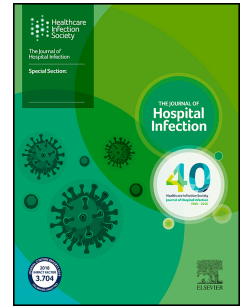


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Role of antiseptics in the prevention and treatment of infections in nursing homes

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1 Review

2 **Role of antiseptics in the prevention and treatment of**
3 **infections in nursing homes**

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1 **Running title: Antiseptics in nursing homes**

2 **Summary (250/250 words)**

3 Inadequate infection control, wound care, and oral hygiene protocols in
4 nursing homes provide challenges to residents' quality of life. Based on the
5 outcomes from a focus group meeting and a literature search, this narrative review
6 evaluates the current and potential roles of antiseptics within nursing home infection
7 management procedures. We examine contemporary strategies and concerns within
8 the management of meticillin-resistant *Staphylococcus aureus* (MRSA; including
9 decolonization regimes), chronic wound care, and oral hygiene, and review the
10 available data for the use of antiseptics, with a focus on povidone-iodine.

11 Compared with chlorhexidine, polyhexanide, and silver, povidone-iodine has a
12 broader spectrum of antimicrobial activity, with rapid and potent activity against
13 MRSA and other microbes found in chronic wounds, including biofilms. As no reports
14 of bacterial resistance or cross-resistance following exposure to povidone-iodine
15 exist, it may be preferable for MRSA decolonization compared with mupirocin and
16 chlorhexidine, which can cause resistant MRSA strains. Povidone-iodine oral
17 products have greater efficacy against oral pathogens compared with other
18 antiseptics such as chlorhexidine mouthwash, highlighting the clinical benefit of
19 povidone-iodine in oral care. Additionally, povidone-iodine-based products, including
20 mouthwash, have demonstrated rapid *in vitro* virucidal activity against SARS-CoV-2
21 and may help reduce its transmission if incorporated into nursing home coronavirus

Abbreviations: CHG: Chlorhexidine; COVID-19: Coronavirus disease; MDRO: Multidrug-resistant organism;
MRSA: Meticillin-resistant *Staphylococcus aureus*; NH: Nursing home; PHMB: Polyhexanide; PVP-I: Povidone-
iodine; SARS-CoV-2: severe acute respiratory syndrome coronavirus 2; SSTI: skin and soft tissue infection.

1 2019 control protocols. Importantly, povidone-iodine activity is not adversely affected
2 by organic material, such as that found in chronic wounds and the oral cavity.

3 Povidone-iodine is a promising antiseptic agent for the management of
4 infections in the nursing home setting, including MRSA decolonization procedures,
5 chronic wound management, and oral care.

6 **Key words:** Povidone-iodine, Decolonization, Oral hygiene, Chronic wound,
7 coronavirus 2019, meticillin-resistant *Staphylococcus aureus*

1 Introduction

2 Nursing homes (NHs) are an important component of the health service
3 network for the elderly population. However, these facilities provide an ideal
4 environment for the introduction and transmission of infections due to the sharing of
5 air, water, food, and healthcare in a crowded setting [1]. Data from a European study
6 conducted in 26 countries indicated the prevalence of long-term care facility
7 residents with at least one healthcare-associated infection was 3.7% (range 0.9–
8 8.5%) [2]. Many NH residents are frail, exposed to multiple medications, and often
9 have underlying chronic diseases, functional dependency, and cognitive impairments
10 [1, 3-5]. These factors, with other cultural and social factors, make older adults more
11 susceptible to infections than younger populations, with significant negative impact
12 on morbidity and functional decline [6].

13 Infection outbreaks in NHs are common, underscoring the need for active
14 infection control programmes in these facilities [1]. Evidence accrued during the
15 recent COVID-19 pandemic demonstrated factors contributing to increased risk for
16 NH epidemics, highlighting the urgent need for adequate healthcare plans for elderly
17 residents [7]. During the first wave of the pandemic, NH residents contributed to a
18 substantial proportion of all deaths due to COVID-19 [8]. Furthermore, investigations
19 have shown a four-fold difference in infection control in acute care hospitals
20 compared with NHs [9]. In infection outbreak models, the presence of NHs
21 substantially potentiated the effect of nosocomial outbreaks on other hospitals,
22 leading to an average 46.2% relative increase in outbreak impact compared with
23 inclusion of hospitals alone [10].

24 Nosocomial infections and multidrug-resistant organisms (MDROs) are
25 significant issues for NHs globally [11]. Between 1.6–3 million infections occur in

1 NHs in the US each year and more than one-third of US NH residents harbour
2 MDROs [12]. Similarly, it has been calculated that the percentage of antimicrobial-
3 resistant bacterial isolates (as a proportion of the number of isolates tested) in
4 Europe is 28.0% among long-term care facility residents across 11 countries [2]. NH
5 residents are disproportionately affected by morbidity and mortality from MDROs,
6 most commonly methicillin-resistant *Staphylococcus aureus* (MRSA) [9, 13, 14].
7 Infections in these facilities and the resultant use of antibiotics are key reasons for
8 the emergence of antibiotic-resistant organisms such as MRSA [15, 16]. In a 2016
9 survey of French NHs, 2.76% of residents were treated with antibiotics; prophylactic
10 treatment was used in 13.7% of cases, and antibiotic treatment duration exceeded 7
11 days in over a third of cases [17].

12 A focus meeting, attended by all authors, on 'antiseptics in the management of
13 infections in the NH setting' was held in December 2020. The discussions resulting
14 from that meeting, including the literature selected and reviewed by the authors, and
15 additional publications identified through subsequent literature searches, form the
16 basis of this narrative review. The aim of this article is to examine available
17 information on (1) MRSA management, including decolonization procedures, (2)
18 chronic wound management, and (3) oral care in NHs. For each of these points we
19 review current practice, limitations, and concerns, and evaluate the role of
20 antiseptics, in particular povidone-iodine (PVP-I), for the management of infections in
21 the NH setting.

22 **Methods**

23 This narrative review was guided using information derived from the focus
24 meeting (December 2020) and a subsequent search of the PubMed database
25 (January 2021). This was not a systematic review, nor was it intended to be

1 exhaustive; instead, we hoped to gain an understanding of current practice in NHs,
2 investigate the resulting limitations and challenges, and identify whether the use of
3 PVP-I might permit improvements in infection control.

4 For the literature review, search terms were chosen based on discussions
5 during the focus meeting. No date restrictions were included in the searches. Various
6 combinations of the following key terms were used for the literature searches:
7 “nursing home”; “povidone-iodine (PVP-I)”; “chlorhexidine (CHG)”; “polyhexanide
8 (PHMB)”; “silver”; “meticillin-resistant *Staphylococcus aureus*”; “mupirocin”;
9 “decolonization”; “chronic wounds”; “infection”; “biofilm”; “resistance”; “oral care”;
10 “periodontitis”; “severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)”.
11 Synonyms of each term were included in all searches. Based on their abstracts, only
12 papers that were considered directly relevant to the three focus areas (MRSA,
13 chronic wounds, and oral care) were included in this review article. Further papers of
14 interest were also identified from reference lists within the papers in the searches.

15 **Results**

16 ***Focus area 1: MRSA management in NHs***

17 MRSA is a key cause of skin and soft tissue infection (SSTI) in NHs [18]. The
18 incidence of SSTIs has risen with a rapid increase in MRSA infections [19, 20]; in a
19 Belgian national study of NHs, 17.5% of residents with infections had skin infections
20 [21]. Among NH residents, the presence of chronic skin diseases or indwelling
21 devices is a risk factor for colonization of MRSA [22, 23].

22 The high prevalence of SSTIs and MRSA infections among residents highlights
23 the need to prevent the spread of MRSA in NHs [9, 24, 25]. Eradication of MRSA is
24 theoretically possible through elimination of MRSA-positive NH admissions over
25 several years [14]; however, this is unlikely to be achieved in practice, in part

1 because there is currently no consensus for MRSA screening at NH admission.
2 Movement of residents and physicians between hospitals and NHs may facilitate
3 MRSA spread within the NH environment [26, 27], and admission of MRSA-
4 colonized residents can cause outbreaks without strict infection control protocols
5 [28].

6 *The role of decolonization*

7 Decolonization, the goal of which is to decrease or eliminate bacterial load on
8 the body, is an integral strategy used to control and prevent the spread of MRSA
9 [29]. Decolonization may reduce strain-specific prevalence of MRSA [14], and
10 decolonization of MRSA carriers in the intensive care unit has been shown to provide
11 downstream benefits [30]. However, broader use of decolonization beyond the
12 intensive care unit would be required to contribute to country-wide eradication efforts
13 [30].

14 In a survey of 13 NHs, MRSA carriage was associated with denial of admission
15 [31]; decolonization may remove this barrier. However, across many regions,
16 systematic screening for MRSA colonization and subsequent decolonization is not
17 required at NH admission; this is a possible avenue for further research.

18 *Current decolonization strategies and limitations*

19 Decolonization of MRSA commonly involves use of an intranasal antimicrobial
20 agent, plus an antiseptic body wash to eliminate bacteria from other body sites [29,
21 32]. Elimination of nasal carriage of *S. aureus* is particularly important to prevent
22 systemic infections [33]. Several studies have shown success in reducing MRSA
23 colonization in NHs with intranasal mupirocin 2% ointment applied to the anterior
24 nares twice daily for 5 days and CHG body wash [34-38].

1 However, previous decolonization strategies in NHs have failed due to factors
2 such as development of resistance and reacquisition of MRSA [39, 40]. Mupirocin
3 resistance was reported in 3.8% of MRSA isolates in 2002 [41], and 12% of isolates
4 in 2013 [42]. Resistance may also be transferred from strains of other bacterial
5 species during mupirocin prophylaxis [43] or decolonization procedures [36, 44]. In
6 many NHs, the prevalence of mupirocin-resistant strains of MRSA increased
7 between 2006 and 2009 [45], supporting an increase in the rate of mupirocin
8 resistance [46, 47]. Persistence of nasal mupirocin-resistant MRSA after
9 decolonization reflects a failure in infection control [48]; hence, extended mupirocin
10 use should be avoided in MRSA-endemic settings [49].

11 *The potential role of antiseptics in MRSA decolonization*

12 Due to the concern of mupirocin-resistance, antiseptics such as CHG and PVP-
13 I have been recommended for evaluation in decolonization protocols [46]. The ideal
14 antiseptic for MRSA decolonization is highly effective against MRSA, including
15 antibiotic- and antiseptic-resistant strains, and does not induce resistance or cross-
16 resistance (Table I) [29].

17 Several studies have shown that use of CHG can lead to resistance in MRSA
18 and other bacterial species [50-54]. CHG exposure may also result in cross-
19 resistance to antibiotics such as daptomycin, ceftazidime, tetracycline, and colistin
20 [54-56].

21 PVP-I has shown superior bactericidal activity against MRSA versus CHG and
22 mupirocin, and is active against both CHG-resistant and mupirocin-resistant MRSA
23 strains [57-60]. Compared with nasal mupirocin, PVP-I had similar efficacy in
24 reducing surgical site infections in patients undergoing orthopaedic surgery [60, 61].
25 Moreover, single nasal applications of 10% PVP-I significantly reduced nasal MRSA

1 1 and 6 hours after application [62]. Importantly, no reports have observed links
2 between PVP-I and induction of bacterial resistance or cross-resistance to
3 antiseptics or antibiotics [60]. In practice, nasal PVP-I swabbing has shown clinical
4 success and cost savings when used as an alternative to MRSA screening for
5 preoperative patients [63].

6 *Focus area 1: summary and recommendations*

7 As outlined in Table I, we recommend decolonization of known MRSA carriers
8 when entering NHs, and of current residents should they test positive for MRSA.
9 Whilst current evidence suggests PVP-I may be an ideal antiseptic for short-term
10 decolonization, further evidence is needed to understand the use of PVP-I for long-
11 term decolonization. Additional research in this area is clearly indicated: widespread
12 application of PVP-I or other antiseptics within decolonization regimes may provide
13 much-needed avenues for MRSA infection control within NHs.

14 ***Focus area 2: chronic wound management in NHs***

15 Chronic, non-healing wounds include vascular leg ulcers, diabetic foot ulcers,
16 and pressure ulcers [64]. As wound healing slows with age, elderly NH residents
17 constitute the age group most susceptible to development of chronic wounds [65]
18 and a subsequent decline in quality of life [66]. NH residents are particularly at risk of
19 developing pressure injuries that progress into an open wound; in European studies
20 of NHs, pressure ulcers comprised 46–50.5% of all chronic wounds [67, 68]. Open
21 wounds may subsequently become colonized with bacteria [69], causing additional
22 complications.

23 MRSA is estimated to be present in 7–30% of chronic wounds, and may enter
24 the bloodstream causing severe illness [70]. One of the most important factors

1 affecting chronic wound healing, is the presence of a biofilm, which can cause
2 chronic wounds to be locked in an inflammatory state and may increase the
3 likelihood of infection [64]. In one analysis, 60% of chronic wounds had a biofilm
4 versus 6% of acute wounds [71]. Mature biofilms in chronic wounds exhibit an
5 enhanced tolerance to many antimicrobial agents, including antibiotics and
6 antiseptics [64, 72, 73].

7 *Current recommendations for treatment of chronic wounds in NHs*

8 In order to minimize antibiotic resistance, systemic antibiotics are not
9 recommended for treatment of chronic wounds [74]. However, a combination of
10 systemic antibiotics and topical antiseptics is recommended in cases of systemic
11 infections, such as sepsis [75]. Antiseptics are preferable to topical antibiotics for
12 treating chronic wounds due to their lower risk of developing bacterial resistance [74,
13 75].

14 Antiseptics should be used to cleanse infected wounds, and on wounds
15 harbouring a biofilm and/or with excessive exudate, debris, or necrotic tissue in the
16 wound bed (Table I). Recommendations for biofilm treatment describe a window of
17 opportunity following initial wound debridement, where the biofilm is susceptible to
18 effective treatment, specifically antiseptics [64, 76]. In a retrospective study of
19 154,644 patients, increased frequency of debridement was significantly associated
20 with improved healing outcomes in chronic wounds, supporting the use of this
21 'treatment window' [77].

22 In NHs, the antiseptic of choice for chronic wounds should: possess rapid and
23 broad-spectrum antimicrobial activity; not induce bacterial resistance or cross-
24 resistance; have potent antibiofilm efficacy; be effective in the presence of organic

1 material; and promote wound healing (Table I) [64, 72, 78-103]. Each of these areas
2 are discussed in greater detail below and in Supplementary Table S1.

3 *Antimicrobial activity*

4 PVP-I possesses a broader antimicrobial spectrum than CHG, silver, and PHMB [64,
5 104]. PVP-I and CHG have also demonstrated rapid antimicrobial activity, however
6 silver and PHMB have not [64, 79, 87, 105, 106].

7 *Bacterial resistance*

8 There are no reports of bacterial resistance or cross-resistance arising in
9 response to PVP-I exposure [60]. Many data exist on bacterial resistance to CHG
10 and silver, including in species commonly found in chronic wound biofilms, such as
11 *S. aureus*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, *Klebsiella*
12 *pneumoniae* and MRSA [64, 78, 80, 86, 93]. In addition to the concern of bacterial
13 resistance, cross-resistance to colistin, ceftazidime, sulfamethoxazole, and
14 imipenem has been described for CHG [54, 55]. Prolonged exposure of MRSA to
15 PHMB *in vitro* has been associated with reduced susceptibility to PHMB and
16 daptomycin [107].

17 *Activity against biofilms*

18 PVP-I has potent antibiofilm activity across a wide range of bacterial species
19 commonly found in chronic wounds (Supplementary Table S1) [81, 82, 87]. In an *in*
20 *vitro* assessment of PVP-I, CHG, and PHMB, PVP-I was the only antiseptic to
21 completely eradicate both *S. aureus* and *P. aeruginosa* biofilms at 15-minute
22 exposures [79]; while CHG was effective in eradicating *S. aureus* biofilms in this
23 study, lower efficacy was observed in a chronic wound biofilm model [79, 83]. In a
24 multispecies biofilm including *K. pneumoniae*, *P. aeruginosa*, and *S. aureus*, only *S.*

1 *aureus* was reduced below detection levels by CHG, indicating limited efficacy in this
2 setting [93]. In a separate *in vitro* study, PHMB was found to be as effective as CHG
3 in reducing the total amount of *P. aeruginosa* biofilm in artificial wound fluid [86]. In
4 an *in vitro* study of mature, multispecies biofilms, PVP-I, but not silver, significantly
5 reduced the amount of bacteria present [82]; no significant difference was observed
6 between the silver dressing and an unimpregnated control dressing [82], suggesting
7 the silver concentration in dressings may be inadequate to treat chronic wounds [86].
8 In a study using a basal perfusion biofilm model, at 7-day exposures, PVP-I was
9 more effective in reducing multispecies biofilms of *P. aeruginosa*, *B. fragilis*, *S.*
10 *pyogenes*, and MRSA than PHMB and silver [84]. Both PVP-I and PHMB eradicated
11 *S. pyogenes*, however silver did not [84].

12 *Efficacy in the presence of organic material*

13 For maximum efficacy in treating chronic wounds, it is important for the
14 antiseptic to have limited inactivation by organic material. The efficacy of PVP-I is not
15 adversely affected in the presence of albumin or blood [104, 108-110]. However, the
16 antimicrobial activities of CHG, PHMB, and silver are reduced in the presence of
17 organic material, relative to PVP-I [103, 108].

18 *Wound healing*

19 PVP-I has demonstrated the ability to promote wound healing in animal studies,
20 clinical studies, and *in vitro* (Supplementary Table S1) [78, 86]. In animal studies,
21 PVP-I increased expression of transforming growth factor beta, promoted
22 neovascularization and re-epithelialization, and simulated wound healing in MRSA-
23 infected skin ulcers [78, 86]. In clinical studies, PVP-I increased healing rates of
24 chronic leg ulcers and exhibited anti-inflammatory effects [90, 91]. CHG has also
25 demonstrated the ability to improve healing of full-thickness skin wounds in rats [95].

1 In an animal study, PHMB demonstrated favourable effects on angiogenesis, re-
2 epithelialization, and blood flow with slight lymphocyte infiltration [99]. Despite
3 evidence of healing effects, CHG and PHMB may cause irritation and inflammation,
4 respectively, which could impact wound healing [96, 100]. Silver dressings inhibited
5 re-epithelialization of wounds in both animal and *in vitro* models [102].

6 *Focus area 2: summary and recommendations*

7 A recent algorithm for the treatment of chronic wounds with critical
8 colonization and/or biofilm recommends a process of mechanical washing with
9 antiseptic solution (PVP-I), debridement, and disinfection with antiseptic (PVP-I)-
10 soaked gauze [64]. It is hoped that widespread uptake and implementation of such
11 processes within NHs will overcome some of the challenges associated with the use
12 of other antiseptics, and improve healing outcomes for patients.

13 ***Focus area 3: oral care in NHs***

14 The elderly population is markedly at risk of more dental problems, such as
15 dental caries and periodontal issues, compared with younger individuals [111]. In our
16 experience, once elderly individuals are admitted to a NH, the frequency of their
17 dental appointments decreases. A 'three interlocking gears' theory has demonstrated
18 that a lack of oral care in NHs may arise through complex interactions affecting
19 caregivers' and residents' behaviours surrounding oral health [112]. Understanding
20 these obstacles surrounding oral care in the elderly may prevent the consequences
21 of poor oral health, improving the quality of life of residents [112].

22 In the NH population, poor oral health has been associated with poor overall
23 health and psychological wellbeing, malnutrition, and mortality [113]. In a study of
24 oral care in NH residents in Japan, those who had their teeth cleaned by

1 toothbrushing and sometimes swabbing with PVP-I had lower occurrences of
2 pneumonia and improvements in daily life [114]. Good oral hygiene of both natural
3 dental tissue and prostheses is important for acceptable oral-health-related quality of
4 life [115].

5 Poor oral care may lead to periodontitis: an infectious and inflammatory oral
6 disease with an adverse impact on systemic health [116]. In susceptible individuals,
7 dysbiosis of the periodontal microbiota can trigger a pathogenic state, causing oral
8 disease [116]. The resulting tooth-associated biofilm may cause respiratory
9 infections, due to the aspiration of bacteria [117]. As aspiration of bacteria is a major
10 cause of pneumonia in NH residents [116], the pathogenic state of periodontitis is
11 likely to increase this risk [117].

12 The oral cavity is also believed to play a role in SARS-CoV-2 transmission [118,
13 119], and healthcare staff providing oral care to NH residents are at risk of viral
14 transmission from residents this way [120]. In patients with COVID-19, periodontitis
15 is associated with higher risk of intensive care unit admission, need for assisted
16 ventilation, and death [121]. Hence, control of oral viral load and hand hygiene is
17 critical to reduce transmission between healthcare staff and residents, and to
18 ameliorate the risk of morbidity and mortality associated with periodontitis.

19 *Practical recommendations for oral care in NHs: oral hygiene*

20 Periodontal disease can be treated with good oral hygiene: use of electric
21 toothbrushes [122], interdental brushes [123], scaling and debridement, antiseptic-
22 containing mouthwash, and cleaning of oral prostheses with antiseptics. In our
23 experience, antiseptic mouthwash should be used at the beginning of dental
24 treatments, after debridement, and, depending on the efficacy of mechanical
25 cleaning, may be used during maintenance of oral health for both natural dental

1 tissue and prostheses (Table I). Findings from treatment of intubated patients with
2 antiseptic mouthwashes also suggest antiseptics may have a limited effect if dental
3 plaque is established and not debrided [124]. Therefore, debridement and
4 subsequent antiseptic mouthwashing may prevent biofilm formation and aspiration of
5 oral bacteria [124].

6 In NHs, post-prandial cleaning of residents' teeth by toothbrushing and weekly
7 professional dental care (including swabbing with PVP-I when necessary) resulted in
8 a significant reduction in pneumonia and death from pneumonia [114, 125]. Wearing
9 dentures during sleep has been shown to increase oral inflammation and microbial
10 burden and double the risk of pneumonia in the very elderly [126], reinforcing the
11 need to clean oral prostheses with antiseptic solution.

12 *The role of antiseptics for oral health maintenance*

13 CHG is currently one of the most widely used antimicrobial agents in dental
14 practice [127], however PVP-I may provide advantages for oral care in NHs [128].
15 CHG mouthwash is recommended as an adjunct strategy for early periodontitis and
16 has demonstrated reduction of gingivitis in patients with mild gingival inflammation
17 after 4–6 weeks of use [129]. PVP-I has been assessed in periodontitis management
18 [128]: PVP-I oral rinsing, in addition to scaling and root planning, significantly
19 enhanced the probing pocket depth reduction in patients with chronic periodontitis
20 [130]. In patients with advanced destructive periodontitis, topical application of PVP-I
21 improved gingival conditions when used in conjunction with mechanical debridement
22 [131].

23 An ideal antiseptic for management of oral care in NHs should be effective
24 against a broad spectrum of common oral pathogens without risk of resistance,
25 reduce the risk of periodontal disease, leave dental tissue and prostheses unstained

1 after use, and should not be inhibited by blood and/or pus (Table I) [128]; each of
2 these attributes is addressed below.

3 *Efficacy and resistance*

4 PVP-I oral products have demonstrated efficacy against more clinically relevant
5 oral pathogens than CHG mouthwash *in vitro* (Supplementary Table S2) [132]. In a
6 clinical study, CHG oral rinse did not reduce incidence of aspiration pneumonia,
7 suggesting lack of efficacy in reducing the periodontal reservoir of pathogenic
8 bacteria [133]. Conversely, application of PVP-I to an artificial biofilm comprised of
9 *Porphyromonas gingivalis* and *Fusobacterium nucleatum*, two periodontal
10 pathogens, demonstrated suppression of these bacteria at concentrations used for
11 daily oral rinses, indicating a clinical use for PVP-I in subgingival biofilm control
12 [134]. Further data are available supporting the use of PVP-I as a component in a
13 rinse with hydrogen peroxide to decrease levels of gingivitis-associated biofilms
14 [135]. While no microbial resistance to PVP-I has been reported to date [60],
15 tolerance of multispecies oral biofilms to CHG has been observed [136]. In another
16 study, after one oral rinse with CHG, oral biofilms presented with significantly higher
17 resistance to CHG than in a control salivary microbiome [137].

18 *Staining*

19 Staining of dental tissue is common in individuals using CHG long-term [138],
20 and newer formulations require an anti-discolouration system to reduce staining
21 [139]. Prolonged use of PVP-I mouthwash has not been shown to stain teeth, cause
22 irritation, affect thyroid function, or cause a change in gustatory function [138, 140,
23 141].

24 *Inhibition by organic materials*

1 As previously discussed, CHG activity is reduced in the presence of organic
2 matter compared with PVP-I activity [104, 108-110, 142]. Thus, PVP-I may be a
3 more appropriate choice for use within oral care regimens for NH residents.

4 *Oral care and viral transmission: lessons from the COVID-19 pandemic*

5 Regular use of antiviral mouth rinses is recommended to decrease the SARS-
6 CoV-2 viral load in droplets emitted by COVID-19 patients [119, 120, 127, 143, 144].
7 The use of PVP-I has been proposed as a pre-treatment preparation for all
8 individuals requiring dental treatment during the COVID-19 pandemic [120].

9 PVP-I has superior virucidal activity compared with CHG [120, 145, 146]. There
10 are limited data demonstrating the virucidal activity of CHG against coronaviruses,
11 and some studies demonstrated that CHG is ineffective at reducing oral viral load
12 and inactivating some coronavirus subtypes, including SARS-CoV-2 [118, 146-149].
13 In a randomized controlled trial evaluating the efficacy of PVP-I, CHG, and
14 cetylpyridinium chloride in reducing salivary SARS-CoV-2 viral load, cetylpyridinium
15 chloride and PVP-I significantly decreased salivary load compared with water
16 mouthwashing in patients with COVID-19 [144]. No significant decrease in salivary
17 SARS-CoV-2 viral load was seen with CHG when compared with water
18 mouthwashing [144]. When comparing PVP-I and hydrogen peroxide in the
19 inactivation of salivary SARS-CoV-2, PVP-I oral rinse completely inactivated the
20 virus at concentrations of 0.5%, 1.25%, and 1.5% after 15- and 30-second
21 exposures [150]; at concentrations of 1.5% and 3.0%, hydrogen peroxide showed
22 minimal virucidal activity after the same exposure times [150].

23 *Focus area 3: summary and recommendations*

1 Collectively, these data suggest that PVP-I fulfils the criteria of an ideal
2 antiseptic for management of general oral health in NHs (Table I). PVP-I has
3 demonstrated rapid *in vitro* virucidal activity against SARS-CoV-2 as a gargle and
4 mouthwash product [151, 152] and also as an antiseptic solution, skin cleanser, and
5 throat spray [152]. Hence, PVP-I may be valuable in NH protocols for control of oral
6 viral load and hand hygiene [152].

7 **Conclusions**

8 NHs are an important component of the health service for the elderly
9 population. However, they are ideal environments for induction and transmission of
10 infections. Antiseptics provide advantages versus antibiotics for infection
11 management in NHs, especially in the management of MRSA decolonization and
12 chronic wounds. While many antiseptics have demonstrated efficacy in some areas
13 of infection management in NHs, PVP-I appears to fulfil the characteristics of the
14 ideal antiseptic for MRSA decolonization, chronic wound care, and oral care. PVP-I
15 may also play an important role in controlling COVID-19 infections in NHs.

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3 The data underpinning this narrative review were obtained from the published
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12 **Authors' contributions**

13 All authors contributed to conceptualization and writing (reviewing and editing) the
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13

1 **Table I**

2 Role of antiseptics and their features in infection control in the nursing home

Procedure in nursing home	Role of antiseptics	Essential features of antiseptic used in procedure	Commonly used antimicrobial agent		
			PVP-I	CHG	Mupirocin
MRSA decolonization	Intranasal application of antiseptic and antiseptic bodywash to eradicate MRSA colonization	Activity against MRSA	✓ [62]	✓ [34, 35, 37, 38]	✓ [34-38]
		No development of bacterial resistance or cross-resistance	✓ [60]		

To be performed when known MRSA carriers enter the nursing home and when a nursing home resident tests positive for MRSA

Activity against antibiotic- and antiseptic-resistant strains of MRSA

✓ [57-60]

Chronic wound care

Antiseptics to be used:

- to cleanse wounds presenting with signs and symptoms of infection (critical colonization or local infection), and in patients with a history of recurrent wound infections

Rapid antimicrobial activity

Broad spectrum of antimicrobial activity

PVP-I

CHG

Silver

PHMB

✓ [64,

79, 87, 105]

✓ [79,

87, 105]

✓ [64,

81, 82, 87, 104]

< PVP-I

[104]

< PVP-I

[64, 104]

< PVP-I

[64, 104]

- on wounds that may harbour a biofilm	No development of bacterial resistance or cross-resistance	✓ [60]			
- on wounds with excessive exudate, debris, or necrotic tissue in the wound bed	Effective in the presence of organic material (e.g. blood)	✓ [88, 104, 108, 110]	< PVP-I [88, 108]	< PVP-I [88, 108]	< PVP-I [88, 108]
- as an adjunct to systemic antibiotics in patients who have signs of spreading wound infection					

Oral care

Antiseptics to be used:

		PVP-I	CHG
- in a mouthwash product as an adjunct to toothbrushing and professional oral care for the maintenance of good oral health	Broad spectrum of antimicrobial activity against oral pathogens	✓ [132]	< PVP-I [132]
	No development of bacterial resistance or cross-resistance	✓ [60]	
	Reduces risk of periodontal disease	✓ [130, 131]	✓ [129]

- for the cleaning of oral prostheses such as dentures or implants	Leaves oral tissue and prostheses unstained	✓ [140, 141]	
	Effective in the presence of organic material (e.g. blood)	✓ [88, 104, 108, 110]	< PVP-I [88, 104, 108, 110]

1 **Abbreviations:** CHG, chlorhexidine; MRSA, meticillin-resistant *Staphylococcus aureus*; PHMB, polyhexanide; PVP-I, povidone-

2 iodine.

3 Table content is based on information provided in the main text

4 < PVP-I, less effective than PVP-I.

5

6