BMJ Open

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Journal:	*BMJ Open*
Manuscript ID	bmjopen-2017-016047
Article Type:	Research
Date Submitted by the Author:	19-Jan-2017
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Primary Subject Heading:	Qualitative research
Secondary Subject Heading:	General practice / Family practice
Keywords:	ORAL & MAXILLOFACIAL SURGERY, Bone diseases < ORTHOPAEDIC & TRAUMA SURGERY, PRIMARY CARE, QUALITATIVE RESEARCH, Adverse events < THERAPEUTICS

Attitudes and perceptions of GPs and community pharmacists towards their role in the prevention of bisphosphonate-related osteonecrosis of the jaw

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Word count: 3832

Key Words:

Bisphosphonate-Related Osteonecrosis of the Jaw, General Practitioners, Pharmacists, Interdisciplinary Communication, Qualitative Research

ABSTRACT

Background: Bisphosphonate-related osteonecrosis of the jaw (BRONJ), is a rare, yet significant, adverse effect of bisphosphonate therapy. A multidisciplinary approach to the prevention of BRONJ is recommended, due to the significant morbidity and difficulty treating the condition. Current evidence suggests that both GPs and community pharmacists have limited knowledge relating to BRONJ and that preventative strategies are rarely implemented.

Objective: To explore the attitudes and perceptions of GPs and community pharmacists on the risks and preventative strategies for the development of BRONJ.

Design: Interpretivist methodological approach using qualitative semi-structured interviews.

Participants: 9 community pharmacists and 8 GPs.

Setting: Primary Care in North East England and Cumbria, UK.

Methods: Using a Grounded Theory methodology and integrating a process of constant comparison in the iterative enrichment of data sets, semi-structured interviews were undertaken, transcribed and analysed using framework analysis. Salient themes were identified and related back to extant literature in the field.

Results: Four salient and inter-related themes emerged: (1) uncertain knowledge, indicating limited exposure of respondents to BRONJ, and limited awareness of the implications of its diagnosis, risk factors and preventative strategies; (2) patient specific, referring to the complexity of patients, patient education and prioritising aspects of care; (3) wider context, indicating a lack of interdisciplinary communication and referral processes between professions, work load pressures, access and patient receptivity to dental services and; (4)

professional, reflecting professional roles and responsibilities, authority and educational initiatives

Conclusions: Effective communication or collaborative care between GPs and community pharmacists for the prevention of BRONJ is not apparent. Interventions to mitigate against the risk of developing BRONJ and clarity of GP and community pharmacy roles are required.

Main strengths and limitations of this study

- This is an under-researched area warranting further study, with the aim of improving patient care
- The patient group is small, but experiences significant morbidity
- A small number of healthcare professionals participated in this study
- The study was conducted in the north east of England and Cumbria, which may impact on transferability of the findings.

INTRODUCTION

Bisphosphonates are a class of drugs used in a variety of therapeutic indications; such as osteoporosis, Paget's disease, hypercalcaemia of malignancy, osteolytic bone metastases and osteolytic lesions of multiple myeloma.[1] In practice, they are most commonly prescribed in the management of osteoporosis.

The prescribing of bisphosphonates has increased considerably over recent years. Statistical evaluation of prescribing in England reveals a rise of 122.6% in the number of individual prescription items dispensed between 2004 and 2014.[2] Alendronic acid is the most commonly prescribed bisphosphonate, with 7,391,000 individual dispensations in 2014.[2] This rise can be attributed to significant increases in the proportion of elderly people in the UK population. Risk for bisphosphonate-related osteonecrosis of the jaw (BRONJ) in people taking bisphosphonates is hypothesised to be related to the unique nature of the blood supply, structure, and function of the jaw bones.[3] Case reports of BRONJ emerged in the early 2000s; it is now well documented in the literature,[4] and has been subject to a number of prescribing safety alerts in recent years.[3, 5]

The actual incidence and prevalence rates of BRONJ are difficult to quantify, with varying reports in the literature. This is potentially attributable to a low incidence of reporting, the variance in diagnostic criteria and a percentage of mild self-resolving cases remaining undiagnosed. A nationwide study in the UK of patients presenting to departments of oral surgery, oral medicine, oral and maxillofacial surgery and dental hospitals identified 369 cases of BRONJ over a specified 2-year period. Oral bisphosphonates had been prescribed for 56% of the patients. Extrapolation of these data suggests that the incidence of BRONJ

may be 8.2-12.8 cases/million of the population/year, which is equivalent to 508-793 patients/year in the UK.[6]

Ideally, optimal dental health should be established before patients commence bisphosphonate therapy.[7] This is to prioritise care that will subsequently reduce mucosal trauma or act prophylactically to aid in the avoidance of subsequent dental extractions or conditions which may further predispose the patient to oral surgery or dental procedures that impact on the osseous structures of the jaw.[8]

A multidisciplinary approach to the prevention of BRONJ is recommended in the management of patients requiring bisphosphonate therapy,[9, 10] incorporating both patient and health professional education of the relative risk of the development of BRONJ.[5] Education of dentists, pharmacists, GPs and patients about BRONJ is indicated,[11] with specific emphasis on the provision of focused preventative measures and detailed oral hygiene instructions.[12]

Available published evidence describing the attitudes of both GPs and pharmacists towards, and their perceptions of, their roles in preventive strategies for BRONJ is limited. A questionnaire survey of GPs (n=120) and pharmacists (n= 60) in North Wales identified that although both sets of healthcare professionals have regular contact with patients who are prescribed bisphosphonates, they have limited knowledge of the dental implications associated with treatment. Both groups of professionals reported awareness of the side effects of bisphosphonates; however, only 11.8% of GPs and 9.7% of pharmacists specifically identified osteonecrosis as a potential unwanted effect of therapy.[13]

Furthermore, even when pharmacists and GPs report some knowledge of BRONJ, is it not clear how this awareness influences their clinical practice. The aim of this study was to

explore the attitudes towards and perceptions of GPs and community pharmacists on the risks and preventative strategies for the development of BRONJ.

METHOD

Design

A Grounded Theory approach,[14] with constant comparison was utilised throughout the research. Semi-structured interviews were carried out by a single researcher (AS), at either the School of Pharmacy or the participant's workplace, depending on participant preference and availability. The interviews were audio-recorded and transcribed verbatim. Integrating a process of constant comparison,[15] an initial topic guide served as a benchmark of questioning, which was subsequently developed iteratively as data were progressively enriched.

Setting

Participants were recruited from a range of urban and rural Primary Care locations in the North East of England and Cumbria. GPs were recruited from both teaching and non-teaching practices and community pharmacists were recruited from independent (single or small chain pharmacies) and multiple pharmacies (companies consisting of numerous pharmacy stores) (see table 2).

Participants

Seventeen participants; 9 community pharmacists and 8 GPs were recruited to the study. Participants were initially recruited via a purposive sampling technique with further recruitment achieved via snowball sampling.

Analysis

Constant comparison allowed enrichment of data and for new concepts to guide subsequent interviews via the strategic development of each subsequent topic guide. Adoption of Ritchie and Spencer's Framework Analysis[16] allowed salient themes from the findings to be identified. Data were analysed by AS, with transcripts and emerging themes cross-checked for interpretation and agreed among the research team. Framework analysis involved a five-stage process: (1) familiarisation with the data – interviews were transcribed by AS and key issues identified through immersion in the data; achieved via iterative cycles of reading and re-reading of transcripts; (2) development of a thematic framework – the initial themes formed the basis of a thematic framework; (3) indexing data – data were then indexed against the thematic framework; (4) charting – charts were produced of the data within the thematic framework; (5) mapping of the data – themes were reviewed until definitive concepts could be produced from the data

Ethics

Ethical approval was obtained from the University of Sunderland (Reference PHW52).

RESULTS

Seventeen healthcare professionals were included in this study (Table 1 and Table 2). Interviews were carried out between January and October 2016; one hour was designated for each interview.

Table 1. Participant Characteristics – GPs

Participant	No. years since registration	Practice Size (patients)	Practice Location	Teaching Practice	Full/part time
GP1	21+	3,000-5,999	Urban	Non-teaching	Full-time
GP2	16-20	12,000+	Urban	Teaching	Part-time
GP3	21+	12,000+	Suburban	Teaching	Part-time
GP4	11-15	9,000-11,999	Semi-rural	Teaching	Full-time
GP5	11-15	12,000+	Suburban	Teaching	Part-time
GP6	16-20	3,000-5,999	Rural	Teaching	Part-time
GP7	21+	9,000-11,999	Semi-rural	Teaching	Full-time
GP8	16-20	9,000-11,999	Semi-Rural	Teaching	Full-time

Table 2. Participant Characteristics – Pharmacists

Participant	No. years since registration	No. Items dispensed per month	Practice Location	Independent /multiple	Full/part time
P1	6-10	6,000-8,999	Suburban	Independent	Full-time
P2	11-15	12,000+	Suburban	Multiple	Full-time
P3	0-5	3,000-5,999	Suburban	Multiple	Full-time
P4	21+	3,000-5,999	Urban	Independent	Part-time
P5	0-5	6,000-8,999	Urban	Independent	Full-time
P6	0-5	6,000-8,999	Urban	Independent	Full-time
P7	6-10	6,000-8,999	Urban	Multiple	Full-time
P8	16-20	6,000-8,999	Rural	Independent	Part-time
P9	11-15	6,000-8,999	Semi-rural	Multiple	Full-time

Four salient inter-related themes emerged. (1) Uncertain knowledge – a lack of familiarity with the subject area, the prevalence and significance of BRONJ and limited exposure to the condition. (2) Patient Specific – complexity of patients, clinical priorities and patient education. (3) Wider context – access/fear of dental services, inter-professional communication and clinical workload. (4) Professional – perceived responsibilities, authority and inter-professional education.

1. Uncertain Knowledge:

All participants perceived themselves to have some degree of knowledge on the adverse effects that are associated with bisphosphonate therapy. The concept of BRONJ was introduced in the participant information sheet and opened up for discussion during the interview; participants actually had minimal knowledge on this topic but all were aware of the potential risk.

"I think it was probably sitting way at the back of my mind…it was probably in a lecture at some point". (GP4)

Although poor dental health and the duration of therapy were frequently identified, all of the participants had limited awareness of the risk factors for the development of BRONJ.

"I am not aware of any, I imagine that significant dental problems would be associated with it, but I am not actually aware of any others". (GP3)

Participants were uncertain on the prevalence of BRONJ and had limited knowledge on the significant morbidity associated with the condition.

"I have never seen it, so I presume it's not very common…I don't really know how serious it is when it does happen". (P3)

One GP had first-hand experience of managing patients with BRONJ, and the significant morbidity that their patients had experienced influenced their attitude towards management of patients who are prescribed bisphosphonates. None of the other participants had been involved with the care of a patient with BRONJ.

"It's the sort of thing that once you see it, you then remember it. They were both very complex patients, but the amount of morbidity involved with the osteonecrosis of the jaw in both of those patients was considerable". (GP1)

2. Patient Specific

Patients prescribed bisphosphonates usually have a number of co-morbidities. They are often elderly and are prescribed multiple medications, and their management can be complex. Indeed, this complexity requires that practitioners assign priorities in their care, relating to both the overall management of the patient and to more specific priorities related to bisphosphonates.

"They are lower down in the pecking order of things that we look at when we are supervising polypharmacy, when we are looking at chronic disease management". (GP3)

All participants identified bisphosphonates as having very specific administration instructions and common side effects; these were the focus of consultations. However, participants were concerned about overloading patients with information and the risk of patients potentially refusing treatment.

"You try not to overload them with too much information because you know that sometimes they can't even take it on board at the best of times". (P2)

Patient education was a key issue that emerged from the data; participants placed importance specifically on the education of patients in relation to administration instructions and common side effects of bisphosphonates. This would usually take the form of a set of predefined counselling points.

"I think when you have a drug like a bisphosphonate, which is complex with its instruction on how to take it and people are tied up in that". (GP1)

Although some participants advised patients to seek dental check-ups, most reported that their patients, in general, appeared to not appreciate the importance of achieving and maintaining good dental health through self-performed daily oral hygiene and regular dental check-ups. This was identified as a barrier in the management of this patient population and a focus for patient education.

"I would say that their oral hygiene was not particularly great. I think it's probably just not wanting to go to the dentist and fear of the dentist". (P9)

Patients often tend to forget the initial advice given to them and reminders or continuous advice are necessary to enhance patient education. Teamwork highlights the importance of specific counselling and reinforces the advice that is given to patients.

"If a new drug is initiated, that is the time to reinforce what the patients been told about the drug and you know to give them the message. I think the more reinforcement and the more information the better". (GP2)

3. Wider Context

Both GPs and pharmacists identified that there is reluctance amongst certain patients to seek dental advice. A number of reasons were proposed for this, including the cost of dental treatment, a general lack of oral health awareness and patients with dental phobias.

"The processes of how you get people to take their dental health seriously are very difficult. The ones that pay for dentistry are likely to be the ones with good teeth, the others who get free treatment just don't access it". (GP3)

Access to dentists was also felt to be an issue that both pharmacists and GPs had encountered, specifically the availability of dental services for patients and referral pathways between professions.

"*Some people don't even have an NHS dentist. I am aware of where I work, there was a dentist upstairs, but it wasn't an NHS dentist. I think when you want to refer someone to another service you know it is going to be a little bit more problematic than just making an appointment with a GP for example". (P2)*

Participants all described a heavy workload and that in the small amount of time that they had with each patient, they would have to prioritise the information they gave to patients.

"In that 2 minutes that you have got to hand something out to somebody, you concentrate on the important things, such as how to take it, to get their concordance and compliance". (P2)

A lack of communication between both GPs/pharmacists and dentists was identified as a major barrier. The absence of a formal referral process between pharmacists, GPs and the dental profession was highlighted throughout. This was felt not only to be an issue related

to BRONJ but represented a wider problem in the management of oral health in primary care. In order to successfully manage the risk of BRONJ, it was clear from interviewees that communication between professionals is key.

"I think maybe there needs to be a little bit more communication involved with pharmacists. The triangle, pharmacist, dentist and prescriber". (P2)

"Some sort of shared record keeping where you could enter into the system. You have done a review and these side effect were discussed with the patient, that would be brilliant. That would make it part of that clinical record, I'd know about it, the patient would know about it. I think that would work very well". (GP7)

One of the key areas identified by all pharmacists and some of the GPs was the benefit of Medication Use Reviews (MURs) and the New Medicine Service (NMS) in community pharmacies. These services provide pharmacies with both the time and structure to provide more detailed advice to patients on medications. Bisphosphonates are not currently specified in either service. Although it was felt that many drugs should be included, all participants identified that bisphosphonates should be included in these services due to their specific administration instructions and potential for side-effects.

"I think during an MUR you certainly have more time to focus on the individual drugs and then it kind of triggers in your brain the more important things that you should be speaking to them about". (P2)

4. Professional

GPs acknowledged their role as the prescriber and the need to counsel patients on the side-effects of their medication. Both prescribers and pharmacists were in agreement that

pharmacists are the experts on medications and they have a role to play in counselling patients on safe and effective use of medicines.

"*I think counselling about medication is far better done by the pharmacists. I think the other reason is perhaps, when a patient sees a doctor they expect to be able to discuss all aspects of their lives and their care. When they see the pharmacist, they know they are seeing the pharmacist about their medication. I think it is much easier for the pharmacist to keep the patient focused on the drugs and the patient to stay focused on the drugs". (GP1)*

Although pharmacists acknowledged their role in counselling patients on medications, a number of them felt that if a patient needs to be dentally fit before commencing bisphosphonate therapy, then it would be the responsibility of the GP to arrange this. Although in many cases GPs would be responsible for initially prescribing bisphosphonates and their continued prescribing, it was commented that bisphosphonates can, at times, be initiated in secondary care. This was certainly the case for intravenous bisphosphonates with all GPs and pharmacists reporting little or no experience with prescribing or dispensing these products. As intravenous bisphosphonates are usually prescribed in secondary care, it was felt by some of the participants that this was a potential risk, as they can be missed on medication lists.

"Making sure that the dental check has been done and that they're healthy should actually be done before you prescribe medication, because if you prescribe a medicine without knowing that, then technically how do you know that it's going to be safe for the patient to take. I think my role as a pharmacist is certainly to promote that it's been done, and if it hasn't to take further steps with the patient". (P7)

A number of participants also described limited education or training in relation to oral and dental health.

"*We have no training in dental care. You know to brush your teeth and that's what you say to people. I think, I don't know, maybe we should have some more training". (GP5)*

"No not really, a little bit maybe in lectures at university but not with dentists, we have worked quite closely with the doctors but not with dentists". (P1)

DISCUSSION

Summary of main findings

It is apparent that both sets of participants (GPs and pharmacists) had limited knowledge of BRONJ, in particular in relation to its prevalence and the morbidity associated with the condition. As BRONJ is relatively uncommon, the majority of participants also lacked first-hand experience of managing affected patients.

Due to the complexity of this patient group and bisphosphonates as a therapeutic class, interviewees assigned priorities in relation to clinical management and in patient education. Consultations would usually focus on the specific administration requirements and more common GI related adverse effects as opposed to the risk of developing BRONJ and the need for good oral and dental health.

Wider issues such as patient reluctance to attend the dentist and difficulties in accessing dental services were thought to be potential barriers for patients. The lack of communication between the professions was also cited as a key issue that needs to be addressed, with the MUR and NMS pharmacy services identified as a potential facilitator.

Pharmacists and GPs reported good working relationships but inter-professional educational opportunities with dental colleagues appear to have been limited in scope or non-existent, and were cited as a potential enabler for improving multidisciplinary working.

Comparison with existing literature

Knowledge on the oral risks associated with bisphosphonate therapy has been reported to be limited,[13] In comparison, all participants interviewed in this research reported being aware of the risk, although this was introduced before the interviews in the participant information leaflet.

Many of the participants would not routinely mention the risk of osteonecrosis of the jaw when prescribing bisphosphonates or when counselling patients about the medication. This is consistent with a small quantitative study that identified only 17% of patients prescribed oral bisphosphonates were aware of the risk of BRONJ, with the majority of these patients acquiring this knowledge from patient information leaflets and not from their GP.[17]

All participants reported reluctance amongst patients to attend dental appointments, with a significant proportion of their patients being either not registered with a dentist or not regular attendees. This is consistent with NHS dental statistics, which state that only 52% of the adult population have seen an NHS dentist within the previous 24 months.[18]

A number of clinical guidelines and patient safety alerts recommend that patients should be counselled on the risk of BRONJ and advised to seek a dental check-up prior to initiating bisphosphonate therapy [5, 8]. Our data suggest that this does not appear to routinely happen. A recent study in Japan reported that 62% (n=629) of physicians did not request oral health care by a dentist before commencing bisphosphonate therapy and 72% of

participants reported no cooperation between physicians and dentists. They concluded that a strategy for sharing information among physicians, dentists, and patients is required to reduce the incidence of osteonecrosis of the jaw associated with osteoporosis treatment.[19]

Participants felt that communication between GPs and pharmacists was more frequent, with closer working relationships than those between pharmacists and dental clinicians. The MUR and NMS were identified as potential facilitators in the prevention of BRONJ. Bisphosphonates are not directly specified in either of these services at present, although participants were in agreement that it would be beneficial for them to be included. The literature to support both services is mixed; a detailed review by the University of Nottingham found that the implementation of the NMS was constrained by the quality of the pharmacist's relationship with GPs. They found that poor communication between the professions and a lack of awareness or understanding by GPs about the service resulted in a lack of referrals; this is consistent with statements from some of the GPs in this study. Pharmacists also suggested that GPs were not interested in the NMS as it potentially encroached on professional boundaries and duplicated work undertaken by the GP.[20] In comparison, the GPs in this study, despite having limited knowledge of the service, were all supportive of its role and the reinforcement of important counselling points was thought to be a key responsibility of the pharmacist.

Pharmacists are subject to organisational pressures to meet targets around the MUR service which has been reported to result in their offering the service to patients who meet the minimum inclusion criteria and avoiding offering the service to more complex patients due to time pressures.[21] This potentially impacts the patient group under study as a clear

theme that emerged from the data was the complexity and polypharmacy issues of patients taking bisphosphonates.

An ethnographic study, utilising observations and patient interviews in two English community pharmacies found that patients generally were positive about the MUR, and patients tended to view the pharmacist as an expert on medicines. However some participants felt wary of the pharmacist's involvement considering that the pharmacists were deliberately or intentionally bypassing the GP. This study also found that there was little evidence to suggest that the professions were collaborating to identify patients who could benefit from the service.[21]

Limitations

The study was based around *a priori* issue of limited knowledge among GPs and pharmacists in the prevention of BRONJ; the concept of BRONJ was introduced during the patient information leaflet, therefore potentially introducing the concept to participants before the interview.

Participants were all located in the North East of England and Cumbria; this therefore may impact on the transferability of findings to other geographical locations or healthcare settings. For example, a variation in the access to dental services in a particular location may influence the practice of participants and patients.

Future work and implications for clinical practice

This study has highlighted a number of areas for future study. However, missing from this study and the wider literature is the dental profession's insight into the interprofessional prevention of BRONJ. A recent publication in *British Dental Journal* highlighted the

opportunities for interprofessional working between pharmacists and dentists; with a particular focus on chronic diseases, it was suggested that dental and pharmacy teams should take action to improve communication and devise schemes for collaborative working.[22] Published clinical guidelines recommend that patients should be referred for dental assessment and treatment prior to initiation on bisphosphonate therapy, but it is apparent this is not happening. The impact of this on dentists and their perspective on how the professions can collaborate to improve patient care would be important to consider before implementing any preventative strategies.

The patient remains the central focus of the healthcare team, and therefore engaging patients in the management of their health is essential when introducing prevention strategies for BRONJ. Attitudes of patients towards the roles of the various team members and their priorities or expectations when being prescribed a new medicine will guide the development of such services.

CONCLUSION

Both GPs and pharmacists demonstrated relatively limited knowledge in relation to BRONJ and the preventative strategies recommended in the literature. Patients prescribed bisphosphonates often have complex medical histories, requiring practitioners to assign priorities in their management and, as such, the measures required to prevent the development of BRONJ can be overlooked.

Prescribing rates of bisphosphonates are increasing, with an ageing population and increasing emphasis on treating and preventing conditions such as osteoporosis. Therefore, the incidence of BRONJ is likely to increase; this will continue to be the case unless changes are made to current practice and effective preventive measures are implemented.

Acknowledgements: We thanks the participants who generously gave their time

Contributors: AS and SW designed the study. AS recruited the participants and carried out the study. AS identified the thematic framework and interpreted the data. AS, SW, PP and CH reviewed and refined the data. AS wrote the paper and all authors revised it

Funding: There was no external funding for this project

Competing interests: None

Ethics approval: University of Sunderland Reference PHW52 – 21/12/2015

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BMJ Open

Attitudes and perceptions of GPs and community pharmacists towards their role in the prevention of bisphosphonate-related osteonecrosis of the jaw. A qualitative study in the North East of England.

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2017-016047.R1
Article Type:	Research
Date Submitted by the Author:	25-May-2017
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Primary Subject Heading:	Qualitative research
Secondary Subject Heading:	General practice / Family practice
Keywords:	ORAL & MAXILLOFACIAL SURGERY, Bone diseases < ORTHOPAEDIC & TRAUMA SURGERY, PRIMARY CARE, QUALITATIVE RESEARCH, Adverse events < THERAPEUTICS

Attitudes and perceptions of GPs and community pharmacists towards their role in the prevention of bisphosphonate-related osteonecrosis of the jaw. A qualitative study in the North East of England.

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Word count: 4139

Key Words:

Bisphosphonate-Related Osteonecrosis of the Jaw, General Practitioners, Pharmacists,

Interdisciplinary Communication, Qualitative Research

ABSTRACT

Background: Bisphosphonate-related osteonecrosis of the jaw (BRONJ), is a rare, yet significant, adverse effect of bisphosphonate therapy. A multidisciplinary approach to the prevention of BRONJ is recommended, due to the significant morbidity and difficulty treating the condition. Current evidence suggests that both general practitioners and community pharmacists have limited knowledge relating to BRONJ and that preventative strategies are rarely implemented.

Objective: To explore the attitudes and perceptions of general practitioners and community pharmacists on the risks and preventative strategies for the development of BRONJ.

Design: Interpretivist methodological approach using qualitative semi-structured interviews.

Participants: 9 community pharmacists and 8 general practitioners.

Setting: Primary Care in North East England and Cumbria, UK.

Methods: Using a Grounded Theory methodology and integrating a process of constant comparison in the iterative enrichment of data sets, semi-structured interviews were undertaken, transcribed and analysed using framework analysis. Salient themes were identified and related back to extant literature in the field.

Results: Four salient and inter-related themes emerged: (1) uncertain knowledge, indicating limited exposure of respondents to BRONJ, and limited awareness of the implications of its diagnosis, risk factors and preventative strategies; (2) patient specific, referring to the complexity of patients, patient education and prioritising aspects of care; (3) wider context, indicating a lack of interdisciplinary communication and referral processes between professions, work load pressures, access and patient receptivity to dental services and; (4)

professional, reflecting professional roles and responsibilities, authority and educational initiatives

Conclusions: Effective communication or collaborative care between general practitioners and community pharmacists for the prevention of BRONJ is not apparent. Interventions to mitigate against the risk of developing BRONJ and clarity of general practitioner and community pharmacy roles are required.

Main strengths and limitations of this study

- This is an under-researched area warranting further study, with the aim of improving patient care
- The patient group is small, but experiences significant morbidity
- A small number of healthcare professionals participated in this study
- The study was conducted in the North East of England and Cumbria, which may impact on transferability of the findings.

INTRODUCTION

Bisphosphonates are a class of drugs used in a variety of therapeutic indications; such as osteoporosis, Paget's disease, hypercalcaemia of malignancy, osteolytic bone metastases and osteolytic lesions of multiple myeloma.[1] In practice, they are most commonly prescribed in the management of osteoporosis.

The prescribing of bisphosphonates has increased considerably over recent years. Statistical evaluation of prescribing in England reveals a rise of 122.6% in the number of individual prescription items dispensed between 2004 and 2014.[2] Alendronic acid is the most commonly prescribed bisphosphonate, with 7,391,000 individual dispensations in 2014.[2] This rise may be attributable to increases in the proportion of elderly people in the UK population, publication of guidance recommending the prescribing of bisphosphonates and the availability of generic products. Risk for bisphosphonate-related osteonecrosis of the jaw (BRONJ) in people taking bisphosphonates is hypothesised to be related to the unique nature of the blood supply, structure, and function of the jaw bones.[3] Case reports of BRONJ emerged in the early 2000s; it is now well documented in the literature,[4] and has been subject to a number of prescribing safety alerts in recent years.[3, 5]

The actual incidence and prevalence rates of BRONJ are difficult to quantify, with varying reports in the literature. This is potentially attributable to a low incidence of reporting, the variance in diagnostic criteria and a percentage of mild self-resolving cases remaining undiagnosed. A nationwide study in the UK of patients presenting to departments of oral surgery, oral medicine, oral and maxillofacial surgery and dental hospitals identified 369 cases of BRONJ over a specified 2-year period. Oral bisphosphonates had been prescribed for 56% of the patients. Extrapolation of these data suggests that the incidence of BRONJ

may be 8.2-12.8 cases/million of the population/year, which is equivalent to 508-793 patients/year in the UK.[6]

Ideally, optimal dental health should be established before patients commence bisphosphonate therapy.[7] This is to prioritise care that will subsequently reduce mucosal trauma or act prophylactically to aid in the avoidance of subsequent dental extractions or conditions which may further predispose the patient to oral surgery or dental procedures that impact on the osseous structures of the jaw.[8]

Several prospective studies have identified that dental screening and preventative strategies reduce the risk of osteonecrosis of the jaw. A study by Dimopoulous (2008) found a statistically significant reduction in the incidence of BRONJ with the implementation of preventative measures and Vandone (2012) reported a 50% reduction in the incidence rate with screening and pre-treatment preventative dental care.[9,10] Although the evidence for preventative measures with oral bisphosphonates is lacking a multidisciplinary approach to the prevention of BRONJ is recommended in the literature for the management of patients requiring bisphosphonate therapy;[11, 12] incorporating both patient and health professional education of the risk of the development of BRONJ.[5] Education of dentists, pharmacists, GPs and patients about BRONJ is indicated,[13] with specific emphasis on the provision of focused preventative measures and detailed oral hygiene instructions.[14]

Available published evidence describing the attitudes of both GPs and pharmacists towards, and their perceptions of, their roles in preventive strategies for BRONJ is limited. A questionnaire survey of GPs (n=120) and pharmacists (n= 60) in North Wales identified that although both sets of healthcare professionals have regular contact with patients who are prescribed bisphosphonates, they have limited knowledge of the dental implications

associated with treatment. Both groups of professionals reported awareness of the side effects of bisphosphonates; however, only 11.8% of GPs and 9.7% of pharmacists specifically identified osteonecrosis as a potential unwanted effect of therapy.[15]

Furthermore, even when pharmacists and GPs report some knowledge of BRONJ, is it not clear how this awareness influences their clinical practice. The aim of this study was to explore the attitudes towards and perceptions of GPs and community pharmacists on the risks and preventative strategies for the development of BRONJ.

METHOD

Design

A Grounded Theory approach,[16] with constant comparison was utilised throughout the research. Semi-structured interviews were carried out by a single researcher (AS), at either the School of Pharmacy or the participant's workplace, depending on participant preference and availability. The interviews were audio-recorded and transcribed verbatim. Integrating a process of constant comparison,[17] an initial topic guide (supplementary document 1) served as a benchmark of questioning, which was subsequently developed iteratively as data were progressively enriched.

Setting

Participants were recruited from a range of urban and rural Primary Care locations in the North East of England and Cumbria. GPs were recruited from both teaching and non-teaching practices and community pharmacists were recruited from independent (single or small chain pharmacies) and multiple pharmacies (companies consisting of numerous pharmacy stores) (see table 1).

Participants

Seventeen participants; 9 community pharmacists and 8 GPs were recruited to the study. An invitation letter and participant information sheet (supplementary document 2) was posted to general practitioners and community pharmacists. An initial convenience sample of participants who responded to the invitation was implemented with further recruitment achieved via snowball sampling.

Analysis

Constant comparison allowed enrichment of data and for new concepts to guide subsequent interviews via the strategic development of each subsequent topic guide. Adoption of Ritchie and Spencer's Framework Analysis[18] allowed salient themes from the findings to be identified. Data were analysed by AS, with transcripts and emerging themes cross-checked for interpretation and agreed among the research team until saturation occurred; a sample transcript has been published alongside this paper (supplementary document 3). Framework analysis involved a five-stage process: (1) familiarisation with the data – interviews were transcribed by AS and key issues identified through immersion in the data; achieved via iterative cycles of reading and re-reading of transcripts; (2) development of a thematic framework – the initial themes formed the basis of a thematic framework; (3) indexing data – data were then indexed against the thematic framework; (4) charting – charts were produced of the data within the thematic framework; (5) mapping of the data – themes were reviewed until definitive concepts could be produced from the data

Ethics

Ethical approval was obtained from the University of Sunderland (Reference PHW52).

RESULTS

Seventeen healthcare professionals were included in this study (Table 1 and Table 2). Interviews were carried out between January and October 2016; one hour was designated for each interview.

Table 1. Participant Characteristics – Pharmacists

Participant	Gender	No. years since registration	No. Items dispensed per month	Practice Location	Independent /multiple	Full/part time
P1	Female	6-10	6,000-8,999	Suburban	Independent	Full-time
P2	Female	11-15	12,000+	Suburban	Multiple	Full-time
P3	Female	0-5	3,000-5,999	Suburban	Multiple	Full-time
P4	Female	21+	3,000-5,999	Urban	Independent	Part-time
P5	Female	0-5	6,000-8,999	Urban	Independent	Full-time
P6	Female	0-5	6,000-8,999	Urban	Independent	Full-time
P7	Male	6-10	6,000-8,999	Urban	Multiple	Full-time
P8	Female	16-20	6,000-8,999	Rural	Independent	Part-time
P9	Male	11-15	6,000-8,999	Semi-rural	Multiple	Full-time

Table.2 Participant Characteristics - GPs

Participant	Gender	No. years since registration	Practice Size (patients)	Practice Location	Teaching Practice	Full/part time
GP1	Female	21+	3,000-5,999	Urban	Non-teaching	Full-time
GP2	Male	16-20	12,000+	Urban	Teaching	Part-time
GP3	Male	21+	12,000+	Suburban	Teaching	Part-time
GP4	Male	11-15	9,000-11,999	Semi-rural	Teaching	Full-time
GP5	Female	11-15	12,000+	Suburban	Teaching	Part-time
GP6	Female	16-20	3,000-5,999	Rural	Teaching	Part-time
GP7	Male	21+	9,000-11,999	Semi-rural	Teaching	Full-time
GP8	Male	16-20	9,000-11,999	Semi-Rural	Teaching	Full-time

Four salient inter-related themes emerged. (1) Uncertain knowledge – a lack of familiarity with the subject area, the prevalence and significance of BRONJ and limited exposure to the condition. (2) Patient Specific – complexity of patients, clinical priorities and patient education. (3) Wider context – access/fear of dental services, inter-professional communication and clinical workload. (4) Professional – perceived responsibilities, authority and inter-professional education.

1. Uncertain Knowledge:

All participants perceived themselves to have some degree of knowledge on the adverse effects that are associated with bisphosphonate therapy. The concept of BRONJ was introduced in the participant information sheet and opened up for discussion during the interview; participants actually had minimal knowledge on this topic but all were aware of the potential risk.

"I think it was probably sitting way at the back of my mind…it was probably in a lecture at some point". (GP4)

Although poor dental health and the duration of therapy were frequently identified, all of the participants had limited awareness of the risk factors for the development of BRONJ.

"I am not aware of any, I imagine that significant dental problems would be associated with it, but I am not actually aware of any others". (GP3)

Participants were uncertain on the prevalence of BRONJ and had limited knowledge on the significant morbidity associated with the condition.

"I have never seen it, so I presume it's not very common…I don't really know how serious it is when it does happen". (P3)

One GP had first-hand experience of managing patients with BRONJ, and the significant morbidity that her patients had experienced influenced their attitude towards management of patients who are prescribed bisphosphonates. None of the other participants had been involved with the care of a patient with BRONJ.

"It's the sort of thing that once you see it, you then remember it. They were both very complex patients, but the amount of morbidity involved with the osteonecrosis of the jaw in both of those patients was considerable". (GP1)

2. Patient Specific

Patients prescribed bisphosphonates usually have a number of co-morbidities. They are often elderly and are prescribed multiple medications, and their management can be complex. Indeed, this complexity requires that practitioners assign priorities in their care, relating to both the overall management of the patient and to more specific priorities related to bisphosphonates.

"They are lower down in the pecking order of things that we look at when we are supervising polypharmacy, when we are looking at chronic disease management". (GP3)

All participants identified bisphosphonates as having very specific administration instructions and common side effects, such as gastro-intestinal or oesophageal problems; these were the focus of consultations. However, participants were concerned about overloading patients with information and the risk of patients potentially refusing treatment.

"You try not to overload them with too much information because you know that sometimes they can't even take it on board at the best of times". (P2)

Patient education was a key issue that emerged from the data; participants placed importance specifically on the education of patients in relation to administration instructions and common side effects of bisphosphonates. This would usually take the form of a set of predefined counselling points.

"I think when you have a drug like a bisphosphonate, which is complex with its instruction on how to take it and people are tied up in that". (GP1)

Although some participants advised bisphosphonate patients to seek dental check-ups, most reported that many of their patients, in general, appeared to not appreciate the importance of achieving and maintaining good dental health through self-performed daily oral hygiene and regular dental check-ups. This was a common theme reported by participants in relation to patients' outlook on oral health issues as a whole and not just related to the specific preventative strategies for BRONJ. This was identified as a barrier in the management of this patient population and a focus for patient education.

"I would say that their oral hygiene was not particularly great. I think it's probably just not wanting to go to the dentist and fear of the dentist". (P9)

Patients often tend to forget the initial advice given to them and reminders or continuous advice are necessary to enhance patient education. Teamwork highlights the importance of specific counselling and reinforces the advice that is given to patients.

"If a new drug is initiated, that is the time to reinforce what the patients been told about the drug and you know to give them the message. I think the more reinforcement and the more information the better". (GP2)

3. Wider Context

Both GPs and pharmacists identified that there is reluctance amongst certain patients to seek dental advice. A number of reasons were proposed for this, including the cost of dental treatment, a general lack of oral health awareness and patients with dental phobias.

"The processes of how you get people to take their dental health seriously are very difficult. The ones that pay for dentistry are likely to be the ones with good teeth, the others who get free treatment just don't access it". (GP3)

Access to dentists was also felt to be an issue that both pharmacists and GPs had encountered, specifically the availability of dental services for patients and referral pathways between professions.

"*Some people don't even have an NHS dentist. I am aware of where I work, there was a dentist upstairs, but it wasn't an NHS dentist. I think when you want to refer someone to another service you know it is going to be a little bit more problematic than just making an appointment with a GP for example". (P2)*

Participants all described a heavy workload and that in the small amount of time that they had with each patient, they would have to prioritise the information they gave to patients.

"In that 2 minutes that you have got to hand something out to somebody, you concentrate on the important things, such as how to take it, to get their concordance and compliance". (P2)

A lack of communication between both GPs/pharmacists and dentists was identified as a major barrier. The absence of a formal referral process between pharmacists, GPs and the dental profession was highlighted throughout. This was felt not only to be an issue related to BRONJ but represented a wider problem in the management of oral health in primary

care. In order to successfully manage the risk of BRONJ, it was clear from interviewees that communication between professionals is key.

"I think maybe there needs to be a little bit more communication involved with pharmacists. The triangle, pharmacist, dentist and prescriber". (P2)

"Some sort of shared record keeping where you could enter into the system. You have done a review and these side effect were discussed with the patient, that would be brilliant. That would make it part of that clinical record, I'd know about it, the patient would know about it. I think that would work very well". (GP7)

One of the key areas identified by all pharmacists and some of the GPs was the benefit of Medication Use Reviews (MURs) and the New Medicine Service (NMS) in community pharmacies. The MUR and NMS services are both Advanced Service within the NHS Community Pharmacy Contractual Framework in England. An MUR is a structured, adherence centred review of patients prescribed multiple medicines and the NMS service provides support for patients with a long-term conditions that's have been newly prescribed a medicine.[19-20]

These services provide pharmacies with both the time and structure to provide more detailed advice to patients on medications. Bisphosphonates are not currently specified in either service. Although it was felt that many drugs should be included, all participants identified that bisphosphonates should be included in these services due to their specific administration instructions and potential for side-effects.

"I think during an MUR you certainly have more time to focus on the individual drugs and then it kind of triggers in your brain the more important things that you should be speaking to them about". (P2)

4. Professional

GPs acknowledged their role as the prescriber and the need to counsel patients on the side-effects of their medication. Both prescribers and pharmacists were in agreement that pharmacists are the experts on medications and they have a role to play in counselling patients on safe and effective use of medicines.

"*I think counselling about medication is far better done by the pharmacists. I think the other reason is perhaps, when a patient sees a doctor they expect to be able to discuss all aspects of their lives and their care. When they see the pharmacist, they know they are seeing the pharmacist about their medication. I think it is much easier for the pharmacist to keep the patient focused on the drugs and the patient to stay focused on the drugs". (GP1)*

Although pharmacists acknowledged their role in counselling patients on medications, a number of them felt that if a patient needs to be dentally fit before commencing bisphosphonate therapy, then it would be the responsibility of the GP to arrange this. Although in many cases GPs would be responsible for initially prescribing bisphosphonates and their continued prescribing, it was commented that bisphosphonates can, at times, be initiated in secondary care. This was certainly the case for intravenous bisphosphonates with all GPs and pharmacists reporting little or no experience with prescribing or dispensing these products. As intravenous bisphosphonates are usually prescribed in secondary care, it was felt by some of the participants that this was a potential risk, as they can be missed on medication lists.

"Making sure that the dental check has been done and that they're healthy should actually be done before you prescribe medication, because if you prescribe a medicine without knowing that, then technically how do you know that it's going to be safe for the patient to take. I think my role as a pharmacist is certainly to promote that it's been done, and if it hasn't to take further steps with the patient". (P7)

A number of participants also described limited education or training in relation to oral and dental health.

"*We have no training in dental care. You know to brush your teeth and that's what you say to people. I think, I don't know, maybe we should have some more training". (GP5)*

"No not really, a little bit maybe in lectures at university but not with dentists, we have worked quite closely with the doctors but not with dentists". (P1)

DISCUSSION

Summary of main findings

It is apparent that both sets of participants (GPs and pharmacists) had limited knowledge of BRONJ, in particular in relation to its prevalence and the morbidity associated with the condition. As BRONJ is relatively uncommon, the majority of participants also lacked first-hand experience of managing affected patients.

Due to the complexity of this patient group and bisphosphonates as a therapeutic class, interviewees assigned priorities in relation to clinical management and in patient education. Consultations would usually focus on the specific administration requirements and more common GI related adverse effects as opposed to the risk of developing BRONJ and the need for good oral and dental health.

Awareness of the issue was thought to be a key barrier to implementing preventative strategies in this patient group; however wider issues in relation to the attitudes of patients towards oral health, a reluctance to attend the dentist and difficulties in accessing dental services were thought to be potential barriers for patients. The lack of communication between the professions was also cited as a key issue that needs to be addressed for the successful implementation of any future collaborative preventative strategies in this patient group, with the MUR and NMS pharmacy services identified as a potential facilitator.

Pharmacists and GPs reported good working relationships but inter-professional educational opportunities with dental colleagues appear to have been limited in scope or non-existent, and were cited as a potential enabler for improving multidisciplinary working.

Comparison with existing literature

Knowledge on the oral risks associated with bisphosphonate therapy has been reported to be limited,[15] All participants interviewed in this research reported being aware of the risk, although this was introduced before the interviews in the participant information leaflet.

Many of the participants would not routinely mention the risk of osteonecrosis of the jaw when prescribing bisphosphonates or when counselling patients about the medication. This is consistent with a small quantitative study that identified only 17% of patients prescribed oral bisphosphonates were aware of the risk of BRONJ, with the majority of these patients acquiring this knowledge from patient information leaflets and not from their GP.[21]

All participants reported reluctance amongst patients to attend dental appointments, with a significant proportion of their patients being either not registered with a dentist or not

regular attendees. This is consistent with NHS dental statistics, which state that only 52% of the adult population have seen an NHS dentist within the previous 24 months.[22]

A number of clinical guidelines and patient safety alerts recommend that patients should be counselled on the risk of BRONJ and advised to seek a dental check-up prior to initiating bisphosphonate therapy [5, 8]. Our data suggest that this does not appear to routinely happen. A recent study in Japan reported that 62% (n=629) of physicians did not request oral health care by a dentist before commencing bisphosphonate therapy and 72% of participants reported no cooperation between physicians and dentists. They concluded that a strategy for sharing information among physicians, dentists, and patients is required to reduce the incidence of osteonecrosis of the jaw associated with osteoporosis treatment.[23]The population studied were all members of the Japan Osteoporosis Society; the nature of this sample and therefore interest in osteoporosis management of the participants could potentially explain the higher rates of dental referrals than reported in other studies.

Participants felt that communication between GPs and pharmacists was more frequent, with closer working relationships than those between pharmacists and dental clinicians. The MUR and NMS were identified as potential facilitators in the prevention of BRONJ. Bisphosphonates are not directly specified in either of these services at present, although participants were in agreement that it would be beneficial for them to be included. The literature to support both services is mixed; a detailed review by the University of Nottingham found that the implementation of the NMS was constrained by the quality of the pharmacist's relationship with GPs. They found that poor communication between the professions and a lack of awareness or understanding by GPs about the service resulted in a

lack of referrals; this is consistent with statements from some of the GPs in this study. Pharmacists also suggested that GPs were not interested in the NMS as it potentially encroached on professional boundaries and duplicated work undertaken by the GP.[24] In comparison, the GPs in this study, despite having limited knowledge of the service, were all supportive of its role and the reinforcement of important counselling points was thought to be a key responsibility of the pharmacist.

Pharmacists are subject to organisational pressures to meet targets around the MUR service which has been reported to result in their offering the service to patients who meet the minimum inclusion criteria and avoiding offering the service to more complex patients due to time pressures.[25] This potentially impacts the patient group under study as a clear theme that emerged from the data was the complexity and polypharmacy issues of patients taking bisphosphonates.

An ethnographic study, utilising observations and patient interviews in two English community pharmacies found that patients generally were positive about the MUR, and patients tended to view the pharmacist as an expert on medicines. However some participants felt wary of the pharmacist's involvement considering that the pharmacists were deliberately or intentionally bypassing the GP. This study also found that there was little evidence to suggest that the professions were collaborating to identify patients who could benefit from the service.[25]

Limitations

The study was based around *a priori* issue of limited knowledge among GPs and pharmacists in the prevention of BRONJ; the concept of BRONJ was introduced during the patient information leaflet, therefore exposing participants to the concept before the interview.

Participants were all located in the North East of England and Cumbria; this therefore may impact on the transferability of findings to other geographical locations or healthcare settings. For example, a variation in the access to dental services in a particular location may influence the practice of participants and patients.

Future work and implications for clinical practice

This study has highlighted a number of areas for future study. However, missing from this study and the wider literature is the dental profession's insight into the interprofessional prevention of BRONJ. A recent publication in *British Dental Journal* highlighted the opportunities for interprofessional working between pharmacists and dentists; with a particular focus on chronic diseases, it was suggested that dental and pharmacy teams should take action to improve communication and devise schemes for collaborative working.[26] Published clinical guidelines recommend that patients should be referred for dental assessment and treatment prior to initiation on bisphosphonate therapy, but it is apparent this is not happening. The impact of this on dentists and their perspective on how the professions can collaborate to improve patient care would be important to consider before implementing any preventative strategies.

Raising awareness of the rare side-effects of medicines is an important consideration when prescribing; explicitly pointing out rare side-effects may create adherence problems and result in non-compliance with a potentially beneficial medicine which needs to be balanced against fully informing patients about the associated risks. Further research with patients to explore this issue would help to guide practitioners and would be applicable to many other rare conditions and medicines.

The patient remains the central focus of the healthcare team, and therefore engaging patients in the management of their health is essential when introducing prevention strategies for BRONJ. Attitudes of patients towards the roles of the various team members and their priorities or expectations when being prescribed a new medicine will guide the development of such services.

CONCLUSION

Both GPs and pharmacists demonstrated relatively limited knowledge in relation to BRONJ and the preventative strategies recommended in the literature. Patients prescribed bisphosphonates often have complex medical histories, requiring practitioners to assign priorities in their management and, as such, the measures required to prevent the development of BRONJ can be overlooked.

Prescribing rates of bisphosphonates are increasing, with an ageing population and increasing emphasis on treating and preventing conditions such as osteoporosis. Therefore, the incidence of BRONJ is likely to increase; this may continue to be the case unless changes are made to current practice . Preventive measures should be implemented and further research performed to assess the effectiveness of such interventions.

Acknowledgements: We thanks the participants who generously gave their time

Contributors: AS and SW designed the study. AS recruited the participants and carried out the study. AS identified the thematic framework and interpreted the data. AS, SW, PP and CH reviewed and refined the data. AS wrote the paper and all authors revised it

Funding: There was no external funding for this project

Competing interests: None

Ethics approval: University of Sunderland Reference PHW52 – 21/12/2015

Data sharing statement – No additional data are available

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Interview Guide

Study Title:

Bisphosphonate related osteonecrosis of the jaw. A study of community pharmacists and general medical practitioners attitudes and perceptions towards the oral implications of bisphosphonate therapy and the influence of this on their practice.

Guide:

This guide should be used as a template and starting point for interviewing participant in the study. Open questioning and providing participants with the opportunity to elaborate on their thoughts and answers should be given priority.

Introduction

Introduce myself explain the format of the interview and confidentiality.

Questions:

How often do you see patients on bisphosphonates?

- Oral/IV
- Initiation or long term patients
- Do you initiate or on secondary care recommendations

Are you aware of the risk of Osteonecrosis of the Jaw?

- Do you know what ONJ is
- Have you encountered patients with ONJ
- Do you see BRONJ as an important issue in practice

- Do you know the risk factors for BRONJ
- Have patients raised concerns regarding dental health

Do you counsel bisphosphonate patients on adverse effects?

- Initiation or long term review
- What do you discuss – do you discuss dental implications
- How do you explain this to patients
- When would you discuss this
- If not, why not

Do you refer bisphosphonate patients to see a dentist?

- Frequency
- Initiation or long term
- All patients or certain patient groups
- If not, why not?

If you don't discuss the risks of BRONJ – why not?

- Lack of knowledge of the risks
- Not perceived as important
- Prioritising of other counselling points

How could this be communicated to the patients?

- Who by
- When
- Referral process to dentists

- Part of NMS/MUR (pharmacists)

Do you feel you should know more about BRONJ?

- Why
- How would you like to achieve this

If a referral process was designed between the professions how would you envisage this working?

Any barriers to this?

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22/02/2016

Dear

My name is Andrew Sturrock; I am a Senior Lecturer in Pharmacy Practice at the University of Sunderland. I am writing to you as an invitation to take part in a research project that I am running in conjunction with Scott Wilkes, Professor of General Practice and Primary Care.

Please find enclosed the participant information sheet, outlining the background to the study and what is required of participants.

If you would like to take part in the study please contact me via email or telephone at the above address.

Yours faithfully

Andrew Sturrock

Senior Lecturer – Pharmacy Practice and Clinical Therapeutics

Participant Information Sheet

Study Title

Attitudes and perceptions of GPs and community pharmacists towards their role in the prevention of bisphosphonate-related osteonecrosis of the jaw. A qualitative study in the UK.

What is the purpose of this study?

- To explore the attitudes and perceptions of general medical practitioners and community pharmacists, on the risks of osteonecrosis of the jaw associated with bisphosphonate treatment.
- To explore the attitudes and perceptions towards patient counselling and referral to a dental professional, by general medical practitioners and community pharmacists, for both newly started and established bisphosphonate patients.
- To explore any perceived barriers or enablers to optimising management of this patient group.

Why have I been approached?

You have been approached to participate in this study as a general medical practitioner or community pharmacist.

Do I have to take part?

No, participation in this study is entirely voluntary and the decision to take part is completely yours. You can withdraw from the study without giving reasons at any time before, during, or up to 7 days after taking part in the interview.

To withdraw from the study contact the principal investigator via the contact details below. You will not be required to give an explanation for withdrawing from the study.

What happens to me if I take part?

Participation in the study will involve an interview, lasting approximately 30-60 minutes. The researcher will ask you a series questions from which there is absolutely no right or wrong answer. Your answers to these questions may lead to further discussion around any point or topics raised. The interview will be audio recorded by the researcher and transcribed for analysis.

What if something goes wrong?

If you have any concerns around the study please contact the principle investigator, Andrew Sturrock.

Any further concerns can be directed to the Chairperson of the University of Sunderland Research Ethics Committee. Contact details are included at the end of this document.

Will my taking part be kept confidential?

Participation in this study will be kept confidential. No personally identifiable information will be included in any write up or publication.

A list of participants, signed consent forms, audio recordings and transcripts will be stored securely by the principle investigator for a period of up to 5 years. Access will be restricted to the principal investigator, supervisor and persons authorised by the University for Quality Assurance purposes.

What happens to the results?

Finding from the study will be written up as part of a research project at the University of Sunderland. In is anticipated that finding will also be published in peer reviewed journals or presented at conferences.

The report and any published work will be made available to participants by contacting the principle investigator.

Who is organising and funding the research?

The research is organised by Andrew Sturrock, Senior Lecturer in Pharmacy Practice and Clinical Therapeutics at the University of Sunderland, Department of Pharmacy, Health and Wellbeing.

This project is not externally funded.

Who has reviewed the study?

This project has been reviewed by the Subcommittee for Faculty of Applied Sciences, Pharmacy, Health and Wellbeing, of the University of Sunderland Research Ethic Committee.

Contact for further information

- Mr Andrew Sturrock

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  Phone: 0191 515 2448

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- Dr Etta Evans

  Chairperson of the University of Sunderland Research Ethics Committee

  Email: etta.evans@sunderland.ac.uk

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Transcribed Interview

Participant GP1

General Medical Practitioner

19/01/2016

Bold **= AS (Interviewer)**

Normal text = Participant

In your practice would you have seen patients regularly on bisphosphonates?

Yes

And would that have been as the prescriber or would that have been initiated from secondary care

Well, initially certainly when they were first starting to be used they were always secondary care initiated, and certainly in the more complex patients. Towards probably the last 4 to 5 years where the guidance changed. For example….it would have been usually if you had….I think someone over the age of 85 who had a fracture…then the guidance was to initiate bisphosphonate without going through the DEXA scans and all the rest……certainly…In the majority of cases, certainly initially and actually even subsequently they were usually initiated by secondary care..

By secondary care….and would that be both oral and IVs

Yes certainly, yes. We came across oral and IVs. The majority of the patients would have been on oral preparations. Erm, but there were a small number where they were either intolerant to the oral preparations for whatever reason they were administered and I know at the point I retired there was one…..they were bringing something in that was going to be able to be administered by specialist nurses in general practice. I think in a sort of shared care arrangement…..But that…..they were all going to be initiated within secondary care.

Within secondary care…..with all shared care arrangement

I think the GP involvement would largely have been in arranging for district nurses to actually give the drug……I think first dose would be given in hospital and then for patient convenience, given at home. I don't quite know what the arrangement would have been…who actually would do the prescribing, whether it was going to be one of these homecare systems, where they deliver the drug at home or whether the GP would be asked to take on the prescribing. That was just sort of…..being mooted in a couple of patient when I left, but it hadn't actually been implemented in those patients. They were both very specialised…sort of …complex patients.

So the majority were oral

Absolutely…..I think just a handful of patients that I could think of, who were on the IV preparation

When you were prescribing bisphosphonates…errmm what sort of things were you aware of, or cautions of, is there anything you were errmm thinking about as you were prescribing that drug particularly.

Errmm…..I think it was largely around, errmm the formulation…..which formulation would be suitable for the patient. Some patients preferred the weekly, but I did have one that preferred to actually take the daily one. It was around interaction with errmm you know times of prescriptions to avoid for example the problem with calcium at the same time. Also….trying to take into account especially elderly patient, concordance issues and the difficulty with the instruction. I knew them by heart.

Very specific instructions

Very specific instructions, that had to be you know……Issued to the patient to make sure that they were taken properly. And then later on with older patients who have got medication dispensed in dosette boxes and mediboxes etc. like that. The difficulty of having a spate one with a drug so…a lot of people……..to do with the practical…..practicalities of actually how they drug and the bisphosphonate and things rather that then the intricacies of how it worked and all the rest of it.

Great….Errmm….so was there any side effects particularly of bisphosphonates you were aware of in practice, or came across regularly.

Ermm I think largely it was….side effects, intolerance, GI intolerance. Having to be aware of the potential for errmm oesophageal ulceration especially if the patient developed dyspepsia. I did have 2 patients that I became aware of osteonecrosis of the jaw.

OK

Once they had actually developed it……They were both very complex patients, but they were……the amount of morbidity involved with the ONJ in both of those patient was considerable….errmm and then later on towards the last 2-3 years of my practice was the discussion about the duration of therapy of bisphosphonate.

Bisphosphonate holidays?

Holidays and things like that…. Certainly when I would have first started to use them, there was absolutely no discussion about the duration of therapy.

Lifelong

That was the assumption at that time, it was lifelong therapy. Errmm and then errmm later on there was discussions about the atypical fractures….in the femur and then bisphosphonate holidays were being mooted and discussed…….Errmm....the major difficulty I encountered was the lack of errmm how should we say…..agreement, if you put it that way…..guidance……There was a lot of discussion about bisphosphonate holidays. I have to say slightly vested interest as my mother had been taking for many years for osteoporosis. I was aware of that and also unable to get any agreed opinion as to how long bisphosphonates should be continued in a patient to giver the maximum benefit. When you should consider the holiday, should you use something else instead…….how long was the holiday going to be for and that guidance at that point just was not there…..Errmm and when we reviewed our patient, we actually did an audit to review…..certainly of patients taking bisphosphonates, and then we ended up having to write to the bone clinic to say what is your advice? Those patients who they did see there didn't seem to be any sort of rationale that I could see, into why decisions were made and what those decisions were. It all seemed to be rather adhoc.

A lot of personal opinion?

I think it was, certainly nothing written there and we are going to develop…we kept hearing developed guidelines would be developed but certainly at the time I had seen nothing relating to that. When I read the patient record of those that had been seen they were seen by the consultant at the clinic and of course that meant considerable waiting time.

Yes

There was a specialist nurse…errmm there didn't seem to be consistency between them either, as to how they were making their decision, it was more like they had a feeling this was the right thing to do. Certainly there was nothing formal to ask in GP land.

As prescribers

As prescribers to actually say, this is the guidance that I was aware of.

OK, interesting. Going back to the two patients which you came across with ONJ errmm were you aware of ONJ before you cam e across these patients.

I was aware of it, as one of the many …you know…one of those that was in there.

On the list

On the list, so I was aware of its potential as a complication and errmm so when one of the patients did develop, he had a persistent dental abscess, the alarm bell did start to ring.

Did he present to you?

He presented to his dental practitioner. As I said he was a complex patient on long term steroids, for complex gout. Very severe, but only a man in his 40s and he after many years errmm as a smoker, drank excessively, diet was poor, a (location) man. After many years he developed an abscess and it didn't…he came for antibiotics. He was told in the end he must see a dentist. I think after about the third time of presenting he decided to go to his dentist and found it was rather more complex.

Did you have difficulty getting that patient to see his dentist?

Yes, that patient was reluctant. I think basically he didn't like going to the dentist and my thinking he also had to pay. My perception is that this is a major barrier.

A barrier

A phenomenal barrier…..Errmm you know I think the dental hygiene of an awful lot of my patients was you know…a cause for concern. And yet they couldn't afford or didn't perceive it was something they could afford to pay for. They weren't registered, we then had to refer them to a dental clinic within the surgery building, but it was only for complex……you know….we couldn't really refer them up.

OK, community dentistry…Really interesting. Errmm so I guess two patients in your career is not a lot of patients to have come across.

But I remember them…because I said it caused significant morbidity to both of them.

Were you aware of the risk factors for developing osteonecrosis of the jaw, other than the bisphosphonates?

I was aware that poor dental hygiene and that would obviously, in combination with the bisphosphonate would be more of an issue. But I wasn't aware of anything specifically.

OK, when you initiated bisphosphonates and you prescribe them….or during medication reviews, would you have counselled patients on adverse effects of bisphosphonates and not just osteonecrosis of the jaw… Other than the sort of dosing instructions

Not particularly……any…I don't think so. I think perhaps because in very few where they actually just taking bisphosphonates….bisphosphonates was one of a large list of other medications they were taking. Unless the patient…I think the one that would have been stressed would have been the dyspepsia……I think…because of the awareness of the ulceration of the oesophagus, and I think somewhere way back in my career I saw someone who had you know oesophageal ulceration from bisphosphonate therapy. It's the sort of thing that once you see it…..you then remember it. I suspect and thinking back now that probably….I was having had 2 patients with osteonecrosis of the jaw I did sort of mention to people when they started, subsequent to that.

After you seen two patients?

Until I had actually…..you know…..it's that sort of thing that how frequently does it happen?….when you have a list.

Not sure on the prevalence? Lacking in awareness?

Certainly, how common was it….certainly you know it is one of those thing were you get osteonecrosis of the jaw…..you get Osteonecrosis of the femoral head……how significant is it….and I think again beginning when bisphosphonates were not being used so much……it is always, its prevalence was going to be much less…..it came to be used more frequently than it was something we were going to be seeing. I think it would have been perhaps less…I don't know in the denture less older patient which is where we were using it in the majority of patients, with false tetchy it wasn't going to be a major issue. I think when it started being used in more complex patients, young people and when it was started being used…..almost prophylactically…..Patients who were taking steroids.

Bone protection

Bone protection became a major issue, with things like steroid use and it started being used in younger patients.

More being prescribed….more

I think it was in the bone protection side of it, rather than in the treatment of osteoporosis. Slightly different demographics

OK, did you ever have patients discuss with you dental concerns who were taking bisphosphonates

Apart from the guy who got the dental abscess….I am…..wasn't…I can't think of anyone particularly who came in and discussed…..certainly no one actually raised it as a particular concern.

Going forward is……would you think counselling on osteonecrosis of the jaw is relevant to prescribers. Should it be part of their……

Yes. I mean it's sort of can be such a potentially serious problem for patients that it's almost a sort of…….the……..I am not explain myself very well……..The two patient I saw were very complex patients, both of them had considerable morbidity, needing surgery and stabilisation, of the jaw etc.

One of them when they tried to fix one side of the jaw, and opened her mouth the other side…..it disintegrated…..She ended up with real problems. I think as I say…..it's that sort of awareness that makes you think twice about it. I know for example in renal transplant placements, pre transplant they don't go onto the list unless they have a dental check-up. It's part of the work up.

Yes

Maybe everyone is a bit blasé about the potential for the problem……Does it….this is a drug that you really need to have, but before we can prescribe it safely for you, you need to have a dental check-up. I don't know if that should come within you know…….who pays for that then? That becomes the difficulty

In an ideal world?

I suppose you say to the patient, if it is an increasing problem it should be part of the checklist. As you wouldn't prescribe…..necessarily to a patient with active peptic ulceration. Then there is the argument for saying you wouldn't give a bisphosphonate without making sure the patient doesn't have dental problems either…..That's my perception of it…if you really want to do it properly and it's a problem. I certainly wouldn't prescribe a bisphosphonate to someone who recently had and endoscopy and found to have peptic ulcers. So……if they had a dental check, then fine, I think the patient would have to make that choice.

If that patient refused the dental check, would you still prescribe?

As long as they…well, up to the patient. If the patient said and I think patient need to be involved in these decisions. "I have heard what you say but I am prepared to accept the risk of what happens to my jaw if I don't have dental check". And the potential benefit of having a bisphosphonate is great, you weigh it up then there is an argument for saying the patient understands the consequences of not having a dental check and that they might develop osteonecrosis of the jaw…..Patient may say I am not having a dental check and I would rather not take the medicines….As long as it is an informed choice.

A lot about patient education

Patient education….and it is engaging patients and also expecting the patient to be more involved.

Responsibility

Taking responsibility and not just saying…what do you think….well have a dental check…I think that, in an ideal world what should be done…..but a lot of the time , certainly with older patients there is a bit of disenfranchise and we think it's a good idea……here are some more tablet for you…so

Coming back to the barrier, we said about cost and patients not prepared. They have come to see you for free, prescribed meds for free and then asking them to go and pay

That right, and I think I have to say I think it would be , perhaps different from the patients point of view if they have recently fallen and had a fracture……they might be more inclined to go for the dental check, because they have had the fracture and can see the potential value having the bisphosphonate. I think doing that in a patient who you were using for bone protection.

Like primary prevention

Yes, primary prevention…..I think it would be very difficult to sell it to a lot of patients on that basis, where and lot of them might say I won't take them….I won't have the dental check-up. I just won't take them.

We then have the risks of them not taking the bisphosphonate

Exactly…..I think doctors and I include myself in this, are not well taught in explaining risk to patients, it's difficult and I think we don't really necessarily understand the risk for every medication and the benefits. To try and explain the risk to the patient and the potential benefit as opposed to the risks of osteonecrosis of the jaw.

Really a thing difficult to get right

Difficult concept…if you are thinking of….you know……some of the less articulate, less educated patients, for them to understand that. Then the feeling that you might then be denying them potentially…

Treatment

Treatment which is actually going to be of benefit to them…yeah

OK, really Interesting…..Would you say that as….the prescriber, would you think that is it your sole responsibility or would you think there other HC professions. Pharmacists?

I think pharmacists are far better… I mean I think….I think the initial prescriber wherever that is initiated it is that is the person who is making the decision

Yeah

To start the drug, in that patient…and I think they should……..do the initial explaining…..The checks and that….but it is a lot of information for patients to take on.

OK

Certainly in a busy hospital environment…and I have to say I think counselling about medication is far better done by the pharmacists….I think the other reason is perhaps……when a patient sees a doctor they expect to be able to discuss all aspects of their lives and their care almost…you know…discuss the cat, the auntie….the uncle….the kids….whatever else, the social drugs etc……..When they see the pharmacist they know they are seeing the pharmacist about their medication…..I think it is much easier for the pharmacist to keep the patient focused on the drugs and the patient to stay focused on the drugs.

On the medication

Rather than to be side tracked on other things…so I certainly think they benefit from the pharmacist, certainly if the patient is collecting prescriptions regularly, is that….therefore the prescription for the pharmacist to reinforce initial advise and the message…..I think that is really where I would see the pharmacist role being invaluable.

And to expand on that advice?

Yes…absolutely…because you know…..advise changes……errmm and concerns change…and benefits change…information about medication changes and I think that when they are having that discussion that that contact with the patient on a regular basis, I think that ideally placed to be able to do that…yep……I certainly….and then within our practice and certainly in some of the community

pharmacies where they were actually undertaking some sort of medication reviews…I think that is the ideal time to be…

To be giving this message

To be giving that….and if the patient is going to a regular pharmacist. If a new drug is initiated, that is the time to reinforce what the patients been told about the drug and you know to give them the message and I think more reinforcement and the more information the better.

So, in terms of….sort of osteonecrosis of the jaw counselling, maybe by a pharmacist. If you are the GP who started the medication errmm you have reviewed the patient and then the pharmacist has brought up this issue of osteonecrosis of the jaw with this patient…would you like to see that patient referred back to yourself or would you like that patient to be

I would be delighted if the pharmacist would refer that patient to the dentist….I think that because….I think the fewer steps in the patients journey…if you see what I mean…the better. Because what I am....going to do if the pharmacist has encountered this…..then the thing to do is to say to the patient to go to the dentist….because all I am going to do when I see the patient is say you need to go to the dentist….and the patient is going to perhaps then going sit there and say…you brought me in to tell me that.

It's another step

It's another step and another….appointment…I think its if….if....you know…I think if the pharmacist says to me I have told the patient they need to see the dentist so perhaps the next time you see them you could reinforce that message and follow up…so you flag it up and say....look the pharmacist did say…or you could do it…..you can reinforce it in different ways…..we would certainly use our repeat prescription systems……on the right side you know…as a reminder you need to see your dentist…have you seen your dentist…..and follow it up that way…errmm and sometimes even a phone call

Yes

Have you been to your dentist yet…so you are reminding them…..I would be very happy in that situation for the pharmacist to?

At the point of the initial prescriptions.

Any time at all, I have no problem as long as its pointed out to the patient at some time…..you know….and you can do it in a way that not going to cause issues…you have been given a lot of information…was it mentioned you ought to see your dentist and this is why……I don't think that does any harm at all… they often…when the drug is initiated there is a lot of other stuff happening with the patient and they may not take on board all of these messages

As the prescriber if…..if the pharmacist is going to refer to the dentist, would you….where would you like to be brought back into that process…..would you like to be informed?

I think…I think it would be…I mean…if we had proper shared records it wouldn't be an issue because the pharmacist could update the records accordingly…

Yeah

But certainly we had….you know…our pharmacist could communicate with us through System One. Certainly some of the pharmacists could…not all of them… and you could even just send a message

saying….I advised this patient to go to the dentist…..so that it can be flagged up…as an alert on the front of the patient records….if this patient needs to be seen....has been checked....follow up that this patient has seen the dentist…I think that's only….I think it does two things….first of all so that we know they have been advised to do it and you can follow up….and we can keep raising it……With the patient as a concern and reinforcing why it is important.

In terms of information that you would like back from the dentist, would you like records of that as well…or

I don't think a record….but I think if the patient is on them…..a note form the dentist to say I have seen Mr so and so has been for his check-up…..all is fine. Or I have concerns I think obviously if there was something negative that …..You know…there was a problem that you might have to reconsider the treatment….then I think…..I would expect the dentist to communicate that back.

Back to you

I think in patients on bisphosphonates....it wouldn't do any harm for the dentist to drop a note round and say…..in the same way as they do for the transplant patients when they have been to the dentist. If it's part of their initiation…..part of their protocol….their checklist….whatever you want to call it….before starting treatment or while they are on treatment….everyone is aware why it is important…I don't think it should be a problem for the dentist to…..just say I have seen this and….it's not a problem to communicate that back so…..so you have got it in the….in the records, in the same way as if a pharmacist gives my patient….one of my patients a flu jab.

Yes…..exactly

I expect them to tell me that they have had something….as its part of their…..their care. So it's important.

OK, errmm I have most of my questions really….I think if the patient went to their GP…as their dentist sort of thought no…..they are not fit for a bisphosphonate….would you....again would be comfortable for that dentist to say….hold on we are going to delay treatment until after we have remedied this or

Yeah…it think if I am sending that patient to….unless there was some very pressing reason that the patient must have bisphosphonates then…in which case I think if it was a complex situation like that and I wasn't sure…..then there are always the specialists…..who I could ask for and say….this is the situation…what do you think I ought to do with this patient…but in that situation if the dentist had a real concern I would be holding off treatment until I had the expert option to say…no it withstanding what the dentist said, this paint needs a bisphosphonate and it ok to go ahead with it…as I say really potentially you are doing harm to the patient with that drug. I think in that situation you need to air on the side of caution.

OK…last question …so…I guess as a GP…when practicing do you feel you would have like to have had more information about bisphosphonate osteonecrosis of the jaw?

I would like to have had more information about the potential serious…the potential morbidity….you know….I am aware it was there in among all the other lists of things…errmm but until I was….

First had experience

Yeah…you know. Osteonecrosis of the jaw…so what…really it was only when I saw it affect those two patients….it was like wow….I do think from what I have seen now an awareness of it…..things like that…I certainly seen cancer specialist and people like…referring patients for a dental …

I think perhaps…perhaps…I think also because they may have encountered cases as well….which has then complicated the patients treatment as they have had to go get this problems sorted out…individual people have developed an awareness of it.

Yes, it's been subject to a number of MHRA alerts over recent years, around dental check-up.

I think it's there…part of the problem…I think is when you have a drug like a bisphosphonate which is complex…with its instruction on how to take it…and people are tied up in that…..and I think also that it is a thing of prioritising side effects as well and when you get osteonecrosis in among all the other lists of side effects…it's where that it…..in terms of…..you know…..how important is it…and something I think you know….almost a way of flagging up the really big side effects…the one I remember is the peptic ulceration as it was always flagged up as potentially lethal, perforating the oesophagus and the patient ending up really ill.

Would you want to know…..in terms of prevalence or more, severity to the patient

I think….I think prevalence is important to know…errmm it gives….it lets the patient know how common and frequently it can occur….and us as well off course…..I think in terms of severity because you can have a prevalent side effect that's not that series…you know if I take amoxicillin it makes me nauseated…that is fairly common but it isn't life threatening…it's not going to hopefully….apart from making me a bit sick not cause a major problem….there are two issues there…prevalence is useful to know but I think the severity of the side effect…you can say to a patient look its very rare…but if it happens you have got a big problem with it….because of what it can do…I don't know if that's explained it very well.

No….No

I think there are some side effects…like a patient on methotrexate who gets oral ulceration…yeah ok…lots of people might…..but in your situation it could be very serious…I think those are ones that we need to flag up as being very serious.

OK, I have no more questions unless there is anything else you would like to discuss..

No.no….that's fine

BMJ Open

Attitudes and perceptions of GPs and community pharmacists towards their role in the prevention of bisphosphonate-related osteonecrosis of the jaw. A qualitative study in the North East of England.

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2017-016047.R2
Article Type:	Research
Date Submitted by the Author:	06-Jul-2017
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Primary Subject Heading:	Qualitative research
Secondary Subject Heading:	General practice / Family practice
Keywords:	ORAL & MAXILLOFACIAL SURGERY, Bone diseases < ORTHOPAEDIC & TRAUMA SURGERY, PRIMARY CARE, QUALITATIVE RESEARCH, Adverse events < THERAPEUTICS

Attitudes and perceptions of GPs and community pharmacists towards their role in the prevention of bisphosphonate-related osteonecrosis of the jaw. A qualitative study in the North East of England.

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Word count: 4091

Key Words:

Bisphosphonate-Related Osteonecrosis of the Jaw, General Practitioners, Pharmacists, Interdisciplinary Communication, Qualitative Research

ABSTRACT

Background: Bisphosphonate-related osteonecrosis of the jaw (BRONJ), is a rare, yet significant, adverse effect of bisphosphonate therapy. A multidisciplinary approach to the prevention of BRONJ is recommended, due to the significant morbidity and difficulty treating the condition. Current evidence suggests that both general practitioners (GPs) and community pharmacists have limited knowledge relating to BRONJ and that preventative strategies are rarely implemented.

Objective: To explore the attitudes and perceptions of general practitioners and community pharmacists on the risks and preventative strategies for the development of BRONJ.

Design: Interpretivist methodological approach using qualitative semi-structured interviews.

Participants: 9 community pharmacists and 8 general practitioners.

Setting: Primary Care in North East England and Cumbria, UK.

Methods: Using a Grounded Theory methodology and integrating a process of constant comparison in the iterative enrichment of data sets, semi-structured interviews were undertaken, transcribed and analysed using framework analysis. Salient themes were identified and related back to extant literature in the field.

Results: Four salient and inter-related themes emerged: (1) uncertain knowledge, indicating limited exposure of respondents to BRONJ, and limited awareness of the implications of its diagnosis, risk factors and preventative strategies; (2) patient specific, referring to the complexity of patients, patient education and prioritising aspects of care; (3) wider context,

indicating a lack of interdisciplinary communication and referral processes between professions, work load pressures, access and patient receptivity to dental services and; (4) professional, reflecting professional roles and responsibilities, authority and educational initiatives

Conclusions: Effective communication or collaborative care between general practitioners and community pharmacists for the prevention of BRONJ is not apparent. Interventions to mitigate against the risk of developing BRONJ and clarity of general practitioner and community pharmacy roles are required.

Main strengths and limitations of this study

- Although BRONJ is not a common finding, affected patients experience significant morbidity, and management of this condition warrants further study to stimulate improved patient care.
- A qualitative approach yielded rich data through in-depth semi-structured interviews with two groups of healthcare professionals (general practitioners and community pharmacists). Constant comparison with concurrent data collection and analysis allowed further exploration and refining of emerging themes
- A study limitation was that, although consistent with the methodological approach, the sample size was relatively small. Furthermore, the study was conducted in the North East of England and Cumbria, which may impact on transferability of the findings to other settings.

INTRODUCTION

Bisphosphonates are a class of drugs used in a variety of therapeutic indications; such as osteoporosis, Paget's disease, hypercalcaemia of malignancy, osteolytic bone metastases and osteolytic lesions of multiple myeloma.[1] In practice, they are most commonly prescribed in the management of osteoporosis.

The prescribing of bisphosphonates has increased considerably over recent years. Statistical evaluation of prescribing in England reveals a rise of 122.6% in the number of individual prescription items dispensed between 2004 and 2014.[2] Alendronic acid is the most commonly prescribed bisphosphonate, with 7,391,000 individual dispensations in 2014.[2] This rise may be attributable to increases in the proportion of elderly people in the UK population, publication of guidance recommending the prescribing of bisphosphonates and the availability of generic products. Risk for bisphosphonate-related osteonecrosis of the jaw (BRONJ) in people taking bisphosphonates is hypothesised to be related to the unique nature of the blood supply, structure, and function of the jaw bones.[3] Case reports of BRONJ emerged in the early 2000s; it is now well documented in the literature,[4] and has been subject to a number of prescribing safety alerts in recent years.[3, 5]

The actual incidence and prevalence rates of BRONJ are difficult to quantify, with varying reports in the literature. This is potentially attributable to a low incidence of reporting, the variance in diagnostic criteria and a percentage of mild self-resolving cases remaining undiagnosed. A nationwide study in the UK of patients presenting to departments of oral surgery, oral medicine, oral and maxillofacial surgery and dental hospitals identified 369 cases of BRONJ over a specified 2-year period. Oral bisphosphonates had been prescribed for 56% of the patients. Extrapolation of these data suggests that the incidence of BRONJ

may be 8.2-12.8 cases/million of the population/year, which is equivalent to 508-793 patients/year in the UK.[6]

Ideally, optimal dental health should be established before patients commence bisphosphonate therapy.[7] This is to prioritise care that will subsequently reduce mucosal trauma or act prophylactically to aid in the avoidance of subsequent dental extractions or conditions which may further predispose the patient to oral surgery or dental procedures that impact on the osseous structures of the jaw.[8]

Several prospective studies have identified that dental screening and preventative strategies reduce the risk of osteonecrosis of the jaw. A study by Dimopoulous (2008) found a statistically significant reduction in the incidence of BRONJ with the implementation of preventative measures and Vandone (2012) reported a 50% reduction in the incidence rate with screening and pre-treatment preventative dental care.[9,10] A multidisciplinary approach to the prevention of BRONJ is recommended in the literature for the management of patients requiring bisphosphonate therapy,[11, 12] incorporating both patient and health professional education of the risk of the development of BRONJ.[5] Education of dentists, pharmacists, general practitioners (GPs) and patients about BRONJ is indicated,[13] with specific emphasis on the provision of focused preventative measures and detailed oral hygiene instructions.[14]

Available published evidence describing the attitudes of both GPs and pharmacists towards, and their perceptions of, their roles in preventive strategies for BRONJ is limited. A questionnaire survey of GPs (n=120) and pharmacists (n= 60) in North Wales identified that although both sets of healthcare professionals have regular contact with patients who are prescribed bisphosphonates, they have limited knowledge of the dental implications

associated with treatment. Both groups of professionals reported awareness of the side effects of bisphosphonates; however, only 11.8% of GPs and 9.7% of pharmacists specifically identified osteonecrosis as a potential unwanted effect of therapy.[15]

Furthermore, even when pharmacists and GPs report some knowledge of BRONJ, is it not clear how this awareness influences their clinical practice. The aim of this study was to explore the attitudes and perceptions of GPs and community pharmacists on the risks and preventative strategies for the development of BRONJ.

METHOD

Design

A Grounded Theory approach,[16] with constant comparison was utilised throughout the research. Semi-structured, one-to-one interviews were carried out by a single researcher (AS), at either the School of Pharmacy or the participant's workplace, depending on participant preference and availability. The interviews were audio-recorded and transcribed verbatim; field notes were not taken due to verbatim transcribing. Integrating a process of constant comparison,[17] an initial topic guide (supplementary document 1) was produced and refined by the research team; this served as a benchmark of questioning, which was subsequently developed iteratively as data were progressively enriched.

Setting

Participants were recruited from a range of urban and rural Primary Care locations in the North East of England and Cumbria. GPs were recruited from both teaching and non-teaching practices and community pharmacists were recruited from independent (single or

small chain pharmacies) and multiple pharmacies (companies consisting of numerous pharmacy stores) (see table 1).

Participants

Seventeen participants, 9 community pharmacists and 8 GPs, were recruited to the study. An invitation letter and participant information sheet (supplementary document 2) were posted to GPs and community pharmacists. An initial convenience sample of participants who responded to the invitation was implemented with further recruitment achieved via snowball sampling. No participants who responded to the invitation refused to participate or dropped out of the study.

Analysis

Constant comparison allowed enrichment of data and for new concepts to guide subsequent interviews via the strategic development of each subsequent topic guide. Adoption of Ritchie and Spencer's Framework Analysis[18] allowed salient themes from the findings to be identified. Data were analysed by AS, using Microsoft Word 2010 and Microsoft Excel 2010, with transcripts and emerging themes cross-checked for interpretation and agreed among the research team until saturation occurred; transcripts were not returned to participants for comment or feedback and repeat interviews were not performed. A sample transcript has been published alongside this paper (supplementary document 3). Framework analysis involved a five-stage process: (1) familiarisation with the data – interviews were transcribed by AS and key issues identified through immersion in the data; achieved via iterative cycles of reading and re-reading of transcripts; (2) development of a thematic framework – the initial themes formed the basis of a thematic framework; (3) indexing data – data were indexed against the thematic framework; (4) charting – charts

were produced of the data within the thematic framework; (5) mapping of the data – themes were reviewed until definitive concepts could be produced from the data.

Ethics

Ethical approval was obtained from the University of Sunderland (Reference PHW52).

RESULTS

Seventeen healthcare professionals were included in this study (Table 1 and Table 2). Interviews were carried out between January and October 2016; one hour was designated for each interview.

Table 1. Participant Characteristics – Pharmacists

Participant	Gender	No. years since registration	No. Items dispensed per month	Practice Location	Independent /multiple	Full/part time
P1	Female	6-10	6,000-8,999	Suburban	Independent	Full-time
P2	Female	11-15	12,000+	Suburban	Multiple	Full-time
P3	Female	0-5	3,000-5,999	Suburban	Multiple	Full-time
P4	Female	21+	3,000-5,999	Urban	Independent	Part-time
P5	Female	0-5	6,000-8,999	Urban	Independent	Full-time
P6	Female	0-5	6,000-8,999	Urban	Independent	Full-time
P7	Male	6-10	6,000-8,999	Urban	Multiple	Full-time
P8	Female	16-20	6,000-8,999	Rural	Independent	Part-time
P9	Male	11-15	6,000-8,999	Semi-rural	Multiple	Full-time

Table.2 Participant Characteristics - GPs

Participant	Gender	No. years since registration	Practice Size (patients)	Practice Location	Teaching Practice	Full/part time
GP1	Female	21+	3,000-5,999	Urban	Non-teaching	Full-time
GP2	Male	16-20	12,000+	Urban	Teaching	Part-time
GP3	Male	21+	12,000+	Suburban	Teaching	Part-time
GP4	Male	11-15	9,000-11,999	Semi-rural	Teaching	Full-time
GP5	Female	11-15	12,000+	Suburban	Teaching	Part-time
GP6	Female	16-20	3,000-5,999	Rural	Teaching	Part-time
GP7	Male	21+	9,000-11,999	Semi-rural	Teaching	Full-time
GP8	Male	16-20	9,000-11,999	Semi-Rural	Teaching	Full-time

Four salient inter-related themes emerged. (1) Uncertain knowledge – a lack of familiarity with the subject area, the prevalence and significance of BRONJ and limited exposure to the condition. (2) Patient Specific – complexity of patients, clinical priorities and patient education. (3) Wider context – access/fear of dental services, inter-professional communication and clinical workload. (4) Professional – perceived responsibilities, authority and inter-professional education.

1. Uncertain Knowledge:

All participants perceived themselves to have some degree of knowledge on the adverse effects that are associated with bisphosphonate therapy. The concept of BRONJ was introduced in the participant information sheet and opened up for discussion during the interview; participants actually had minimal knowledge on this topic but all were aware of the potential risk.

"I think it was probably sitting way at the back of my mind…it was probably in a lecture at some point". (GP4)

Although poor dental health and the duration of therapy were frequently identified, all of the participants had limited awareness of the risk factors for the development of BRONJ.

"I am not aware of any, I imagine that significant dental problems would be associated with it, but I am not actually aware of any others". (GP3)

Participants were uncertain on the prevalence of BRONJ and had limited knowledge on the significant morbidity associated with the condition.

"I have never seen it, so I presume it's not very common…I don't really know how serious it is when it does happen". (P3)

One GP had first-hand experience of managing patients with BRONJ, and the significant morbidity that her patients had experienced influenced their attitude towards management of patients who are prescribed bisphosphonates. None of the other participants had been involved with the care of a patient with BRONJ.

"It's the sort of thing that once you see it, you then remember it. They were both very complex patients, but the amount of morbidity involved with the osteonecrosis of the jaw in both of those patients was considerable". (GP1)

2. Patient Specific

Patients prescribed bisphosphonates usually have a number of co-morbidities. They are often elderly and are prescribed multiple medications, and their management can be complex. Indeed, this complexity requires that practitioners assign priorities in their care,

relating to both the overall management of the patient and to more specific priorities related to bisphosphonates.

"They are lower down in the pecking order of things that we look at when we are supervising polypharmacy, when we are looking at chronic disease management". (GP3)

All participants identified bisphosphonates as having very specific administration instructions and common side effects, such as gastro-intestinal or oesophageal problems; these were the focus of consultations. However, participants were concerned about overloading patients with information and the risk of patients potentially refusing treatment.

"You try not to overload them with too much information because you know that sometimes they can't even take it on board at the best of times". (P2)

Patient education was a key issue that emerged from the data; participants placed importance specifically on the education of patients in relation to administration instructions and common side effects of bisphosphonates. This would usually take the form of a set of predefined counselling points.

"I think when you have a drug like a bisphosphonate, which is complex with its instruction on how to take it and people are tied up in that". (GP1)

Although some participants advised bisphosphonate patients to seek dental check-ups, most reported that many of their patients, in general, appeared to not appreciate the importance of achieving and maintaining good dental health through self-performed daily oral hygiene and regular dental check-ups. This was a common theme reported by participants in relation to patients' outlook on oral health issues as a whole and not just

related to the specific preventative strategies for BRONJ. This was identified as a barrier in the management of this patient population and a focus for patient education.

"I would say that their oral hygiene was not particularly great. I think it's probably just not wanting to go to the dentist and fear of the dentist". (P9)

Patients often tend to forget the initial advice given to them and reminders or continuous advice are necessary to enhance patient education. Teamwork highlights the importance of specific counselling and reinforces the advice that is given to patients.

"If a new drug is initiated, that is the time to reinforce what the patients been told about the drug and you know to give them the message. I think the more reinforcement and the more information the better". (GP2)

3. Wider Context

Both GPs and pharmacists identified that there is reluctance amongst certain patients to seek dental advice. A number of reasons were proposed for this, including the cost of dental treatment, a general lack of oral health awareness and patients with dental phobias.

"The processes of how you get people to take their dental health seriously are very difficult. The ones that pay for dentistry are likely to be the ones with good teeth, the others who get free treatment just don't access it". (GP3)

Access to dentists was also felt to be an issue that both pharmacists and GPs had encountered, specifically the availability of dental services for patients and referral pathways between professions.

"*Some people don't even have an NHS dentist. I am aware of where I work, there was a dentist upstairs, but it wasn't an NHS dentist. I think when you want to refer someone to*

another service you know it is going to be a little bit more problematic than just making an appointment with a GP for example". (P2)

Participants all described a heavy workload and that in the small amount of time that they had with each patient, they would have to prioritise the information they gave to patients.

"In that 2 minutes that you have got to hand something out to somebody, you concentrate on the important things, such as how to take it, to get their concordance and compliance". (P2)

A lack of communication between both GPs/pharmacists and dentists was identified as a major barrier. The absence of a formal referral process between pharmacists, GPs and the dental profession was highlighted throughout. This was felt not only to be an issue related to BRONJ but represented a wider problem in the management of oral health in primary care. In order to successfully manage the risk of BRONJ, it was clear from interviewees that communication between professionals is key.

"I think maybe there needs to be a little bit more communication involved with pharmacists. The triangle, pharmacist, dentist and prescriber". (P2)

"Some sort of shared record keeping where you could enter into the system. You have done a review and these side effect were discussed with the patient, that would be brilliant. That would make it part of that clinical record, I'd know about it, the patient would know about it. I think that would work very well". (GP7)

One of the key areas identified by all pharmacists and some of the GPs was the benefit of Medication Use Reviews (MURs) and the New Medicine Service (NMS) in community pharmacies. The MUR and NMS services are both Advanced Service within the NHS

Community Pharmacy Contractual Framework in England. An MUR is a structured, adherence-centred review of patients prescribed multiple medicines and the NMS service provides support for patients with long-term conditions that have been newly prescribed a medicine.[19-20]

These services provide pharmacies with both the time and structure to provide more detailed advice to patients on medications. Bisphosphonates are not currently specified in either service. Although it was felt that many drugs should be included, all participants identified that bisphosphonates should be included in these services due to their specific administration instructions and potential for side-effects.

"I think during an MUR you certainly have more time to focus on the individual drugs and then it kind of triggers in your brain the more important things that you should be speaking to them about". (P2)

4. Professional

GPs acknowledged their role as the prescriber and the need to counsel patients on the side-effects of their medication. Both prescribers and pharmacists were in agreement that pharmacists are the experts on medications and they have a role to play in counselling patients on safe and effective use of medicines.

"*I think counselling about medication is far better done by the pharmacists. I think the other reason is perhaps, when a patient sees a doctor they expect to be able to discuss all aspects of their lives and their care. When they see the pharmacist, they know they are seeing the pharmacist about their medication. I think it is much easier for the pharmacist to keep the patient focused on the drugs and the patient to stay focused on the drugs". (GP1)*

Although pharmacists acknowledged their role in counselling patients on medications, a number of them felt that if a patient needs to be dentally fit before commencing bisphosphonate therapy, then it would be the responsibility of the GP to arrange this. Although in many cases GPs would be responsible for initially prescribing bisphosphonates and their continued prescribing, it was commented that bisphosphonates can, at times, be initiated in secondary care. This was certainly the case for intravenous bisphosphonates with all GPs and pharmacists reporting little or no experience with prescribing or dispensing these products. As intravenous bisphosphonates are usually prescribed in secondary care, it was felt by some of the participants that this was a potential risk, as they can be missed on medication lists.

"Making sure that the dental check has been done and that they're healthy should actually be done before you prescribe medication, because if you prescribe a medicine without knowing that, then technically how do you know that it's going to be safe for the patient to take. I think my role as a pharmacist is certainly to promote that it's been done, and if it hasn't to take further steps with the patient". (P7)

A number of participants also described limited education or training in relation to oral and dental health.

"*We have no training in dental care. You know to brush your teeth and that's what you say to people. I think, I don't know, maybe we should have some more training". (GP5)*

"No not really, a little bit maybe in lectures at university but not with dentists, we have worked quite closely with the doctors but not with dentists". (P1)

DISCUSSION

Summary of main findings

It is apparent that both sets of participants (GPs and pharmacists) had limited knowledge of BRONJ, in particular in relation to its prevalence and the morbidity associated with the condition. As BRONJ is relatively uncommon, the majority of participants also lacked first-hand experience of managing affected patients.

Due to the complexity of this patient group and bisphosphonates as a therapeutic class, interviewees assigned priorities in relation to clinical management and in patient education. Consultations would usually focus on the specific administration requirements and more common GI-related adverse effects as opposed to the risk of developing BRONJ and the need for good oral and dental health.

Awareness of the issue was thought to be a key barrier to implementing preventative strategies in this patient group; however wider issues in relation to the attitudes of patients towards oral health, a reluctance to attend the dentist and difficulties in accessing dental services were thought to be potential barriers for patients. The lack of communication between the professions was also cited as a key issue that needs to be addressed for the successful implementation of any future collaborative preventative strategies in this patient group, with the MUR and NMS pharmacy services identified as a potential facilitator.

Pharmacists and GPs reported good working relationships but inter-professional educational opportunities with dental colleagues appear to have been limited in scope or non-existent, and were cited as a potential enabler for improving multidisciplinary working.

Comparison with existing literature

Knowledge on the oral risks associated with bisphosphonate therapy has been reported to be limited,[15] All participants interviewed in this research reported being aware of the risk, although this was introduced before the interviews in the participant information leaflet.

Many of the participants would not routinely mention the risk of osteonecrosis of the jaw when prescribing bisphosphonates or when counselling patients about the medication. This is consistent with a small quantitative study that identified only 17% of patients prescribed oral bisphosphonates were aware of the risk of BRONJ, with the majority of these patients acquiring this knowledge from patient information leaflets and not from their GP.[21]

All participants reported reluctance amongst patients to attend dental appointments, with a significant proportion of their patients being either not registered with a dentist or not regular attendees. This is consistent with NHS dental statistics, which state that only 52% of the adult population have seen an NHS dentist within the previous 24 months.[22]

A number of clinical guidelines and patient safety alerts recommend that patients should be counselled on the risk of BRONJ and advised to seek a dental check-up prior to initiating bisphosphonate therapy [5, 8]. Our data suggest that this does not appear to routinely happen. A recent study in Japan reported that 62% (n=629) of physicians did not request oral health care by a dentist before commencing bisphosphonate therapy and 72% of participants reported no cooperation between physicians and dentists. They concluded that a strategy for sharing information among physicians, dentists, and patients is required to reduce the incidence of osteonecrosis of the jaw associated with osteoporosis treatment.[23]The population studied were all members of the Japan Osteoporosis Society; the nature of this sample and therefore interest in osteoporosis management of the

participants could potentially explain the higher rates of dental referrals than reported in other studies.

The MUR and NMS were identified as potential facilitators in the prevention of BRONJ. Bisphosphonates are not directly specified in either of these services at present, although participants were in agreement that it would be beneficial for them to be included. The literature to support both services is mixed; a detailed review by the University of Nottingham found that the implementation of the NMS was constrained by the quality of the pharmacist's relationship with GPs. They found that poor communication between the professions and a lack of awareness or understanding by GPs about the service resulted in a lack of referrals; this is consistent with statements from some of the GPs in this study. Pharmacists also suggested that GPs were not interested in the NMS as it potentially encroached on professional boundaries and duplicated work undertaken by the GP.[24] In comparison, the GPs in this study, despite having limited knowledge of the service, were all supportive of its role and the reinforcement of important counselling points was thought to be a key responsibility of the pharmacist.

Pharmacists are subject to organisational pressures to meet targets around the MUR service which has been reported to result in their offering the service to patients who meet the minimum inclusion criteria and avoiding offering the service to more complex patients due to time pressures.[25] This potentially impacts the patient group under study as a clear theme that emerged from the data was the complexity and polypharmacy issues of patients taking bisphosphonates.

An ethnographic study, utilising observations and patient interviews in two English community pharmacies found that patients generally were positive about the MUR, and

patients tended to view the pharmacist as an expert on medicines. However some participants felt wary of the pharmacist's involvement, considering that the pharmacists were deliberately or intentionally bypassing the GP. This study also found that there was little evidence to suggest that the professions were collaborating to identify patients who could benefit from the service.[25]

Limitations

The study was based around the *priori* issue of limited knowledge among GPs and pharmacists in the prevention of BRONJ; the concept of BRONJ was introduced during the patient information leaflet, therefore exposing participants to the concept before the interview.

Participants were all located in the North East of England and Cumbria; this therefore may impact on the transferability of findings to other geographical locations or healthcare settings. For example, a variation in the access to dental services in a particular location may influence the practice of participants and patients.

Future work and implications for clinical practice

This study has highlighted a number of areas for future study. However, missing from this study and the wider literature is the dental profession's insight into the interprofessional prevention of BRONJ. A recent publication in *British Dental Journal* highlighted the opportunities for interprofessional working between pharmacists and dentists; with a particular focus on chronic diseases, it was suggested that dental and pharmacy teams should take action to improve communication and devise schemes for collaborative working.[26] Published clinical guidelines recommend that patients should be referred for

dental assessment and treatment prior to initiation on bisphosphonate therapy, but it is apparent this is not happening. The impact of this on dentists and their perspective on how the professions can collaborate to improve patient care would be important to consider before implementing any preventative strategies.

Raising awareness of the rare side-effects of medicines is an important consideration when prescribing; explicitly pointing out rare side-effects may create adherence problems and result in non-compliance with a potentially beneficial medicine which needs to be balanced against fully informing patients about the associated risks. Further research with patients to explore this issue would help to guide practitioners and would be applicable to many other rare conditions and medicines.

The patient remains the central focus of the healthcare team, and therefore engaging patients in the management of their health is essential when introducing prevention strategies for BRONJ. Attitudes of patients towards the roles of the various team members and their priorities or expectations when being prescribed a new medicine will guide the development of such services.

CONCLUSION

Both GPs and pharmacists demonstrated relatively limited knowledge in relation to BRONJ and the preventative strategies recommended in the literature. Patients prescribed bisphosphonates often have complex medical histories, requiring practitioners to assign priorities in their management and, as such, the measures required to prevent the development of BRONJ can be overlooked.

Prescribing rates of bisphosphonates are increasing, with an ageing population and increasing emphasis on treating and preventing conditions such as osteoporosis. Therefore, the incidence of BRONJ is likely to increase; this may continue to be the case unless changes are made to current practice. Preventive measures should be implemented and further research performed to assess the effectiveness of such interventions.

Acknowledgements: We thanks the participants who generously gave their time

Contributors: An interest in the subject area was developed by AS as an extension to the interprofessional learning opportunities delivered at the University of Sunderland School of Pharmacy. The multidisciplinary team was assembled to reduce bias and provide rigor in the investigation. AS and SW designed the study. AS recruited the participants and carried out the study. AS identified the thematic framework and interpreted the data. AS, SW, PP and CH reviewed and refined the data. AS wrote the paper and all authors revised it. AS received training in qualitative research skills by the research team and through attendance at a Qualitative Research Methods in Health Course at University College London.

Funding: There was no external funding for this project

Competing interests: None

Ethics approval: University of Sunderland Reference PHW52 – 21/12/2015

Data sharing statement – No additional data are available

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Interview Guide

Study Title:

Bisphosphonate related osteonecrosis of the jaw. A study of community pharmacists and general medical practitioners attitudes and perceptions towards the oral implications of bisphosphonate therapy and the influence of this on their practice.

Guide:

This guide should be used as a template and starting point for interviewing participant in the study. Open questioning and providing participants with the opportunity to elaborate on their thoughts and answers should be given priority.

Introduction

Introduce myself explain the format of the interview and confidentiality.

Questions:

How often do you see patients on bisphosphonates?

- Oral/IV
- Initiation or long term patients
- Do you initiate or on secondary care recommendations

Are you aware of the risk of Osteonecrosis of the Jaw?

- Do you know what ONJ is
- Have you encountered patients with ONJ
- Do you see BRONJ as an important issue in practice

- Do you know the risk factors for BRONJ
- Have patients raised concerns regarding dental health

Do you counsel bisphosphonate patients on adverse effects?

- Initiation or long term review
- What do you discuss – do you discuss dental implications
- How do you explain this to patients
- When would you discuss this
- If not, why not

Do you refer bisphosphonate patients to see a dentist?

- Frequency
- Initiation or long term
- All patients or certain patient groups
- If not, why not?

If you don't discuss the risks of BRONJ – why not?

- Lack of knowledge of the risks
- Not perceived as important
- Prioritising of other counselling points

How could this be communicated to the patients?

- Who by
- When
- Referral process to dentists

- Part of NMS/MUR (pharmacists)

Do you feel you should know more about BRONJ?

- Why
- How would you like to achieve this

If a referral process was designed between the professions how would you envisage this working?

Any barriers to this?

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22/02/2016

Dear

My name is Andrew Sturrock; I am a Senior Lecturer in Pharmacy Practice at the University of Sunderland. I am writing to you as an invitation to take part in a research project that I am running in conjunction with Scott Wilkes, Professor of General Practice and Primary Care.

Please find enclosed the participant information sheet, outlining the background to the study and what is required of participants.

If you would like to take part in the study please contact me via email or telephone at the above address.

Yours faithfully

Andrew Sturrock

Senior Lecturer – Pharmacy Practice and Clinical Therapeutics

Participant Information Sheet

Study Title

Attitudes and perceptions of GPs and community pharmacists towards their role in the prevention of bisphosphonate-related osteonecrosis of the jaw. A qualitative study in the UK.

What is the purpose of this study?

- To explore the attitudes and perceptions of general medical practitioners and community pharmacists, on the risks of osteonecrosis of the jaw associated with bisphosphonate treatment.
- To explore the attitudes and perceptions towards patient counselling and referral to a dental professional, by general medical practitioners and community pharmacists, for both newly started and established bisphosphonate patients.
- To explore any perceived barriers or enablers to optimising management of this patient group.

Why have I been approached?

You have been approached to participate in this study as a general medical practitioner or community pharmacist.

Do I have to take part?

No, participation in this study is entirely voluntary and the decision to take part is completely yours. You can withdraw from the study without giving reasons at any time before, during, or up to 7 days after taking part in the interview.

To withdraw from the study contact the principal investigator via the contact details below. You will not be required to give an explanation for withdrawing from the study.

What happens to me if I take part?

Participation in the study will involve an interview, lasting approximately 30-60 minutes. The researcher will ask you a series questions from which there is absolutely no right or wrong answer. Your answers to these questions may lead to further discussion around any point or topics raised. The interview will be audio recorded by the researcher and transcribed for analysis.

What if something goes wrong?

If you have any concerns around the study please contact the principle investigator, Andrew Sturrock.

Any further concerns can be directed to the Chairperson of the University of Sunderland Research Ethics Committee. Contact details are included at the end of this document.

Will my taking part be kept confidential?

Participation in this study will be kept confidential. No personally identifiable information will be included in any write up or publication.

A list of participants, signed consent forms, audio recordings and transcripts will be stored securely by the principle investigator for a period of up to 5 years. Access will be restricted to the principal investigator, supervisor and persons authorised by the University for Quality Assurance purposes.

What happens to the results?

Finding from the study will be written up as part of a research project at the University of Sunderland. In is anticipated that finding will also be published in peer reviewed journals or presented at conferences.

The report and any published work will be made available to participants by contacting the principle investigator.

Who is organising and funding the research?

The research is organised by Andrew Sturrock, Senior Lecturer in Pharmacy Practice and Clinical Therapeutics at the University of Sunderland, Department of Pharmacy, Health and Wellbeing.

This project is not externally funded.

Who has reviewed the study?

This project has been reviewed by the Subcommittee for Faculty of Applied Sciences, Pharmacy, Health and Wellbeing, of the University of Sunderland Research Ethic Committee.

Contact for further information

- Mr Andrew Sturrock

  Principal Investigator

  Senior Lecturer – Pharmacy Practice and Clinical Therapeutics, University of Sunderland

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  Phone: 0191 515 2448

- Professor Scott Wilkes

  Project Supervisor

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- Dr Etta Evans

  Chairperson of the University of Sunderland Research Ethics Committee

  Email: etta.evans@sunderland.ac.uk

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Transcribed Interview

Participant GP1

General Medical Practitioner

19/01/2016

Bold **= AS (Interviewer)**

Normal text = Participant

In your practice would you have seen patients regularly on bisphosphonates?

Yes

And would that have been as the prescriber or would that have been initiated from secondary care

Well, initially certainly when they were first starting to be used they were always secondary care initiated, and certainly in the more complex patients. Towards probably the last 4 to 5 years where the guidance changed. For example….it would have been usually if you had….I think someone over the age of 85 who had a fracture…then the guidance was to initiate bisphosphonate without going through the DEXA scans and all the rest……certainly…In the majority of cases, certainly initially and actually even subsequently they were usually initiated by secondary care..

By secondary care….and would that be both oral and IVs

Yes certainly, yes. We came across oral and IVs. The majority of the patients would have been on oral preparations. Erm, but there were a small number where they were either intolerant to the oral preparations for whatever reason they were administered and I know at the point I retired there was one…..they were bringing something in that was going to be able to be administered by specialist nurses in general practice. I think in a sort of shared care arrangement…..But that…..they were all going to be initiated within secondary care.

Within secondary care…..with all shared care arrangement

I think the GP involvement would largely have been in arranging for district nurses to actually give the drug……I think first dose would be given in hospital and then for patient convenience, given at home. I don't quite know what the arrangement would have been…who actually would do the prescribing, whether it was going to be one of these homecare systems, where they deliver the drug at home or whether the GP would be asked to take on the prescribing. That was just sort of…..being mooted in a couple of patient when I left, but it hadn't actually been implemented in those patients. They were both very specialised…sort of …complex patients.

So the majority were oral

Absolutely…..I think just a handful of patients that I could think of, who were on the IV preparation

When you were prescribing bisphosphonates…errmm what sort of things were you aware of, or cautions of, is there anything you were errmm thinking about as you were prescribing that drug particularly.

Errmm…..I think it was largely around, errmm the formulation…..which formulation would be suitable for the patient. Some patients preferred the weekly, but I did have one that preferred to actually take the daily one. It was around interaction with errmm you know times of prescriptions to avoid for example the problem with calcium at the same time. Also….trying to take into account especially elderly patient, concordance issues and the difficulty with the instruction. I knew them by heart.

Very specific instructions

Very specific instructions, that had to be you know……Issued to the patient to make sure that they were taken properly. And then later on with older patients who have got medication dispensed in dosette boxes and mediboxes etc. like that. The difficulty of having a spate one with a drug so…a lot of people……..to do with the practical…..practicalities of actually how they drug and the bisphosphonate and things rather that then the intricacies of how it worked and all the rest of it.

Great….Errmm….so was there any side effects particularly of bisphosphonates you were aware of in practice, or came across regularly.

Ermm I think largely it was….side effects, intolerance, GI intolerance. Having to be aware of the potential for errmm oesophageal ulceration especially if the patient developed dyspepsia. I did have 2 patients that I became aware of osteonecrosis of the jaw.

OK

Once they had actually developed it……They were both very complex patients, but they were……the amount of morbidity involved with the ONJ in both of those patient was considerable….errmm and then later on towards the last 2-3 years of my practice was the discussion about the duration of therapy of bisphosphonate.

Bisphosphonate holidays?

Holidays and things like that…. Certainly when I would have first started to use them, there was absolutely no discussion about the duration of therapy.

Lifelong

That was the assumption at that time, it was lifelong therapy. Errmm and then errmm later on there was discussions about the atypical fractures….in the femur and then bisphosphonate holidays were being mooted and discussed…….Errmm....the major difficulty I encountered was the lack of errmm how should we say…..agreement, if you put it that way…..guidance……There was a lot of discussion about bisphosphonate holidays. I have to say slightly vested interest as my mother had been taking for many years for osteoporosis. I was aware of that and also unable to get any agreed opinion as to how long bisphosphonates should be continued in a patient to giver the maximum benefit. When you should consider the holiday, should you use something else instead…….how long was the holiday going to be for and that guidance at that point just was not there…..Errmm and when we reviewed our patient, we actually did an audit to review…..certainly of patients taking bisphosphonates, and then we ended up having to write to the bone clinic to say what is your advice? Those patients who they did see there didn't seem to be any sort of rationale that I could see, into why decisions were made and what those decisions were. It all seemed to be rather adhoc.

A lot of personal opinion?

I think it was, certainly nothing written there and we are going to develop…we kept hearing developed guidelines would be developed but certainly at the time I had seen nothing relating to that. When I read the patient record of those that had been seen they were seen by the consultant at the clinic and of course that meant considerable waiting time.

Yes

There was a specialist nurse…errmm there didn't seem to be consistency between them either, as to how they were making their decision, it was more like they had a feeling this was the right thing to do. Certainly there was nothing formal to ask in GP land.

As prescribers

As prescribers to actually say, this is the guidance that I was aware of.

OK, interesting. Going back to the two patients which you came across with ONJ errmm were you aware of ONJ before you cam e across these patients.

I was aware of it, as one of the many …you know…one of those that was in there.

On the list

On the list, so I was aware of its potential as a complication and errmm so when one of the patients did develop, he had a persistent dental abscess, the alarm bell did start to ring.

Did he present to you?

He presented to his dental practitioner. As I said he was a complex patient on long term steroids, for complex gout. Very severe, but only a man in his 40s and he after many years errmm as a smoker, drank excessively, diet was poor, a (location) man. After many years he developed an abscess and it didn't…he came for antibiotics. He was told in the end he must see a dentist. I think after about the third time of presenting he decided to go to his dentist and found it was rather more complex.

Did you have difficulty getting that patient to see his dentist?

Yes, that patient was reluctant. I think basically he didn't like going to the dentist and my thinking he also had to pay. My perception is that this is a major barrier.

A barrier

A phenomenal barrier…..Errmm you know I think the dental hygiene of an awful lot of my patients was you know…a cause for concern. And yet they couldn't afford or didn't perceive it was something they could afford to pay for. They weren't registered, we then had to refer them to a dental clinic within the surgery building, but it was only for complex……you know….we couldn't really refer them up.

OK, community dentistry…Really interesting. Errmm so I guess two patients in your career is not a lot of patients to have come across.

But I remember them…because I said it caused significant morbidity to both of them.

Were you aware of the risk factors for developing osteonecrosis of the jaw, other than the bisphosphonates?

I was aware that poor dental hygiene and that would obviously, in combination with the bisphosphonate would be more of an issue. But I wasn't aware of anything specifically.

OK, when you initiated bisphosphonates and you prescribe them….or during medication reviews, would you have counselled patients on adverse effects of bisphosphonates and not just osteonecrosis of the jaw… Other than the sort of dosing instructions

Not particularly……any…I don't think so. I think perhaps because in very few where they actually just taking bisphosphonates….bisphosphonates was one of a large list of other medications they were taking. Unless the patient…I think the one that would have been stressed would have been the dyspepsia……I think…because of the awareness of the ulceration of the oesophagus, and I think somewhere way back in my career I saw someone who had you know oesophageal ulceration from bisphosphonate therapy. It's the sort of thing that once you see it…..you then remember it. I suspect and thinking back now that probably….I was having had 2 patients with osteonecrosis of the jaw I did sort of mention to people when they started, subsequent to that.

After you seen two patients?

Until I had actually…..you know…..it's that sort of thing that how frequently does it happen?….when you have a list.

Not sure on the prevalence? Lacking in awareness?

Certainly, how common was it….certainly you know it is one of those thing were you get osteonecrosis of the jaw…..you get Osteonecrosis of the femoral head……how significant is it….and I think again beginning when bisphosphonates were not being used so much……it is always, its prevalence was going to be much less…..it came to be used more frequently than it was something we were going to be seeing. I think it would have been perhaps less…I don't know in the denture less older patient which is where we were using it in the majority of patients, with false tetchy it wasn't going to be a major issue. I think when it started being used in more complex patients, young people and when it was started being used…..almost prophylactically…..Patients who were taking steroids.

Bone protection

Bone protection became a major issue, with things like steroid use and it started being used in younger patients.

More being prescribed….more

I think it was in the bone protection side of it, rather than in the treatment of osteoporosis. Slightly different demographics

OK, did you ever have patients discuss with you dental concerns who were taking bisphosphonates

Apart from the guy who got the dental abscess….I am…..wasn't…I can't think of anyone particularly who came in and discussed…..certainly no one actually raised it as a particular concern.

Going forward is……would you think counselling on osteonecrosis of the jaw is relevant to prescribers. Should it be part of their……

Yes. I mean it's sort of can be such a potentially serious problem for patients that it's almost a sort of…….the……..I am not explain myself very well……..The two patient I saw were very complex patients, both of them had considerable morbidity, needing surgery and stabilisation, of the jaw etc.

One of them when they tried to fix one side of the jaw, and opened her mouth the other side…..it disintegrated…..She ended up with real problems. I think as I say…..it's that sort of awareness that makes you think twice about it. I know for example in renal transplant placements, pre transplant they don't go onto the list unless they have a dental check-up. It's part of the work up.

Yes

Maybe everyone is a bit blasé about the potential for the problem……Does it….this is a drug that you really need to have, but before we can prescribe it safely for you, you need to have a dental check-up. I don't know if that should come within you know…….who pays for that then? That becomes the difficulty

In an ideal world?

I suppose you say to the patient, if it is an increasing problem it should be part of the checklist. As you wouldn't prescribe…..necessarily to a patient with active peptic ulceration. Then there is the argument for saying you wouldn't give a bisphosphonate without making sure the patient doesn't have dental problems either…..That's my perception of it…if you really want to do it properly and it's a problem. I certainly wouldn't prescribe a bisphosphonate to someone who recently had and endoscopy and found to have peptic ulcers. So……if they had a dental check, then fine, I think the patient would have to make that choice.

If that patient refused the dental check, would you still prescribe?

As long as they…well, up to the patient. If the patient said and I think patient need to be involved in these decisions. "I have heard what you say but I am prepared to accept the risk of what happens to my jaw if I don't have dental check". And the potential benefit of having a bisphosphonate is great, you weigh it up then there is an argument for saying the patient understands the consequences of not having a dental check and that they might develop osteonecrosis of the jaw…..Patient may say I am not having a dental check and I would rather not take the medicines….As long as it is an informed choice.

A lot about patient education

Patient education….and it is engaging patients and also expecting the patient to be more involved.

Responsibility

Taking responsibility and not just saying…what do you think….well have a dental check…I think that, in an ideal world what should be done…..but a lot of the time , certainly with older patients there is a bit of disenfranchise and we think it's a good idea……here are some more tablet for you…so

Coming back to the barrier, we said about cost and patients not prepared. They have come to see you for free, prescribed meds for free and then asking them to go and pay

That right, and I think I have to say I think it would be , perhaps different from the patients point of view if they have recently fallen and had a fracture……they might be more inclined to go for the dental check, because they have had the fracture and can see the potential value having the bisphosphonate. I think doing that in a patient who you were using for bone protection.

Like primary prevention

Yes, primary prevention…..I think it would be very difficult to sell it to a lot of patients on that basis, where and lot of them might say I won't take them….I won't have the dental check-up. I just won't take them.

We then have the risks of them not taking the bisphosphonate

Exactly…..I think doctors and I include myself in this, are not well taught in explaining risk to patients, it's difficult and I think we don't really necessarily understand the risk for every medication and the benefits. To try and explain the risk to the patient and the potential benefit as opposed to the risks of osteonecrosis of the jaw.

Really a thing difficult to get right

Difficult concept…if you are thinking of….you know……some of the less articulate, less educated patients, for them to understand that. Then the feeling that you might then be denying them potentially…

Treatment

Treatment which is actually going to be of benefit to them…yeah

OK, really Interesting…..Would you say that as….the prescriber, would you think that is it your sole responsibility or would you think there other HC professions. Pharmacists?

I think pharmacists are far better… I mean I think….I think the initial prescriber wherever that is initiated it is that is the person who is making the decision

Yeah

To start the drug, in that patient…and I think they should……..do the initial explaining…..The checks and that….but it is a lot of information for patients to take on.

OK

Certainly in a busy hospital environment…and I have to say I think counselling about medication is far better done by the pharmacists….I think the other reason is perhaps……when a patient sees a doctor they expect to be able to discuss all aspects of their lives and their care almost…you know…discuss the cat, the auntie….the uncle….the kids….whatever else, the social drugs etc……..When they see the pharmacist they know they are seeing the pharmacist about their medication…..I think it is much easier for the pharmacist to keep the patient focused on the drugs and the patient to stay focused on the drugs.

On the medication

Rather than to be side tracked on other things…so I certainly think they benefit from the pharmacist, certainly if the patient is collecting prescriptions regularly, is that….therefore the prescription for the pharmacist to reinforce initial advise and the message…..I think that is really where I would see the pharmacist role being invaluable.

And to expand on that advice?

Yes…absolutely…because you know…..advise changes……errmm and concerns change…and benefits change…information about medication changes and I think that when they are having that discussion that that contact with the patient on a regular basis, I think that ideally placed to be able to do that…yep……I certainly….and then within our practice and certainly in some of the community

pharmacies where they were actually undertaking some sort of medication reviews…I think that is the ideal time to be…

To be giving this message

To be giving that….and if the patient is going to a regular pharmacist. If a new drug is initiated, that is the time to reinforce what the patients been told about the drug and you know to give them the message and I think more reinforcement and the more information the better.

So, in terms of….sort of osteonecrosis of the jaw counselling, maybe by a pharmacist. If you are the GP who started the medication errmm you have reviewed the patient and then the pharmacist has brought up this issue of osteonecrosis of the jaw with this patient…would you like to see that patient referred back to yourself or would you like that patient to be

I would be delighted if the pharmacist would refer that patient to the dentist….I think that because….I think the fewer steps in the patients journey…if you see what I mean…the better. Because what I am....going to do if the pharmacist has encountered this…..then the thing to do is to say to the patient to go to the dentist….because all I am going to do when I see the patient is say you need to go to the dentist….and the patient is going to perhaps then going sit there and say…you brought me in to tell me that.

It's another step

It's another step and another….appointment…I think its if….if....you know…I think if the pharmacist says to me I have told the patient they need to see the dentist so perhaps the next time you see them you could reinforce that message and follow up…so you flag it up and say....look the pharmacist did say…or you could do it…..you can reinforce it in different ways…..we would certainly use our repeat prescription systems……on the right side you know…as a reminder you need to see your dentist…have you seen your dentist…..and follow it up that way…errmm and sometimes even a phone call

Yes

Have you been to your dentist yet…so you are reminding them…..I would be very happy in that situation for the pharmacist to?

At the point of the initial prescriptions.

Any time at all, I have no problem as long as its pointed out to the patient at some time…..you know….and you can do it in a way that not going to cause issues…you have been given a lot of information…was it mentioned you ought to see your dentist and this is why……I don't think that does any harm at all… they often…when the drug is initiated there is a lot of other stuff happening with the patient and they may not take on board all of these messages

As the prescriber if…..if the pharmacist is going to refer to the dentist, would you….where would you like to be brought back into that process…..would you like to be informed?

I think…I think it would be…I mean…if we had proper shared records it wouldn't be an issue because the pharmacist could update the records accordingly…

Yeah

But certainly we had….you know…our pharmacist could communicate with us through System One. Certainly some of the pharmacists could…not all of them… and you could even just send a message

saying….I advised this patient to go to the dentist…..so that it can be flagged up…as an alert on the front of the patient records….if this patient needs to be seen....has been checked....follow up that this patient has seen the dentist…I think that's only….I think it does two things….first of all so that we know they have been advised to do it and you can follow up….and we can keep raising it……With the patient as a concern and reinforcing why it is important.

In terms of information that you would like back from the dentist, would you like records of that as well…or

I don't think a record….but I think if the patient is on them…..a note form the dentist to say I have seen Mr so and so has been for his check-up…..all is fine. Or I have concerns I think obviously if there was something negative that …..You know…there was a problem that you might have to reconsider the treatment….then I think…..I would expect the dentist to communicate that back.

Back to you

I think in patients on bisphosphonates....it wouldn't do any harm for the dentist to drop a note round and say…..in the same way as they do for the transplant patients when they have been to the dentist. If it's part of their initiation…..part of their protocol….their checklist….whatever you want to call it….before starting treatment or while they are on treatment….everyone is aware why it is important…I don't think it should be a problem for the dentist to…..just say I have seen this and….it's not a problem to communicate that back so…..so you have got it in the….in the records, in the same way as if a pharmacist gives my patient….one of my patients a flu jab.

Yes…..exactly

I expect them to tell me that they have had something….as its part of their…..their care. So it's important.

OK, errmm I have most of my questions really….I think if the patient went to their GP…as their dentist sort of thought no…..they are not fit for a bisphosphonate….would you....again would be comfortable for that dentist to say….hold on we are going to delay treatment until after we have remedied this or

Yeah…it think if I am sending that patient to….unless there was some very pressing reason that the patient must have bisphosphonates then…in which case I think if it was a complex situation like that and I wasn't sure…..then there are always the specialists…..who I could ask for and say….this is the situation…what do you think I ought to do with this patient…but in that situation if the dentist had a real concern I would be holding off treatment until I had the expert option to say…no it withstanding what the dentist said, this paint needs a bisphosphonate and it ok to go ahead with it…as I say really potentially you are doing harm to the patient with that drug. I think in that situation you need to air on the side of caution.

OK…last question …so…I guess as a GP…when practicing do you feel you would have like to have had more information about bisphosphonate osteonecrosis of the jaw?

I would like to have had more information about the potential serious…the potential morbidity….you know….I am aware it was there in among all the other lists of things…errmm but until I was….

First had experience

Yeah…you know. Osteonecrosis of the jaw…so what…really it was only when I saw it affect those two patients….it was like wow….I do think from what I have seen now an awareness of it…..things like that…I certainly seen cancer specialist and people like…referring patients for a dental …

I think perhaps…perhaps…I think also because they may have encountered cases as well….which has then complicated the patients treatment as they have had to go get this problems sorted out…individual people have developed an awareness of it.

Yes, it's been subject to a number of MHRA alerts over recent years, around dental check-up.

I think it's there…part of the problem…I think is when you have a drug like a bisphosphonate which is complex…with its instruction on how to take it…and people are tied up in that…..and I think also that it is a thing of prioritising side effects as well and when you get osteonecrosis in among all the other lists of side effects…it's where that it…..in terms of…..you know…..how important is it…and something I think you know….almost a way of flagging up the really big side effects…the one I remember is the peptic ulceration as it was always flagged up as potentially lethal, perforating the oesophagus and the patient ending up really ill.

Would you want to know…..in terms of prevalence or more, severity to the patient

I think....I think prevalence is important to know…errmm it gives….it lets the patient know how common and frequently it can occur….and us as well off course…..I think in terms of severity because you can have a prevalent side effect that's not that series…you know if I take amoxicillin it makes me nauseated…that is fairly common but it isn't life threatening…it's not going to hopefully….apart from making me a bit sick not cause a major problem….there are two issues there…prevalence is useful to know but I think the severity of the side effect…you can say to a patient look its very rare…but if it happens you have got a big problem with it....because of what it can do…I don't know if that's explained it very well.

No….No

I think there are some side effects…like a patient on methotrexate who gets oral ulceration…yeah ok…lots of people might…..but in your situation it could be very serious…I think those are ones that we need to flag up as being very serious.

OK, I have no more questions unless there is anything else you would like to discuss..

No.no….that's fine

Consolidated criteria for reporting qualitative studies (COREQ): 32-item checklist

Developed from:
Tong A, Sainsbury P, Craig J. Consolidated criteria for reporting qualitative research (COREQ): a 32-item checklist for interviews and focus groups. *International Journal for Quality in Health Care*. 2007. Volume 19, Number 6: pp. 349 – 357

YOU MUST PROVIDE A RESPONSE FOR ALL ITEMS. ENTER N/A IF NOT APPLICABLE

No. Item	Guide questions/description	Reported on Page #	Details
Domain 1: Research team and reflexivity			
Personal Characteristics			
1. Inter viewer/facilitator	Which author/s conducted the interview or focus group?	21	Andrew Sturrock (AS)
2. Credentials	What were the researcher's credentials? E.g. PhD, MD	1	AS has an MSc in Clinical Pharmacy
3. Occupation	What was their occupation at the time of the study?	1	Senior Lecturer – Pharmacy Practice and Clinical Therapeutics
4. Gender	Was the researcher male or female?	1	Male
5. Experience and training	What experience or training did the researcher have?	1 + 21	AS received training in qualitative research skills by the research team and through attendance at a Qualitative Research Methods in Health Course at University College London.
Relationship with participants			
6. Relationship established	Was a relationship established prior to study commencement?	7	Invitation letter and participant information sheets were posted out prior to the study.
7. Participant knowledge of the interviewer	What did the participants know about the researcher? e.g. personal goals, reasons for doing the research	Supplementary document 2	A participant information sheet was provided to all participants.
8. Interviewer characteristics	What characteristics were reported about the inter viewer/facilitator? e.g. Bias, assumptions, reasons and interests in the research topic	1+21	AS is a pharmacist. Interest in the research topic was developed due to teaching commitments on the MPharm programme at the University of Sunderland. The multidisciplinary team was assembled to reduce bias in the research process.
Domain 2: study design			
Theoretical framework			
9. Methodological orientation and Theory	What methodological orientation was stated to underpin the study? e.g. grounded theory, discourse analysis, ethnography,	6	A Grounded Theory approach, with constant comparison.

	phenomenology, content analysis		
Participant selection			
10. Sampling	How were participants selected? e.g. purposive, convenience, consecutive, snowball	7	A convenience and snowball sampling method were adopted
11. Method of approach	How were participants approached? e.g. face-to-face, telephone, mail, email	7	An invitation letter was posted to participants
12. Sample size	How many participants were in the study?	7	17 participants
13. Non-participation	How many people refused to participate or dropped out? Reasons?	7	No participants who responded to the invitation refused to participate or dropped out of the study.
Setting			
14. Setting of data collection	Where was the data collected? e.g. home, clinic, workplace	6	Data were collected at a time and place convenient to the interviewee; this was usually at their place of work
15. Presence of non-participants	Was anyone else present besides the participants and researchers?	6	Interviews were held on a one-to-one basis.
16. Description of sample	What are the important characteristics of the sample? e.g. demographic data, date	8-9	As displayed in table 1 and table 2
Data collection			
17. Interview guide	Were questions, prompts, guides provided by the authors? Was it pilot tested?	6	Interview guide was developed and refined by the research team. Included as supplementary document 1
18. Repeat interviews	Were repeat inter views carried out? If yes, how many?	7	No repeat interview were performed
19. Audio/visual recording	Did the research use audio or visual recording to collect the data?	6	Audio recording
20. Field notes	Were field notes made during and/or after the inter view or focus group?	6	No field notes were taken due to the verbatim transcribing
21. Duration	What was the duration of the interviews or focus group?	8	Up to 1 hour
22. Data saturation	Was data saturation discussed?	7	Data were analysed by AS, with transcripts and emerging themes cross-checked for interpretation and agreed amongst the research team until saturation occurred
23. Transcripts returned	Were transcripts returned to participants for comment and/or correction?	7	No

Domain 3: analysis and findings			
Data analysis			
24. Number of data coders	How many data coders coded the data?	21	AS identified the thematic framework and interpreted the data
25. Description of the coding tree	Did authors provide a description of the coding tree?	N/A	A description of the coding tree is not provided.
26. Derivation of themes	Were themes identified in advance or derived from the data?	7	Themes were derived from the data
27. Software	What software, if applicable, was used to manage the data?	7	Microsoft Word 2010 and Microsoft Excel 2010
28. Participant checking	Did participants provide feedback on the findings?	7	No
Reporting			
29. Quotations presented	Were participant quotations presented to illustrate the themes/findings? Was each quotation identified? e.g. participant number	10-15	Quotation are presented with clearly identifiable participant numbers
30. Data and findings consistent	Was there consistency between the data presented and the findings?	10-15	Yes
31. Clarity of major themes	Were major themes clearly presented in the findings?	9-15	Yes
32. Clarity of minor themes	Is there a description of diverse cases or discussion of minor themes?	9-15	Yes

Correction: Attitudes and perceptions of GPs and community pharmacists towards their role in the prevention of bisphosphonate-related osteonecrosis of the jaw: a qualitative study in the North East of England

Sturrock A, Preshaw P, Hayes C, *et al*. Attitudes and perceptions of GPs and community pharmacists towards their role in the prevention of bisphosphonate-related osteonecrosis of the jaw: a qualitative study in the North East of England. *BMJ Open* 2017;**7**:e016047. doi: 10.1136/bmjopen-2017-016047.

The middle initial of author 'Philip Preshaw' is missing from the article. This name should be written 'Philip M Preshaw'.

BMJ Open 2017;**0**:e016047corr1. doi:10.1136/bmjopen-2017-016047corr1