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A systematic review
Topical treatment for controlling malignant wound odour

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The prevalence of malignant wounds is currently unknown. However, it is estimated that around 5%–10% of breast cancer cases, sarcomas and melanomas result in malignant wounds. This article describes a study which identified and analysed the scientific evidence on the use of topical treatments for controlling odour from malignant wounds.

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ABSTRACT

Background

The prevalence of malignant wounds (MWs) is currently unknown. However, it is estimated that around 5%–10% of breast cancer cases, sarcomas and melanomas result in MWs.

Aim

This study aimed to identify and analyse the scientific evidence on the use of topical treatments for controlling odour from MWs.

Methods

We used a PRISMA checklist to systematically review articles in the following databases: PubMed, ProQuest, Science Direct, CINAHL, Wiley, Springer, CANCERLIT and Google Scholar, published from 2011 to 2018. We structured the research questions with the use of PICO elements. Although 111 articles were obtained from the search, only eight articles met the inclusion criteria. We analysed these articles with the aid of a CASP checklist and classified them based on the levels of evidence and recommendation grade.

Results

Among the eight shortlisted articles, four were intervention studies (three RCTs and one non-controlled study), three were case studies and one was a cohort study. The MWs in these articles were predominantly located on the breast, head/neck, cervix, vulva/vagina, groin, spine, lower limbs, penis and rectum/anus. Wound odour was measured using the verbal rating scale (VRS). Six products were used as topical therapies to manage wound odour: Polyhexamethylene biguanide, metronidazole, green tea, Manuka honey, nanocrystalline silver nanoparticles and charcoal dressing. These were associated with level of evidence 2b and recommendation grade B. Further, the charcoal dressing was associated with level of evidence 4 and recommendation grade C.

Conclusions

The following topical therapeutic products for control or management of MW Fodour were of recommendation grade B: polyhexamethylene biguanide, metronidazole, green tea, manuka honey and nanocrystalline silver nanoparticles.

Implications for clinical practice

The topical products discussed in this review can be used for controlling MW odour. Six interventions in the form of topical therapies were identified to reduce wound odour, namely Polyhexamethylene biguanide, metronidazole, green tea, manuka honey and nanocrystalline silver nanoparticles with level of evidence 2b and recommendation grade B. The use of oral metronidazole as topical therapy in wounds is not recommended, because it shows poor results. It is better to use metronidazole gel proved to be effective and safe for reduce bad odour.

INTRODUCTION

Cancer is known as one of the leading causes of death worldwide. Estimates of the global incidence of cancer obtained from the Global Burden Cancer (GLOBOCAN) database show that around 18.1 million new cancer cases and 9.6 million cancer deaths occurred in 2018.[1,2] In 2017, around 1,688,780 cases of cancer were recorded in the United States (US).[3] In Indonesia, the cancer prevalence in 2013 was 347,792 (1.4%).[4] It is also known that cancer can metastasise to the lungs, liver, bones, brain and skin.[5]

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Conflicts of Interest:
None

Malignant wounds are a form of skin metastasis.[6] They often occur when cancerous cells infiltrate the skin, supporting blood vessels and lymph nodes. This in turn leads to loss of vascularisation and tissue death.[10] Malignant wounds are also described as fungating wounds, ulcerative tumours, ulcerative cancer, malignant skin wounds and neoplastic lesions.[7,8] These wounds are cancer-related skin lesions characterised by ulceration and necrosis.[9]

Currently, no accurate data exists on the prevalence of MWs worldwide. However, 5%–10% of MWs are estimated to occur in breast cancer, sarcomas and melanomas.[11,12,6] About 0.6%–9% of MWs occur in patients with advanced stages of cancer who are receiving palliative care.[12] Thus, MW is a serious health problem and efforts for the prevention as well as control of symptoms are required.

Malignant wounds have various symptoms, such as pain, exudate, infection, bleeding and odour.[6] Previous studies have found that the most disturbing symptom of MWs is unpleasant odour and pain.[13] These symptoms interfere with the patients' quality of life.[14] Therefore, comprehensive palliative care is needed for the control of these symptoms.

The latest publication by the European Oncology Nursing Society (EONS) recommends a number of methods and products for controlling infections and odour from MWs. These include wound cleaning and irrigation, debridement, topical application or oral intake of metronidazole, silver dressings, changing dressings (twice a day) and opiate use for pain management during wound care.[15,13,16]

Malignant wounds are known to be associated with the final stages of life for patients with cancer[17] and eliminating or controlling MW odour remains a challenge for nurses when performing wound care. In addition, tools for measuring wound odour are subjective. Few studies have been conducted to determine the best topical treatments for controlling MW odour. The aim of this study is therefore to identify and analyse scientific evidence on the use of topical therapies for controlling MW odour. The study is based on a research design that included malignant wound type, wound odour instruments, and different types of topical therapeutics for controlling this odour. It is important to emphasise that information in the literature regarding interventions to control MW odour was minimal. For this reason, we utilised review articles that contain both study interventions (randomised and non-randomised) and cohort or case studies.

METHODS

We used the PRISMA 2009 checklist to assess the literature.[18] We searched the following databases: PubMed, ProQuest, Science Direct, CINAHL, Wiley, Springer, CANCERLIT and Google Scholar. Research questions were structured using PICO elements (patient, intervention, comparison and outcome)[19,20], as follows: P: patients with malignant wounds, I: topical treatment, C: no comparison, O: control of wound odour. Keywords were based on the databases in the MeSH Term (Figure 1).

Using the PICO method, a research question was formulated as follows: "What topical treatments are used in controlling wound odour in patients with MWs?" We identified 111 articles from eight electronic databases that

Figure 1. Description of keywords used in the literature search using the PICO method (patient, intervention, comparison and outcome)

PICO COMPONENT	
P	Fungating OR malignant OR melanoma, malignant, of soft parts OR neoplasm, malignant OR adenomas, malignant OR adenoma, malignant OR neoplasm OR neoplasm, skin OR skin cancers OR skin cancer OR cancer, skin OR Skin ulcer OR skin ulcers OR ulcer, skin OR ulcers, skin. Infection, wound OR wounds, injury OR wounds and injuries OR wounds and injury OR injury and wounds OR wound OR injury OR injuries, wounds.
I	Biological dressing OR biologic dressing OR dressing OR dressing, occlusive OR silver sulfadiazine OR bandage, hydrogel OR hydrogel OR alginates OR honey OR phosphorylcholine OR gels OR powders OR administration, topical drug OR administration, topical OR anti-bacterial agents. Metronidazole OR nitroimidazole OR 2 methyl 5 nitroimidazole 1 ethanol OR metrogel OR metrogyl OR metronidazole phosphate OR metronidazole hydrochloride OR metrodzhil.
C	No comparison in this literature review
O	Odour OR odours OR smell OR sense of smell OR malodorous OR malodour OR odour OR smelly tumours

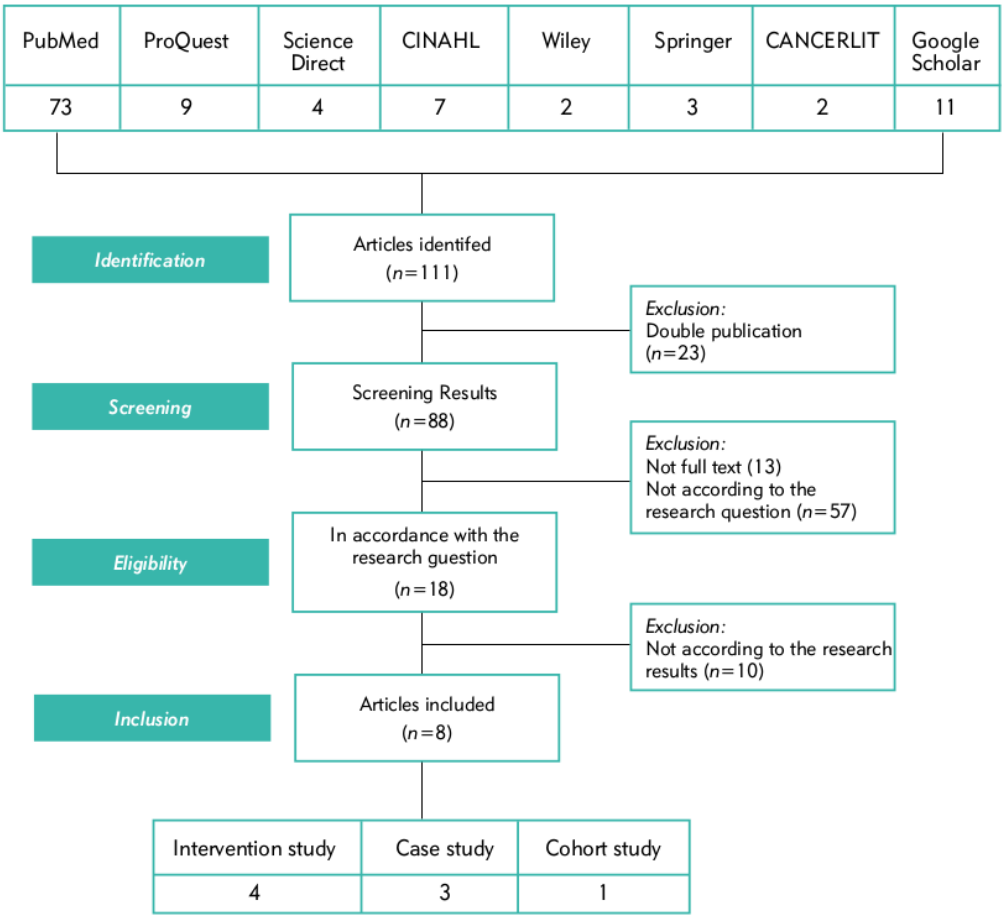

Figure 2. Flowcharts for study selection and inclusion

were published from 2011 to 2018; all these articles were studies conducted with humans as subjects. We excluded 23 articles out of the 111 because of double publications; 13 others were also excluded because they were not complete texts, and another 57 were excluded because they were not relevant to our research objectives.

The criteria for inclusion in our studies were: 1) focus on interventions to control MW odour, 2) English as the language of the manuscript, and 3) published from 2011 to 2018. Of the eighteen articles that met these criteria, ten were not eligible because they not relevant to our research objectives. Thus, only eight articles fulfilled the inclusion criteria, and these were four intervention articles, three case studies and one cohort study. Figure 2 illustrates the study inclusion process.

The articles that fulfilled the inclusion criteria were classified using the Critical Appraisal Skill Program (CASP) checklist21 and critical appraisal from the Center for Evidence-Based Management.[22]

Studies were selected according to the level of evidence, level of recommendation and quality of the study. The level of recommendation is a quality measure associated with the level of research evidence and helps in the interpretation of recommendations. In analysing the quality of clinical studies, the Oxford Centre for Evidence-Based Medicine (CEBM) was employed to classify research articles into five levels of evidence in accordance with their research designs (1, 2, 3, 4 and 5). The studies were grouped into four levels of recommendations (A, B, C and D). Grade A is a level 1 study (1a, 1b and 1c) used for systematic review of randomised clinical trials and representing a higher level of evidence. Grade B (2a, 2b, 2c, 3a and 3b) is used for systematic reviews of cohort studies, outcome

research, systematic reviews of case-control studies and case-control studies. Grade B represents a moderate level of evidence. Values C (4) and D (5) represent the lowest level of evidence. Grade C is used for case studies, and Grade D is for expert opinion.[23]

RESULTS

Research design

In this systematic review, eight articles were identified that fitted the objectives set for our research. These articles were mainly about clinical studies that used topical therapeutics in controlling MW odour. There were four intervention studies, which were made up of three randomised controlled trials (RCTs)[8,24,25] and one non-controlled study[26]; further, there were three case studies[27,28,29] and one cohort study.[30]

Malignant wound type

The types of MWs varied for each study that used topical therapeutics in managing wound odour. Castro and colleagues found that MWs were predominantly located on the lower limbs (n = 12; 50.0%), followed by the head and neck (n = 6; 25.0%), breast (n = 3; 12.5%), penis (n = 2; 8.3%) and hypochondrium (upper abdomen, inferior to the thorax, and underneath the lower rib cage) (n = 1; 4.2%).[8] In another study, Watanabe and colleagues examined patients with breast cancer (n = 21; 100%) and found MWs on all the patients examined.[26] Lian and colleagues found MWs located on the breast (n = 24), neck (n = 2), groin (n = 2), spine (n = 1) and anus (n = 1).[24] In addition, Lund-Nielsen and colleagues examined breast cancer (n = 55; 80%), head and neck cancer (n = 8; 12%) as well as other cancer-related diagnoses (n = 6; 8%).[25]

Results for a case study by Haynes included the following: foot vein ulcer (n = 2), pressure ulcer (n = 2), fungating tumour (n = 2), fungating breast wound (n = 1), metastasis (n = 1), squamous cell cancerous buttock (n = 1) and arterial leg ulcer (n = 1).[29] In another study, Drain and Fleming examined one case of squamous cell carcinoma of the oral cavity.[27] Similar to Fleming's work, Wong and colleagues examined one case with a MW on the right arm.28 Meanwhile, a cohort study conducted by George and colleagues identified 179 patients with malodour related to necrotic cancer. The locations of these patients' MWs were as follows: cervix (n = 80; 44.7%), head and neck (n = 71; 39.7%), breast (n = 6 3.5%, rectum/anal (n = 5; 2.8%), vulva/vagina (n = 4; 2.2%) and others (n = 13; 7.3%).[30]

Odour Wound Instrument

With regards to the measurement of wound odour, four studies did not report how they assessed wound odour.[27,28,29,30] Three studies used verbal rating scale (VRS) instruments for the measurement of wound odour. Lund-Nielsen and colleagues used VRS instruments from Haughton and Young (1995)[31], and reported their results in 4 categories as follows: 1 = no malodour, 2 = slight malodour, 3 = moderate malodour and 4 = strong malodour.[25] Lian and colleagues, however, used a verbal numeric scale (VNS) with a range of 0–10 (0 = odourless and 10 = the worst smell imaginable).[24] Another study conducted by Watanabe and colleagues used a scale range of 0–4 (0 = no smell; 1 = smell present but not offensive, slight smell close to the ulcer about 20 cm; 2 = mildly offensive smell, more pronounced smell close to the ulcer about 20 cm; 3= moderately offensive smell, at the bedside about 1 m; 4 = extremely offensive smell, at the entrance of the room).[32]

One study assessed odour intensity, quality and impact. To assess the intensity, 5 scales were used as follows: 0 = no odour, 1 = odour is detected only after removing the bandage, 2 = smell is felt when approaching the patient, 3 = odour detected when entering the room and 4 = odour detected before entering the room. For odour quality, 5 scales were used: 0 = no odour, 1 = smell is felt but not offensive, 2 = smell is felt and is slightly offensive, 3 = smell is felt and moderately offensive, and 4 = smell is perceived as extremely offensive. In addition, to assess the impact of odour, the respondents showed the effect of the odour by choosing 1 or more of 5 reactions: 1 = the smell is being detected, 2 = worry that other people are realising the smell, 3 = the patient is reluctant to socialise because of the smell, 4 = odour negatively affects the appetite and 5 = nausea because of the smell. Furthermore, the odour effect was assessed later on according to the number of reactions chosen by the patient: 0 score indicated all registered descriptions are selected; 1 for 4 selected descriptions; 2 for 3 selected descriptions; 3 for 2 selected descriptions; 4 for 1 selected description; and 5 if no description is selected.[8]

Types of topical malignant wound treatments and duration of interventions:

a. Polyhexamethylene biguanide (0.2%) as well as metronidazole (0.8%) can significantly reduce the smell of malignant wounds in 4 days (p value of each intervention was <0.001 with level of evidence 2b and recommendation grade B).[8]
b. Metronidazole (0.75%) gel proved effective and safe for reduce bad odour in anaerobic bacteria-infected neoplastic fungating tumours during 14 days of treatment, with clinical success rates (score 0 or 1) of 95.2% (20 of 21 patients); the 90% confidence interval (exact two-tailed significance level) was 79.3%–99.8%, thus confirming the research hypothesis, which suggested that the success rate must not fall below 70% if the level of evidence was 2c and recommendation g rade was B.[32]
c. Green tea dressings and metronidazole topical powder

Topical Intervention	Citations in Studies	Levels of evidence	Grade of Recommendation
Polyhexamethylene	1	2b	B
Biguanide	4	2b	B
Metronidazole	1	2b	B
Green tea	2	2b	B
Manuka honey	2	2b	B
Nanocrystalline silver coated	1	4	C
Charcoal			

Table 1. Synthesis of evidence regarding topical treatment for controlling MW odour.

were effective in controlling the smell of malignant fungating wounds, and this treatment was carried out for 7 consecutive days. With level 2b of evidence and recommendation grade B24, malodour control was better when metronidazole treatment was used. Outcomes were poor during the period when only topical or intermittent oral metronidazole was used. Topical use gradually decreased (97% vs 55%) and the proportion of patients receiving maintenance oral metronidazole increased (0% in 2003–2004 vs 93% in 2011). Concurrently, there was a reduction in documented malodour (12.5% of visits per patient in 2003–2004 vs 1.5% in 2011, p<0.01).[30]

d. Honey-coated and silver-coated bandages were effective for treating MW odour for a period of 4 weeks, with level of evidence 2b and recommendation grade B.[25] A case study conducted by Wong and colleagues used silver dressings and manuka honey to control MW odour. In this study, the level of evidence was 4 and recommendation grade was C.[28]
e. Activated charcoal dressings have also proven effective and comfortable in managing wound odour with level of evidence 4 and recommendation grade C.[29] However, the duration of this intervention was not stated in this article.

DISCUSSION

Overall, six intervention products were identified as topical therapeutics for controlling MW odour: Polyhexamethylene biguanide, metronidazole, green tea, manuka honey and nanocrystalline silver nanoparticles. These products were associated with level of evidence 2b and recommendation grade B. Charcoal dressing was associated with level of evidence as 4 and recommendation grade C.

Metronidazole was discussed in four studies with level of evidence 2b and recommendation grade B. Previously, researchers found that anaerobic bacteria cause malodour in fungating wounds and that metronidazole is an effective antibacterial drug in treating fungating, bad-smelling wounds.[33] It is a synthetic antimicrobial drug, which is very effective against anaerobic bacteria and protozoa.[34] Some metronidazole products, such as topical metronidazole 0.8%, metronidazole gel 0.75%, and metronidazole topical powder, were found to be effective.[8,32]

A 0.8% metronidazole topical solution reduced MW odour in 4 days, and the patient's quality of life improved as their wound odour was controlled.[8] In addition, using 0.75% metronidazole gel (applied 1-2 times/day for 14 days) proved to be effective and safe for reducing malodour from anaerobic bacteria-infected neoplastic fungating tumours.[32] In another study, the use of metronidazole topical powder for seven days controlled the smell of malignant fungating wounds.[24] However, a study that used a retrospective case note review stated that topical use of oral metronidazole showed poor results, but when metronidazole is used appropriately, it has better malodour control.[30] Therefore, the use of metronidazole topical powder should be considered as a topical treatment for MW.

Polyhexamethylene biguanide (PHMB) 0.2% showed no significant difference in comparison with 0.8% metronidazole topical solution in controlling MW odour for 4 days.[8] In addition, green tea dressings applied for seven days can be used to control MW odour.[24] Other effective interventions include manuka honey and nanocrystalline silver nanoparticles. Factors to consider when selecting a treatment for MW odour include wound size, level of cleanliness, exudation, foul odour and wound pain[25] with the level of evidence was 2b and recommendation grade was B. Manuka honey is also proven to be safe and effective as a palliative treatment for reducing odour and inflammation in wounds secondary to squamous cell carcinoma of the oral cavity.[27] Likewise, silver dressings can be considered in managing chronic fungating wounds. This intervention is applied with the concept of "TIME" (T-Tissue management, I-Inflammation and infection control, M-Moisture balance, E-Epithelial advancement).[28]

Charcoal dressings contain activated carbon incorporated into a dressing, which is protected by viscose and polyamide rayon layers. However, one systematic review found that the level of evidence for activated carbon dressing was 2c while its recommendation grade was B.[33]

Products including charcoal consist of activated carbon. Activated carbon is usually made from natural sources such as rice, coconut shells or other types of wood; this material provides a large area for the adsorption of various types of gases, bacteria and liquids.[35] Activated carbon has been used in various biomedical applications.[36] These dressings contain 85%–88% charcoal cloth active carbon.[35] Some products can be used in combination with antibiotics or as primary dressings to neutralise the bacteria captured in the charcoal.[37]

Six interventions were identified for topical treatment to control odour in MW. Polyhexamethylene biguanide, metronidazole, green tea, manuka honey and nanocrystalline silver nanoparticles. These were associated with level of evidence 2b and recommendation grade B. Charcoal Dressing is associated with level of evidence 4 and recommendation grade C (Table 1).

Our aim of identifying evidence for controlling MW odour has been achieved. However, our review has some limitations including few available RCTs, small sample sizes and absence of instruments or scales to measure odours objectively. Odour perception is induced by stimulation of chemicals sensory receptor; thus, odour perception differs from person to person.[38] For this reason, an objective tool or measurement for measuring wound odour is necessary.

CONCLUSION

Among the eight shortlisted articles, four were intervention studies (three RCTs and one non-controlled study), three were case studies and one was a cohort study. The MWs in these articles were predominantly located on the breast, head/neck, cervix, vulva/vagina, groin, spine, lower limbs, penis and rectum/anus. Wound odour was measured using the verbal rating scale (VRS).

In the literature search, we identified eight clinical studies using topical therapies for controlling odour in MW. Six interventions in the form of topical therapies were identified for namely Polyhexamethylene biguanide, metronidazole, green tea, manuka honey and nanocrystalline silver nanoparticles with level of evidence 2b and recommendation grade B. Charcoal Dressing produces level 4 evidence and has a recommendation grade C.

Some of the main limitations of our study are the limited availability of RCTs on MW odour control, small sample sizes and absence of instruments or scales to measure MW odour objectively.

IMPLICATIONS FOR CLINICAL PRACTICE

The topical products discussed in this review can be used for controlling MW odour. Six interventions in the form of topical therapies were identified to reduce wound odour, namely Polyhexamethylene biguanide, metronidazole, green tea, manuka honey and nanocrystalline silver nanoparticles with level of evidence 2b and recommendation grade B. The use of oral metronidazole as topical therapy in wounds is not recommended, because it shows poor results. It is better to use metronidazole gel proved to be effective and safe for reduce bad odour. ■

Table 2. Description of studies on topical treatment for odour control in malignant wounds

RESEARCHER, COUNTRY	RESEARCH DESIGN	AIM	SAMPLE SIZE
Castro, Santos and Woo (2018), Brazil	RCT	To compare the effect of polyhexamethylene biguanide 0.2% with metronidazole 0.8% on malignant wound odour, quality of life and pain during application	Randomly 24 participants malignant wounds were divided into 2 groups (12 in each group)
Watanabe et al (2016), Japan	Multicentre, open-label, non-controlled, phase III study	To evaluate the effectiveness and safety of metronidazole gel 0.75% in reducing malodour in anaerobic infected neoplastic fungating tumours	21 participants

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	INTERVENTION	EVALUATION OF ODOUR WITH INSTRUMENTS	OUTCOME
	Intervention Group: using polyhexamethylene biguanide 0.2% Control group: using metronidazole 0.8% topical solution. Treatments were carried out for 0 days, 4 days and 8 days	Smell was measured in terms of intensity, quality and impact, which was assessed by researchers, nurses and patients	Significantly, polyhexamethylene biguanide 0.2% and metronidazole 0.8% can reduce malignant wound odour in 4 days. Thus, the patient's quality of life increases due to controlled wound odour. Meanwhile, pain measurements between the 2 groups did not show a significant difference over time
	Metronidazole gel 0.75% was applied 1-2 times / day, up to a maximum daily dose of 30 g for 14 days Fungating wounds were thoroughly cleaned and covered with dressings such as gauze, silicone gauze or wound dressing coated with topical metronidazole	The smell of wounds was assessed by researchers, nurses and patients using 5 scales (0-4)	Metronidazole gel 0.75% is an effective and safe treatment for reducing bad odour in anaerobic infected neoplastic fungating tumours

Table 2. Description of studies on topical treatment for odour control in malignant wounds

RESEARCHER, COUNTRY	RESEARCH DESIGN	AIM	SAMPLE SIZE
Lian, Xu, Goh and Aw (2014), Singapore	Prospective randomised experimental study	To compare the effectiveness of green tea with metronidazole topical powder regarding the level of malodorous score reduction using the verbal numeric scale (VNS)	Randomly 30 participants with fungating malignant wounds were divided into 2 groups (12 in each group)
Lund-Nielsen, Adamsen and KoMWos (2011), Denmark	RCT	To determine the effect of honey-coated bandages compared with silver-coated bandages in the treatment of malignant wounds, looking at the size of the wound, the cleanliness, odour, exudation and wound pain	Randomly 69 cancer patients with malignant wounds were divided into 2 groups (group A: 34, group B: 35)
Drain and Fleming, (2015), USA	Case Study	To evaluate the effectiveness of manuka honey in an 80-year-old woman suffering from malodorous squamous cell carcinoma of the mouth	An 80-year-old woman with squamous cell carcinoma in the oral cavity was treated in a nursing home. The patient was experiencing distress associated with extreme malodour
Wong, Brahim, Aminuddinand Nasiruddin (2017), Malaysia	Case Study	To evaluate bad odour fungating wound management with silver coated nanocrystalline dressings	A 68-year-old woman with a four-year history of bad-odour related to wounds on her right arm
Haynes (2018)	Case Study	To assess the clinical effects and comfort of charcoal dressings in the management of wound odour	10 patients with: leg vein ulcer (n = 2), pressure ulcer (n = 2), fungating tumour (n = 2), fungating breast wound (n = 1), metastasis (n = 1), squamous cell cancer of the buttock (n = 1), arterial leg ulcer (n = 1)
George et al (2017), India	Cohort study	To explore the effectiveness of topical or oral metronidazole for malodour in necrotic cancer and to propose a protocol for the use of metronidazole in MW malodour management	179 patients with malodour in necrotic cancer

	INTERVENTION	EVALUATION OF ODOUR WITH INSTRUMENTS	OUTCOME
	Each group of patients was treated for 7 consecutive days using randomised dressings Intervention Group: Using green tea solution. Meanwhile, the control group received the conventional method with metronidazole topical powder	Verbal Numeric Scale (VNS) scale 0-10	No significant difference found between green tea dressings and metronidazole topical powder in controlling the smell of malignant fungating wounds
	Using modern wound care: Cleaning with water faucet and soap liquid (pH 4.5) and continued with the help of tweezers, metzenbaum scissors and non-woven pads Group A: Honey-coated bandages, absorbent dressings and foam bandages Group B: Nanocrystalline silver-coated bandages and foam bandages The intervention was carried out for 4 weeks	Verbal Numeric Scale (VNS) scale 0-10	No statistically significant differences between groups. Namely, honey-coated and silver-coated bandages were both effective for the treatment of MWs. Factors considered were wound size, cleanliness, exudation, bad odour and wound pain in malignant wounds
	Calcium alginate infused with Manuka honey was applied to external wounds and Manuka honey paste was applied twice daily in the oral cavity using a stick Manuka honey paste was chosen for mouth sores due to its good viscosity	Not mentioned	Manuka honey is proven to be a safe and effective palliative treatment for reducing odour and inflammation in wounds secondary to squamous cell carcinoma of the oral cavity
	Wounds were assessed using the concept of "TIME" (T-Tissue management, Inflammation and infection control, M-Moisture balance, E-Epithelial advancement) The wound was cleaned with distilled water. Hydrogel was applied to soften the slough then coated with silver antimicrobial nanocrystalline. The dressing was placed at the base of the wound, detached from its side and moistened with distilled water. Then it was covered with sterile gauze	Not mentioned	Silver dressings can be considered in managing chronic fungating wounds if other conventional methods do not lead to any improvement
	The dressings used in this clinical evaluation were activated charcoal dressings, which are protected by viscose and polyamide rayon layers	Not mentioned	Charcoal dressings where effective and comfortable in managing wound odour
	179 patients with malodour in necrotic cancer	Not mentioned	This study showed better malodour control when metronidazole was used. However, the results were poor during the intermittent period when using only topical oral metronidazole Topical use gradually decreased (97% vs 55%) and the proportion of patients receiving oral metronidazole treatment increased (0% in 2003–2004 vs. 93% in 2011) There was a reduction in malodour (12.5% of visits per patient in 2003-2004 vs. 1.5% in 2011, $p < 0.01$)

Table 3. Critical Appraisal

NO	CRITICAL APPRAISAL INTERVENTION STUDY (21)	CASTRO ET AL (2018)	WATANABE ET AL (2016)	LIAN ET AL (2014)	LUND-NIELSEN ET AL (2011)	
1	Did the trial address a clearly focused issue?	Yes	Yes	Yes	Yes	
2	Was the assignment of patients to treatments randomised?	Yes	No	Yes	Yes	
3	Were all of the patients who entered the trial properly accounted for in the conclusion?	Yes	Yes	Yes	Yes	
4	Were patients, health workers and study personnel 'blind' to treatment?	Yes	No	No	Yes	
5	Were the groups similar at the start of the trial?	Yes	Yes	Yes	Yes	
6	Aside from the experimental intervention, were the groups treated equally?	No	No	No	No	
7	How large was the treatment effect?	Yes	Yes	Yes	Yes	
8	How precise was the estimate of the treatment effect?	Yes	Yes	Yes	Yes	
9	Can the results be applied to the local population, or in your own context?	Yes	Yes	Yes	Yes	
10	Were all clinically important outcomes considered?	Yes	Yes	Yes	Yes	
11	Are the benefits worth the harms and costs?	Yes	Yes	Yes	Yes	
	Level of evidence; grade of recommendation (23)	2b;B	2b;B	2b;B	2b;B	

	CRITICAL APPRAISAL COHORT STUDY (21)	GEORGE ET AL (2017)	CRITICAL APPRAISAL CASE STUDY (22)	DRAIN AND FLEMING (2015)	WONG ET AL (2017)	HAYNES (2018)
	Did the study address a clearly focused issue?	Yes	Did the study address a clearly focused question / issue?	Yes	Yes	Yes
	Was the cohort recruited in an acceptable way?	Yes	Is the research method (study design) appropriate for answering the research question?	Yes	Yes	Yes
	Was the exposure accurately measured and bias minimised?	Yes	Are the setting and subjects representative with regard to the populationto which the findings will be applied?	No	No	No
	Was the outcome accurately measured to minimise bias?	Yes	Is the researcher's perspective clearly described and taken into account?	Can't Tell	Can't Tell	Can't Tell
	Were any confounding factors in the design and/or analysis been taken into account?	No	Are the methods for collecting data clearly described?	Yes	Yes	Yes
	Was the follow up of subjects complete enough?	No	Are the methods for analysing the data likely to be valid and reliable? Are quality control measures used?	Can't Tell	Can't Tell	Can't Tell
	What are the results of this study?	Yes	Are quality control measures used?	Yes	Yes	Yes
	How precise are the results?	Yes	Was the analysis repeated by more than one researcher to ensure reliability?	Can't Tell	Can't Tell	Can't Tell
	Do you believe the results?	Yes	Are the results credible, and if so, are they relevant for practice?	Yes	Yes	Yes
	Can the results be applied to the local population?	Yes	Are the conclusions drawn justified by the results?	Yes	Yes	Yes
	Do the results of this study fit with other available evidence?	Yes	Are the findings of the study transferable to other settings?	Yes	Yes	Yes
	Level of evidence; grade of recommendation (23)	2b;B	Level of evidence; grade of recommendation (23)	4;C	4;C	4;C

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ORIGINALITY REPORT

%20	%7	%14	%11
SIMILARITY INDEX	INTERNET SOURCES	PUBLICATIONS	STUDENT PAPERS

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