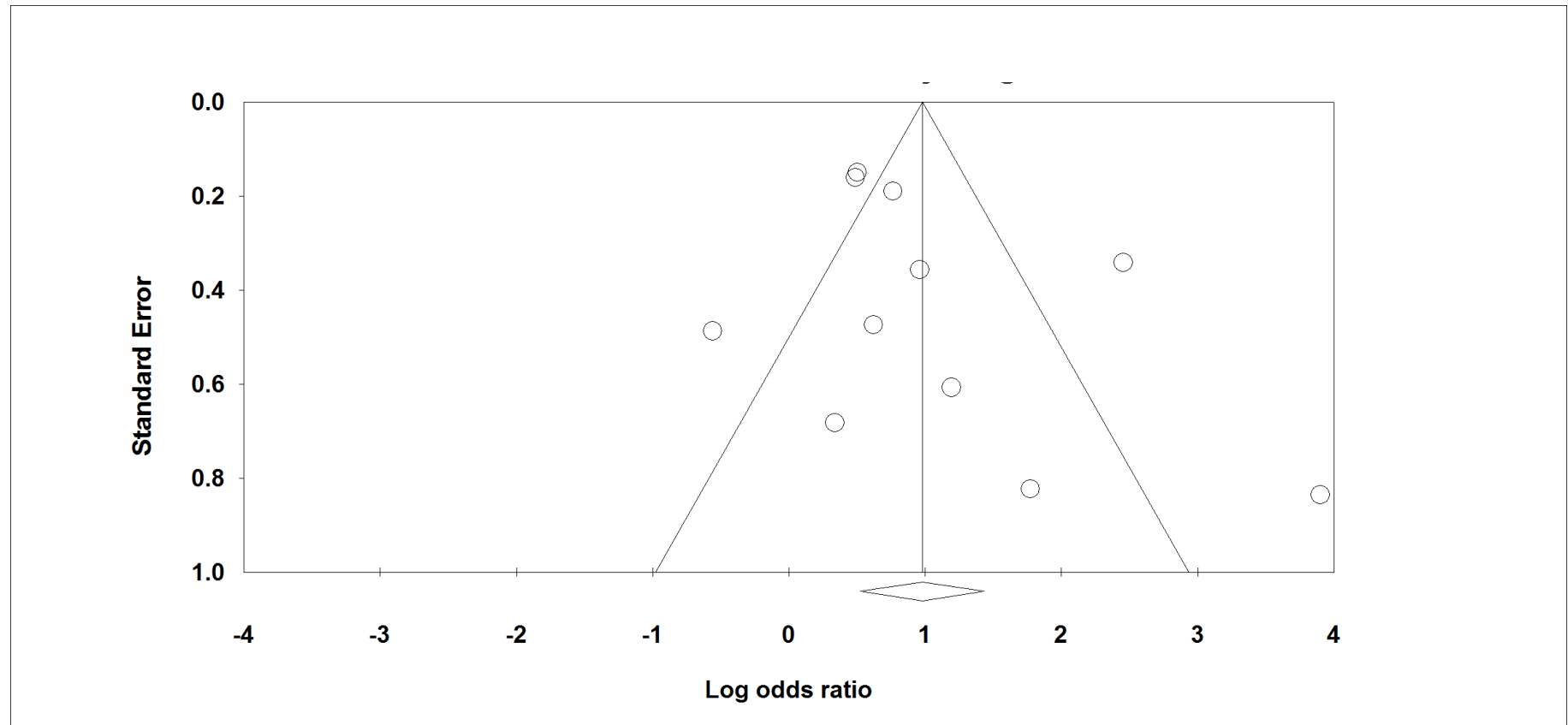


Egger's regression:
Intercept = 1.76
95% lower limit (2-tailed) = -1.08
95% upper limit (2-tailed) = 4.60
d/f = 9.00
P-value (2 tailed) = 0.19

**Figure 39: Funnel Plot: Meta-Analysis of all Wounds - Odds Ratio (17 studies)**
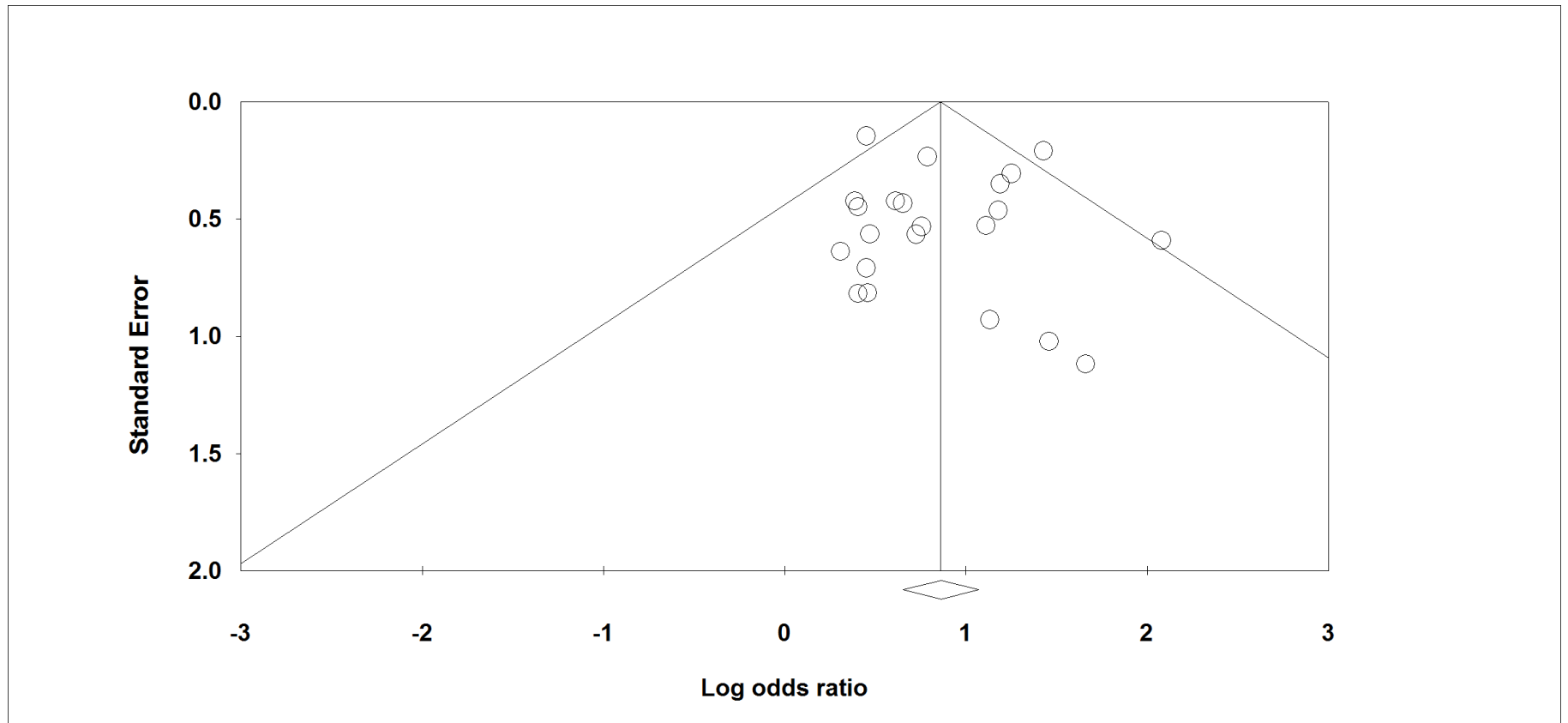


Egger's regression:
Intercept = 0.30
95% lower limit (2-tailed) = -1.72
95% upper limit (2-tailed) = 1.33
d/f = 20.00
P-value (2 tailed) = 0.54

**Figure 40: Funnel Plot: Meta-Analysis of Sex (Male vs Female) - Odds Ratio (18 studies)**
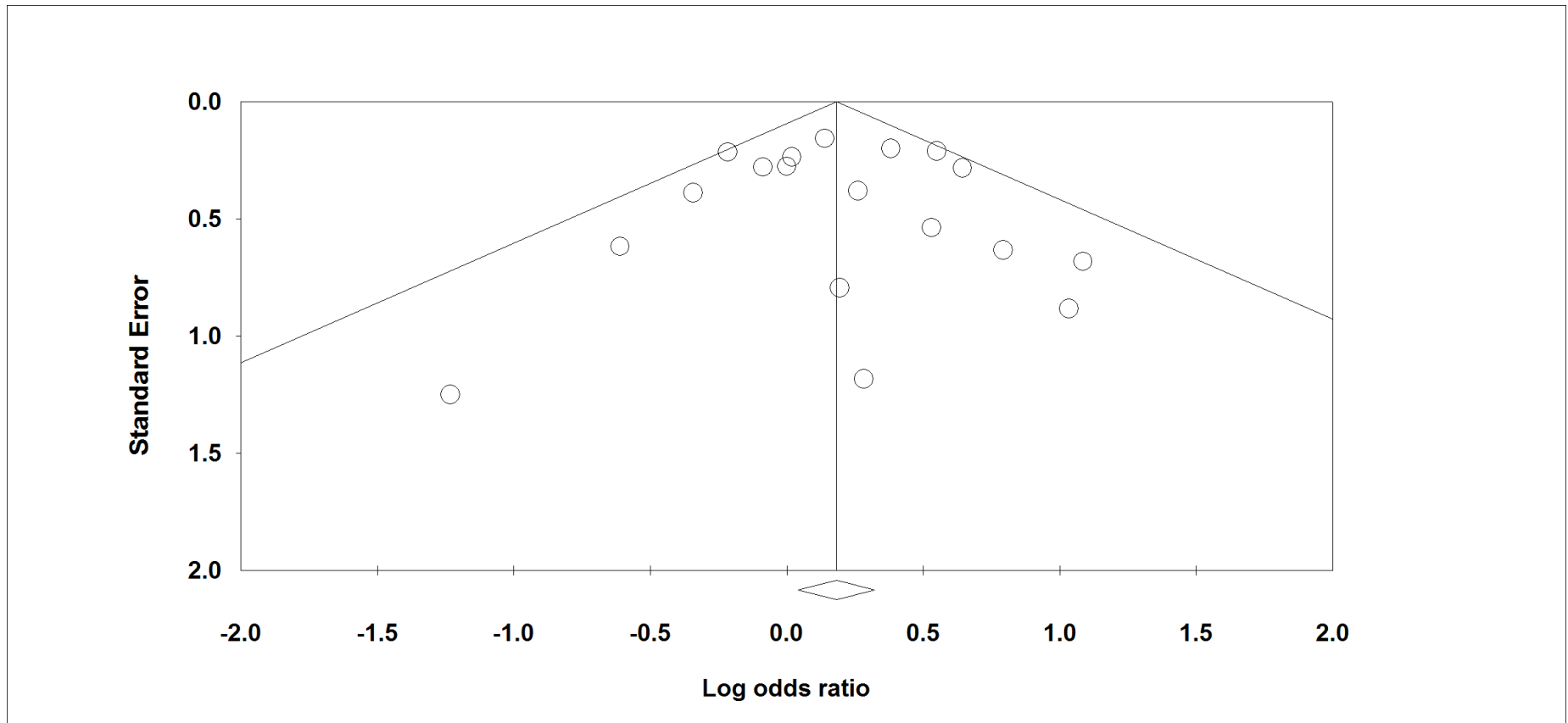


Egger's regression:
Intercept = 0.09
95% lower limit (2-tailed) = -1.06
95% upper limit (2-tailed) = 1.25
d/f = 16.00
P-value (2 tailed) = 0.86

**Figure 41: Funnel Plot: Meta-Analysis of Sex (Male vs Female) - Risk Ratio (16 studies)**
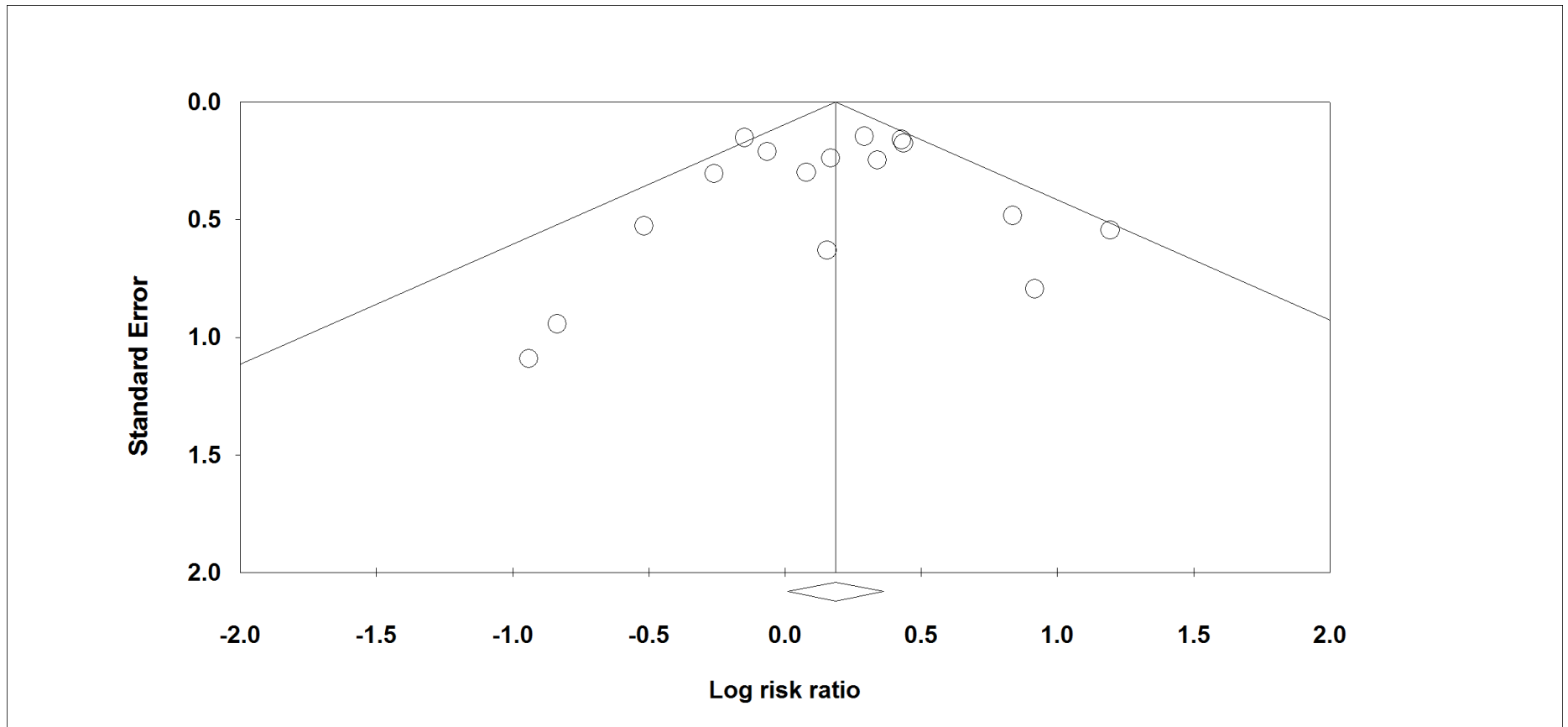


Egger's regression:
Intercept = - 0.17
95% lower limit (2-tailed) = -1.57
95% upper limit (2-tailed) = 1.23
d/f = 14.00
P-value (2 tailed) = 0.80

**Figure 42: Funnel Plot: Meta-Analysis of Invasive Devices - Odds Ratio (19 studies)**
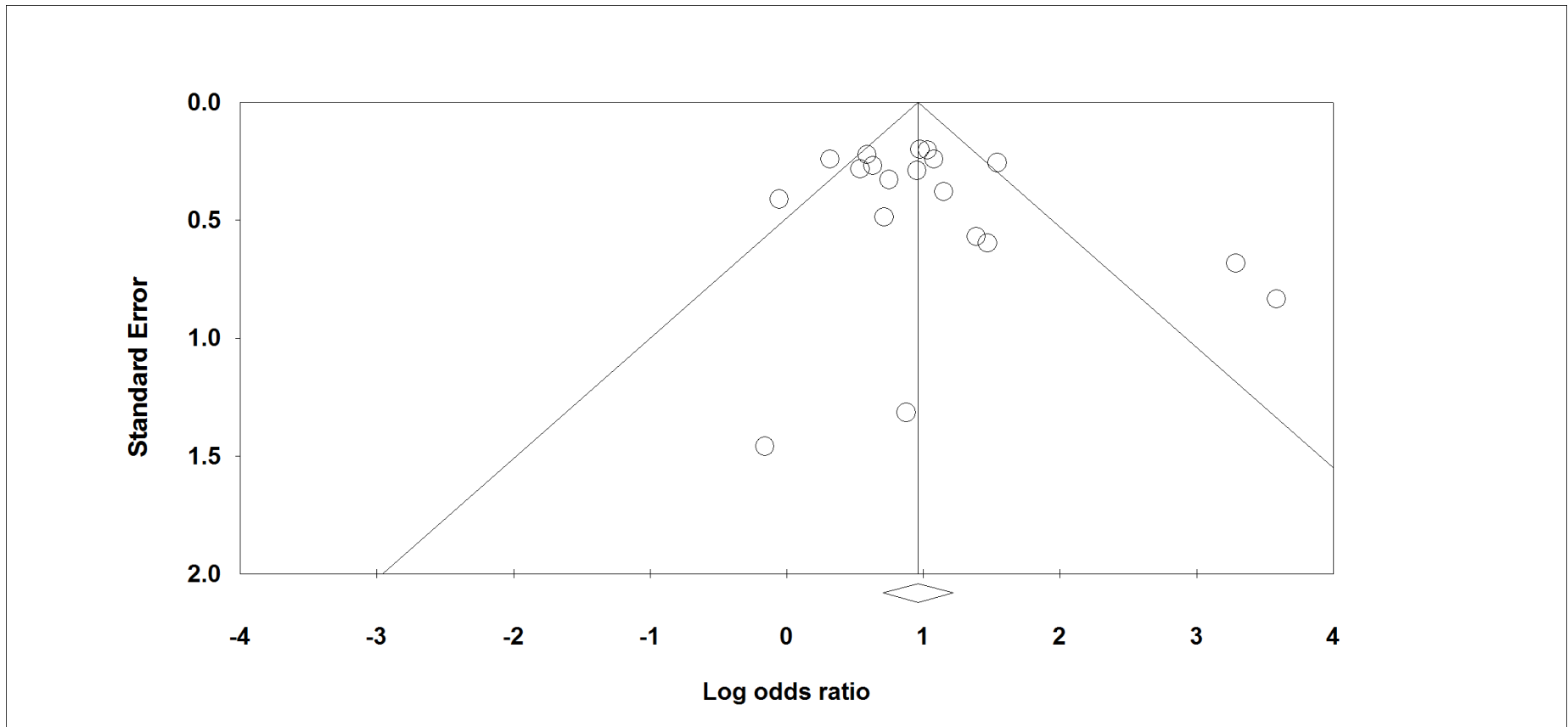
Egger's regression:
Intercept =  - 1.11
95% lower limit (2-tailed) = -0.74
95% upper limit (2-tailed) = 2.96
d/f = 17.00
P-value (2 tailed) = 0.22

**Figure 43: Funnel Plot: Sub-group analysis of IDUC/CUD Devices - Odds Ratio (14 studies)**
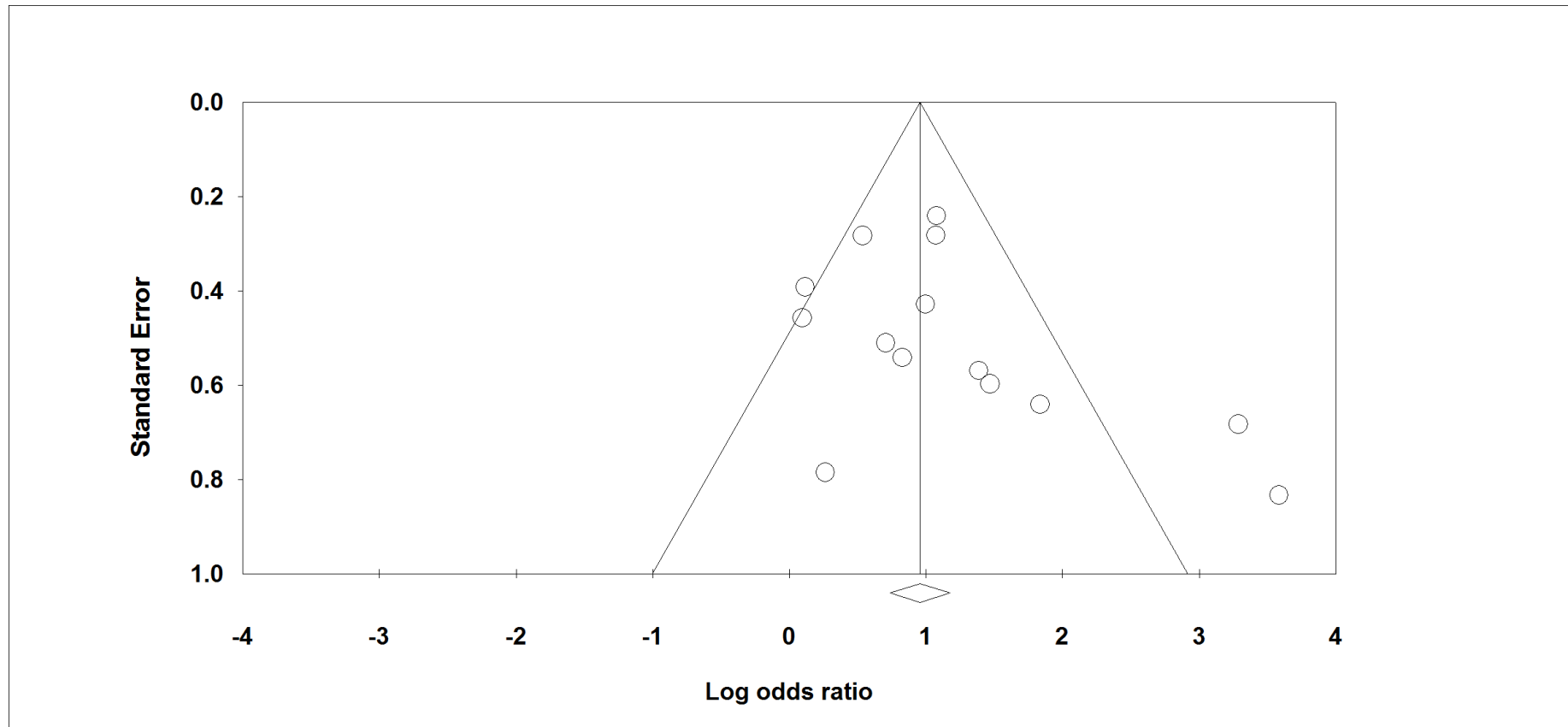
Egger's regression:
Intercept = 1.76
95% lower limit (2-tailed) = -0.74
95% upper limit (2-tailed) = 4.27
d/f = 12.00
P-value (2 tailed) = 0.15

**Figure 44: Funnel Plot: Meta-Analysis of Antibiotic Use - Odds Ratio (22 studies)**
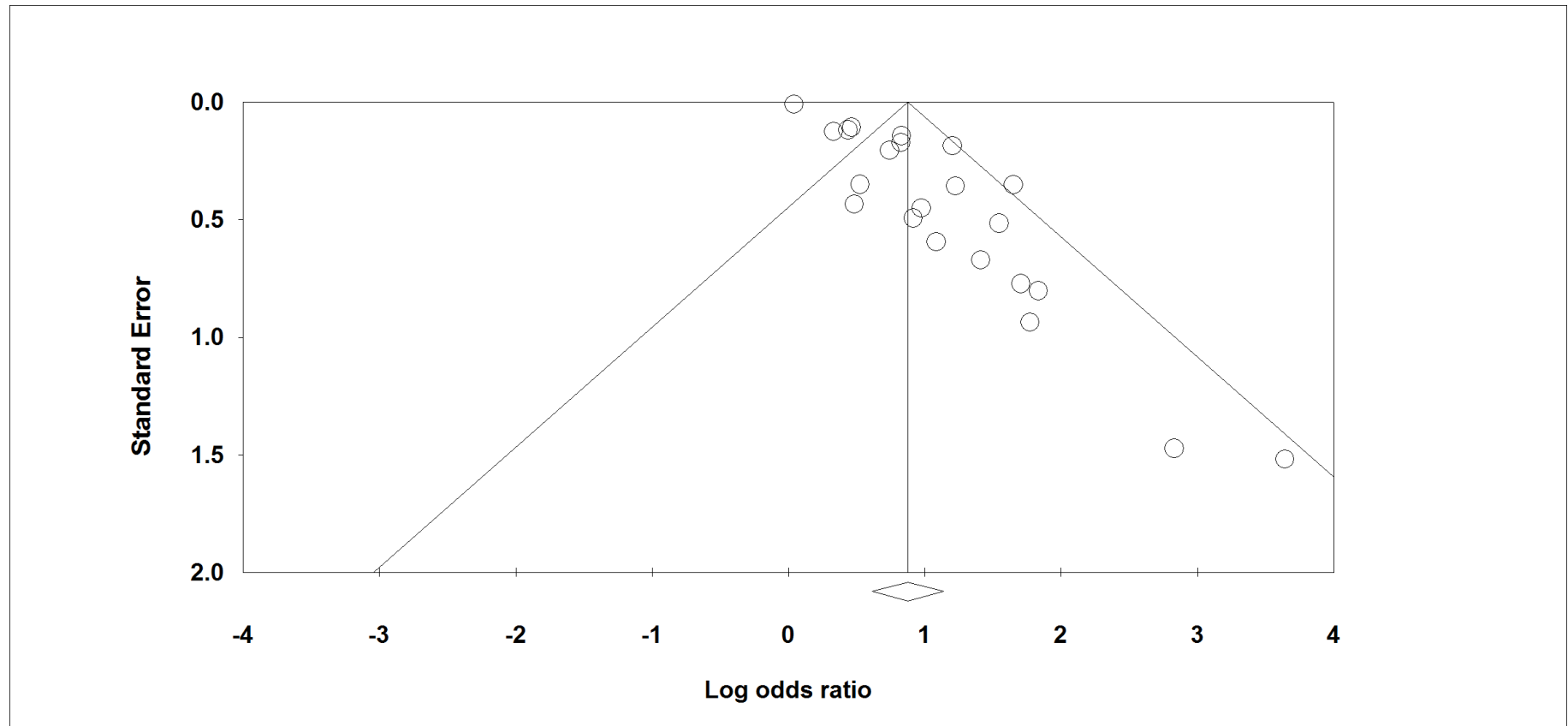
Egger's regression:
Intercept = 2.94
95% lower limit (2-tailed) = 2.27
95% upper limit (2-tailed) = 3.62
d/f = 20.00
P-value (2 tailed) = 0.00

# Figure 45: Funnel Plot: Meta-Analysis of Antibiotic Use - Risk Ratio (11 studies)
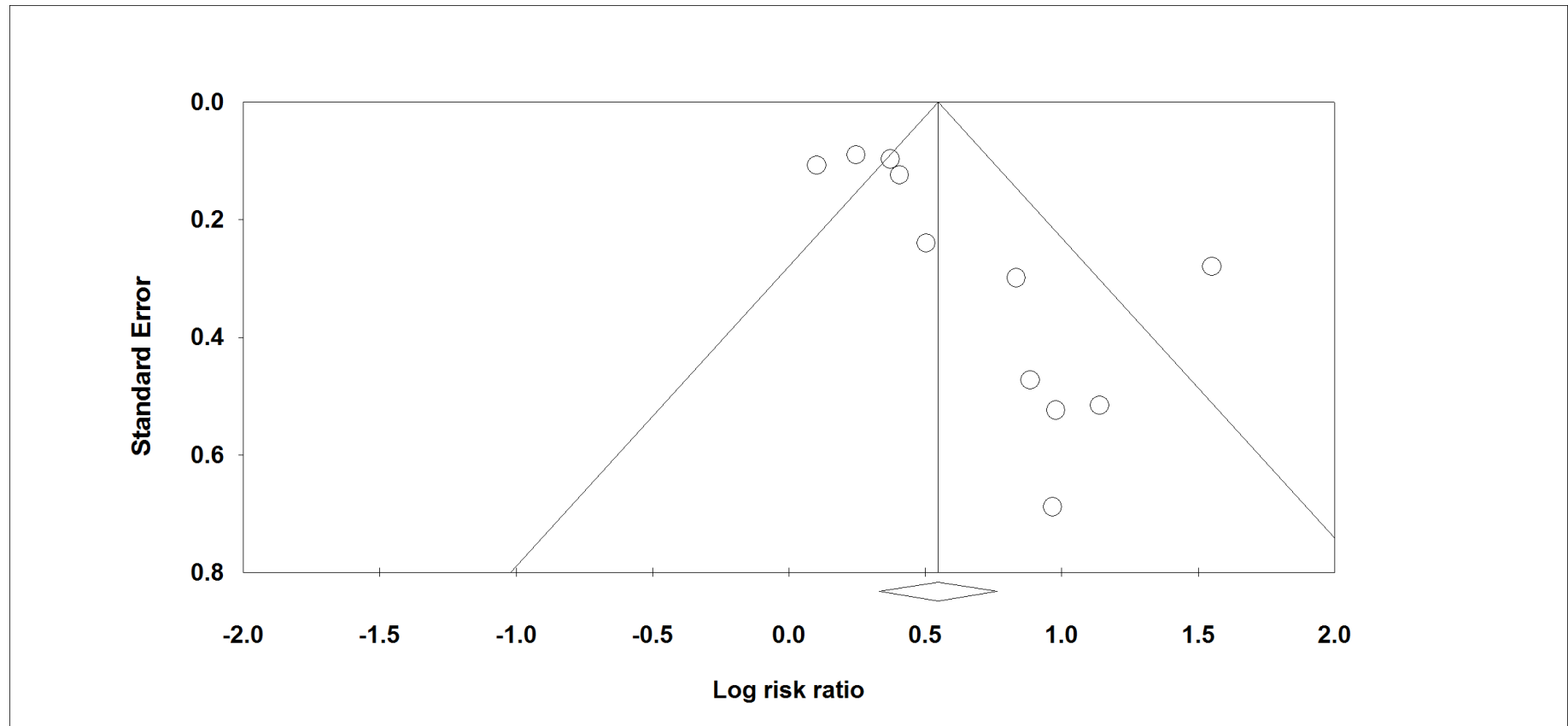


Egger's regression:
Intercept = 2.29
95% lower limit (2-tailed) = 0.68
95% upper limit (2-tailed) = 3.90
d/f = 9.00
P-value (2 tailed) = 0.01

Figure 46: Funnel Plot: Sub-group analysis of Antibiotic Use in last 12 weeks - Odds Ratio (11 studies)

Egger's regression:
Intercept = 3.50
95% lower limit (2-tailed) = 2.20
95% upper limit (2-tailed) = 4.80
d/f = 9.00
P-value (2 tailed) = 0.00

**Figure 47: Funnel Plot: Meta-Analysis of Hospital Stay Meta-analysis: Odds Ratio (16 studies)**



Egger's regression:
Intercept = 1.31
95% lower limit (2-tailed) = -0.29
95% upper limit (2-tailed) = 2.92
d/f = 14.00
P-value (2 tailed) = 0.10

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