

Medication related osteonecrosis of the jaw: a qualitative study investigating the understanding and knowledge of local oncology clinical nurse specialists

Abstract

Purpose: To explore oncology clinical nurse specialists (CNS) knowledge and understanding of medication related osteonecrosis of the jaw (MRONJ).

Method: A qualitative study involving semi-structured interviews with four oncology CNS and subsequent interpretative phenomenological analysis.

Results: Findings were reported under three themes; the importance of medication related osteonecrosis of the jaw, education on medication related osteonecrosis of the jaw and patient access to dental care. The key aspects highlighted were the important role of the oncology clinical nurse specialists and the need to improve communication and links between medical and dental specialties. A prominent subtheme was the aspiration of the oncology clinical nurse specialists to develop their understanding of medication related osteonecrosis of the jaw.

Conclusions: The study provides new knowledge on oncology clinical nurse specialists understanding of medication related osteonecrosis of the jaw. It reinforces that improvements are to be made when it comes to oncology clinical nurse specialists understanding of oral health problems. It highlights the importance of reinforcing oral health needs as part of the holistic view of patients by the medical specialties and it affirms the valuable role of the clinical nurse specialists.

Keywords: medication related osteonecrosis of jaw, oncology, clinical nurse specialists, oral health

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Andrews LV,¹ Devlin B,² Hall DK,³ Curtin C⁴

¹Community Dental Service, Aneurin Bevan University Health Board, Cwmbran Health Centre, UK

²Keyll Darree Health and Social Care Education & Training Centre, Isle of Man

³Morrison Hospital, Heol Maes Eglwys, UK

⁴University Dental Hospital Wales, UK

Correspondence: Laura Andrews, Community Dental Service, Aneurin Bevan University Health Board, Cwmbran Health Centre, Tudor Road, Cwmbran, NP44 3PJ, UK, Email lauravandrews7@hotmail.co.uk

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Introduction

Ruggiero et al.¹ described medication related osteonecrosis of the jaws (MRONJ) as a patient with:

1. Presence of exposed bone (or bone that can be probed through an intra-oral or extra-oral fistula) in the maxillofacial region over a period of 8 weeks.
2. Current or previous treatment with anti-resorptive or anti-angiogenic agents.

3. No history of radiation therapy to the jaw or obvious metastatic disease to the jaw.

MRONJ lesions can occur in both the mandible and the maxilla with the mandible being most frequently affected.² This most likely occurs due to the restricted blood supply to the mandible, the increased cortical bone in the mandible, high bone metabolism and ready exposure to bacteria through breaches in the thin oral mucosa.² There are many drugs currently associated with MRONJ (Table 1).

Table 1 Medications associated with MRONJ³

Medications associated with MRONJ arranged by type of drug	
Drug Type	Name
Bisphosphonates	Zoelndronic Acid
	Pamidronate
	Risedronate
	Ibandronic acid
	Alendronic acid
	Clodronate

Table Continued...

Medications associated with MRONJ arranged by type of drug	
Drug Type	Name
Tyrosine kinase inhibitors	Sunitinib
	Cabozantinib
	Imatinib
	Sorafenib
	Regorafenib
	Axitinib
	Pazopanib
	Dasatinib
	Methotrexate
	Corticosteroids
Immunosuppressants	Thalidomide
	Rituximab
	Adalimumab
	Ipilimumab
	Infliximab
Selective estrogen modulator receptors (SERM)	Romosozumab
	Raloxifene
Monoclonal antibodies	Bevacizumab
	Denosumab
	Sirolimus
Mammalian target of rapamycin (mTOR)	Temsirolimus
	Everolimus
Radiopharmaceuticals	Radium 223
Fusion proteins	Aflibercept

At present, MRONJ is a relatively uncommon condition with the incidence ranging from 0 to 12%. It is higher in patients treated with bone-modifying agents and anti-angiogenics for the treatment of breast cancer in the adjuvant setting, patients with metastatic bone disease, myeloma and treatment of hypercalcaemia of malignancy.³⁻⁵ These drugs reduce the occurrence of skeletal related events including bone pain, pathological fracture and spinal cord compression.⁶ As the survival rate and time for oncology patients continues to improve, the number of patients taking anti-resorptive and anti-angiogenic drugs is predicted to rise resulting in a subsequent increase of the number of MRONJ cases.⁷ The risk of MRONJ is increased by various risk factors which include type of drug, the disease process for which the drug is being used, duration of treatment, total cumulative dose and dental intervention.³

It has been widely reported that dental extractions and dentures carry the highest risk for the development of MRONJ.⁸ A systematic

review estimated the incidence of MRONJ after tooth extraction in oncology patients as 2.9%.⁹ Several studies report that among patients with MRONJ, tooth extraction is a common predisposing event ranging from 52 to 61%.¹⁰⁻¹² However, MRONJ can occur “spontaneously” without the patient having undergone any recent invasive dental treatment. An emphasis on improving oral health is likely to decrease the probability of tooth removal as well as the necessity of denture use and insertion of dental implants in patients at increased risk of MRONJ.¹³ MRONJ significantly impairs quality of life with an increasing effect with stage severity and it often persists for many years with increased pain, eating discomfort, self-consciousness, poor diet, interrupted meals, irritability and decreased life satisfaction.¹⁴ There are various classifications proposed for MRONJ; however, the American Association of Oral and Maxillofacial Surgeons published in 2014 remains the most widely used and accepted (Table 2).¹

Table 2 American association of oral and maxillofacial surgeons staging and treatment strategies for MRONJ¹

Stage	Description	Treatment
0	No clinical evidence of necrotic bone, but non-specific clinical findings, radiographic changes and symptoms	<ul style="list-style-type: none"> - Systemic management, including the use of pain medication and antibiotics - Antibacterial mouth rinse
1	Exposed and necrotic bone, or fistulae that probes to bone, in patients who are asymptomatic and have no evidence of infection	<ul style="list-style-type: none"> - Clinical follow up on a quarterly basis - Patient education and review of indications for continued BMA or AA therapy - Symptomatic treatment with oral antibiotics
2	Exposed and necrotic bone, or fistulae that probes to bone, associated with infection as evidenced by pain and erythema in the region of the exposed bone with or without purulent drainage	<ul style="list-style-type: none"> - Oral antibacterial mouth rinse - Pain control - Debridement to relieve soft tissue irritation and infection control - Antibacterial mouth rinse
3	Exposed and necrotic bone or a fistula that probes to bone in patients with pain, infection, and one or more of the following: exposed and necrotic bone extending beyond the region of alveolar bone, (i.e., inferior border and ramus in the mandible, maxillary sinus and zygoma in the maxilla) resulting in pathologic fracture, extra-oral fistula, oral antral/oral nasal communication, or osteolysis extending to the inferior border of the mandible or sinus floor	<ul style="list-style-type: none"> - Antibiotic therapy and pain control - Surgical debridement/resection for longer term palliation of infection and pain

The current lack of curative MRONJ treatment options highlights the important role of prevention in reducing the burden of disease. There is some low quality evidence, mainly based on observational studies that dental prevention regimes can decrease the risk of MRONJ.¹⁵⁻²¹ These recommendations stress the importance of oral cavity examination before, during and post therapy and guiding the patient to maintain good dental health and optimal oral hygiene in order to limit the risk of MRONJ.²³

With all this in mind consideration should be placed on how best we can aid patients to understand their MRONJ risk. Clinical nurse specialists (CNS) play a vital role in the delivery of care and support for oncology patients as they have a sympathetic presence, provide individualised advice, and develop strong relationships.²² CNS are in a prime position to aid in the prevention of the development of MRONJ in at risk oncology patients through patient education. To do this however, they need to be empowered with knowledge of MRONJ. A number of published studies have shown a lack of knowledge of MRONJ amongst healthcare professionals (HCPs) although none of these studies examined the knowledge of oncology CNS specifically.²³⁻³⁴ It would be advantageous for the CNS to be well versed on educating the patient on the importance of dental prevention and MRONJ risk reduction prior to commencing anti-resorptive or anti-angiogenic treatments.

Material and method

Design

The purpose of the study was to explore what the oncology CNS understanding of MRONJ and prevention of MRONJ was and what methods can be developed and maintained to improve that

knowledge. A qualitative approach and in particular the interpretive phenomenological analysis (IPA) paradigm was most appropriate for this study as it is founded on the principle that “there is no attempt to test a predetermined hypothesis of the researcher; rather the aim is to explore, flexibly and in detail, an area of concern”.³⁵ The analysis is a product of the interactions between the participants and the researcher, and it is considered to be both phenomenological (participants’ accounts) and interpretative (researcher’s interpretations of participants’ accounts). Secondly, it is particularly appropriate in an area where a review of the literature had revealed a lack of previous research.³⁵

Population and sample

Smith & Osborn³⁵ suggest that IPA sampling tends to be purposive and broadly homogenous to ensure the topic is relevant for the sample and can be explored in depth. There are several populations of patients who are at risk of MRONJ and have the drugs administered in multiple medical departments so it was important to focus the question further as it would be impractical to focus on such a broad population for this study. The population group was purposive and narrowed to oncology CNS who administer anti-angiogenics and anti-resorptives for cancer patients as the literature has found these patients are at a higher risk of MRONJ due to the malignant nature of their condition and treatment regime.¹ All four CNS in this department were invited to take part in the study.

Researcher positioning

The principal researcher and author was a dentist working as a Special Care Dental Officer (SCDO) in the Community Dental setting. In the author’s clinical practice they found it challenging when a

patient is referred for a dental assessment by oncology, as the majority of patients are unaware of the importance of a dental assessment prior to their oncology treatment. The majority of the patients appeared to lack understanding of the long-term implication of the risk of MRONJ and how to prevent it. The patient may have already been given information on MRONJ by their oncology team but coming to terms with a recent cancer diagnosis may have led to poor retention of the drug information at that time.

Inclusion and exclusion criteria

The inclusion criteria comprised only of registered CNS working in the local Oncology Department at a small rural hospital. There were no exclusion criteria for this study.

Data collection

The CNS were invited to participate via email. Confidentiality of the participants was maintained and ethical principles and research standards were adhered to.³⁶ Each interview lasted approximately 30 minutes followed by debriefing by the principle researcher. All four oncology CNS invited to participate consented. In IPA studies the researcher aims to enable participants to share their personal experience of the phenomenon under investigation. For this reason semi-structured, face to face interviews were chosen as they are regarded to be the most appropriate form of data collection for IPA studies.³⁷ An interview guide containing open-ended questions and probes was used to encourage free narrative, reflection and detailed responses as required for IPA (Appendix 1).³⁷ The interviews were audio-recorded and transcribed verbatim on Microsoft® Word by the principle researcher. The principal researcher had no pre-existing relationship with the participants and being a dentist with knowledge in that field it may be more difficult to establish rapport through empathic neutrality. This may have unintentionally had the 'Hawthorne effect' undermining validity.³⁷ The oncology nurses may have felt uneasy disclosing information as they may not have wanted to seem as if they did not understand or they were not acting within their professional duty; they may have felt there was a power dynamic between the interviewer and participant.³⁸

Data analysis

Qualitative analysis is a subjective process and IPA recognises that a researcher's perspective invariably affects the analysis.³⁹ IPA was employed by the principle researcher to analyse the transcripts.³⁵ Each transcript was read several times to encourage familiarity. The transcript from Participant 1 was used to produce a list of themes and the other transcripts were studied to identify recurrences of these themes, contradictor or related themes and any additional themes. The themes were illustrated with supporting quotes from the transcript to ensure they were adequately represented and grounded in the data. The themes were analysed and where they appeared to be linked and related, were clustered together to produce a list of super-ordinate themes. The final list of themes comprised of three superordinate themes that were explored through a number of sub themes. An analytic memo was kept during data collection and analysis to help reflect on my thoughts and offer a decision trail for others to be able to follow the research process as a method of auditability, which enhances the trustworthiness of the findings.³⁸

Results

The main points are illustrated by anonymous quotations followed by a number in brackets that indicated each oncology nurse.⁴⁰

Theme 1: The importance of MRONJ

Subtheme: Oncology CNS understanding of MRONJ

The CNS studied felt they lacked knowledge on MRONJ as it was a condition that they rarely encountered and one CNS appeared to consider that they did not need to understand MRONJ as it was the dentists' role to treat the condition.

- a. "We don't have a lot to do with it (MRONJ)... they go to specialist dental teams..."(N3)
- b. "I wouldn't know a lot about that (MRONJ)..."(N4)

Subtheme: Patient Quality of Life

Oral health related quality of life is a multi-dimensional phenomenon with oral status and oral health part of general health.¹⁴ All of the CNS were aware of the negative impact MRONJ had on the patients, based on seeing a handful of patients who had developed it in their clinic.

1. "...apart from the pain and discomfort was the anxiety associated with not carrying on with their treatment..."(N1)
2. "...a bad taste in their mouth all the time, awful bad breath..."(N2)

Subtheme: CNS understanding of the prevention of MRONJ

Oral health is often a neglected aspect of nursing care, which may be owing to a lack of knowledge and understanding among nursing staff.⁴¹ However, the CNS in this study were passionate about the importance of oral health for their patients undergoing treatment in their department as the following extract elucidates:

- i. "It's essential... interferes with their ability to eat and drink... the one thing that patients complain about the most is if their mouth is bad..."(N2)
- ii. One CNS reported that two patients with MRONJ were late in reporting symptoms therefore, it may be advantageous for CNS to enquire about any oral problems the patients may be having on a regular basis.
- iii. "...more thrush and ulcers... I don't see it (MRONJ) as frequently as I thought..."(N1)
- iv. "...we have two...who didn't report any problems right at the beginning so it (MRONJ) has become a big problem..."(N2)
- v. All of the CNS placed importance on patients having a dental assessment prior to starting their oncology treatment.
- vi. "We don't start anyone on treatment until they have a referral to and feedback from a dentist..."(N1)
- vii. "It's our policy for (patients)...to be seen by the dentist..."(N2)

There was agreement amongst all the CNS of the importance of preventing MRONJ but none of them were sure as to what patient advice to give.

- a) "No I haven't thought of that...we do it with our chemo patients (give oral health advice)...not as much as we should do with our bisphosphonate patients"(N3)
- b) "We could do a bit more on oral hygiene...it would probably be better advised by specialists in oral hygiene..."(N2)
- a) In contrast, all of the CNS were well versed on explaining oral

health complications and prevention for patients undergoing chemotherapy.

- b) "...if they are on chemo... from the start we talk about looking after your mouth, keeping it clean, mouthwashes..."(N3)
- c) **1.4 Subtheme: Awareness of MRONJ guidelines**
- d) Three of the CNS were aware of the Scottish Dental Clinical Effectiveness Programme⁴² guidelines related to the prevention of MRONJ; however they relied heavily on the dental team to advise patients on the risk of MRONJ.
- e) "...we talk to you guys (Special Care Dental team) more than anything, you are the biggest resource that we have"(N3)

Subtheme: CNS understanding of the patient cohort at risk of MRONJ

Two of the CNS recognised and discussed in some detail about the increasing number of patients who are at risk of developing MRONJ as survival rates of cancers continue to improve. One CNS recognised that the cohort of patients receiving adjuvant treatment for breast cancer are a relatively new patient group prescribed extensive and prolonged anti-resorptive treatment which places them at an increased risk of MRONJ.

1. "...we are keeping patients for a long lot of years on treatment... that may become more of a problem than the cancer."(N2)
2. "I think we are getting more and more patients...We are chronically managing a lot of our patients now for years and years and they carry on with these drugs until it becomes an issue..."(N3)

Theme 2: Education on MRONJ

Subtheme: CNS education on MRONJ

This subtheme relays how all of the CNS showed a genuine interest in developing a better understanding of MRONJ. They all felt that training for CNS on oral health for patients at risk of MRONJ was lacking and would be beneficial.

- a. "...I wouldn't really think to advise somebody who is on bisphosphonates (about MRONJ)..."(N4)
- b. "I haven't had any education...I don't always look in somebody's mouth as I don't know what I am looking for..."(N1)

Subtheme: Patient education on MRONJ

Three of the CNS felt education for their patients on the prevention of MRONJ needed to be improved. They felt that verbal information from CNS or the doctors was insufficient and it would be advantageous to have written and visual aids for the patient to take home. All of the patients are supplied with written leaflets by non-dental sources.

1. "I give...a book from denosumab...Macmillan information leaflet on zoledronic acid."(N1)
2. "It would be nice to have...more information for the patients as we give basic stuff...information stands in the waiting area... Maybe an education package or poster or leaflets."(N2)

Subtheme: Patient MRONJ education responsibility

The CNS felt that medication information should be supplemented throughout the duration of treatment and not just at the beginning. It is important to reiterate information and check for patient understanding

at multiple points along the patient journey.⁴³ Packham et al.⁴⁴ found CNS were preferential sources of information over other HCPs, particularly those with more complex disease, supporting the integral role CNS play in the multidisciplinary team.

- a. "Education...tends to get...lost when we are giving treatment all the time. It tends to be at the beginning and if we have problems."(N2)
- b. "I think the more you can tell people the better it is. Some people don't want to be told..."(N4)
- c. All the CNS were of the opinion that MRONJ education was both the doctors and the CNS responsibility. Due to time constraints on the doctors, the CNS said that they often had to reinforce information and answer patient questions.
- d. "It's our responsibility as once they (patient) come to us then it has perhaps sunk in a little bit...I feel it's important to mention it subsequent times as well."(N4)
- e. "...the doctor is taking consent...but it's my job to reinforce it and to make sure they (patient) understand the importance of it."(N1)

Theme 3: Patient access to dental treatment

Subtheme: Communication between the Special Care Dental and Oncology teams

The CNS were unsure as to how oncology patients could access their dental assessment which highlights communication between the oncology and the Special Care Dental (SCD) team could be improved. The CNS all agreed with recent service pressures to the SCD department they were unsure where to refer patients leading to discontinuity in care. Instead they had been sending patients to the oral surgery department leading to a question over access to patients for holistic care as oral surgery would be an extraction only approach and possibly onward referral to the SCD department resulting in a delay in treatment. This has highlighted the need for clearer clinical pathways and increased collegiality and teamwork between medical and dental departments with patient-centred care being the focus.

- I. "...your service was getting busy... I refer patients that maybe don't have their own dentist...should the patient's dentist be doing the dental assessment? Is that good enough?"(N1)
- II. "It makes sense to send them (patients) to you (Special Care Dental team)...you can provide the whole service, but your service is busy and under stress like every other service..."(N1)

Subtheme 3.2: Patient access to National Health Service (NHS) dental care

Two CNS highlighted the ethical dilemma of dental charges both for NHS and private patients for essential treatment that the patient may not be able to afford leading to potential health inequalities.

- "...private patient...incurring quite an expense for her...the patient needs the dental treatment done before she has her treatment (oncology)...where do we sit with it? Do we (NHS) pay for it? She knew she needed it (dental treatment)...but had been putting it off." (N1)

Discussion

This was an important first study to explore oncology CNS understanding and knowledge of MRONJ. This concurs with the

published literature demonstrating a deficiency in MRONJ knowledge amongst HCPs in general.^{23–34} A lack of knowledge in relation to risk and suitable preventive strategies by HCPs is potentially placing patients at risk of MRONJ which has significant quality of life associations and represents a medication safety issue. An awareness of MRONJ among HCPs that come into contact with patients at risk of this condition is key to ensuring that an appropriate risk assessment is completed and effective education of patients on preventative advice is given.^{3,32,42} It was important to determine the oncology CNS understanding of MRONJ as the role of the oncology CNS should not be underestimated in relation to patient medication understanding and effective prevention education. McCormack & McCance⁴⁵ identify CNS as relatively inexpensive members of the healthcare team who address patients' psychosocial needs, develop patients' knowledge and enhance patient empowerment leading to reduced anxiety and depression. Al Saffar et al.⁴⁶ supported this concluding the provision of information concerning medication at the time of diagnosis in the doctor's clinic was not always absorbed by patients and therefore CNS have an important role to play in reinforcing the information.

One CNS divulged they would not think to advise a patient on their risk of MRONJ which highlights the importance of improving CNS oral health education. This is supported by multiple studies that conclude patients are being poorly informed about their risk of MRONJ and that preventive dental care is rarely being implemented at the point of prescribing implicated medications.^{32,47,48} Oral health is currently only a very small component of the undergraduate nursing curriculum;⁴⁹ thus nurses cannot be expected to feel confident and impart evidence based knowledge to patients without education and training over their postgraduate careers.⁵⁰ There have been other events in healthcare when education of HCPs has resulted in positive outcomes such as training HCPs in infection prevention and control and antimicrobial stewardship.^{51,52}

The adoption of recommendations that stress the importance of oral care and prevention by both medical and dental professionals is a significant factor in reducing the incidence of MRONJ.^{3,13,42} Thus, the benefits of oncology CNS facilitating important discussions on the need to maintain good oral hygiene and oral health at various stages during the patients' treatment and signposting patients to the appropriate dental services cannot be ignored. Ohrn & Sjoden⁵³ and Sturrock et al.³² found patients had a positive attitude to discussions on oral hygiene performed by allied HCPs. This supports the notion that oncology CNS are key persons in the multidisciplinary team for patient education on the prevention of MRONJ. The CNS involved in this study, showed a willingness to learn about MRONJ and oral health. As MRONJ can in many cases, be prevented with appropriate oral health education and preventive care the dissemination and adoption of the Scottish Dental Clinical Effectiveness Programme⁴² and UK Chemotherapy Board³ followed by educational sessions from dentists managing oncology patients may be an effective way to improve the knowledge of CNS and other HCPs involved in the care of oncology patients.

Importantly this study highlights the desire to improve patient MRONJ education. Packham et al.⁴⁴ found specialist sources including nurses and doctors and patient information leaflets (PILs) most useful for patient drug education. Patients have reported that PILs are a valuable supplement to the oral information provided.⁵⁴ Specifically tailored patient information leaflets, dental alert cards, visual aids and/or message boards within the oncology department can enhance the information being delivered verbally on the importance of oral

health and the prevention of MRONJ.^{3,55} This would enable access to dental information for all patients attending the oncology clinic for treatment.

A multidisciplinary approach to the prevention of MRONJ is recommended in the literature.^{3,7,42,56–58} Within this study the communication between the oncology and dental teams could be improved. To refine patient multi-disciplinary care a joint meeting of all the medical and dental specialties involved to review the current clinical pathway is required. With consideration to implement a managed clinical network (MCN) including oncologists and local representatives from the primary, community and hospital dental services to implement a MRONJ risk reduction pathway.⁵⁸ As service pressures were highlighted for the SCD department the aim of the MCN would be to reduce reliance on secondary care dental services so the oncology team would refer patients to their own dentists for dental screening/treatment before commencing drug therapy that increased the risk of MRONJ.^{3,42} The ultimate objective of the MCN would be to enable timely and effective communication between oncologists, oral surgeons and dentists, reducing disruption to oncology treatment and improve patient-centred care.

Possible barriers in implementing the multidisciplinary prevention of MRONJ should be highlighted such as effectively engaging patients in recognising the need for oral care and potentially placing higher demands on staff time and already stretched NHS resources.³² Access to dental care was a concern discussed by the CNS, in particular with regards to ethical issues such as access to NHS care and dental charges. This is a thought-provoking topic which is going to become increasingly important and would be a decision the local health board or government would have to make to ensure potential oral health inequalities are reduced.⁵⁹ In line with the Scottish Dental Clinical Effectiveness Programme⁴² guidance patients who are not registered with a dentist should be referred to their local community or SCD department.

Study limitations

The relatively small sample size could be seen as a limitation of this study although it was appropriate for the methodology used. The emerging consensus for IPA is to use smaller samples as the difficulties exploring testimonies in-depth from large samples can lead to superficial understanding.³⁵ Smith³⁹ suggests five or six as a reasonable sample size. Another limitation is that the researcher only explored oncology CNS understanding in one healthcare organisation which was in a rural setting. Although the CNS selected do reflect the key setting in which nurses typically prescribe anti-resorptives to patients with malignant conditions, the transferability of findings to other settings has yet to be confirmed.³⁸ Given IPA's recognition of the dynamic role of the researcher, it is important to acknowledge the particular influence that the researchers experience of MRONJ has inevitably had on the research process, namely being a dentist, working in a SCD department and having an interest in MRONJ. This inevitably led to the introduction of concepts within the data collection process and ultimately themes that were generated reflected the researchers interests and focus. This could have been addressed with more rigorous reflective examination and the use of multiple transcript analysts.⁶⁰ Furthermore the semi-structured interview questions could be less explicit and loaded but sufficient to let the respondent know what the area of interest is. The research findings, therefore, should be considered as tentative however, can contribute to an increased understanding of the lack of awareness of MRONJ and guide an individual's practice locally and potentially externally.

Conclusion

The study provided new knowledge on local CNS understanding of MRONJ and adds to the plethora of articles that the awareness and understanding of MRONJ is deficient amongst HCPs in general. The study highlighted the need for MRONJ education and prevention to be improved through collaboration with multi-disciplinary teams consisting of both medical and dental professionals and the creation of efficient clinical pathways. It reinforces the fact that improvements are still to be made with respect to CNS understanding of oral health problems. This study also highlights the importance of reinforcing oral health needs as part of the holistic view of patients by the medical specialties and it affirms the valuable role of the CNS.

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Conflicts of interest

The authors declare that there is no conflicts of interest.

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