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Volume 11 • Issue 10 • December 2023

ISSN 2050-4322

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DOI 10.3310/JBPT2117

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Disclosure of interests

Full disclosure of interests: Completed ICMJE forms for all authors, including all related interests, are available in the toolkit on the NIHR Journals Library report publication page at https://doi.org/10.3310/10.3310/JBPT2117.

Primary conflicts of interest: David Wright received speaker fees from Desitin Pharma and speaker fees and unrestricted education grants from Rosemont Pharmaceuticals during the conduct of the study. Christine Bond reports personal fees as the Editor-in-Chief of *International Journal of Pharmacy Practice* during the conduct of the study. Carmel Hughes reports membership of HS&DR Commissioned Panel member (2015–19). Garry Barton reports membership of a CTU funded by the NIHR (up to 2021). Lee Shepstone reports membership of EME Funding Committee member (2010–14). Antony Arthur reports membership of HS&DR Commissioned Board member (2014–16). Arnold Zermansky reports membership of HTA MPOH Panel (2011–18) Pharmaceuticals Panel.

Published December 2023
DOI: 10.3310/JBPT2117

This report should be referenced as follows:

Wright D, Holland R, Alldred DP, Bond C, Hughes C, Barton G, *et al*. The Care Home Independent Pharmacist Prescriber Study (CHIPPS): development and implementation of an RCT to estimate safety, effectiveness and cost-effectiveness. *Programme Grants Appl Res* 2023;**11**(10). https://doi.org/10.3310/JBPT2117

Programme Grants for Applied Research

ISSN 2050-4322 (Print)

ISSN 2050-4330 (Online)

Programme Grants for Applied Research (PGfAR) was launched in 2013 and is indexed by Europe PMC, NCBI Bookshelf, DOAJ, Ulrichsweb™ (ProQuest LLC, Ann Arbor, MI, USA) and Scopus® (Elsevier, Amsterdam, Netherlands).

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This report

The research reported in this issue of the journal was funded by PGfAR as project number RP-PG-0613-20007. The contractual start date was in May 2015. The final report began editorial review in July 2021 and was accepted for publication in October 2022. As the funder, the PGfAR programme agreed the research questions and study designs in advance with the investigators. The authors have been wholly responsible for all data collection, analysis and interpretation, and for writing up their work. The PGfAR editors and production house have tried to ensure the accuracy of the authors' report and would like to thank the reviewers for their constructive comments on the final report document. However, they do not accept liability for damages or losses arising from material published in this report.

This report presents independent research funded by the National Institute for Health and Care Research (NIHR). The views and opinions expressed by authors in this publication are those of the authors and do not necessarily reflect those of the NHS, the NIHR, CCF, PGfAR or the Department of Health and Social Care. If there are verbatim quotations included in this publication the views and opinions expressed by the interviewees are those of the interviewees and do not necessarily reflect those of the authors, those of the NHS, the NIHR, the PGfAR programme or the Department of Health and Social Care.

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Abstract

The Care Home Independent Pharmacist Prescriber Study (CHIPPS): development and implementation of an RCT to estimate safety, effectiveness and cost-effectiveness

David Wright,[1*] Richard Holland,[2*] David Phillip Alldred,[3,4] Christine Bond,[5] Carmel Hughes,[6] Garry Barton,[7] Fiona Poland,[8] Lee Shepstone,[7] Antony Arthur,[8] Linda Birt,[8] Jeanette Blacklock,[1] Annie Blyth,[1] Stamatina Cheilari,[7] Amrit Daffu-O'Reilly,[9] Lindsay Dalgarno,[5] James Desborough,[1] Joanna Ford,[10] Kelly Grant,[5] Janet Gray,[11] Christine Handford,[11] Bronwen Harry,[12] Helen Hill,[13] Jacqueline Inch,[5] Phyo Kyaw Myint,[14] Nigel Norris,[15] Maureen Spargo,[6] Vivienne Maskrey,[16] David Turner,[7] Laura Watts[7] and Arnold Zermansky[17]

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Background: Medicine prescribing, monitoring and administration in care homes can be significantly enhanced. Effective interventions to improve pharmaceutical care and resident outcomes are required. The enablement of pharmacists to prescribe provides an opportunity for pharmacist independent prescribers to assume responsibility for improving pharmaceutical care, medication-related outcomes and resident safety whilst reducing general practitioner workload.

Objective(s): To determine the effectiveness and cost-effectiveness of pharmacist independent prescribing in care homes.

Design: Development work was undertaken through five work packages before the delivery of the definitive trial. Triads of pharmacist independent prescribers, care home and general practice with responsibility over 20 care home residents were recruited and cluster randomised to intervention or usual care for 6 months. Researchers were blinded at recruitment stage only. Recruitment of 880 residents was required to provide 80% statistical power, to show a 21% reduction in falls over 6 months, assuming 20% attrition. Randomisation was undertaken electronically at triad level, stratified by geographical area. Intention-to-treat analysis undertaken using a negative binomial model. Parameters were estimated using a generalised estimating equation approach. Costs were captured from an NHS perspective. Quality of life (EuroQol; five domain; five level) was collected by proxy to enable cost/quality-adjusted life-year estimation. A concurrent process evaluation was performed. Safety was monitored through a review of pharmacist independent prescriber activities, independent concerns reporting and review of adverse events.

Participants: Forty-nine triads of general practitioners, pharmacist independent prescribers and care homes were recruited with 454 residents allocated to the intervention arm and 428 to the control arm.

Intervention: Medication review and care planning, medication reconciliation, staff training, support with care home medication-related procedures, deprescribing and authorisation of monthly prescriptions.

Main outcome measure: Fall rate per person over 6 months.

Results: Data for 449 intervention and 427 control residents available for final analysis.

The 6-month fall rate ratio in favour of intervention was 0.91 (95% confidence interval 0.66 to 1.26; p=0.58). No significant difference in secondary outcomes was identified except Drug Burden Index (rate ratio 0.83, 95% confidence interval 0.75 to 0.92; p<0.001).

No harms were identified. One quarter of medication-related interventions were associated with a reduced risk of falls. The intervention was positively received.

Limitations:

- Participant self-selection bias may have affected the generalisability of findings.
- Open-label cluster randomised controlled trial limited by 6-month follow-up.
- Potential ceiling effect due to concurrent pharmacist-led interventions.
- Falls potentially insufficiently proximal to the intervention.

Conclusions: To enhance effectiveness and acceptance of the proposed model, effective integration into care home and general practitioner teams was identified as a central requirement. A core outcome set and a training package were developed.

The final model of care, whilst being safe and well received and resulting in a reduction in drug burden, demonstrated no improvement in the primary outcome of falls. With no improvement in quality-adjusted life-years identified, the pharmacist independent prescriber intervention was not estimated to be cost-effective.

Future work: To develop and evaluate better models of care for enhancing medication outcomes and safety in care homes or re-test with a longer intervention and follow-up period and a stronger primary outcome.

Trial registration: This trial is registered as ISRCTN10663852, definitive trial: ISRCTN17847169.

Study registration: This study is registered as PROSPERO CRD20150907.

Funding: This award was funded by the National Institute for Health and Care Research (NIHR) Programme Grants for Applied Research programme (NIHR award ref: RP-PG-0613-20007) and is published in full in *Programme Grants for Applied Research*; Vol. 11, No. 10. See the NIHR Funding and Awards website for further award information.

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AE	adverse event
CEAC	cost-effectiveness acceptability curve
CH	care home
CI	confidence interval
CHIPPS	Care Homes Independent Pharmacist Prescriber Study
CHM	care home manager
CHS	care home staff
COS	core outcome set
CPD	continuing professional development
CQC	Care Quality Commission
cRCT	cluster randomised controlled trial
DBI	Drug Burden Index
EAP	expert advisory panel
EOI	expression of interest
EQ-5D-5L	EuroQol Five Dimensions and Five Levels Rating Scale
GP	general practitioner
ICER	incremental cost-effectiveness ratio
MI	multiple imputation
MMSE	Mini-Mental State Examination
MOCH	Medicines Optimisation in Care Homes
MRC	Medical Research Council
NICE	National Institute for Health and Care Excellence
NPT	normalisation process theory
NRES	National Research Ethics Service
PCA	prescription cost analysis
PCP	pharmaceutical care plan
PIP	pharmacist independent prescriber
PPI	patient-public involvement
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-analyses
PSS	personal social services
QALY	quality-adjusted life-year
RA	research associate
RCT	randomised controlled trial
RR	rate ratio
SAE	serious adverse event
SUSAR	suspected unexpected serious adverse reaction
TDF	theoretical domains framework
WP(n)	work package (number)
WPOA	welfare power of attorney

Plain language summary

The purpose of this study was to explore whether a pharmacist who can prescribe drugs could work with care homes and general practitioners to improve how medicines are prescribed, how they are monitored to see whether they are working or causing problems and how the medicines are then given to the residents. The question was whether this approach was likely to be safe, to improve care for residents and to be a good way for utilising NHS money.

The project included six parts:

- *Listening* to everyone to help us design a service to create something that was likely to be acceptable and effective
- *Thinking* about what the best way would be to capture whether the service worked or not [i.e. what outcome(s) to measure]
- *Thinking* about the costs and benefits of the service and how best to capture these to find out whether the service was likely to provide value for money to the NHS
- *Designing* a training package for the pharmacists to increase the chances of them being effective in their role
- *Testing* the study design to make sure that we had thought about everything
- *Running* the main study that involved 882 residents and 72 care homes where half of them received the pharmacist service and half did not, to find out whether the pharmacist service reduced falls (a common side effect of medication).

The service presented no safety concerns. The pharmacists switched and stopped the medication, of which one quarter should have reduced the chances of falls. The service was generally liked. However, there is no evidence to suggest that the service reduced the number of falls or that it represented good value for NHS money.

Our public and patient involvement members have helped us at every stage of the process. They were a central part of our final reporting event.

Scientific summary

Background

The predominant UK care home (CH) model for enhancing pharmaceutical care currently consists of a pharmacist visit at least yearly to conduct a medication review and support medication management processes. Evidence for improvements in clinical outcomes resulting from this is inconsistent and lacks consensus. Non-medical independent prescribing provided an opportunity for pharmacist independent prescribers (PIPs) to assume greater responsibility for improving pharmaceutical care for residents in CHs, whilst saving general practitioner (GP) time in prescribing activities.

Objectives

- Identify and describe the components stakeholders would specify in a feasible and acceptable PIP service.
- Identify the most appropriate outcomes to measure the impact of the Care Home Independent Pharmacist Prescriber Study (CHIPPS) intervention through the development of a core outcome set (COS).
- Identify and develop the components of a training package, which would prepare PIPs for the role.
- Test and refine the service specification and proposed study processes to inform a definitive trial.
- Estimate the effectiveness, cost-effectiveness and safety of a pharmacist independent prescribers assuming responsibility for providing pharmaceutical care to residents in CHs.

Methods

The study sites were located in Northern Ireland (one site), Scotland (one site) and England (two sites). Ethical approval was received for each work package (WP).

WP1 development of service specification

Views of residents, relatives, CH staff, CH managers, GPs, and pharmacists with experience of living or working in, or with, CHs regarding how to develop the PIP service were obtained by focus groups and through interviews.

Transcripts were iteratively analysed, using the Theoretical Domains Framework, to identify key components, initial codes and themes to inform our study design.

WP2 outcomes identification

We followed recognised methodology to develop a COS to identify and select potential outcomes for the CHIPPS trial.

Phase I: We generated a long list of outcomes through the literature review and stakeholder involvement (semi-structured interviews and focus groups) constituted for WP1, WP2 and WP4.

Phase II: We convened a consensus panel to rate the importance of the long list of outcomes and provide additional recommendations for new outcomes. The panel was then asked to re-rate those outcomes for which consensus was not achieved and any newly recommended outcomes. Consensus for inclusion was achieved when 70% of respondents rated an outcome as critical.

WP3 health economics

Costs were estimated in Great British pounds (£) at 2017/2018 financial year levels. PIPs maintained training and activity logs to enable their time to be costed. Details of healthcare use were obtained from GP/CH records. Unit costs were obtained from published resources.

Quality of life was measured using EuroQol Five Dimensions and Five Levels Rating Scale (EQ-5D-5L), which was completed by proxy. Mean quality-adjusted life-year (QALY) scores were estimated for the 6-month follow-up.

WP4 training package development

A training package was developed through six phases overseen by an expert advisory panel (EAP).

Systematic review and narrative synthesis

The review was registered with PROSPERO (20150907) and reported according to PRISMA guidelines. Published articles were selected by two independent reviewers if they provided primary empirical data describing a pharmacist intervention in the care home environment, including information regarding education and training. Systematic reviews and abstracts were excluded. Data were extracted to enable description of knowledge requirements for the role.

Initial stakeholder engagement

Within the interviews and focus groups outlined in WP1, participants were asked for views with respect to education and training requirements for PIPs.

Training-specific interviews and focus groups

Focus groups were convened with primary care pharmacists, GPs, community pharmacists and care home staff to obtain their views on the first draft of the training package derived by the EAP from Phases I and II.

Stakeholder engagement and consensus

Panels were held at each site to obtain consensus on the proposed training package.

Feasibility testing

A focus group was convened with PIPs to obtain feedback on the training package following feasibility testing.

Evaluation

All intervention PIPs received the training package during the definitive trial (WP6). Evaluation consisted of training day evaluation forms (PIP, n = 21), online survey (PIP n = 16) and semi-structured interviews (PIP, n = 14). The dataset was analysed separately and then triangulated.

WP5 feasibility study

Four triads (one in each location), consisting of a GP, PIP and care home (providing care to older persons) with 10 residents (65 years and older, prescribed at least one medicine), were recruited. PIPs were trained and provided the intervention for 3 months.

Data on recruitment and retention were collated. Outcome measures identified in WP2 were tested for suitability for inclusion within the main trial.

A safety assessment process was developed involving an independent review of PIP pharmaceutical care plans (PCPs) and adverse events, i.e. hospitalisations and deaths, plus enablement of independent reporting of concerns through a specific email address.

Post-intervention face-to-face semi-structured interviews were held with participants and a focus group was held with the PIPs. Proceedings were digitally recorded and transcribed verbatim.

WP6 definitive trial with internal pilot

This was a cluster randomised controlled trial (cRCT) involving the training of PIPs to collaborate with the care home residents' GP, care home staff and residents, to assume responsibility for medication management over 6 months.

Recruitment

General practices, CHs and PIPs were recruited in triads according to the following inclusion and exclusion criteria:

Inclusion criteria

- Pharmacists had to be an independent prescriber (PIP).
- General practices had to be caring for sufficient care home residents to enable recruitment of 20 eligible participants.
- Care homes had to be caring for adults aged ≥65 years and associated with a participating general practice.
- Care home residents had to be under the care of a participating general practice, ≥65 years old and prescribed at least one regular medicine.

Exclusion criteria

- Care homes in regular (monthly or more) receipt of a medication-focused review service or under formal investigation by a regulator.
- Care home residents receiving end-of-life care or participating in another study.

Identification

Pharmacist independent prescribers were identified using local networks. Care home(s) were approached by participating GPs.

General practices identified and screened residents against the inclusion and exclusion criteria. Eligible residents were provided with invitation packs by care home managers to obtain verbal permission for a researcher to approach for consent. For residents without capacity, consent packs were posted to the resident's next of kin.

Randomisation and blinding

Randomisation was at a general practice (triad) level and was stratified by the four geographical areas, using a web-based electronic system. Research associates were blinded to allocation during recruitment. PIPs, CHs and GPs were unblinded.

Training

Intervention PIPs undertook the training package, revised after WP5, over 6 weeks. Time-zero for the intervention was 6 weeks post-randomisation.

Intervention

The PIP intervention, 4 hours allocated per week per 20 residents, included

- developing and implementing PCPs
- assuming prescribing responsibilities
- supporting ordering, prescribing and administration processes
- medication management training of care home staff
- liaison between all parties to optimise medication-related activities.

Control
Pharmacist independent prescribers allocated to the control arm did not participate. Care homes and residents received usual care.

Sample size
Overall, 880 participants (440 in each arm) were required to detect a 21% decrease in fall rate from 1.50 per resident over 6 months with 80% power, at the 5% significance level and with an intra-class correlation coefficient of ≤0.05. We assumed a 20% loss to follow-up.

Primary outcome measure

- Fall rate per person from care home falls record over 6 months.

Secondary outcome measures

- Quality of life (EQ-5D-5L)
- Barthel Index
- Drug Burden Index (DBI)
- Hospital admissions
- GP visits
- Mortality

Statistical methods
Intention-to-treat analysis was performed with between-arm comparison of falls using a negative binomial model. Analyses were conducted using the generalised estimation equation approach adjusted for the clustered design. The final model included baseline fall rate, prognostic variables and arm as fixed factors.

Safety reporting of serious adverse events
Serious adverse events (SAEs), defined as hospitalisation or death, identified through routine monitoring, were assessed for association with PIP activity by residents' GPs.

An independent email address was created to enable concerns regarding the intervention to be confidentially reported.

A random 20% sample of PCPs and associated resident documents were assessed by study geriatricians during the intervention period for clinical appropriateness and safety.

Process evaluation
Quantitative (surveys of care home staff, GPs and PIPs, PIP activity logs, PCP review and trial outcomes) and qualitative (interviews with care home staff, residents, GPs and PIPs) data were collected.

Results

WP1 development of service specification
Twenty-seven pharmacists (care home and community), 24 GPs, 6 care home managers, 9 care home staff and 14 residents and relatives provided input.

The concept was broadly welcomed by all. Potential barriers were identified as pharmacists' knowledge of chronic disease management and older people's medication, the care home environment, requirement to provide clarity with respect to the role and the need to become integrated both socially and professionally within CHs and general practice teams.

Participants agreed that the PIP should assume responsibility and provide support for all elements of medication management within the home.

WP2 outcomes identification

Sixty-three outcomes were identified in Phase I (22 from the literature and 41 from stakeholders).

Twelve outcomes met consensus criteria for inclusion in round 1, with 17 achieving no consensus and the remainder achieving consensus for exclusion. Two outcomes were further included after round 2, yielding a final list of 14 potential outcomes.

WP3 health economics

The estimated mean per resident cost of the PIP intervention was £323 (including training). The mean (per resident) incremental cost of the PIP intervention, after considering other NHS costs and personal social services (PSS) and adjusting for any differences between arms, was £280. The mean incremental effect was estimated to be −0.004 QALYs. As the PIP intervention was estimated to be associated with higher costs and no improvement in quality of life, it was not estimated to be cost-effective.

WP4 training package development

Literature provided therapeutic and clinical knowledge requirements. Qualitative work added the importance of understanding local cultures and requirement to integrate into teams. Recognising that PIPs started from different baselines, the final training package consisted of

- face-to-face training for 2 days
- underpinning knowledge pack
- personal development framework
- personal development planning and implementation with mentor
- time to integrate into teams and understand local cultures
- oral competency assessment by a mentor and an independent medical assessor.

Pharmacist independent prescribers reported that all elements were useful and appropriate, enhancing their confidence for the role. Additional training on how to build effective relationships was recommended.

WP5 feasibility study

Four triads, each with 10 residents, were successfully recruited; 30% of the residents in CHs were found unsuitable following screening and 30% of those invited declined to participate or failed to reply.

Two outcome measures [Mini-Mental State Examination (MMSE) and QUALIDEM] were removed following testing. Differences in outcome measures pre- and post-intervention suggested that the intervention had the potential to enhance care.

No adverse events related to PIP activity occurred, and no major concerns were identified from reviewing PCPs.

Qualitative feedback confirmed acceptability of the intervention and identified potential for the intervention to improve patient care and safety and to save GP and care home staff time and effort.

WP6 definitive trial with internal pilot

Recruitment

Forty-nine triads (49 GPs and PIPs and 72 CHs) were randomly allocated to the intervention (n = 25) and control (n = 24) arms. Additionally, 454 residents were recruited to the intervention arm and 428 to the control arm.

Baseline characteristics

Baseline characteristics were largely similar between arms. The control arm had a greater proportion of CHs with nursing residents (59% vs. 42%) and lower performance with respect to activities in daily living. Residents in the intervention arm had a higher mean number of falls in the 3 months before service implementation (0.78 for intervention vs. 0.57 for control).

Primary outcome

A greater number of falls were recorded in the intervention arm in the 6-month follow-up. Once adjusted for differences at baseline, the result was non-significantly in favour of the intervention [rate ratio (RR): 0.91, 95% confidence interval (CI) 0.66 to 1.26; $p = 0.99$].

Secondary outcome measures

The intervention reduced residents' DBI by 25% compared with that by 15% in the control arm (RR 0.83, 95% CI 0.75 to 0.92; $p<0.001$). It had no effects on mortality, hospitalisation, activities of daily living or quality of life in the intervention and control arms.

Safety

No SAEs were related to PIP activity. Independent review of care plans revealed no safety concerns, and no concerns regarding PIP activity were received through email.

Process evaluation

Pharmacist independent prescribers largely adhered to service specification, varying provision according to need. Two-thirds of PIP time was spent on resident-related activities, of which approximately 24% was face-to-face. They spent 24% of their time on other general activities in the care home and 10% of their time travelling. Five PIPs stated that 4 hours per week was not enough, eight PIPs found it sufficient and three PIPs found it too much.

Overall, 668 interventions were recorded, of which 566 were clinical, including 379 for medication discontinuation or dose reduction, 86 for medication initiation or dose increase, 49 for medication change and 52 for monitoring. Among the 566 interventions, 189 (33.5%) involved medication for treating diseases of the central nervous system. Among the 189 interventions, 148 reduced the likelihood of falls, 37 increased it and 4 were unclassifiable. Moreover, 179 interventions reduced drug burden and 10 increased it.

The service was valued by most of the stakeholders. This was believed to be more effective where there was good communication, a readily accessible PIP, confidence on PIP competence, stable care home management and resonance between PIP activities and GP and care home needs.

Conclusions

Service specification, COS, training package and study design were delivered for use within a definitive trial designed to evaluate this model of care. The trial recruited and retained to target. Three PIPs (12%) failed to deliver any part of the intervention.

The intervention was well received and believed to enhance resident care and safety. Several medicines were discontinued or stopped, resulting in a significantly reduced drug burden. However, no difference in falls, the primary outcome measure, was identified. The PIP intervention was also not estimated to be cost-effective, as it was associated with an increase in costs and no improvement in QALYs.

Given the evidence of suboptimal prescribing in CHs, further work is recommended to develop interventions that improve resident clinical outcomes and are likely to be cost-effective.

Trial registration

This trial is registered as ISRCTN10663852, definitive trial: ISRCTN17847169.

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This study is registered as PROSPERO CRD20150907.

Funding

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SYNOPSIS

Summary of programme alterations

There were no substantive changes to the original study aims and objectives or changes to the investigators or grant holders.

Programme delivery

There have been a few changes in the programme to improve procedures or optimise effectiveness.

Qualitative evaluation

A focus group and an online survey were planned to capture the PIP's experience at the end of the feasibility study; this was changed to a face-to-face workshop to facilitate a fuller understanding of the intervention delivery and research procedures.

Recruitment of triads

The unit of recruitment was refined to triads consisting of a PIP/general practitioner (GP)/care home(s). To manage workload, triad recruitment was divided into three time phases to ensure that peak activity points did not overlap.

Recruitment of resident participants

The target of residents recruited in each triad was changed from '20' to a 'mean of 20'.

Health economic model beyond trial

This was not undertaken because the intervention was estimated to increase costs and reduce quality-adjusted life-years (QALYs), such that the extrapolation would not change the outcome.

Validation of methods for capturing quality of life

This was not undertaken as EuroQol Five Dimensions (EQ-5D) was the only utility measure used in the final trial. Previously, a validation work for use in care homes (by proxy) has already been undertaken.

Coronavirus

The trial was delayed in Scotland for the triads recruited at the end of Phase III. Final data collection was undertaken remotely immediately after the first lockdown was eased and with appropriate approval. The dissemination events were conducted on Zoom.

Background

The idea for Care Home Independent Pharmacist Prescriber Study (CHIPPS) resulted from three publications originating from the core research team. The 2009 Care Homes' Use of Medicines Study (Alldred) reported that prescribing, monitoring and administration of medicines could be significantly improved[1] and resulted in a Department of Health alert requiring significant overhaul in the ways in which medication was managed within this environment.[2] A Cochrane review (Hughes, updated in 2018) suggested no improvement in clinical outcomes from interventions to improve the appropriate use of polypharmacy in care homes.[3] An exploratory trial (Bond, Holland, Wright) to determine the potential effectiveness of PIPs providing care for individuals with chronic pain demonstrated significant improvements in clinical outcomes.[4]

The hypothesis proposed in 2012 was that improvements in clinical outcomes could be realised by allowing PIPs to assume responsibility for pharmaceutical care provision for residents within care

homes. Furthermore, PIPs would be able to support all medication-related activities, thereby reducing medication errors resulting from prescription, ordering, storage, administering and recording.

The team deliberately chose not to use 'errors' as an outcome measure within an open-label trial owing to previous experience of a significant control arm reactivity bias in response to being planned to be observed for medication errors.[5]

Whilst we were confident that with the ability to support and monitor all medication-related practices in the care home, a PIP would be able to demonstrate a positive clinical effect; we were unsure as to which clinical outcome measure would be most appropriate and created WP2 to explore this.

Recognising that the use of PIPs in care homes was a step change from current models of care within this environment, we planned to listen to all stakeholders to understand what would be appropriate to be included in such an intervention and how it should be best implemented (WP1). WP3 resulted from the need for cost-effectiveness to be captured.

With a desire to enhance intervention fidelity and recognition that pharmacist prescribers are required to be competent within their defined area of practice, we developed a training package (WP4).

Following Medical Research Council (MRC) guidance regarding the development and evaluation of complex interventions,[6] we included feasibility (WP5), pilot and definitive trial stages (WP6) (see *Figure 1*). Latterly, we used the MRC guidance for process evaluation[7] informed by the logic model, which was refined as the project progressed.

The programme of work was carried out in four locations: Norfolk (England), Yorkshire (England), Grampian (Scotland) and Belfast (Northern Ireland).

Work package 1: development of service specification

Approvals

Research ethics approved by the NRES Committee Yorkshire and the Humber Sheffield REC Ref.: 15/YH/0172.

NHS Research and Development approved by NHS Grampian R&D Ref.: IRAS: 173232.

Aim

To qualitatively explore stakeholders' expectations and understanding of introducing a new service to inform ways to introduce an acceptable service, anticipating and mitigating potential barriers.

Research question

What components stakeholders would specify in a feasible and acceptable PIP service and what did they consider were barriers and enablers to implementing it?

Objectives

To access stakeholders in four demographically and culturally diverse study sites [England (two), Scotland and Northern Ireland (one in each)] to collect their views through focus group discussions and interviews and validate analytic themes through consensus discussions.

Method

A purposive sampling approach gained stakeholders' views with experience of living or working in, or with, care homes, to maximise the range of data relevant to the research goals.[8] Stakeholders were

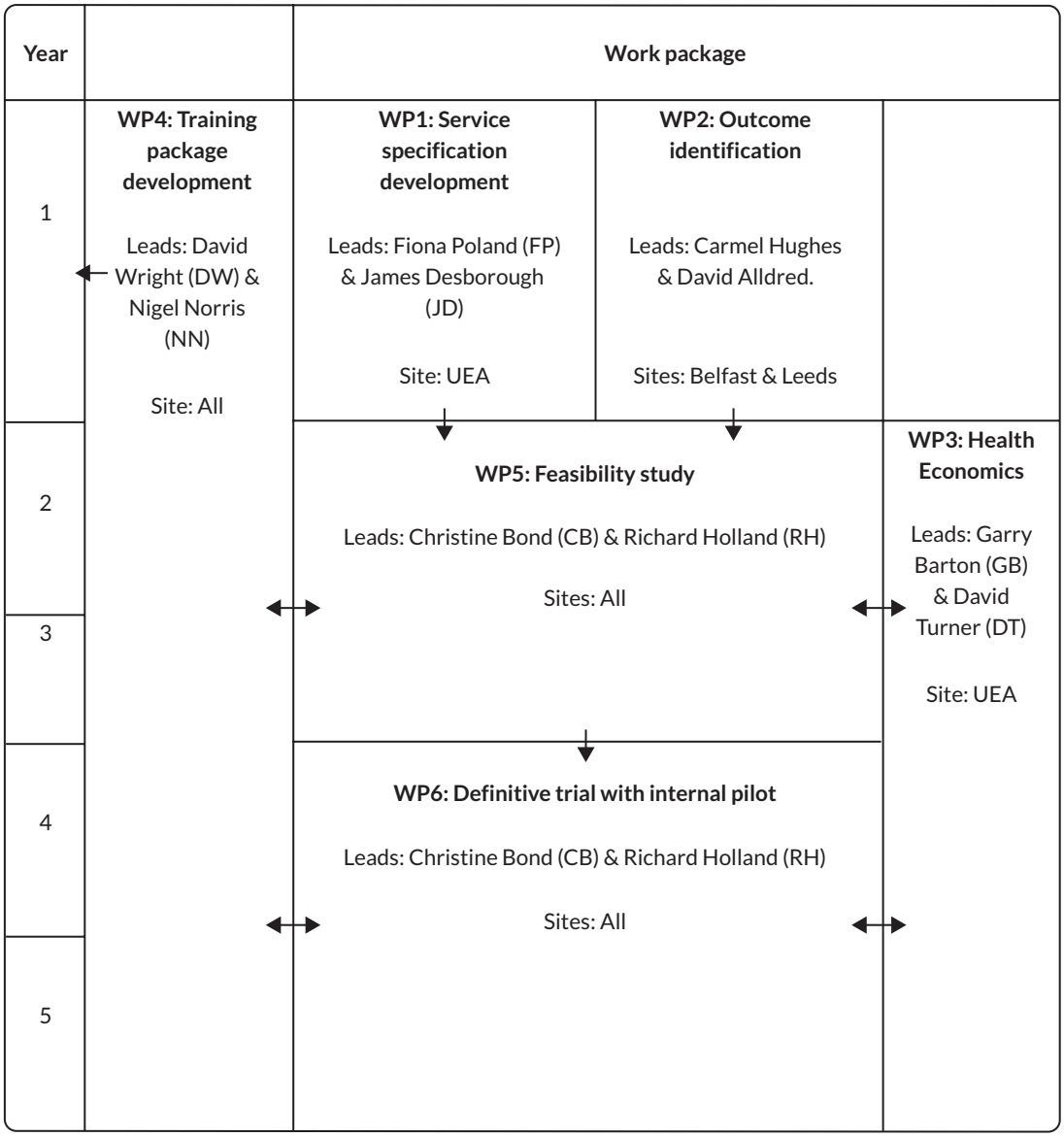

FIGURE 1 Research pathway diagram.

GPs, pharmacists (Ps), care home managers (CHMs), care home staff (CHS), care home residents and residents' relatives.

Our semi-structured topic guide was informed by the Theoretical Domains Framework (TDF) for behaviour change[9] to identify expected characteristics, barriers for and benefits of the proposed PIP role (see *Appendix 1*, *Table 1*).

We drew on the interdisciplinary research team's broad experience to identify theory- and practice-related data collection topics relevant to

- working in current medication management
- stakeholders' knowledge of scientific, procedural or environmental factors shaping care home practices
- how a PIP service and GP-PIP partnership might work
- potential benefits and risks
- social and professional roles and identity
- topics for PIP training (reported in WP4).

We contacted GPs, pharmacists and care homes – through our own and local professional networks. Additional care homes were recruited through national and site-specific regulatory bodies, local primary care and care home networks. Our maximum variation sample targeted: differently managed care homes, varying resident needs, nursing and care residents and diverse funding arrangements.

Transcripts were iteratively analysed using the TDF to identify key components, initial codes and themes for our study design.

Results

Thirteen stakeholder group-specific focus groups (*n* = 72 participants) and interviews (*n* = 13 participants) were held with GPs, pharmacists (P), one pharmacy technician, care home managers, care home staff, residents and residents' relatives in four study sites (see *Appendix 1*, *Table 2*). Fifteen pharmacists described themselves as being employed in primary care, 11 within community pharmacy and one as split across the two (see *Appendix 1*, *Table 3*).

All focus group, interview and workshop stakeholders largely welcomed introducing the PIP service as offering benefits for residents, care homes and doctors. Reasons included viewing this new role as relevant for improving medication management, benefiting residents, overcoming communication lapses between care home, GP practice and pharmacy, residents and their relatives. Nonetheless, stakeholders identified specific potential *contextual* and *implementation* barriers and facilitators specifically in relation to

- chronic disease management (*contextual*)
- knowledge of older people's medication and care homes (*contextual*)
- clarity of PIPs' role and responsibilities (*implementation*)
- integrated social and professional team-working (*implementation*).

GPs' working patterns, together with multiple care home staff involved in medication, were seen to constrain effective chronic disease management and effective communication around residents' medication needs.

All stakeholders prioritised regular, responsive medication reviews by PIPs to address gaps in managing chronic disease and enhance the safety of residents living with comorbidities.

GPs' onerous workload limited their capacity for 'time-consuming' procedures and 'complexities' in reviewing and managing medication (GP8-FG), and pharmacists argued that PIPs could do 'more proactive work' (P10-FG).

Contextual barriers and facilitators

Knowledge of older people's medication, chronic disease management and care homes was seen as underpinning an effective PIP service.

Chronic disease management

All stakeholders emphatically identified chronic disease management as core in managing medication in care homes. Any viable PIP service must successfully address 'many points in the circuit of prescribing where it can go wrong' (GP15-FG), including working patterns that disrupted continuity of residents' care, infrequent medication reviews and communication shortcomings in ordering and overseeing medications. GPs admitted that they found it 'difficult managing all the complexity and the comorbidity' (GP6-FG). If a PIP oversaw and bridged gaps in these processes, much communication 'mayhem' between care homes, pharmacies and GP practices could be eliminated (GP7-FG).

Knowledge of older people's medication and care homes

Knowledge of older people's conditions and their life in a care home was considered essential for the PIP, taking into account the whole person, how care homes operate and care homes' practices and cultures. Stakeholders prioritised well-developed communication skills to interact and share knowledge with residents, 'particularly [those] with cognitive impairment' (P1-FG).

Implementation barriers and facilitators

Stakeholders questioned how PIPs' specific responsibilities and roles should be understood and incorporated into care home environments. They highlighted two implementation issues: (1) clarity of a PIP's roles and responsibilities, and (2) integrated team-working with the PIP.

- clarity of a PIP's roles and responsibilities

Stakeholders advocated clarity about the PIP's role. GPs, who hold ultimate responsibility for patients' healthcare, argued for monitoring information with the PIP, based on effective, regular mutual communication, eliminating duplicate orders and preventing omissions of medication responsibilities. For care home staff, residents and relatives, shared understanding of the PIP's role would help improve communication in medication management.

- integrated social and professional team working

Stakeholders believed that to embed the new service, PIPs must take time to establish communicative relationships with GP practices and care homes, to promote shared understanding of roles, working co-operatively, developing trust, providing service continuity and gaining contextual knowledge of older residents' health.

Many participants reflected on their previous positive experiences of multi-professional working for integrating PIPs into teams, including 'effective working relationships' between GPs and pharmacists (GP6-FG) (P5-FG). Some GPs and care home managers envisaged PIPs educating care home staff to raise their medications' awareness, which resonated with residents' wishes to know about their medications as: … nobody [is there] to ask things about your medication, (RR4-FG) with staff and residents able to see PIPs as part of a resident's 'care package' team, rather than 'checking up on [staff]' (P6-FG).

Stakeholders emphasised clarity in team-working to integrate PIPs to strengthen, not complicate, their working collaborations in care homes. Welcoming a PIP was therefore conditional on a clearly defined PIP role communicated to stakeholders; collaborating across doctors, PIPs and care home staff; dialogue with residents and relatives on developing the service and trustful and effective communication.

Discussion

Work package 1 explored stakeholders' expectations of the components and context for a feasible PIP service, with a TDF-informed approach identifying components, stakeholders and contextual practices as relevant to mitigate implementation barriers. This identified care home environments as complex, with diverse participants, organisational processes, systems and resources providing care to frail older people, posing chronic disease management and review challenges.

A PIP model was envisaged to offer means to address this, but only if well informed about older people's medication and care homes. Stakeholders believed that an acceptable service required the PIP to offer means to strengthen mechanisms to ensure efficient, effective 'whole team' approach to prescribing in care homes.[1] All stakeholders gave priority to a PIP conducting medication reviews to save GPs' time/work. They welcomed PIP-related relationships as enhancing trustful communication around medication issues, mutually recognising remits and competencies.

We gained comprehensive understanding from stakeholders about processes to maximise chances of the impact of the PIP intervention on practice.[10] Central here was for everyone involved to 'understand each other's systems' by recognising established organisational and cultural practices in care homes and primary care during implementation and improving communication around related changes. Care home managers, residents and relatives saw PIPs spending time with residents to explain and reassure around medication, to be more fully partners in their own care.[11]

Integrated team-working was another key component: stakeholders were more likely to consider the PIP's role as acceptable and viable if effective team-working were embedded in implementing such healthcare change.[12] GPs and pharmacists strongly preferred PIPs to be integrated into their practice teams.

Clearly defined PIP roles were considered crucial at micro-level experiences of individual actions and at macro-level experiences in care home and GP practice organisation. Residents and relatives were more likely to accept the new service if its purpose was carefully explained to them. GPs and pharmacists required explicit agreement on areas for PIP prescribing.

Contextual factors framed how stakeholders envisaged implementation issues. For example, effective team-working with the PIP, in GP practices and care homes (an *implementation concern*), depended upon the PIP acquiring appropriate knowledge of older people's medication and frailties (a *contextual issue*). Guidelines and existing research underscore that specifically addressing both context and implementation barriers can better guarantee improved outcomes for older people in residential settings.[13] Multiple stakeholders shared the belief that for any proposed PIP innovation to be acceptable and viable, it would be dependent on all stakeholders understanding each other's systems.[14]

Work package 2: outcomes identification

Aim

This WP aimed to identify the most appropriate outcomes to measure the impact of the CHIPPS intervention through the development of a core outcome set (COS).

Objectives

The purpose of determining the effectiveness of the CHIPPS service was to

- identify potentially appropriate outcome measures
- rate and select outcome measures based on validity, reliability, utility and proximity to the intervention.

Method

In WP2, we followed methodology for the development of a COS (standardised set of outcomes that should be measured and reported at minimum in all clinical trials)[15] for CHIPPS. The full study has been published.[16]

The methodology used was informed by published guidance[17] and conducted in two phases. Phase I encompassed the first three steps recommended by Williamson *et al.*: (1) to explicitly describe the scope of the COS, (2) to identify existing outcomes, and (3) to identify outcomes that are important to key stakeholders. This resulted in a long list of outcomes that fed into Phase II, corresponding to step (4) of the aforementioned guidance – prioritising the most important outcomes using a consensus method.

Phase I: Generating and refining a long list of outcomes

Step 1: Scope of COS

- Health condition and population: older adults with any type/number of health conditions.
- Intervention: those aiming to optimise prescribing.
- Setting: care homes, defined as nursing and/or residential homes, skilled nursing, assisted living and aged-care facilities.

Step 2: Literature review

A relevant Cochrane review, assessing interventions to optimise prescribing in care homes, was used, as it reported outcomes pertinent to COS development.[18] Briefly, 12 randomised controlled trials (RCTs) involving over 10,000 older adults residing in 355 care homes were included.

Step 3: Stakeholder involvement

Focus groups and semi-structured interviews were conducted with GPs, pharmacists, care home managers/staff and care home residents/relatives from the four CHIPPS study sites to determine outcomes for inclusion. These stakeholder consultations were conducted primarily for the development of the CHIPPS intervention and are described elsewhere in this report (WP1: Service Specification Development).[14] Transcripts of the focus groups and interviews were independently analysed by two researchers who recorded verbatim all outcomes proposed by stakeholders. The stakeholder study was approved by the National Research Ethics Service (NRES) Committee Yorkshire and the Humber, Sheffield; reference: 15/YH/0172.

The resulting long list of outcomes was reviewed, with removal of duplicate items and process measures. Four members of the CHIPPS WP2 team then independently assessed the remaining outcomes and voted anonymously to determine whether each outcome should progress to Stage 2. All four team members involved in this process had either practised clinically or undertaken clinical trials in care homes previously.

Phase II: Delphi consensus exercise

We used the Delphi technique to achieve consensus on a final COS.

The Delphi Panel

The Delphi panel comprised the 19 members of the wider CHIPPS management team (excluding the four aforementioned team members). The group included academic pharmacists (n = 3), geriatricians (n = 2), patient-public involvement (PPI) representatives (n = 2), health economists (n = 2), senior CHIPPS research fellows (n = 2), a prescribing advisor pharmacist (n = 1), an academic sociologist (n = 1), a research governance manager (n = 1), a care home quality director (n = 1), an educationalist (n = 1), an academic doctor (n = 1), a GP (n = 1) and an academic nurse (n = 1).

The questionnaires

The first questionnaire was structured around the Phase I long list of outcomes. Each outcome formed a single questionnaire item, accompanied by a brief explanation, to prevent misinterpretation. For example, 'Duplicate drugs' was described as a situation where two medicines of the same pharmacological class were prescribed, such as the prescribing of two concurrent opiates.[19]

Questionnaires were distributed using a web-based survey tool (Survey Gizmo®; Alchemer, Louisville, CO, USA). Panellists were emailed a link to each questionnaire and asked to complete within 4 weeks. Reminder emails were sent as needed. Panellists responding to the first questionnaire were invited to participate in the second round.

Panellists rated the importance of including each outcome in the COS, using a scoring system derived from the Grading of Recommendations Assessment, Development and Evaluation (GRADE) Working Group.[20] Scoring was based on a Likert scale, ranging from 1 to 9. Scores of 1–3 indicated an outcome of 'limited importance', 4–6 indicated 'important but not critical' and 7–9 indicated 'critical'. Panellists were also given the option to select 'unable to score'. During the first round, panellists were invited to suggest additional outcomes for inclusion, which were reviewed and discussed by the WP2 study team.

The second questionnaire (with the same rating method) included a revised list of outcomes, inclusive of 'non-consensus' outcomes (see below for a definition of consensus) and any new outcomes generated from the first round. A summary of first-round scores for each outcome (including individual score, group mean score and group median score) accompanied the link to the second questionnaire. Panellists were encouraged to consider this information whilst re-scoring outcomes.

Definition of consensus

Consensus for inclusion of an outcome in the COS (consensus 'in') was defined as ≥70% of respondents rating an outcome 7–9, that is, 'critical' and fewer than 15% of respondents rating it 1–3, that is, 'of limited importance'. Similar thresholds have been previously reported.[21,22] Consensus for exclusion (consensus 'out') from the COS was defined as fewer than 15% of respondents rating an outcome 7–9, that is, 'critical' and ≥70% of respondents rating it 1–3, that is, 'of limited importance'. All other score distributions were categorised as 'no' consensus.

Data analysis

Responses were analysed using Statistical Package for the Social Sciences Statistics version 22 (IBM Corporation, Armonk, NY, USA). The proportion of respondents rating the outcome as 'critical', 'important but not critical' or 'not important' was calculated for each outcome to determine whether consensus had been reached, as described above.

After the first Delphi round, outcomes that reached consensus 'in' were included in the COS, and outcomes that reached consensus 'out' were excluded. 'No' consensus outcomes proceeded to the second round. This approach was also used after the second round; however, 'no' consensus outcomes were excluded from the final COS.

Key findings

An overview of the COS development process is provided in *Appendix 1*, *Figure 2*.

Phase I

Sixty-three outcomes for potential inclusion in the COS were identified in Phase I (22 from 12 studies included in the Cochrane review and 41 from stakeholder focus groups and interviews). Sixteen duplicates were removed. Further 16 were classified as process outcomes (e.g. 'satisfaction with PIP service') and excluded. Two outcomes ('pain' and 'accidents') were also excluded unanimously by the CHIPPS review panel. A total of 29 outcomes (see *Appendix 1*, *Figure 2* and *Table 1*) were considered by the Delphi panel in the consensus exercise.

Phase II

The first round of the Delphi consensus exercise was completed by all 19 Delphi panellists (100% response rate). Twelve outcomes met the consensus criteria for inclusion in the COS. No outcomes met the exclusion criteria, and no consensus was achieved for 17 outcomes.

Outcomes (n = 6) suggested by the panel during the first Delphi round were discussed by three members of the research team (AM, CH and DA). The outcomes were 'patient mobility'; 'making sure drug charts are kept up to date'; 'anticholinergic burden'; 'nutritional status', for example, Malnutrition Universal Screening Tool score or 'use of nutrition supplements'; and 'appropriate use of covert

medication.' 'Anticholinergic burden' was added to the second Delphi round. 'Patient mobility' was not added because it was considered a subset of 'physical functioning'. The other suggestions were considered beyond the COS scope. Another outcome, 'number of medicines (and associated costs)', was reformulated into two separate outcomes: 'number of medicines' and 'costs of medicines'.

The 17 outcomes for which consensus had not been achieved, together with the three outcomes added/reformulated based on panel feedback, resulted in a total of 20 outcomes being included in the second Delphi round (see *Appendix 1*, *Table 4*).

The second round was completed by 18 of the 19 respondents (94.7% response). Two outcomes ('number of medicines' and 'anticholinergic burden') met the criteria for inclusion in the COS, with the remainder (*n* = 18) being excluded (see *Appendix 1*, *Table 5*).

Therefore, a total of 13 individual outcomes met the inclusion criteria in the COS (see *Appendix 1*, *Table 6*).

Discussion

This WP was informed, in part, by the stakeholder engagement activities organised in WP1. Stakeholder engagement is a crucial part of COS development methodology to ensure that outcomes represent those that are considered of importance to service users and/or their representatives.

The final COS provided the basis for planning the next phases of the trial, notably the feasibility study (WP5), internal pilot and main trial (WP6).

Work package 3: health economics

A summary of the health economic work undertaken is given below. More details on the *Methods* and *Results* for the health economics component of the main trial/WP6 are given in the associated health economics report (see *Appendix 8*).

Background

Medication administration errors are common within care homes.[1] The PIP intervention therefore has the potential to improve outcomes. However, not all treatments can be provided. We therefore undertook an economic evaluation of the PIP intervention to assess whether it represented a good use of scarce resources. This was deemed feasible for the full trial (outlined in WP6) based on, amongst other things, the high response rate achieved for proxy EQ-5D scores in the feasibility study (see WP5). The methods of resource use data collection were also informed in a previous work in the care home setting.[23]

Objective

To estimate the cost-effectiveness of the PIP intervention.

Methods

Study overview

The economic evaluation was conducted alongside the CHIPPS cluster randomised trial (see *WP6 of this report*).

Costs

The methods used to estimate costs are described in the associated health economics report (see *Appendix 8*). In brief, costs were estimated in Great British pounds (£) at 2017/2018 financial year levels, from the perspective of the NHS and PSS, over the 6-month trial (no discounting was undertaken).

To estimate the cost of the PIP intervention applied in WP6, each PIP was asked to complete a training log and a log of all activity associated with the intervention, including contacts with others, for

example, care home residents, care home staff, GP or any other professionals (geriatricians, community pharmacists, district nurses, etc.). Subsequently, unit costs[24] (see *Appendix 1*, *Table 22*) were assigned to estimated times for all PIPs and other staff time.

It was envisaged that the PIP intervention would enable GPs to spend less time undertaking prescription management for intervention arm participants. Accordingly, based on previously published work,[24] the estimated GP time (cost) saving per resident was also estimated.

The total PIP intervention cost was subsequently estimated by summing the PIP training and activity costs and deducting the estimated GP time/cost saving.

Other costs

As informed in previous research,[24,25] GP and practice nurse visit data were extracted from primary care records, along with medication data, outpatient attendances, inpatient stays, tests and investigations. All other health professional contacts (phone calls, visits and their location) were extracted from care home records.

Data for the previous 3 months were collected at baseline and those for the previous 6 months were collected at 6-month follow-up. Unit costs[24,26] were assigned to each contact/admission in line with Underwood *et al.*;[27] medication costs were extracted from the prescription cost analysis (PCA).[28,29]

Outcomes

Quality of life was measured using the EuroQol Five Dimensions and Five Level Rating Scale (EQ-5D-5L).[30] The EQ-5D-5L (proxy version) was chosen as it is deemed the preferred measure of utility in the National Institute for Health and Clinical Excellence (NICE) methods guide[31] and in the light of work undertaken in the CHIPPS feasibility study[32] (see *WP5*). The latter included an assessment of outcome measures used in the CHIPPS feasibility study where the EQ-5D-5L was chosen to be used in the full RCT, as it had been previously validated,[33] and had a relatively good completion rate and low time taken to collect. It is recommended that QALYs are used to measure and value health effects, as QALY is a generic measure of health benefit that considers both mortality and health-related quality of life.[34]

For all participants, proxy respondents were asked to report participants' level of problems (none to extreme/unable) in five dimensions (mobility, self-care, usual activities, pain/discomfort and anxiety/depression) at baseline, 3- and 6-month follow-up. In line with the NICE position statement,[33] the crosswalk mapping function was used to convert these responses into utility scores.[35] Those who were known to have died by the particular follow-up points were assigned a utility score of zero. QALY scores were subsequently estimated based on the total area under the curve method and the assumption of linear interpolation.[36]

Analyses

Base-case results were based on those with complete cost data at both baseline and 6-month follow-up and those with complete EQ-5D data at baseline, 3- and 6-month follow-up. Bivariate regression[37] was used to analyse the cost and QALY data, based on the intention-to-treat approach, enabling the mean incremental cost (mean difference in cost between the two arms) and the mean incremental effect (the mean difference in QALYs) to be estimated. The cost-effectiveness acceptability curve (CEAC)[38] was also used to estimate the probability of the PIP intervention being cost-effective at the λ value of £20,000/QALY compared with standard care. In addition, three key sensitivity analyses were undertaken: using multiple imputation to account for missing values, removing training costs (as they are one-off cost) and undertaking a threshold analysis to establish at what threshold the intervention would be effective (in terms of cost or effect).

Results

PIP intervention costs

The training logs were returned by 23/25 PIPs, and the activity logs by 22/25 PIPs. Training costs were assigned to the two non-responding PIPs, but activity costs were not assigned to three non-responding

PIPs, as they did not implement the PIP intervention. Overall, the mean reported activity time for each PIP was equivalent to an average of just over 3 hours per resident (see *Appendix 1*, *Table 23*). The total PIP intervention cost was subsequently estimated to be £323 per resident by summing the PIP training and activity costs and deducting the estimated GP time/cost saving.

Other costs

It is notable that the mean cost associated with the intervention was lower than that associated with overall medication costs, GP/practice nurse contacts, other professional contacts and in-patient stays. In terms of total (NHS and PSS) costs, the (unadjusted) mean difference between arms was £246. This might suggest that some of the aforementioned PIP intervention costs were partially offset, for example, by lower medication costs (see *Appendix 1*, *Table 24*).

Outcomes

EQ-5D scores are shown in *Appendix 1*, *Table 25*, where it can be seen that both arms had lower mean scores at the 3- and 6-month follow-up points. Although the mean QALY score was higher for the intervention arm, the mean baseline EQ-5D score was also higher for these participants. This means we cannot infer that the intervention was more effective based on these results and that there is a need to adjust for, amongst other things, the baseline difference in EQ-5D scores between arms.

Analyses

A total of 609 participants (70%) had complete cost and EQ-5D data. Bivariate regression estimated that the mean (95% confidence interval) incremental cost of the intervention, compared with standard care, after adjusting for baseline costs, age and gender was £279.86 (£19.39–540.33). The estimated mean incremental effect was −0.004 (−0.016 to 0.009) QALYs. The PIP intervention was therefore estimated to be dominated, as it was associated with higher costs and lower effect, and the CEAC estimated that it had a 3.8% probability of being cost-effective at the £20,000/QALY value. These results suggest that there would be no added benefit of a long run model as (given lower effect and higher cost) as the results of a long-term model would be unchanged/in line with the within trial analysis, that is, the PIP intervention would not be estimated to be cost-effective. All sensitivity analyses were not found to change conclusions from the above findings.

Discussion

In terms of overall costs, the estimated mean incremental cost of £280 was lower than the estimated cost of the PIP intervention, suggesting that intervention costs were partially offset by certain lower costs, for example, medication. However, as the PIP intervention had higher mean costs and was not estimated to be associated with an improved QALY score, it is not estimated to be cost-effective. These conclusions are based on the 6-month within trial analysis for those with complete data, but the conclusions were the same when multiple imputations or other sensitivity analyses were carried out (see *Appendix 1*, *Table 26*).

Work package 4: development of PIP training package

Approvals

Research ethics approved by the Faculty of Medicine and Health Sciences Research Ethics Committee Ref.: 20142015-77.

NHS Research and Development approved by NHS Grampian Research and Development Ref.: NRS15/PH18.

Aim

Develop a training package to ensure that pharmacist independent prescribers are appropriately prepared to deliver the service.

Method

WP4 consisted of six phases:

- systematic review and narrative synthesis
- initial stakeholder engagement
- training specific interviews and focus groups
- stakeholder engagement and consensus
- feasibility testing
- validation.

Systematic review

The systematic review was registered with PROSPERO (CRD42015026693) and adheres to PRISMA.[39] Papers and abstracts were selected for review to inform both content and design of any future pharmacist training package.

Synonyms for care home (population), pharmacist (intervention), education and training (outcome) and pharmaceutical care (intervention) were used. This review included articles published until 30 June 2015.

Inclusion criteria:[1]

- Description of education and training of pharmacists before service/intervention delivery in a care home, OR
- Description of expertise of the pharmacist, for example, title denoting additional expertise or training to perform role, OR
- Training provided by pharmacists to care home staff for which they would need to have sufficient knowledge to deliver, OR
- Materials provided to support the pharmacist in service delivery in care homes, AND
- English language.

Exclusion criteria:[2]

- Studies not primarily focused on provision of services to older people residing in care homes
- Studies where the primary focus was to determine the effectiveness of an individual drug, OR
- Papers without empirical data for example, editorials, opinion pieces commentaries, OR
- Abstracts, OR systematic reviews and narrative syntheses.

Databases searched (July 2015) were Academic Search Complete, EBSCOH, Ovid MEDLINE® and EMBASE, OvidSP, ASSIA (Applied Social Sciences Index and Abstracts), CSA, ProQuest XML, Cochrane Database of Systematic Reviews, Cochrane Reviews (Issue 6 of 12, June 2015), E-theses online service (EThOS), Ingenta Connect (Ingenta), Wiley Online Science, EPOC Group Specialised Register, Reference Manger, Ageline (EbscoH), CINAHL (Cumulative Index to Nursing and Allied Health Literature), EBSCOH, International Pharmaceutical Abstract (OvidSP) and PsycINFO (EbsoH).

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Titles, abstracts and full-text papers were screened for eligibility, independently by two authors. Differences were resolved by consensus. A PRISMA diagram[39] was populated, and Kappa coefficients[40] calculated.

As the narrative synthesis focused on learning from the content of published care home interventions, the quality of the included papers was not appraised.

In line with Cochrane guidance, the following information was extracted from papers and abstracts by two independent researchers (DW and VM):

- year, design, location, setting
- main findings
- pharmacist expertise
- education and training provided
- service delivery support tools provided
- training of care staff provided by pharmacist
- clinical and therapeutic area(s) of intervention focus (three most commonly reported)
- intervention description.

The results were compared and again agreed by consensus by two independent reviewers.

Analytical approach

Data were themed and collated to inform the development of a care home pharmacist training package. All training methods outlined within selected papers were extracted.

Initial stakeholder engagement

As part of the main programme of CHIPPS work, focus groups and interviews were undertaken primarily to define the PIP service specification.[14] Incorporated into the topic guides was a question regarding the pharmacist-training package.

The elements from the content analysis were combined with those from the previously reported literature review[41] by NN and DW to create a training package including a personal development framework (PDF) consisting of domains (i.e. our grouping name for a selection of similar competencies), competencies and behaviours. This was presented to the External Advisory Panel (EAP) to review and amend.

Training-specific focus groups and interviews

Focus groups with different healthcare professional groups were organised and located across four locations as follows:

- primary care pharmacists (Yorkshire and Humber)
- general practitioners (Aberdeen)
- community pharmacists (Belfast)
- care home staff (Norwich).

Within each location, an appropriate healthcare professional with significant local care home experience regarding medication management was interviewed to enable identification of local environmental and contextual factors.

The current draft of the training package was provided before focus groups and interviews. The topic guide consisted of the following:

- initial views on the draft training package

- therapeutic and clinical areas to be included
- care home-specific processes which pharmacists would need to be aware of
- knowledge required to be effective
- inter-professional related knowledge required
- advice relating to pharmacist preparation.

Where possible, consensus on how best to amend and enhance the training package and framework was identified within the focus groups. All the focus groups/interviews were recorded digitally and transcribed verbatim. Interviews and focus groups were content analysed by DW and validated by NN.

To create the next draft of the training package, where consensus was not clear, a final decision was sought from the EAP.

Expert consensus

A consensus day held at each study site (outlined in WP1), included a session to obtain feedback on the draft training package regarding:

- training content
- PDF
- assessment processes
- Points of dissonance identified within the stakeholder focus groups and interviews.

Detailed notes were taken from the consensus panels and used by NN and DW to create a final draft training package for feasibility testing.

Feasibility testing

Four PIPs and four care homes, each with 10 consented residents, were recruited and PIPs trained to deliver the intervention over 3 months.[42] At the end of the feasibility phase, a face-to-face focus group with the PIPs was convened to obtain feedback regarding

- personal development planning and support process
- PDF
- assessment processes
- impact of the training
- elements that worked well and those that worked less well.

Focus groups were recorded, transcribed verbatim and content analysed to create the final draft training package for use within the main trial.

Validation

All intervention PIPs undertook the final training plan. The PIPs' experience of the training days and the aligned professional development and assessment of competence were evaluated through training day evaluation forms (PIP *n* = 21), online survey (PIP *n* = 17) and semi-structured interviews (PIP *n* = 14). Using a mixed-methods approach, each dataset was analysed separately and then triangulated to provide a detailed evaluation of the process. The evaluation forms and online survey were described quantitatively and tabulated. Qualitative interview data were coded by two researchers, and descriptive categories and interpretative themes identified through thematic analysis were agreed upon among the researchers.

Results

Systematic review

Paper selection and description

Fifty-two papers were selected for the review (see *Appendix 1*, *Figure 3*). Characteristics of the included papers are provided in *Appendix 1*, *Table 7*. All studies reported that their intervention was effective.

Pharmacist, education and training characteristics

Descriptions regarding qualifications and training provided before pharmacist role in care homes were generally vague. Six papers reported the pharmacists being provided with a tool to support the service.

Two papers described the pharmacists being trained in inter-professional relationship development. Ten papers described some form of training in a limited manner.

Codified and practical knowledge

A summary of the main clinical and therapeutic areas identified and the most commonly cited activities is provided in *Appendix 1*, *Table 8*.

Care home–specific cultural knowledge

Care home staff training was seen as important for developing relationships and changing care home medication-related cultures, for example, requests for medication such as antibiotics, antipsychotics, analgesia and laxatives[43] and willingness to implement changes in therapy. Care home culture was cited in one paper as a reason for medication changes not being implemented.[43,3]

Stakeholder engagement

Thirteen interviews and 13 focus groups with 72 participants were undertaken. The main results have been reported elsewhere.[44] The different types of knowledge identified as important through the interviews and focus groups are summarised in *Appendix 1*, *Box 1*. *Appendix 1*, *Figure 3*: Draft 1 provides a copy of the first draft of the PDF used to underpin the training package.

A variety of activities were added to enable the development of identified cultural knowledge requirements, for example, spending time with different medical practice and care home staff to identify expectations and preferences and learning to use local systems.

The practical knowledge identified as important was how to provide pharmaceutical care for older people with frailty.

The EAP identified the need for 'context' to be included as a domain within the PDF and to change the 'chronic disease management' domain to 'managing complexity in late life' (see *Appendix 1*, *Figure 4*: Draft 2).

Training-specific focus groups and interviews

Six primary care pharmacists, six GPs, five community pharmacists, six care home staff and four local experts participated. Additional changes to the training package were identified as being required, including the addition of activities to enable the PIP to understand local cultures and to integrate into the teams.

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Expert consensus

Four consensus panels were held (Grampian *n* = 12, Yorkshire and Humber *n* = 12, Norfolk *n* = 15, Belfast *n* = 14). The content of the face-to-face training days was agreed along with the expectation that a geriatrician should be involved in delivery.

The consensus panel emphasised the need for a significant amount of time to be allocated to the development of relationships and that training care home staff was an important element within this.

A number of further changes to competencies and behaviours were recommended.

A large number of topics about which PIPs should be knowledgeable were identified (see *Appendix 1*, *Box 2*). It was agreed to provide this information through a knowledge pack, consisting of relevant links.

It was proposed that the PIPs would use the PDF for self-assessment purposes and they should be allocated a mentor (senior care home pharmacist) to support them through the process.

Completion of these competencies would be signed off both by their mentor and by a medical practitioner with expertise in providing medical care to care home residents (independent assessor). Sign-off by both parties would provide the 'accreditation' for the PIPs.

A copy of the training package and PDF created following this exercise and before feasibility testing is provided in *Appendix 1* and *Figure 5*.

Feasibility testing

The PIPs reported that the process of personal development planning, being supported by a mentor and assessed on their final competence through oral viva, was appropriate and effective. Greater guidance on evidence collection for assessment purposes was requested at the outset.

The elements of the face-to-face training that were perceived as particularly effective were the case studies surrounding the management of complexity, legal issues and covert administration and the session on the management of psychotropic medication.

The training was viewed positively and reported to be motivational, helping to enhance confidence. This resulted in no major changes to the training package.

Evaluation

All PIPs found the training useful, specifically the input from the geriatric specialists who produced case studies on medication management in older people: '*probably about the best CPD I've done for a long time*'. Overwhelmingly, the PIPs strongly agreed that the training content was appropriate.

- Comprehensive training, mentorship, competency assessment and explanation of research processes amply equipped these experienced PIPs to carry out their role.
- Input from older people psychiatric specialists and specific training on antipsychotics was reported to be of huge value to the majority of PIPs, increasing their confidence and understanding around this area of medication management.

Post-training mentorship by a qualified pharmacist with extensive care home experience was reported as being extremely helpful in guiding their CPD and in preparing a portfolio of evidence for the assessment of competence by a GP. All PIPs achieved competency at first attempt and within expected timelines. Only one PIP stated that mentorship was not very useful at this stage. The PIPs reported that they had less contact with the mentor as the intervention progressed.

The training days and mentoring appeared to increase confidence, especially in PIPs with limited experience in older people medicine. Even for those with extensive experience in older people medicine, the training provided a chance to consolidate knowledge. Alongside consolidating clinical knowledge, the PIPs needed to be able to successfully develop relationships with care home staff and primary care staff if they were joining a new practice. PIPs reported arranging peer support through the cloud-based messaging app 'Telegram'. Mentorship and peer support was reported as useful in the early stages of the intervention but use tailed off as individuals' confidence grew.

The need to demonstrate competency through completion of the competency framework and professional discussion with a GP was appreciated by the PIPs. Evidence from the PCP reviews suggested all were competent in the role. PIPs' comments on their practice during the trial, evidence the increased competency and confidence they had due to the training programme:

> *There were a few people that we'd got off a medication, antipsychotics particularly, because that's something I probably wouldn't have touched, but after having the training session, and the group discussions, and more of an awareness, I felt more comfortable*

Pharmacist independent prescribers suggested that individualised country-specific sessions could run in tandem during main training days without affecting the length of the training programme. An additional refresher event mid-intervention was recommended as was advice on building relationships in CHs where work cultures may be new to pharmacists.

Discussion

The results from the feasibility study suggest that the iteratively designed training package is likely to ensure that PIPs are competent to undertake their envisaged role. Evaluation within WP6 will enable the researchers to determine whether it is generalisable to a broader range of PIPs.

Work package 5: feasibility study[4]

Approvals

Research ethics approved by NRES East of England – Essex REC Ref: 16/EE/0284 and Scotland A REC Ref.: 16/SS/0125.

Health Research Authority approved Ref: IRAS 206970.

Aims

To test and refine the service specification and proposed study processes to inform the cRCT (WP6).

Objectives

To

- test processes for participant identification, recruitment and consent and assess retention rates
- determine suitability of outcome measures and data collection processes from care homes and GP practices
- assess service and research acceptability
- test and refine the service specification.

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Method

Design

This was a single-arm, open-feasibility study conducted in care homes for older people in all four locations across the UK from August 2016 to April 2017.

The recruitment target was one eligible general practice, one PIP and up to three care homes associated with each participating practice in each location. Each GP/PIP/care home(s) triad had a target of recruiting 10 residents.

Inclusion criteria

GP practice

General practitioner practice managing sufficient care home residents to recruit a minimum of 10 residents in up to three (in case one or more care homes did not have sufficient eligible participants) care homes. An existing arrangement with a PIP was preferred, but not mandatory.

PIPs

Pharmacists registered with the General Pharmaceutical Council or Pharmaceutical Society of Northern Ireland as independent prescribers.

Care homes

Care home primarily caring for residents aged ≥65 years, registered as caring for adults aged ≥5 years.

Residents

Permanent residents under the care of the participating GP practice, prescribed at least one regular medication, aged ≥65 years; they should be able to provide informed consent/assent, or for this to be provided by a nominated representative.

Residents on an end-of-life care pathway were excluded.

Patient identification and recruitment

PIPs and GP practices

Each location used locally defined strategies and networks (see *Appendix 2*) to obtain expressions of interest (EOIs) from GP practices and PIPs, for either the feasibility study or the planned main RCT.

Care homes

The consenting GP practice in each study location approached up to three care homes. Care home managers expressing interest were sent a formal invitation pack by the local researchers. A second or third care home was contacted only if there were insufficient residents in one home.

Residents

General practitioners identified eligible care home residents from their computerised records. An invitation pack [letter from the GP, participant information sheet (spoken version, if necessary) and consent form] was distributed to each resident by the care home manager. After a minimum of 24 hours, the care home manager visited each resident and obtained verbal consent from residents willing to discuss the study with the study research associate (RA) who then visited the care home, met with interested residents and assessed resident capacity to give consent. Where a resident was identified

by the care home manager or RA as lacking capacity, a legally appropriate third party [e.g. relative/friend known as consultee (England and Northern Ireland)] or welfare power of attorney (WPOA; Scotland), was contacted by mailed invitation pack, through the care home. Reminder letters were issued after 2 weeks as needed. In England and Northern Ireland, a member of the care home staff could be nominated as the consultee, but in Scotland, a member of staff could not be the WPOA. The recruitment process is outlined in *Appendix 1*, *Figure 5*.

Sample size

No formal power calculation was conducted. The recruitment target was 10 participants per site (a total of 40), judged as sufficient to assess feasibility.[45]

Intervention

The intervention included medication review; prescribing and deprescribing; care home staff training, medication-related support and communication (see *Appendix 3*). It spanned for 90 days (4 hours per week per PIP per 10 patients). Before the intervention, PIPs attended training (described in WP4). Pharmaceutical care plans (see *Appendix 4*) were used by the PIPs to document each intervention. A random sample of eight PCPs (two per location) was selected for review of appropriateness (based on professional judgement) by one of the two specialists in 'care-of-the-elderly' grant holders.

Estimating the participating proportion of the eligible population

The proportion of general practices, pharmacists, care homes and residents approached and consented was recorded along with the proportion of residents followed up at 3 months to assess recruitment and retention.

Suitability of outcome measures

Potential outcome measures identified in WP2 (see *Appendix 1*, *Box 3*) were collected at baseline and 3-month follow-up for each participant. To determine their suitability for inclusion in the RCT, each outcome measure was assessed against the following criteria: availability of the data source, potential for bias, potential for missing data, resident centeredness, sensitivity to the intervention, reliability, whether validated, potential for third party completion, ability to blind and time taken to collect per patient and quantity of data. At minimum, the measure had to be judged objective, discriminating and efficient to collect.

Assessment of service acceptability and trial feasibility

Participant views

After the intervention, face-to-face semi-structured interviews were held with stakeholders at each location and a focus group held with the PIPs. Proceedings were digitally recorded and transcribed verbatim.

Serious adverse drug events

All admissions to hospital and deaths were recorded as serious adverse events (SAEs) and assessed for causality by a medical doctor in the study management team, using professional judgement.

Data analysis

Descriptive statistics were used for the quantitative outcome measures at baseline and follow-up. No statistical comparisons were conducted. Interview and focus group transcripts were thematically analysed.

Approvals and registration information

A favourable ethical opinion was received from East of England – Essex Research Ethics Committee (5 September 2016: 16/EE/0284) and Scotland A Research Ethics Committee (8 September 2016:rec ref. number 206970) with subsequent approval from the Health Research Authority/NHS Research and Development.

The trial was registered on the ISRCTN registry Registration number ISRCTN10663852.

Results

Recruitment and retention

In total, 4 PIPs, 4 GPs, 6 care homes and 40 residents were recruited (see *Appendix 1*, *Table 9* and *Figure 6*). The four recruited PIPs were employed directly either by the practice (1) or by the NHS (one with no existing relationship with a GP) (2) or were self-employed (1). The GP or PIP identified 122 residents from GP records and invited 86. Thirty-six (30%) residents were excluded on screening and 33 (27%) of those invited declined the invitation or did not reply. Forty were recruited and retained for 3 months.

Suitability of outcome measures

There were data for all outcome measures (see *Appendix 1*, *Table 10*) for all or most residents, other than the MMSE, which could be completed only by 40% and 35% of residents, respectively, at baseline and follow-up. The direction of change between baseline and follow-up suggested that the intervention could improve care.

Appendix 5 provides a review of the suitability of outcome measures following feasibility testing. The outcome 'falls per patient' met most criteria and was selected as the primary outcome measure with Drug Burden Index (DBI),[46] hospitalisations, mortality, Barthel (proxy)[47] and ED-5Q-5L (face-to-face and proxy).[30,33] Whilst hospitalisations and mortality were also considered as the potential clinical primary outcome, when considering the sample size necessary to detect a clinically important difference, falls was the only feasible option. STOPP/START was not used due to perceived subjectivity.[19] The QUALIDEM[48] and MMSE[49] were excluded as too time-consuming to complete, a better measure was available (to replace the QUALIDEM) or a high potential for bias existed and/or data were missing.

Quality of pharmaceutical care plans and adverse events

Eight pharmaceutical care plans (PCPs) were reviewed. Six PCPs were considered appropriate. Two included insufficient detail to fully judge appropriateness. Just over 10% of residents [5/40 (12.5%)] were admitted to hospital (11 hospital admissions), and two residents (5%) died. None of these events were related to the intervention.

Participants' views of service and research acceptability

All 28 participants invited to interviews agreed (6 care home managers, 6 GPs, 12 care home staff, 12 residents, 3 relatives and 1 dietician). Lack of capacity restricted the number of residents interviewed.

Perceived benefits of the service

All participants expressed positive views about the service. The main themes are summarised below and illustrated with exemplar quotes detailed in *Appendix 1*, *Table 11* and indicated in the text.

Improved patient care and safety

Regular medication review led to improved patient care and quality of life (quote 1). The key pharmacist skills were their knowledge, ability to prescribe, professionalism, autonomy and ability to provide training and communication (quote 2). Care home managers highlighted that medication practice had become safer (quote 3) and efficiency was increased. The PIP facilitated prompt implementation of medication changes and acute prescriptions (quote 4) and saved care home manager time (quote 5). A nurse highlighted the value of having pharmacists who could prescribe (quote 6). The PIP had time to communicate with relatives and care home staff (quote 7) and had more time than GPs to complete detailed medication reviews (quote 8).

The PIP service freed up GP time and was the most 'efficient' way of conducting medication reviews (quote 9), with the ability of the PIP to work autonomously being valued (quote 10). Conversely, some care home managers did not feel it freed up any time for them (quote 12), but neither did it impede care home processes (quote 11). However, it did reduce stress levels and improve communication (quote 13).

Potential disadvantages of the service

Few disadvantages were mentioned. The main one was that the PIP was not as familiar with the patients as the GP (quote 14). GPs also expressed concern that they would become less familiar with the residents and the care home staff if they were less involved (quote 15).

Refinements to service specification

Only two of four PIPs attended the focus group. Two were unwell, and views were obtained by later telephone interviews. Few changes were proposed. Delivering the service took more than the indicative 4 hours per week, not having an existing relationship with the GP was a disadvantage, and PCPs needed simplifying.

Discussion

The acceptability of the service and feasibility of proceeding to the main trial were confirmed. The processes to identify and recruit trial participants (GPs, PIPs, care homes and residents) were successful and scalable, including those for participants without capacity. Participants were retained for 3 months. The primary outcome measure for the main trial was confirmed as the fall rate per person. In contrast to other potential outcomes, a clinically important difference in falls would be detectable with acceptable power within a realistic sample size. Minor areas of refinement to the service specification and the research process were identified. For example, using the professional judgement of a study team member to assess causality between reported adverse event(s) (AEs) and the intervention was subject to bias, and an alternative approach was developed, that is, using independent GPs for WP6. Similarly, a review of the PCPs, conducted subjectively by the study team members, could have been biased, and WP6 includes details of the standardised protocol and reporting templates used in the main trial.

The participant demographics were similar to those of the UK care home population.[1] Participation rates were high, suggesting there had not been selective recruitment. The PIPs participating in this study included pharmacists employed by either primary care or the GP practice, providing evidence that this service specification is adaptable to either model; PIPs with a pre-existing relationship with the GP found it easier to arrange meetings.

The level of EOI confirmed that there would be sufficient participants for the main trial, and the consent rate of residents informed the target number of care home patients required to be registered with the participating GP.

Work package 6: definitive trial with internal pilot

Approvals

Research ethics approved by NRES East of England Central Cambridge REC Ref.: 17/EE/0360 and Scotland A REC Ref.: 17/SS/0118.

Health Research Authority approved, Ref.: IRAS 233964.

Aim

To estimate the effectiveness, cost-effectiveness and safety of a PIP assuming responsibility for providing pharmaceutical care to residents in care homes.

Methods

This was a cRCT conducted in primary care involving triads of a GP practice, PIP and a sufficient number of care homes to provide 20 care home residents per triad.[50]

Recruitment

Inclusion and exclusion criteria

Pharmacist Independent Prescribers were excluded if they were already providing an intensive service to the care home or could have a conflict of interest by holding employment with the community pharmacy supplying the home(s).

General practitioner practices were included where they managed sufficient care home residents to support recruitment of our target of approximately 20 eligible participants.

Care homes needed to be primarily caring for adults aged ≥65 years and associated with a participating general practice. Homes were excluded if they already received a regular medication-focused review service (monthly or more) or were under formal investigation by a regulator [e.g. Care Quality Commission (CQC) for England].

Care home residents needed to be under the care of the participating GP practice if they were ≥65 years old, a permanent resident in a participating care home, prescribed one or more medications and able to provide (directly or through an appropriate representative) informed consent or advice. They were excluded if they were receiving end-of-life care or additional instructions on their residence (e.g. held securely) or were participating in another study.

Participant identification and recruitment

Pharmacist Independent Prescribers were identified using local networks and related GPs (if links already established) were recruited concurrently, followed by their relevant care home(s) who were approached by participating GPs. Where one single linked home had too few potential resident participants, up to two further homes were recruited.

Resident recruitment

General practitioners identified residents in participating care homes taking one or more medications and screened them against the study inclusion and exclusion criteria. Care home managers handed out invitation packs to potential residents, re-visited each resident after at least 24 hours and obtained verbal consent for the local researcher to approach them to discuss study participation. For residents who were considered to lack capacity, packs were posted to the resident's next of kin. The process is summarised in *Figure 7*.

Randomisation and blinding

Randomisation was at triad level to minimise contamination occurring between two homes in the same practice where one received the intervention but the other did not. Residents were not individually randomised, as part of the intervention was for PIPs to help care homes improve their overall medication management processes. Randomisation was stratified by the four geographical areas, using a web-based electronic system integrated into the study database, in an allocation ratio of one intervention triad to one control triad. Because of the nature of the intervention, PIPs, care homes and GPs were not blinded to their allocation arm once the intervention began. Researchers, however, were blinded to arm allocation during the recruitment phase.

Six weeks were provided for PIP training to be undertaken and completed. Consequently, time zero for data collection purposes was standardised at 6 weeks after randomisation.

Intervention

This was delivered by trained PIPs for a period of 6 months and involved the PIP, in collaboration with the care home resident's GP and care home staff, assuming responsibility for managing the medication of each resident, including

- reviewing the resident's medication and developing and implementing a PCP
- assuming prescribing/deprescribing responsibilities
- supporting systematic ordering, prescribing and administration processes with each care home, general practice and supplying pharmacy where needed
- providing care home staff training
- liaising with GP practice, care home and supplying community pharmacy.

We anticipated each PIP providing approximately 4 hours of intervention per week per 20 residents for 6 months.

Control: Triads allocated to the control arm received usual GP-led care, which could include pharmacist review/services to care homes where routinely provided, excluding those of an intensity equivalent to the study intervention.

Outcome measures

The primary outcome was fall rate per person over 6 months after time zero, as documented in care home falls record for those residents recruited into the trial only.

Secondary outcomes, all at 6 months after time zero unless stated otherwise:

- Resident (i.e. self-report) or proxy resident quality of life (EQ-5D-5L) at 3 months and 6 months: utility scale where a score of 0 indicates equivalent to death and that of 1 indicates full health.[30]
- Proxy modified physical functioning score (Barthel): a score of 0 is most dependent on 20, which indicates least dependent.[47]
- DBI: a measure of anti-cholinergic and sedative drug exposure, which was collected through GP-recorded medication data: higher scores indicate greater anticholinergic potential and increased risk of drug-related morbidity.[46]
- Health service utilisation (and associated costs); notably unplanned hospital admissions in the past 6 months, at 6-month follow-up, collected from care home and GP records (see WP3 for health economics results of WP6).
- Mortality.

Sample size

A sample size calculation indicated that 880 participants (440 in each arm) would detect a 21% decrease in fall rate from 1.50 per resident over 6 months with 80% power, at the 5% significance level and an assumed intraclass correlation coefficient not more than 0.05. With approximately 20 patients per triad, this equated to 44 triads. The relative reduction of 21% was half of that detected within a UK-based, pharmacist-led medication review service provided to care homes.[51] Furthermore, we assumed a loss to follow-up of 20% based on mortality and loss observed in the CAREMED study.[23]

Statistical methods

All analyses were by intention-to-treat, and it was anticipated that the primary outcome ('falls per resident') would follow a Poisson distribution; hence, the between-arm comparison of falls was to be made using a Poisson Regression model. Data subsequently demonstrated that the best fit was in fact a negative binomial model and parameters were estimated using a generalised estimating equation approach adjusted for the clustered design. The final model included baseline fall rate, prognostic variables (specifically DBI, Barthel Index and Charlson scores) and home status (nursing/residential) with arm as a fixed factor.

Safety

Processes were developed for recording sudden unexpected serious adverse reactions (SUSARs), SAEs and AEs. SAEs were defined as inpatient hospitalisation and death requiring immediate reporting. If SAEs were believed to be related to the study intervention, then they were reported as SUSARs. We used a mixture of prospective and retrospective SUSAR notification by asking GPs to report SUSARs immediately, and retrospectively, and by our trial manager proactively contacting care homes each month to ask about SAEs. The resident's GP was then assessed for causality of the SAE, and whether it was linked, or not, to the PIP intervention.

Concerns could also be confidentially raised by any member of care home staff using a dedicated email address.

A random (computerised number generation) 20% sample of the PCPs and associated resident documents were assessed by a study geriatrician, to ensure clinical appropriateness and safety.

Process evaluation

Complementary to the main RCT, a process evaluation was conducted,[52] following MRC guidance.[7] This evaluation used a mixed methods approach to inform interpretation of trial findings and subsequent implementation, should the intervention be effective. Objectives were as follows: to provide description of the intervention in terms of quality, quantity and variability in delivery; to explore the effect of individual components on the primary outcome; to investigate the mechanisms of action; to describe views of the intervention (including training of PIPs and care home staff) from GP, care home, PIP, resident and relative perspectives; to describe the characteristics of each arm and to estimate how 'normalised' the intervention became.

A mix of quantitative (surveys of care home staff, GPs and PIPs, PIP activity logs, PCP review and the trial outcomes) and qualitative (interviews with care home staff, residents, GPs and PIPs) approaches were used. Data were collected relating to delivery of detailed tasks required to implement the new service, to collect data to confirm the mechanism of action as hypothesised in the logic model (see *Appendix 6*), to collect explanatory process data and data on contextual factors that could have facilitated/hindered effective and efficient delivery of the service. Detailed analysis of PCPs additionally involved determining which medication-related changes would be associated with the risk of falls guided by recent comprehensive systematic reviews.[53–55]

All data were collected, from intervention arm participants only, after the study period for each home had finished. The tasks, aims, data and data sources are summarised in *Appendix 1*, *Tables 18–21*.

Interviews schedules were informed by normalisation process theory (NPT),[56,57] and questionnaires included a set of NoMaD questions that translates NPT domains for survey use.[58] Interviews were conducted face-to-face or by telephone; all were audio recorded and transcribed verbatim. Thematic analysis of qualitative data was based on the NPT framework, but a complementary inductive approach enabled recognition of unexpected emergent themes. All data sets (qualitative and quantitative) were integrated to identify relationships, explain findings and identify optimal intervention contexts.[52] Full details are published elsewhere.[50]

Ethics

Ethics approval was provided by East of England Central Cambridge Research Ethics Committee (for England and Northen Ireland) – Ref.: 17/EE/0360; and by Scotland A REC – Ref.: 17/SS/0118.

Protocol

This is published and is available at: https://trialsjournal.biomedcentral.com/articles/10.1186/s13063-019-3827-0.

Results

As shown in *Appendix 1*, *Figure 8* (CONSORT diagram), we recruited 49 triads (49 general practices, 49 PIPs and 72 care homes) between December 2017 and May 2019. Of these 49 triads, 25 were randomly allocated to the intervention arm and 24 to the control arm. There were 454 residents in the intervention arm and 428 residents in the control arm. Almost all losses were due to resident deaths (134/166 losses = 81%). Three intervention PIPs (12%) failed to deliver the service due to personal reasons.

Baseline comparison between arms is provided in *Appendix 1* and *Table 12*. Whilst most variables including age, medications, admissions, DBI, Charlson comorbidity, and EQ-5D-5L proxy scores were similar between arms, the control arm had a slightly greater proportion of male residents (33% vs. 28%), and a considerably greater proportion in nursing home care (59% vs. 42%). In line with those findings, the intervention arm had a higher Barthel score (8.34 vs. 7.07 of 20, where higher scores imply greater independence) and those self-reporting EQ-5D (11% of participants) reported better health 0.50 versus 0.35 (scale 0–1, 1 = perfect health). Residents in the intervention arm had a mean number of falls of 0.78 in the previous 90 days compared with that of 0.57 in residents of the control arm. Follow-up data collection commenced in September 2018 and concluded in July 2020 (this was delayed by 4 months for the final triads due to COVID-19).

Primary outcome analysis

Although there were a greater number of falls recorded in the intervention arm in the 6-month follow-up period (697 vs. 538) and a higher crude rate of falling, when adjusted for baseline falls, no difference was observed between arms (RR = 1.00, 95% CI 0.73 to 1.36; $p = 0.99$). Further adjustment for key potential confounders reduced the RR, in favour of the intervention, to 0.91, although this too was not statistically significant (95% CI 0.66 to 1.26; $p = 0.58$; see *Appendix 1*, *Table 13*).

Similarly, there was no evidence of an effect on fall rate at 3 months. The RR favoured the intervention arm (RR = 0.86, 95% CI 0.63 to 1.19; $p = 0.36$), but this was not statistically significant.

Mortality

There were 66 (14.7%) deaths in the intervention arm compared with 71 (16.6%) deaths in the control arm, with a mean time to death of 109 versus 103 days. However, a Cox's proportional hazards model indicated no evidence of a beneficial effect on the death rate (hazard ratio = 0.93, 95% CI 0.64 to 1.35; $p = 0.68$). *Appendix 1* and *Figure 9* illustrate the Kaplan–Meier survival curves.

Other secondary outcomes

The remaining secondary outcomes included DBI, hospitalisation, Barthel score (see *Appendix 1*, *Table 14*), and quality of life as measured using the EQ-5D (see *Appendix 1*, *Table 15*). Of these outcomes, the intervention improved (decreased) residents' DBI by 8% from 0.72 at baseline to 0.66 at 6 months. By contrast, the DBI among control arm residents increased from 0.70 to 0.73. When analysed using a natural log transform, the rate ratio of DBI scores at 6 months between the intervention and control arms was 0.83 (95% CI 0.75 to 0.92; $p < 0.001$), suggesting that more effective deprescribing occurred in the intervention arm. No other secondary outcome showed a statistically significant difference. No evidence of a decrease in hospital admissions between arms was found (RR = 0.98, 95% CI 0.66 to 1.46; $p = 0.93$), nor was there any evidence of any difference between arms with respect to the Barthel Index at 6 months, although scores favoured the intervention arm (ratio of means = 1.20, 95% CI 0.96 to 1.49; $p = 0.11$).

Quality of life scores were collected as self-reported or by proxy, as shown in *Table 15* (see *Appendix 1*). Few residents were able to report their own scores (only 6.5% at 6 months) and for those who could report, scores favoured the intervention arm at baseline by 0.14 points (>40% higher). There was no evidence of any effect of the intervention on self-reported EQ-5D scores at either 3 months (mean difference = 0.079, 95% CI: −0.028 to 0.186; $p = 0.146$) or 6 months (mean difference = 0.010, 95%

CI: −0.115 to 0.135; p = 0.873). Proxy reported EQ-5D scores were available from almost 70% of residents. These scores were very similar at baseline between arms and changed very little through follow-up, with a small, non-significant difference observed at 3 months (mean difference = −0.017, 95% CI −0.073 to 0.039; p = 0.556), and 6 months (mean difference = 0.030, 95% CI −0.021 to 0.080; p = 0.249).

Exploratory/additional analyses

Several additional post hoc analyses were performed on the primary outcome to explore our findings further. First, those lost to follow-up, or died within 10 days or 28 days of baseline, were excluded on the basis that those residents would have been unlikely to benefit from any intervention. Excluding these individuals left 811 and 809 residents, respectively (i.e. over 92% of the study sample). The RR of falls between arms was almost identical in both analyses at 0.91 (95% CI 0.66 to 1.26), and neither was statistically significant (p = 0.58). These estimates did not differ substantially from those including the full study sample.

Some residents fell very often, with one resident falling 59 times during follow-up. This led to a highly skewed distribution. Excluding those with the very highest rate of falls (the top 5%) also made little difference to the estimated RR (0.96, 95% CI 0.73 to 1.26; p = 0.78). The analysis was also conducted removing residents who were immobile, on the basis that they were not able to fall and, therefore, could not contribute to the primary outcome. Removing these individuals left 60% of the sample in the model (n = 526), but again little difference was observed (RR = 1.07, 95% CI 0.79 to 1.45; p = 0.66).

Finally, dividing residents into those who fell before baseline and those who did not fall found quite different rates of falling during follow-up, that is, a rate of 1.3 falls per annum amongst 'non-fallers' and 7.3 falls per annum amongst 'fallers'. However, there was no evidence of a differential effect between the intervention and control arms with respect to these two arms: 1.27 and 1.33 falls per annum for non-fallers in the intervention versus control arms; and 7.41 and 6.12 falls per annum amongst fallers in each arm, respectively. An interaction term (faller status*arm) was not statistically significant (p = 0.16).

Process evaluation

Overall, the PIPs adhered to the service specification and delivered all aspects of the role, although to varying degrees in different homes according to need. Some care home managers had said there was no need for any training to be delivered to staff. Across all PIPs, 24% of their time was spent face-to-face with residents, 43% of their time spent on resident-related desk activities; 24% of their time spent on other general activities in the care home and 10% of the time spent on travelling. In questionnaire responses, eight reported that they personally visited the care home monthly and eight visited weekly. Regarding sufficiency of time, five stated that 4 hours was not enough, eight found it sufficient and three stated it was too much time. Resident-related prescribing changes are summarised in *Appendix 1*, *Table 16*, and the data are based on the analysis of 368 completed PCPs with a total of 668 interventions. British National Formulary therapeutic categories are reported in *Appendix 1*, *Table 17*. Of the 566 clinical interventions, 202 (35%) were related to medication likely to cause falls, of which medication discontinuation (94) and dose reduction (54) would reduce fall risk (148/566; 26.1%). By contrast, there were dose increases (17), medication changes (9) and new medication initiation (20), which increased the risk of falls (46/566; 8.1%). A detailed PCP review also suggested that the PIPs identified the majority of medication changes that could have reduced a resident's fall risk.

No safety concerns were identified from the review of PCPs or independent assessment of SAEs. No reports of safety concerns were received through the bespoke email address.

When interviewed, the GPs were very positive about the pharmacists' interventions (saved them time, or reassured them about medication appropriateness and safety) as were the care home managers who sometimes specifically commented how they had observed the benefit of the reduced medications on the patient (see example quotes in *Appendix 1*, *Box 4*) as well as increased efficiencies.

For optimum implementation, all stakeholders need to believe in the idea of the service and actively support it. A detailed analysis of the different triads against this framework illustrates how this worked in practice, as shown in *Appendix 1*, *Box 5*.

Finally, there were 26 questionnaires returned (PIP × 16, GP × 8, CHM × 2) and 38 interviews conducted (PIP × 14, GP × 8, CHM/staff 15, resident 1). Both questionnaires and interviews asked about satisfaction with specific aspects of the role and overall satisfaction. Very high overall satisfaction was reported (see *Appendix 1*, *Figure 10*) reflecting the vast majority of quotes (see *Appendix 1*, *Box 6*).

Discussion

This large, rigorously conducted, cRCT did not demonstrate that PIPs who took responsibility for medication management for older patients in care homes could reduce falls significantly. Moreover, health economic analysis showed an overall cost per resident of £280, with no effect on quality of life.

However, the PIPs did contribute to a decrease in the residents' mean DBI compared with that of the controls, suggesting the occurrence of effective deprescribing, and the data suggest there were savings in medication costs. In the longer term, a reduced DBI would have theoretical health benefits. All outcomes' point estimates, after adjustment for baseline differences, including Barthel index, mortality, hospital admission, proxy quality of life and falls favoured the intervention arm although not reaching statistical significance.

Drug burden is associated with increased mortality,[59] falls,[60] hip fractures,[61] frailty[62] and reduced quality of life.[62] Consequently, the significant reduction in DBI is predictive of improved resident outcomes. With data on DBI and risk based on a minimum 12 months of observation,[60–63] the 6-month follow-up in this study may again have been unlikely to fully realise clinical improvements.

Whilst we should be cautious in overinterpreting such findings, the data combined with the generally very positive views from the stakeholders and confirmed safety suggest that this intervention merits further refinement and investigation. In particular, the facilitating contextual factors need to be further explored in light of the ongoing NHS roll out of this and similar pharmacist-led medication-related services.

Involvement of patients and the public

We worked with our local public and patient in research (PPIRES) arm from the outset with feedback received on the original idea from PPIRES members and subsequent involvement in the grant application as it developed. At that early stage, with support from our care home expert (HH), we visited a care home to undertake a focus group of residents to listen to their views regarding the idea underpinning the project and what we needed to consider from a resident's perspective. They were clear that whilst they had no concerns regarding a pharmacist prescriber looking after their medicines, they wanted residents to be involved in all decisions. Training regarding this was incorporated into the final model.

On receipt of the grant, we recruited four patient and public involvement members, with an interest in care homes, through PPIRES: two members for the management group and to support the process as it developed [Kate Massey (KM) and Christine Handford (CHD)] and two members for the independent steering committee (Joyce Groves and Elaine Bounds). KM and CHD were invited to, and actively involved in, all project management meetings, with pre-meetings organised with team members beforehand to inform them of the main issues. Their views were sought at all points in the process to ensure that they were an integral part of the research process.

Whilst preparing our protocols for submission for ethical approval, we actively involved KM and CM in reviewing participant information leaflets and consent forms. KM and CHD reviewed qualitative data,

which had been generated within WP4 to ensure our interpretations matched theirs. The insights of both KM and CHD increased our confidence in what we believed was being said but, at times, provided a different perspective.

Kate Massey and CHD provided excellent feedback on the training materials that we had created for the pharmacists to train care home staff, enabling us to be confident that the information was pitched at an appropriate level. We also routinely invited KM and CHD to review abstracts and papers before publication.

Kate Massey wrote and published an editorial on her positive experiences of working within CHIPPS, promoting this to the pharmacy research community.[45] Very sadly and unexpectedly, Kate passed away before the article was published. Three years into the project, we therefore recruited Janet Gray (JG) as her replacement. CHD and JG were actively involved in preparing our dissemination strategy and identifying the areas within which they could most effectively participate. As a result, we engaged with the Patients' Association to seek their support in the grant's final year with respect to dissemination of the findings, allowing Frances Hollwey to join the project team. CHD, JG and FH were all active members of the small team responsible for organising our final dissemination event and contributed to the session with pre-recorded videos where they expressed their views and opinions on the process.

In summary, our PPI members have been an integral part of the CHIPPS process, engaging effectively and helping the research team throughout all stages.

Reflections

Within this report, we present the results of 5 years of work where we have carefully considered each element of the research process and assiduously followed MRC guidance.[6] The model of care, which we developed, was well received by all stakeholders. We developed a COS, which can be used internationally for all interventions of a similar nature, and a unique training programme, which supported competent service delivery. Our feasibility study found that our proposed service specification was likely acceptable and the research design was appropriate. We recruited to target, had sufficient power at the end of the trial to test our hypothesis and, excepting COVID-19, we would have completed the programme of work to time.

We originally requested a 6-month no-cost extension recognising that, given the complexity of the data, we would not have completed the final report within the required 2 weeks of project completion. Fortuitously, this extension enabled final data collection from two Scottish sites, recruited at the end of Phase III, whose 6-month follow-up was scheduled during the first COVID-19 lockdown. R&D permission was sought and gained to collect the data remotely in July 2020, and following data cleaning, analysis started in August 2020.

With the delivery of a successful project, the focus of the reflection is therefore on the final outcome, as the intervention did not have a significant effect on our primary outcome measure. We note however that, with the exception of the QALY scores, once baseline data and confounding factors were considered, the differences identified in all outcomes favoured the intervention arm, although only the change in DBI was statistically significant.

Given what we learned from the listening exercise in WP1, it was unsurprising that the predominant messages from the earlier WPs were the need for the PIP to integrate into these teams, as opposed to being 'an external body coming in to improve practices' and that effective communication with all stakeholders would be the key to their success.

In retrospect, a 12-month intervention, rather than a 6-month one, would have allowed the PIPs to have more time to not only integrate but also to ensure that all medication-related systems were appropriate within the home alongside their work to manage patients' medication. Furthermore, the PIPs would have had more time to prioritise their activities and interventions.

The selection of a suitable primary outcome measure for a generic medicine–related intervention is difficult, and this had been identified as a potential failure point within the application process by one of the original reviewers. WP2 identified three possible primary measures (falls, hospitalisation and quality of life), but within the project budget, 'falls' was the only practical choice. Our decision was, however, bolstered by recent systematic reviews, suggesting that 'falls' had been significantly reduced by pharmacist interventions in care homes.[64,65]

Through our process evaluation, we found that the PIPs made appropriate medication changes for the majority of residents: more than a quarter of these medication changes had the potential to reduce falls, and approximately 5% had the potential to increase them. Consequently, as an indicator of intervention effectiveness, it was proximal to the primary outcome for only one third of the PIP interventions. Furthermore, when considering the relationship between medication and falls, the two are not co-located chronologically, that is, by stopping a medicine known to be associated with falls, a reduction in falls is not immediately seen. It is the probability of falling, which is reduced, and this effect may not be seen, if at all, until sometime in the future. Consequently, again the 6-month follow-up may have been too short.

The introduction of the Medicines Optimisation in Care Homes (MOCH) initiative by NHS England mid-way through CHIPPS, where national funding was found to employ pharmacists to work within care homes, had the potential to contaminate our results. By raising standards in homes across the board, it could theoretically have created a ceiling effect, thereby minimising our opportunity to enhance care within the intervention arm, but we have no evidence to suggest this occurred.

The number of interventions per resident was slightly lower than that reported in the SHINE Project, where a single medication review was performed.[66] This may reflect the fact that homes were already receiving pharmacist visits and that this was not precluded from the CHIPPS control homes. We perhaps should have captured the nature of this activity in the control arms more carefully at the end of the study as control arm care may have been better than expected.

Limitations

Work package 1

Minimal representation of residents and relatives in intervention-development workshops, held on university premises outside their usual residence. Participant self-selection may bias them toward favourable expectations for the PIP role.

Work package 2

Delphi panel participants, drawn from the research team, were located in the UK, which limited generalisability. We included just two PPI representatives in our panel where other COS developers have recruited PPI representatives and professionals to their Delphi panels in a 2:1 ratio.[67,68] Outcomes that had not received consensus following the second round were excluded from the COS. Further rounds may have resulted in consensus for more outcomes. For pragmatic reasons, a final face-to-face 'consensus meeting' did not occur, potentially limiting further consideration of some outcomes. This approach has been used in other COS research.[67–69]

Work package 3

We were unable to collect data in relation to all items of resource use. Assumptions were made about the GP time saved due to no longer approving prescriptions, but there could have been other

differences, for example, shorter GP medication reviews and length of home visits. The analysis also did not include any time implications for care home staff. Estimated PIP intervention costs were also based on data reported by PIPs in the activity logs, which suggested under-reporting as mean reported time tended to be lower than the time remunerated for.

Work package 4

The training package was tested for final validation purposes only on 25 PIPs.

Work package 5

Research processes and service specification tested in one triad only in each location, that is, four PIPs, four general practices and six care homes in total.

Work package 6

Whilst GP selection of care homes may have introduced an element of selection bias, the number of homes available to them was frequently limited and there was no evidence of obvious selection bias in the final cohort of randomised homes.

Three PIPs (12%) failed to deliver the intervention.

Follow-up was carried out for 6 months only, and this may have been an insufficient time period. Some residents' PCPs had agreed only 3 months into the intervention period. Furthermore, where medication changes reduced the likelihood of falls, this is rarely an immediate effect.

The primary outcome of falls was proximal to only a third of the PIP interventions, and therefore, more focused inclusion criteria based on the risk of falls due to medication may have been more appropriate.

The concurrent national roll out of MOCH in England may have reduced intervention opportunities.

Conclusions

WP1 service specification development

To effectively embed this new pharmaceutical care service in care homes, stakeholders highlighted that securing PIP role acceptability and viability would require time and steps to ensure that all involved could 'understand each other's systems'. This should address contextual and implementation barriers and identify what practices were feasible for addressing residents' medication-related safety issues. GP and care homes required reassurance that the model was likely safe.

WP2 outcome identification and selection

Using the evidence-based and stakeholder views, we conducted a Delphi consensus exercise to identify outcomes that should be measured to evaluate the service and published this as a COS for trials testing prescribing interventions in care homes. This was registered on the COMET database. The outcomes meeting our criteria were subsequently feasibility tested in WP5.

WP3 health economics

The methods used to estimate cost-effectiveness in WP6 were developed through WP1 to WP4 and tested in WP5. The mean incremental cost of the PIP intervention, compared with that in control participants, was estimated to be £280. This suggests that the cost of the PIP intervention might be partially offset by, for example, lower medication costs. However, no improvement in QALYs was identified, and consequently, based on the results presented, the PIP intervention was not estimated to be cost-effective.

WP4 training package

The CHIPPS training package consisted of 2-day face-to-face training, a PDF, personal development planning with supported mentorship, time to 'understand each other's systems' and independent formative assessment by oral viva, which enabled the PIPs to practice safely.

WP5 feasibility study

Feasibility testing demonstrated that the PIP service was acceptable and practical. Trial processes for recruitment, retention, data collection and choice of outcome measures were confirmed. A robust process for monitoring safety of the PIP medication changes was developed, which involved independent assessment of all deaths and hospitalisations, independent review of PIP-created PCPs through sampling and provision of an independent email address to enable reporting of safety concerns.

WP6 definitive trial with internal pilot

No differences were found in the primary outcome of falls. This can be explained by the relatively small proportion of interventions that were identified as potentially affecting this outcome. The intervention did significantly reduce residents' drug burden. No differences in the other secondary outcomes were identified, although all outcomes favoured the intervention arm. Proactive monitoring found the model of care to be safe.

Frequent discontinuation of medication used within the central nervous system explained the reduction in drug burden seen. Most, but not all, PIPs delivered the intervention as intended. The view of stakeholders was generally very positive. Care home staff valued the pharmacist's advice and prompt resolution of queries. GPs reported reduced workload, improved patient safety and less inappropriate prescribing. To be successful in integrating the new systems of working, PIPs need to become fully integrated into GP and care home teams.

Recommendations for future research

Future research should

- determine the optimal model, processes and time for integrating pharmacists effectively into care home and GP practice teams
- determine the optimum follow-up time for interventions focused on fall reduction
- identify mechanisms of action leading to proactive deprescribing to enhance current practice
- develop an outcome measure that is meaningful to patients and practical for researchers, which accurately captures the impact of pharmacist interventions.

Implications for practice and decision makers

The challenge of optimising medication regimens in care homes is well recognised, and the CQC identified the proper and safe use of medicines as one area of care that requires regular review and that continues to fall below the expected standards (see *Appendix 1*, *Box 7*).[70] Pharmacists have been identified as health care professionals with the skills and knowledge to improve care home medication use (see *Appendix 1*, *Box 8*).[71]

As a result, pharmacists increasingly work in the care home environment ranging from 12-monthly visits to assuming full responsibility for medication within the home. However, these service changes have been introduced without robust evidence. In the SHINE project[66] on which the Medicines Optimisation in Care Homes project in England[71] was based, there was an estimated savings of £100 per resident per annum but no evidence of clinical effectiveness. Savings were based on medication costs only under the assumption that residents lived for 1 year on average.

The CHIPPS RCT demonstrated a significant reduction in individual DBI, thus lowering the likelihood of long-term negative drug effects on morbidity and mortality. Although the PIPs saved some of the GP time, our model of a session per week per 20 residents did not save money once the cost of the pharmacist time and additional monitoring costs were considered. Given that the PIPs visited each home every week over 6 months, it was relatively inexpensive and a reduction in DBI could be used to justify the importance of integrating a prescribing pharmacist into the care home setting, providing the amount of resource required was believed to justify this outcome.

Feedback from GPs and care home staff provided evidence that this pharmacist service is valued by, and acceptable to, the key stakeholders. GPs felt reassured about the safety and appropriateness of a resident's medication regimen and reported time saved, with independent prescribing authority core to this. Care home managers and staff reported that residents received better care, many improved visibly and systems became more efficient. Thus, CHIPPS has provided (across the programme) a holistic account of the more intangible benefits of this new pharmacy service. This is particularly relevant to jurisdictions where there is not yet a formal programme for involving pharmacists in care homes, such as Scotland (whose care home policy does not mention a pharmacy role) and Northern Ireland.

A second important policy and practice relevant finding is a theoretically informed understanding of the optimum way to implement the service. Mutual trust and a strong and established relationship between the PIP and the responsible GP are key; the care home staff also need time to establish that mutual trust with the pharmacist too. All stakeholders need a shared understanding of the service and a will to make it work.

The PIP service was, however, not found to be cost-effective based on standard UK government assessment criteria. Therefore, the CHIPPS model, as tested in the trial, cannot be recommended for adoption and implementation at this time. However, the reduction in DBI, a finding that all other measures favoured the intervention, suggests the merit in assessing this intervention for longer (c. 12 months) and with a stronger primary outcome.

Acknowledgements

This research was supported by the National Institute for Health and Care Research (NIHR) Yorkshire and Humber Patient Safety Translational Research Centre (NIHR YH PSTRC). The views expressed in this article are those of the author(s) and not necessarily those of the NHS, the NIHR or the Department of Health and Social Care.

This report is dedicated to Kate Massey, an active and enthusiastic member of the CHIPPS patient and public involvement team who sadly passed away during the delivery of this study.

Contributions of authors (see *Appendix 7*)

David Wright (https://orcid.org/0000-0003-3690-9593) (Professor of Pharmacy Practice) co-led WP4 to develop the training package for pharmacist independent prescribers and was Co-Chief Investigator for the CHIPPS Programme.

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Christine Bond (https://orcid.org/0000-0003-0429-5208) (Professor of Primary Care, Pharmacy) co-led WP5 to test and refine the service specification, proposed study processes and co-led WP6 to perform a definitive trial, led the WP6 process evaluation and was Principal Investigator for Scotland.

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Garry Barton (https://orcid.org/0000-0001-9040-011X) (Professor of Heath Economics) led WP3 to estimate the cost-effectiveness of the intervention and conducted analysis of the economic data.

Fiona Poland (https://orcid.org/0000-0003-0003-6911) (Professor of Social Research Methodology) co-led WP1 to develop the service specification and supported qualitative analysis in WP6.

Lee Shepstone (https://orcid.org/0000-0001-5524-7818) (Professor of Medical Statistics) conducted statistical analysis and prepared the results for publication.

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Lindsay Dalgarno (https://orcid.org/0000-0001-9994-5861) (Research Fellow) conducted local recruitment of Scotland sites and participants, collected study data and contributed to the WP6 process evaluation analysing and interpreting qualitative datasets.

James Desborough (https://orcid.org/0000-0001-5807-1731) (Senior Lecturer in Pharmacy) co-led WP1, contributed to the delivery of training in WP4 and aided in the delivery of WP5 and WP6 in Norwich.

Joanna Ford (https://orcid.org/0000-0002-8480-393X) (Consultant Geriatrician) contributed to the training, provided specialist advice on medication reviews and working with primary care–based pharmacists and reviewed pharmaceutical care plans and related records to ensure the safety of the participants.

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Janet Gray (Public and Patient Representative) provided service user perspectives throughout the programme and developed plain language summary.

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Bronwen Harry (https://orcid.org/0000-0002-6938-567X) (Junior Clinical Trial Manager) supported the delivery of the definitive trial.

Helen Hill (https://orcid.org/0000-0002-8036-1935) (Independent Consultant) provided expertise in the development of medication management policies and shared experiences of management within the adult social care and care of older people settings.

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Maureen Spargo (Research Fellow) conducted local recruitment of Northern Ireland sites and participants, collected study data and contributed to process evaluation.

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Arnold Zermansky (General Practitioner, Research Fellow) provided general practice expertise and supported local recruitment of general practices.

Ethics statement

Ethics approval was provided by East of England Central Cambridge Research Ethics Committee (for England and Nothern Ireland) – Ref.: 17/EE/0360; and by Scotland A REC – Ref.: 17/SS/0118.

Data-sharing statement

We will make data available to the scientific community with as few restrictions as feasible, while retaining exclusive use until the publication of major outputs. All data requests will be submitted to the corresponding author for consideration.

Data from the randomised controlled trial described in WP6 have been added to the Virtual International Care Homes Trials Archive (VICHTA). Access to anonymised data may be granted following review and appropriate agreements being in place. It is envisaged VICHTA data will be available at www.virtualtrialsarchive.org from December 2023 [see Irvine L, Burton JK, Ali M, Quinn TJ, Goodman C. Protocol for the development of a repository of individual participant data from randomised controlled trials conducted in UK adult care homes (The Virtual International Care Homes Trials Archive, VICHTA)]. Submitted to BMC Trials, August 2020 www.dachastudy.com).

The authors will be happy to discuss potential collaborations regarding other data and will make anonymised data available on that basis.

Publications

WP	Date	Venue	Title	Output	URL (where available), *Also listed as a reference in References in the report	Citation
Prog	4 December 2015	RCN RPS Joint Summit	CHIPPS: Care Homes Independent Pharmacist Prescribing Service: Development and delivery of a cluster randomised controlled trial to determine both its effectiveness and cost-effectiveness.	Poster	Publications and Conferences – Groups and Centres – UEA Scroll down to download the document	Wright D on behalf of the CHIPPS team. CHIPPS: Care Homes Independent Pharmacist Prescribing Service: Development and delivery of a cluster randomised controlled trial to determine both its effectiveness and cost-effectiveness.
WP1	22 July 2016	Health Services Research in Pharmacy Practice conference (HSRPP)	GP views on the potential role for pharmacist independent prescribers within care homes: Care Homes Independent Pharmacist Prescribing Study (CHIPPS)	Presentation	Abstracts of the 19th International Social Pharmacy Workshop, 19–22 July 2016, Aberdeen, UK: International Journal of Pharmacy Practice: Vol 24, No. S2 https://onlinelibrary.wiley.com/toc/20427174/2016/24/S2 Select Oral Abstracts/PDF and scroll down to page 6	Bond C, Lane K, Poland F, Maskrey V, Blyth A, Desborough J, Barton G, Alldred D, Hughes C, Arthur A, Myint P, Massey K, Holland R, Wright D. GP Views on the potential role for pharmacist independent prescribers within care homes: Care Homes Independent Pharmacist Prescribing Study (CHIPPS). Journal of Pharmacy and Practice, 2016, 24:S2
WP1	6–8 July 2016	British Society of Gerontology (BSG) conference	Envisioning pharmacists in care homes for older people: inter-disciplinary research to develop a new role	Poster	https://research-portal.uea.ac.uk/en/publications/envisioning-pharmacists-in-care-homes-for-older-people-inter-disc	Lane K, Alldred D, Blyth A, Bond C, Desborough J, Holland R, Hughes C, Maskrey V, Millar A, Myint P, Wright D, Poland F. Envisioning pharmacists in care homes for older people: Inter-disciplinary research to develop a new role. BSG; 2016, Communities in Later Life: Engaging with Diversity Conference Handbook
WP1	29 August 2016	International Social Pharmacy Workshop Conference – SP16	Care Homes Independent Pharmacist Prescribing Study (CHIPPS): GP views on the potential role for pharmacist independent prescribers within care homes	Presentation	https://onlinelibrary.wiley.com/doi/epdf/10.1111/ijpp.12278 Scroll down to page 6	Bond C.M, Maskrey V, Alldred DP, Blyth A, Daffu-O'Reilly A, Inch J, Millar A, Notman F, Hughes C, Holland R, Wright D. Care Homes Independent Pharmacist Prescribing Study (CHIPPS): GP views on the potential role for pharmacist independent prescribers within care homes. International Journal of Pharmacy and Practice 2016: S2, page 6

WP	Date	Venue	Title	Output	URL (where available), *Also listed as a reference in References in the report	Citation
WP5	12–14 July 2017	SAPC	Care Homes Independent Pharmacist Prescribing Study (CHIPPS). Feasibility study early experiences	Presentation	https://sapc.ac.uk/conference/2017/abstract/care-homes-independent-pharmacist-prescribing-study-chipps-feasibility	Bond C.M, Maskrey V, Alldred DP, Blyth A, Daffu-O'Reilly A, Inch J, Millar A, Notman F, Hughes C, H0olland R, Wright D. Care Homes Independent Pharmacist Prescribing Study (CHIPPS). Feasibility Study early experiences. SAPC ASM 2017, 3A.5
WP4	29 August 2016	RPS Royal Pharmaceutical Society	Development of a training plan for pharmacists to assume responsibility for medicines management in care homes: Results from a rapid review of the literature	Poster	https://onlinelibrary.wiley.com/toc/20427174/2016/24/S3 Select 'Poster/PDF' and scroll down to page 60, No. 0083	Wright D, Norris N, Maskrey V, Blyth A, Lane K, Arthur A, Desborough J, Holland R, Poland F, Bond C, Myint P, Hughes C, Millar A, Alldred D, Massey K. Development of a training plan for pharmacists to assume responsibility for medicines management in care homes: Results from a rapid review of the literature. International Journal of Pharmacy and Practice, 2016, Supplement 3, no. 0083
WP2	5 September 2016	RPS Royal Pharmaceutical Society	Development of a core outcome set (COS) for studies relating to prescribing in care homes: The Care Homes Independent Pharmacist Prescriber Study (CHIPPS)	Poster	https://onlinelibrary.wiley.com/toc/20427174/2016/24/S3 Select 'Medicines Optimisation/PDF' and scroll down to page 17, No. 0161	Millar A, Hughes C, Alldred D, Wright D, Holland R, Maskrey V, Blyth A, Desborough J, Norris N, Arthur A, Barton G, Lane K, Poland F, Shepstone L, Bond C, Myint P, Massey K, Ford J. Development of a core outcome set (COS) for studies relating to prescribing in care homes: The Care Homes Independent Pharmacist Prescriber Study (CHIPPS). International Journal of Pharmacy and Practice, 2016, Supplement 3, no. 0161
WP2	28 September 2016	International Day of the Older Person: Medicines Optimisation Showcase	CHIPPS: Care Home Independent Pharmacist Prescribing Study	Poster	Publications and Conferences – Groups and Centres – UEA Scroll down to download the document	Wright D, Holland R, Alldred D, Arthur A, Barton G, Blyth A, Bond C, Daffu-O'Reilly A, Desborough J, Handford C, Hill H, Inch J, Lane K, Maskrey V, Massey K, Myint PK, Norris N, Notman F, Poland F, Shepstone L, Small I, Swart AM, Symms C, Turner D, Zermansky A. CHIPPS: Care Home Independent Pharmacist Prescribing Study
WP1	5–7 October 2016	European Union Geriatric Medicine Society (EUGMS)	Integrating independent pharmacist prescribers into care homes: Messages from a year of listening and learning	Presentation	Publications and Conferences – Groups and Centres – UEA Scroll down to download the document	Desborough J. Integrating independent pharmacist prescribers into care homes: Messages from a year of listening and learning

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WP	Date	Venue	Title	Output	URL (where available), *Also listed as a reference in References in the report	Citation
WP1, WP2, WP4	6 November 2016	RPS Royal Pharmaceutical Society	Development and delivery of a cluster randomised controlled trial to determine both its effectiveness and cost-effectiveness	Presentation	Publications and Conferences – Groups and Centres – UEA Scroll down to download the document	Wright D on behalf of the CHIPPS team. Development and delivery of a cluster randomised controlled trial to determine both its effectiveness and cost-effectiveness
WP1, WP2, WP4	29 November 2016	National Care Homes Research and Development Forum	Development and delivery of a cluster randomised controlled trial to determine both its effectiveness and cost-effectiveness	Presentation	Publications and Conferences – Groups and Centres – UEA Scroll down to download the document	Wright D on behalf of the CHIPPS team. Development and delivery of a cluster randomised controlled trial to determine both its effectiveness and cost-effectiveness
WP1, WP2, WP4	17 January 2017	Primary Care Pharmacy Association (PCPA) Care Homes Group Symposium 2017	Development and delivery of a cluster randomised controlled trial to determine both its effectiveness and cost-effectiveness	Presentation	Publications and Conferences – Groups and Centres – UEA Scroll down to download the document	Wright D on behalf of the CHIPPS team. Development and delivery of a cluster randomised controlled trial to determine both its effectiveness and cost-effectiveness.
WP1	26 January 2017	National Conference of Scottish Departments of General Practice (NADEGS)	GP views on the potential role for pharmacist independent prescribers within care homes: Care Homes Independent Pharmacist Prescribing Study (CHIPPS): 'There has to be something in it for me'	Presentation	n/a	n/a
WP2	30 January 2017	The Pharmaceutical Care Network Europe	Developing core outcome sets for pharmaceutical care	Workshop	n/a	n/a
WP2	12 April 2017	Trials	Development of a core outcome set for effectiveness trials aimed at optimising prescribing in older adults in care homes	Paper	https://doi.org/10.1186/s13063-017-1915-6 * Reference number[16]	Millar A, Daffu-O'Reilly A, Hughes CM, Alldred DP, Barton G, Bond CM, *et al.* Development of a core outcome set for effectiveness trials aimed at optimising prescribing in older adults in care homes. Trials. 2017;18(1):175

WP	Date	Venue	Title	Output	URL (where available), *Also listed as a reference in References in the report	Citation
WP5	4 September 2017	RPS Royal Pharmaceutical Society	Care Homes Independent Pharmacist Prescribing Study (CHIPPS): Early experiences	Presentation	Publications and Conferences – Groups and Centres – UEA Scroll down to download the document	Bond C on behalf of the CHIPPS team. Care Homes Independent Pharmacist Prescribing Study (CHIPPS): Early experiences
WP5	14 September 2017	Community Pharmacy Scotland (CPS) – University Research Day	Care Homes Independent Pharmacist Prescribing Study (CHIPPS): Feasibility Study – Early experiences	Poster	Publications and Conferences – Groups and Centres – UEA Scroll down to download the document	Bond C, Notman F, Inch J on behalf of the CHIPPS team. Care Homes Independent Pharmacist Prescribing Study (CHIPPS): Feasibility study – Early experiences
WP5	1 October 2017	RPS Royal Pharmaceutical Society Workshop at the Scottish National Seminar	Care Homes Independent Pharmacist Prescribing Study (CHIPPS): Feasibility study	Presentation	Publications and Conferences – Groups and Centres – UEA Scroll down to download the document	Frances Notman on behalf of CHIPPS team. Care Homes Independent Pharmacist Prescribing Study (CHIPPS): Feasibility Study
WP5	5 December 2017	RPS Winter Summit	Care Homes Independent Pharmacist Prescribing Study (CHIPPS): experiences from a non-randomised feasibility study	Presentation	Publications and Conferences – Groups and Centres – UEA Scroll down to download the document	Bond C on behalf of CHIPPS team. Care homes Independent Pharmacist Prescribing Study (CHIPPS): experiences from a non-randomised feasibility study
WP1, WP2, WP4	20 September 2017	CRN Eastern	Development and delivery of a cluster randomised controlled trial to determine both its effectiveness and cost-effectiveness	Presentation	Publications and Conferences – Groups and Centres – UEA Scroll down to download the document	David Wright on behalf of CHIPPS team. Development and delivery of a cluster randomised controlled trial to determine both its effectiveness and cost-effectiveness
WP5	31 January 2018	Primary care Pharmacy Association (PCPA) Care Homes Group Symposium 2018	Care Homes Independent Pharmacist Prescribing Study (CHIPPS): Early experiences	Presentation	Publications and Conferences – Groups and Centres – UEA Scroll down to download the document	Wright D on behalf of the CHIPPS team. Care Homes Independent Pharmacist Prescribing Study (CHIPPS): Early experiences

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WP	Date	Venue	Title	Output	URL (where available), *Also listed as a reference in References in the report	Citation
WP5	18 March 2018	NHS Excellence in Pharmaceutical Care in Grampian One day Conference	Care Homes Independent Pharmacist Prescribing Study (CHIPPS). Feasibility study	Poster	n/a	n/a
WP5	23 July 2018	ISPW – International Social Pharmacy Workshop	Care Homes Independent Pharmacist Prescribing Study (CHIPPS): experiences from a non-randomised feasibility study	Presentation	Publications and Conferences – Groups and Centres – UEA Scroll down to download the document	Bond C on behalf of CHIPPS team. Care-homes Independent Pharmacist Prescribing Study (CHIPPS): experiences from a non-randomised feasibility study.
WP5	6 September 2018	FIP World Congress of Pharmacy and Pharmaceutical Sciences	Care Homes Independent Pharmacist Prescribing Study (CHIPPS): experiences from a feasibility study	Poster	Publications and Conferences – Groups and Centres – UEA Scroll down to download the document	Bond C, Notman F, Inch J on behalf of the CHIPPS team. Care Homes Independent Pharmacist Prescribing Study (CHIPPS): Feasibility study- Early experiences
WP5	2 November 2018	Pharmacy Together – Care Homes – The Next Steps	Care Homes Independent Pharmacist Prescribing Study (CHIPPS): Feasibility study- Early experiences	Poster	Publications and Conferences – Groups and Centres – UEA Scroll down to download the document	Bond C, Notman F, Inch J on behalf of the CHIPPS team. Care Homes Independent Pharmacist Prescribing Study (CHIPPS): Feasibility study- Early experiences
WP5	11 July 2019	Pilot & Feasibility Studies Journal	The Care Home Independent Prescribing Pharmacist Study (CHIPPS)-A non-randomised feasibility study of independent pharmacist prescribing in care homes	Paper	https://doi.org/10.1186/s40814-019-0465-y * Reference number[32]	Inch J, Notman F, Bond C, Alldred D, Arthur A, Blyth A, Daffu-O'Reilly A, Ford J, Hughes C, Maskrey V, Millar A, Myint P, Poland F, Shepstone L, Zermansky A, Holland R, Wright D & On behalf of the CHIPPS Team. The Care Home Independent Prescribing Pharmacist Study (CHIPPS)-A non-randomised feasibility study of independent pharmacist prescribing in care homes. Pilot & Feasibility Studies, 2019;5(89)
Prog	4 May 2018	International Journal of Pharmacy Practice	Not just a 'tick box exercise' – meaningful public involvement in research	Paper	https://doi.org/10.1111/ijpp.12450 * Reference number[72]	Massey K. Not just a 'tick box exercise' – meaningful public involvement in research. The International Journal of Pharmacy Practice. 2018;26(3):197–8.

WP	Date	Venue	Title	Output	URL (where available), *Also listed as a reference in References in the report	Citation
WP4	12 November 2019	International Journal of Pharmacy Practice	Systematic review and narrative synthesis of pharmacist provided medicines optimisation services in care homes for older people to inform the development of a generic training or accreditation process	Paper	https://doi.org/10.1111/ijpp.12591 * Reference number[41]	Wright DJ, Maskrey V, Blyth A, Norris N, Alldred DP, Bond CM, Desborough J, Hughes C, Holland R. Systematic review and narrative synthesis of pharmacist provided medicines optimisation services in care homes for older people to inform the development of a generic training or accreditation process. The International Journal of Pharmacy Practice. 2020;28(3):207–19.
WP5	9 December 2019	ASHP Midyear Clinical Meeting	Care Homes Independent Pharmacist Prescriber Study (CHIPPS): Results from an open-label, non-randomised feasibility study	Presentation	n/a	Wright D on behalf of the CHIPPS team. Care Homes Independent Pharmacist Prescribing Study (CHIPPS): Feasibility test results
WP5	19 August 2019	Dementia Forum, UEA	Care Homes Independent Pharmacist Prescribing Study (CHIPPS): Feasibility test results	Presentation	Publications and Conferences – Groups and Centres – UEA Scroll down to download the document	Wright D on behalf of the CHIPPS team. Care Homes Independent Pharmacist Prescribing Study (CHIPPS): Feasibility test results
WP6	20 May 2020	Trials	Protocol for the process evaluation of a cluster randomised controlled trial to determine the effectiveness and cost-effectiveness of independent pharmacist prescribing in care home: the CHIPPS study	Paper	https://doi.org/10.1186/s13063-020-04264-8 * Reference number[52]	Bond CM, Holland R, Alldred DP, Arthur A, Barton G, Birt L, Blyth A, Desborough J, Ford J, Handford C, Hill H, Hughes C, Maskrey V, Massey K, Myint P, Poland F, Shepstone L, Zermansky A, Wright D & On behalf of CHIPPS Team. Protocol for the process evaluation of a cluster randomised controlled trial to determine the effectiveness and cost-effectiveness of independent pharmacist prescribing in care home: the CHIPPS study. Trials. 2020;21(1):439.
WP1	2 March 2020	Health and Social Care in the Community	Everyone needs to understand each other's systems: Stakeholder views on the acceptability and viability of a Pharmacist Independent Prescriber role in care homes for older people in the UK	Paper	https://doi.org/10.1111/hsc.12970[14] * Reference number[14]	Lane K, Bond C, Wright D, Alldred DP, Desborough J, Holland R, Hughes C, Poland F. 'Everyone needs to understand each other's systems': Stakeholder views on the acceptability and viability of a Pharmacist Independent Prescriber role in care homes for older people in the UK. Health & Social Care in the Community. 2020;28(5):1479–87

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WP	Date	Venue	Title	Output	URL (where available), *Also listed as a reference in References in the report	Citation
WP6	21 January 2020	Trials	Protocol for a cluster randomised controlled trial to determine the effectiveness and cost-effectiveness of independent pharmacist prescribing in care home: the CHIPPS study	Paper	https://doi.org/10.1186/s13063-019-3827-0 * Reference number[52]	Bond CM, Holland R, Alldred DP, Arthur A, Barton G, Blyth A, *et al*. Protocol for a cluster randomised controlled trial to determine the effectiveness and cost-effectiveness of independent pharmacist prescribing in care homes: the CHIPPS study. Trials. 2020;21(1):103.
WP6	1–3 July 2020	British Society of Gerontology (BSG) conference	A pharmacist calls: exploring the role of pharmacist independent prescribers in care homes across the UK	Abstract Cancelled due to the COVID-19 pandemic	n/a	Birt L, Delgarno L, Bond C, Poland F, Wright D. A pharmacist calls: exploring the role of pharmacist independent prescribers in care homes across the UK
WP6	9–11 September 2020	SSM Society for Social Medicine and Population Health, Scientific Meeting 2020	The CHIPPS study: a cluster randomised controlled trial to determine the effectiveness and cost-effectiveness of independent pharmacist prescribing in care homes	Abstract Virtual conference	n/a	Holland R on behalf of CHIPPS team. The CHIPPS study: a cluster randomised controlled trial to determine the effectiveness and cost-effectiveness of independent pharmacist prescribing in care homes
WP6	19 June 2020	RPS Science & Research Summit 2020	Care Homes Independent Pharmacist Prescriber Study (CHIPPS): Using MRC guidance on complex interventions to effectively deliver a UK wide trial	Abstract Cancelled due to the COVID-19 pandemic	Abstracts – 2020 – International Journal of Pharmacy Practice – https://onlinelibrary.wiley.com/doi/full/10.1111/ijpp.12633 Scroll down to abstract number 4	Wright D., Bond C, Hughes C, Alldred A. Care Homes Independent Pharmacist Prescriber Study (CHIPPS): Using MRC guidance on complex interventions to effectively deliver a UK wide trial. The International Journal of Pharmacy Practice. 2020; Abstracts, 4
WP6	16–17 April 2020	Health Services Research in Pharmacy Practice (HSRPP)	Development and testing of an effective model for monitoring patient safety within the Care Homes Independent Pharmacist Prescribing Study (CHIPPS)	Abstract Cancelled due to the COVID-19 pandemic	Publications and Conferences – Groups and Centres – UEA Scroll down to download the document	Wright D, Bond C, Hughes C, Alldred D, Holland R on behalf of the CHIPPS team. Development and testing of an effective model for monitoring patient safety within the Care Homes Independent Pharmacist Prescribing Study (CHIPPS)

WP	Date	Venue	Title	Output	URL (where available), *Also listed as a reference in References in the report	Citation
WP6	15 July 2020	Society of Academic Primary Care (SAPC)	The CHIPPS study: a cluster randomised controlled trial to determine the effectiveness and cost-effectiveness of independent pharmacist prescribing in care homes	Abstract Cancelled due to the COVID-19 pandemic	https://sapc.ac.uk/conference/2020/abstract/chipps-study-cluster-randomised-controlled-trial-determine-effectiveness | SAPC	Bond C, Wright D, Holland R, Alldred D, Hughes C, Poland F on behalf of the CHIPPS Team. The CHIPPS study: a cluster randomised controlled trial to determine the effectiveness and cost-effectiveness of independent pharmacist prescribing in care homes. SAPC ASM 2020, U.1
WP5	11 February 2020	SAGE Research Methods Cases	Lessons learned from CHIPPS (Care Homes Independent Pharmacist Prescribing Study): how feasibility studies informed ultimate randomised controlled trial design	Paper	https://research-portal.uea.ac.uk/en/publications/lessons-learned-from-chipps-care-homes-independent-pharmacist-pre	Bond C, Alldred D, Hughes C, Holland R, Poland F, Wright D. Lessons learned from CHIPPS (Care Homes Independent Pharmacist Prescribing Study): how feasibility studies informed ultimate randomised controlled trial design. 2020; SAGE Research Methods Cases Part 2
WP4	21 May 2021	International Journal of Pharmacy Practice	Development and feasibility testing of an evidence-based training programme for pharmacist independent prescribers responsible for the medicines-related activities within care homes	Paper	https://doi.org/10.1093/ijpp/riab025	Wright, DJ., Blyth, A., Maskrey, V., Norris, N., Bond, CM., Hughes, CM., Alldred, DP., Holland, RC., CHIPPS Team. International Journal of Pharmacy Practice. 29(4):376–84
WP6	2 October 2021	BMC Health Services Research	Process evaluation for the Care Homes Independent Pharmacist Prescriber Study (CHIPPS)	Paper	https://doi.org/10.1186/s12913-021-07062-3	Linda Birt, Lindsay Dalgarno, David J Wright, Mohammed Alharthi, Jackie Inch, Maureen Spargo, Jeanette Blacklock, Fiona Poland, Richard C Holland, David P. Alldred, Carmel M. Hughes & Christine M. Bond on behalf of the CHIPPS study team
WP4	15 July 2022	BMC Medical Education	Evaluation of a training programme for Pharmacist Independent Prescribers in a care home medicine management intervention	Paper	https://doi.org/10.1186/s12909-022-03575-5	Linda Birt, Lindsay Dalgarno, Christine M. Bond, Richard C Holland, David P. Alldred, Carmel M. Hughes, Annie Blyth, Laura Watts & David J. Wright, on behalf of the CHIPPS study team BMC Medical Education 22; 551

Planned remaining publications

Short title	Title
Main trial	Effectiveness and cost-effectiveness of integrating a pharmacist independent prescriber into care homes for older people. A cluster randomised controlled trial.
The qualitative benefits	Pharmacist Independent Prescriber a linchpin in multidisciplinary primary care: a qualitative investigation of the impact of a pharmacy-intervention in UK care homes.
Researcher reflection	From study protocol to sitting in a cupboard: account of trial researchers experience of set-up and data collection during an RCT sited in care homes
The NOMAD results	The 'work' of normalising the place of prescribing pharmacists within UK care homes: understanding supportive and disruptive practices using Normalization Process Theory
The logical model methodology	Logic models a tool to enhance understanding of the relationships between resources, activities, outputs and the outcomes and impact of a programme of practice

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Appendix 1 Synopsis tables, figures and boxes

Work package 1 tables

TABLE 1 Topic guide for focus groups and interviews linked to domains in the theoretical domains framework (where applicable)

	Question
	What is your role?
Knowledge Professional role Skills Environmental context	How are medicines managed at the moment in your experience for care home residents?
Knowledge Beliefs about capabilities of a PIP service? Beliefs about consequences Skills	What might be the key ingredients?
Beliefs about capabilities Environmental context and resources	What organisational barriers could affect putting this into practice?
Social professional role and identity Social influences	What professional barriers could affect putting this into practice?
Intention Goals	What might be the solutions to these barriers
Skills Behavioural regulation	What could we include in training pharmacists undertaking this role?
	Is there anything else important about this proposed service you want to mention?

PIP, pharmacist independent prescriber.

TABLE 2 Number of participants per stakeholder group

Stakeholder group	Study sites involved	No. of focus groups (groups)	Interviews	Total
Pharmacists	All 4 sites	25 (4)	2	27
General Practitioners	All 4 sites	24 (4)	5	29
Care home managers	All 4 sites	3 (1)	3	6
Care home staff	England (2) and Northern Ireland	6 (2)	3	9
Residents and relatives	England and Scotland	7 residents, 7 relatives	0	14
Total		72	13	85

TABLE 3 Characteristics of pharmacy professional participants

Sector	Prescribing pharmacists	Non-prescribing pharmacists	Pharmacy technician	Total
Primary care	2	13		15
Community	1	9	1	11
Portfolio[a]	1	–		1
Total	4	22	1	27

a Employed in a split role across primary care and community pharmacy.

Work package 2 tables

TABLE 4 Delphi questionnaire round 1 results

Outcome	Mean Delphi score	Median Delphi score	Respondents scoring 7–9 'critically important' (%)	Respondents scoring 1–3 'not important' (%)	Result (in, out or no consensus)
Number of medications (and associated costs)	7.7	8.5	83.3	0	In
Medication wastage (and associated costs)	6.6	7	68.4	10.5	No consensus
Polypharmacy (≥4 medicines)	6.5	7	57.9	10.5	No consensus
Medication appropriateness (potentially inappropriate prescribing)	8.2	9	84.2	0	In
Duplicate drugs	7.2	7.5	72.2	5.6	In
Use of antipsychotics	7.4	8	73.7	0	In
Medication changes made (by anyone)	6.9	8	63.2	10.5	No consensus
Number of medication reviews conducted (by anyone)	6.7	7	63.2	10.5	No consensus
Admissions to hospital (and associated costs)	8.2	8	100	0	In
Accident & emergency visits (and associated costs)	7.8	8	83.3	0	In
Visits to outpatients (and associated costs)	5.3	5	26.3	31.6	No consensus
Visits to/from GP (and associated cost)	7.1	7	63.2	5.3	No consensus
Visits to/from nurse (and associated cost)	6.1	6	42.1	5.3	No consensus
Adverse drug events	8.4	9	94.7	0	In
Falls	7.4	7	84.2	0	In
Acute kidney injury	6.7	6	46.7	0	No consensus

TABLE 4 Delphi questionnaire round 1 results (*continued*)

Outcome	Mean Delphi score	Median Delphi score	Respondents scoring 7–9 'critically important' (%)	Respondents scoring 1–3 'not important' (%)	Result (in, out or no consensus)
Prescribing errors	7.9	8	89.5	5.3	In
Harmful interactions	7.7	8	84.2	5.3	In
All-cause mortality	7.5	9	78.9	5.3	In
Physical functioning	6.5	7	57.9	15.8	No consensus
Behaviour	6.6	7	63.2	5.3	No consensus
Cognitive functioning	6.6	7	57.9	5.3	No consensus
Depression	6.3	7	55.6	5.6	No consensus
Quality of life	7.7	8	83.3	0	In
Compliance with NICE guidelines	6.3	7	52.6	10.5	No consensus
Compliance with medicines	6.7	7	68.4	5.3	No consensus
Care home staff job satisfaction	5	5	26.3	36.8	No consensus
Efficiency of medication administration by care home staff	6.3	6	42.1	5.3	No consensus
Accuracy of administration of medications by care home staff	6.9	7	57.9	5.3	No consensus

GP, general practitioner; NICE, National Institute for Health and Care Excellence.

TABLE 5 Delphi questionnaire round 2 results

Outcome	Mean	Med	Respondents scoring 7–9 'critically important' (%)	Respondents scoring 1–3 'not important' (%)	Consensus result (in, out or no consensus)
Number of medications	7.3	8.0	83.3	11.1	In
Costs of prescribed medication	6.3	7.0	61.1	11.1	No consensus
Medication wastage (and associated costs)	6.6	7.0	66.7	5.6	No consensus
Polypharmacy (≥4 medicines)	6.6	7.0	66.7	5.6	No consensus
Medication changes made (by anyone	6.5	7.0	55.6	5.6	No consensus
Number of medication reviews conducted (by anyone)	6.6	7.0	66.7	5.6	No consensus

continued

TABLE 5 Delphi questionnaire round 2 results (*continued*)

Outcome	Mean	Med	Respondents scoring 7–9 'critically important' (%)	Respondents scoring 1–3 'not important' (%)	Consensus result (in, out or no consensus)
Visits to outpatients (and associated costs)	5.6	5.0	33.3	5.6	No consensus
Visits to/from GP (and associated cost)	6.6	6.5	50.0	0	No consensus
Visits to/from nurse (and associated cost)	6.1	6.5	50.0	0	No consensus
Acute kidney injury	6.8	7.0	53.3	0	No consensus
Physical functioning	6.5	7.0	61.1	5.6	No consensus
Behaviour	6.9	7.0	61.1	5.6	No consensus
Cognitive functioning	6.8	7.0	61.1	0	No consensus
Depression	6.7	7.0	61.1	0	No consensus
Compliance with NICE guidelines	6.4	7.0	55.6	16.7	No consensus
Compliance with medicines	6.9	7.5	61.1	5.6	No consensus
Care home staff job satisfaction	5.1	5.0	22.2	5.6	No consensus
Efficiency of medication administration by care home staff	6.4	6.0	38.9	0	No consensus
Accuracy of administration of medications by care home staff	7.3	7.0	55.6	0	No consensus
Anticholinergic burden	7.3	7.0	75.0	0	In

GP, general practitioner; NICE, National Institute for Health and Care Excellence.

TABLE 6 Final core outcome set for effectiveness studies in optimising prescribing in older adults in care homes

Outcome	Explanation from Delphi questionnaire
Medication appropriateness (potentially inappropriate prescribing)	Potentially inappropriate prescribing 'encompasses the use of medicines that introduce a significant risk of an adverse drug-related event where there is evidence for an equally or more effective but lower-risk alternative therapy available for treating the same condition … also includes the use of medicines at a higher frequency and for longer than clinically indicated, the use of multiple medicines that have recognised drug-drug interactions and drug-disease interactions, and importantly, the under-use of beneficial medicines that are clinically indicated but not prescribed for ageist or irrational reasons' (Gallagher *et al.*, 2007)[73]
Number of prescribed medicines	Number of medications prescribed for a care home resident

TABLE 6 Final core outcome set for effectiveness studies in optimising prescribing in older adults in care homes (*continued*)

Outcome	Explanation from Delphi questionnaire
Duplicate drugs	'Duplicate drugs' described a situation where an individual is prescribed two medicines of the same pharmacological class, e.g. the prescribing of two concurrent opiates (O'Mahony *et al.*)[47]
Use of antipsychotics	The prescription of antipsychotic medicines in care homes residents. 'Antipsychotic drugs are also known as "neuroleptics" and (misleadingly) as "major tranquillisers". In the short term, they are used to calm disturbed patients whatever the underlying psycho-pathology … The balance of risks and benefits should be considered before prescribing antipsychotic drugs for elderly patients' (Joint Formulary Committee, 2016)[74]
Harmful interactions	A 'harmful interaction' in a care home resident may describe the prescription of a medication that causes or has the potential to cause a clinically significant drug-drug or drug-disease interaction. A drug-drug interaction is when a medicine affects the pharmacological effect of another medicine. A drug-disease interaction is when a medicine, which may be used to treat or prevent a disease, can have a detrimental effect on another existing disease/condition in the individual (Mallet *et al.*)[75]
Anticholinergic burden	This refers to the anticholinergic burden associated with care home residents' medication regimens. Medicines with anticholinergic effects are commonly prescribed for various conditions; however, increased overall exposure to anticholinergics has been associated with an increased risk of cognitive impairment, falls and all-cause mortality in older adults (Ruxton *et al.*)[76]
Adverse drug events	Adverse drug events experienced by care home residents. 'An adverse drug event is any undesirable event experienced by a patient whilst taking a medicine, including physical harm, mental harm or loss of function' (Bates *et al.*)[77]
Prescribing errors	Prescribing errors in care home residents' medication regimens. A prescribing error is 'a prescribing decision that results in an unintentional, significant reduction in the probability of treatment being timely and effective or a significant increase in the risk of harm, when compared with that in generally accepted practice' (Dean *et al.*)[78]
Falls	Falls occurring amongst care home residents. A fall is 'an event that results in a person coming to rest inadvertently on the ground or floor or other lower level' (World Health Organization)[79]
Quality of life	A measure of care home residents' quality of life. Quality of life is 'a ubiquitous concept that has different philosophical, political and health-related definitions. Health-related quality of life includes the physical, functional, social and emotional well-being of an individual' (Fallowfield)[80]
All-cause mortality	All deaths of care home residents
Admissions to hospital (and associated costs)	The number of care home residents having a hospital admission/number of hospital admissions per resident (and the associated cost)
Accident and Emergency visits to hospital (and associated costs)	The number of care home residents attending Accident and Emergency departments/ number of Accident and Emergency visits per resident (and the associated cost)

Work package 4 tables

TABLE 7 Summary of studies, services and outcomes included within the review

Author	Location	Year	Setting	Study type	Service	Main outcome
Roberts, MS, *et al.*[43]	Australia	2001	Nursing home	Randomised controlled trial	Medication review	Reduction in the number of medicines
King, MA, *et al.*[81]	Australia	2001	Nursing home	Service evaluation	Medication review	Non-significant reductions in medication orders, cost and mortality
Smith, MA, *et al.*[82]	Australia	2002	Nursing home	Service evaluation	Medication review	Significant reduction in the number of doses of regular medicine prescribed
Crotty, M, *et al.*[83]	Australia	2004	Residential aged care	Randomised controlled trial	Pharmacist supported patient transit from hospital	Improved pain control and hospital usage in the intervention arm
Beer, C, *et al.*[84]	Australia	2011	Residential aged care	Randomised controlled trial	Withdrawal of one target medicine	Trial acceptable to patients
Khalil, H[85]	Australia	2011	Aged care facility	Service evaluation	Medication review	Clinical recommendations implemented
Verrue, CL, *et al.*[86]	Belgium	2010	Nursing home	Service evaluation	Training on medication administration	Reduction in medication administration errors
Verrue, C, *et al.*[87]	Belgium	2012	Nursing home	Controlled study	Medication review service	Modest improvement in medication appropriateness
Soon, JA[88]	Canada	1985	Nursing home	Service evaluation	Adverse drug reaction monitoring program	Earlier detection and resolution of adverse drug reactions
Kroger, E, *et al.*[89]	Canada	2015	Nursing home	Service evaluation	Medication review	Service to optimise medicine use is feasible
Norgaard, LS, *et al.*[90]	Denmark	2015	Residential care setting	Service evaluation	Medication review and medicine reconciliation	Reduction in drug-related problems
Legueline, G, *et al.*[91]	France	2013	Nursing home	Controlled study	Medication review	Significant reduction in adverse drug event risk
Frankenthal, D, *et al.*[92]	Israel	2014	Chronic geriatric facility	Randomised controlled trial	Medication review with STOPP/START	Significant reduction in the number of medicines
Finkers, F, *et al.*[93]	The Netherlands	2007	Nursing home	Service evaluation	Medication review	Significant reduction in drug-related problems

TABLE 7 Summary of studies, services and outcomes included within the review (*continued*)

Author	Location	Year	Setting	Study type	Service	Main outcome
Stujit, CCM, *et al.*[94]	The Netherlands	2008	Residential home	Service evaluation	Medication review	Significant improvement in medication appropriateness
Stujit, CCM, *et al.*[95]	The Netherlands	2013	Nursing home	Service evaluation	Training in medication administration for patients with dysphagia	Significant reduction in medication administration errors
Connolly, MJ, *et al.*[96]	New Zealand	2014	Long-term care facility	Cluster randomised controlled trial	Nurse-led staff education Multi-professional review	No effect on hospitalisations and mortality; fewer acute admissions
Ruths, S, *et al.*[97]	Norway	2003	Nursing home	Service evaluation		
Bellingan, M, *et al.*[98]	South Africa	1996	Elderly care facility	Service evaluation	Medication review	Significant reduction in drug-related problems and polypharmacy
Jodar-Sanchez, F, *et al.*[99]	Spain	2014	Nursing home	Controlled study	Medication review	Number of medicines significantly reduced
Bergman, A, *et al.*[100]	Sweden	2006	Nursing home	Service evaluation	Medication appropriateness review	70% of prescriptions potentially inappropriate
Kuo, CN, *et al.*[101]	Taiwan	2013	Nursing home	Service evaluation	Medicine reconciliation	Reduction in medication discrepancies
Newman, GR[102]	UK	1982	Residential aged care	Service evaluation	Medication handling intervention	Positive feedback on scheme from participants
Narula, N, *et al.*[103]	UK	1992	Residential home	Service evaluation	Review of medication administration problems	Problem report form developed
Rees, JK, *et al.*[104]	UK	1995	Residential home	Service evaluation	Medication review	Clinical recommendations implemented
Furniss, L, *et al.*[105]	UK	2000	Nursing home	Randomised controlled trial		Significant reduction in medicines; no effect on mortality
Zermansky, A, *et al.*[51]	UK	2006	Care home for elderly people	Randomised controlled trial	Medication review	Significant difference in the number of drug changes per patient

continued

TABLE 7 Summary of studies, services and outcomes included within the review (*continued*)

Author	Location	Year	Setting	Study type	Service	Main outcome
Alldred, DP, *et al.*[106]	UK	2007	Care home for elderly people	Randomised controlled trial	Medication review	Clinical recommendations implemented
Saaed, M, *et al.*[107]	UK	2010	Nursing home	Service evaluation	Audit medication administration records	Reduction in medication errors
Patterson, SM, *et al.*[108]	UK	2011	Nursing home	Randomised controlled trial	Medication review	Significant improvement in antipsychotic medication appropriateness
Hampson, N[109]	UK	2012	Care home	Service evaluation	Medication review	Reduction in medication costs
Cooper, JW, *et al.*[110]	USA	1978	Long-term care facility	Service evaluation	Medication review	Number of medicines reduced
Cooper, JW[111]	USA	1985	Long-term care facility	Service evaluation	Medication review	Reduction in drug use
Andolesk, K[112]	USA	1987	Long-term care facility	Service evaluation	Medication review	Number of medicines reduced
Pucino, F[113]	USA	1988	Long-term care facility	Service evaluation	Therapeutic drug monitoring service	Anecdotal improvements in patient control
Cooper, JW[114]	USA	1995	Nursing facility	Controlled study	Medication review	Significant reduction in hypoglycaemic and hyperglycaemic events in home where the pharmacist is authorised to make changes independently
Cooper, JW[115]	USA	1997	Geriatric nursing facility	Service evaluation	Medication review	Clinical recommendations implemented
Jeffrey, S, *et al.*[116]	USA	1999	Long-term care facility	Service evaluation	Medication review	Reduction in the number of unnecessary medicines
Elliott, RA, *et al.*[117]	USA	1999	Nursing home	Service evaluation	Medication review	Reduction in medication costs
Lai, LL, *et al.*[118]	USA	2001	Nursing home	Service evaluation	Antibiotic medication review	Clinical recommendations implemented
Christensen, D, *et al.*[119]	USA	2004	Nursing home	Service evaluation	Medication review	Reduction in polypharmacy
Crotty, M, *et al.*[120]	USA	2004	Long-term care facility	Randomised controlled trial	Medication review	Significant improvement in medication appropriateness
Buhr, GT, *et al.*[121]	USA	2006	Nursing home	Service evaluation	Quality improvement project to improve pain management	Staff pain management knowledge improved

TABLE 7 Summary of studies, services and outcomes included within the review (*continued*)

Author	Location	Year	Setting	Study type	Service	Main outcome
Cooper, JW, *et al.*[122]	USA	2007	Geriatric nursing facility	Service evaluation	Medication review	Clinical recommendations implemented
Hursh, D, *et al.*[123]	USA	2010	Nursing facility	Service evaluation	Improving antipsychotic medication use	Reduced antipsychotic medication use
Gunning, K, *et al.*[124]	USA	2010	Assisted living facility	Service evaluation	Integration of pharmacists into the team	Students valued the experience, felt valued as medication experts
Lapane, KL, *et al.*[125]	USA	2011	Nursing home	Randomised controlled trial	Implementation of Geriatric Risk Assessment MedGuide	Significantly lower rate of potential delirium onset
Motycka, C, *et al.*[126]	USA	2012	Long-term care facility	Service evaluation	Warfarin medication review	Significantly greater proportion of patients in the therapeutic range
Zarowitz, BJ, *et al.*[127]	USA	2012	Nursing home	Service evaluation	Quality improvement project to improve methotrexate administration	Reduction in methotrexate administration errors
Nye, A[128]	USA	2012	Nursing home	Service evaluation	Medication review	Clinical recommendations implemented
Phillippe, HM[129]	USA	2012	Long-term care facility	Service evaluation	Anticoagulation service	Improved time in therapeutic range
Lemay, CA, *et al.*[130]	USA	2013	Nursing home	Survey	Education needs for staff regarding antipsychotic medication	Multifaceted intervention to improve care home staff knowledge regarding the antipsychotics required

TABLE 8 Identified codified and practical knowledge requirements

Codified knowledge		Practical knowledge
Therapeutic area (*n*)	**Clinical area (*n*)**	**Activity (*n*)**
Psychotropic (15)	Dementia (10)	Medication review (40)
Cardiovascular (11)	Pain (5)	Medicine discontinuation (24)
Gastrointestinal (6)	Diabetes (4)	Medicine change (23)
Benzodiazepines (4)	Cardiovascular disease (4)	Monitoring recommendations (20)
Analgesia (4)	Stroke (2)	Multidisciplinary intervention (20)
Nutrition and blood (3)	Dysphagia (2)	Medicine initiation (12)
Anticoagulants (2)	Infection (1)	Care home staff training (8)
Antimicrobials (2)	Behavioural problems (1)	Error management (6)
Urinary tract (1)	Pulmonary disease (1)	Medicine reconciliation (4)
	Fall prevention (1)	Use of the STOPP/START tool (2)
		Medicine administration (1)

Work package 5 tables

TABLE 9 Baseline and follow-up recruitment and retention

	Total number invited	Total number of EOIs (%)	Number participating at baseline	Number participating at follow-up (%)
GP practices[a]	346	33 (9.5)	4	4 (100)
PIPs	22	14 (57.1)	4	4 (100)
Care homes	6	n/a	6	6 (100)
Residents	86	53 (62.2)	40	40 (100); 2 died

EOI, expression of interest; GP, general practitioner; PIP, pharmacist independent prescriber.

a The number of GP practices invited was high as two sites sent invitations to all GP practices (300) in their area whereas the other two sites only sent invitations to GP practices that provided a service to care homes or through a PIP working with the practice.

TABLE 10 Outcome measures: data generated by the proposed measure at baseline and follow-up

Measure	Baseline	Follow-up
STOPP		
Mean (per patient) (range) SD	3.27 (0–7) 1.96	2.54 (0–5) 1.24
Median (IQR)	3.0 (2.0–4.25)	2.0 (2.0–3.25)
START		
Mean (per patient) (range) SD	2.35 (0–6) 1.42	2.05 (0–6) 1.55
Median (IQR)	2 (1–3)	2.0 (1.0–3.0)
Falls in the past 3 months (total number)[a]	12	10
Falls in the past 3 months (number of patients falling)	9/40 (20%)	7/40 (17.5%)
Falls per person		
Mean (range) SD	0.33 (0–3) 0.694	0.25 (0–2) 0.588
Median (IQR)	0.0 (0–0)	0.0 (0–0)
	(*n* = 40)	(*n* = 38)
Barthel Index		
Mean (range) SD	6.53 (0–17) 5.50	6.38 (0–19) 5.51
Median (IQR)	6.5 (1–9)	6.0 (1.0–10.0)
MMSE		
Mean (range) SD	20.13 (9–30) 7.03	20.79 (11–29) 5.90
Median (IQR)	21.0 (14.25–25.5)	20.5 (15–26)
Number	(*n* = 16)	(*n* = 14)
Drug Burden Index		
Score 0 (*n* (%))	14 (35%)	14 (35%)
Drug Burden Index[b]		
N Score > 0 (*n* (%)	26 (65%)	26 (65%)
Mean (range) SD	1.11 (0.14–3.37) 0.74	0.93 (0.14–3.34) 0.67
Median (IQR)	1.035 (0.5–1.5)	0.76 (0.5–1.17)
Number of medicines per patient[c]		
Mean (range) SD)	9.3 (1–26) 5.9	8.7 (0–31) 6.0
Median (IQR)	8.5 (6–12)	8 (5–10)
Total QUALIDEM		
Mean (range) SD	93 (67–130) 15.55	77.85 (31–109) 18.32
Median (IQR)	91.0 (79.25–101.5)	79.0 (71.0–92.5)
Care relationship		
Mean (range) SD	15.33 (10–23) 3.53	15.83 (4–21) 5.00
Median (IQR)	14.0 (12.25–18.0)	16.0 (13.0–20.0)

continued

TABLE 10 Outcome measures: data generated by the proposed measure at baseline and follow-up (*continued*)

Measure	Baseline	Follow-up
Positive affect		
Mean (range) SD	14.33 (6–24) 5.50	12.43 (2–18) 4.33
Median (IQR)	14.5 (9.0–18.75)	14.0 (8.5–16.0)
Negative affect		
Mean (range) SD	8.25 (3–12) 2.25	5.35 (0–9) 2.28
Median (IQR)	9.0 (6.0–10.0)	5.0 (4.0–7.0)
Restless/tense behaviour		
Mean (range) SD	8.48 (3–12) 2.59	5.13 (0–9) 2.41
Median (IQR)	9.0 (6.25–10.0)	5.0 (4.0–7.0)
Positive self-image		
Mean (range) SD	7.88 (3–11) 1.88	6.23 (0–9) 2.24
Median (IQR)	8.0 (6.0–9.0)	6.0 (4.25–8.75)
Social relations		
Mean (range) SD	12.03 (7–22) 3.68	11.13 (1–18) 4.79
Median (IQR)	11.0 (10.0–13.0)	10.5 (8.25–15.75)
Social isolation		
Mean (range) SD	6.00 (3–11) 1.45	4.60 (10–9) 1.99
Median (IQR)	6.0 (5.0–7.0)	5.0 (4.0–6.0)
Feeling at home		
Mean (range) SD	8.88 (6–14) 2.22	9.68 (1–12) 2.74
Median (IQR)	8.0 (7.0–11.0)	11.0 (8.0–12.0)
EQ-5D-5L (self)[d]		
Mean (range) SD	0.449 (−0.281 to −0.951) 0.335	0.572 (−0.027 to −1.000) 0.327
Median (IQR)	0.379 (0.279–0.719)	0.585 (0.34–0.77)
N	16	13
EQ-5D-5L (proxy)[d]		
Mean (range) SD	0.434 (−0.027 to −0.896) 0.229	0.406 (−0.019 to −0.887) 0.236
Median (IQR)	0.356 (0.267–0.664)	0.341 (0.206–0.581)
N	39	38
EQ-5D-5L baseline VAS (self)[d]		
Mean (range) SD	57.5 (0–100) 31.9	62.9 (10–99) 30.2
Median (IQR)	67.5 (32.5–75)	75 (30–85)
N	14	11

TABLE 10 Outcome measures: data generated by the proposed measure at baseline and follow-up (*continued*)

Measure	Baseline	Follow-up
EQ-5D-5L baseline VAS (proxy)[d]		
Mean (range) SD	51.6 (2–99) 23.9	50.2 (2–90) 27.3
Median (IQR)	57.5 (38.75–66.25)	50 (30–70)
N	38	37
Adverse drug events related to the intervention in the past 3 months	0/40 (0%)	0/40 (0%)

IQR, interquartile range; MMSE, Mini-Mental State Examination; NICE, National Institute for Health and Care Excellence; SD, standard deviation; VAS, visual analogue scale.
a NICE (2017) defines a fall as an unintentional or unexpected loss of balance resulting in coming to rest on the floor, the ground, or an object below knee level.
b Calculation based only on those with any Drug Burden Index score.
c Includes topical preparations.
d EQ-5D-5L index obtained from Devlin (2016) on *https://euroqol.org*, accessed June 2017.

TABLE 11 Themes on views of the service and exemplar quotes

Theme	Sub theme	Quote no., quote, interviewee type
Perceived benefits of the service	Improved patient care	*1. 'I think you know overall it just had led to better patient care, better medicines management you know for those patients and nursing homes'.* ***(GP)***
		2. *'She's very professional in the fact that you know that she knows what she's talking about so there's no question about it, XXX (PIP) gonna know the answer for us and she doesn't take time up to do anything'.* ***(Care home manager)***
	Improved patient safety	***3.*** *'Swallowing issues, what medicines are suitable for crushing, different formulations especially when we're looking at medications where people can no longer take, the refusals, all due to their cognitive behaviours, you know, looking at whether we should, well you know we know about crushing and then changing it to liquid form, having the pharmacist part of the care home makes it safer again for that reason because GPs will just automatically say oh well crush because we can't afford to give you liquid'.* ***(Care home manager)***
	Saving staff time and effort – more efficient	***4.*** *'Sometimes I find when you go through GPs it takes much longer if, you know, if you ask them to reduce something, … then they pass it on. I found with XXX (PIP) after her phone call, it's implemented straight away, you know, there's no hanging around, which is good, I like that'.* ***(Care home manager)***
		5. *'I also know there's a professional behind me that's doing something that I don't have to double check at all. I don't have to turn round and double check what she's doing as this day of audits and auditing everything that happens, with somebody like that around I have got somebody else to share the job'* ***(Care home manager)***
		6. *'Well I really welcomed it because I think all the care homes could do with an independent practitioner …… having to wait 48 hours for an urgent prescription and it's just been horrendous before you came in regards to trying to get what we need from the surgery so having XXX (PIP) here was wonderful'.* ***(Dementia nurse)***

continued

TABLE 11 Themes on views of the service and exemplar quotes (*continued*)

Theme	Sub theme	Quote no., quote, interviewee type
		7. *'I have said to her, you know, could you explain to the relatives about this for me. It takes another 20 minutes out of my day'.* ***(Care home manager)***
Perceived benefits of the service	Saving staff time and effort – more efficient	**8.** *'I think the pharmacist was able to spend more time with us and the resident looking at the medications that they were on, speaking to the staff who knew the residents really well and getting a detailed history which unfortunately we know the GPs haven't got the time to do that so we thought it was really …… really helpful, yeah'.* ***(Care home manager)***
		9. *The most worthwhile thing is that it's not a GP that's doing it, that it's someone qualified and the right person to do it … it's good that that's done with a back-up from us and it's done in the most efficient time-responsible way which is I guess having a pharmacist to do it'.* ***(GP)***
		10. *'It was very good. XXX (PIP) did most of the work. I had some involvement with looking at the plans and reviewing them and also kind of any bits of advice, but she did most of the work herself and led it herself so I wasn't hugely involved'.* ***(GP)***
		11. *'It didn't really impede on the day to day running of the home, it wasn't really intrusive to the residents' day to day lives'.* ***(Deputy care home manager)***
		12. *'There was some increased workload for the staff because of the time that we needed to give to the pharmacist to discuss the resident in more detail and sought of you know providing the relevant care plans … but generally any changes were done at the beginning of the monthly cycle so there wasn't that much extra work involved'.* ***(Care home manager)***
		13. *'Absolutely, if we could have a XXX (PIP) in every single practice, and I know that's hopefully what's gonna happen, it would make my job so much easier …. I can see it could make my job a lot less stressful if we had that service right across the board'.* ***(Care home manager)***
Perceived disadvantages of the service	Knowledge of the patient	**14.** *'With the lady in question she was saying but the pharmacist doesn't know her, the pharmacist doesn't know her history'.* ***(Care home manager)***
		15. *'because XXX (PIP) is going in and dealing with maybe some of the issues that we would have dealt with in the past, that there's the potential that you see your patients less and you have less of a close relationship with some patients in the nursing homes so that would be a potential negative going forward …. you would have less contact with the nursing home staff cos quite a number of our contacts with nursing homes are you know medication issues so if a pharmacist was picking up them, yeah, we may have less contact, but I don't think there would be any major negative impact from such a scheme'.* ***(GP)***

GP, general practitioner; PIP, pharmacist independent prescriber.

Work package 6 tables

TABLE 12 Trial arms at baseline

	Intervention, *N* = 449 residents	Control, *N* = 427 residents	Overall, *N* = 876 residents
Age at consent in years, mean (SD)	85.1 (7.7)	85.4 (7.6)	85.3 (7.7)
Gender, *n* (%)			
Male	125 (27.8%)	141 (33.0%)	266 (30.4%)
Female	324 (72.2%)	286 (67.0%)	610 (69.6%)
Consent, *n* (%)			
Participant	59 (13.1%)	51 (11.9%)	110 (12.6%)
Consultee	390 (86.9%)	376 (88.1%)	766 (87.4%)
Resident care home status, *n* (%)			
With nursing	188 (42.3%)	250 (59.0%)	438 (50.5%)
Residential only	256 (57.7%)	174 (41.0%)	430 (49.5%)
Missing	5	3	8
Number of medications:			
Median ($q_{0.25}$, $q_{0.75}$)	6 (4, 9)	6 (4, 9)	6 (4, 9)
Minimum, maximum	1, 19	1, 19	1, 19
Missing	2	4	6
Falls in previous 90 days			
Median ($q_{0.25}$, $q_{0.75}$)	0 (0, 1)	0 (0, 1)	0 (0, 1)
Minimum, maximum	0, 30	0, 18	0, 30
Mean (SD)	0.78 (2.30)	0.57 (1.43)	0.68 (1.93)
Hospital admissions in previous 90 days			
Median ($q_{0.25}$, $q_{0.75}$)	0 (0, 0)	0 (0, 0)	0 (0, 0)
Minimum, maximum	0, 2	0, 3	0, 3
Mean (SD)	0.07 (0.26)	0.08 (0.30)	0.09 (0.33)
Barthel Index, mean (SD)	8.34 (5.78)	7.07 (5.77)	7.74 (5.81)
Missing	10	35	45
Drug Burden Index, mean (SD)	0.72 (0.75)	0.70 (0.69)	0.71 (0.72)
Missing	5	2	7
Charlson Comorbidity Index: mean (SD)	5.94 (1.84)	5.98 (1.52)	5.96 (1.69)
Missing	5	6	11
EQ-5D Self-Utility Score, mean (SD)	0.49 (0.37)	0.33 (0.36)	0.41 (0.37)
Missing	396	377	773
EQ-5D Proxy Utility score, mean (SD)	0.31 (0.35)	0.29 (0.37)	0.30 (0.36)
Missing	33	53	86

SD, standard deviation.

TABLE 13 Falls at 6 months – summary

	Intervention, *N* = 449	Control, *N* = 427	Rate ratio[a] (model 1)	Rate ratio[b] (model 2)
Total falls	697	538		
Follow-up (person-days)	79 803	76 904		
Crude fall rate/year and rate ratio	4.78	3.71	1.00	0.91
Confidence interval			0.73–1.36	0.66–1.26
p-value			0.580	0.992
Minimum, maximum	0, 59	0, 27		
Q_{25}, Q_{75}	0, 2	0, 1		
Median	0	0		

a Model 1 – adjusted for falls at baseline (in 90 days before enrolment).
b Model 2 – adjusted for falls at baseline, Barthel Index, Drug Burden Index, Charlson Comorbidity Index and Home status (nursing/residential).

TABLE 14 Further secondary outcomes at 6 months

	Intervention, *N* = 449	Control, *N* = 427	Comparison[a]	Fully adjusted comparison[b]
Hospitalisations per person				
Median ($q_{0.25}$,$q_{0.75}$)	0 (0, 0)	0 (0, 0)		
Minimum, maximum	0, 4	0, 3		
Mean (SD) or RR	0.19 (0.50)	0.18 (0.47)	0.98	0.90
95% CI			0.66–1.46	0.60–1.31
p-value			0.932	0.573
Barthel Index				
Mean (SD) or RR	8.12 (5.84)	6.46 (5.66)	1.19	1.20
95% CI			0.96–1.49	0.96–1.49
p-value			0.116	0.107
Missing	113	110		
Drug Burden Index				
Mean (SD) or RR	0.66 (0.74)	0.73 (0.69)	0.83	0.83
95% CI			0.75 to 0.93	0.74–0.92
p-value			<0.001	<0.001
Missing	10	9		

CI, confidence interval; RR, rate ratio; SD, standard deviation.
a Comparison adjusted for baseline values of the main variable only.
b Comparison adjusted for baseline value of the main variable, Barthel Index, Charlson Comorbidity Index, home status and Drug Burden Index.

TABLE 15 EuroQol Five Dimensions outcomes at 3 and 6 months

	Intervention, *N* = 449	Control, *N* = 427	Absolute difference between intervention and control[a]	Absolute difference fully adjusted comparison[b]
Three months				
EQ-5D Self-Utility score				
Mean (SD)	0.32 (0.37)	0.18 (0.33)	0.079 (−0.028 to 0.186)	0.047 (−0.021 to 0.114)
Missing	372	352	*p* = 0.146	*p* = 0.175
EQ-5D Proxy Utility score				
Mean (SD)	0.28 (0.35)	0.28 (0.35)	−0.017 (−0.073 to 0.039)	−0.043 (−0.092 to 0.006)
Missing	77	47	*p* = 0.556	*p* = 0.082
Six months				
EQ-5D self-utility score				
Mean (SD)	0.18 (0.33)	0.14 (0.29)	0.010 (−0.115 to 0.135)	0.012 (−0.114 to 0.139)
Missing	353	326	*p* = 0.873	*p* = 0.849
EQ-5D proxy utility score				
Mean (SD)	0.26 (0.35)	0.21 (0.33)	0.030 (−0.021 to 0.080)	0.042 (−0.043 to 0.052)
Missing	53	47	*p* = 0.249	*p* = 0.862

SD, standard deviation.
a Comparison adjusted for baseline values of EQ-5D only.
b Comparison adjusted for baseline values of EQ-5D, Barthel Index, Charlson Comorbidity Index, home status and Drug Burden Index.

TABLE 16 Number and type of pharmacist independent prescriber interventions per patient

Category		
Interventions per resident (average)		1.8
Technical interventions [*n* (%)]		99 (11.2)
Educational intervention [*n* (%)]		3 (0.4)
Clinical interventions [*n* (%)]		566 (85)
Type of clinical intervention	Medicine discontinuation/dose reduction [*n* (%)]	379 (67)
	Start new medication [*n* (%)]	60 (10.6)
	Change medication [*n* (%)]	49 (8.6)
	Dose increase [*n* (%)]	26 (4.6)
	Monitoring [*n* (%)]	52 (9.2)

TABLE 17 Clinical interventions categorised by therapeutic area (*N* = 566)

BNF therapeutic area		Pharmacist independent prescriber medication intervention						
		Dose increase	Medication discontinuation	Changing the medication	Dose reduction	Starting new medication	Drug monitoring recommendation	Total, *n* (%)
1	Gastrointestinal system	3	43	2	20	21	0	89 (15.8)
2	Cardiovascular system	6	53	11	18	8	7	103 (18.2)
3	Respiratory system	1	15	2	0	6	0	24 (4.3)
4	Nervous system	10	81	15	51	3	29	189 (33.5)
6	Endocrine system	4	17	4	5	3	8	41 (7.3)
9	Blood and nutrition	2	43	5	1	13	5	69 (12.2)
13	Skin	0	10	10	0	0	3	23 (4)
	Others	0	22	0	0	6	0	28 (4.6)
Total *n* (%)		26 (4.6)	284 (50.3)	49 (8.6)	95 (16.6)	60 (10.6)	52 (9)	566 (100)

BNF, British National Formulary.

TABLE 18 Contextual factors collected as part of process evaluation

Contextual factor		Data collected	Data source
Barriers to delivering the intervention		Feedback from stakeholders	Care home staff interview
			GP interview
			PIP interview
			NoMAD[16] survey to GPs/PIPs and care home staff
			Other anecdotal feedback
Facilitators to delivering the intervention		Feedback from stakeholders	Care home staff interviews
			GP interview
			PIP interview
			NoMAD[16] survey to GPs/PIPs and care home staff
			Other anecdotal feedback
Site and participant factors	Inter-PIP variation	Competency	Variation in outcomes
			Review of PCPs for both safety and missed opportunity
			GP interview
			Care home interviews
		Employment status	Baseline PIP questionnaire
		Qualifications	Baseline PIP questionnaire
	Inter-site variation	Care home factors	Baseline CH survey
		Resident factors	Baseline resident data
	Inter-location variation	Views of researchers	Meeting minutes

TABLE 18 Contextual factors collected as part of process evaluation (*continued*)

Contextual factor		Data collected	Data source
Normalisation of the intervention into routine practice	Actions taken by participants to ensure the intervention works	Coherence (making sense of the service)	NoMAD survey[16] to PIPs, CH staff, GPs
			GP Interview CH staff Interviews
			PIP interview
		Cognitive participation (engaging with the service)	NoMAD[16] survey to PIP, CH staff, GPs
			Interviews (GP and CH staff)
			PIP interview
		Collective action (delivering the service/responding to the service)	NoMAD[16] survey to PIP, CH staff, GPs
			GP interview CH staff interviews
			PIP interview
		Reflexive monitoring (appraising and reviewing the service)	NoMAD[16] survey to PIP, CH staff, GPs
			GP interview CH staff interviews
			PIP interview

CH, care home; GP, general practitioner; PIP, pharmacist independent prescriber.

TABLE 19 Process evaluation task assessed, data collected and source

Task assessed	Data collected	Data source
Effectiveness of training	PIPs' views on training	Post-training feedback forms
		PIP Interview
		PIP questionnaire
		Online survey
	Competency	Competency assessments
		Appropriateness of PCPs (20% of the sample)
		Missed opportunities (50% of the sample)
		Views of stakeholders (interviews)
Intervention fidelity	Services provided and frequency with which provided	PIP activity logs
		No. of pharmaceutical care plans
		PIP questionnaire
	Quality of medication review	Review of 20% of PCPs

PCP, pharmaceutical care plan; PIP, pharmacist independent prescriber.

TABLE 20 Mechanism of impact and data collected as part of process evaluation (This draws on the logic model and hypotheses for addressing the identified issues)

Impact	Mechanism of impact	Data collected	Data source
Medication changes identified	PIP medication review	Recommendations for change and rationale	Pharmaceutical care plans PIP interview PIP questionnaire
Medication changes made	PIP prescribing	Total no. of medications per patient at baseline and 6 months	Pharmaceutical care plans GP records
		No. of medications stopped per patient at 6 months	Pharmaceutical care plans GP records
		No. of medications started per patient at 6 months	Pharmaceutical care plans GP records
		No. of medications amended, e.g. dose change, formulation change	Pharmaceutical care plans GP records
		No. of antipsychotics/psychotropics prescribed at baseline and 6 months	Pharmaceutical care plans GP records
		Categorised description of drugs changed, stopped and started	Resident medical records
Biochemical monitoring	PIP medication review	Recommendations made for biochemical monitoring	Pharmaceutical care plans
Medication errors	PIP medication review	No. of prescribing, dispensing and administration errors	Pharmaceutical care plans GP records
Non-patient facing activities improved, e.g. medication storage advice	PIP support for care home	Services provided and frequency	PIP activity log
		Views on the usefulness of services	Care home staff interviews PIP interview PIP questionnaire
Better/tailored training for staff	PIP training for care home staff	Training provided and frequency	PIP activity log
		Views on the usefulness of training	Care home staff interviews PIP interview PIP questionnaire
Quality of communication between care home, GP and community pharmacy	PIP input into communication	Views of care home staff	Care home staff interviews
		Views of GPs	GP interview
		Views of PIPs	PIP interview PIP questionnaire

GP, general practitioner; PIP, pharmacist independent prescriber.

TABLE 21 Outcomes and data collected as part of process evaluation

Aim	Outcome	Data collected	Data source
To improve quality of care for those over 65 years old resident in care homes	Falls	Fall rate per person at 3 months	Care home fall record
		Fall rate per person at 6 months	Care home fall record
	Quality of life	Self-reported quality of life	Face-to-face self-reported EQ-5D-5L (applicable only for participants with capacity) at baseline, 3 months and 6 months
		Carer-assessed quality of life	Proxy EQ-5D-5L (quality of life) at baseline, 3 months and 6 months
	Physical functioning	Carer-assessed physical functioning	Proxy Barthel Index (physical functioning) at baseline and 6 months
	Health service utilisation and associated costs	Costs of care (medication, health care team contacts, monitoring and tests)	GP records at baseline and 6 months
	Drug Burden Index	Calculate Drug Burden Index based on medications	GP records at baseline and 6 months
To assess intervention safety	Mortality	Information on the number of residents dying	Monthly call to care homes
	Hospitalisations (not always a negative marker of safety)	Information on the number of residents hospitalised	Monthly call to care homes
	Global view[a]	Perceptions of GPs	GP interview
		Perceptions of care home staff	Care home staff interviews
		Perception of residents/consultee/WPOA	Resident/consultee/WPOA interviews
		Perceptions of PIPs	PIP interview
	Adverse events[a]	New drug-related symptoms	Stakeholder feedback using the standard template
	Serious adverse events[a]	See hospitalisations/deaths	Monthly call to care homes
	Sudden unexpected serious adverse events[a]	See hospitalisations/deaths	Feedback from GPs/independent medical assessor on the causal link with the PIP intervention

GP, general practitioner; PIP, pharmacist independent prescriber; WPOA, welfare power of attorney.
a Other than those asterisked, these are also primary and secondary outcomes for the main trial.

TABLE 22 Unit costs assigned to different resource use items (with associated reference source)

Resource item	Unit cost (£)			
	Per hour of employment	Care home visit	Hospital/community visit	Telephone call
PIP (band 7)	53[24]			
PIP mentor/ trainer (8a)	63[24]			
GP	110[24]	85[24]	28[24]	21[24]
Practice nurse		27[24]	16[24]	6[24]
Ambulance call out		192[24]	252[24]	
A&E visit			138[24]	
Pharmacist (not CHIPPS PIP)		29[24]	29[24]	9[24]
District nurse		33[24]	33[24]	8[24]
Nurse specialist		43[24]	43[24]	11[24]
Dietitian		86[24]	86[24]	7[24]
Podiatrist		43[24]	43[24]	11[24]
Physiotherapist		57[24]	57[24]	14[24]
Occupational therapist		81[24]	81[24]	20[24]
Speech therapist		96[24]	96[24]	24[24]
Community care assistant		11[24]	11[24]	
MRI			146[24]	
ECG			136[24]	
CT scan			104[24]	
DEXA scan			77[24]	
Ultrasound			55[24]	
Radiography			31[24]	
Directly accessed pathology services			2[24]	

A&E, accident and emergency; CT, computed tomography; DEXA, dual X-ray absorptiometry; ECG, electrocardiogram; GP, general practitioner; MRI, magnetic resonance imaging; PIP, pharmacist independent prescriber.

Note
For stays with a length of stay of less than 2 days, a weighted average of the NHS reference costs for short stays was used (£616). For non-elective stays of ≥2 days, a weighted average of all non-elective stays from the NHS reference costs (£3117) was used. Where noted, data of the length of visit and/or the ratio (of, e.g., cost per hour of client contact to cost per hour of employment) from the reference (136) were applied to more recent cost per hour of employment data.[24]

TABLE 23 Mean levels of resource use per participant[a]

Resource use item	Time period	PIP intervention (*n* = 449)	Control (*n* = 427)
Training: PIP time (hours per PIP)	6-month FU	32.30 (*n* = 449)	-
Total PIP activity time (minutes)	6-month FU	191.33 (*n* = 449)	
Medication (number of different items prescribed/packs ordered)	Baseline[b]	26.95 (*n* = 448))	27.74 (*n* = 425)
	6-month FU	34.85 (*n* = 448)	33.66 (*n* = 425)
Outpatient attendances	Baseline[b]	0.10 (*n* = 448)	0.10 (*n* = 426)
	6-month FU	0.18 (*n* = 443)	0.20 (*n* = 420)
Inpatient admissions	Baseline[b]	0.08 (*n* = 449)	0.07 (*n* = 427)
	6-month FU	0.16 (*n* = 448)	0.15 (*n* = 426)
Tests/investigations	Baseline[b]	1.36 (*n* = 44)	1.75 (*n* = 427)
	6-month FU	3.10 (*n* = 443)	2.57 (*n* = 420)
GP/practice nurse visits/ telephone calls	Baseline[b]	3.24 (*n* = 448)	3.32 (*n* = 426)
	6-month FU	5.26 (*n* = 443)	5.95 (*n* = 420)
Other healthcare professional visits/telephone calls	Baseline[b]	3.55 (*n* = 446)	3.66 (*n* = 422)
	6-month FU	6.91 (*n* = 398)	6.36 (*n* = 402)

FU, follow-up; GP, general practitioner; *n*, number of residents for whom data were available; PIP, pharmacist independent prescriber.
a Mean values per participant unless otherwise stated.
b Three-month period before randomisation.

TABLE 24 Summary costs

Resource use, mean (SD) (*n*)	Time period	PIP intervention (*n* = 449)	Control (*n* = 427)
PIP training cost[a]	6-month FU	£137.90 (£0.00) (*n* = 449)	
PIP activity cost[a]	6-month FU	£205.29 (£170.31) (*n* = 449)	-
GP time saving	6-month FU	−£20.60 (£0.00) (*n* = 449)	-
Total PIP intervention cost	6-month FU	£322.59 (£170.31) (*n* = 449)	-
Overall medication costs	Baseline	£248.28 (£289.39) (*n* = 448)	£279.25 (£300.58) (*n* = 425)
	6-month FU	£443.53 (£577.36) (*n* = 448)	£504.92 (£618.02) (*n* = 425)
Outpatient attendances	Baseline[b]	£12.57 (£46.07) (*n* = 448)	£12.38 (£47.03) (*n* = 426)
	6-month FU	£21.91 (£78.20) (*n* = 443)	£23.40 (£76.33) (*n* = 420)
Inpatient stays	Baseline[b]	£229.28 (£911.06) (*n* = 449)	£160.42 (£669.52) (*n* = 427)
	6-month FU	£518.08 (£1338.60) (*n* = 448)	£509.79 (£1303.44) (*n* = 426)
Tests/investigations	Baseline[b]	£3.83 (£9.43) (*n* = 448)	£5.19 (£16.38) (*n* = 427)
	6-month FU	£11.26 (£26.24) (*n* = 444)	£8.38 (£19.51) (*n* = 421)

TABLE 24 Summary costs (*continued*)

Resource use, mean (SD) (*n*)	Time period	PIP intervention (*n* = 449)	Control (*n* = 427)
GP/practice nurse visits/ telephone calls	Baseline[b]	£182.16 (£222.58) (*n* = 448)	£183.01 (£185.22) (*n* = 426)
	6-month FU	£302.30 (£330.63) (*n* = 443]	£340.53 (£282.36) (*n* = 420)
Other healthcare professional visits/telephone calls	Baseline[b]	£160.52 (£229.49) (*n* = 446)	£170.23 (£253.22) (*n* = 422)
	6-month FU	£337.20 (£400.25) (*n* = 398)	£321.01 (£398.46) (n = 402)
Total other (non-medication) costs	Baseline[b]	£590.56 (£1050.61) (*n* = 445)	£532.82 (£820.47) (*n* = 422)
	6-month FU	£1189.44 (£1544.28) (*n* = 398)	£1213.31 (£1584.07) (*n* = 401)
Total costs	Baseline[b]	£840.27 (£1122.87) (*n* = 445)	£811.83 (£881.58) (*n* = 422)
	6-month FU	£1970.42 (£1690.20) (*n* = 398)	£1724.82 (£1746.38) (*n* = 401)

FU, follow-up; *n*, number of residents for whom data were available; PIP, pharmacist independent prescriber; SD, standard deviation.
a This includes costs associated with the input time for other professionals.
b Three-month period before randomisation.

TABLE 25 Outcome scores on the EuroQol Five Dimensions

Item, mean (SD) (*n*) (% response rate)	Intervention (*n* = 449)	Control (*n* = 427)
Baseline EQ-5D-5L score	0.313 (0.350) [416] (92.7%)	0.287 (0.369) [374] (87.6%)
Three-month EQ-5D-5L score	0.284 (0.349) [372] (82.9%)	0.278 (0.349) [380] (89.0%)
Three-month change in the EQ-5D-5L score	−0.056 (0.256) [353] (82.7%)	−0.018 (0.271) [347] (81.3%)
Six-month EQ-5D-5L score	0.263 (0.348) [396] (88.2%)	0.209 (0.330) [380] (89.0%)
Six-month change in EQ-5D-5L score	−0.061 (0.279) [369] (82.2%)	−0.071 (0.262) [344] (80.9%)
QALY score	0.150 (0.160) [316] (70.4%)	0.136 (0.161) [322] (75.4%)

n, number for whom data were available; QALY, quality-adjusted life-year; SD, standard deviation.

TABLE 26 Estimates of incremental cost, incremental effect and cost-effectiveness of the pharmacist independent prescriber intervention in the base-case and sensitivity analyses

Analysis (Nc, Ni)	Incremental cost (95% CI)	Incremental effect (95% CI)	ICER	CEAC (%)[a]
		QALYs		
Base-case: complete case (303, 306)	£279.86 (£19.39 to £540.33)	−0.004 (−0.016 to 0.009)	Dominated	3.8
SA1: imputed (449, 427)	£239.32 (£26.26 to £452.39)	−0.003 (−0.049 to 0.042)	Dominated	26.6
SA2: complete case, no training costs (303, 306)	£141.96 (−£118.51 to £402.43)	−0.004 (−0.016 to 0.009)	Dominated	14.1

Dominated, higher mean costs and lower mean effect; ICER, incremental cost-effectiveness ratio; Nc (Ni), number randomised to the control arm (PIP group) who were included in the analysis; PIP, pharmacist independent prescriber; QALY, quality-adjusted life-year at 6 months; SA1 and SA2 refer to the first and second sensitivity analyses, respectively, described in the Methods.
a Probability of bringing cost-effectiveness on the cost-effectiveness acceptability curve at the threshold (λ) of £20,000 per QALY.

Work package 2 figures

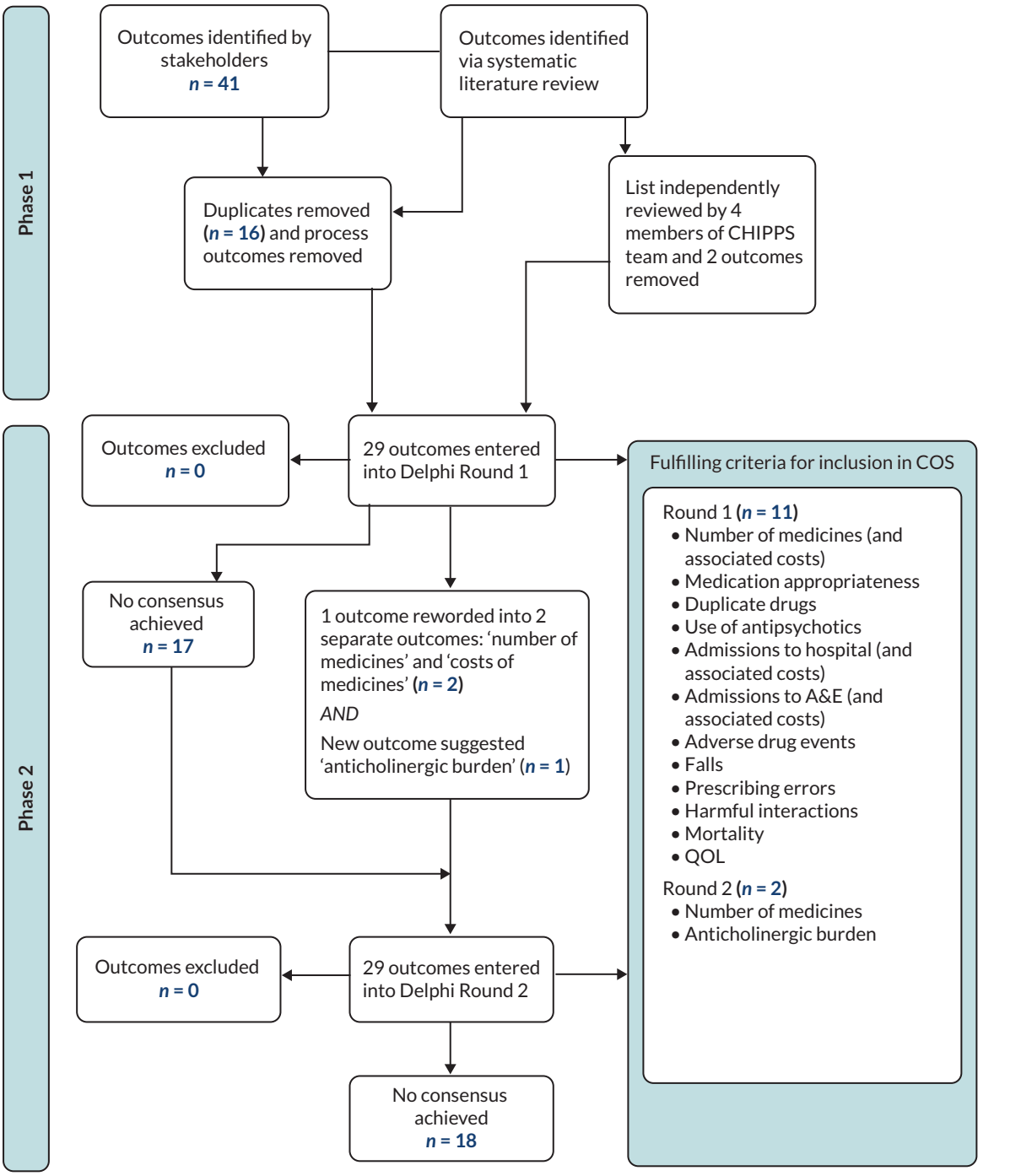


FIGURE 2 Overview of core outcome set development.

Work package 4 figures

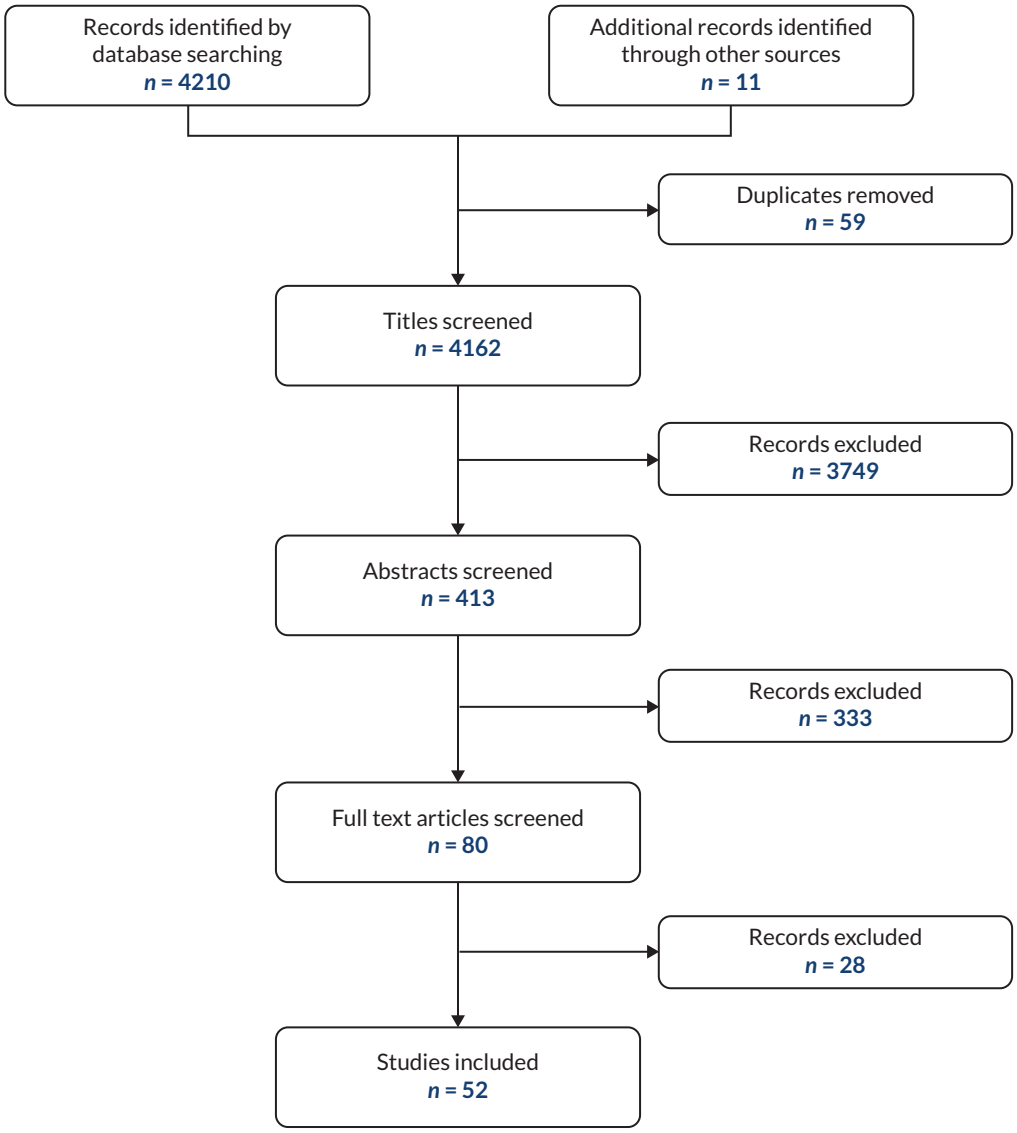


FIGURE 3 PRISMA diagram showing the literature review process.

Draft 1		Draft 2	
Domain	**Competency**	**Domain**	**Competency**
Prescribing	Effective monitoring of therapy	Prescribing	Effective monitoring of therapy
	Safe and effective therapy alteration		Safe and effective therapy alteration
	Recognises limitations of competence		Recognises limitations of competence
Medicines management	Medicines storage, handling and record keeping	Medicines management	Medicines storage, handling and record keeping
	Medicines reconciliation		Medicines reconciliation
	Safe and effective medicines administration		Safe and effective medicines administration
Communication	Maintenance of records related to prescribing and medication review	Communication	Maintenance of records related to prescribing and medication review
	Relationship building and maintenance		Relationship building and maintenance
Chronic disease management	Pain management	Managing complexity in later life	Pain management
	Cognitive impairment		Cognitive impairment
	Cardiovascular disease		Nutrition
			Polypharmacy
		Context	Cultural awareness
			Policy awareness
			Duty of candour

FIGURE 4 First two personal development framework iterations.

The training package consisted of:
- Two training days (study design & project delivery, preparation for role)
- Development of underpinning knowledge (Box 2)
- Self-assessment against personal development framework and agreement of personal development plan with mentor (Next page)
- Relationship building and competency development (below)
- Sign off for role through mentor and independent assessor.

Relationship building and competency development

Developing relationships with GPs, general practice, staff, care home manager(s), care home staff, community pharmacist by undertaking the following relevant activities
- Discusses and agrees prescribing boundaries and methods of working
- Identifies efficient approaches to manage urgent medicine requests from home
- Agrees frequency and preferred modes of communication
- Identifies support available from other healthcare professionals referral processes
- Develops list of useful contacts.

Additionally, within the general practice
- Learns how to use IT system and agrees content of records
- Obtains access to prescription pad
- Meets lead prescriber and local primary care pharmacist responsible for prescribing within general practice to obtain local medicines related problems and policies
- Visits care home with GP when undertaking a routine visit and jointly perform medication review on non-study residents
- Learns how to use IT system and agrees content of records.

Additionally, within the care home:
- Understands recording systems including MAR charts
- Observe medication administration rounds to identify how best to support staff
- Identify senior members of team, roles and medicines related culture
- Provides care home staff training depending on identified needs.

Arrange to meet the following if available and deemed useful:
- Local safety expert
- Care home pharmacist specialist
- Consultant geriatrician working in primary care
- Community matron with responsibilities for care homes
- Local CQC or national equivalent inspector
- District nurse (dressings, catheter, barrier cream policies).

FIGURE 5 Final training package. (*continued*)

Personal Development Framework

Domain	Competency	Behaviours
Prescribing	Safe and effective therapy alteration	• Discontinues or changes therapy in line with best practice • Implements appropriate monitoring plans for safety and efficacy for medicines which have been initiated, changed or discontinued
	Effective monitoring of therapy	• Implements monitoring according to local requirements and expectations • Ensures that prescribing and monitoring practices relating to high risk therapy e.g. anti-platelet and anticoagulant therapy, are appropriate
	Recognises limitations of competence	• Identifies complex prescribing decisions outside of competency and seeks appropriate support and guidance • Identifies where patients transfer from chronic disease management to terminal care and hands responsibility back to medical practitioner
Medicines Management	Medicines storage, handling and record keeping	• Supports the home in meeting national requirements for safe medicines management • Identifies and recommends practical solutions to improve medicines related activities e.g. addresses inequivalence, reduces wastage and likelihood of medication related errors • Recognises advantages and disadvantage of medication administration systems and identifies approaches to optimise their use
	Medicines reconciliation	• Supports effective transfer of medicines related information when residents are hospitalised • Ensures that medicines related information transferred from hospital to the care home is accurate and complete
	Safe and effective medicines administration	• Ensures that care staff know how to administer medicines safely and appropriately e.g. when it is appropriate to crush/disperse medicines • Identifies patients for whom administration of medicines is challenging and supports care staff accordingly
	Responds appropriately to medicines related errors and critical incidents	• Performs critical incident analysis, identifying and implementing strategies to prevent future recurrence • Supports recording and reporting of incidents in line with local and national policy
Communication	Maintenance of records related to prescribing and medication review	• Uses IT systems within care home and general practice effectively • Ensures all activities and rationale for them are communicated effectively and recorded contemporaneously
		• Ensures records of activities are accessible to care home staff and members of healthcare professional team • Language used within records appropriate for all stakeholders
	Relationship building and maintenance	• AVppropriately uses and refers to all members of healthcare team responsible for care within the home • Whenever practical and appropriate involves residents, families and carers in prescribing decisions • Regularly reviews role and boundaries to maintain effective relationship
	Trains others	• Delivers effective small group teaching sessions • Provides feedback on performance sensitively and constructively
Managing complexity in later life	Pain management	• Recognises the symptoms associated with pain in patients with and without cognitive impairment • Ensures that 'as required' pain relief is supplied when necessary e.g. paracetamol
	Cognitive impairment	• Regularly reviews all antipsychotic, sedative and anticholinergic therapy for need and appropriateness
	Nutrition	• Ensures that resident nutritional needs are regularly reviewed and related prescribing is in line with local policy and guidance • Ensures that appropriate nutritional support is provided to enhance bone protection
	Polypharmacy	• Reviews and rationalises therapy in light of risk and benefits in a complex older person • Appropriately reviews therapies which are known to increase the likelihood of falls
Context	Cultural awareness	• Practices in line with expectations of general practitioners with respect to inter professional working and prescribing practices • Identifies medicines related cultures (e.g. use of antipsychotics, sedatives, antibiotics, analgesia & laxatives) within the care homes and works with staff to implement best practice • Educates and supports care staff in the management of behavioural disturbances and the use of antipsychotic medication
	Policy awareness	• Supports home in meeting relevant legislative frameworks e.g. CQC requirements • Ensures patient rights under mental capacity act e.g. covert administration, right of refusal
	Duty of candour	• Iato

FIGURE 5 Final training package.

Work package 5 figures

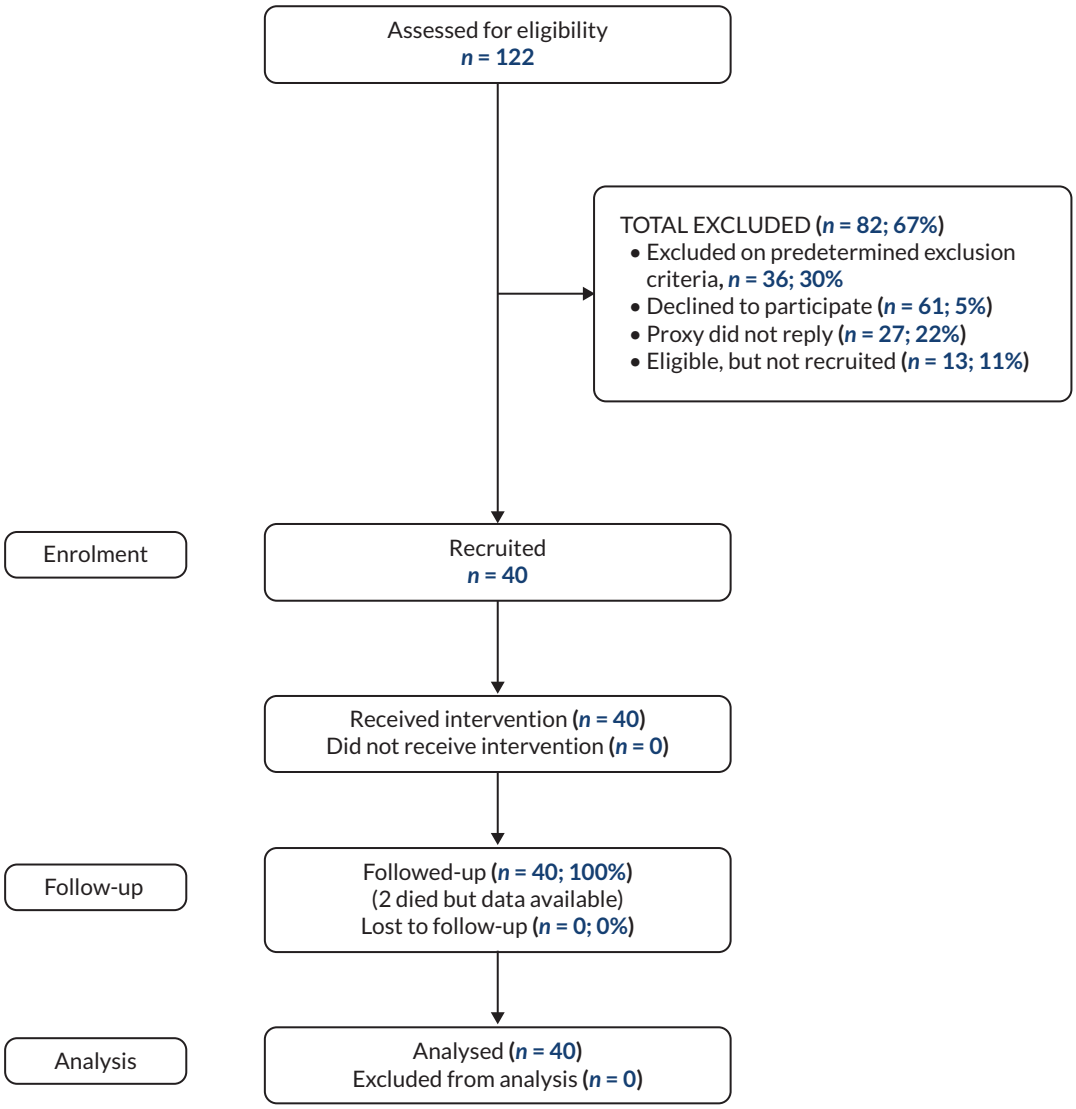


FIGURE 6 Care Home Independent Pharmacist Prescriber Study work package 5 feasibility study CONSORT diagram.

Work package 6 figures

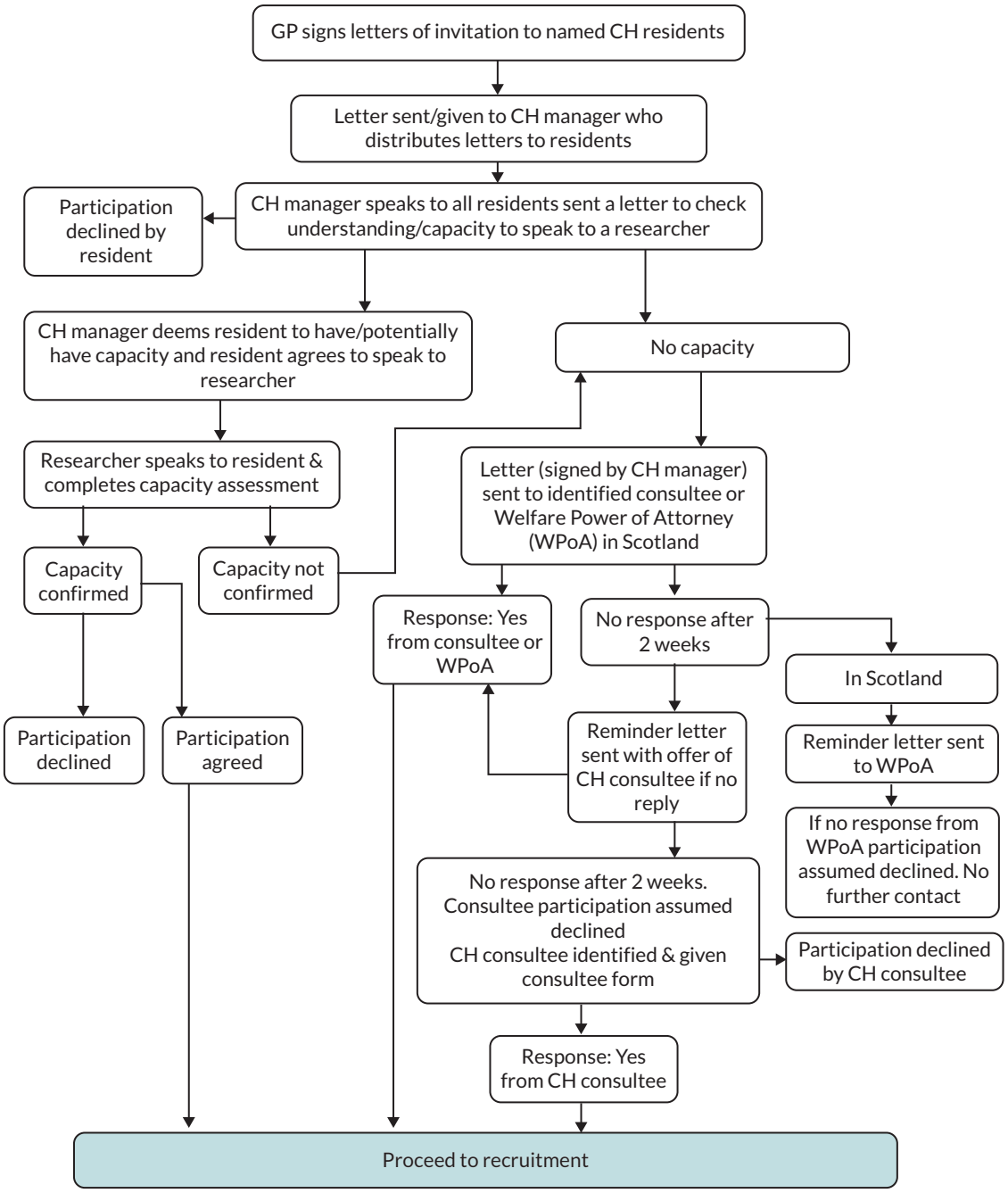


FIGURE 7 Flowchart of care home resident recruitment.

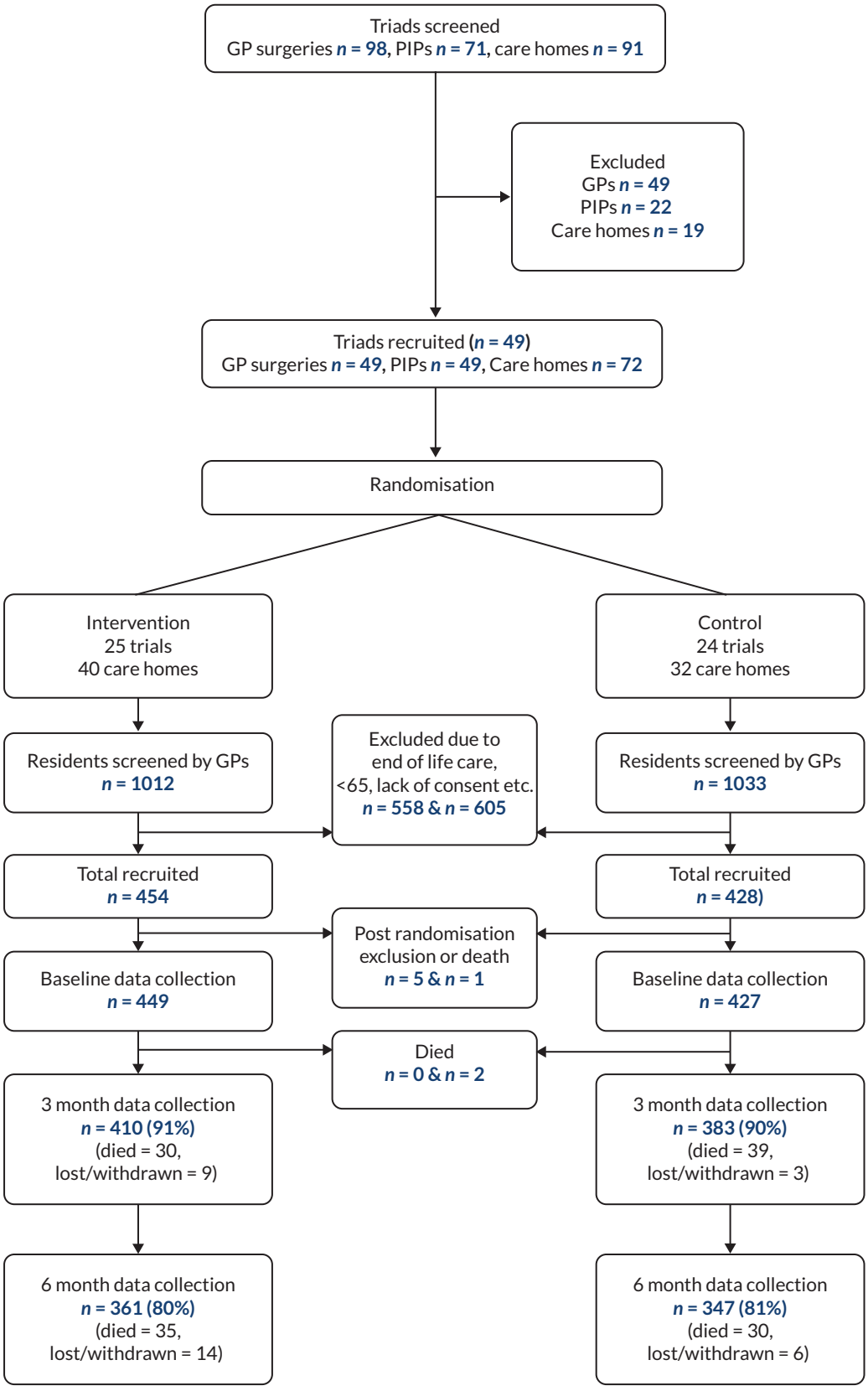


FIGURE 8 Consort diagram of a cluster randomised controlled trial.

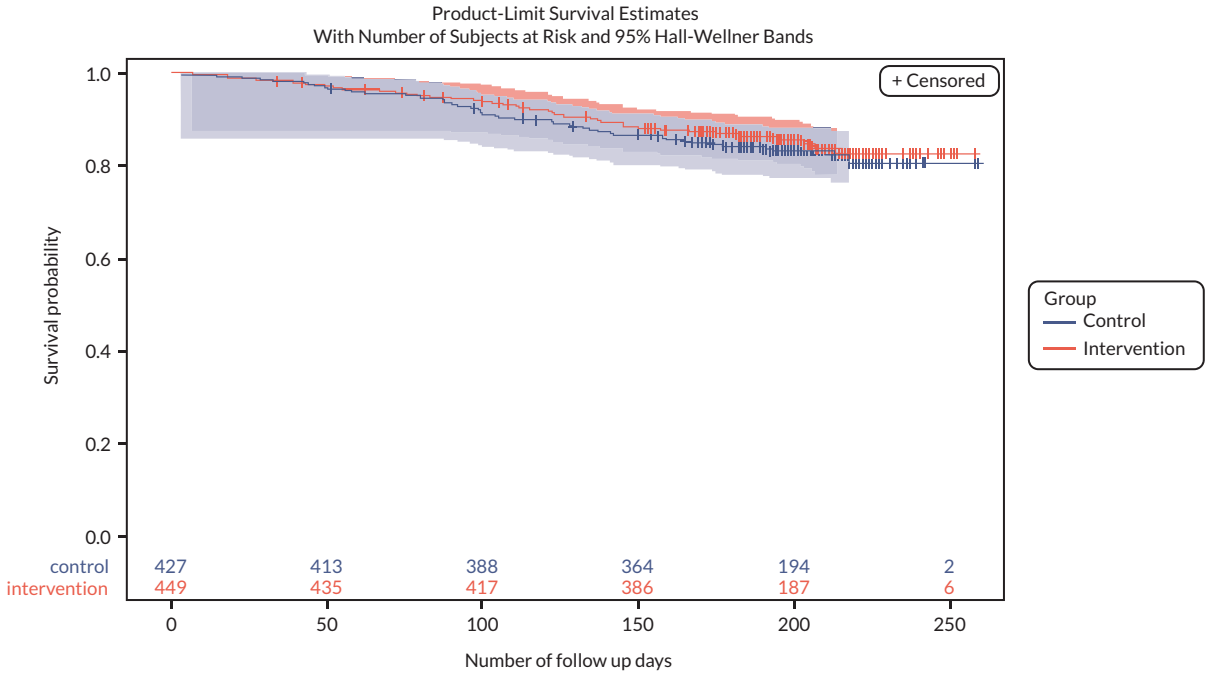


FIGURE 9 Survival analysis comparing arm 1 (intervention arm) with arm 2 (control arm).

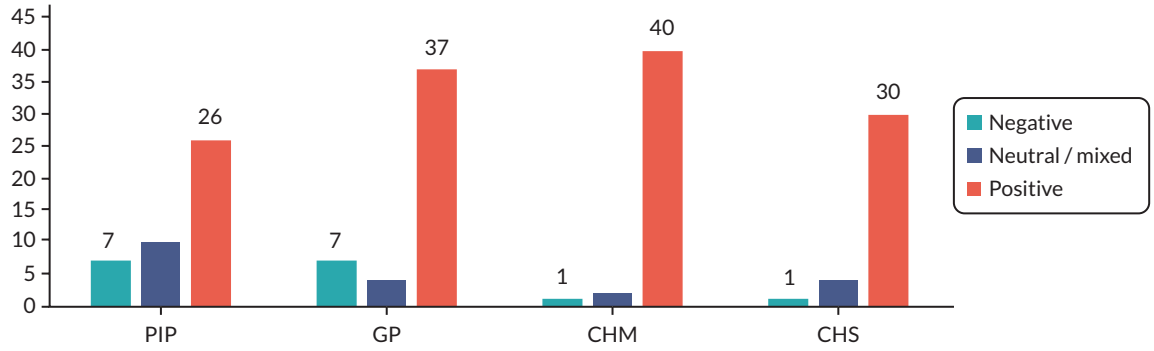


FIGURE 10 Responses to the satisfaction statement by stakeholder group.

Work package 4 boxes

BOX 1 Summary of knowledge requirements and recommendations for training delivery design

Codified knowledge

- Frailty.
- Harmful drugs for older people.
- Capacity and how to support residents without it.
- End-of-life care.
- Role and boundaries of self and others.
- Management of geriatric conditions.
- Medicines regulations in care homes.
- Importance of involving residents and relatives in decision making.

Practical knowledge

- Know limitations and to work within them.
- How to integrate into a team.
- Good communication with the team, with residents and relatives.
- Need for the use of IT systems at home and in medical practice.

BOX 1 Summary of knowledge requirements and recommendations for training delivery design (*continued*)

Care Home Cultural knowledge

- Develop relationships with everyone involved in team.
- How medical practice servicing the home operates.
- Care home culture with respect to medicines.
- Impact of medicines within the care home.
- Medicine ordering and supply processes to enable effective access to medicines.

Training delivery design

- To support integration into the team.
- Ensure includes effective communication about the role of a PIP to the home and wider team members.
- Mentoring and/or shadowing, as part of training, doctors and care workers.
- PIPs to communicate to staff regarding the importance of managing medicines effectively.
- PIPs to understand and support good medicine administration practices.

BOX 2 Specific knowledge identified as required to practice safely in a care home

Conditions

- Parkinson's disease.
- Cognitive impairment and behavioural disturbances.

Symptoms

- Delirium.
- Common skin conditions seen in care homes.
- Dysphagia.

Non-pharmacological therapy

- Wound management and catheter prescribing guidelines.[a]
- Nutrition guidelines.[a]
- Pain.
- Dose optimisation based on renal function.

Pharmacological therapy

- Cardiovascular (hypertension, secondary prevention, heart failure).
- Asthma and chronic obstructive pulmonary disease.
- Anticoagulant.
- Anticholinergics and burden.
- Antipsychotic.
- Sedatives.
- Antidepressants.
- Gastrointestinal (laxatives, proton pump inhibitors).
- Diabetes.

Legislation

- Mental Capacity Act or local equivalent and gaining consent.
- Covert administration.
- Controlled drugs.

a Locally derived

Work package 5 boxes

BOX 3 Outcome measures used in a feasibility study

- Adverse drug events as would normally be reported by a care home.
- STOPP/START (medication appropriateness tool).
- Mortality.
- Fall rate per patient as per standard care home safety data collection.
- Barthel Index (physical functioning).
- Mini-Mental State Examination (MMSE).
- Drug Burden Index.
- Number of medicines.
- QUALIDEM.
- EuroQoL EQ-5D-5L (Proxy version 1). The proxy (care home staff, key worker) was asked to rate how they (i.e., the proxy), would rate the subject's health (quality of life).
- EuroQol EQ-5D-5L face-to-face with the resident.
- Adverse drug events as would normally be reported by a care home.

Work package 6 boxes

BOX 4 Example quotes of views on medication changes

- 'Having a pharmacist who had good knowledge of all kinds of medications, going through polypharmacy, with a fine-tooth comb and picking up on any errors or things'. GP 2
- 'It has **reduced the time taken to see patients** as …. their meds are all up to date, tests required for routine monitoring have been flagged up and I have been able to action these. From a **safety and medicine waste point of view things have much improved**' GP 52
- 'A resident was on a huge amount of anti-psychotic drugs … seeing PIP on a weekly basis meant we were able to make some huge reductions; I don't think I have had any falls from her for a couple of months ….'. CHM 32.

BOX 5 Comparison of characteristics of triads in which Care Home Independent Pharmacist Prescriber Study service well and is less well embedded

Characteristics of triads where CHIPPS service well	Characteristics of triads where CHIPPS service is less well embedded
Resonance between PIPs' activities and GP and CH needs	Dissonance within relationships
GPs welcomed second clinical professional input and resident safety improvements	Lack of understanding of roles and responsibilities
PIP and GP have established working relationships GP and CH trust in the PIP's clinical competency Stable CH management	No established GP-PIP working relationship 'I found it very difficult that I was not an employee of the GP practice … having to start from scratch building relationships … I was not a known entity'. PIP 41
Communication channels enabling discussion of residents' clinical care	New ways of working did not become embedded
Regular PIP access to the CH, PIP readily available, including as the main contact for medication queries	PIP was not seen as key contact for medication queries
PIP service seen to continue post-intervention	PIP service did not continue post-intervention

CH, care home; GP, general practitioner; PIP, pharmacist independent prescriber.

BOX 6 Example quotes of stakeholder satisfaction

> '**I want it back!** *It was very helpful …* **it took the workload** *off … and* **reduced medications** *that we tend to leave the patients on' GP 54*
>
> *'It* **made ordering easier, a little bit simpler, put the MAR charts into place** *a bit better … things … that were no longer needed were taken off' CH staff 11*
>
> *'Her husband is much more positive about his experiences when he visits her … that's really positive' CHM 32*
>
> *It was just pushing it a bit, looking at the patient as a whole,* **and being able to do a little bit more** *and involved the families* **…… it made me more thorough as a prescriber and a pharmacist***' PIP 8*

BOX 7 Care Quality Commission Standard 4 for the Proper and Safe Use of Medicines[131]

Standard 4 How does the provider ensure the proper and safe use of medicines?

S4.1 Is the service's role in relation to medicines clearly defined and described in relevant policies, procedures and training? Is current and relevant professional guidance about the management of medicines followed?
S4.2 How does the service make sure that people receive their medicines (both prescribed and non-prescribed) as intended (including controlled drugs and 'as required' medicines), and that this is recorded appropriately?
S4.3 How are medicines ordered, transported, stored and disposed of safely and securely in ways that meet current and relevant legislation and guidance?
S4.4 Are there clear procedures for giving medicines covertly, in line with the Mental Capacity Act 2005?
S4.5 How does the service make sure that people's behaviour is not controlled by excessive or inappropriate use of medicines?
S4.6 How do staff assess the level of support a person needs to take their medicines safely, particularly where there are difficulties in communicating, when medicines are being administered covertly, and when undertaking risk enablement assessments designed to promote self-administration?
S4.7 How does the service engage with healthcare professionals in relation to reviews of medicines at appropriate intervals?
S4.8 How do staff make sure that accurate, up-to-date information about people's medicines is available when people move between care settings? How do medicines remain available to people when they do so?

BOX 8 Recent and ongoing policy initiatives in devolved nations involve employment of pharmacists in care homes

- NHS England.
  1. The Medicines Optimisation in Care Homes (MOCH) 2016: funding for 200 pharmacists and pharmacy technicians to be employed across the country.
  2. Primary Care Networks funded to employ pharmacists with one target to enhance health in care homes in 2020.
  3. National review of overprescribing with a particular focus on problematic polypharmacy.
- NHS Scotland.
  4. Strategy for pharmaceutical care 2015 noted the need for high-quality pharmaceutical care in care homes.
  5. Health and Social Care Delivery Plan—every GP practice to have access to a pharmacist with advanced clinical skills by 2021.

Appendix 2 Recruitment strategies for GP and PIPs

Locations	GP practice	PIP
Aberdeen	Letters of invitation and EOI forms were sent through the Scottish Clinical Research Network co-ordinator to 25 GP practices identified as providing services to care homes. Seven GP practices returned the EOI forms stating they had a PIP working at their practice	The seven PIP pharmacists identified through the GP invitations were sent invitation letters and EOI forms regarding the CHIPPS feasibility study. The third PIP pharmacist contacted was happy to take part in the feasibility study and fulfilled all our inclusion criteria. No other PIPs were contacted
Belfast	EOI forms were sent out to a random selection of 100 GP practices identified using the Business Services Organisation website. Twelve GP practices expressed an interest to take part but none employed a PIP at that time The GP practice that was eventually recruited resulted from a suggestion made by the recruited PIP who had previous experience working with the practice	EOIs were sent to eight PIPs in Northern Ireland identified using local networks. Four PIPs expressed an interest. The first PIP contacted who could attend the training was recruited
Leeds	The GP practice was approached through the CCG pharmacist who was recruited for CHIPPS. The PIP made initial contact on our behalf	Found locally through the Principal Investigator
Norwich	The Clinical Research Network Eastern Primary Care Locality Manager for Norfolk Great Yarmouth and Waveney invited GP practices on the Research Active list to express an interest in the study. Ultimately, however, the GP practice selected for the feasibility study was approached directly by a PIP based on the PIP's familiarity with the practice and travel logistics (to ensure that the shortest time possible of the PIP's 16 hours/month would be used for travel during the intervention)	Norfolk PIPs received invitation emails either from the Medicines Management lead for Norfolk CCGs or from the Local Clinical Research Network Pharmacist lead for the East of England. They were asked to express an interest in the study to the CHIPPS research team

CCG, Clinical Commissioning Group; EOI, expression of interest; GP, general practitioner; PIP, pharmacist independent prescriber.

Appendix 3 Service specification used in the feasibility study

Service outline

CHIPPS is a National Institute for Health and Care Research (NIHR) programme grant to develop and deliver a cluster randomised controlled trial to determine the effectiveness and cost-effectiveness of making pharmacist prescribers part of a team working alongside care home staff and general practitioners (GPs) in care homes for older people. CHIPPS will provide a pharmacist independent prescriber (PIP) to review and optimise prescribing in recruited residents and facilitate and support cost effective evidence-based prescribing and medicine management in care homes for older people.

Aims and objectives

The aim of the service is to improve health outcomes and well-being of care home residents and ensure medicines are prescribed and managed in a safe, effective and cost-effective manner.

To meet the stated aims, recruited GP practices and care homes will work with a PIP who has demonstrated competency in care home medicine management and prescribing in older people. The PIP will be based at the GP practice, for the duration of the study, and will have developed an excellent working relationship with the GP practice and care home before commencing the service delivery. The service will run for a period of 3 months.

Inclusion/exclusion criteria for the service

Pharmacist independent prescriber

Inclusion criteria

- Registered as a PIP.
- Following training can demonstrate competence to deliver the service (see *Service requirements*).
- Ability to work flexibly and commit a minimum of 16 hours a month to deliver the service for 3 months.

Exclusion criteria

- Substantive employment with the community pharmacy (branch/store) that supplies medicines to the care home with which the PIP would work.

Care home

Inclusion criteria

- CQC registered specialism as caring for adults aged ≥65 years.
- Primarily caring for residents over 65 years.

Exclusion criteria

- Care homes that receive additional medication-focused services with a visit frequency of monthly or more.
- Care homes that provide only carer or support remotely (they do not have carers onsite 24 hours a day).
- Care homes that are currently under formal investigation with the CQC or an equivalent body.

Residents

Inclusion criteria

- Resident under the care of the participating GP practice.
- Residents currently prescribed at least one medicine.
- Residents or their appropriate representative who are/is able to provide informed consent/assent.
- Permanent resident in a care home (not registered for respite care/temporary resident).
- Residents must be aged ≥65 years.

Exclusion criteria

- Residents who are currently receiving end-of-life care [equivalent to yellow (stage C) of the Gold Standards Framework prognostic indicator].
- Resident with additional limitations on their residence (e.g. held securely).
- Participating in another research study.

Service requirements

Recruitment and employment of the pharmacist independent prescriber

Initial identification and recruitment of the PIP will be conducted by the CHIPPS management committee. The PIP will require

- excellent interpersonal, communication and IT skills
- familiarity with relevant GP software systems
- experience of providing prescribing and medicine management advice and support
- previous experience of working in a GP practice environment
- be able to travel to site locations
- a mobile phone to be contactable for the purposes of delivering this service
- appropriate indemnity insurance for prescribing.

The PIP will be employed according to local arrangements and seconded to the relevant GP practice for the study duration and during training and competency assessments (see *Training and competency assessment of PIP*).

Training and competency assessment of the PIP

See text in main paper.

PIP roles and responsibilities (NB: categorised as essential or not)

The PIP will, where appropriate:

Review each resident's medication and develop and implement a pharmaceutical care plan[5] (essential)

- Optimise prescribing ensuring clear indication and evidence base for each medication (taking into consideration national and local pathways, guidelines and formularies), informed by tools such as STOPP/START.
- Minimise the potential for adverse effects.
- Optimise the dose of all medications.
- Co-ordinate appropriate monitoring and associated tests for all medicines and conditions.
- Agree the initial care plan with GP, care staff and resident (where appropriate).
- Document and maintain records relating to the review and care plan in GP and care home records as appropriate.

Prescribing (essential)

- Authorise repeat prescriptions.
- Co-ordinate appropriate monitoring and associated tests for all medicines and conditions.
- Deprescribe medicines according to the agreed pharmaceutical care plan.
- Document medication changes in GP and care home records and notify supplying pharmacy of all changes to medication within 24 hours.
- Initiate only new medicines for existing diagnoses or for common ailments that can be managed with medicines classified by the Medicines and Healthcare products Regulatory Agency (MHRA) as Pharmacy (P) or General Sales List (GSL).
- Any additional areas of prescribing must be agreed and documented with the GP practice before prescribing (e.g. antibiotics for simple urinary tract infections).

Communication (essential)

- Agree local protocols for communication with GP practice and care home before commencing service. This should include the following aspects.
- Process of communication and messaging when the PIP is not available.
- Documentation location and level of detail for all interventions made by the PIP.
- Process and communication of referrals for activities outside the competence of the PIP.
- Inform supplying community pharmacy about the service and role (before the start of the service).
- Communicate all changes in medication to supplying pharmacy.
- Complete all documentation and recording of activities as required by the study team.

Support systematic ordering, prescribing and administration processes with each care home, GP practice and supplying pharmacy where needed: (undertaken at the PIP's discretion)

- Provide instructions on how to administer each drug.
- Synchronise residents prescription quantities for monthly cycles.
- Add or clarify directions for all medications where it is currently not clear.
- Provide advice on repeat prescription ordering processes to minimise missed items and optimise quantities.
- Optimise the use of homely remedies within the care home.
- Reconcile resident medication following transfer of care.

5 A pharmaceutical care plan is defined as a plan for the responsible provision of medicine-related care for the purpose of achieving defined outcomes that improve the patient's quality of life. It involves gathering information, identifying problems, assessing problems and achieving desired improvements.

Training provision (undertaken at the PIP's discretion)

- Review training needs of care home and GP practice and draft proposed training package.
- Provide training to care home staff on training needs basis from the agreed list of potential topics/areas.
- Provide guidance to relevant GP practice on training needs basis from the agreed list of potential topics/areas.

Safe and effective service provision

- The PIP will be contactable and respond to messages within 24 hours (Monday–Friday).
- The GP practice will triage all medicine-related contacts for CHIPPS participants following a locally agreed protocol for referral to the PIP [see *Training provision (undertaken at PIP's discretion)*].
- PIP will have full (read/write) access to the GP record system to issues prescriptions and update records.
- Where possible, the PIP will use remote access to update records when changes are made to GP-held records.
- Where remote access is not feasible, the PIP must update records within 24 hours of making a change.
- PIP will have full (read/write) access to care home records to update records during all visits using appropriate local reporting systems.
- The PIP will visit/contact the care home at least once a week.
- The PIP will visit/contact the GP practice at least once a week.
- All annual leaves must be agreed at least 4 weeks before the leave and clear system for the transfer of responsibility communicated to GP, care home and supplying pharmacy.
- The PIP will work within the local prescribing formularies of GP practice and primary care organisation.
- The PIP will report and document all significant clinical events or near misses using local reporting procedures and study documentation.
- The PIP will ensure that all records are aligned.

Outcomes from the service

As part of the feasibility study, we will measure levels of resource use associated with the PIP intervention, which will be estimated using the PIP log, which the PIP will complete every day.

End-of-service transitional arrangements

The duration of service will be clearly documented in study documentation and signed agreement to service provision completed by Care Home and GP practice before commencing the study.

- All original policy and procedure documentation will be kept before the amendments are made during service provision.
- Transfer meeting with PIPs, GP practice and care home at least 3 weeks before the end of service.
- Agree transfer of responsibilities from the PIP.
- Agree named contact point for medication-related issues at GP practice.
- Communicate current plans for each resident.
- Transfer of care plan and set review date.
- Agree changes in policy and procedures.

Appendix 4 Pharmaceutical care plan

Medical History			
Active problems/ current diagnosis			**Significant past diagnosis/problems**
1			
2			
3			
4			
5			
6			
7			
8			
Are any medicines being administered covertly (Y/N). (If yes please specify)			**Self- medicating (Y/N) (If yes please specify what medicines are being taken)**
Known allergies (please specify or write none known)			

Further information			
Nutritional support (Y/N)(Please specify)		Mobility	Immobile ☐ Walks with aids ☐ walks unaided ☐
Incontinent			
	Of urine ☐ Of faeces ☐	Falls risk (Y/N)	

Data Sources used (please tick all that apply)
GP records ☐ Care home record/Kardex ☐ Homely remedies ☐ falls book ☐ other (please state) ☐ _____

Medication Review		
Current prescribed medicines from GP records - *Repeat list and acute prescriptions* (include form, strength, and dose frequency - *cut and paste from GP record if practicable)*		**Indication in this patient**
1.		
2.		
3.		
4.		
5.		
6.		
7.		
8.		
9.		
10.		
11.		
12.		
13.		
14.		
15.		
16.		
17.		
18.		
19.		
20.		
21.	*Add additional rows to document as required (right click>insert>insert row below)*	

OTC/herbal medication/homely remedies used (Y/N) specify

Initial review - list only relevant clinical observations and biochemical tests (most recent measurements) *add/delete from list as necessary*

Date of test	**Test - *Electrolytes***	Level/result	Date of test	**Test - *Liver***	Level/result	Date of test	**Test – *Lipid / FBC***	Level/result
	Na (mmol/L)			Bilirubin- total (µmol/l)			Chol- total (mmol/L)	
	K (mmol/L)			ALP (IU/L)			Hb (g/dL)	
	Chloride (mmol/l)			AST (IU/L)			MCV (fL)	
	Urea (mmol/L)			ALT (IU/L)			HbA1c (%)	
	Cr (µmol/L)			GGT (IU/L)			***Observations:***	
	eGFR (mL/min/1.73m^2)			Albumin (g/L)			Heart rate (bpm)	
							BP (mmHg)	

Other relevant tests and measurements (most recent measurements) *add to list as required*

Date of test	Test	Level/ result	Date of test	Test	Level/result	Date of test	Test	Level/result
	Height (cm)							
	Weight (kg)							
	BMI							
	Creatinine clearance							

Other key information

Pharmaceutical Care Issues

Date identified	**Care Issues** (E.g. unmet need, ADR, drug interaction etc.)	**Recommended actions** (If starting a new medication include form, strength & dose frequency)	**Duration**	**Date actioned**	**Follow-up (date)**	**Outcome & agreed action at follow-up** (If Care issue not resolved complete continuation sheet and cross reference care issue number)	**PIP initials**	**STOPP START criteria code or n/a**
	1.E.g. Itch	*Antipruritic- Cetirizine 10mg i o/d*	*2 weeks*	*11.11.16*	*25.11.16*	*No itch anymore. Fbc normal. Discussed with nurse, stop drug*	*XX*	
	2.							
	3.							
	4.							
	5.							
	6.							
	7.							
	8.							

	9.							
	10.	*Add additional rows to document as required (right click>insert>insert row below)*						

Date identified	**Other problems**	**Suggested Interventions**	**Agreed actions**	**Date**	**PIP initials**	**STOPP START criteria code or n/a**
			Add additional rows to document as required (right click>insert>insert row below)			

Continuation sheet for unresolved issues								
Date identified	**Care Issues** (E.g. unmet need, ADR, drug interaction etc.)	**Recommended actions** (If starting a new medication include form, strength & dose frequency)	**Duration**	**Date actioned**	**Follow-up (date)**	**Outcome & agreed action at further follow-up**	**PIP initials**	**STOPP START criteria code or n/a**
		Add additional rows to document as required (right click>insert>insert row below)						
Additional notes:								

Date of PIP intervention	**Type of intervention** (paper-based/ discussion with care home staff/ discussion with GP/face-to-face with patient)	**PIP Signature**

Appendix 5 Assessment of outcome measures based on data from Cochrane review and experience of the feasibility study

Outcome	Data source	Potential for bias	Potential for missing data	Resident centred	Sensitivity to intervention	Reliability	Validated?	Third party completion	Ability to blind?	Time taken to collect	Quantity of data	Inclusion in RCT
EQ-5D (Quality of Life)	Direct interview with resident	High	High	++	None of included studies used this measure of QOL	++	✓	x	-	10–15 min	Poor	Secondary outcome measure
EQ-5D proxy (Quality of life)	Care home staff	Low (if completed by the same person)	Low	+	None of the included studies used this measure of QOL	+	✓	✓	-	3–5 min	Good; 100%	Secondary outcome measure
MMSE (cognitive function)	Direct interview with resident	High	High	+	No significant difference reported	++	✓	x	-	10–20 min	Poor	Not included
Barthel Index (proxy)	Care home staff	Medium	Low	+	No significant difference reported	++	✓	✓	-	2–10 min	Good; 100%	Secondary outcome measure
QUALIDEM (proxy)	Care home staff	Low	Low	+	Recommend QOL tool for those with dementia	+	Dementia Care Home population only	✓	-	5–10 min	Good; 100%	Not included
Falls	Care home register	Low	Low	+	Three studies found no significant difference, two reported a significant difference	++	N/A	✓	+	1–30 min	Good	Primary outcome measure
Adverse drug events	Care home record	High	High	+	Verification between the medicine and the event is difficult. No significant difference reported	-	N/A	✓	-	2–30 min	None recorded	Monitor for patient safety only

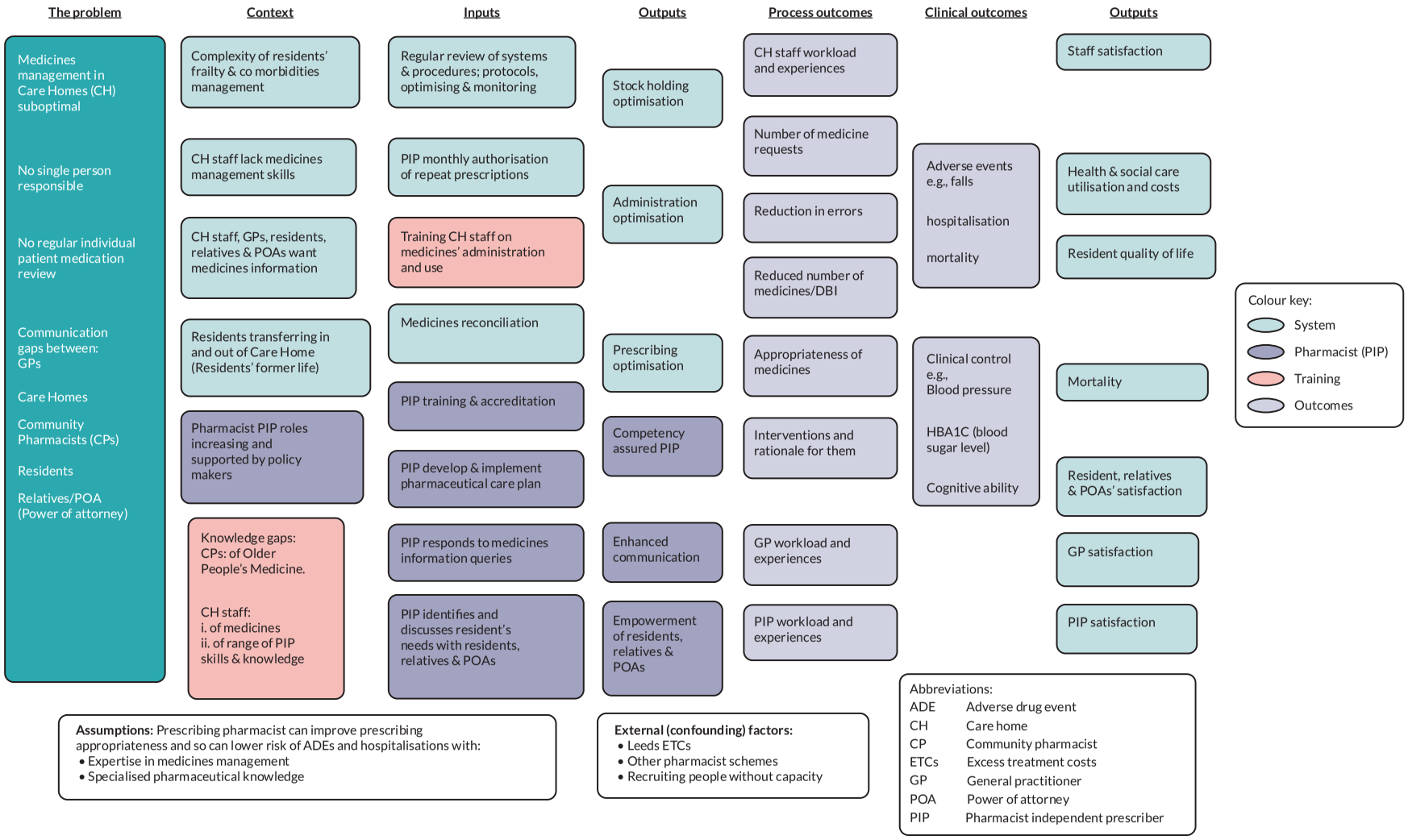
Outcome	Data source	Potential for bias	Potential for missing data	Resident centred	Sensitivity to intervention	Reliability	Validated?	Third party completion	Ability to blind?	Time taken to collect	Quantity of data	Inclusion in RCT
STOPP/START	GP medical records	High	Medium	-	Significant improvement in two studies	-Concerns about inter-rater reliability- not designed as a research tool	✓clinical tool only	✓	+	10–20 min	Good	Secondary outcome measure – reduced list
No. of medicines	GP records	Low	Low	-	Three studies no significant effect Two studies significant decrease	++	N/A	✓	+	None	Good	Process measure
Drug Burden Index	GP record	Low	Low	-	Not previously reported- only relates to anticholinergic medicines	+	✓	✓	+	5 min	Good	Secondary outcome measure
Hospitalisations	Care home	Low	Low	+	No effect found in three studies Positive in two	+	N/A	✓	-	5 min	Good	Secondary outcome measures
Mortality	Care home	Low	Low	-	No effect reported in five studies	++	N/A	✓	+	5 min	Good	Secondary outcome measure

GP, general practitioner; MMSE, Mini-Mental State Examination; N/A, not applicable; QOL, quality of life; RCT, randomised controlled trial.
A fall is defined as 'an event whereby an individual comes to rest on the ground or another lower level with or without loss of consciousness' (World Health Organization 2007).

Note
✓, Meets the criterion; ++, + and –, Extent to which it meets the criterion (meets the criterion fully, meets the criterion partially and does not meet the criterion, respectively).

Appendix 6 Final Logic Model v9 FINAL, 6 February 2019 (vs. 1–8 in Supplementary file)

2019.02.06 CHIPPS Logic Model v9.0 Final



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Research participants

Care homes and their staff
GP practices and their staff
PIPs

Appendix 8 Health economics report

Methods

Costs

Costs were estimated in Great British pounds (£) at 2017/2018 financial year levels from the perspective of the NHS and personal social services (PSS). No discounting was undertaken due to the time frame of the study (costs were estimated over a 3-month period before the baseline/intervention and a 6-month follow-up period).

Estimating the cost of the PIP intervention

To estimate the PIP costs, each PIP was asked to complete two particular items over the 6-month post-randomisation period: a training log and an activity log. The training log enabled the PIP to record the time spent with others/courses undertaken as part of their training/professional development, for example, in-person training, contacts with a mentor, GP, community pharmacist, as well as any self-directed learning. The PIPs were also asked to record any activities associated with the PIP role within the PIP activity log, including the duration of (1) any contacts with others, for example, care home residents (participants), care home staff, GP, or any other professionals (e.g. geriatricians, community pharmacists, and district nurses), and (2) any other non-contact activity, for example, resident prescription management, care home medication storage, staff training and travel.

For both training and activity, log estimates of the cost per hour of employment were assigned to estimated times for the PIP and other professionals (including care home staff), where it was assumed that the PIP would have band 7 costs and their mentors/trainers band 8a costs.[24] Overheads were included as part of these unit costs, and these were deemed to cover any additional costs associated with the intervention.

As in the intervention arm, the PIP's role enabled the undertaking of prescription management for the individual care home residents, and it was envisaged that this would enable GPs to spend less time undertaking prescription management for intervention arm participants. We estimated the GP time saving that would have occurred, for each individual participant, because of no longer undertaking prescription time management, would have been as follows. It has been estimated that the mean time spent per prescription-related event is 56.0 seconds (28). Based on this figure, if each participant were to have two prescriptions issued each month (each of which contain up to four items), which no longer required GP approval, then this would equate to a total GP time saving of 11.2 minutes (per resident across the 6-month study period). At a cost of £110 per hour for a GP[24], this equates to a total cost saving, for GP time, of £20.60 per resident/participant.

Subsequently, the total PIP intervention cost was estimated by summing the per-participant PIP training and PIP activity costs and deducting the estimated GP time/cost saving.

Other costs

As it was considered that there was the potential for the introduction of the PIP role to improve outcomes/impact the use of other NHS and PSS resource-items, the following items were extracted from medical records.

Medication details were extracted from primary care records for both the 3-month period before baseline and the 6-month study follow-up period. In terms of unit cost, when extracting the medication data (directly into an electronic format), researchers were able to select medication details from the 2015 version of the Prescription Cost Analysis (PCA),[28,29] This was undertaken with a view to reduce the number of misspelt medications to which it would not be possible to attach cost at the end of the

study (it was still possible to enter a medication name if the drug was not listed in the 2015 PCA). Unit costs were automatically selected from the 2015 PCA as part of the data collection process, and no adjustment was made to these costs, as the average cost per prescription item has not increased in recent years.[28,29] Medications that were not automatically assigned a 2015 PCA price at the time of data entry were assigned a unit cost from the 2018 PCA.[28,29] The above enabled overall medication costs to be estimated.

Details of outpatient attendances, inpatient stays, tests and investigations and GP and practice nurse visits/phone calls were also extracted from primary care records. Conversely, informed by previous research,[23] the details of all other health professional contacts were extracted from care home records, where professional data of the number of visits (and location: care home/community) and number of phone calls were extracted. For all items, data in relation to the previous 3 months were collected at baseline and those for the previous 6 months were collected at the 6-month follow-up. Unit costs were subsequently assigned to each of these resource items (see *Appendix 1*, Table 1) and totalled to estimate the total other (non-medication) costs.

Finally, the total PIP intervention cost, overall medication costs and other (non-medication) costs were summed to estimate the total (NHS and PSS) cost.

Outcomes

In line with the National Institute for Health and Clinical Excellence (NICE) methods guidelines,[31] quality of life was measured using the EQ-5D-5L.[30] For all participants, proxy respondents were asked to report the participants' level of problems (on a range from none to extreme/unable) on five dimensions (mobility, self-care, usual activities, pain/discomfort and anxiety/depression) at baseline, 3-month follow-up and 6-month follow-up. As recommended in the NICE position statement,[33] the crosswalk mapping function[35] was used to convert these responses into utility scores, where a score of zero corresponds to death and one to full health. Participants who were known to have died were assigned a utility score of zero at the time points where this was known. Quality-adjusted life-year (QALY) scores were subsequently estimated for each individual based on the total area under the curve method and the assumption of linear interpolation.[36]

Analyses

The base-case analysis was based on the complete case approach (24) and included only those with complete total (NHS and PSS) cost data at baseline and 6-month follow-up and complete QALY scores. Because of the potential for skewed data/correlation between costs and effects, bivariate regression[37] was used to analyse the cost and QALY data, based on the intention-to-treat principle, that is, according to allocation arm (regardless of, e.g., whether the PIP intervention was received). Each regression included trial arm, age and gender as covariates, with the cost regression also including baseline costs and the QALY regression including the baseline EQ-5D score. Together, this enabled the mean incremental cost and the mean incremental effect (mean difference in QALYs) associated with the PIP intervention to be estimated.

If the PIP intervention were found to be more costly and less effective, then it would be dominated (by the other intervention), and not be recommended for implementation (money could be better spent elsewhere). Alternatively, the incremental cost-effectiveness ratio (ICER) (mean incremental cost/mean incremental effect) would be estimated, where an ICER (incremental cost per QALY) below the cost-effectiveness threshold (λ) value of £20,000–30,000 per QALY can be inferred to be cost-effective.[31]

Analyses of uncertainty

To estimate the level of uncertainty associated with the decision regarding cost-effectiveness, we depict results on the cost-effectiveness acceptability curve,[38] where we report the probability of the PIP intervention being cost-effective at the λ value of £20,000/QALY compared with that with standard care.

Additionally, to assess the robustness of the results to assumptions made in the above base-case analysis, the following sensitivity analyses were undertaken. First, as missing data can lead to bias,[132] multiple imputation (MI) was undertaken.[133] Specifically, the Stata mi impute command was used to create multiple datasets, which were then pooled using Rubin's rules.[134] The MI model included the trial arm, age, gender and the aforementioned component costs and EQ-5D scores at baseline and at 3- and 6-month follow-ups (cost components were included as they had different levels of missing data, whereas levels of missing data did not tend to differ across the dimensions of the EQ-5D). Total costs and QALY scores were then estimated based on the component costs and EQ-5D scores, respectively. In the second sensitivity analysis, the PIP training costs were excluded from the total costs. This (best case scenario) was justified on the basis that, as training has now been undertaken, in certain circumstances, no further training would be required if the intervention were continued. In both these sensitivity analyses, the analysis was otherwise as reported above, that is, bivariate regression was undertaken to estimate mean incremental cost and mean incremental effect, and the probability of the PIP intervention being cost-effective at the λ value of £20,000/QALY was also estimated.

Finally, threshold analysis was undertaken in order to identify when the decision as to whether an intervention is cost-effective switches, for example, from being estimated to be not cost-effective, to being estimated to be cost-effective.[34] In particular, we sought to identify the estimated cost (effect), holding the effect (cost) as in the base-case, at which the decision as to cost-effectiveness would change. Thus, showing the range of costs (effects) where the PIP intervention would be estimated to be cost-effective.

Results

A total of 25 (449) triads (participants) were allocated to the intervention, and 24 (427) to the control. Aside from the intervention group having a lower proportion of participants in nursing home care (42% vs. 59%), a higher mean Barthel score (8.34 vs. 7.07, i.e. greater independence), and a greater number of falls (0.78 vs. 0.57 mean falls in the previous 90 days), the groups were otherwise broadly similar.

Cost of the PIP intervention

The training logs were returned by 23/25 PIPs, and the activity logs by 22/25 PIPs. Certain assumptions were therefore necessary to deal with this and other types of missing data, in order that mean PIP costs be estimated for all PIPs/participants. By way of example, in cases where a particular training/activity was reported, but the associated time was not, the mean time listed for that particular training/activity by other PIPs was estimated and assigned to the described activity. This meant, for example, that the mean cost for the 23 PIPs who returned the training logs was applied to the two PIPs who did not as it was known that these two PIPs had completed their training.

The mean training time per PIP was 4.3 days (see *Table 2*), where this included a 2-day course, approximately a further day of contact time with other professionals, for example, mentor/GP along and a further day of self-directed learning. The mean total training cost (including the costs for contacts with other professionals) was estimated to be £61,916.07, which was equivalent to £2476.64 per PIP or £137.90 per study participant. Though these costs are based on actual study data, they may overestimate future training costs as in practice training could be delivered to more individuals at once, and the costs spread across more residents, reducing the cost per resident (this is assessed as part of the aforementioned second sensitivity analysis).

No PIP activity costs were assigned to intervention participants in the care homes where the three PIPs did not return their activity logs (these PIPs did not deliver the intervention and zero PIP time/costs were therefore assigned to the residents under their care). Conversely, one PIP reported activities that amounted to a time of 19.4 days (assuming a 7.5-hour working day) per resident. As such, there was wide variation around the mean PIP reported activity time of 7.6 days (this equates to 191 minutes per participant, see *Appendix 1*, *Table 23*).

In terms of costs, the mean PIP activity cost was £205.29 (range: £0–1168.67) per participant, where the mean PIP cost was £169.68 per participant, compared to £35.61 per participant for other professionals' time. When added to the aforementioned training cost, and the assumed GP cost saving due to them undertaking fewer prescriptions, this gives an estimated mean PIP intervention cost of £322.59 (see *Appendix 1*, *Table 24*).

Other costs

In terms of the other NHS and PSS resource-items that it was considered could change due to the introduction of the PIP role (medication, out-patient attendances, in-patient stays, tests and investigations, GP and practice nurse visits/phone calls and other health professional visits/phone calls), the associated mean estimated levels of resource use and costs are reported in *Tables 2* and *3*, respectively, where it can be seen that overall medication costs and other (non-medication) costs are broadly similar between groups. Accordingly, the mean total (NHS and PSS) cost was estimated to be higher in the PIP intervention group (see *Appendix 1*, *Table 24*), where this difference between groups was largely due to the costs associated with the PIP intervention.

Outcomes

The response rates for both groups and mean utility scores at the baseline, 3- and 6-month follow-up points, along with mean QALY scores, are shown in *Appendix 1*, *Table 25*. It can be seen that the mean utility scores tended to fall over time in both groups (i.e. somewhat explained by zero scores being assigned to those who died). The baseline imbalance in EQ-5D scores between groups also demonstrates why this variable should be adjusted for when estimating the incremental QALY scores.

Analyses

A total of 609 participants (70%) had complete cost and EQ-5D data. The base-case estimated mean incremental cost and effect (mean difference in QALYs) are provided in *Appendix 1*, *Table 26*. It can be seen that the PIP intervention is estimated to be both more costly, and less effective, with only a 4% probability of being cost-effective at the effective at the λ value of £20,000/QALY. Within the two sensitivity analyses the PIP intervention was again estimated to be more costly and less effective.

In terms of threshold analysis, the aforementioned base-case analysis estimated that the PIP intervention was associated with higher costs (£279.86) and a (marginally) lower effect (−0.004), and thus was estimated not to be cost-effective. When considering a cost-effectiveness threshold of £20,000/QALY, assuming the same base-case cost (£279.86) the PIP intervention would be estimated to switch to being cost-effective if the QALY gain was estimated to be ≥0.14. Additionally, for the same base-case effect (−0.004) a cost-saving of ≥£72.02 would be necessary for the PIP intervention to switch to being estimated to be cost-effective (have a cost/QALY <£20,000/QALY). Both of the above threshold values are outside the 95% CI surrounding both the base-case mean cost and the mean effect, which would suggest that one would consider it unlikely that these thresholds would be reached based on the data collected, and associated assumptions, in this analysis.

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