Title Page

Clinical deterioration and hospital-acquired complications in adult patients with isolation precautions for infection control: A systematic review

Running Head

Isolation precautions and outcomes

Authors

Debra BERRY[2, 3]

Erin WAKEFIELD[4]

Maryann STREET [1, 2]

Julie CONSIDINE[1, 2]

[1] Deakin University, Geelong, Australia: School of Nursing and Midwifery; Centre for Quality and Patient Safety Research & Institute for Health Transformation.

[2] Centre for Quality and Patient Safety – Eastern Health Partnership, Box Hill, Australia.

[3] Deakin University, Geelong, Australia: School of Nursing and Midwifery & Institute for Health Transformation.

[4.] Eastern Health, 8 Arnold Street, Box Hill, Vic. 3128, Australia.

This is an unfunded systematic review.

Author Contribution Table

Author	Conceived and designed the review	Developed the search strategy and	Screening of the literature	Selection of Studies	Synthesis	Wrote manuscript

This is the author manuscript accepted for publication and has undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1111/JAN.14435

		undertook search				
DB	✓	✓	✓	✓	✓	✓
EW		✓	✓	✓		✓
MS					✓	✓
JC	✓				✓	✓

Corresponding author

Ms Debra BERRY

Deakin University Centre for Quality and Patient Safety Research – Eastern Health Partnership

Level 2, 5 Arnold St, Box Hill, VICTORIA, 3128.

E: debra.berry1@deakin.edu.au T: +61 (03) 9094 9618

Twitter: @Debra_L_Berry

MS DEBRA BERRY (Orcid ID : 0000-0002-8780-054X)

DR MARYANN STREET (Orcid ID : 0000-0002-5615-141X)

PROFESSOR JULIE CONSIDINE (Orcid ID : 0000-0003-3801-2456)

Article type : Review

CLINICAL DETERIORATION AND HOSPITAL-ACQUIRED COMPLICATIONS IN ADULT PATIENTS WITH ISOLATION PRECAUTIONS FOR INFECTION CONTROL: A SYSTEMATIC REVIEW

ABSTRACT

Aim

To review and synthesise literature examining clinical deterioration and hospital-acquired complications in adult patients with isolation precautions for infection control.

Background

Isolation precautions are a common infection prevention and control strategy which may impact on safety and quality of care.

Design

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines guided this systematic review, which was registered with PROSPERO [CRD42019131573].

Data sources

A search of Medline, Embase and Cumulative Index to Nursing and Allied Health Literature was conducted for studies published in English up to 5 April 2019.

Review methods

Risk of bias was determined using Critical Appraisal Skills Program tools. Quality appraisal was performed using the Grades of Recommendation, Assessment, Development and Evaluation approach. The primary outcomes of interest were clinical deterioration events and hospital-acquired complications. In-hospital death and hospital length of stay were secondary outcomes. Data were synthesised using a narrative approach.

Results

The search yielded 785 citations after removal of duplicates, of which, six studies were relevant. Certainty of evidence for outcomes of interest was low to very low.

Conclusion

There is no strong evidence that adult medical and surgical ward patients in isolation precautions for infection control are more or less likely to experience clinical deterioration or hospital-acquired complications.

Key words: nurses, nursing, review, infection, hospital-acquired, precautions, isolation

Impact

What problem did the study address?

- Are patients in isolation precautions more likely to experience clinical deterioration or hospital-acquired complications than non-isolated patients?

What were the main findings?

- There is no strong evidence that clinical deterioration and hospital-acquired complications are more likely to occur to patients in isolation precautions for infection control.

Where and on whom will the research have an impact?

- This research is of relevance to acute care nurses.

Keywords

• Clinical Deterioration; Complications; Hospitals, Isolation; Infection Control; Nursing; Nursing Assessment; Patient Isolation; Systematic Review

1. INTRODUCTION

Healthcare-associated infections (HIA) are a common adverse event in healthcare and have significant impact in terms of patient morbidity, mortality and quality of life and preventable financial burdens to healthcare systems, (World Health Organization 2016) (WHO). Up to 7% of patients in developed countries and 10% in developing countries will acquire at least one HIA (WHO 2016). Thus, reducing HIA through effective infection prevention and control is a global patient safety priority and vital to the safety of healthcare professionals (WHO 2016).

Although the benefits of using isolation for infection prevention and control are well documented, isolation may result in unintended consequences for patients. There is a risk that patients may receive less attention from and contact with, health professionals that may result in lower levels of surveillance, suboptimal documentation of care and increased preventable adverse events (Stelfox et al. 2003, Croft et al. 2015, NHMRC 2019, Godsell et al. 2013, Abad et al. 2010, Morgan et al. 2011) . There are also reports of adverse mental health events for patients such as depression, anxiety and feelings of stigmatisation (Gandra et al. 2014, Karki et al. 2013, Croft et al. 2015, Lupión-Mendoza et al. 2015, Tran et al. 2017, NHMRC 2019, Godsell et al. 2013). There is no strong evidence from hospital design research that single rooms per se' compromise patient safety (Maben 2015, Simon 2016). However, staff perceive that single rooms inhibit visibility, surveillance and monitoring (Maben 2015) and there are reports in the literature of temporary increases in falls and medication errors (Simon 2016) after transition from multi-bedrooms to single rooms.

None of the studies of single rooms to date were conducted in the context of the use of single rooms for isolation so do not account for specific constraints that isolation places on the patient or nurse. Constraints include: closed-door care; restrictions on patient movement and ambulation; limited equipment; and the need to don and doff personal protective equipment. The patient experience of isolation is well documented from a psychological perspective (Catalano et al. 2003, Gammon 1999, Tarzi et al. 2001, Abad et al. 2010). It is important to

understand whether there are patient safety implications from the use of isolation, specifically whether there are unintended consequences in terms of recognition and response to clinical deterioration and development of hospital-acquired complications.

1.1 Background

Infection prevention and control in acute care hospitals are grounded in the use of standard precautions and transmission-based precautions. Standard precautions include hand hygiene; use of personal protective equipment; safe handling and disposal of sharps; environmental management; respiratory hygiene and cough etiquette; and appropriate handling and disposal of waste and linen. Standard precautions are applied to all patients, irrespective of infection status and are the cornerstone of infection prevention and control (National Health and Medical Research Council 2019) (NHMRC). Transmission-based precautions aim to interrupt the mode of transmission of infection and include contact precautions; droplet precautions and airborne precautions (NHMRC 2019). Transmission-based precautions include caring for the patient in a single closed-door room with its own bathroom facilities (isolation); use of appropriate personal protective equipment; using patient-dedicated equipment; specific air management strategies and restricting the movement of patients and healthcare professionals (NHMRC 2019). The use of isolation (single rooms) is indicated for patients who require airborne precautions and recommended for patients requiring contract or droplet precautions (NHMRC 2019).

2. THE REVIEW

2.1 Aims

The aim of this systematic review is to examine and synthesise published peer-reviewed studies of clinical deterioration and hospital-acquired complications in adult medical and surgical ward patients with isolation precautions for infection control.

2.2 Design

This systematic review was planned, conducted and reported according to the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) Statement (Liberati et al. 2009) and was registered with the International Prospective Register of Systematic

Reviews (PROSPERO) (Registration number: CRD42019131573). The population, intervention, comparator and outcome (PICO) format was used to develop the following research question for this systematic review (Considine et al. 2017): in adult acute medical and surgical ward patients (P); what is the effect of isolation precautions for infection control (I); compared with no isolation (C); on clinical deterioration events and hospital-acquired complications (O)?

The primary outcomes of interest were:

i) clinical deterioration events; Rapid Response System (RRS) activations, unplanned Intensive Care Unit (ICU) admissions, in-hospital cardiopulmonary arrests (IHCA) and

ii) hospital-acquired complications; pressure injuries, falls with injury, venous thromboembolism, medication-related complications, delirium, malnutrition and dehydration.

The hospital-acquired complications were adapted from the Australian Commission on Safety and Quality in Health Care Hospital-acquired complications list (ACSQHC2019). In-hospital death and hospital length of stay (LOS) were secondary outcomes of interest.

2.3 Search methods

The search strategy was developed and conducted independently by two researchers (DB and EW) and reviewed by a Health Librarian. Key terms included: patient isolation; infection control; universal precautions; clinical deterioration; adverse events; patient safety; and treatment outcome. The complete search strategy for each database can be found in Appendix 1. A systematic search of Medline, Cumulative Index to Nursing and Allied Health Literature (CINAHL) and Excerpta Medica Database (EMBASE) was conducted 5-9 April 2019 with the limiters of English language studies and studies of adults (however defined in the specific database). No time limiters were applied. Studies had to be peer-reviewed and published as full-text: abstract only papers and opinion, discussion or review papers were excluded. The search was re-run on 13 November 2019 to ensure there were no new studies for inclusion and none were found.

2.4 Search outcome

After removal of duplicates, the search yielded 785 citations for screening. Citations were uploaded into Rayyan software (Ouzzani et al. 2016) and two researchers (DB and EW) independently assessed titles and abstracts for eligibility using the exclusion and inclusion criteria. Discrepancies were resolved by discussion and ratified by the research team. Thirteen full-text papers were again independently reviewed by two researchers (DB and EW) and discrepancies were resolved by discussion and ratified by the research team. A total of five studies met the inclusion criteria for this systematic review. One further study was found through hand-searching of reference lists. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) (Liberati et al. 2009) flow diagram shows the results of the search and screening processes (Figure 1).

2.5 Quality appraisal

Quality appraisal of each study was conducted independently by two researchers (DB and EW) and discrepancies were resolved by discussion with a third investigator (JC). The Critical Appraisal Skills Program (CASP) (Critical Appraisal Skills Programme UK 2018) clinical appraisal tools were used to undertake the quality and risk of bias assessments for the individual studies. The CASP clinical appraisal tools are widely accepted validated tools used to critique quality at the individual study level (Purssell 2020). Specific CASP tools are available for a variety of study designs and the relevant tool was used to appraise each study in this review (Critical Appraisal Skills Programme UK 2018).

Quality appraisal at an outcome level was undertaken using the Grades of Recommendation, Assessment, Development and Evaluation (GRADE) (Atkins et al. 2004). GRADE has been used widely by highly regarded international bodies, including the World Health Organisation and the Cochrane Collaboration (Meader et al. 2014). GRADE provides a structured and transparent approach to the quality appraisal of evidence at the outcome level (Thornton et al. 2013). Using the GRADE approach, the following five specific domains were assessed: (i) risk of bias in terms of limitations of study design and execution; (ii) inconsistency; (iii) indirectness; (iv) imprecision; and (v) publication bias (Atkins et al. 2004). An evidence profile table was created with one row per outcome. Quality appraisal was undertaken independently by two reviewers (DB & JC) and verified by the research team.

2.6 Data abstraction

Two researchers (DB & EW) independently extracted the following data from each included study: author, year, country, study design, population, intervention, comparison, outcomes of interest and major findings relevant to the PICO. A third researcher reviewed and verified the extracted data (JC).

2.7 Synthesis

A narrative synthesis (Popay et al. 2006) was used to analyse extracted data and present the results of this systematic review.

3. RESULTS

3.1 Study Selection

Six studies (Stelfox et al. 2003, Karki et al. 2013, Gandra et al. 2014, Lupión-Mendoza et al. 2015, Croft et al. 2015, Tran et al. 2017) were relevant to this systematic review (Figure 1).

3.2 Study Characteristics

Characteristics and results of individual studies are summarised in Table 1. Five studies were observational design (Stelfox et al. 2003, Karki et al. 2013, Gandra et al. 2014, Croft et al. 2015, Tran et al. 2017) and one study used a mixed methods approach (Lupión-Mendoza et al. 2015). Studies were published between 2003 - 2017 and conducted in nine tertiary hospitals situated in four countries (United States of America, Canada, Australia and Spain).

The sample sizes of five studies (Stelfox et al. 2003, Karki et al. 2013, Croft et al. 2015, Lupión-Mendoza et al. 2015, Tran et al. 2017) ranged from 144 (Lupión-Mendoza et al. 2015) – 4,478 (Tran et al. 2017) adult patients. The sample size in Gandra et al. (2014) was unclear with all admitted medical and surgical patients included but the specific number of isolated and non-isolated patients not reported. A sensitivity analysis using data from 200 patients was completed (Gandra et al. 2014) and these data are used in this systematic review.

Isolation with contact precautions was reported in all studies (Stelfox et al. 2003, Karki et al. 2013, Gandra et al. 2014, Lupión-Mendoza et al. 2015, Croft et al. 2015, Tran et al. 2017). In addition, one study (Lupión-Mendoza et al. 2015) included patients in either contact (80.6%, N=58) or airborne precautions (19.4%, N= 14) and Tran et al. (2017) included patients in either droplet (67.1%, N=1506) or contact precautions (32.9%, N=745).

The clinical deterioration events of in-hospital cardiac arrest and unplanned ICU admission were reported by Croft et al. (2015). No studies reported on RRS activations. The hospital-acquired complications reported were falls with injury (Tran et al. 2017, Croft et al. 2015, Lupión-Mendoza et al. 2015, Gandra et al. 2014, Karki et al. 2013, Stelfox et al. 2003); pressure injuries (Croft et al. 2015, Lupión-Mendoza et al. 2015, Gandra et al. 2014, Karki et al. 2013, Stelfox et al. 2003); medication-related adverse events (Tran et al. 2017, Croft et al. 2015, Karki et al. 2013, Stelfox et al. 2003); venous-thromboembolism (Croft et al. 2015) and delirium (Croft et al. 2015). No studies reported on the frequency of malnutrition or dehydration. Secondary outcomes were in-hospital death that was reported in three studies (Tran et al. 2017, Karki et al. 2013, Stelfox et al. 2003) and hospital LOS that was reported in four studies (Tran et al. 2017, Croft et al. 2015, Gandra et al. 2014, Stelfox et al. 2003)

3.3 Risk of Bias within Studies

The risk of bias within studies is displayed in Table 2. All studies applied an appropriate study method (Tran et al. 2017, Croft et al. 2015, Lupión-Mendoza et al. 2015, Gandra et al. 2014, Karki et al. 2013, Stelfox et al. 2003) to address a focussed research question.

Most studies controlled for confounding through matching of the cohorts (Tran et al. 2017, Croft et al. 2015, Lupión-Mendoza et al. 2015, Stelfox et al. 2003). Four of the studies adjusted for co-morbidity (Lupión-Mendoza et al. 2015, Croft et al. 2015, Gandra et al. 2014, Stelfox et al. 2003). Both Croft et al. (2015) and Karki et al. (2013) explicitly state that they were unable to control for the severity of illness in their studies.

Medical records were used for retrospective data collection (Tran et al. 2017, Croft et al. 2015, Gandra et al. 2014, Karki et al. 2013, Stelfox et al. 2003) with the potential for bias due to misclassification or omission of data. It is unclear how Lupión-Mendoza et al. (2015) obtained pressure ulcer and falls data.

3.4 Synthesis of results

A summary of the findings for outcomes of interest across studies is shown in Table 3. Analyses of included studies mostly showed no significant difference in participant characteristics between isolation and non-isolation patient groups. All studies were of adults, however, it is to be noted that the youngest mean age was fifty-two years old (Croft et al. 2015) with the oldest group being isolated patients with respiratory illness having a mean age of 71.7 years old (Tran et al. 2017).

The certainty of evidence for individual outcomes of interest was low to very low. Several limitations of individual studies precluded their inclusion in specific elements of the GRADE process: Gandra et al. (2014) was excluded due to lack of clarity regarding sample size that could not be resolved by contacting the author; Stelfox et al. (2003) did not report exact numbers regarding falls and pressure ulcers but grouped them under supportive care failure; Karki et al. (2013) reported falls with injury data within a category of non-pressure injury data; and Stelfox et al. (2003) reported critical care admission as a single category so did not differentiate elective and unplanned ICU admissions. Risk of bias for the outcomes of interest is shown in Table 4.

For the primary outcome of clinical deterioration events, no identified studies reported on RRS activations. For the outcome of in-hospital cardiac arrest, we identified low certainty evidence from one observational study representing 296 patients (Croft et al. 2015). The evidence was downgraded due to lack of blinding and lack of randomisation (Table 4). There was no significant difference in in-hospital cardiac arrest between isolated and non-isolated patients: no patient in either group had an in-hospital cardiac arrest (Croft et al. 2015). For the primary outcome of unplanned ICU admission, we identified low certainty evidence from the same observational study representing 296 patients (Croft et al. 2015). There was no significant difference in ICU admissions during hospitalisation (8 versus 14, p=0.18) (Croft et al. 2015).

For the primary outcome of hospital-acquired complications, no studies identified reported on malnutrition or dehydration. For the outcome of pressure injuries, we identified very low certainty evidence from three observational studies representing 932 patients. The evidence was downgraded for risk of bias (Table 4). In two studies, the isolated patients had significantly more pressure injuries (Gandra et al. 2014, Stelfox et al. 2003) but there was no significant difference between groups in three studies (Lupión-Mendoza et al. 2015, Croft et al. 2015, Karki et al. 2013).

All studies reported falls with injury (Tran et al. 2017, Lupión-Mendoza et al. 2015, Croft et al. 2015, Gandra et al. 2014, Karki et al. 2013, Stelfox et al. 2003). Due to the limitations described previously only three studies, representing 4,918 patients, could be included in the GRADE tables and the certainty of evidence was very low (Tran et al. 2017, Croft et al. 2015, Lupión-Mendoza et al. 2015). Evidence was downgraded for risk of bias and inconsistency (Table 4). The six studies had conflicting results with three finding no significant difference between groups (Tran et al. 2017, Lupión-Mendoza et al. 2015, Croft et al. 2015) and three reporting that patients in isolation had significantly more falls with injury (Gandra et al. 2014, Karki et al. 2013, Stelfox et al. 2003).

For the outcome of VTE, low certainty evidence from one observational study representing 296 patients (Croft et al. 2015) was identified. The evidence was downgraded for study design. Patients in isolation had significantly lower VTE than non-isolated patients (0 versus 2, p=0.02) (Croft et al. 2015).

For the outcome of medication-related events, we identified very low certainty evidence from four observational studies representing 5,022 patients (Tran et al. 2017, Croft et al. 2015, Karki et al. 2013, Stelfox et al. 2003). The evidence was downgraded for risk of bias and inconsistency (Table 4). Three studies found no difference in medication-related adverse events between isolated and non-isolated patients (Tran et al. 2017, Croft et al. 2015, Stelfox et al. 2003) and one study reported that isolated patients had significantly more medication administration errors and fewer prescription/pharmacy-related errors than non-isolated patients (Karki et al. 2013).

For the outcome of delirium, very low certainty evidence from one observational study representing 296 patients (Croft et al. 2015) was identified. The evidence was downgraded for risk of bias (Table 4). There was no significant difference between groups and no isolated patient was diagnosed with delirium (0 versus 2, p=0.28) (Croft et al. 2015).

In-patient death and hospital LOS were secondary outcomes. For the outcome of in-hospital death, we identified low certainty evidence from three observational studies representing 5,420 patients (Tran et al. 2017, Karki et al. 2013, Stelfox et al. 2003). The evidence was downgraded for study design (Table 4). Stelfox et al. (2003) and Tran et al. (2017) found no difference in in-hospital deaths between isolated and non-isolated patients. Karki et al. (2013) studied the same patient group with and without isolation precautions and reported 29% in-hospital deaths.

Hospital LOS was an outcome of interest in four studies with two finding no significant difference (Croft et al. 2015, Gandra et al. 2014) and two finding an increased LOS for the isolated patient group (Tran et al. 2017, Stelfox et al. 2003). For the outcome of hospital LOS, we identified low certainty evidence from observational studies representing 5,536 patients (Tran et al. 2017, Croft et al. 2015, Stelfox et al. 2003). The evidence was downgraded for study design (Table 4).

4. DISCUSSION

To our knowledge this is the first systematic review to identify and synthesise findings examining clinical deterioration and hospital-acquired complications among patients in isolation precautions for infection control as compared with non-isolated patients. The overall certainty of evidence is low to very low across all outcomes of interest reported. This will reduce the reliability and validity of findings.

There was no identified evidence suggesting patients in isolation were more likely to suffer clinical deterioration events. However, there was only one study that specifically reported on in-hospital cardiac arrest and unplanned ICU admissions (Croft et al. 2015) and no studies were identified that reported on RRS activations. In-hospital cardiac arrest is a relatively

infrequent event occurring in 1–6 per 1000 admissions (Schluep et al. 2018) making large scale research of these events challenging given the rarity of the outcome of interest. In addition, targeting a patient cohort who experience in-hospital cardiac arrest whilst in isolation further narrows eligibility for studies focused on in-hospital cardiac arrest as the primary outcome.

Reporting of unplanned ICU admissions is a quality and patient safety indicator used by health services (Haller et al. 2005). Unplanned ICU admission is commonly required as an outcome of clinical deterioration to patients (Delgado et al. 2013) with the multi-national multi-site ACADEMIA (Antecedents to Cardiac Arrests, Deaths and Emergency Intensive Care Admissions in Australia, New Zealand and the United Kingdom) study conducted over three days reporting a 29.6% unplanned ICU admission rate (Kause et al. 2004). Croft et al. (2015) found no significant difference in unplanned ICU admission for isolated and non-isolated patients. Other studies (Delgado et al. 2013, Frost et al. 2009) have found that whilst the presence of infection, especially respiratory infections, was a predictor of unplanned ICU admission, pre-existing co-morbidities and age were also pertinent factors. Croft et al. (2015) matched for co-morbidity and age and therefore have adjusted for these confounders.

Recognition and response to clinical deterioration is an essential nursing responsibility (Considine and Currey 2015, Odell et al. 2009) with patient safety implications (National Institute for Health and Clinical Excellence 2007). Appropriate identification and response strategies should be in place for all patients, irrespective of the model of care employed (Australian Commission of Safety and Quality in Healthcare 2017). The average number of RRS activations per 1000 admissions is estimated to be 16.3 in adults and 16.8 in children (Maharaj et al. 2015) so RRS activation is a common occurrence in acute care hospitals. The lack of published research related to RRS activations for patients in isolation has highlighted a major gap in the research to date.

Pressure injury mean incidence rates during hospitalisation are 6.48 (SD 4.53) globally (Al Mutairi and Hendrie 2018) and have a detrimental effect on patients, including increased pain (Briggs et al. 2013) and increased hospital LOS with both personal and economic impacts (Bennett et al. 2004, Nguyen et al. 2015, Graves et al. 2005). Immobilisation is a precipitating factor for the development of pressure injuries (European Pressure Ulcer

Advisory Panel et al. 2019). The opportunity to mobilise more freely is reduced when in isolation precautions, however, this does not explain three (Gandra et al. 2014, Karki et al. 2013, Stelfox et al. 2003) studies finding a significant increase in pressure injuries in the isolated patient groups and two (Lupión-Mendoza et al. 2015, Croft et al. 2015) finding no between-group difference. None of the five studies that reported on pressure injuries, commented on other measures which may have been in place to reduce pressure injury risk, for example, pressure relieving devices, specification of mattress or the frequency of repositioning of patients (Gillespie et al. 2014, European Pressure Ulcer Advisory Panel et al. 2019). The presence or absence of pressure-relieving initiatives may have had am impact on results. The understanding and application of evidence-based initiatives by nurses to prevent pressure injury should be undertaken regardless of clinical setting.

Falls prevention is a focus for healthcare services worldwide (Di Giacomo-Geffers 2016, Bouldin et al. 2012), as falls cause harm to patients (Australian Commission on Safety and Quality in Health Care 2009) and increase LOS (Dunne et al. 2014) which offers an explanation for inclusion of falls as an outcome of interest in all included studies (Tran et al. 2017, Croft et al. 2015, Lupión-Mendoza et al. 2015, Gandra et al. 2014, Karki et al. 2013, Stelfox et al. 2003). The Australian Institute of Health and Welfare (2018) reports that in 2015–16 falls occurred in 3.2 per 1,000 hospitalisations in Australian hospitals. The reported rate of falls in acute-care hospitals varies with higher rates on medical wards compared with surgical wards (Stephenson et al. 2016, Bouldin et al. 2012). Predisposing factors for falls in hospital include older age, comorbidity, impaired cognition and severity of illness (Cox et al. 2015, Brand and Sundararajan 2010). The patient environment (Stephenson et al. 2016) and nursing skill mix (Cox et al. 2015) have also been found to be contributing factors to in-hospital falls. In this systematic review, three studies found no significant difference in falls between isolated versus non-isolated patients (Tran et al. 2017, Lupión-Mendoza et al. 2015, Croft et al. 2015) and three studies reported that patients in isolation had more falls with injury (Gandra et al. 2014, Karki et al. 2013, Stelfox et al. 2003). The reason for these conflicting results is unclear. Most patients in the included studies were older adults and many had pre-existing co-morbidity but there was matching of cases to control for these issues. None of the included studies reported on the skill-mix of the nurses caring for the patients, nor did they report on the patient environments of isolated versus non-isolated

patients. The implementation of best evidenced-based falls prevention strategies should be initiated for all patients in all clinical environments.

Medication errors are a common event and cause of harm to patients; a systematic review of 91 studies across 16 countries found a median medication administration error rate of 19.6% (8.0% with timing errors removed) (Keers et al. 2013b). In a further systematic review Keers et al. (2013a) classified causes of medication administration errors into three main groups; unsafe acts; local workplace factors; and organisational decisions (Keers et al. 2013a). Workplace factors include, but are not exclusive to, the patient, communication, local working and culture, general work environment (Keers et al. 2013a). The aspects of the potential precipitators or preventative measures for medication administration error present in the clinical settings of included studies are unclear and may have had an impact on findings. It is unclear if there were any workplace factors contributing to medication administration errors. If hospital processes for medication safety are robust, then patients in isolation should be at no greater risk of medication errors than those not in isolation. Of the four studies that examined medication errors, three found no difference (Tran et al. 2017, Croft et al. 2015, Stelfox et al. 2003). The one study that found increased medication administration errors to isolated patients (Karki et al. 2013) was a retrospective pre-post cohort study. Further research using prospective methods and a controlled design are warranted.

Hospital LOS is influenced by many factors, including hospital-acquired complications such as pressure injury (Bennett et al. 2004, Nguyen et al. 2015, Graves et al. 2005) and in-hospital falls (Dunne et al. 2014). In this systematic review, there were conflicting findings regarding the impact of isolation on hospital LOS with two studies showing no significant difference (Croft et al. 2015, Gandra et al. 2014) and two studies reporting an increased LOS for the isolated patients (Tran et al. 2017, Stelfox et al. 2003). However, none of the included studies adjusted for the effect of hospital-acquired complications, with or without isolation and the effect on LOS.

The finding of no difference for in-hospital mortality may be explained, in part, by the matching of cases and controls in the two studies (Tran et al. 2017, Stelfox et al. 2003) which reported this outcome. Stelfox et al. (2003) matched by primary diagnosis (congestive cardiac

failure) and hospital bed and Tran et al. (2017) used propensity scoring to match cases and controls that took into account age, gender, resource requirements, number of hospital readmissions within 90 days, total LOS for hospital admissions within 90 days, site of admission, month and year of isolation and case mix group. Age, sex, co-morbidity, type of admission and admission diagnosis have been found to be predictors of in-hospital mortality (Michael et al. 2012) therefore it is possible that overmatching may have resulted in no significant differences in in-hospital deaths. The one study that did not match or adjust for co-morbidity (Karki et al. 2013) was a cohort study using the same patient group so it was not possible to determine whether isolation had an effect on in-hospital mortality.

This systematic review is strengthened by adherence to the PRISMA guidelines (Liberati et al. 2009). Hand searching of reference lists was undertaken to reduce the risk of missing relevant literature. There are, however, some limitations that should be considered when interpreting the findings. There were only six studies that met the inclusion criteria for this systematic review, and all were observational studies, highlighting the need for further research into the safety of isolation precautions for infection control. Search limiters for 'adult' classification varied between databases: Medline defines adults as being aged 19 years however CINAHL and EMBASE define an adult as 18 years and older. Publication bias needs to be considered as only studies published in the English language were included and studies with no significant between group differences may not have been published.

5. CONCLUSION

This systematic review of literature has identified low to very low certainty evidence that shows patients in isolation precautions for infection control were at no greater risk of clinical deterioration events or hospital-acquired complications compared with non-isolated patients. In theory, patient assessment, interventions and escalation of care responses should be the same for all patients irrespective of isolation status, however this systematic review highlights that the patient safety implications of isolation precautions for infection control are poorly understood.

5.1 Further Research

This systematic review highlighted several gaps in the literature to date that should be the focus of further research. There are no published studies related to recognition of patient

deterioration and Rapid Response Systems use or identification of malnutrition and dehydration in the patient with isolation precautions for infection control and these areas have significant implications for patient safety and recovery from illness or surgery. There is a clear lack of randomised controlled studies of the impact of isolation precautions for infection control on patient safety outcomes.

ANONYMISED CONFLICT OF INTEREST STATEMENT

No conflict of interest has been declared by the authors.

REFERENCES

Abad, C., Fearday, A. & Safdar, N. (2010) Adverse effects of isolation in hospitalised patients: a systematic review. Journal of Hospital Infection, (2), 97.

Al Mutairi, K.B. & Hendrie, D. (2018) Global incidence and prevalence of pressure injuries in public hospitals: A systematic review. Wound Medicine, **22**, 23.

Atkins, D., Best, D., Briss, P.A., Eccles, M., Falck-Ytter, Y., Flottorp, S., Guyatt, G.H., Harbour, R.T., Haugh, M.C., Henry, D., Hill, S., Jaeschke, R., Leng, G., Liberati, A., Magrini, N., Mason, J., Middleton, P., Mrukowicz, J., O'Connell, D., Oxman, A.D., Phillips, B., Schünemann, H.J., Edejer, T.T.-T., Varonen, H., Vist, G.E., Williams, J.W., Jr. & Zaza, S. (2004) Grading quality of evidence and strength of recommendations. BMJ (Clinical Research Ed.), **328**(7454), 1490-1490.

Australian Commission of Safety and Quality in Healthcare. (2017). National Consensus Statement: essential elements for recognising and responding to acute physiological deterioration. Second Edition. Retrieved from

https://www.safetyandquality.gov.au/sites/default/files/migrated/National-Consensus-Statement-clinical-deterioration_2017.pdf

Australian Commission of Safety and Quality in Healthcare. (2019). Hospital-acquired complications (HACs). 2.0. Retrieved from https://www.safetyandquality.gov.au/our-work/indicators/hospital-acquired-complications#hospital-acquired-complications-list

Australian Commission on Safety and Quality in Health Care. (2009). Preventing falls and harm from falls in older people : best practice guidelines for Australian community care. Retrieved from http://www.activeandhealthy.nsw.gov.au/assets/pdf/Hospital_Guidelines.pdf

Australian Institute of Health and Welfare. (2018). Australia's Health 2018. Retrieved from https://www.aihw.gov.au/getmedia/256a903d-a3ab-449b-ae52-c9cfe78381e0/aihw-aus-221-chapter-7-9.pdf.aspx

Bennett, G., Dealey, C. & Posnett, J. (2004) The cost of pressure ulcers in the UK. Age And Ageing, **33**(3), 230-235.

Bouldin, E.L. andresen, E.M., Dunton, N.E., Simon, M., Waters, T.M., Liu, M., Daniels, M.J., Mion, L.C. & Shorr, R.I. (2012) Falls among Adult Patients Hospitalized in the United States: Prevalence and Trends. Vol. 60, pp. S12-S12.

Brand, C.A. & Sundararajan, V. (2010) A 10-year cohort study of the burden and risk of in-hospital falls and fractures using routinely collected hospital data. Quality and Safety in Health Care, **19**(6), e51.

Briggs, M., Collinson, M., Wilson, L., Rivers, C., McGinnis, E., Dealey, C., Brown, J., Coleman, S., Stubbs, N., Stevenson, R., Nelson, E.A. & Nixon, J. (2013) The prevalence of pain at pressure areas and pressure ulcers in hospitalised patients. BMC Nursing, **12**(1), 19-24.

Catalano, G., Houston, S.H., Catalano, M.C., Butera, A.S., Jennings, S.M., Hakala, S.M., Burrows, S.L., Hickey, M.G., Duss, C.V., Skelton, D.N. & Laliotis, G.J. (2003) Anxiety and depression in hospitalized patients in resistant organism isolation. Southern Medical Journal, **96**(2), 141-145.

Considine, J. & Currey, J. (2015) Ensuring a proactive, evidence-based, patient safety approach to patient assessment. Journal Of Clinical Nursing, **24**, 300-307.

Considine, J., Shaban, R.Z., Fry, M. & Curtis, K. (2017) Evidence based emergency nursing: designing a research question and searching the literature. International Emergency Nursing **32**, 78-82.

Cox, J., Thomas-Hawkins, C., Pajarillo, E., DeGennaro, S., Cadmus, E. & Martinez, M. (2015) Factors associated with falls in hospitalized adult patients. Applied Nursing Research, **28**(2), 78-82.

Critical Appraisal Skills Programme UK. (2018). CASP checklists. Retrieved from https://casp-uk.net/casp-tools-checklists/

Croft, L.D., Liquori, M., Ladd, J., Day, H., Pineles, L., Lamos, E., Arnold, R., Mehrotra, P., Fink, J.C., Langenberg, P., Simoni-Wastila, L., Perencevich, E., Harris, A.D. & Morgan, D.J. (2015) The Effect of Contact Precautions on Frequency of Hospital Adverse Events. Infection Control And Hospital Epidemiology, **36**(11), 1268-1274.

Delgado, K., Liu, V., Pines, J., Kipnis, P., Gardner, M. & Escobar, G. (2013) Risk factors for unplanned transfer to intensive care within 24 hours of admission from the emergency department in an integrated healthcare system. Journal of Hospital Medicine, (1), 13.

Di Giacomo-Geffers, E. (2016) Sentinel Event Alert aimed at preventing falls. Briefings on Accreditation & Quality, **27**(1), 7-11.

Dunne, T.J., Gaboury, I. & Ashe, M.C. (2014) Falls in hospital increase length of stay regardless of degree of harm. Journal of Evaluation in Clinical Practice, (4), 396.

European Pressure Ulcer Advisory Panel, National Pressure Injury Advisory Panel & Pan Pacific Pressure Injury Alliance. (2019). Prevention and Treatment of Pressure Ulcers/Injuries: Quick Reference Guide. Third Edition. Retrieved from https://pppia.org/guideline/

Frost, S.A., Alexandrou, E., Bogdanovski, T., Salamonson, Y., Parr, M.J. & Hillman, K.M. (2009) Unplanned admission to intensive care after emergency hospitalisation: Risk factors and development of a nomogram for individualising risk. Resuscitation, **80**(2), 224-230.

Gammon, J. (1999) The psychological consequences of source isolation: a review of the literature. Journal Of Clinical Nursing, **8**(1), 13-21.

Gandra, S., Barysauskas, C.M., Mack, D.A., Barton, B., Finberg, R. & Ellison, R.T., 3rd (2014) Impact of contact precautions on falls, pressure ulcers and transmission of

MRSA and VRE in hospitalized patients. The Journal Of Hospital Infection, **88**(3), 170-176.

Gillespie, B., Chaboyer, W., McInnes, E., Kent, B., Whitty, J.A. & Thalib, L. (2014) Repositioning for pressure ulcer prevention in adults (Review). Cochrane Library Cochrane Database of Systematic Reviews, (4), 1-36.

Godsell, M.-R., Shaban, R.Z. & Gamble, J. (2013) "Recognizing rapport": Health professionals' lived experience of caring for patients under transmission-based precautions in an Australian health care setting. AJIC: American Journal of Infection Control, **41**(11), 971-975.

Graves, N., Birrell, F. & Whitby, M. (2005) Effect of Pressure Ulcers on Length of Hospital Stay. Infection Control and Hospital Epidemiology, **26**(3), 293.

Haller, G., Myles, P.S., Weeks, A.M., Stoelwinder, J., McNeil, J. & Wolfe, R. (2005) Validity of unplanned admission to an intensive care unit as a measure of patient safety in surgical patients. Anesthesiology, **103**(6), 1121-1129.

Karki, S., Leder, K. & Cheng, A.C. (2013) Patients under contact precautions have an increased risk of injuries and medication errors: a retrospective cohort study. Infection Control And Hospital Epidemiology, **34**(10), 1118-1120.

Kause, J., Smith, G., Prytherch, D., Parr, M., Flabouris, A. & Hillman, K. (2004) A comparison of Antecedents to Cardiac Arrests, Deaths and EMergency Intensive care Admissions in Australia and New Zealand and the United Kingdom—the ACADEMIA study. Resuscitation, **62**(3), 275-282.

Keers, R.N., Williams, S.D., Cooke, J. & Ashcroft, D.M. (2013a) Causes of medication administration errors in hospitals: a systematic review of quantitative and qualitative evidence. Drug Safety, (11), 1045.

Keers, R.N., Williams, S.D., Cooke, J. & Ashcroft, D.M. (2013b) Prevalence and Nature of Medication Administration Errors in Health Care Settings: A Systematic Review of Direct Observational Evidence. Vol. 47, pp. 237-256.

Liberati, A., Altman, D.G., Tetzlaff, J., Mulrow, C., Gøtzsche, P.C., Ioannidis, J.P.A., Clarke, M., Devereaux, P.J., Kleijnen, J. & Moher, D. (2009) The PRISMA Statement for Reporting Systematic Reviews and Meta-Analyses of Studies That Evaluate Health

Care Interventions: Explanation and Elaboration. Annals of Internal Medicine, **151**(4), W65-W94.

Lupión-Mendoza, C., Antúnez-Domínguez, M.J., González-Fernández, C., Romero-Brioso, C. & Rodriguez-Bano, J. (2015) Effects of isolation on patients and staff. American Journal Of Infection Control, **43**(4), 397-399.

Maben, J., Griffiths, P., Penfold, C., Simon, M., Pizzo, E. anderson, J., Robert, G., Hughes, J., Murrells, T., Brearley, S. and Barlow, J. No 3.3 (2015) Evaluating a major innovation in hospital design: workforce implications and impact on patient and staff experiences of all single room hospital accommodation. Health Services and Delivery Research. , **3**(3).

Maharaj, R., Raffaele, I. & Wendon, J. (2015) Rapid response systems: a systematic review and meta-analysis. Critical Care, **19**(1), 254.

Michael, J.C., Richard, M.J., James, F., Ravi, M. & Jon, N. (2012) Developing a summary hospital mortality index: retrospective analysis in English hospitals over five years. BMJ: British Medical Journal, **344**(7848), 19.

Morgan, D.J., Day, H.R., Harris, A.D., Furuno, J.P. & Perencevich, E.N. (2011) The impact of contact isolation on the quality of inpatient hospital care. PLoS ONE, **6**(7).

National Institute for Health and Clinical Excellence. (2007). Acutely Ill Patients in Hospital: Recognition of and Response to, Acute Illness in Hospitalised Adults. . Retrieved from https://www.nice.org.uk/guidance/cg50

Nguyen, K.H., Whitty, J.A. & Chaboyer, W. (2015) Pressure injury in Australian public hospitals: A cost-of-illness study. Australian Health Review, **39**(3), 329-336.

National Health and Medical Research Council. (2019). Australian Guidelines for the Prevention and Control of Infection in Healthcare. Retrieved from https://www.nhmrc.gov.au/about-us/publications/australian-guidelines-prevention-and-control-infection-healthcare-2019#block-views-block-file-attachments-content-block-1

Odell, M., Victor, C. & OHMRliver, D. (2009) Nurses' role in detecting deterioration in ward patients: systematic literature review. Journal of Advanced Nursing, (10), 1992.

Ouzzani, M., Hammady, H., Fedorowicz, Z. & Elmagarmid, A. (2016) Rayyan--a web and mobile app for systematic reviews. Systematic Reviews, (1).

Popay J, R.H., Sowden A, Petticrew M, Arai L, Rodgers M, Britten, N, Roen, K, & Duffy, S. (2006) Guidance on the conduct of narrative synthesis in systematic reviews. A product from the ESRC (European Social Research Council) methods programme, Lancaster University, UK.

Schluep, M., Gravesteijn, B.Y., Stolker, R.J., Endeman, H. & Hoeks, S.E. (2018) One-year survival after in-hospital cardiac arrest: a systematic review and meta-analysis. Resuscitation, **132**, 90-100.

Simon, M., Maben, J., Murrells, T., & Griffiths, P. (2016) Is single room hospital accommodation associated with differences in healthcare-associated infection, falls, pressure ulcers or medication errors? A natural experiment with non-equivalent controls. . Journal of health services research & policy, **21**(3), 147-155.

Stelfox, H.T., Bates, D.W. & Redelmeier, D.A. (2003) Safety of patients isolated for infection control. JAMA, The Journal of the American Medical Association, (14), 1899.

Stephenson, M., McArthur, A., Giles, K., Lockwood, C., Aromataris, E. & Pearson, A. (2016) Prevention of falls in acute hospital settings: A multi-site audit and best practice implementation project. International Journal for Quality in Health Care, **28**(1), 92-98.

Tarzi, S., Kennedy, P., Stone, S. & Evans, M. (2001) Methicillin-resistant Staphylococcus aureus: psychological impact of hospitalization and isolation in an older adult population. The Journal Of Hospital Infection, **49**(4), 250-254.

Tran, K., Bell, C., Stall, N., Tomlinson, G., McGeer, A., Morris, A., Gardam, M. & Abrams, H.B. (2017) The Effect of Hospital Isolation Precautions on Patient Outcomes and Cost of Care: A Multi-Site, Retrospective, Propensity Score-Matched Cohort Study. Journal of General Internal Medicine, **32**(3), 262-268.

World Health Organisation (2016) Guidelines on Core Components of Infection Prevention and Control Programmes at the National and Acute Health Care Facility Level, WHO Document Production Services, Geneva.

Critical Appraisal Skills Programme UK. (2018). CASP checklists. Retrieved from https://casp-uk.net/casp-tools-checklists/

Croft, L.D., Liquori, M., Ladd, J., Day, H., Pineles, L., Lamos, E., Arnold, R., Mehrotra, P., Fink, J.C., Langenberg, P., Simoni-Wastila, L., Perencevich, E., Harris, A.D. & Morgan, D.J. (2015) The Effect of Contact Precautions on Frequency of Hospital Adverse Events. Infection Control And Hospital Epidemiology, **36**(11), 1268-1274.

Gandra, S., Barysauskas, C.M., Mack, D.A., Barton, B., Finberg, R. & Ellison, R.T., 3rd (2014) Impact of contact precautions on falls, pressure ulcers and transmission of MRSA and VRE in hospitalized patients. The Journal Of Hospital Infection, **88**(3), 170-176.

Karki, S., Leder, K. & Cheng, A.C. (2013) Patients under contact precautions have an increased risk of injuries and medication errors: a retrospective cohort study. Infection Control And Hospital Epidemiology, **34**(10), 1118-1120.

Lupión-Mendoza, C., Antúnez-Domínguez, M.J., González-Fernández, C., Romero-Brioso, C. & Rodriguez-Bano, J. (2015) Effects of isolation on patients and staff. American Journal Of Infection Control, **43**(4), 397-399.

Meader, N., King, K., Llewellyn, A., Norman, G., Brown, J., Rodgers, M., Moe-Byrne, T., Higgins, J.P.T., Sowden, A. & Stewart, G. (2014) A checklist designed to aid consistency and reproducibility of GRADE assessments: Development and pilot validation. Systematic Reviews, **3**(1).

Purssell, E. (2020) Can the Critical Appraisal Skills Programme check-lists be used alongside Grading of Recommendations Assessment, Development and Evaluation to improve transparency and decision-making?

Stelfox, H.T., Bates, D.W. & Redelmeier, D.A. (2003) Safety of patients isolated for infection control. JAMA, The Journal of the American Medical Association, (14), 1899.

Thornton, J., Alderson, P., Tan, T., Turner, C., Latchem, S., Shaw, E., Ruiz, F., Reken, S., Mugglestone, M.A., Hill, J., Neilson, J., Westby, M., Francis, K., Whittington, C., Siddiqui, F., Sharma, T., Kelly, V., Ayiku, L. & Chamberlain, K. (2013) Introducing GRADE across the NICE clinical guideline program. Journal Of Clinical Epidemiology, **66**(2), 124-131.

Tran, K., Bell, C., Stall, N., Tomlinson, G., McGeer, A., Morris, A., Gardam, M. & Abrams, H.B. (2017) The Effect of Hospital Isolation Precautions on Patient Outcomes and

Cost of Care: A Multi-Site, Retrospective, Propensity Score-Matched Cohort Study. Journal of General Internal Medicine, **32**(3), 262-268.

Table 1: summary of included studies

Author (Year) Country	Design	Population	Intervention	Comparison	Outcomes of interest	Results
Tran et al. (2017) Canada	Retrospective matched cohort study	Adult patients, ≥18 years, admitted to medical services at three tertiary hospitals with a length of stay ≥2 days Cases: • patients in droplet precautions for respiratory illness(n=1502) • patients in contact precautions for MRSA[1] (n=737) Controls: • non-isolated patients matched to cases by propensity scores 1:1	Isolation with droplet precautions for respiratory illnesses and contact precautions for MRSA	Isolated patients with MRSA and respiratory illness compared to non-isolated patients	Adverse events Falls Medication-related incidents Length of stay In-hospital mortality	For the patients with respiratory illness, isolation vs non-isolation made no significant difference to • adverse events [9.1% versus 8.9%, effect 0.2; 95% CI[2]: -2.9 to +3.4, p=0.88[NS]] • inpatient mortality [6.9% versus 8.5%, effect -1.6; 95% CI: -3.9 to +0.6, p=0.15 [NS]] • falls [4.2% versus 5.1%, effect -0.9; 95% CI: -3.2 to +1.3, p=0.42 [NS]] • medication incidents [2.1% versus 1.6%, effect 0.5; 95% CI: -0.7 to +1.7, p=0.41 [NS]] For the patients with MRSA, isolation vs non-isolation made no significant difference to • adverse events [12.4% versus 10.7%, effect 1.7; 95% CI: -2.3 to +5.7, p=0.4100 [NS]] • inpatient mortality [8.0% versus 7.0%, effect 1.0; 95% CI: -1.0 to +3.1, p=0.3276 [NS]] • falls [10.3% versus 8.0%, effect 2.3; 95% CI: -1.5 to +6.1, p=0.2309 [NS]] • medication incidents [2.2% versus 2.4%, effect -0.3; 95% CI: -1.7 to +1.2, p=0.7274 [NS]] There was a significant difference in Length of stay to both MRSA and Respiratory cohorts when compared to non-isolated patients. [MRSA; 12.8 vs 7.6 days, p=<0.0001 [NS] and Respiratory; 8.5 vs 7.6, p=<0.0001 [NS]]

Author (Year) Country	Design	Population	Intervention	Comparison	Outcomes of interest	Results
Lupión-Mendoza et al. (2015) Spain	Mixed methods i) Matched case-control study ii) semi-structured interviews with cases and health-care workers	Adult patients admitted to medical or surgical wards in single site hospital Cases: patients in isolation for ≥5 days i) case-control(n=72 pairs) ii) semi-structured interviews cases (n=28) and health-care workers (n=28) Controls: patients from same ward, same week, similar length of hospital stay (±2 days), similar Charlson scores (±1)	In isolation for ≥5 days • 80.6% contact precautions & • 19.4% airborne precautions	Isolated patients compared to non-isolated patients	Falls Pressure ulcers, new during admission	Isolation made no significant difference to: • falls [n=1 versus n=0, p=0.61[§]] • new pressure injuries [n=2 versus n=0, p=0.47[*]]

Croft et al. (2015) USA	Prospective matched cohort study Matched by length of stay and admitting unit	Adult medical and surgical patients admitted to single-site tertiary hospital with a hospital length of stay of ≥3 days (n=296; 148 isolated patients and 148 non-isolated patients)	Isolation (contact precautions) for duration of hospital stay	Isolated patients compared to non-isolated patients	All non-infectious adverse events Severe non-infectious adverse events Preventable non-infectious adverse events **Adverse events by physiological systems** • cardiovascular including cardiac arrest • respiratory system including pulmonary embolus • haematological system including thromboembolic venous event • neurological system including over sedation and delirium • other types of harm, including falls and pressure injuries • Intensive Care Unit admissions during hospitalisation	Isolated patients had: • less non-infectious adverse events [n=62 versus n=84, p=0.01†; rate ratio =0.69; 95% CI: 0.51-0.94, p=0.02] • less thromboembolic venous events [n=0 versus n=2, p=0.02† for haematological adverse events] There was no significant difference between isolated and non-isolated patients in • severe non-infectious adverse events [n=20 versus n=27, p=0.27†] • preventable non-infectious adverse events [n=37 versus n=41, p=0.60†; adjusted rate ratio =0.85; 95% CI: 0.59-1.24, p=0.41] (adjusted for gender, comorbidities) • cardiac arrests [n=0 in both groups, p=0.50† for cardiovascular adverse events] • pulmonary embolus [n=0 in both groups, p=1.00† for respiratory adverse events] • delirium [n=0 versus n=2], over-sedation [n=6 versus n=0] and inadequate analgesia n=0 versus 0, p=0.28† for neurological adverse events] • falls [n=1 versus n=0] and pressure injuries [n=1 in both groups, p=0.67† for other adverse events] • intensive care unit admissions during hospitalisation [n=8 versus n=14, p=0.18†] no increase in Length of Stay [4.7 vs 5.5 median days (IQR 3.3-7.1 vs 3.7-8.1), p=0.16‡]

Author (Year) Country	Design	Population	Intervention	Comparison	Outcomes of interest	Results
					Length of stay	
Gandra et al. (2014) USA	Retrospective matched cohort study Matched by hospital ward and admission date (±30 days)	Adult patients admitted to a single-site tertiary hospital (n=unable to determine)[3]	Isolation (contact precautions) MRSA and/or VRE[4]	Isolated MRSA /VRE patients versus non-isolated medical-surgical patients	Falls Pressure Ulcers Length of stay	Isolated vs non-isolated patients had: • increased falls [4.57 vs 2.04 per 1000 patient days, p=<0.0001†] • Increased pressure injuries [4.87 vs 1.22 per 1000 patient days, p=<0.0001†] • No significant increase in Length of Stay; [patients who fell whilst isolated vs fall when non-isolated; 15.4 vs 18.2 mean days, p=0.27‡ and patients with pressure ulcers during isolation vs pressure injury when non-isolated; 30.1 vs 23.8 mean days, p=0.08‡]

Karki et al. (2013) Australia	Retrospective pre-post cohort study	Adult patients with VRE detection admitted to single-site tertiary hospital (n=246)	Isolation (contract precautions) for patients with VRE	Compared the period prior to isolation with period following initiation of isolation	Total adverse events New pressure injury during stay Non-pressure injury (including from falls) Medication –related errors Death	Initiation of isolation increased: • non pressure injuries (including falls & self-injury) [n=18 versus n=5; incidence rate 0.87/1000 patient-days versus 2.81/1000 patient-days; incidence rate ratio 3.24; 95% CI: 1.16 - 11.17, p=0.013#] • medication administration errors [n=62 versus n=36; incidence rate 6.24/1000 patient-days versus 9.69/1000 patient-days; incidence rate ratio 1.55; 95% CI: 1.01 -2.41, p=0.003#] Initiation of isolation decreased: • prescription and pharmacy related errors [n=22 versus n=12; incidence rate 3.82/1000 patient-days versus 1.88/1000 patient-days; incidence rate ratio 0.49; 95% CI: 0.22 -1.03, p=0.05#] Initiation of isolation made no significant difference to: • adverse events [n=214 versus n=186; incidence rate 32.2/1000 patient-days versus 33.4/1000 patient-days; incidence rate ratio 1.04; 95% CI: 0.85-1.27, p=0.7#] • pressure injuries during hospital stay [n=19 versus n=9; incidence rate 1.56/1000 patient-days versus 2.97/1000 patient-days; incidence rate ratio 1.91; 95% CI: 0.82-4.77, p=0.1#] • uncomplicated falls while alone [n=25 versus n=24; incidence rate 4.16/1000 patient-days versus 3.91/1000 patient-days; incidence rate ratio 0.94; 95% CI: 0.51-1.71, p=0.8#] • uncomplicated falls while accompanied [n=6

Author (Year) Country	Design	Population	Intervention	Comparison	Outcomes of interest	Results
						versus n=9; incidence rate 1.56/1000 patient-days versus 0.94/1000 patient-days; incidence rate ratio 0.614; 95% CI: 0.17-1.88, p=0.3[#]] In-hospital mortality was 29% (n=79/246)
Stelfox et al. (2003) Canada and USA	Matched cohort study 1 case: 2 controls	Adult patients admitted to two hospitals (one Canadian, one USA) Cases: consecutive patients isolated for ≥2 days with MRSA • all-diagnoses (n=78) • congestive cardiac failure (n=72) Controls: non-isolated patients • all-diagnoses (n=156) • congestive cardiac failure (n=144)	Isolation (contact precautions) for ≥2 days with MRSA	Isolated versus non-isolated patients	Adverse events • all • preventable versus non-preventable Specific Outcomes; • supportive care failures (including falls and pressure injuries) • medication-related adverse events • length of stay • death	Isolated patients: • had more adverse events [31 vs 15 events per 1000 days, p=0.001[§§]] • had more preventable adverse events [20 vs 3 events per 1000 days, p=<0.001[§§]] • were 8 times more likely than control patients to experience supportive care failures which included falls and pressure areas [rate ratio = 8.3; 95%CI: 3.1-22.1, p=<0.001[§§]] • had an increased length of stay [general cohort; 31 vs 12 median days (10-69 IQR vs 7-24 IQR) and congestive heart failure cohort; 8 vs 6 median days (4-13 IQR vs 4-9 IQR), p=<0.001[§§]] There were no significant difference in • non-preventable adverse events [11 vs 12 events per 1000 days, p=0.98[§§]] • adverse drug-related events [rate ratio = 1.5; 95%CI: 0.8-2.8, p= 0.23[§§]] • in-hospital mortality [17% vs 10%, odds ratio = 1.7; 95%CI: 0.5-3.2, p=0.1[§§]]

Author (Year) Country	Design	Population	Intervention	Comparison	Outcomes of interest	Results

[1]MRSA=methicillin-resistant Staphylococcus aureus; [2]95% CI = 95% confidence interval; [3]Number of events per patient days reported; [4]VRE= vancomycin-resistant enterococcus; [NS] Not Stated-specific statistical test not stated; [§]p -values were calculated by conditional logistic regression; [†] Chi-Square test; [‡] t-test; [#] Incident Rate Ratio (IRR) from number of events and the number of patient days at risk before and after contact precautions assuming a Poisson distribution; [§§] Linear, logistic and Poisson regression analyses used to test for between-group difference

Table 2: Risk of bias assessments*

Bibliography: Stelfox et al. (2003); Karki et al. (2013); Gandra et al. (2014); Lupión-Mendoza et al. (2015); Croft et al. (2015); Tran et al. (2017)

	Stelfox et al. (2003)	Karki et al. (2013)	Gandra et al. (2014)	Croft et al. (2015)	Lupión-Mendoza et al. (2015)	Tran et al. (2017)
The study addressed a clearly focused issue?	Yes	Yes	Yes	Yes	Yes	Yes
Was the cohort recruited in an acceptable way?	Yes	Yes	Can't tell	Yes	Yes	Yes
Was the exposure accurately measured to minimise bias?	Yes	Yes	Can't tell	Can't tell	Can't tell	Can't tell
Was the outcome accurately measured to minimise bias?	Can't tell	Can't tell	Can't tell	Yes	Can't tell	Yes
Have the authors identified all important confounding factors?	Yes	No	Can't tell	Yes	Yes	Yes
Have the authors taken account of the	Yes	Can't tell	Yes	Yes	Yes	Yes

confounding factors in design/and or analysis?						
Was the follow-up of subjects complete enough?	Yes	Yes	Can't tell	Yes	Yes	Yes
Was the follow-up of subjects long enough?	Yes	Yes	Can't tell	Yes	Yes	Yes
*CASP - (Critical Appraisal Skills Programme UK 2018)						

Table 3: Outcomes of Interest (Patients in isolation vs patients not in isolation)

Study and type of isolation precautions	**Adverse Events**	**Falls with injury**	**Pressure Injury**	**Medication - related**	**Delirium**	**Venous thrombo-embolism**	**Unplanned ICU admission**	**In-hospital cardiac arrest**	**In-hospital death**	**Hospital LOS**
Tran et al. (2017) Contact or droplet precautions	No significant difference 21.5% vs 19.5% (481/2239 vs 438/2239) p=0.8830 [NS]	No significant difference 14.5% vs 13.0% (324/2239 vs 293/2239) p=0.4236 [NS]	Not Reported	No significant difference 4.3% vs 3.9% (96/2239 vs 89/2239) p=0.4122 [NS]	Not Reported	Not Reported	Not Reported	Not Reported	No significant difference 14.8% vs 15.5% (333/2239 vs 347/2239) p=0.1578 [NS]	**↑ in isolation group** MRSA 11.9 vs 9.1 days; (effect 1.30; CI 1.22,1.39) Respiratory 8.5 vs 7.6 days p=<0.0001[NS] (effect 1.17; CI 1.09, 1.25)
Lupion-Mendoza et al. (2015) Contact or airborne precautions	Not Reported	No significant difference 1.4% vs 0% (1/72 vs 0/72) p=0.61[§]	No significant difference 2.8% vs 0% (2/72 vs 0/72) p=0.47[§]	Not Reported	Not Reported	Not Reported	Not Reported	Not Reported	Not Reported	Not Reported
Croft et al. (2015) Contact precautions	**↓ in isolation group** 42% vs 57%	No significant difference 0.7% vs 0% (1/148 vs 0/148)	No significant difference 0.7% in both groups	No significant difference in over-sedation events 4.0% vs 0%	No significant difference 0% vs 1.3% (0/148 vs 2/148)	↓ in isolation group 0% vs 1.3%	No significant difference 5.4% vs 9.4% (8/148 vs 14/148)	No significant difference 0/148 vs 0/148	Not Reported	No significant difference Mdn(IQR)[*]

Study and type of isolation precautions	Adverse Events	Falls with injury	Pressure Injury	Medication - related	Delirium	Venous thrombo-embolism	Unplanned ICU admission	In-hospital cardiac arrest	In-hospital death	Hospital LOS
	(62/148 vs 84/148) p=0.01†	p=0.67†	(1/148 vs 1/148) p=0.67†	(6/148 vs 0/148) p=0.28†	p=0.28†	(0/148 vs 2/148) p=0.02†	p=0.18†			4.7 (3.3-7.1) vs 5.5 (3.7-8.1) days p=0.16‡
Gandra et al. (2014) Contact precautions	Not Reported	**↑ in isolation group** 4.57 vs 2.04/1000 patient days p=<0.0001†	**↑ in isolation group** 4.87 vs 1.22/1,000 patient days p<0.0001†	Not Reported	Not Reported	Not Reported	Not Reported	Not Reported	Not Reported	No significant difference Mean (SD†) • Falls cohort 15.4 (14.7) vs 18.2 (17.6) days • Pressure Ulcer cohort 30.1 (24.7) vs 23.8 (18.6) days p=0.08‡

Study and type of isolation precautions	**Adverse Events**	**Falls with injury**	**Pressure Injury**	**Medication - related**	**Delirium**	**Venous thrombo-embolism**	**Unplanned ICU admission**	**In-hospital cardiac arrest**	**In-hospital death**	**Hospital LOS**
Karki et al. (2013) Contact precautions	No significant difference 87% vs 75.6% (214/246 vs 186/246) p=0.7[#]	**↑ in isolation group** Numbers not available as included within non-pressure injury data p=0.013[#]	No significant difference 7.7% vs 3.6% (19/246 vs 9/246) p=0.1[#]	Medication administration **↑ in isolation group** 62/246 vs 36/246 p=0.003[#] Prescription/ Pharmacy related errors **↓ in isolation group** 12/246 vs 22/246 p=0.05[#]	Not Reported	Not Reported	Not Reported	Not Reported	29% 72/246 (same patient sample)	Not Reported

Study and type of isolation precautions	Adverse Events	Falls with injury	Pressure Injury	Medication - related	Delirium	Venous thrombo-embolism	Unplanned ICU admission	In-hospital cardiac arrest	In-hospital death	Hospital LOS
Stelfox et al. (2003) Contact precautions	**↑ in isolation group** 72% vs 17.6% (108/150 vs 53/300) p=0.001[§]	**↑ in isolation group** Included in 'supportive care' data and reported as 8 times greater occurrence in isolated patients p=<0.001[§]	**↑ in isolation group** Included in 'supportive care' data and reported as 8 times greater occurrence in isolated patients p=<0.001[§]	No significant difference 17.3% vs 6.3% (26/150 vs 19/300) p= 0.23[§]	Not Reported	Not Reported	Not Reported	Not Reported	No significant difference 12% vs 2.7% (18/150 vs 8/300) p=0.1[§]	**↑ in isolation group** Mdn (IQR)[†] • General cohort 31 (10-69) vs 12 (7-24) days p=<0.001[§§] • Heart failure cohort 8 (4-13) vs 6 (4-9) days p=<0.001[§§]

ICU = Intensive Care Unit; LOS=Length of Stay; CI=95% Confidence Interval; [*]Mdn=median; IQR=Interquartile Range; SD[†]=Standard Deviation; [NS] Not Stated- specific statistical test not stated; [§]p-values were calculated by conditional logistic regression; [†] Chi-Square test; [‡] t-test; [#] Incident Rate Ratio (IRR) from number of events and the number of patient days at risk before and after contact precautions assuming a Poisson distribution; [§§] Linear, logistic and Poisson regression analyses used to test for between-group difference

Table 4: Risk of bias at outcome level*: patients in isolation versus patients not in isolation

Author(s): Berry, D., Wakefield, E., Street, M. & Considine, J.

Date: 17TH July 2019

Question: What is the effect of isolation precautions for infection control, compared with no isolation, on clinical deterioration events and hospital-acquired complications?

Setting: Acute medical and surgical ward patients

Bibliography: Stelfox et al. (2003); Karki et al. (2013); Lupión-Mendoza et al. (2015); Croft et al. (2015); Tran et al. (2017)

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**isolation**	**non isolation**	**Relative (95% CI)**	**Absolute (95% CI)**		
Adverse events; Tran et al. (2017); Croft et al. (2015); Karki et al. (2013); Stelfox et al. (2003)												
4	observational studies	serious [a,b,c,d,e]	not serious [d]	serious [c]	not serious	none	852/2537 (33.6%)	732/2687 (27.2%)	not estimable		⊕◯◯◯ VERY LOW	CRITICAL
In-hospital cardiac arrest; Croft et al. (2015)												
1	observational studies	not serious [a,b]	not serious	not serious	not serious	none	0/148 (0.0%)	0/148 (0.0%)	not estimable		⊕⊕◯◯ LOW	CRITICAL
Unplanned intensive care unit admission; Croft et al. (2015)												
1	observational studies	not serious [a,b,e]	not serious	not serious	not serious	none	8/148 (5.4%)	14/148 (9.5%)	not estimable		⊕⊕◯◯ LOW	IMPORTANT
Pressure Injury; Lupión-Mendoza et al. (2015); Croft et al. (2015); Karki et al. (2013)												

3	observational studies	serious [a,b,f]	not serious [g]	not serious	not serious	none	22/466 (4.7%)	10/466 (2.1%)	not estimable		⊕◯◯◯ VERY LOW	IMPORTANT
Falls with injury; Lupión-Mendoza et al. (2015); Croft et al. (2015); Tran et al. (2017)												
3	observational studies	serious [a,b,e]	serious [h]	not serious	not serious	none	326/2459 (13.3%)	293/2459 (11.9%)	not estimable		⊕◯◯◯ VERY LOW	IMPORTANT
VTE; Croft et al. (2015)												
1	observational studies	not serious [a,b]	not serious	not serious	not serious	none	0/148 (0.0%)	2/148 (1.4%)	not estimable		⊕⊕◯◯ LOW	IMPORTANT
Medication adverse events; Tran et al. (2017); Croft et al. (2015); Karki et al. (2013); Stelfox et al. (2003)												
4	observational studies	serious [a,b,c,e,f]	serious [d]	not serious	not serious	none	190/2783 (6.8%)	108/2239 (4.8%)	not estimable		⊕◯◯◯ VERY LOW	IMPORTANT
Delirium; Croft et al. (2015)												
1	observational studies	serious [a,b,e]	not serious	not serious	not serious	none	0/148 (0.0%)	2/148 (1.4%)	not estimable		⊕◯◯◯ VERY LOW	IMPORTANT
In-hospital death; Tran et al. (2017); Karki et al. (2013); Stelfox et al. (2003)												
3	observational studies	not serious	not serious	not serious	not serious	none	423/2635 (16.1%)	427/2785 (15.3%)	not estimable		⊕⊕◯◯ LOW	CRITICAL
Hospital LOS (assessed with: days); Tran et al. (2017); Croft et al. (2015); Stelfox et al. (2003)												

3	observational studies	not serious	not serious	not serious	not serious	none	2696	2840	↑ **in isolation group** • Tran et al. (2017): mean difference 5.2 days (MRSA group) and 0.7 days (respiratory group) • Stelfox et al. (2003): median difference 19 days (general cohort) and 2 days (heart failure cohort) **No significant difference** Croft et al. (2015)	⊕⊕◯◯ LOW	IMPORTANT
Malnutrition - not reported												
-	-	-	-	-	-	-	-	-	-	-	-	IMPORTANT
Dehydration - not reported												
-	-	-	-	-	-	-	-	-	-	-	-	IMPORTANT
Rapid Response Systems – not reported												
-	-	-	-	-	-	-	-	-	-	-	-	IMPORTANT

*GRADEPro; CI: Confidence interval

Explanations

a. Intervention not blinded; Karki et al. (2013); Gandra et al. (2014); Lupión-Mendoza et al. (2015); Croft et al. (2015); Tran et al. (2017)

b. Patients not randomised; Stelfox et al. (2003); Karki et al. (2013); Gandra et al. (2014); Lupión-Mendoza et al. (2015); Croft et al. (2015); Tran et al. (2017)

c. Different definitions of adverse events; Stelfox et al. (2003); Karki et al. (2013); Croft et al. (2015); Tran et al. (2017)

d. Two studies had patients with contact precautions only (Stelfox et al. 2003; Croft et al. 2015). One study used contact or droplet precautions (Tran et al. 2017).

e. Potential for information bias; Tran et al. (2017); Lupión-Mendoza et al. (2015); Croft et al. (2015); Gandra et al. (2014); Karki et al. (2013); Stelfox et al. (2003)

f. Confounding; Karki et al. (2013)

g. One study used patients in contact precautions only (Karki et al. 2013). One study used patients in contact or airborne precautions (Lupion-Mendoza et al. 2015)

h. One study had patients in contact precautions only (Croft et al. 2015), one used patients in either contact or airborne precautions (Lupion-Mendoza et al. 2015) and one had patients in either contact or droplet precautions (Tran et al 2017).

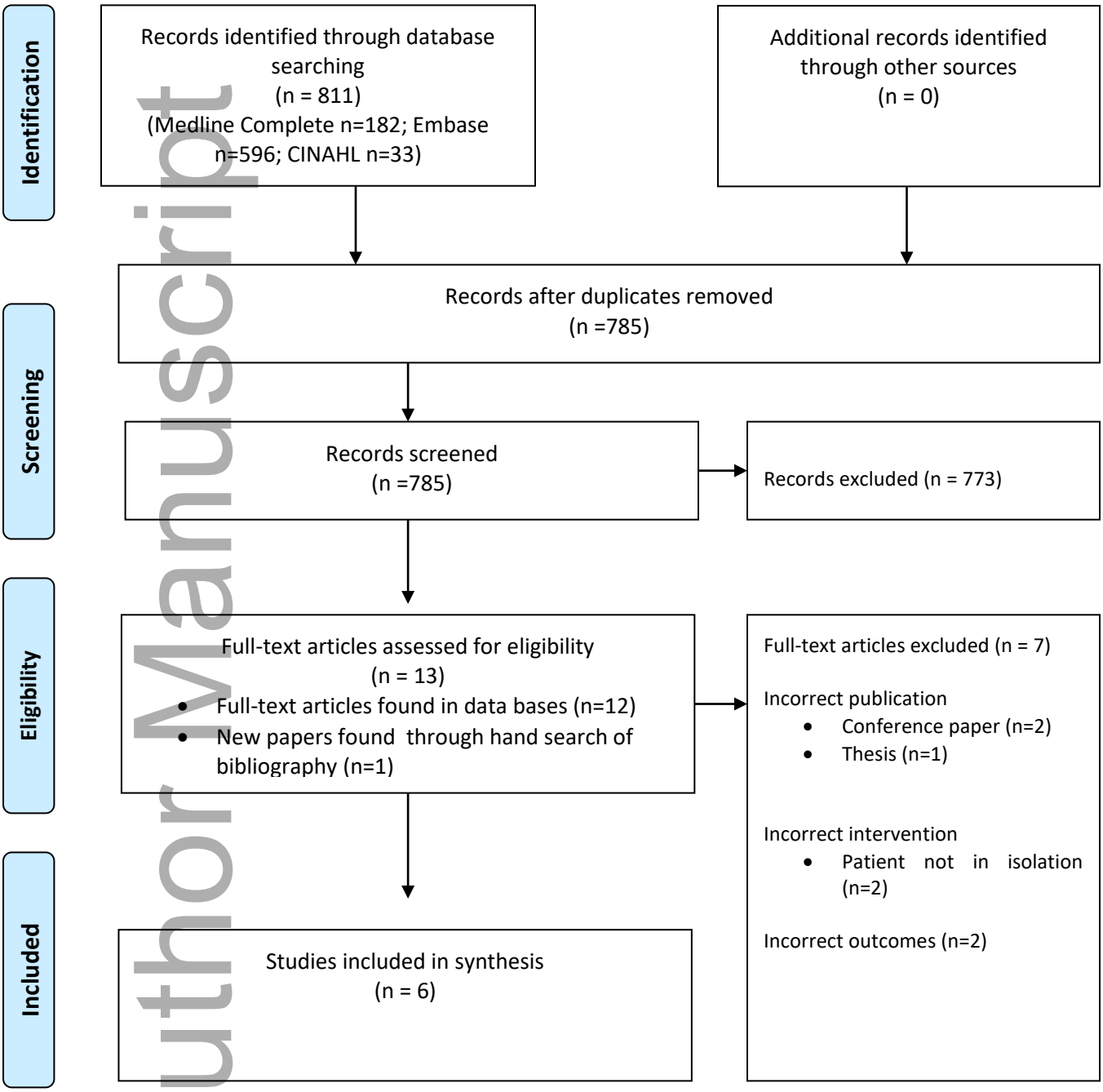

Figure 1: PRISMA FLOW CHART Adapted from: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). *P*referred *R*eporting *I*tems for *S*ystematic Reviews and *M*eta-*A*nalyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

Author/s:
Berry, D;Wakefield, E;Street, M;Considine, J

Title:
Clinical deterioration and hospital-acquired complications in adult patients with isolation precautions for infection control: A systematic review.

Date:
2020-09

Citation:
Berry, D., Wakefield, E., Street, M. & Considine, J. (2020). Clinical deterioration and hospital-acquired complications in adult patients with isolation precautions for infection control: A systematic review.. J Adv Nurs, 76 (9), pp.2235-2252. https://doi.org/10.1111/jan.14435.