Title: Poor oral hygiene, oral microorganisms and aspiration pneumonia risk in older people in residential aged care: a systematic review

Abstract

Background: Aspiration pneumonia increases hospitalization and mortality of older people in residential aged care.

Objectives: Determine potentially pathogenic microorganisms in oral specimens of older people with aspiration pneumonia and the effect of professional oral care in reducing aspiration pneumonia risk.

Data Sources: PUBMED/MEDLINE, CINAHL, EMBASE, COCHRANE, PROQUEST, Google Scholar, Web of Science.

Study Eligibility Criteria: Published between January 2001 and December 2019 addressing oral microorganisms, aspiration pneumonia, oral health, and treatment.

Participants: People 60 years and older in residential aged care.

Study Appraisal and Synthesis Methods: The Newcastle Ottawa Scale and SPIRIT checklist.

Results: Twelve studies (four cross-sectional, five cohort and three intervention) reported colonization of the oral cavity of older people by microorganisms commonly associated with respiratory infections. Aspiration pneumonia occurred less in people who received professional oral care compared with no such care. Isolation of *Candida albicans*, *Staphylococcus aureus*, methicillin-resistant *S. aureus*, and *Pseudomonas aeruginosa* was related to mortality due to aspiration pneumonia. An interesting finding was isolation of *Escherichia coli,* a gut bacteria.

Limitations: More information may be present in publications about other comorbidities that did not meet inclusion criteria. A high degree of heterogeneity prevented a meta-analysis. Issues included sampling size; no power and effect size calculations; different oral health assessments; how oral specimens were analysed; and how aspiration pneumonia was diagnosed.

Conclusions and Implications of Key Findings: Pathogenic microorganisms colonizing the oral microbiome are associated with aspiration pneumonia in older people in residential care; professional oral hygiene care is useful in reducing aspiration pneumonia risk.

Keywords: Aspiration pneumonia, pathogenic microorganisms, older people, oral health, residential aged care

Key points:

- Pathogenic microorganisms colonizing the oral microbiome were significantly associated with poor oral health and a higher incidence of aspiration pneumonia in older people in residential aged care.
- Professional oral hygiene care reduced the growth of potentially pathogenic microorganisms found in the mouths of older people in residential aged care compared to non-professional oral hygiene care.
- Professional oral hygiene care reduced the risk of aspiration pneumonia in older people.

INTRODUCTION

Rationale

Aspiration pneumonia (a dominant form of community or healthcare acquired pneumonia) is a preventable condition, resulting in clinical deterioration, escalation of preventable hospital admissions, increased mortality and greater cost of care, particularly for older people in residential care (1, 2). Risk is heightened by the presence of co-morbidities, including dementia and stroke (3, 4). Aspiration pneumonia develops when regurgitated gastric contents or oropharyngeal secretions, often mixed with food and liquid, are mis-directed into the respiratory system and the lungs cannot clear the aspirated material (5) (6).

Many older people in residential care are frail and with cognitive impairment. These conditions are frequently accompanied by dysphagia, esophageal dysmotility, and gastrointestinal (GI) reflux. Frequently prescribed multiple medications for chronic co-morbidities can adversely affect GI function, and dry the oral mucosa and saliva needed for a healthy mouth and efficient swallowing (7-9). Older people's dependence on care, including care for the mouth and assistance with eating, increases the risk of poor oral hygiene with associated colonization of large numbers of potentially pathogenic microorganisms (10). These include *Escherichia coli* (*E. coli*), *Klebsiella pneumoniae* (*K. pneumoniae*), *Staphylococcus aureus* (*S. aureus*) and others that are not part of the oral microbial flora (11-13). If dysphagia is present, weakened and/or unco-ordinated muscles of the tongue, oropharynx and larynx can reduce clearance of food, liquid, and saliva and misdirect the bolus during a swallow. Subsequent aspiration, combined with pathogenic colonizers of the oral cavity from an unclean mouth may lead to aspiration pneumonia (14).

Sensitive and specific markers for the early diagnosis of aspiration pneumonia are scarce (15) and understanding the contribution of potentially pathogenic microorganisms colonizing the oral microbiome is important. The human mouth harbours approximately 700

different microbial species (16). These microbiomes can be mapped by extraction of DNA from oral samples, and amplification of bacterial marker genes by Polymerase Chain Reaction (PCR) analysis (17). Competitive inhibition of pathogenic microorganisms by the normal flora helps maintain a healthy oral cavity (16). However, this inhibition is often challenged by age, hygiene, mental health, immune status, and lifestyle choices, including frequent sugar intake (18), along with poor access to dental care (19, 20). Frequent sugar intake and reduced saliva increase oral acidity (as a metabolic by-product of normal endogenous flora). If untreated, resultant acid tolerant bacteria destroy tooth enamel, increase plaque and caries, and heighten aspiration pneumonia risk (21). Older people with periodontitis and/or dental caries (22) have a higher load of microorganisms that are associated with the risk of hospitalization (23) and chronic co-morbidities including aspiration pneumonia, compared to those with better oral health (24-28).

Aspiration of droplet nuclei containing pathogenic microorganisms is the hallmark of aspiration pneumonia which leads to lung pathology (6). Potentially pathogenic colonizers of the oral microbiome commonly associated with aspiration pneumonia include organisms of oral origin (*Haemophilus influenzae* [*H. influenzae*], *Candida albicans* [*C. albicans*], *Streptococcus pneumoniae* [*S. pneumoniae*]) and organisms of non-oral origin (*Pseudomonas aeruginosa* [*P. aeruginosa*], *S. aureus*, and *K. pneumoniae*) (11-13, 29-35). Some pathogens (e.g., *C. albicans*, *S. pneumoniae*) also inhabit the GI tract (36). The microbial community undergoes continuous change during the life course and reflects issues such as immune status (37), age, and mental health disorders (38). The oral microbiome in older adults in residential care can be significantly different compared to healthy individuals (39) (40). It is therefore important to characterize the structure of the oral microbiome in older people to further understand its role in health and disease (41).

Two systematic reviews have reported a significant association between oral hygiene and bacterial pneumonia (42, 43). However, the literature is scarce in identifying the

association between poor oral hygiene and microorganisms found in the mouth that are commonly associated with increased risk of aspiration pneumonia for older people in residential care. As the number of older people increases globally, maintaining their health is an increasingly important public health priority.

Objectives

This systematic review sought to determine the presence of potentially pathogenic microorganisms in oral specimens of older people with aspiration pneumonia in residential care and the effect of professional oral hygiene care in reducing aspiration pneumonia risk.

METHODS

Protocol

Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, along with Population Intervention Comparator Outcome (PICO) criteria were followed to construct the research question: "Which microorganisms in the oral microbiome are a risk factor for aspiration pneumonia for older adults in residential care?"

Eligibility criteria

To address the research question and objectives, eligibility criteria were original studies, published in English between January 2000 and December 2019, of people 60 years and older; of people with dementia; of people in residential aged care; reporting aspiration pneumonia as an outcome; and describing oral microorganisms. Studies focusing on people younger than 60 years, commentaries, reviews, systematic reviews, literature reviews, mini reviews, dissertations, letters to the editor, in vivo studies, and non-English papers were excluded.

Information sources

Information was sourced from seven databases: PUBMED/MEDLINE, CINAHL, EMBASE, COCHRANE, PROQUEST, Google Scholar and Web of Science. Snowballing was used to find further publications that matched the eligibility criteria. Relevant search terms

were identified using National Library of Medicine Medical Subject Headings (MESH) and free text terms and are presented in Supplementary Table 1. The search of the databases was conducted from December 16, 2019 to January 20, 2020.

Search

An example of a full electronic search strategy is presented in Supplementary Table 1.

Study selection

Two authors (SK1, SK2) independently screened the titles and abstracts of identified papers. These authors then read the full texts of the papers that met the eligibility criteria. Any disagreements were resolved by a third author (SB).

Data collection process and data items

Data were extracted from the selected papers using a form devised by the writing team. This form documented (i) study characteristics: country, setting, design, participants' demographics; (ii) participants' diagnoses including dementia, cognitive impairment, and aspiration pneumonia; (iii) oral microbial sampling techniques and analyses; (iv) load and type of microorganisms found in the mouth; (v) interventions; and (vi) key findings. The form confirmed that the selected studies addressed the primary and secondary objectives of this systematic review; namely, to determine (1) the presence of potentially pathogenic microorganisms in oral specimens of older people with aspiration pneumonia in residential care, and (2) the effect of professional oral hygiene care in reducing the risk of aspiration pneumonia.

Quality appraisal

Two authors (SK1, SK2) independently applied the Newcastle-Ottawa Quality Assessment Scale (NOS) to appraise the quality of the identified cross-sectional and cohort studies. The NOS uses a star (☆) system based on three categories of selection (maximum 5 stars), comparability (maximum 2 stars) and outcomes (maximum 3 stars). The Standard Protocol

Items: Recommendations for Intervention Trials (SPIRIT) statement was used to assess the quality of intervention studies.

RESULTS

Study selection

The database search produced 574 studies. After removal of duplicates, 467 studies were identified for title and abstract screening. After screening, 25 studies remained for full text review; 13 were excluded as they focused on people less than 60 years of age, people with a mental health condition, contained no oral specimen sampling, or collected samples from broncho-alveolar lavage. One study by Terpenning et al. (44) involving participants aged 55 years and above was included for review. Data were analysed only for participants aged 60 years and older, whenever available. Figure 1 shows the PRISMA diagram of the literature search and study selection process.

Study characteristics

Of the 12 included studies, nine were observational [five cohort (44-48), four cross-sectional (13, 49-51)] and three were intervention (52-54) (Supplementary Tables 2 and 3). The studies were from three countries: Israel (50), Japan (13, 45-49, 52-54) and the United States (44, 51). Observational studies included a follow-up period ranging from six months to nine years or until participants were no longer living. The duration of the intervention studies was five months in one (54) and 24 months in the other two (52, 53). Ten studies included people in residential communities (44-47, 49-54).

Variables among the studies

Diagnosis of aspiration pneumonia

The diagnosis of aspiration pneumonia varied and was based on fever ≥37.8°C, number of febrile days, chest X-radiographs (finding areas of increased density), auscultatory findings, cough, sputum, dyspnea or pleuritic chest pain or positive pleuritic fluid cultures, and white blood cell (WBC) count >5000 cells/mm^3.

Collection of oral specimens

Oral specimens were obtained from the tongue, palatal and buccal mucosa, oropharynx and palatoglossal arches. Most studies used a culture technique to identify microorganisms (13, 44, 47-50, 52-54). Others used DNA extraction, (PCR analysis and Terminal Restriction Fragment Length Polymorphism, T-RFLP) (45), Pulsed-Field Gel Electrophoresis (PFGE) (51), and Di-Electrophoretic Impedance Measurement (DEPIM) (46).

Oral health assessment

Determination of oral health focused on number of teeth present; number with dental caries; measurement (mm) of depth of periodontal pockets to document periodontal disease; use of dentures and any other removable prosthesis; indices to document plaque on teeth and coating on tongue surface; moistness of oral mucosa and tongue; presence of food debris to indicate possible chewing and swallowing difficulty; general oral hygiene and presence of active oral disease.

Further variables

Studies also varied in their inclusion of participants' medical and dental histories, current health and dental conditions and health-related behaviour (e.g. smoking and alcohol intake), personal oral hygiene, current medications, dependency for oral care, complaints of xerostomia, dietary intake, exercise and sleep patterns, and self-perception of health status.

Quality assessment

Observational (cohort and cross-sectional) studies. Results of the NOS quality assessment for the non-intervention studies are presented in Supplementary Table 4. Most studies were of fair to good quality based on the threshold of stars obtained.

*Intervention studies***.** All three intervention studies (52-54) divided participants into (a) an experimental group receiving weekly professional oral hygiene care (POHC) and (b) a control group receiving basic oral care - swabbing with a sponge brush and denture cleaning (52, 53) or gargling with 0.35 % povidone iodine once a day (54). Weekly professional oral care included cleaning the teeth, dentures, oral mucosa and tongue with hand scalers, electric toothbrush, irrigation, and interdental and sponge brushing. SPIRIT assessments of the quality of these studies are presented in Supplementary Table 5.

Addressing the Primary Objective of this review: Determining the presence of pathogenic microorganisms in oral specimens of older people with aspiration pneumonia in residential care.

Cohort and cross-sectional studies: Outcomes of these studies (participant size =71-697 [cohort] and 49-138 [cross-sectional]) are presented in Supplementary Table 6. These studies reported the colonization of the oral biofilms of older people by pathogenic microorganisms commonly associated with respiratory infections. One study (44) used a logistic regression model to calculate the risk of developing aspiration pneumonia in the presence of particular bacteria in the oral cavity. For example, *S. aureus* in saliva was higher (odds ratio: 4.3, 95% confidence interval= 2.0-9.3) in participants with aspiration pneumonia. Participants with aspiration pneumonia had a significantly higher load of *Porphyromonas gingivalis* (45), *Streptococcus sobrinus* (45)*,* and *S. aureus* (44, 49) as demonstrated by microbiological analysis of saliva and tongue swabs. Analysis of tongue coating samples documented that microbiological complexity (24, 45), oral bacterial count $\geq 10^{8.5}$ CFU/ml (46) and presence of

Haemophilus parainfluenzae (13, 49), *K. pneumoniae* (13, 49), *P. aeruginosa* (13) and *Candida* species (48) were significantly associated with an increased risk of aspiration pneumonia. Dental plaque microbiological profiling documented that methicillin-resistant *S. aureus* (45%), enteric Gram-negative bacilli (42%) and *P. aeruginosa* (13%) were significantly associated with pneumonia in older people (51).

Intervention studies: All three studies found a high prevalence of potent respiratory pathogens e.g. *Staphylococcus species* and *P. aeruginosa* (Supplementary Table 7).

Confounding factors: The putative confounders significantly associated with microorganisms present in the oral cavity and risk for aspiration pneumonia were: frailty, pulmonary disease, type 2 diabetes, dementia, incidence of stroke, low Body Mass Index, low physical activity, high number of dental caries, periodontal disease, increased depth of periodontal pockets, high tongue plaque and high dental plaque index scores, presence of dentures, chewing and swallowing difficulties, and xerostomia.

Addressing the Secondary Objective of this review: to determine the effect of professional oral care in reducing the risk of aspiration pneumonia.

Results of the three intervention studies (participant size = 98-202) showed that weekly professional oral care was effective in reducing aspiration pneumonia risk (Supplementary Table 7). The oral microbiological analyses documented that the loads of *C. albicans, S. aureus, methicillin-resistant S. aureus, P. aeruginosa*, and *E. coli* were significantly lower in people who received weekly professional oral hygiene care compared to those who received daily basic oral hygiene care from non-professional staff, complemented by gargling with 0.35 % povidone iodine (52-54).

DISCUSSION

Summary of evidence

This review identified *S. aureus*, *S. pneumoniae*, *H. influenzae*, *K. pneumoniae*, *P. aeruginosa*, *E. coli*, and *Candida* species as potentially pathogenic microorganisms colonizing the oral microbiome and microbiological evidence of aspiration pneumonia in older adults, particularly for those in residential care. The five cohort (44-48), four cross-sectional (13, 49-51) and three intervention studies (52-54) documented that poor oral hygiene set the stage for these potential pathogens and was associated with an increased risk of aspiration pneumonia. The detection of *E. coli*, along with *K. pneumoniae* and *P. aeruginosa* in the mouths of older people with aspiration pneumonia was an important finding. *E. coli* and *Klebsiella species* are normal flora in the GI tract. Their presence in the mouth may be related to the gastro-esophageal reflux experienced by many older people, especially those with dysphagia. This suggests that professionals providing oral care to older people need to understand the signs and symptoms of reflux for appropriate clinical management and reduction of aspiration pneumonia risk.

However, a more likely explanation centres in transfer from the environment. Most bacterial genera that comprise the coliform group (e.g., *Escherichia*, *Klebsiella*) are within the family Enterobacteriaceae and can inhabit the gastrointestinal tract. Members of the genera *Klebsiella*, *Enterobacter*, *Serratia*, and others are considered coliforms but are also found in the environment and are not a common component of the gut microbiome. Similarly, pseudomonad (e.g., *Pseudomonas)* are ubiquitous in food and environmental sources. *Pseudomonas* species normally inhabit soil, water, and vegetation and can be isolated from the skin, teeth, throat, and stool of healthy persons. Airborne and fomite transmission in health care has also been implicated in outbreaks of other infections from *Pseudomonas*. These microorganisms are common agents of health care-associated infection in older people (55, 56)

and frequently exhibit resistance to antimicrobials (57). Thus, poor handwashing procedures by staff and residents, tainted food, food debris remaining in the mouth, and poor denture cleaning are some possible reasons accounting for the transfer of gut bacteria to the mouths of vulnerable older adults in residential care.

The concept of a microbial oral reservoir, reflecting colonization of the oral ecosystem by extra-oral and pathogenic bacteria and compounding aspiration pneumonia risk is a concern. The oral cavity of older people, especially those in residential care, can serve as a reservoir for opportunistic pathogens (58, 59). Poor oral hygiene increases the possibility of virulent pathogenic microorganisms in the oral cavity, with subsequent oral disease, aspiration pneumonia, and systemic illness. An imbalance in the oral microenvironment (60) increases the proliferation of pathogenic microorganisms associated with gingivitis, increased periodontal pocket depth, alveolar bone and tooth loss (61), and oral ulcerations (62). As an example, the acid-tolerant *Streptococcus mutans*, *Veillonella* species and *Lactobacillus* species, have been related to demineralization of tooth enamel favoring the formation of dental plaque (37). Dental plaque accumulates approximately 100 million bacteria per mm^3 (63) including Gram negative proteolytic and Gram positive acidogenic bacteria (64). In normal health, saliva prevents the formation of plaque and deposition of pathogenic microorganisms through its flushing action and antimicrobial properties (65). However, reduced saliva production increases plaque formation (66, 67) and the systemic spread of aspirated oral plaque microorganisms into the lower respiratory tract can cause aspiration pneumonia (68, 69).

The clinical manifestation of aspiration pneumonia is the result of the body's inflammatory response to a proliferating microbial population. For example, increased leukocyte migration in the inflamed area causes purulent sputum production (65). Repeated lung infections, or episodic aspiration pneumonia, increase sarcopenia, the loss of skeletal muscle mass and strength, causing a decline in the function of swallowing musculature and

cough physiology. This, in turn, increases frailty and an older person's ability to fight off infection. As their burden of co-morbidities increases, older people's cognitive and socio-emotional health may decline (70, 71).

Many people in residential aged care are dependent on others for feeding and oral care. Difficulty with swallowing heightens the risk of aspirating food, liquid and/or saliva, especially if people are fed too fast or given unsafe liquids to drink. More importantly, if food debris remains in the mouth due to poor oral care, this facilitates the colonization of potentially pathogenic microorganisms (30). Thus, co-dependent older people are at increased risk for the repeated aspiration of infectious particles present in the oral cavity resulting in a vicious cycle of dysphagia – aspiration pneumonia – dysphagia and declining health (5).

Inflammation of the oral cavity is also associated with the blood-borne spread of pathogenic microbes to distant body sites resulting in systemic infection, e.g., bacterial endocarditis (72). Similarly, the spread of microbial toxins (i.e. endotoxins, heat shock proteins) and immunological products of inflammation can cause fever, toxic shock syndrome (29) and amplify the severity of type 2 diabetes (73). Thus, the effects of poor oral health and an adverse oral microbial environment can be evident in whole-body systems (60-62).

The effect of poor oral health is not limited to clinical diseases. It affects an individual's ability to eat well, speak clearly, and communicate with confidence. Oral diseases (dental caries and periodontitis) impair the production of saliva making it difficult to chew (64) and swallow food (72), resulting in altered dietary intake (72) and malnutrition (74). Undernourishment, in turn, is related to enamel hypoplasia, changes in the composition of saliva and diminished functioning of salivary glands, continuing the cycle of poor oral health-malnutrition-poor oral health (74). Oral malodor, a consequence of tongue and dental plaque, putrefaction of food debris, and secretions in the oral cavity by Gram negative bacteria, is a cause of anxiety and psychosocial embarrassment (75).

Oral health is vital to overall health and physical, social and psychological wellbeing for older people in residential care. A collaborative interprofessional approach to establish and maintain residents' oral health and minimize potentially pathogenic microorganisms from colonizing the oral microbiome needs to involve dentists, nurses, and allied health providers (e.g. speech pathologists, dietitians/nutritionists, pharmacists, oral health therapists, physiotherapists) through both pathogen- and function-oriented therapy (5, 76, 77). Studies suggest that weekly professional oral hygiene care is effective in decreasing the load of potentially pathogenic oral microflora, respiratory pathogens and risk of aspiration pneumonia (78). When provided in a collaborative interprofessional approach, such care can improve older people's independence in functional activities of daily living, promote health, and reduce societal and personal health care costs (78).

Limitations

Further information may be present in publications about other comorbidities that did not meet eligibility criteria. A high degree of heterogeneity prevented a meta-analysis. Issues included sampling size; no power and effect size calculations; different oral health assessment measures; how oral specimens were analysed; and how aspiration pneumonia was diagnosed.

Conclusions

Regardless of the documented variations in the studies, there was agreement that poor oral hygiene from lack of oral care increases the colonization of potentially pathogenic and identifiable microorganisms in the oral cavity. These microorganisms are *S. aureus, S. pneumoniae, Candida* species*, H. influenzae, K. pneumoniae, P. aeruginosa* and *E. coli*. Their presence in the mouth is associated with a significantly increased risk for aspiration pneumonia. Professional weekly oral care is an effective measure in decreasing the load of potentially pathogenic microorganisms that can colonize the oral microbiome and reducing the risk of aspiration pneumonia related to poor oral health.

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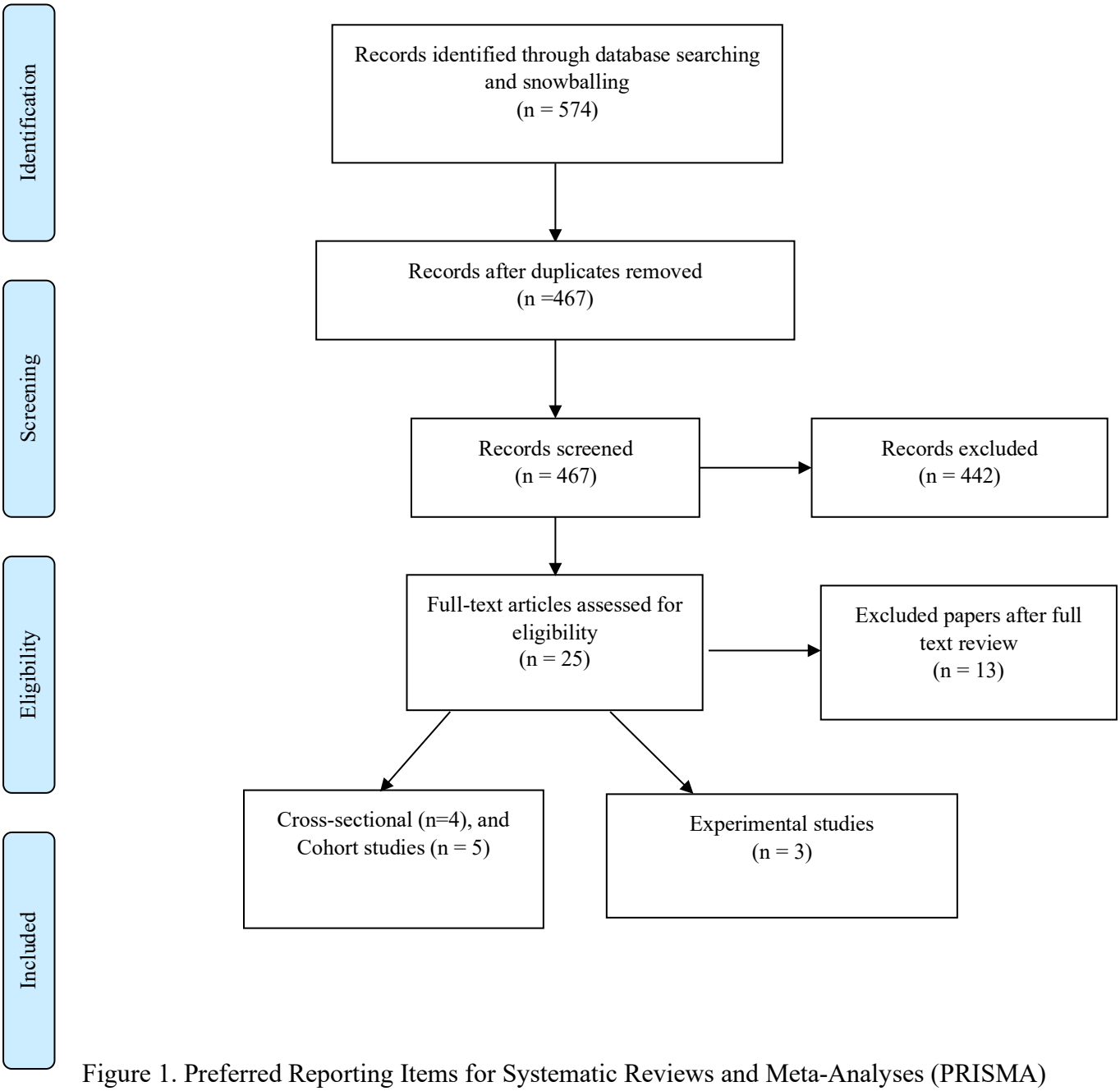

Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) for literature search and paper selection process.