MSc Evidence Based Healthcare (Medical Statistics)

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PROJECT DETAILS
MSc Evidence Based Healthcare (Medical Statistics)
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FUNDING STATEMENT
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Outline any extension requests granted by PRUK (200 words max)

This section should outline any extension requests that were approved (extensions to the bursary duration or additional monies) and the reasons for the extension.

Describe the nature of the training undertaken (300 words max)

Please provide an overview of the training that you have undertaken as part of the bursary.

This is a list of the modules that have been completed:
Essential Medical Statistics
Introduction to Statistics for Health Care Research
Statistics for clinical trials
Big data epidemiology
Complex Reviews
Qualitative Research Methods
Programming in R and Stata
Systematic Literature Review Cochrane

Background (500 words max)

This section should outline the existing literature and a background to the research conducted.

Osteoporosis is a disease defined as a bone mineral density less than 2.5 standard deviations below the average female(Johnell *et al.*, 2003). It is estimated that one in two women and one in five men over 50 will have a broken bone for the remainder of their life. Unfortunately, due to the insidious nature of the condition, testing and diagnosis occur predominately after a patient experiences a fragility fracture. These fragility fractures are a significant cause of disability, morbidity and mortality, with 20% of hip fractures resulting in death within one year(Barceló *et al.*, no date).

Oral bisphosphonates have repeatedly demonstrated their cost-effectiveness in reducing the risk of subsequent fractures. Newer agents such as denosumab, intravenous bisphosphonates, teriparatide and romozumab have also shown significant benefits. However, the treatments are often second-line agents(NICE, 2008). Despite the clear advantage of reducing fracture risk, treatment adherence remains suboptimal, leading to further fractures impacting patients, families and healthcare systems. Some studies estimate commitment as low as 20% in one year. This represents a significant care gap(Rabenda *et al.*, 2008; Hadji *et al.*, 2015; Cho *et al.*, 2018; Fatoye *et al.*, 2019).

One solution to improve adherence was to commission pharmacists to review patients newly initiated anti-osteoporosis therapy under the new medicines service (NMS). The three stages of the service provide an opportunity for the pharmacist to understand the use, beliefs and concerns about their medication and condition. As a result, the service has shown improved adherence(Elliott *et al.*, no date).

It is worth noting that the outcomes for osteoporosis are different. In asthma, for example, there is a physical manifestation which correlates with the state of the conditions, i.e. as asthma gets worse the is an increased number of “wheezes”. Osteoporosis is like hypertension or hyperlipidaemia that are asymptomatic; there is no such manifestation per se, but rather an increasing probability of a fragility fracture as the condition worsens. As such, it would not be prudent to transpose the evidence from one to another. There is a paucity of evidence relating to the effect of pharmacist intervention on osteoporosis-associated outcomes.

Aims & Objectives (300 words max)
Please outline the aims and objectives of the research conducted.

This systematic review aims to evaluate the effect of pharmacist interventions in any setting (GP practice, hospital, community, nursing home and others) on short-term and long-term adherence.

Primary

Compared with usual care in patients with osteoporosis, does pharmacist intervention improve MPR above 80% one year after the intervention?

Secondary

To assess the effect of pharmacist intervention on the number of hip fractures.
To assess the effect of pharmacist intervention on the number of BMD scans.

Tertiary
The effect of providing the service has on job satisfaction.

Method (500 words max)
Please describe the methodologies employed on the research, including any other relevant assessments conducted.

Eligibility criteria

Study Design
This review will consider all types of study designs. The primary source will likely be pre and post. However, we do not expect to find many RCT but will include any study type. We will limit languages to English only.

Participants
Patients any of the following Initiated either in primary or secondary care:
Alendronate
Risedronate
Ibandronate
Strontium
Raloxifene
Denosumab (60mg ONLY brand name Prolia™)
Intravenous Zoledronate
Intravenous Ibandronate
Teriparatide

Exclusion:
Patients on anti-osteoporosis medication(AOM) and:
Glucocorticoids / Steroids
HIV medication
Osteoporosis medication used at cancer doses

Interventions
Any intervention carried out by, Community Pharmacist, Community Pharmacist visiting care home, GP Pharmacist PCN Pharmacist, Care home pharmacist (residential)

The intervention itself can be a standalone assessment or as a part of a wider-based intervention. The intervention will be included if any component performed by a pharmacist We expect interventions to fall into the following, either singularly or in combinations, phone calls, face-to-face, video, and printed material.

Comparators
Usual pharmacy Care
Usual FLS care
Usual GP care

Outcomes
Adherence at one year using MPR > 80%
-patient/carer questionnaire
-clinician assessed the questionnaire
-refill rates
-MPR
-PDC

Timings
3 months
6 months
12 months
24 months

Setting
There is no limit on Settings; however, sub-group analysis will determine if the setting impacts the magnitude of the effect. This will be the pharmacy's location (i.e. community, primary care, secondary care)

Outcomes
Adherence was defined as the mean possession ratio and measured using prescription data, patient reports and physician data. Adherence will be assessed as being short-term (3 months to one year) and long-term (one year and over) (primary outcome) to anti-osteoporosis medication (AOMs). The review will answer the following questions. The comparator group will be GP practice, normal pharmacy practice, and Fracture Liaison Service. We will measure the intervention from initiation of therapy until discontinuation or end of the study.

Information sources
The following databases will be searched:
Ovid Embase
Ovid Medline
EBSCO CINAHL
Scopus
Web of Science Core Collection
Cochrane Database of Systematic Reviews
Cochrane CENTRAL
Grey literature will not be included. These studies recognise the potential use of grey literature in understanding the landscape on a given topic. It is important to note that this literature may not be subject to the same scrutiny as published material.

Results (500 words max)

Please describe the main results of the research and an outline of the analyses conducted to produce the results.

422 abstracts were screened. From these, only three remained eligible.

Proactive pharmaceutical care interventions decrease patients' non-adherence to osteoporosis medication
Method: Medication Monitoring and Optimization (MEMO) Program
Intervention Description:
At first dispensing pharmacist provides information. 2 weeks after, a pharmacist conducts second counselling. Every three months, pharmacists search for non-adherence patients.
Persistence details: Discontinuation was defined as permanently stopping osteoporosis medication.
Comparator: Pre-implementation of the MEMO program.
Results:
N=937
Rate of discontinuation
3 months Intervention 7.79%, control 17.2% no p-value as the values have been estimated
6 months Intervention 12.54% control 21.98% no p-value as the values have been estimated
12 months Intervention 19.0% control 32.8%. p<0.001
No BMD assessments
Pharmacist satisfaction was included in a second paper but not in English.

Effects of pharmaceutical care on adherence and persistence to bisphosphonates in postmenopausal osteoporotic women
Method: Intervention counselling package. 4 visits (months 0,3,6,12) over 12 months. The counselling package includes an explanation of osteoporosis, risk factors, lifestyle modifications, goals of osteoporosis therapy, side effects and the importance of medication adherence. Verbal counselling was reinforced with an osteoporosis booklet. The pharmacist also reviewed the participant's medications and conducted monthly follow-ups via telephone for the first six months, then every three months until month 12.
Persistence details: Persistence (defined as the time in days from the date of the first dose of bisphosphonate until treatment discontinuation) was obtained from supply records using the pharmacy information system v8.6 (Ascribe, Bolton, UK).
Comparator: No counselling.
Results:
N=167
Persistence
12 months intervention 87.0% control 89.8%. Not significant.
No BMD assessments
Pharmacist satisfaction was included in a second paper but not in English.

Impact of a pharmacist-directed intervention in postmenopausal women after fracture
Method: clinical-pharmacy-based osteoporosis management service (CPOMS). IN CPOM, a clinical pharmacy specialist at each facility reviews the patient's medical record to develop a therapeutic plan and send it to the primary care provider for input or approval. The therapeutic program, could consist of recommendations for BMD screening, initiation of osteoporosis therapy (i.e., bisphosphonates, estrogen replacement therapy, raloxifene, calcitonin, teriparatide), or calcium and vitamin D supplementation as indicated. Once the primary care provider authorized a final

plan, the clinical pharmacy specialist contacted the patient to implement the plan. All patients were followed monthly as needed by telephone, postal mail, or e-mail for six months after their fracture to ensure adherence. Persistence was defined based on the last medication purchase prior to the 365-day cutoff date. If the days' supply multiplied by 1.2 was greater than or equal to the number of days between the final prescription purchase and the cutoff date, medication use was considered persistent
Comparator: Comparator (nurse led) control
Results:
N=362
Persistence
12 months pharmacist 54% FLS pharmacist 45%, p = 0.19.
BMD CPOMs 35% Intervention 31%

Due to the low number of papers, a meta-analysis was not conducted.

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Discussion (500 words max)

Please use this section to analyse the findings of your research and link it back to the original hypothesis.

The evidence shows overall shows mixed results. Only one study which involved the MEMO programme appeared to be effective, resulting in an almost fifty-per cent reduction in discontinuation. However, other studies indicate no difference when compared to the comparator.

Essentially the studies can be organised into comparisons. The MEMO and CPROM studies both compared intervention to no intervention. The MEMO study demonstrated a significant beneficial effect, whereas the CPROM failed to find one. In addition, the MEMO study had a greater breadth of drugs being explored beyond bisphosphonates; by comparison, CPROMS was limited to alendronate and risedronate.

It is well-documented that bisphosphonates are the most likely to be discontinued of the osteoporosis treatments(Ettinger, Gallagher and MacCosbe, 2006; Penning-van Beest *et al.*, 2006; Weiss *et al.*, 2007; Confavreux *et al.*, 2012; Hiligsmann *et al.*, 2012; Li *et al.*, 2012; Hadji *et al.*, 2015; Fatoye *et al.*, 2019; Torre *et al.*, 2019). Thus the inclusion of other non-bisphosphonates drugs would improve the apparent effect. Conversely, limiting to bisphosphonates would deflate an effect.

The second comparison being made is against a trained HCP. In this study, the pharmacist, after training, was able to deliver a service which was non-inferior to that provided by a trained nurse. This study highlights that persistence rates are comparable to specialised professionals with training and specific service. But was the adherence good in either aim (>80% MRP)

The implication is that a service where pharmacists can deliver clinically meaningful support to patients is one in which there is where pharmacists are supported, and persistence is assessed beyond the early stages. For example, in the MEMO study, pharmacists delivered service at regular intervals. No clinically specific training was provided, but it improved persistence in pre-service delivery. In the Malaysia study, in addition to specific service delivery, there was training that enabled them to work as effectively pharmacists can deliver clinically meaningful support to patients is one in which there is where pharmacists are supported, and persistence is assessed beyond the early stages. For example, in the MEMO study, pharmacists delivered service at regular intervals. No clinically specific training was provided, but it improved persistence in pre-service delivery. In the Malaysia study, in addition to specific service delivery, there was training that enabled them to work as effectively as specifically trained nurses.

Some features in the studies raise issues about the generalisability of the studies in a broader context. For example, current literature puts one-year persistence close to 50%, whereas, in the MEMO study without intervention, the persistence after one year was 60%. Aside from the differences in the programme, contextual factors may have influenced the results and thus affected generalisability. This includes each country's actual and perceived role and scope of practice.

Only the CPROMs study looked at the number of BMD tests. It found that the intervention group had a higher percentage of BMD scans. This is reassuring, but it does not address the primary outcome of adherence. The paucity of data highlights the need for further research in this area. The studies look at preventing fractures over a year, significantly longer than the 3 weeks for the NMS service.

Conclusion (300 words max)
Please provide a succinct conclusion to the report and provide the key take-home message for the reader to understand.

Overall evidence suggests there is potential for pharmacists to play a role in improving the long-term persistence of osteoporosis therapy but the evidence base is very small and inconsistent. However it does indicate that for such a service to be successful, it would require the appropriate service design with training. Services which provide clinically specific training with a service which regularly monitors patients results in better outcomes compared to others The current framework has the potential to undervalue pharmacy contribution as the setup is not conducive to providing or demonstrating success.

Summary of outputs (300 words max)
Please include a list of dissemination activities carried out during the life of the project, in addition to future activities planned.

Current dissemination:
Published:
Janjua, SS, Boardman, HF, Sami, A, Johansen, A, Toh, LS, Javaid, KM. Anti-osteoporosis medication dispensing by clinical commissioning groups in England – an ecological study of variability in practice and of the effect of the Covid-19 pandemic. Pharmacoepidemiol Drug Saf. 2022; 1- 8. doi:10.1002/pds.5544

Unpublished:
Osteoporosis medication adherence interventions involving pharmacists: A scoping review to develop an Initial Programme Theory – in collaboration team from Nottingham

Planned:
A systematic review of pharmacist interventions on adherence to osteoporosis medication.

Outline the next steps in your research career (500 words max)
We are interested in the next steps you will be taking in your research journey. We also want to understand how this project will support you to take those next steps.

This project has been vital in providing the skills to become a clinical academic.

My next step would be to apply for a DPhil programme at the University of Oxford. Funding will be applied from NIHR.

Currently, I have applied in collaboration with Emma Clarke from Bristol University to test Vfrac (Vertebral fracture assessment) in a community pharmacy. We have reached the 2nd round and are awaiting a decision and comments.

References
Please use the Harvard referencing format.

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NICE (2008) 'Alendronate, etidronate, risedronate, raloxifene, strontium ranelate and teriparatide for the secondary prevention of osteoporotic fragility fractures in postmenopausal women [TA161]'. NICE.
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