Process evaluation of the SPPiRE trial: a GP delivered medication review of polypharmacy, deprescribing and patient priorities in older people with multimorbidity

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Abstract

Background: The SPPiRE cluster randomised controlled trial (RCT) found that a GP delivered medication review that incorporated screening potentially inappropriate prescriptions (PIP), a brown bag review and a patient priority assessment, resulted in a significant but small reduction in the number of medicines and no significant reduction in PIP.

Objective: To explore the experiences of GPs and patients engaged in the SPPiRE intervention and the potential for system wide implementation.

Design: Mixed methods process evaluation; quantitative data was collected from the SPPiRE intervention website and qualitative data via semi-structured interviews.

Setting and participants: 51 general practices throughout Ireland, and 404 participants with multimorbidity aged ≥65 years, prescribed ≥15 medicines participated in the RCT. Qualitative data was collected with purposive samples of intervention GPs (18/26) and patients (27/208).

Methods: Quantitative data was analysed descriptively, qualitative data thematically and both were integrated using a triangulation protocol.

Results: The analysis generated three themes, intervention implementation, mechanisms of action, and both were underpinned by the theme of context. One fifth of patients had no review, primarily due to insufficient GP time. The brown bag review component resulted in the most medication changes, particularly stopping a medicine. GPs felt it easier to change medicines if the patient was well known to them, and patients were generally receptive to change. GPs identified lack of integration into practice software systems and resources as barriers to future implementation.

Conclusion: Consideration of implementation of successful interventions is key to informing policy and integration into clinical practice. GPs and patients viewed the intervention positively, but implementation will depend on resourcing and integration into practice software systems.

Trial registration number: ISRCTN12752680

Key words: deprescribing, multimorbidity, polypharmacy, potentially inappropriate prescribing, process evaluation

Key points:

- Process evaluations elucidate how complex interventions are implemented and mediate their effect.
- GP staff shortages affected implementation and 22% of intervention patients did not have a medication review.
- Despite describing PIP identification as important, GPs identified less PIP than anticipated, based on assessment of baseline prescriptions, and this may explain the lack of effect of the intervention on PIP.
- The brown bag review process, where each medicine is reviewed in turn resulted in the most medication changes.
- Deep seated views on medical decision making influenced engagement with components of the intervention especially assessing patient treatment priorities.

Introduction

There is a growing population of older people living with multiple chronic conditions or multimorbidity [1]. Prescribing for patients with multimorbidity, especially those with more significant polypharmacy can be risky due to potential drug – drug and drug – disease interactions [2]. The application of multiple single disease guidelines to an individual person with multimorbidity is often not feasible or advisable and can lead to an unacceptable treatment burden [3]. Multimorbidity and polypharmacy guidelines advise identifying patients at risk of medication related harm, screening for potentially inappropriate prescriptions (PIP) and tailoring care to individual patient priorities [4-6]. However a 2019 overview of multimorbidity and polypharmacy guidelines recognised that despite these guiding principles of tailoring care, specific recommendations are often missing [7].

The Supporting Prescribing in Older Patients with Multimorbidity in Primary Care (SPPiRE) cluster randomised controlled trial (RCT) demonstrated that the SPPiRE intervention was effective in reducing the number of medicines but did not demonstrate an effect on PIP, in patients aged ≥65 years and prescribed ≥15 repeat medicines in Irish primary care [8]. The development of the SPPiRE intervention is described in detail elsewhere [9]. The SPPiRE intervention compromised professional training in the form of online training videos and a web guided medication review where GPs were supported in identifying PIP (from a predefined list of 34 indicators based predominantly on the STOPP/START version 2 criteria [10], see Appendix 1), provided with suggested treatment alternatives for identified PIP, and prompted to perform a brown bag medication review and assess patient treatment priorities. The SPPiRE intervention was a complex pragmatic intervention as it had a number of interacting components and a degree of flexibility in how it was delivered [11]. As recommended by the Medical Research Council, as part of their framework on complex interventions, a process evaluation was performed alongside the effectiveness evaluation of the SPPiRE intervention, to assess how the intervention was implemented and resulted in change and how participants (both GPs and patients) responded to it [12].

The overall aim of the SPPiRE process evaluation was to assess the potential for system wide implementation. Objectives included exploration of intervention implementation and the mechanism of action of the intervention. Specifically; what were the effective and ineffective components of the intervention, how did GPs and patients respond to it, and how did the overall context effect intervention implementation?

Methods

The methods for this mixed methods parallel process evaluation have been described in the published protocol [13] and were developed based on a framework that was designed to guide the conduct of process evaluations for cluster RCTs [14]. Quantitative and qualitative data collection techniques were employed and data was analysed in isolation and integrated using triangulation to gain a comprehensive understanding of intervention implementation and mechanism of action.

Study Population

The SPPiRE study was conducted in 51 general practices throughout the Republic of Ireland, who identified and recruited 404 patients aged ≥65 years and prescribed ≥15 repeat medicines. Twenty-six practices (208 patients) were allocated to the intervention group and 25 practices (196 patients) to control. Given that the primary aim of the process evaluation was to assess intervention implementation, only intervention GPs and patients were invited to take part in semi-structured telephone interviews. Eighteen of 26 intervention GPs and a purposive sample of 27 of 208 intervention patients were interviewed, to include a mix of male and female patients and those who had some and no medication changes.

Data Collection

To address the objectives, quantitative and qualitative data sources were used to evaluate the themes of implementation, mechanism of action, and the over-arching theme of context.

Quantitative data was collected from the SPPiRE website for all intervention patients who had a SPPiRE medication review. GPs inputted PIP data, medication related concerns during the brown bag review

and recorded patient treatment priorities. For each PIP, concern or priority identified the GP was prompted to discuss and record the outcome (which included no action). GPs also recorded an immediate pre and post intervention medication count. Quantitative data was also collected from a general practice profile questionnaire which was submitted by all recruited practices and included details on practice demographics and repeat prescribing systems. Quantitative data on patient demographics was collected from a self-administered postal questionnaire. Quantitative data from the main trial outcomes was used to compare PIP prevalence.

Qualitative data was collected using semi structured telephone interviews and study manager logs of patient and practice contact during recruitment, intervention delivery and follow-up. The GP interview topic guide focused on pre - intervention prescribing practices, intervention implementation and overall views on participation, (see Appendix 2). The patient interview topic guide focused on attitudes towards medicines and experience of the SPPiRE medication review (see Appendix 3). Interviews were conducted by CMC and BK, who are GPs by professional background, and were trained by BC, a senior researcher with experience in qualitative methods. Patient interviews lasted an average of 11.0 minutes (min 4.0–max 25.9), while GP interviews lasted an average of 19.5 minutes (min 11.3–max 32.1).

Data Analysis

Quantitative data was analysed using descriptive statistics in Stata version 17.

Telephone interviews were all audiotaped and transcribed verbatim. Interview audio files and transcripts were listened to and read repeatedly by two researchers (IP and CMC) to ensure familiarisation with the data. Transcripts were uploaded into NVIVO 12 and analysed thematically. Codes were generated both inductively from recurring themes in the data and deductively using the four Normalisation Process Theory (NPT) constructs to describe implementation [15]. NPT is a contemporary social theory that has been used to understand the factors in intervention implementation and has four constructs; coherence, cognitive participation, collective action and reflexive monitoring. The initial codes were developed by a researcher who was independent from

the main trial (IP) and reviewed by another researcher, who was also the study manager (CMC) and final codes and sub codes were agreed by all members of the process evaluation study team. Participating practices were coded by number for example GP1, and their participating patients were coded using the practice code with a patient code, e.g. GP1P1.

Integration

Qualitative and quantitative data were integrated using a triangulation protocol [16]. Data were initially analysed in isolation and during the integration process identified themes from qualitative data and quantitative results were further explored from the alternative data sources and the relationship between the two data sources coded as either being in agreement, partial agreement, silent or dissonant.

Results

The analysis generated three themes, intervention implementation and mechanisms of action, both of which were underpinned by the third theme of context.

Characteristics of the sample

Practices self-classified as either urban, rural or mixed and were categorised into three groups based on the size of the practice. There were 14 urban (54%), 4 rural (15%) and 8 mixed practices (31%). Of the 18 intervention GPs interviewed, 11 were male. Of the 27 intervention patients interviewed 12 were male, the mean age was 73.7 years (SD 5.4) and this was slightly younger than the mean age for all intervention patients at baseline (76.7 years). Looking at the immediate post intervention medication count recorded by GPs, interviewed patients had on average 1.59 medicines stopped (SD 2.50) compared to 1.71 medicines in all reviewed patients (SD 2.31).

Intervention implementation

Between 2nd January 2018 and 11th May 2020, 163 of 208 (78%) intervention patients had a SPPiRE medication review. Intervention practices were given six months from the date of allocation to complete all medication reviews. Eleven practices completed within this time frame (see Appendix 4)

and the remainder were on average 7 weeks late in completing the intervention (range of 20 weeks early and 47 weeks late). The most commonly reported reasons for these delays were practice time constraints and staffing issues. Overall, a higher proportion of participants from smaller and rural practices had their SPPiRE review and within the designated time frame (see Appendix 4), however there was significant variation and a small number of practices in the rural category.

Data from the study research logs highlighted that of the 45 patients who did not have a review, 38 were because the GP reported they did not have enough time to complete the review(s). Three patients did not have a review because they had died and four were either too unwell or in hospital and thus unable to attend for a review. Figure 1 illustrates the number of participants per practice who had a SPPiRE medication review and the immediate mean reduction in the number of medicines per practice, illustrating the intra practice variation in deprescribing. Included in the 45 patients who did not have a review, were 20 patients from three intervention practices who did not perform any reviews within the specified time, the GPs again cited time constraint and staffing issues as the reasons.

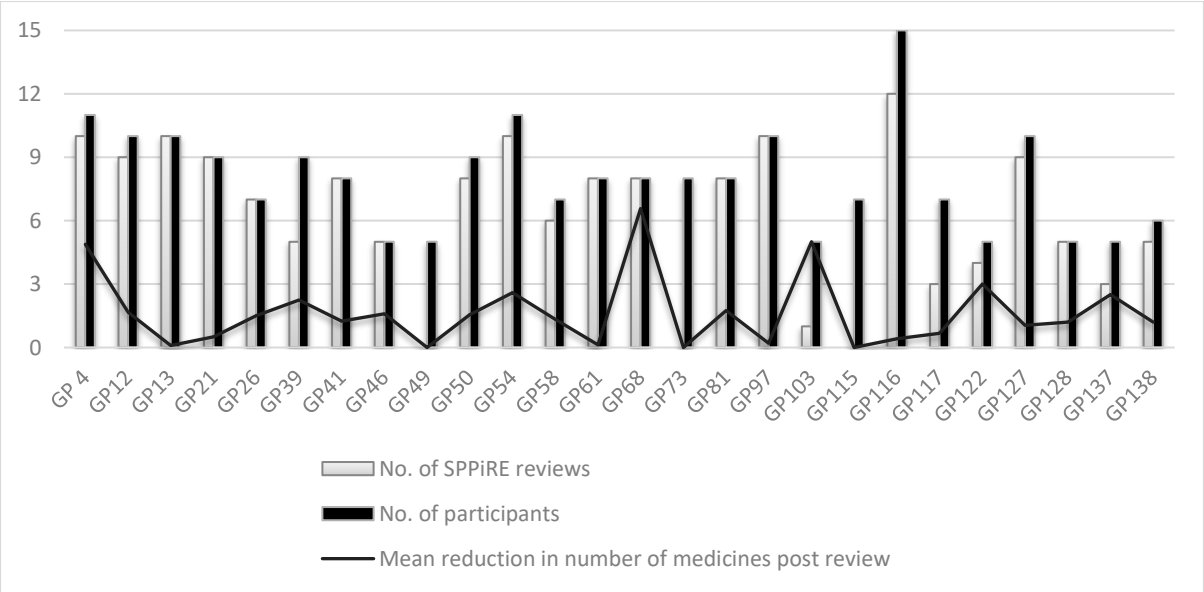

Figure 1 Mean reduction in number of medicines per practice post intervention

In terms of the NPT construct coherence (sense making of the intervention) seven of the 27 interviewed patients had difficulty remembering their review as separate or different to routine care.

Patients described significant treatment burden and recounted instances of medicines being stopped in hospital clinics or during admissions, and so might have had difficulty differentiating SPPiRE from other care. On the other hand, GPs generally saw the SPPiRE review process as separate to routine care, and this was viewed positively by some "*it felt like a luxury that you could sit down in practice and take the time to go through it" (GP61).* Despite viewing SPPiRE as separate to routine care most GPs made few changes or adaptations to the rest of their practice to incorporate reviews and frequently participated in SPPiRE in isolation from the rest of their practice activity, see Table 1 for illustrative quotations. For example, two GPs described coming in on days off or after hours to complete the reviews as they felt this was the only way they could get them done. In terms of collective action (practical work of doing the intervention), all GPs identified PIP and most reviewed the patients' notes prior to the face-to-face patient consultation, "*just to familiarize ourselves again with all the past medical history and try and see what the indication was for each of the medications" (GP26).* Adherence to the brown bag review and assessment of patient priorities processes varied. Although GPs reported finding the brown bag review process useful, the majority of interviewed patients did not bring all their medicines in with them *"I thought if it was on the list, there wasn't much point in carrying it in…because everything is on the computer" (GP39P41)*. Of the 23 intervention practices that implemented either some or all of the reviews, 11 recorded at least one treatment priority for all patients, in the remaining 12 practices the proportion of patients with at least one recorded priority varied from 30% to 88%. Overall patients and GPs were positive in their appraisal and evaluation of the intervention (reflexive monitoring), *"There was nothing I didn't like about it, I felt it was useful...it was generally useful and informative." (GP26P6),* but GPs felt adequate resourcing and integration with practice electronic health record systems would be vital for system wide implementation.

Table 1 Thematic analysis of SPPiRE medication review implementation using NPT

NPT Core Construct	Construct components	Example quotes
Coherence Making sense of the intervention	GPs saw the SPPiRE review as	*"I suppose these are patients we were seeing them anyway, so it wasn't as if we were creating extra appointments trying to get them back in again....*

NPT Core Construct	Construct components	Example quotes
	a ***separate process to routine care*** that would be beneficial	*But we're seeing them when we were forearmed, I guess forewarned with other information, with stuff that we could be doing better or mistakes that were being made." (GP21)* *"It was really good and again, it felt like a luxury that you could sit down in practice and take the time to go through it." (GP61)*
	GPs often ***took on the process alone;*** only 6 interviewed GPs said that other GPs from the practice were involved	*"...it wasn't that they were antagonistic. When the proposal came in and we brought it up at the practice (meeting) and said...we'd all like to do that. But like with the best will in the world it just didn't get communicated to everybody." (GP39)*
	GPs felt their ***role was central*** to ensuring safe prescribing for these patients	*"I suppose maybe we're the only central person to their prescriptions." (GP12)* *"I mean it's one of the most important, one of the most important aspects of our role, and the most medico-legal aspect of our role." (GP46)*
Cognitive Participation Involvement with the intervention	***Adaptation of the practice*** varied. Practices were advised to book double time slots for SPPiRE reviews.	*"I actually did it outside of hours...so it didn't really impact and probably is a bit artificial but they didn't really impact on you know, day-to-day working because I wanted to give it enough time." (GP4)* *"So I ended up just going in on time off and doing it and then you can just kind of dedicate a couple of sessions to doing it and getting it done properly that way." (GP61)* *"...we had to make sure that when they made their appointment that the receptionist knew that it was actually for the study and that they gave a half an hour doctor appointment so that we had enough time." (GP26)* *"The practice manager giving me protected time to complete it." (GP54)*
	Positive experience with the ***training videos***, particularly that they were short and easy to access	*"..the training materials were very good...having everything in one place and links to points on the online reviews was just invaluable. You know you could find the stuff you needed to make a decision quickly." (GP128)* *"They were actually very good. And so would take from this is that I would probably run them now as a teaching session in the practice...and suggest that this is what we do and this is how we do a medication review and that we plan to do it in a more structured way' (GP39)* *"I thought they were really good. They weren't too long which was great, so it was easy to get through them quite quickly and they were to the point." (GP26)*

NPT Core Construct	Construct components	Example quotes
Collective action How practical work of doing the intervention is carried out	***Familiarisation with the notes*** and medicines prior to the review	*"I ran the SPPiRE thing first before they come in, so that is at least flagged up what issues there might be with their prescription." (GP39)* *"Obviously I did a review of their medications first; checking for interactions, checking for were they on the appropriate dose, checking that they were being monitored correctly, and that you know things were co prescribed appropriately." (GP12)* *"Before we called the patient in we would have had a good look through the file just to familiarize ourselves again with all the past medical history and try and see what the indication was for each of the medications." (GP26)*
	Adherence to the SPPiRE review process: most patients did not bring their medicines with them, half of GPs felt including patient priorities was either challenging or not helpful	*"Not the actual medicines, no. I would have had a list. Well, the doctor had a list of them anyhow." (GP54P28)* *"Yeah, I sort of got the feeling they didn't really know what I meant or and maybe I didn't word it very well." (GP128)*
Reflexive Monitoring Evaluation and appraisal of the intervention	GPs felt they had a ***better awareness of PIP***, were more ***confident stopping medicines*** but had not anticipated the ***amount of time*** involved	*"I found it...educational because a lot of stuff they had mentioned in terms of drugs to look out for maybe I wasn't familiar with or wasn't doing it on a day to day basis, that then prompted how I would prescribe in the future if that makes sense." (GP4)* *"I suppose I think since I did the SPPiRE study I have probably become a lot more aware of trying to stop things in elderly particularly." (GP26)* *"It does take up more sort of energy and time then we may have anticipated." (GP54)*
	Patient's generally felt ***reassured*** and ***better informed*** about their medicines	*"There was nothing I didn't like about it, I felt it was useful...it was generally useful and informative." (GP26P6)* *"I suppose just to be able to chat to him about my concerns...it made me feel more comfortable taking them because I knew exactly, what was what." (GP41P8)*
	Suggested solutions and improvements	*"...perhaps asking them what your priorities are earlier before they even came into you, instead of just springing it on them in the consultation would have proven more useful." (GP4)* *"I suppose if people got an extra fee for it that would always be an incentive you know yourself." (GP137)* *"I think it would have to be something that's integrated into our software system that we work from." (GP12)*

Mechanism of action of the intervention

The SPPiRE intervention was effective in reducing the number of medicines but had no effect on PIP outcomes [8]. Practice characteristics that might influence the mechanism of action such as size and location were included as covariates in the trial analyses, and did not significantly influence the results. In terms of the effect of practice organisation, a sensitivity analysis indicated that there was no difference in the results when "presence of a written practice repeat prescribing policy" was included as a covariate. Including patient factors such as patients' attitudes to deprescribing [17] also had no significant effect on the results. The qualitative data suggested that most participants were open to stopping medicines but there was reluctance or fear in stopping some medicines, particularly those that had been prescribed for a long time, *"It's funny when you're taking tablets and if it's working for you. It's like everything else, if it works don't break it. You know what I mean, you're afraid." (GP50P1).* In particular there was a reluctance to discontinue benzodiazepines, *"The only category that they're not always happy with is the benzos because they're so …used to those benzos and sleeping tablets" (GP97).* With respect to their SPPiRE review most patients who described a change during their review viewed this positively, even in an instance where the change did not work out and a medicine that had been stopped had to be restarted; *"...I feel fine about it. They did their best to try to reduce my medication, which is a good thing. The less you take, the less side effects you're going to have. So I was all for it" (GP4P13).* Whether a medicine was stopped or changed depended on multiple factors including the patients' attitude, the medicine and the doctor patient relationship. Most patients were well known to the GP however, five GPs described doing reviews with patients not well known to them and most felt this made the process more complicated. Another factor that influenced the decision to stop medicines was the complexity of the patient; *"She's a complex patient who you tweak rather than make any real, you tweak to keep her propped up really" (GP137).*

Patients' background views on their medicines varied with four patients being wary of too many medicines and others who were hoping for a *"miracle medicine" (GP122P11).* Patients' views also varied in how involved they liked to be in making decisions about their medicines. Many described

complete and unquestioning trust in their doctor, *"Whatever I'm ordered to take, I take and that's it" (GP54P25)* but others described being wary of *"pill popper" (GP50P1)* or doctors *"adding on something all the time" (GP39P41).*

With respect to changes in prescribing activity recorded on the SPPiRE website, GPs identified 282 PIP in the 163 patients who had a review (1.73 PIP per person), resulting in 133 different medication changes and eight referrals for blood monitoring. The same PIP criteria were used in the intervention and for trial outcomes and GPs identified less PIP compared to the baseline assessment of intervention prescriptions (n=208) by the trial's blinded pharmacist, who identified 517 PIP (2.49 PIP per person). When compared to the baseline numbers in the 163 participants who had a review there was a total of 410 PIP (2.52 per person). There were also differences in the proportions of PIP identified with GPs less commonly identifying proton pump inhibitor (PPI) and anticholinergic related PIP, see Appendix 5 for the numbers and proportions of the top 10 identified PIP. The website also captured data on the outcome for identified PIP. Overall the identification of a PIP resulted in either no change (28%) or stopping a medication (22%) the majority of times (see Appendix 6). For PPIs, the most common outcome was a dose change (46%) and for benzodiazepines was no change (55%), consistent with the qualitative findings. The prescription of an anticholinergic medicine with a specific co-morbidity resulted in no change in over 50% of identified cases. The reasons for this were not obvious from the qualitative data. On further review of website data, the PIP was frequently an antimuscarinic inhaler which GPs may have judged to be less likely to cause systemic side effects. In at least one other case the PIP was a urinary anti-spasmodic, initiated in secondary care for urgency symptoms secondary to benign prostatic hypertrophy.

With respect to the brown bag review, a total of 237 different medication concerns in 97 patients (58.3%) were recorded. Examples of concerns included non-adherence to a medicine, side effects and monitoring issues and these were identified by either the patient or GP and the most common outcome for identified concerns was stopping a medicine (40.9%). See Appendix 7 for outcomes of identified medication related concerns. As previously described, the majority of interviewed patients

reported not bringing their medicines to the review, however a majority of interviewed GPs found this process very useful, *"I think the learning for me is that you know people get stuck on, get put on tablets and sometimes haven't the vaguest of ideas of what they're taking them for, you know?" (GP58).* In instances where the patient did not bring their medicines, interviewed GPs described working off a list instead but the qualitative data indicated that this process was more effective when the patient brought their medicines with them; *"I found one or two that were on a list, on a drug that they're getting a prescription for but they haven't taken it for months" (GP39).* It was not possible to ascertain from the quantitative data if more changes were made when the patient had brought the medicines in with them.

The final process prompted the GP to ask the patient about his or her priorities for treatment. GPs identified 226 different priorities for 128 patients (78.5%), most commonly treating pain and other symptoms, see Figure 2. Assessing treatment priorities resulted in a medication change for 51 of these patients, usually a dose change.

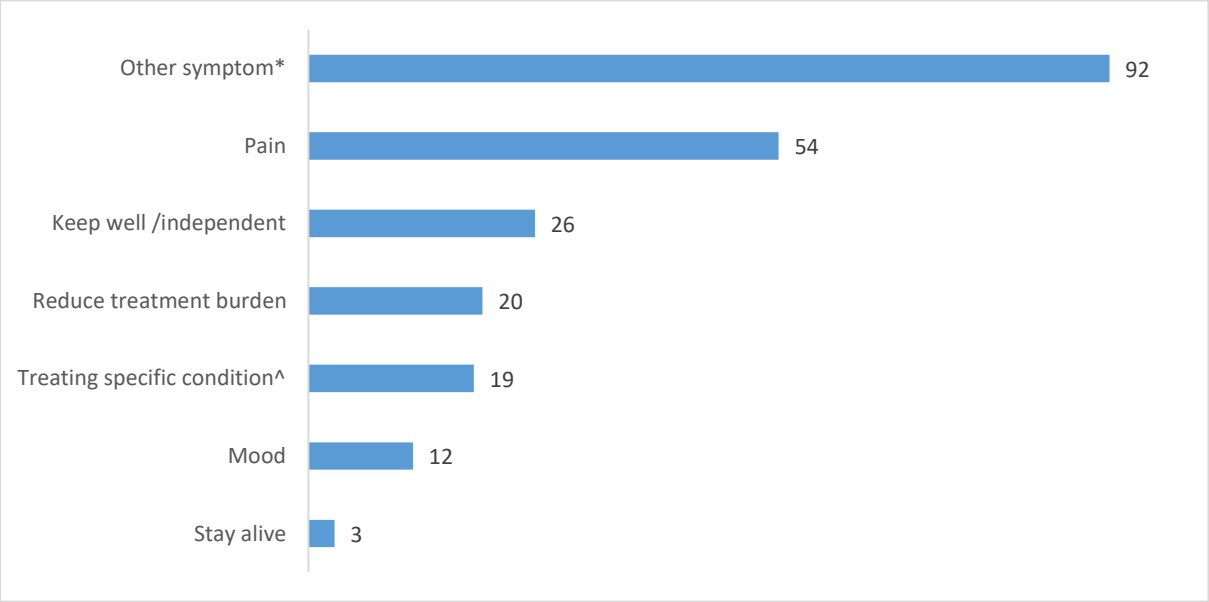

Figure 2 Patient treatment priorities recorded by GP

^ Examples included Type 2 Diabetes Mellitus targets, blood pressure targets and avoiding a specific outcome such as another heart attack or stroke

** Common examples included constipation, diarrhoea, urinary incontinence, fatigue, shortness of breath, insomnia and dizziness*

GPs views on the elicitation of patient priorities varied considerably. Four of the 18 interviewed reported that they already knew their patients' priorities and so they didn't need to ask, five found it challenging and said the patients struggled to understand the question or focused on multiple symptoms. Only three GPs reported finding this process useful, see table 2. There is little data from patient interviews as many found it difficult to answer questions about their treatment priorities, *"I don't understand what it's all about" (GP4P13)*. One patient, who previously worked as a healthcare professional spoke positively about the process, describing it as a way of *"having an over look at the whole body, the whole beast",* whereas previously, *"Nobody was looking at the big picture. I feel different people, different consultants prescribe different things" (GP39P41).*

Table 2 GP responses to assessing patients' treatment priorities

GP Response	Example quotes
Unengaged (4)	*"I really didn't delve in too much for that. Some of them were probably incapable of understanding it or didn't want to understand it." (GP21)*
Useful (3)	*"All of these patients will be people we would in general tend to know very well. So we do make assumptions. So actually, getting them to verbalise what their priorities are is, I think, very useful." (GP122)*
Not useful (4)	*"When you see a patient who's on a lot of medications, generally speaking that's because they've got quite a few medical problems and so therefore their priorities were sort of, you know, to have the medical problems addressed if possible." (GP58)*
Challenging (5)	*"Yeah, that was actually a bit tricky. I'm not sure, I didn't want to try and put words in their mouth." (GP128)*

Table 3 integrates and summarises the results of the qualitative and quantitative analyses with respect to the three intervention processes.

Table 3 Summary of the mechanisms of action of SPPiRE: Integration of qualitative and quantitative analyses

Process	Qualitative data	Quantitative data	Integration
PIP identification	GPs felt PIP identification was important GPs described feeling more confident in identifying PIP and stopping medicines	GPs identified less PIP than baseline pharmacist PIP identification resulted in change <50% of the time	Dissonance
Brown bag review	Not all patients brought their medicines in with them, although GPs thought this component was useful	Although concerns were only identified in less than 60% patients, this process resulted in the most medication changes	Partial agreement

Process	Qualitative data	Quantitative data	Integration
Recording treatment priorities	A minority of GPs found this process helpful. Most found it either challenging or didn't buy into the process. There is little data from patient interviews as many found it difficult to answer questions about their treatment priorities.	Although almost 80% of participants had at least one priority recorded, this process rarely resulted in medication change	Agreement

Discussion

Summary of findings

This mixed-methods process evaluation revealed that the SPPiRE intervention was implemented as intended in the majority of practices. However, 22% of intervention patients had no review, three of the 26 intervention practices were unable to complete any reviews and adherence to the various sub components of the review varied. The overall context of staff shortages and resource issues as well as deep seated views on medicines affected both how the intervention was implemented and exerted its effect, see Appendix 8.

Interestingly, GPs identified less PIP than anticipated and acted on them less than half of the time despite describing this process as important and valuable in interviews. GPs may have identified less PIP during the medication review than the trial pharmacist for a range of reasons. Firstly, there may have been actual differences in PIP between baseline data collection and the medication review (typically a 6 to 12 month time period), as GPs may have been prompted to review prescriptions when patients were identified for the trial. Both intervention and control GPs identified eligible participants (aged ≥65 tears and prescribed ≥15 medicines) by running a finder tool that was embedded in practice management software and were advised to check prescriptions to ensure the participant was currently on ≥15 medicines. Although control GPs were given no information about PIP, improvements in PIP in the control group during the study suggest that the identification of these patients on ≥15 medicines did result in medication change [8]. Secondly, GPs are likely to be less familiar with the application of explicit prescribing criteria than pharmacists, particularly a pharmacist working in a

research setting, and thirdly because PIP identified by the pharmacist may have been judged by the GP to be specifically appropriate to the individual patient and not recorded as a PIP. Examples that appeared in website data (these were recorded as PIP, but an explanation was left by the GP) included the use of dual antiplatelet therapy for more than one year post percutaneous cardiac intervention in patients at very high risk of having another event, or the use of a therapeutic dose PPI on the recommendation of secondary care. It is possible there were similar occurrences where the GP, knowing the context, did not record the PIP. The brown bag review, where GPs reviewed each medicine with their patient and recorded any concerns identified either by the patient or GP, resulted in the most medication changes out of the various components of the review (146 medication changes related to 237 identified concerns). Most of the time this was stopping a medicine, suggesting that the intervention effect may have been mediated mostly through this process and is consistent with the overall trial results where there was evidence of an effect on number of medicines, but not PIPs [8]. Patient treatment priorities were mostly symptom based, particularly treating pain and this process led to fewer medication changes than PIP identification and the brown bag review. Only three of the 18 GPs viewed the identification of patient priorities as useful and patients often found it difficult to describe their priorities. Although training material was viewed positively as informative and succinct, the purpose and process of assessing patient treatment priorities may not have been adequately covered.

Strengths and weaknesses

The aims of the SPPiRE process evaluation were pre-specified and based on a framework that was designed to guide the conduct of process evaluations for cluster RCTs [14]. In addition, NPT was used to guide qualitative analysis and make sense of how the intervention was implemented. Triangulation of the qualitative and quantitative analyses allowed the results to be explored from different perspectives [18]. The process evaluation was carried out parallel to the main trial, reducing the likelihood of bias, where investigators may be more focussed on explaining the results rather than unearthing unintended consequences. The disadvantage of this approach was that we were unable to

explain the deprescribing and improvements in PIP that were seen in the control group once the results for the main trial were analysed. Half of the GP interviews were carried out by the study manager who had significant contact with GPs during recruitment and intervention delivery increasing the likelihood of social desirability bias among interviewees. Another limitation of this work is that control practices were not interviewed as the focus was on intervention implementation but it means we have less understanding of the changes in PIP that occurred in control practices.

Comparison to other literature

Qualitative work describing GPs' approaches to managing patients with multimorbidity has suggested that GPs are reticent to "rock the boat" in these older complex patients [19]. Similarly qualitative work with patients and their carers has suggested that both can be reluctant to stop a medicine that is not currently giving any perceived benefit for fear of missing out on possible future benefits [20]. SPPiRE patients and GPs voiced similar views however most GPs felt patients were receptive to change and patients were generally positive in their description of medication changes that occurred during their SPPiRE review.

SPPiRE was not effective at reducing PIP, unlike the Data-driven Quality Improvement in Primary care (DQIP) cluster RCT that showed that a GP oriented intervention comprising education, informatics and financial incentives was effective in improving the safety of prescribing [21]. Results from the DQIP process evaluation suggested that the financial incentives may have been important for initiation of the intervention and for recruitment but were not considered an important "active ingredient" [22]. Although SPPiRE practices received a small remuneration (€60 per patient recruited) to cover some of the practice costs for taking part, this was not part of the intervention and the use of financial incentives may have helped with the delays seen in initiating intervention implementation. Another effective component of the DQIP intervention that was important with initiation in larger practices, and was missing from SPPiRE, was discussion with the practices about potential practice processes to do the work [22]. A final difference was that SPPiRE guided GPs in the identification of PIP but the DQIP tool identified and alerted GPs to PIP. As described previously, failure in identification of PIP by

GPs may partially explain the lack of effect on this outcome measure in SPPiRE. There was a sustained effect from the DQIP intervention and their process evaluation suggested this may have been due to potential changes in the initiation of high risk prescribing [23]. SPPiRE GPs also reported a better awareness of PIP and more caution about initiating certain classes of medicines after participating in the intervention.

SPPiRE was unique when compared with other recently published medicines management multimorbidity interventions in that it targeted a much more clinically vulnerable group with very significant polypharmacy and in that no other health care professionals, aside from the GP, were involved in the intervention [24-31]. One of these studies, the 3D study, has published a process evaluation which showed that reach was lower than anticipated with a similar proportion to SPPiRE, having at least one review but only 49% having the full intervention (comprising a nurse and GP review) [32]. Similar to SPPiRE, staff shortage was the primary reason cited for this. Conversely to SPPiRE, the identification of patient priorities was the most consistently delivered component of the 3D intervention (99%) [32]. This may be because this was the first component of the review or because this process was delivered by the practice nurse. Interestingly, one of the SPPiRE GPs commented that this process may have been better suited to the nurse and that the patients may have been more free and forthcoming with their problems with the nurse. Another GP suggested that this process may have been improved if the patients had some fore warning and time to consider their priorities rather than the question being sprung on them at the review. This approach, where patients are sent a questionnaire and encouraged to consider their goals for treatment prior to the medication review, has been adopted for a similar intervention which is set in primary care in Canada and being evaluated by an individually randomised clinical trial [33]. A similar intervention study set in primary care in Germany, where patients had a full 30 minute interview with their GP to discuss priorities prior to a medication review, led to increased prescriptions for analgesics in the intervention group [34]. Although pain was frequently identified as a priority for SPPiRE patients, this did not lead to the addition of new prescriptions for analgesics, this may be because the priority assessment process was

not effective in addressing priorities or given the high number of medicines at baseline, pain was addressed by adjusting and augmenting current analgesic prescriptions. The most common medication change related to priority assessment in SPPiRE was a dose change (compared to stopping a medicine for the PIP assessment and brown bag processes), indicating that optimising medications in polypharmacy is not just about changes in the number of medicines.

The PINCER trial demonstrated the clinical and cost effectiveness of pharmacist delivered medication reviews in primary care in the UK [35], and their process evaluation showed that GPs acted on pharmacist recommendations the majority of times [36]. SPPiRE GPs acted on self-identified PIP less than half of the time. It may be that collaboration with a colleague facilitates making medication changes and a medicines management multimorbidity intervention that adopts this approach [37] has recently been piloted in Irish primary care [38]. Primary care pharmacists are not a part of routine care in Ireland however given the context of GP shortage in Irish primary care a potentially more feasible approach may be an intervention that involves other health care professionals. Recently a small uncontrolled study based in Irish primary care has demonstrated the feasibility of pharmacist delivered medication reviews in primary care [39].

Conclusion

This mixed-methods process evaluation showed that overall SPPiRE was implemented as planned in the majority of practice but that the context of resource and staff shortage affected implementation. In addition, deep seated patient and doctor views around medicines and medical decision-making influenced adherence to the various sub-components of the review. The SPPiRE intervention had a significant but small effect in reducing the number of medicines and this appears to have been mediated by the brown bag review element of the intervention. The intervention was not effective in reducing PIP and this may be because GPs were less familiar with the application of explicit prescribing criteria, especially given that the qualitative results indicated that GPs were motivated to identify and address PIP, although part of the lack of effect seen on PIP was due to improvements in the control group. A systems approach that is embedded in practice management software systems may be more

effective, and override the need for the GP to identify PIP. The majority of participants had at least one priority identified and these were primarily symptom based. GPs' views on this process varied considerably. Overall the majority of patients and GPs viewed SPPiRE positively, but adequate resourcing and integration into practice systems would be necessary for system wide implementation.

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Supplementary material Contents

Appendix 1: SPPiRE PIP Criteria

Drug group	PIP	Reason
Drug groups frequently associated with preventable drug related morbidity		
NSAIDS	with diuretic and ACEi/ARB (1)	Risk of renal impairment
	with chronic kidney disease (eGFR <50) (1, 2)	
	for ≥ 12 weeks with no gastroprotection (1)	Risk of GI bleed
	that is not COX 2 selective, with a history of PUD with no gastroprotection (2)	
	and antiplatelet with no gastroprotection (2)	
	with an anticoagulant (2, 3)	
	with severe hypertension or heart failure (2)	Risk of hypertension/ heart failure exacerbation
	COX-2 selective with concurrent cardiovascular disease (2)	Increased risk of MI/CVA
Antiplatelets	and history of PUD with no gastroprotection (1, 3)	Risk of GI bleed
	and anticoagulant with no gastroprotection (1, 3)	
	dual antiplatelet therapy with no gastroprotection (1)	
	consider intended duration of treatment if taking dual anti-platelet therapy for over one year post PCI (2)	Not usually indicated
Anticoagulants	for first uncomplicated DVT for >6 months duration (2)	Not indicated
	for first uncomplicated PE for >12 months duration (2)	
	dabigatran (Pradaxa®) if eGFR <30 ml/min/ 1.73m^2 or if renal function is unknown (2)	Risk of bleeding
	rivaroxaban (Xarelto®)or apixaban (Eliquis®) if eGFR <15 ml/min/ 1.73m^2 or if renal function is unknown (2)	
Diuretics	and no U&E check in the last 48 weeks (1)	Risk of renal impairment and electrolyte abnormality
	loop diuretic and thiazide diuretic and no U&E in the last 24 weeks (1)	
	loop diuretic for dependent oedema and no heart failure, liver failure or nephrotic syndrome (2)	Risks usually out-weigh benefits
	thiazide diuretic with a history of gout (2)	Risk of precipitating gout
Drugs groups associated with morbidity in the elderly		
Anticholinergic drugs	With comorbidities (3) Dementia Narrow angle glaucoma Cardiac conduction abnormalities Chronic prostatism	Exacerbation of co-morbidity

Drug group	PIP	Reason
	Concomitant use of two or more drugs with anticholinergic properties (2)	Risk of anticholinergic toxicity
	tricyclic antidepressant as first line antidepressant (2)	Increased risk of adverse effects in older patients and alternatives available
	antimuscarinic antihistamine (2)	
Benzodiazepines OR Z drugs	for longer than 4 weeks (2) (1)	Risk of sedation, confusion, impaired balance, falls. NNT 13 and NNH 6 when used for insomnia (4)
Antipsychotics	with dementia and no psychosis (1, 2)	Increased risk of stroke, only use when all other means have failed and shortest possible dose for shortest duration (5)
Miscellaneous drug groups; included because of prevalence or high risk		
Methotrexate	not prescribed as weekly (1)	Increased risk of potentially fatal medication errors
	prescribed > 1 strength tablet (1)	
Opioids	used regularly with no laxative (2)	Risk of severe constipation
Corticosteroids	use ≥ 12 weeks with no bone protection (2)	Risk of fracture
PPI	for uncomplicated PUD/erosive peptic oesophagitis at full therapeutic dose ≥ 8 weeks (2)	Not indicated
Metformin	with eGFR < 30 ml/min/ 1.73m^2 (2)	Risk of lactic acidosis

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Appendix 2: SPPiRE Interview Topic Guide – Intervention GPs

Prescribing for older patients

- Can you talk me through how repeat prescriptions for older patients are reviewed in your practice?
    - Dedicated medication review visit Vs opportunistic
    - Who does it?
    - How are changes made when reviewing repeat prescriptions?
    - If problems are identified how are they managed, eg message left for patient/pharmacist through admin staff or GP contacting patient or written message left for patient with prescription?
- Can you describe some of the issues you face when reviewing prescriptions for these patient?
    - Uncertainty over who started the medicine and why
    - Uncertainty over potential benefits and risks
    - Reluctance to make too many changes due to fear of adverse consequences/the need for added visits
    - Patient preferences/demands
    - Previous positive or negative experiences of changing or discontinuing repeat medicines

Summary of intervention use

NPT Construct	**Questions/Prompts**
Coherence: making sense of the intervention	What did you think would be the benefits of taking part in SPPiRE? What were you wary of in terms of taking part? How did you see these medication reviews fitting into your day to day practice?
Cognitive Participation: involvement with the intervention	Can you describe who else was from the practice was involved in the SPPiRE intervention. What do you feel their views of this were? What did you see your role as being? Describe how the practice has had to adapt to incorporate the implementation of the intervention. Can you tell me what you thought about the training videos?
Collective Action: how practical work of *doing* the intervention is carried out within the organization	Can you talk me through the steps that were involved in performing the medication review? • How were the appointments arranged, did the patients turn up? • Use of the SPPiRE website? • Was the review performed in one sitting? Was the patient present?

	• What worked well? What didn't work so well? Was the website easy to use? • PIP identified? How did patient respond to suggested changes? • Brown bag • Patient priorities Can you describe how compatible this was with existing practice?
Reflexive Monitoring: evaluation and appraisal of the intervention	Overall how would you describe your experience of taking part? Was it worthwhile? Would you like to see this or something similar in routine use (if yes, any suggestions as to what changes would be needed to improve intervention, if no reasons why it would be unfeasible in routine practice)? What you would change? In what way do you think it has had any impact? Are there any aspects of the intervention that you have now incorporated into your routine practice? Added workload, ADWEs?

Concluding comments

- Overall is there anything else you would like to comment on?

Appendix 3: SPPiRE Interview Topic Guide – Intervention Patients

Medications in general

- You were invited to take part in this study because of the number of medicines you are currently prescribed. How do you feel about the number of medicines you are prescribed?
    - What do you think is a lot of medicines to take?
    - How important/necessary do you feel they are?
    - Do you feel you know what medicines you are taking and why?
    - If you had a concern about your medicines, who would you talk to?
    - Do you feel you can talk to your GP about your medicines?
    - Do you like to be involved in decisions about your medicines?

Summary of intervention use

- As part of this study you would have been invited to attend a medication review visit with your GP.
    - What did you expect would happen?
    - Can you describe how that visit went?
    - Did you bring your medicines in with you to the visit?
    - How were your ideas, concerns and priorities addressed?
    - Were any changes made to your medicines? How did you feel about this?
    - Which things did you like the best about it? What did you not like/what would you change?
- What, if any, difference do you feel it has made to you
    - happier about medicines
    - reassured they were reviewed
    - concerns and priorities were addressed
    - left you feeling concerned or worried about your medicines
- Would you like to see something like this routinely used?
    - If yes, any suggestions are to how to improve or sustain it?
    - If no, why?

Concluding comments

Is there anything else the participant would like to add?

Appendix 4: Practice characteristics and SPPiRE intervention implementation

GP ID	Practice size[¥]	Practice Location	Reviewed/ Recruited	No. days late	PIP* N (%)	Concern^ N (%)	Priority[§] N (%)	Meds stopped (Mean)
4	37	Rural	10/11	0	8 (80)	9 (90)	10 (100)	4.89
12	35	Urban	9/10	0	9 (100)	5 (56)	9 (100)	1.67
13	45	Urban	10/10	0	6 (60)	2 (20)	3 (30)	0.10
21	9	Mixed	9/9	100	7 (78)	0	3 (33)	0.50
26	28	Urban	7/7	0	6 (86)	4 (57)	7 (100)	1.50
39	54	Mixed	5/9	317	4 (80)	2 (40)	3 (60)	2.25
41	8	Rural	8/8	0	6 (75)	7 (88)	8 (100)	1.25
46	21	Urban	5/5	0	5 (100)	1 (20)	3 (60)	1.60
49	34.5	Mixed	0/5	N/A	N/A	N/A	N/A	N/A
50	53	Urban	8/9	3	5 (63)	7 (88)	7 (88)	1.56
54	30	Rural	10/11	243	10 (100)	7 (70)	8 (80)	2.60
58	29	Mixed	6/6	0	5 (83)	5 (83)	5 (83)	1.33
61	18	Urban	8/8	330	6 (75)	4 (50)	8 (100)	0.13
68	14	Urban	8/8	0	7 (88)	3 (38)	8 (100)	6.57
73	88	Urban	0/8	N/A	N/A	N/A	N/A	N/A
81	43	Mixed		0	5 (63)	5 (63)	3 (38)	1.75
97	10	Mixed	10/10	110	10 (100)	4 (40)	8 (80)	0.20
103	22	Mixed	1/5	266	1 (100)	1 (100)	1 (100)	5.00
115	16	Urban	0/7	N/A	N/A	N/A	N/A	N/A
116	34	Urban	12/15	298	10 (83)	12 (100)	12 (100)	0.42
117	24	Urban	3/7	12	3 (100)	1 (33)	3 (100)	0.67
122	40	Mixed	4/5	5	3 (75)	3 (75)	4 (100)	3.00
127	30	Urban	9/10	14	5 (56)	7 (78)	6 (67)	1.05
128	12.5	Urban	5/5	0	3 (60)	4 (80)	2 (40)	1.20
137	24	Urban	3/5	0	1 (33)	2 (67)	2 (67)	2.50
138	32	Rural	5/6	30	5 (100)	0 (0)	5 (100)	1.20

[¥] Measured by the number of GP sessions per week, whereby one session is one half day (either a morning or afternoon clinic).

** The number of participants and proportion of those reviewed, with at least 1 PIP identified.*

^ The number of participants and proportion of those reviewed, with at least 1 concern identified.

[§] The number of participants and proportion of those reviewed, with at least 1 priority identified.

Appendix 5: Difference in prevalence between baseline pharmacist and intervention GP PIP assessment

PIP	GP N=163 (%)	Trial pharmacist N=208 (%)
The use of a benzodiazepine or z drug for longer than 4 weeks	56 (34.4)	86 (41.3)
Full dose PPI for longer than 8 weeks	56 (34.4)	126 (60.6)
Regular opioid with no laxative	28 (17.2)	39 (18.8)
Therapeutic duplication	27 (16.6)	40 (19.2)
Anticholinergic with co-morbidities	19 (11.7)	24 (11.5)
Two or more anticholinergic drugs	17 (10.4)	71 (34.1)
Loop diuretic for dependent oedema	16 (9.8)	46 (22.1)
Any diuretic use and no RP in past 48 weeks	10 (6.1)	34 (16.3)
NSAID with diuretic and ACEi	9 (5.5)	8 (3.8)
Loop and thiazide diuretic and no RP in last 24 weeks	5 (3.1)	3 (1.4)

Abbreviations: PIP: potentially inappropriate prescription, PPI; proton pump inhibitor, RP; renal profile, NSAID; Non-steroidal anti-inflammatory drug, ACEi; Angiotensin converting enzyme inhibitor.

Appendix 6: GP identified PIP and outcome action

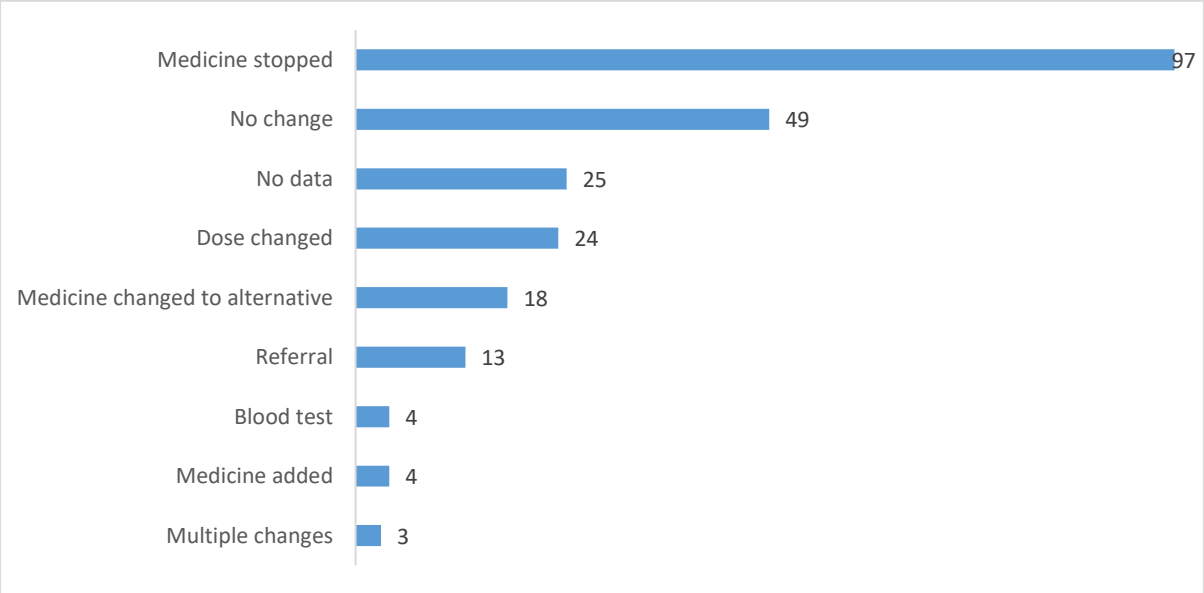
PIP	N=163	Medicine stopped	Dose changed	No change	No data[1]	Other[2]
The use of a benzodiazepine or z drug for longer than 4 weeks	56	5	12	31	4	4
Full dose PPI for longer than 8 weeks	56	9	26	13	6	2
Regular opioid with no laxative	28	2	3	9	4	10
Therapeutic duplication	27	11	0	6	4	6
Anticholinergic with co-morbidities	19	4	1	10	3	1
Two or more anticholinergic drugs	17	8	1	5	2	1
Loop diuretic for dependent oedema	16	7	1	3	2	3
Diuretic use and no RP within 48 weeks	10	2	1	0	2	5
NSAID with diuretic and ACEi	9	5	0	1	0	3
Loop and thiazide diuretic and no RP within 24 weeks	5	3	0	0	0	2
Total	**252**	**57 (22.6%)**	**46 (18.3%)**	**80 (31.7%)**	**29 (11.5%)**	**40 (15.9%)**

[1]GP did not fill out action data for PIP

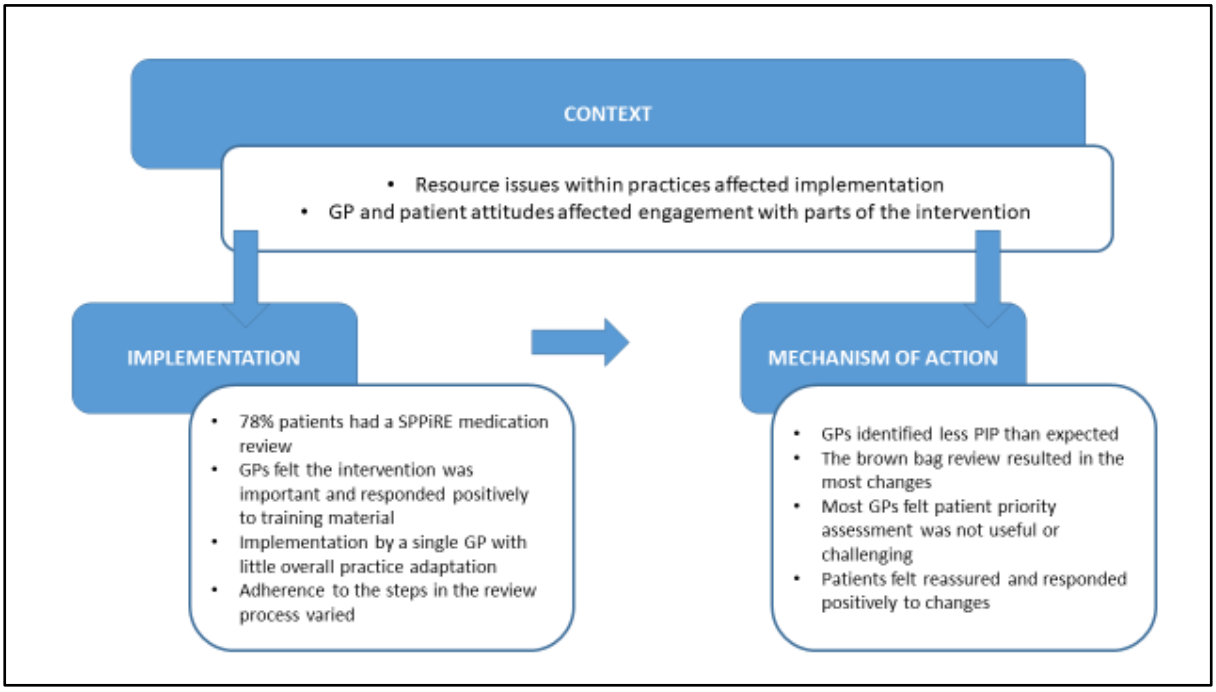
[2]Either specialist referral, blood test, medicine added or multiple medication changes

Abbreviations: PIP; potentially inappropriate prescription, PPI; proton pump inhibitor, RP; renal profile, NSAID; Non-steroidal anti-inflammatory drug, ACEi; Angiotensin converting enzyme inhibitor.

Appendix 7: Outcome of medication concerns identified during the brown bag review



Appendix 8: Summary of SPPiRE process evaluation results



Summary of context, implementation and mechanism of action of the SPPiRE intervention [1, 2]

1. Kyne K, McCarthy C, Kiely B, Smith SM, Clyne B. Study protocol for a process evaluation of a cluster randomised controlled trial to reduce potentially inappropriate prescribing and polypharmacy in patients with multimorbidity in Irish primary care (SPPiRE). *HRB open research*. 2019;2:20.
2. Moore GF, Audrey S, Barker M, Bond L, Bonell C, Hardeman W, et al. Process evaluation of complex interventions: Medical Research Council guidance. *BMJ (Clinical research ed).* 2015;350:h1258.