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Strategies to Reduce Non-Ventilator-Associated Hospital-Acquired Pneumonia: A Systematic Review

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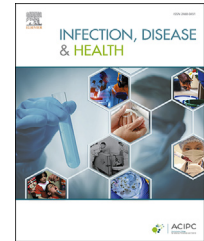Brett G. Mitchell, Philip L. Russo, Allen Cheng, Andrew Stewardson, Hannah Rosebrock, Stephanie J. Curtis, Sophia Robinson, and Martin Kiernan

INFECTION, DISEASE & HEALTH

Review

Strategies to reduce non-ventilator-associated hospital-acquired pneumonia: A systematic review

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Abstract *Background*: Point prevalence studies identify that pneumonia is the most common healthcare associated infection. However, non-ventilator associated healthcare associated pneumonia (NV-HAP) is both underreported and understudied. Most research conducted to date, focuses on ventilator associated pneumonia. We conducted a systematic review, to provide the latest evidence for strategies to reduce NV-HAP and describe the methodological approaches used.

Methods: We performed a systematic search to identify research exploring and evaluating NV-HAP preventive measures in hospitals and aged-care facilities. The electronic database Medline was searched, for peer-reviewed articles published between 1st January 1998 and 31st August 2018. An assessment of the study quality and risk of bias of included articles was conducted using the Newcastle—Ottawa Scale.

Results: The literature search yielded 1551 articles, with 15 articles meeting the inclusion criteria. The majority of strategies for NV-HAP prevention focussed on oral care (n = 9). Three studies evaluated a form of physical activity, such as passive movements, two studies used

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dysphagia screening and management; and another study evaluated prophylactic antibiotics. Most studies (n = 12) were conducted in a hospital setting. Six of the fifteen studies were randomised controlled trials.

Conclusion: There was considerable heterogeneity in the included studies, including the type of intervention, study design, methods and definitions used to diagnose the NV-HAP. To date, interventions to reduce NV-HAP appear to be based broadly on the themes of improving oral care, increased mobility or movement and dysphagia management.

Highlights

- There is considerable heterogeneity in the study design, interventions, methods and definitions used in NV-HAP studies.
- Improving oral care, increased mobility or movement and dysphagia management appear to be key strategies in reducing NV-HAP.
- Further research in a hospital setting, using robust designs are needed.

Introduction

In recent years, there have been numerous initiatives to reduce certain healthcare-associated infections (HAIs), such as bloodstream infections [1], urinary tract infections [2] and surgical site infections [3]. In some countries, there have also been government targets, incentives and penalties for specific HAIs, including central line-associated bloodstream infections, catheter-associated urinary tract infections, surgical site infections (colon and hysterectomy), methicillin-resistant *Staphylococcus aureus* bacteremia and *Clostridium (Clostridioides) difficile* infections [4]. However, despite hospital-acquired pneumonia (HAP) reported as one of the most common HAIs [5–7], this infection has received little attention to date.

Point prevalence studies (PPS) in Europe and the United States highlight the type and proportion of different HAIs. Data from Europe identified HAP as the most frequent HAI in prevalence studies conducted in England, Northern Ireland, Scotland, Wales [6] and Switzerland [8]. In 2015, a multi-site PPS conducted in the United States also identified pneumonia as the most common HAI, with a prevalence of 26% [5]. Thirty-five percent of the pneumonia cases were classified as ventilator-associated pneumonia (VAP) and 65% as non-ventilator-associated hospital-acquired pneumonia (NV-HAP) [5], the two subcategories of HAP. A common definition of VAP is where a case of pneumonia where the patient is on mechanical ventilation for >2 calendar days on the date of event and the ventilator was in place on the date of event or the day before, other cases being considered NV-HAP [9].

While the impact of both VAP and NV-HAP on healthcare services and patients is significant, evidence suggests that NV-HAP occurs more frequently, is associated with higher healthcare costs and is equally as dangerous as VAP [10]. Findings from a multi-centred study from the United States suggests that 18.8% of patients with NV-HAP required transfer into the intensive care unit [11]. NV-HAP also results in a prolonged hospital stay and increased patient morbidity and mortality [12,13]. However, NV-HAP is both underreported and understudied with most research conducted on VAP, thereby prompting recent calls for an urgent need to prioritise research on NV-HAP [14]. This paper therefore focuses on NV-HAP, rather than VAP.

Risk factors for the development of NV-HAP are quite varied and similar to those for HAP in general [14]. Some identified risk factors include age (>70 years), male sex, length of hospital stay, multiple comorbidities, dysphagia and chronic obstructive pulmonary disease [12,15–17]. In some cases, patients may also present with few to no risk factors [14]. Poor oral hygiene associated with dental plaque build up has also been identified as an important risk factor [18], with identical genetic profiles found between respiratory pathogens isolated from dental plaque and bronchoalveolar lavage fluid [19]. Various studies have demonstrated the benefits of implementing comprehensive oral care management protocols in reducing the incidence of NV-HAP [14,20–22], highlighting the potential health and financial gains that could result from widespread implementation of such strategies for this problematic HAI [16,23]. Previous reviews have indicated that interventions that target potential modifiable risk factors may reduce NV-HAP, including improved oral hygiene, hand hygiene, early mobilisation, identification and appropriate management of dysphagia particularly in post-stroke patients, and prevention of viral infections [16,23]. We present a contemporary review, which seeks to provide the latest evidence for strategies to reduce NV-HAP and describe the methodological approaches used. Based on this, we will present key gaps in the literature and methodological considerations to inform future interventional studies.

Methods

A systematic review to identify research exploring and evaluating NV-HAP preventive measures in hospitals and aged-care facilities was undertaken. Reporting of this systematic review complied with the preferred reporting

items for systematic reviews and meta-analyses (PRISMA) guidelines [24].

Search strategy

We performed a systematic search of the literature. Using the key words stated below, we searched the electronic database Medline and reviewed the reference lists of eligible articles to identify any additional relevant articles. The electronic search was limited to articles published between 1st January 1998 and 31st August 2018 in peer-reviewed journals, with no limits placed on language. A combination of Medical Subject Heading (MeSH) and free-text terms was used, based on a prior review of the literature [16].

The first search involved the following terms: ('pneumonia' OR 'respiratory tract infection' OR 'respiratory infection') AND ('nosocomial' OR 'hospital-acquired' OR 'healthcare associated' OR 'healthcare-associated') AND ('prevention'). We performed an additional search and combined this with the results from the previous search.

The keywords used in the second search were ('pneumonia' OR 'respiratory tract infection' OR 'respiratory infection') AND ('nosocomial' OR 'hospital-acquired' OR 'healthcare associated' OR 'healthcare-associated') AND.

○ 'hand hygiene' OR 'hand washing' OR
○ 'oral care' OR 'oral hygiene' OR 'oral decontamination' OR 'oral health' OR 'mouthwashes'
○ 'bed position' OR 'head position' OR 'body position' OR 'bed rest' OR 'bed protocol'
○ 'mobilization' OR 'mobility' OR 'motility' OR 'physical activity' OR 'physiotherapy'
○ 'dysphagia' OR 'swallowing' OR 'swallowing disorder' OR 'aspiration' OR 'aspirative'
○ 'viral infection' OR 'viral' OR 'virus' OR 'flu'
○ 'stress bleeding prophylaxis' OR 'gastric' OR 'gastric protection' OR 'acid-suppressive therapy' OR 'acid-suppressive' OR 'proton pump inhibitor' OR 'omeprazole' OR 'ranitidine'

Selection criteria

The inclusion criteria were all randomised controlled trials and observational studies (cohort, case control, observational, cross sectional or case/short reports) that examined measures (excluding vaccination and systematic antimicrobial therapy) to reduce HAP in hospitals and aged-care facilities. Only studies examining adult populations were included. Studies that did not analyse the effect of any prevention measure were initially included but subsequently removed for sub-analysis. Exclusion criteria were studies examining VAP, all grey literature, non-peer-reviewed literature, reviews, editorials and commentaries.

Definitions

For the purpose of this systematic review, we used the following definitions:

- 'Healthcare-associated infection' refers to any infection as defined or accepted by the authors as being healthcare-associated, hospital-acquired or nosocomial.
- 'Measure' refers to interventions, clinical practice or policy. It excludes systematic antimicrobial treatment and vaccination measures.
- We accepted the definitions and application of defining pneumonia as stated in the paper.

Study selection

We examined and assessed the titles and abstracts of all the publications identified in the electronic database for relevance and appropriateness to the review question and excluded those that were irrelevant. Of the remaining articles, we reviewed the full texts to assess their further eligibility. Articles deemed to have data relevant to the systematic review were included. Trained research assistants performed the study selection process and other stages of the review. Ten percent of the original articles were cross-checked with the study eligibility criteria by two of the research assistants. In addition, an experienced research member randomly selected 10% of the original articles retrieved in the initial search and reviewed them as a cross-check against the study eligibility criteria. Two members of the research team resolved any discrepancies that were observed in the application of either the inclusion or the exclusion criteria.

Data extraction

For each eligible study, the following data were extracted using a data extraction form developed in Excel (Microsoft, USA): author(s); year of publication; country of study; study design; study population; sample; setting; outcome measures; results for both the control and intervention groups, and conclusions. All data extracted were cross-checked by a second member of the team. We did not attempt to contact the authors of papers that contained missing data or unclear information.

Risk of bias

An assessment of the study quality and risk of bias in the articles included in the review was conducted using the Newcastle—Ottawa Scale [25,26]. The Newcastle—Ottawa Scale, is a collaboration between several universities, to assess the quality of studies with its design, content and ease of use directed to the task of incorporating the quality assessments. The scales uses a 'star system' to judge articles in three broad perspectives: the selection of the study groups; the comparability of the groups; and the ascertainment of either the exposure or outcome of interest for case-control or cohort studies respectively [27]. A maximum of nine stars to be awarded to a study. The content validity and inter-rater reliability of this tool have been established [26]. One researcher undertook this assessment independently, with a random 10% of the articles reviewed by a second researcher. There were no

discrepancies in the application of the risk of bias assessment found, when the random sample of articles was compared by a second reviewer.

Data analysis

Extracted data from the included studies were synthesised and summarised in evidence tables. Given the significant heterogeneity in the included studies, we did not attempt to conduct a meta-analysis.

Results

Overview

The literature search yielded 1551 articles. Of these, 56 articles remained for a full text review following a review of the titles and abstracts and the exclusion of duplicates. After screening the 56 articles against the study's inclusion and exclusion criteria, we excluded 43 articles either because they did not report on NV-HAP, they did not evaluate the impact of an intervention, or they were reviews. With the addition of three eligible articles that were known to the research team from manual searches (one from an excluded review, two from references lists of included articles), 15 articles met the inclusion criteria and were included in the final systematic review (Fig. 1).

In this review of literature, we identified 15 studies that involved an intervention aimed at reducing NV-HAP. There was considerable heterogeneity in these studies, including the type of intervention, study design, methods and definitions used to diagnose the NV-HAP. To date, interventions to reduce NV-HAP appear to be based broadly on the themes of improving oral care, increased mobility or movement and dysphagia management.

Study characteristics

Table 1 provides an overview of the 15 studies included in the review. The majority of strategies for NV-HAP prevention focussed on oral care (n = 9), with four oral care approaches using dental professionals [28—31]. Three studies evaluated a form of physical activity, such as passive movements [32—34]; two studies used dysphagia screening and management [35,36]; and another study evaluated prophylactic antibiotics [37]. Most studies (n = 12) were conducted in a hospital setting. Six of the fifteen studies were randomised controlled trials.

Risk of bias assessment

We undertook a risk of bias assessment on the 15 studies included in the review. The maximum star rating using the Newcastle—Ottawa Scale is nine stars. Four studies received a star rating of eight [31,36—38], six studies received a rating of seven [20,29,32—34,39] and five studies received a rating of five or less [14,28,30,35,40]. Table 2 provides an overview of the risk of bias assessment for each study.
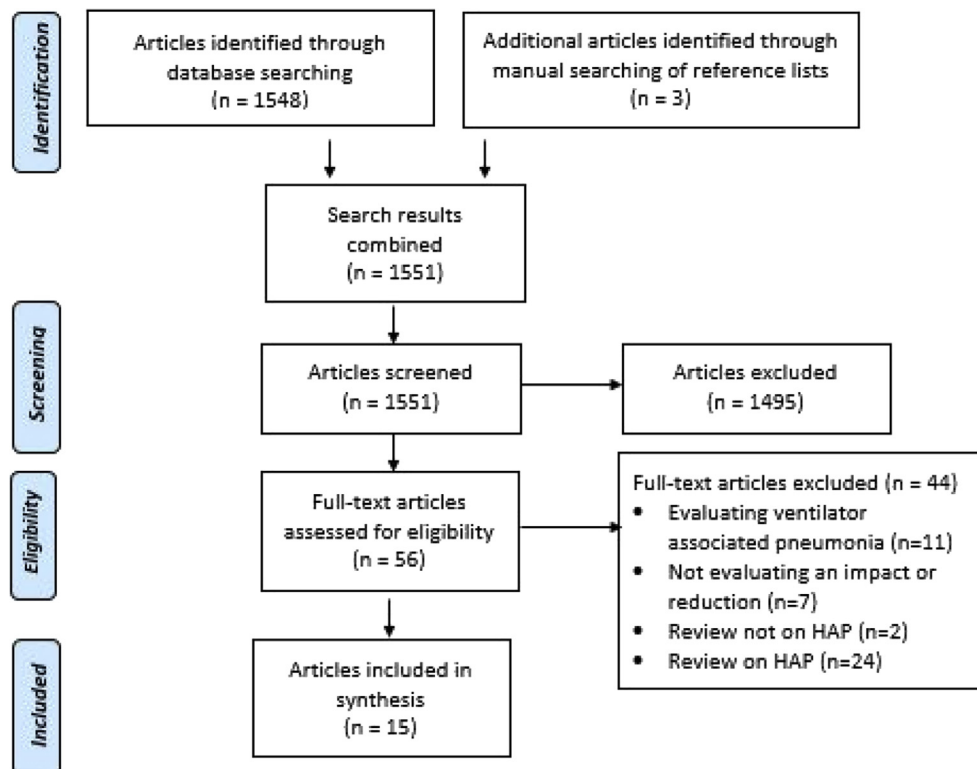

Figure 1   Flow diagram for selection of articles.

Table 1 Studies included in the review.

Author, Year	Design	Sample	Setting	Broad intervention strategy	Significant change in pneumonia
Adachi et al., 2002 [28]	RCT	141	Nursing home	Oral care (professional)	YES
Bellisimo-Rodrigues et al., 2014 [29]	RCT	254	Hospital (Intensive Care Unit)	Oral care (professional)	YES
Boden et al., 2018 [32]	RCT	441	Hospital	Physical activity	YES
Bouringault et al., 2010 [30]	RCT	2513	Nursing home	Oral care (professional)	NO
Chen et al., 2016 [40]	Cohort	873	Hospital (Intensive Care Unit)	Oral care	YES
Cuesy et al., 2010 [33]	RCT	223	Hospital	Physical activity	YES
Johansen et al., 2016 [37]	Cohort	88	Hospital (Ear, Nose and Throat Department)	Prophylactic antibiotics	YES
McNally et al., 2018 [38]	Quasi-experimental	2891	Hospital (non-ICU)	Oral care	NO
Quinn et al., 2014 [14]	Quasi-experimental		Hospital	Oral care	Decrease+
Robertson et al., 2013 [20]	Quasi-experimental	85	Hospital (acute neurosurgical unit)	Oral care	YES
Schrock et al., 2018 [35]	Cohort	2372	Hospital	Dysphagia screen	YES
Stolbrink et al., 2014 [34]	Quasi-experimental	156	Hospital (respiratory and elderly wards)	Physical activity	YES
Titsworth et al., 2013 [36]	Cohort	2334	Hospital	Dysphagia screen	YES
Wagner et al., 2016 [39]	Cohort	1656	Hospital	Oral care	YES
Yoneyama et al., 2012 [31]	RCT	366	Nursing Home	Oral care (professional)	NO

Note: + significance values not provided.

Oral care and NV-HAP prevention

Nine studies in this review involved an oral care intervention to reduce the incidence of NV-HAP. Four of the nine studies involved professional oral care, such as oral care provided by a dentist or hygienist. All of these studies were randomised controlled studies [28—31], and three of them were performed in nursing homes [28,30,31]. The remainder of the studies (n = 5), did not use professional dental care as part of the oral care intervention [14,20,38—40]. None of these five studies used a randomised controlled design.

Non-professional oral care

There was considerable heterogeneity among interventions in the studies that involved routine oral care (i.e. non-professional dental care). No two studies had the same intervention, and where an antiseptic was used as part of oral care, the type of antiseptic differed between studies. The interventions included: oral care kits that contained an antiseptic (cetylpyridinium chloride and 1.5% hydrogen peroxide) [39]; oral care by swabbing with an antiseptic (chlorhexidine gluconate vs. metronidazole) [40]; increased volume of oral care and the use of an antiseptic (0.05% cetylpyridinium chloride) [38]; oral care kits and the use of a toothbrush containing sodium bicarbonate and an antiseptic (antiseptic unspecified) [14]; and moisturiser, toothbrushes and oral swabs impregnated with sodium bicarbonate and an antiseptic rinse (1.5% hydrogen peroxide) [20]. The outcomes from the oral care interventions were largely associated with a reduction in NV-HAP (Table 3).

Professional oral care

Four studies involved the use of a dentist or dental hygienist in the delivery of oral care [28—31]. The interventions in the studies included.

- Dental hygienists performed professional oral health care weekly [28]

- dental care provided by a dental surgeon, 4—5 times a week [29] Patients receiving dental care were compared to those receiving routine oral care.
- annual visit to the dentist, tooth, tongue and mucosa brushing three times a day and after each meal [30] In addition, those receiving the intervention received used an chlorhexidine mouth wash.
- annual visit to the dentist, tooth, tongue and mucosa brushing three times a day and after each meal [31]

Two of the four studies identified a reduction in NV-HAP associated with the intervention (Table 3) [28,31]. One study recorded no cases of NV-HAP during the intervention phase [29], while the fourth and largest study did not identify a reduction in NV-HAP [30].

Dysphagia and NV-HAP prevention

Two non-randomised studies used dysphagia screening as the primary method for NV-HAP prevention [35,36]. Schrock and colleagues used a pre-post quasi-experimental study to evaluate rates of NV-HAP in patients with ischemic and haemorrhagic stroke both before and after the use of a dysphagia screen [35]. In the post study phase, a dysphagia screening test was applied to all acute stroke patients in the emergency department. For patients In the haemorrhagic group, the incidence of NV-HAP decreased from 19% to 15% (P < 0.001), while in the ischemic stroke groups, NV-HAP rates decreased from 13.8% to 8% (P = 0.007) [35]. Titsworth et al. also examined an intervention in patients with ischemic or haemorrhagic stroke [36]. The intervention was a nurse-led bedside dysphagia screen and a rapid clinical swallow undertaken by a speech pathologist. The authors suggest that this quality improvement initiative coincided with a reduction in NV-HAP from 6.5% to 2.8% among the stroke patients (P < 0.001) [36].

Table 2 Risk of bias assessment.

First Author	Year	Elements of Newcastle—Ottawa Scale			
		Selection (0—4)	Comparability (0—2)	Exposure (0—3)	Total stars
Adachi	2002	4	0	0	4
Bellisimo-Rodrigues	2014	2	2	3	7
Boden	2018	2	2	3	7
Bourigaulta	2010	4	1	0	5
Chen	2016	3	0	2	5
Cuesy	2010	3	1	3	7
Johansen	2016	3	2	3	8
McNally	2018	3	2	3	8
Quinn	2014	2	0	3	5
Robertson	2013	4	0	3	7
Schrock	2018	3	0	2	5
Stolbrink	2014	3	2	2	7
Titsworth	2013	4	2	2	8
Wagner	2016	3	2	2	7
Yoneyama	2002	4	1	3	8

Table 3 Summary of findings involving oral care and healthcare associated pneumonia.

Study (first author)	Outcome	Intervention (n)		Control (n)		Comments
		Event	Total	Event	Total	
Professional dental care						
Adachi	Fatal aspiration pneumonia	2	40	8	48	Significant reduction (p < 0.05). Original sample = 141, participants lost to follow-up. Observed over 24 month period.
Bellisimo-Rodrigues	Pneumonia in non-ventilated patients	0	127	1	127	No cases during intervention. 294 sample, 40 excluded as died or discharged from ICU within 48 h. Pneumonia in non-ventilated patients was secondary outcome.
Yoneyama	Pneumonia	21	184	34	182	Significant reduction (p < 0.05). 51 participants excluded from analysis because they died from causes other than pneumonia during follow-up.
	Fatal pneumonia	14	184	30	182	Significant reduction (p < 0.05)
Bourigault	Patients with pneumonia	93	868	203	1645	No difference
	Fatal pneumonia	15	868	26	1645	No difference
Non-professional dental care						
Chen	Hospital acquired pneumonia	84	661	44	212	Significant reduction (p < 0.05)
McNally	Hospital acquired pneumonia	25	1403	26	1487	No difference
Quinn	Hospital acquired pneumonia	Unclear	Unclear	Unclear	Unclear	Incidence decreased from 0.49 to 0.3 per 1000 patient days (38.8%).
Robertson	Hospital acquired pneumonia	2	32	13	51	Significant reduction (p < 0.05)
Wagner	Hospital acquired pneumonia (post-stroke)	98	949	99	707	Significant reduction (p < 0.05)

Note: The raw numerator and denominator data from this study in the pre and post intervention phases are not able to be extracted from this study. No confident intervals are provided around the incidence rates.

Mobility and NV-HAP prevention

We identified three studies that involved a form of physical activity as a way of reducing the incidence of NV-HAP [32–34]. Cuesy et al. conducted a randomised controlled trial examining the effect of turning and passive mobilisation on patients with acute ischemic stroke [33]. The turn-mob program, instigated during the intervention phase, included modifying the patient from supine position to right and left lateral recumbent position every 2 h, in addition to passive mobilizations of the 4 limbs through each segment's entire range of motion, every 6 h. Family members were also involved in this process. The intervention was associated with a decrease in NV-HAP (relative risk of 0.39; 95% CI 0.19–0.79; P = 0.008) [33]. A randomised controlled trial undertaken by Boden et al. also reported a reduction in NV-HAP [32]. The intervention included preoperative patient education, early ambulation and self-directed breathing exercises, and additional pre-operative physiotherapy. Although the primary outcome was post-operative pulmonary complications, a reduction in NV-HAP was also identified (HR 0.45; 95% CI 0.26–0.78, P = 0.005) [32]. Stolbrink et al. also undertook a physiotherapy-based intervention that involved early mobilisation in patients following a hip fracture [34]. In this quasi-experimental study, the intervention was associated with a lower incidence of NV-HAP (HR 0.39; 95% CI 0.22–0.68; P = 0.001) [34].

Differences in NV-HAP definitions used in included articles

The articles included in this review used different definitions for determining cases of NV-HAP. These included chest radiography with clinical symptoms of pneumonia [31–35], Administrative coding data [14,38,39], Clinical Pulmonary Infection Score [20], Centers for Disease Control and Prevention (CDC) definition [29,36], and national professional guidelines [20]. Some articles were less clear or did not specify the diagnostic approach [28,30].

Discussion

In this review, interventions from studies aimed at reducing NV-HAP, appear to be based broadly on the themes of improving oral care, increased mobility or movement and dysphagia management. The most common preventive strategy used to reduce NV-HAP was oral care. The studies included in our review focussed on improving oral care through education, increasing frequency and or consistency of oral care provided and use of an antiseptic. Further, the highest quality studies evaluating the impact of improved oral care all utilised professionals in the field of dentistry, such as dentists and/or dental hygienists. However, while most of these studies were randomised controlled trials, they were largely conducted in residential aged care facilities, with only one randomised controlled study conducted in a hospital setting. The feasibility of implementing an intervention requiring dentistry input in a hospital setting is limited at best. There are challenges in improving the provision of oral care in the hospital setting. A recent

study illustrated this with an average of 1.6 tooth brushings per day, when the goal of the intervention was three per day by the nursing staff [38]. A recent review also identified variation in the reported frequency of oral care provided by nurses (range 2–3.5 times a day) and the documented frequency of oral care in nursing notes (range 1.2–3.5 times a day) for non-ventilated patients [41]. Further, the lack of nurse-led randomised studies for NV-HAP prevention identified in this review highlights a critical issue for patient care. As nurses are primarily responsible for the daily care needs of patients, they have a vital role to play in the prevention of HAIs, including NV-HAP [42]. Three studies, Quinn et al. [14], McNally et al. [38] and Robertson et al. [20], all emphasised the importance of nurse-led initiatives along with interdisciplinary collaboration as being vital to successful oral care interventions. Improvements in oral care are considered a modifiable risk factor for NV-HAP [14,43].

The differing antiseptic agents used as part of oral care interventions in the studies included in this review also warrant discussion, as uncertainty remains regarding the most appropriate antiseptic for oral care in the prevention of NV-HAP. Antiseptic agents such as chlorhexidine gluconate, sodium bicarbonate, hydrogen peroxide and cetylpyridinium chloride are examples of antiseptics that were used in the included studies. Povidone-iodine is also an antiseptic agent known to be used for oral care in the prevention of HAP in general [44]. Findings from our review do not add to the existing evidence base regarding the use of chlorhexidine gluconate in oral care for the prevention of pneumonia in the literature [43,45–47]. Further research on the effectiveness of chlorhexidine and other antiseptics for oral care in HAP prevention has been called for, including cost effectiveness analyses [43,46].

Our review also identified dysphagia screening and physical activity or movement, as effective strategies for preventing NV-HAP. This supports findings from a narrative review of the literature by Pássaro et al. [16], which also showed a reduction in NV-HAP following the use of early mobilization interventions as well as prompt diagnosis and treatment of dysphagia. However, given the lack of studies assessing these strategies in patients with NV-HAP (two studies for dysphagia and three for physical activity) and the lack of randomised control designs, their effectiveness is uncertain, thus suggesting the need for further evaluation of these strategies.

The diversity of interventions used for NV-HAP prevention and settings makes comparisons, generalisability and translation into practice difficult. In addition, the small sample size of published studies [20,28] poses a limitation to the generalisability of the findings. Hence, the challenges in designing future NV-HAP intervention studies include diagnoses, adequate sample sizes and ethical considerations around accessing a high-risk population. As noted in our review, the methods used to diagnose NV-HAP varied and included definitions from the CDC guidelines [14], Association of Medical Microbiology and Infectious Diseases Canada guidelines [20], clinical symptoms and signs, and radiological features [31]. While it is recognised that there is no gold standard for the diagnosis of NV-HAP or VAP [47], we suggest that future studies should use NV-HAP definitions from point

prevalence studies, such as the European Centre for Disease Prevention and Control [48]. The use of standard definitions allows infection control and prevention professionals and hospital epidemiologists to make sensible comparisons among data from hospitals or against national data [42]. The use of definitions that are already familiar from current use may also improve the reliability of their application in studies.

While HAP is one of the most prevalent HAIs among hospitalised patients, the incidence of NV-HAP in hospitalised patients is relatively low [11]. Hence, a large sample size providing sufficient statistical power will be required for any study seeking to determine the effects of NV-HAP interventions. This large sample size, coupled with both the need to undertake prospective diagnoses and difficulties in implementing oral care interventions, presents a major challenge. The incidence of NV-HAP is higher in high-risk groups, such as the elderly or those with multiple co-morbidities; therefore, studying this type of group may aid a reduction in sample size. However, the challenge with studying this type of group pertains to informed consent and the associated selection bias. Therefore, a stepped wedge design may be a useful study design for future NV-HAP studies [49].

Our review has several limitations. The variability in the definitions of NV-HAP and the substantial clinical and methodological heterogeneity between the included studies made it impossible to undertake a meta-analysis. The quality and risk of bias of one-third of the studies included in the review had ratings of five or less, and therefore were considered to have a high risk of bias and the potential to impact the study findings. In view of the findings from this paper, it appears that improving the quality and frequency of oral care, in addition to mobilisation may be useful interventions in reducing the incidence of NV-HAP. Nurse led randomised studies, to assess the effectiveness of an intervention or interventions to reduce the incidence of NV-HAP are required. Such studies need to be rigorously conducted and sufficiently powered.

Authorship statement

BM, PR, AC and AS conceived this study. HR, SC, SR contributed to data collection. All authors reviewed the manuscript and provided critical input. All authors approved the final version of this paper. BM was the lead for this project.

Conflict of interest

Three of the authors have an editorial affiliation with the journal. They played no role whatsoever in the peer review process or decisions relating to this manuscript.

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Ethics

Not required, this is a systematic review of the literature.

References

[1] Duerden B, Fry C, Johnson AP, Wilcox MH. The control of methicillin-resistant Staphylococcus aureus blood stream infections in England. Open Forum Infect Dis 2015;2(2): ofv035—.

[2] Saint S, Greene MT, Krein SL, Rogers MA, Ratz D, Fowler KE, et al. A program to prevent catheter-associated urinary tract infection in acute care. N Engl J Med 2016;374(22):2111—9.

[3] National Health Safety Network. Surgical site infection (SSI) documentation review checklist. 2019. https://www.cdc.gov/nhsn/pdfs/checklists/ssi-checklist-508.pdf. [Accessed 12 February 2019].

[4] Centers for Medicare & Medicaid Services. Hospital-acquired condition reduction program fiscal year 2019 fact sheet. 2019. https://www.cms.gov/Medicare/Medicare-Fee-for-Service-Payment/AcuteInpatientPPS/Downloads/HAC-Reduction-Program-Fact-Sheet.pdf. [Accessed 12 February 2019].

[5] Magill SS, O'Leary E, Janelle SJ, Thompson DL, Dumyati G, Nadle J, et al. Changes in prevalence of health care—associated infections in US hospitals. N Engl J Med 2018;379(18):1732—44.

[6] European Centre for Disease Prevention and Control. Point prevalence survey of healthcare associated infections and antimicrobial use in European acute care hospitals. Stockholm: ECDC; 2013.

[7] Magill SS, Edwards JR, Bamberg W, Beldavs ZG, Dumyati G, Kainer MA, et al. Multistate point-prevalence survey of health care-associated infections. N Engl J Med 2014;370(13): 1198—208.

[8] Metsini A, Vazquez M, Sommerstein R, Marschall J, Voide C, Troillet N, et al. Point prevalence of healthcare-associated infections and antibiotic use in three large Swiss acute-care hospitals. Swiss Med Wkly 2018;148:w14617.

[9] Centres of Disease Control and Prevention. Pneumonia (ventilator -associated [VAP] and non-ventilator -associated pneumonia [PNEU]) event. 2019. https://www.cdc.gov/nhsn/pdfs/pscmanual/6pscvapcurrent.pdf. [Accessed 3 June 2019].

[10] Davis J, Finley E. The breadth of hospital-acquired pneumonia: nonventilated versus ventilated patients in Pennsylvania. Penn Patient Saf Auth 2012;9(3):99—105.

[11] Baker D, Quinn B. Hospital acquired pneumonia prevention initiative-2: incidence of nonventilator hospital-acquired pneumonia in the United States. Am J Infect Contr 2018; 46(1):2—7.

[12] Micek ST, Chew B, Hampton N, Kollef MH. A case-control study assessing the impact of nonventilated hospital-acquired pneumonia on patient outcomes. Chest 2016;150(5):1008—14.

[13] Giuliano KK, Baker D, Quinn B. The epidemiology of non-ventilator hospital-acquired pneumonia in the United States. Am J Infect Control 2018;46(3):322—7.

[14] Quinn B, Baker DL, Cohen S, Stewart JL, Lima CA, Parise C. Basic nursing care to prevent nonventilator hospital-acquired pneumonia. J Nurs Scholarsh Offic Publ Sigma Theta Tau Int Honor Soc Nurs 2014;46(1):11—9.

[15] Walter J, Haller S, Quinten C, Kärki T, Zacher B, Eckmanns T, et al. Healthcare-associated pneumonia in acute care hospitals in European Union/European Economic Area countries: an

analysis of data from a point prevalence survey, 2011 to 2012. Euro Surveill Bull Eur Sur Les Maladies Transmissibles — Eur Commun Dis Bull 2018;23(32).

[16] Pássaro L, Harbarth S, Landelle C. Prevention of hospital-acquired pneumonia in non-ventilated adult patients: a narrative review. Antimicrob Resist Infect Contr 2016;5:43.

[17] Sopena N, Heras E, Casas I, Bechini J, Guasch I, Pedro-Botet ML, et al. Risk factors for hospital-acquired pneumonia outside the intensive care unit: a case-control study. Am J Infect Contr 2014;42(1):38—42.

[18] Kanzigg LA, Hunt L. Oral health and hospital-acquired pneumonia in elderly patients: a review of the literature. J Dent Hyg JDH 2016;90(Suppl. 1):15—21.

[19] Heo S-M, Haase EM, Lesse AJ, Gill SR, Scannapieco FA. Genetic relationships between respiratory pathogens isolated from dental plaque and bronchoalveolar lavage fluid from patients in the intensive care unit undergoing mechanical ventilation. Clin Infect Dis 2008;47(12):1562—70.

[20] Robertson T, Carter D. Oral intensity: reducing non-ventilator-associated hospital-acquired pneumonia in care-dependent, neurologically impaired patients. Can J Neurosci Nurs 2013; 35(2):10—7.

[21] Munro S, Baker D. Reducing missed oral care opportunities to prevent non-ventilator associated hospital acquired pneumonia at the department of veterans affairs. Appl Nurs Res 2018;44:48—53.

[22] Talley L, Lamb J, Harl J, Lorenz H, Green L. HAP prevention for nonventilated adults in acute care: can a structured oral care program reduce infection incidence? Nurs Manag 2016; 47(12):42—8.

[23] Pedersen PU, Larsen P, Håkonsen SJ. The effectiveness of systematic perioperative oral hygiene in reduction of post-operative respiratory tract infections after elective thoracic surgery in adults: a systematic review. JBI Database Systemat Rev Implement Rep 2016;14(1):140—73.

[24] Moher D, Liberati A, Tetzlaff J, Altman DG, The PG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. PLoS Med 2009;6(7):e1000097.

[25] Higgins Julian PT, Green Sally. Cochrane handbook for systematic reviews of interventions. 5.1.0 ed. Cochrane Collaboration; 2011.

[26] Wells G, Shea B, O'connell D, Peterson J, Welch V, Losos M, et al. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomized studies in meta-analysis. 2011. http://www.ohrica/programs/clinical_epidemiology/oxfordasp2016.

[27] Ottawa Hospital Research Institute. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomized studies in meta-analyses. 2019. http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp. [Accessed 12 June 2019].

[28] Adachi M, Ishihara K, Abe S, Okuda K, Ishikawa T. Effect of professional oral health care on the elderly living in nursing homes. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2002; 94(2):191—5.

[29] Bellissimo-Rodrigues WT, Menegueti MG, Gaspar GG, Nicolini EA, Auxiliadora-Martins M, Basile-Filho A, et al. Effectiveness of a dental care intervention in the prevention of lower respiratory tract nosocomial infections among intensive care patients: a randomized clinical trial. Infect Control Hosp Epidemiol 2014;35(11):1342—8.

[30] Bourigault C, Lietard C, Golmard JL, Maman L, Nabet C, Carrat F, et al. Impact of bucco-dental healthcare on the prevention of pneumonia in geriatrics: a cluster-randomised trial. J Hosp Infect 2011;77(1):78—80.

[31] Yoneyama T, Yoshida M, Ohrui T, Mukaiyama H, Okamoto H, Hoshiba K, et al. Oral care reduces pneumonia in older patients in nursing homes. J Am Geriatr Soc 2002;50(3): 430—3.

[32] Boden I, Skinner EH, Browning L, Reeve J, Anderson L, Hill C, et al. Preoperative physiotherapy for the prevention of respiratory complications after upper abdominal surgery: pragmatic, double blinded, multicentre randomised controlled trial. BMJ (Clin Res Ed) 2018;360:j5916.

[33] Cuesy PG, Sotomayor PL, Piña JOT. Reduction in the incidence of poststroke nosocomial pneumonia by using the "turn-mob" program. J Stroke Cerebrovasc Dis — Offic J Natl Stroke Assoc 2010;19(1):23—8.

[34] Stolbrink M, McGowan L, Saman H, Nguyen T, Knightly R, Sharpe J, et al. The Early Mobility Bundle: a simple enhancement of therapy which may reduce incidence of hospital-acquired pneumonia and length of hospital stay. J Hosp Infect 2014;88(1):34—9.

[35] Schrock JW, Lou L, Ball BAW, Van Etten J. The use of an emergency department dysphagia screen is associated with decreased pneumonia in acute strokes. Am J Emerg Med 2018;12:2152—4.

[36] Titsworth WL, Abram J, Fullerton A, Hester J, Guin P, Waters MF, et al. Prospective quality initiative to maximize dysphagia screening reduces hospital-acquired pneumonia prevalence in patients with stroke. Stroke 2013;44(11): 3154—60.

[37] Johansen NJ, Hahn CH. Prophylactic antibiotics at the time of tracheotomy lowers the incidence of pneumonia. Dan Med J 2015;62(7).

[38] McNally E, Krisciunas GP, Langmore SE, Crimlisk JT, Pisegna JM, Massaro J. Oral care clinical trial to reduce non-intensive care unit, hospital-acquired pneumonia: lessons for future research. J Healthc Qual 2019;41(1):1—9.

[39] Wagner C, Marchina S, Deveau JA, Frayne C, Sulmonte K, Kumar S. Risk of stroke-associated pneumonia and oral hygiene. Cerebrovasc Dis (Basel, Switzerland) 2016;41(1—2): 35—9.

[40] Chen Y, Mao E-Q, Yang Y-J, Zhao S-Y, Zhu C, Wang X-F, et al. Prospective observational study to compare oral topical metronidazole versus 0.2% chlorhexidine gluconate to prevent nosocomial pneumonia. Am J Infect Control 2016;44(10): 1116—22.

[41] Emery KP, Guido-Sanz F. Oral care practices in non-mechanically ventilated intensive care unit patients: an integrative review. J Clin Nurs 2019;28(13-14):2462—71.

[42] Collins AS. Preventing health care—associated infections. In: Hughes R, editor. Patient safety and quality: an evidence-based handbook for nurses. Rockville, MD: Agency for Healthcare Research and Quality; 2008.

[43] Tablan OC, Anderson LJ, Besser R, Bridges C, Hajjeh R. Guidelines for preventing health-care-associated pneumonia, 2003: recommendations of CDC and the healthcare infection control practices advisory committee. MMWR Recomm Rep — Morb Mortal Wkly Rep Recomm Rep 2003; 53(RR-3):1—36.

[44] Labeau SO, Van de Vyver K, Brusselaers N, Vogelaers D, Blot SI. Prevention of ventilator-associated pneumonia with oral antiseptics: a systematic review and meta-analysis. Lancet Infect Dis 2011;11(11):845—54.

[45] Vogelaers D, Deschepper M, Blot S. Oral care with chlorhexidine gluconate: time to focus on outcomes that matter. J Crit Care 2017;40:308—9.

[46] Torres A, Niederman MS, Chastre J, Ewig S, Fernandez-Vandellos P, Hanberger H, et al. International ERS/E-SICM/ESCMID/ALAT guidelines for the management of hospital-acquired pneumonia and ventilator-associated pneumonia: guidelines for the management of hospital-acquired pneumonia (HAP)/ventilator-associated pneumonia (VAP) of the European Respiratory Society (ERS), European Society of Intensive Care Medicine (ESICM), European Society of Clinical Microbiology and Infectious Diseases (ESCMID) and

Asociación Latinoamericana del Tórax (ALAT). Eur Respir J 2017;50(3).

[47] Kalil AC, Metersky ML, Klompas M, Muscedere J, Sweeney DA, Palmer LB, et al. Management of adults with hospital-acquired and ventilator-associated pneumonia: 2016 clinical practice guidelines by the Infectious Diseases Society of America and the American Thoracic Society. Clin Infect Dis 2016;63(5): e61—111.

[48] European Centre for Disease Prevention and Control. Point prevalence survey of healthcare-associated infections and antimicrobial use in European acute care hospitals — protocol version 5.3. Stockholm: European Centre for Disease Prevention and Control; 2016.

[49] Prost A, Binik A, Abubakar I, Roy A, De Allegri M, Mouchoux C, et al. Logistic, ethical, and political dimensions of stepped wedge trials: critical review and case studies. Trials 2015;16(1):351.