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Supporting GPs and people with hypertension to maximise medication use to control blood pressure: a pilot cluster RCT of the MIAMI intervention





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RESEARCH

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Supporting GPs and people with hypertension to maximise medication use to control blood pressure: a pilot cluster RCT of the MIAMI intervention

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Abstract

Background Hypertension, or high blood pressure, is a key modifiable risk factor for heart disease and stroke. International guidelines have highlighted 'poor adherence to treatment' and 'physician inertia' as major barriers to effective blood pressure management. The *Maximising Adherence, Minimising Inertia* (MIAMI) intervention, a theory-based complex intervention, supports General Practitioners (GPs) and people with hypertension in maximising medication use to manage blood pressure. This pilot cluster randomised control trial (RCT) aimed to collect and analyse feasibility data to refine the MIAMI intervention and assess the feasibility of a definitive RCT.

Method A pilot cluster RCT with a MIAMI intervention arm and usual care control arm was conducted. Quantitative data collection consisting of clinical measures and a self-report questionnaire took place at baseline and twelve week follow up. Semi-structured interviews with GP and patient participants were conducted. Fidelity (as measured by a protocol checklist and through qualitative interviews) and health economics costings were assessed.

Results Six GP practices (intervention arm $n=3$, control arm $n=3$) and 52 patients (intervention arm $n=25$, control arm $n=27$) took part. All six GP practices and 92% of patients were retained. Fidelity, as measured by a checklist and through qualitative interviews, was good but three deviations from protocol were identified. Outcomes and measures used were acceptable. The implementation cost of the MIAMI intervention was estimated at €490 per participant. The qualitative data demonstrated that the intervention was considered acceptable and feasible by both GP and patient participants, except for the urine test component, which GPs found difficult to incorporate into practice due to logistical challenges.

Conclusions The MIAMI intervention was considered largely acceptable and feasible. Some changes to both intervention components and trial processes are required but with these in place a definitive RCT could be considered worthwhile.

Trial registration ISRCTN registry, ISRCTN85009436, registered 17/1/23.

Keywords Hypertension, Primary care, Adherence, Feasibility

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Background

Hypertension is a prevalent, potent, and modifiable risk factor for multiple chronic conditions; including those linked to cardiovascular disease, chronic kidney disease and dementia [1, 2]. There is a strong evidence base supporting the efficacy and effectiveness of multiple pharmacological agents in lowering blood pressure (BP) and there is good consensus internationally for the role of long-term medications in reducing morbidity and mortality associated with hypertension [3, 4]. Therefore, pharmacotherapy with antihypertensive agents is the bedrock of contemporary medical management of hypertension [5].

One significant obstacle to realising the potential treatment benefits of antihypertensive medications concerns the variability in how these medications are used in the community by patients [6, 7]. Several decades of evidence using multiple methods demonstrates that medications are often not used as initially agreed with prescribers. This is termed 'non-adherence' in the literature and has been disaggregated into three temporal phases: initiation, persistence, and discontinuation [8]. These phases represent the continuum from starting to take the medication following diagnosis and prescription, through to the continued use of the medication over time and finally to the point where medication may be no longer sought and/or used by patient [9].

Much of hypertension management occurs in the community, for example, in general practice and similar primary care settings [10, 11]. This setting provides an important context where challenges with medication-taking can be identified, and appropriate interventions can be delivered to support effective medication use. Indeed, there are several studies that have evaluated behavioural interventions to support medication use for hypertension in general practice; however, these included a heterogeneous range of interventions and contexts [12–15].

Following a programme of work on medication use in hypertension over a series of studies [12, 16–19], we focused on medication-taking behaviour and physician inertia as two key behaviours for intervention. Informed by the MRC framework and using the Behaviour Change Wheel [45] as the overarching development framework, we used Collective Intelligence methodology to develop an intervention package called the *Maximising Adherence, Minimising Inertia* (MIAMI) intervention (comprehensive description reported elsewhere, [20]). It aims to support General Practitioners (GPs) and people with hypertension to maximise medication use to control BP. A key feature of this work has been the close collaboration with key stakeholders and a consistent systematic

approach to the co-design of this intervention with patient and public involvement (PPI) throughout intervention design and evaluation.

Aims of the MIAMI cluster pilot RCT

The specific aim of the MIAMI pilot cluster randomised controlled trial (RCT) was to gather and analyse feasibility data to allow us to (1) refine the MIAMI intervention, and (2) determine the feasibility of a definitive RCT.

Specifically, the MIAMI pilot cluster RCT had the following objectives:

1. To investigate if the MIAMI intervention is acceptable to participants - GPs and people with hypertension;
2. To collect pilot qualitative and quantitative data to assess the feasibility of recruitment and retention of both practices and participants;
3. To collect pilot qualitative and quantitative data to assess the feasibility of outcomes and measures used;
4. To conduct a pilot health economic assessment of the MIAMI intervention;
5. To inform the sample size calculation, including the optimal number of GP practices (clusters) and people with hypertension (participants), for a definitive cluster RCT;
6. To collect pilot quantitative and qualitative data to assess the feasibility of a 'Study Within A Trial' focused on the impact of an informational video on study retention levels.

Methods

This study has been registered (ISRCTN85009436, 17/1/23) and a detailed protocol has been published [21]. Here we briefly summarise our methods – please see protocol for detail. All study materials and data can be accessed at <https://osf.io/xusby/>.

Design

This is a pilot cluster RCT with an intervention arm and a usual care control arm.

Inclusion and exclusion criteria

See Table 1 for inclusion and exclusion criteria.

Sample size calculations

To generate the reliable estimates needed, it was proposed that six clusters (three in the intervention arm, three in the control arm) each containing 10 patient participants be recruited.

Table 1 Inclusion and exclusion criteria for GP practices, GP participants and patient participants

Inclusion criteria for GP practices	Inclusion criteria for GP participants	Inclusion criteria for patient participants
<ul style="list-style-type: none"> • Located within the catchment area of the bio-chemistry lab at University Hospital Galway • Use the Socrates™ practice management software system [22] 	<ul style="list-style-type: none"> • Doctors who provide patient care in the practice 	<ul style="list-style-type: none"> • Confirmed diagnosis of hypertension • Age over 65 years • Currently prescribed two or more anti-hypertensive medications • Not achieving recommended blood pressure levels, i.e., clinic readings are higher than 140/90 mmHg or day ABPM^a reading is higher than 135/85 mmHg [23] • In the judgement of the GP regarding a change in medication, the balance of risk / benefit lies in favour of benefit <p>Exclusion criteria for patient participants</p> <ul style="list-style-type: none"> • Inability to give informed consent • Resident in a nursing home • Currently attending a hospital resistant hypertension clinic

^a ABPM ambulatory blood pressure monitor

Recruitment

GP practice recruitment

A convenience sample of 10 GP practices who had previously participated in similar hypertension research [24] and who met the inclusion criteria were identified and invited to participate by letter. If invited practices expressed interest in taking part, research staff followed up with a telephone call, and then a practice visit, to provide further details about the study. All participating practices were offered €100 per recruited patient participant to cover the additional administration costs, as well as a right to keep a 24-hour ambulatory blood pressure monitor (ABPM) after the study ended.

Patient participant recruitment

Recruitment commenced in December 2022 and initially happened through random sampling, where member of the practice team searched the practice records, first electronically and then manually, using the inclusion and exclusion criteria to identify all eligible patient participants. Once identified, the practice then posted a letter of invitation and information sheet to a random selection of 20 patients. Patients were asked to contact the research team if interested in taking part. If there was no response after 10 days, the practice contacted eligible patients by phone, explained the information in the letters and offered an opportunity to ask questions. If the target of 10 participants was not met at that point, another 10–20 letters were sent out, dependent on the response to date. However, after the first practice began recruitment, this approach was deemed too resource-intensive by practice staff.

A new recruitment strategy of case-finding [25] was introduced in February 2023, where instead of the entire patient record, the practice team searched recent and future bookings for ABPMs, and screened patients using the eligibility criteria. Once identified, the practice then contacted the patient, asked if they were interested in hearing more about the research, and asked for the patient's permission to be contacted by the research team. If the patient consented, a member of the research team contacted them by phone, explained the study and posted out the information sheet. The team member then followed up with another phone call to see if the patient wanted to take part. If so, the patient was booked in for a clinic appointment. All patient participants were offered a €40 payment to cover costs associated with their participation (e.g., travel to the practice for study visits).

Cluster randomisation

After all practices were recruited, three GP practices were randomised to the MIAMI intervention and three to the usual care control. The code to generate the randomisation plan was written in R (using a reproducible random generation seed) and implemented by an independent statistician.

Intervention procedures

The MIAMI intervention is delivered at a minimum of one GP appointment during a twelve-week period. The intervention arm and control arm are described below.

MIAMI intervention arm

The MIAMI intervention is a structured set of supports for GPs and patients with hypertension to facilitate adequate information exchange within consultations about long-term antihypertensive medication use and adherence skill development. All GP intervention materials were provided to GPs at the beginning of the study, to ensure enough time to undertake training. Full details are provided in Table 2.

Urine samples were collected at practice visits 1 and 4 and brought to the local hospital laboratory in University Hospital Galway. From there, they were sent to the National Centre for Drug Adherence Testing at University Hospitals of Leicester for urine analysis via spectrometry testing [27]. Results were then sent back to the local laboratory and subsequently disseminated to GP practices.

The patient flow through the intervention arm can be seen in Fig. 1.

Control group

Participants in the control group received usual care (see protocol for description of usual care, [21]). Urine samples were collected at practice visit 3 and followed the same testing procedures as outlined above.

Patient flow through the control arm can be seen in Fig. 2.

Data collection**Participant quantitative data collection**

Patients Patient data collection occurred at two time points, baseline (T1) and follow up (T2; twelve weeks later). A full description of patient outcome measures can be seen in Table 3.

GPs A questionnaire to gather demographic and personal information including length of time working in primary care, employment basis (full-time, part-time, and other), practice location (urban/rural) and practice size was administered at T1.

Feasibility and acceptability data

The following was also measured:

1. Recruitment of GP practices was assessed by documenting the number of invitations sent, the number of refusals and number of acceptances.
2. Recruitment of patients was assessed by documenting the number of invitations sent, the number of initial responses, the number of follow-up phone-calls

required, the number of refusals, and the number of acceptances.

3. Attrition of participants was documented at every time-point.
4. Levels of missing data in returned questionnaires was measured.
5. The comprehensibility and acceptability of all questionnaires were measured by asking participants how the questionnaires might be improved and how long they took to complete.

Qualitative evaluation of feasibility and acceptability

A descriptive qualitative approach [33] was used to explore the perceptions and experiences of patients ($n=6$) and GPs ($n=3$) of participating in the MIAMI study and their views as to the acceptability of the intervention. Patient participants were interviewed at study mid-point (week 6) and again at end-point (week 12). GP participants were interviewed at study end-point. Patient participants ($n=6$) and GPs ($n=3$) in the control arm were interviewed at study end-point and the focus of this was the acceptability of taking part in a pilot RCT in the control arm. Reflexive thematic analysis as outlined by Braun & Clarke [34] was used to analyse the data and NVivo 14 was used to manage the data.

Fidelity

A checklist embedded as a 'Drop-Down Menu' in the Socrates practice software system was developed for the distinct components in the MIAMI intervention. This checklist was completed by GP participants during each consultation and subsequently reviewed by the research team.

Fidelity was also explored in the qualitative interviews with patient and GP participants.

Health economic analysis

A pilot health economic assessment of the MIAMI intervention relative to the usual care control arm was undertaken. Resource use associated with delivery of the MIAMI intervention was prospectively identified, measured and costed. In particular, implementation resources related to GP and other staff time input, consumables (e.g. urine bottles and disposable gloves), urine tests, and the ABPM process were identified, measured, and costed. In addition, a data collection form for healthcare service resource usage was included in the participant questionnaire at baseline and twelve-week follow-up. A number of sensitivity analyses were employed to address uncertainty

Table 2 The MIAMI intervention

Target	Intervention component	Timepoint of delivery	Detail
GP	Training videos	Pre-intervention commencement	30-minute training package (six short videos and quiz) <ul style="list-style-type: none"> • Part 1: Adherence to medication, including the extent of non-adherence, key factors associated with adherence, and types of non-adherence • Part 2: Three case studies to illustrate how you might support patients' medication adherence in different scenarios • Part 3: Skills and strategies to support adherence • Part 4: A case study illustrating the use of the MIAMI intervention
GP	MIAMI booklet	Pre-intervention commencement	Booklet contains: <ul style="list-style-type: none"> • BP thresholds (American College of Cardiology) [26] • A list of oral anti-hypertensive drugs (American College of Cardiology) [26] • Core drug treatment strategy for uncomplicated hypertension (European College of Cardiology) [23] • A list of available single pill combinations in Ireland • Simple reiteration of key training messages
GP	Consultation guide available through a drop-down menu integrated into practice management software	Pre-intervention commencement	Drop-down menu on computer which contains a guide to the consultation. <ul style="list-style-type: none"> • Discussed ABPM: YES/NO • Discussed urine results: YES/NO • Made an agreed plan which may include: single pill combinations, 'blister pack' specification: YES/NO • Asked patient to form a habit (pair medication taking with another stable behaviour e.g., a mealtime/brushing teeth/Coronation Street): YES/NO • Wrote out the agreed plan on the 'MIAMI pre-consultation tool': YES/NO • Sent relevant text message: YES/NO Text that the GP can copy and paste into a text message to the patient: <i>You can set up text messages to remind you to take your medication at dontforget.ie</i> <i>Information about blood pressure and blood pressure medication is available on the Croí website: https://croi.ie/health/heart-conditions/high-blood-pressure/</i>
Patient	Pre-consultation plan	Practice visit 2 and 5 (see Fig. 1)	Short document containing: <ul style="list-style-type: none"> • 'What do you want to talk about at your blood pressure appointment today?' (to be filled in prior to consultation) • Textbox for BP reading and whether it is in target • Textbox for goal setting and action planning (to be used during consultation)
Patient	GP consultation	Practice visit 3 and 6 (see Fig. 1)	Discussion of ABPM and chemical adherence urine test results. Use of pre-consultation plan to create shared action plan GP to review prescription and adjust to include single pill combinations and blister pack if appropriate GP to advise on habit creation GP to send text messages on dontforget.ie and Croí website if appropriate
Patient	Croí website	Practice visit 3 and 6 (see Fig. 1)	Page on website containing (both text and video format): <ul style="list-style-type: none"> • Information on BP • BP values • How medication works • Benefits of medication • Possible side-effects

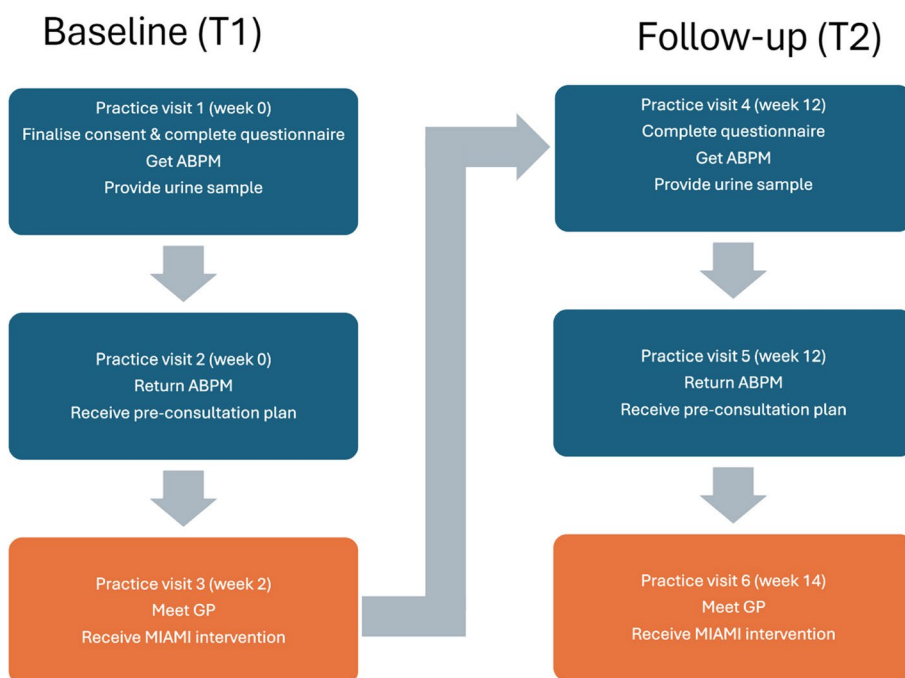


Fig. 1 Patient flow through the MIAMI intervention. Blue denotes data collection visit and orange denotes intervention visit

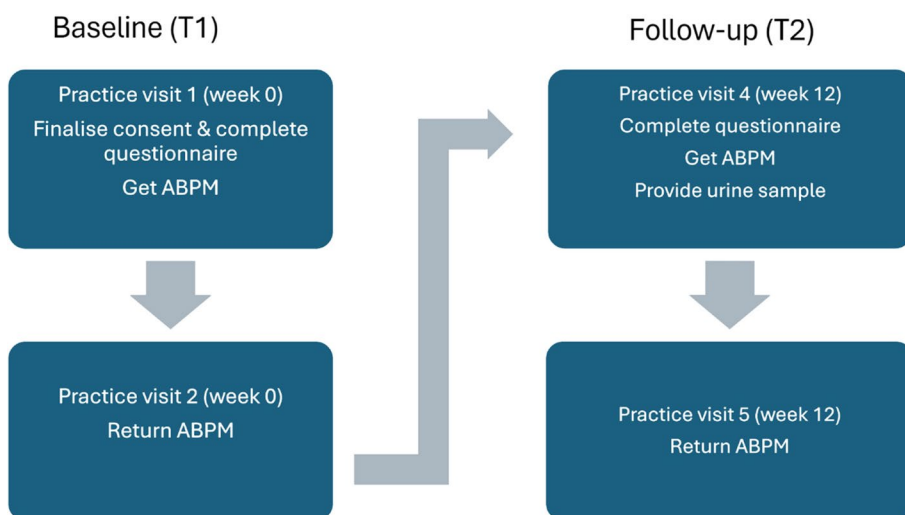


Fig. 2 Patient participant flow through the usual care control arm

in the cost analysis. In terms of health outcomes, Quality Adjusted Life Years (QALYs) were estimated based on participant response data to the EuroQol EQ-5D-5 L instrument at baseline and twelve weeks, and the Irish EQ-5D-5 L value set [35]. Summary statistics in the form of means and standard deviations are presented to compare healthcare costs and QALYs gained at twelve-week follow-up.

Statistical analysis

Suitable summary statistics (e.g., mean, standard deviation, and frequency) were calculated for the main outcomes.

Sample size estimates for a future definitive trial were calculated from the improvement (i.e. Post – Baseline) in systolic BP measures using the pilot study data. To allow for clustering, an estimate of the sample size for an

Table 3 Patient outcome measures

Outcome	Measurement	When	Source
Systolic BP	24-hour ABPM (average day reading)	T1 & T2	Direct researcher entry
Diastolic BP	24-hour ABPM (average day reading)	T1 & T2	Direct researcher entry
BP control	24-hour ABPM (readings above or below 140/90 mmHg)	T1 & T2	Direct researcher entry
Medication adherence	Urine screen (Adherence ratio ^a)	(T1) & T2 ^b	Chart review by researcher
Medication adherence	Prescription refill record	T1 & T2	Chart review by researcher
Medication adherence	Medication Adherence Report Scale [28] Scored from 1–5, with higher score indicating greater adherence	T1 & T2	Patient self-report
Beliefs about medication	Beliefs about Medicines Questionnaire [29] Scored from 1–5, with higher scores indicating greater necessity beliefs and greater concerns beliefs Illness Perceptions Questionnaire–Revised ('treatment control' & 'consequences' items) [30] Treatment control: scored 5–25, higher scores represent more positive beliefs about controllability of the illness Consequences: scored 5–30, higher scores represent more strongly held beliefs about the negative consequences of the illness	T1 & T2	Patient self-report
Habit strength	Self-Report Behavioural Automaticity Index [31] Scored from 4–28, with higher scores indicating greater medication-taking habit strength	T1 & T2	Patient self-report
Patient assessment of care	Patient Assessment of Chronic Illness Care [32] ^c Scored from 1–5, with higher scores indicating greater perceived receipt of aspects of patient-centred structured chronic care	T1 & T2	Patient self-report
Medication prescription/pill burden	Quantity of medications	T1 & T2	Chart review by researcher
Health related QoL	EuroQoL-5D-5 L Scored 1–5, with lower scores indicating a better health state	T1 & T2	Patient self-report
Wellbeing	ICECAP-O Scored 1–5, with higher scores indicating greater wellbeing	T1 & T2	Patient self-report

^a This outcome will not be captured at baseline in the control arm, due to a concern around the provision of clinical information to GPs without guidance on management. It will be captured at follow up in the control arm, as all GPs will have access to intervention materials at study end

^b Ratios are calculated for each patient – based on the medications that could be detected – by dividing the total number of antihypertensive medications detected in spot urine into the total number of detectable antihypertensive medications prescribed, whereby total non-adherence was equal to 0 and perfect adherence was equal to 1

^c Four of the five subscales – recent psychometric evaluation evidence indicates that the 'Follow-up/Coordination' sub-scale and item 10 are the least psychometrically robust and that a 14-item measure with an underlying four-factor structure provides more psychometrically robust measurement than the original 20-item scale with a five-factor structure [10]

individually randomised trial was adjusted and inflated by the design effect given by $1 + (\bar{n}-1)\rho$, where \bar{n} was the average cluster size and ρ was the estimated intra-class correlation coefficient (ICC) for this study [36, 37].

Progression to a full RCT

The following pre-defined stop/go criteria in Table 4 were used to inform the decision on whether to proceed to a full trial.

The Decision-making after Pilot and feasibility Trials (ADePT) process involves examining 14 methodological issues that are pertinent to feasibility research [38, 39]. We used this process, as well as the progression criteria, findings from the qualitative research, and discussions with the study research team, trial management group, trial steering committee, and the public and patient involvement (PPI) panel to make a decision on whether to progress to full RCT.

Study within a trial (SWAT)

A small-scale pilot SWAT was conducted as part of this pilot RCT. Full details and results can be found at <https://osf.io/xusby/>.

Ethical approval

Ethical approval was granted by the Irish College of General Practitioners (ICGP_REC_22_014). An amendment was sought and approved for the change to recruitment strategy.

Results

The completed CONSORT extension to pilot and feasibility trials checklist can be seen in Appendix 1.

Sample characteristics

Demographic characteristics for all patient and GP participants can be seen in Table 5.

Table 4 Stop/go criteria for progression to a full scale RCT

	Go – proceed with full RCT	Amend – proceed to full RCT with changes	Stop – do not proceed unless major changes are possible
1. Feasibility of practice recruitment Can 6 practices be recruited to take part in 3 months?	If ≥ 5 practices are recruited to take part in 3 months	If ≥ 5 practices are recruited, but it takes longer than predicted (e.g. 3–6 months)	Unable to recruit at least 4 practices.
2. Feasibility of patient recruitment Can 10 patients per practice (total n = 60) be recruited?	If 8–10 patients are recruited in one month per practice: total of 60 (100%)	If 6–7 patients are recruited in one month per practice: total of 36–60 (60% to ≤ 100%)	If < 6 patients are recruited in one month per practice: total of ≤ 36 (< 60%)
3. Feasibility of practice retention Can all 6 practices be retained in the study until completion?	≥ 5 retained	≥ 4 retained	≤ 3 retained
4. Feasibility of patient retention ^a Can at least 90% of recruited patients be retained in the study until completion?	> 9 patients (90%) retained per practice	7–8 patients (70–80%) retained per practice	< 7 patients (< 70%) retained per practice
5. Intervention feasibility	Delivery of intervention judged strongly feasible by qualitative data	Delivery of intervention judged mainly feasible by qualitative data	Delivery of intervention judged problematic by qualitative data

^a Retention defined as availability of primary outcome at follow-up

Table 5 Demographic characteristics of patient and GP participants

Patient participants	Control n = 27	MIAMI intervention n = 25
<i>Age (mean, SD)</i>	75.04 (5.48)	73.8 (6.19)
<i>Sex</i>		
Male (n, %)	17 (63%)	18 (72%)
Female (n, %)	10 (37%)	7 (28%)
<i>Marital status</i>		
Single (n, %)	2 (7.4%)	3 (12%)
Cohabiting (n, %)	1 (3.7%)	1 (4%)
Married (n, %)	18 (66.7%)	12 (48%)
Widowed (n, %)	5 (18.5%)	7 (28%)
Divorced (n, %)	0	2 (8%)
Missing (n, %)	1 (3.7%)	0
<i>Living situation</i>		
Living alone (n, %)	2 (7.4%)	8 (32%)
Living with partner (n, %)	13 (48.1%)	10 (40%)
Living with family (n, %)	10 (37%)	6 (24%)
Missing (n, %)	2 (7.4%)	1 (4%)
<i>Education</i>		
Primary school only (n, %)	6 (22.2%)	9 (36%)
Some secondary school (n, %)	5 (18.5%)	3 (12%)
Complete secondary school (n, %)	7 (25.9%)	4 (16%)
Technical or vocational qualification (n, %)	4 (14.8%)	4 (16%)
Some third level (n, %)	2 (7.4%)	4 (16%)
Complete third level (n, %)	2 (7.4%)	0
Missing (n, %)	1 (3.7%)	1 (4%)
<i>Employment status</i>		
Full time employee (n, %)	1 (3.7%)	4 (16%)
Part time employee (n, %)	0	2 (8%)
Self-employed (n, %)	4 (14.8%)	3 (12%)
Homemaker (n, %)	2 (7.4%)	0
Retired (n, %)	19 (70.4%)	16 (64%)
Missing (n, %)	1 (3.7%)	0
<i>Medical card (n, %)</i>	13 (48.1%)	20 (80%)
<i>Health insurance (n, %)</i>	16 (59.3%)	11 (44%)
<i>Length of hypertension diagnosis</i>		
< 1 year (n, %)	1 (3.7%)	2 (8%)
1-5 years (n, %)	2 (7.4%)	5 (20%)
> 5 years (n, %)	21 (77.8%)	17 (68%)
Missing (n, %)	3 (11.1%)	1 (4%)
<i>Blood pressure (mean, SD)</i>	147.59/80.74 (11.27/11.82)	143.68/78.72 (11.81/11.12)
GP participants	n = 3	n = 3
<i>Sex</i>		
Male (n)	3	2
Female (n)	0	1
<i>Years working as a GP (mean, SD)</i>	22.67 (11.06)	20.66 (7.5)
<i>Practice Location</i>	Urban: 2 Rural: 0 Mixed: 1	Urban: 1 Rural: 1 Mixed: 1

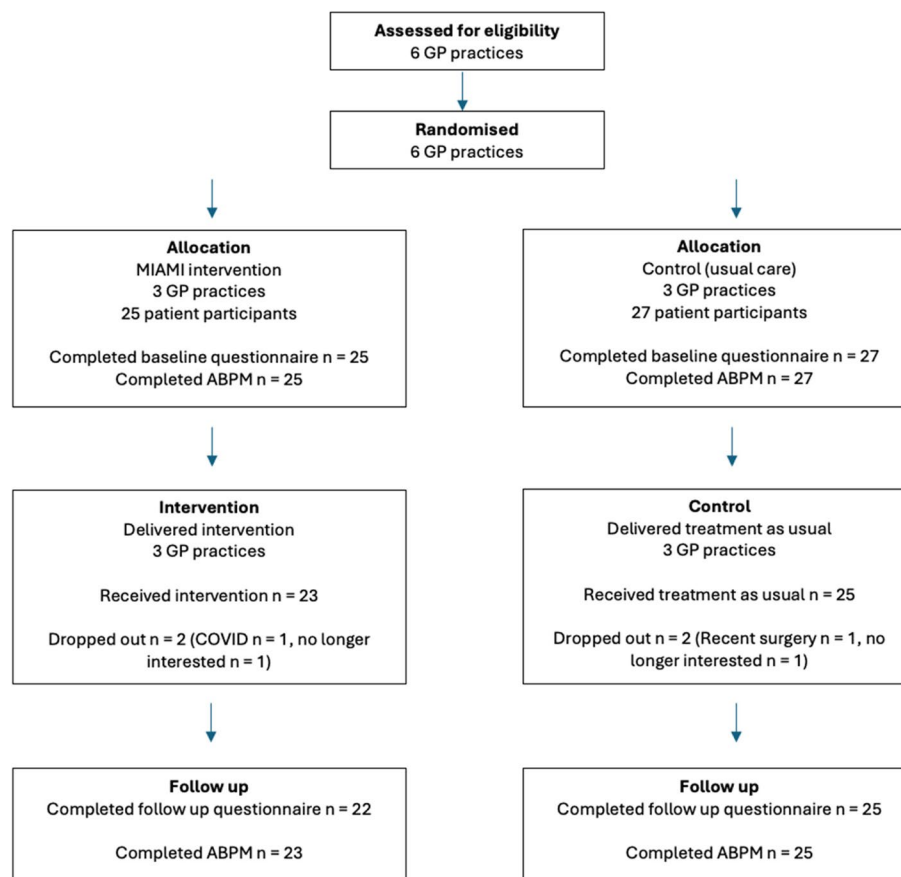


Fig. 3 CONSORT flow diagram

Recruitment

The CONSORT diagram (Fig. 3) illustrates the flow of patient participants through the study.

Letters of invitation were sent to ten practices and six were successfully recruited over five months. In terms of patient recruitment, as mentioned in the Method section, the initial recruitment strategy of random sampling was considered too burdensome by practice staff. A case-finding method was introduced, which was considered more acceptable to staff. This led to a faster recruitment process; however, this meant that data was no longer possible to collect on the number of invitations sent and responses. Five sites recruited eight or more patients, and one site recruited four.

Retention

All six GP practices were retained. The attrition rate for the patient sample from baseline to follow up was 7.69% ($n = 4$). Two patients dropped out of the MIAMI intervention arm and two patients dropped out of the control arm. Reasons for dropout included COVID-19, recent surgery, and no longer being interested (see Fig. 3).

Outcome measures

Table 3 gives a full description of outcome measures and Table 6 presents the results for the blood pressure outcome measures at baseline and follow up for intervention and control arms. The results of the remaining outcomes measures are included in the [Supplementary material](#).

A number of the outcomes were self-reported (see Table 3) and the mean length of time reported to complete the questionnaire was 22 minutes (range 10-60 minutes). Missing data was minimal, except for the health economics section where there were frequent instances of missing or incorrectly reported data (see Table 7). Feedback on the questionnaire was generally positive.

“The questionnaire was straightforward and clearly laid out.” (Female, age 74, intervention arm).

All questionnaires were completed ($n = 52/52$, 100%) at baseline. At follow-up, 90% (47/52) of questionnaires were completed (four patients left the study – see CONSORT flow diagram).

Table 6 Blood pressure measures at baseline and follow up

	Control	MIAMI intervention	Overall
Baseline	<i>n</i> = 27	<i>n</i> = 25	
<i>Daytime average SBP</i>			
Mean (SD)	142 (14.9)	143 (10.6)	142 (12.9)
Median [Min, max]	147 [105, 167]	141 [127, 168]	143 [105, 168]
<i>Daytime average DBP</i>			
Mean (SD)	81.7 (7.72)	84.0 (9.02)	82.8 (8.37)
Median [Min, max]	82.0 [64.0, 94.0]	86.0 [59.0, 97.0]	84.0 [59.0, 97.0]
Twelve week follow up	<i>n</i> = 25	<i>n</i> = 23	
<i>Daytime average SBP</i>			
Mean (SD)	139 (14.4)	137 (13.1)	138 (13.7)
Median [Min, max]	137 [118, 172]	136 [106, 166]	137 [106, 172]
<i>Daytime average DBP</i>			
Mean (SD)	81.0 (7.62)	80.4 (8.33)	80.7 (7.88)
Median [Min, max]	81.0 [68.0, 101]	80.0 [59.0, 96.0]	81.0 [59.0, 101]

Table 7 Resource use, costs, EQ-5D-5 L scores and QALY estimates at baseline and follow up (twelve weeks)

Resource Items	Intervention (<i>n</i> = 25)		Control (<i>n</i> = 27)		Intervention (<i>n</i> = 25)		Control (<i>n</i> = 27)	
	Baseline – costs incurred in previous 12 months Mean (SD)		Baseline – costs incurred in previous 12 months Mean (SD)		Follow Up – costs incurred in previous 3 months Mean (SD)		Follow Up – costs incurred in previous 3 months Mean (SD)	
	Usage	Cost €	Usage	Cost €	Usage	Cost €	Usage	Cost €
GP Visits	4.80 (2.57)	254(136)	4.39 (2.52)	233 (134)	1.85 (2.54)	98(135)	1.35 (0.81)	72 (43)
Practice Nurse Visit	2.53(2.44)	114(110)	1.43(1.83)	64(82)	0.61(0.70)	28(31)	0.60(0.75)	27(34)
Outpatient Visits BP related	0.05 (0.22)	7(33)	0.05(0.21)	7(31)	0.14 (0.35)	20(51)	0.00(0.00)	0(0)
Outpatient Visits non- BP related	0.95(1.36)	139(198)	1.52(2.79)	222(407)	0.38(0.50)	56(73)	0.48(0.85)	70(123)
Inpatient Days	0.05(0.22)	37(168)	0.33(1.09)	257(840)	0.05(0.21)	35(164)	0.00(0.00)	0(0)
Inpatient Nights	0.48 (1.63)	473(1,621)	0.38(1.06)	373(1,049)	0.86 (2.35)	852(2,337)	0.30(1.46)	303(1,451)
A&E Visits	0.14(0.35)	41(105)	0.17(0.38)	50(114)	0.11 (0.32)	32(95)	0.00(0.00)	0(0)
ICU night	0.17(0.83)	463(2,220)	0.00(0.00)	0(0)	0.14(0.65)	380(1,742)	0.00(0.00)	0(0)
MIAMI Intervention					25(100)	490(0)	0(0)	0 (0)
Health Outcomes								
EQ-5D-5 L Score	0.80(0.20)		0.78(0.30)		0.78 (0.27)		0.77 (0.31)	
QALYs Gained					0.19 (0.05)		0.19 (0.07)	

A&E Accident and emergency, ICU Intensive care unit, QALYs Quality adjusted life years. Unit costs in € 2022 prices

EQ-5D-5 L responses were transformed using an algorithm into a single health state index score, based on values elicited via the time trade-off and discrete choice approach for the Irish population [26]

Completeness of data:

Intervention: Baseline – 24% missing data for GP visits, 24% for practice nurse visits, 20% for outpatient BP-related visits, 20% for outpatient non BP related visits, 12% for A&E visits, 16% for inpatient days, 16% for inpatient nights, 8% for ICU visits, 8% for EQ-5D-5L 1,2,4,5. and 12% for EQ-5D-5L 3

Intervention: Follow up – 20% missing data for GP visits, 28% for practice nurse visits, 12% for outpatient BP-related visits, 16% for outpatient non BP related visits, 24% for A&E visits, 12% for inpatient days, 16% for inpatient nights, 16% for ICU visits, 12% for EQ-5D-5L, 1,3,4,5, 16% for EQ-5D-5L,2 and 24% for QALYs

Control: Baseline – 33% missing data for GP visits, 22% for practice nurse visits, 19% for outpatient BP-related visits, 22% for outpatient non-BP related visits, 11% for A&E visits, 11% for inpatient days, 11% for inpatient nights, 11 for ICU visits, and 4% for EQ-5D-5L

Control: Follow up – 26% missing data for GP visits, 26% for practice nurse visits, 19% for outpatient BP-related visits, 15% for outpatient non-BP related visits, 15% for A&E visits, 15% for inpatient days, 15% for inpatient nights, 15% for ICU visits, 15% for EQ-5D-5L and 14% for QALYs

Sample size calculation

This sample size calculation used a mean improvement of 5mmHg in systolic BP as a clinically important difference with a standard deviation of 14mmHg (based on the

improvements observed in the pilot study). An estimate of the ICC of 0.005 was provided from the random effect due to the clustering in a linear mixed model of systolic BP at follow up adjusting for treatment arm and baseline

Table 8 Study results mapped to stop/go criteria

	Go – proceed with full RCT	Amend – proceed to full RCT with changes	Stop – do not proceed unless major changes are possible
1. Feasibility of practice recruitment Can 6 practices be recruited to take part in 3 months?	If ≥ 5 practices are recruited to take part in 3 months	If ≥ 5 practices are recruited, but it takes longer than predicted (e.g. 3–6 months)	Unable to recruit at least 4 practices
2. Feasibility of patient recruitment Can 10 patients per practice (total n = 60) be recruited?	If 8–10 patients are recruited in one month per practice: total of 60 (100%)	If 6–7 patients are recruited in one month per practice: total of 36–60 (60% to ≤ 100%)	If < 6 patients are recruited in one month per practice: total of ≤ 36 (< 60%)
3. Feasibility of practice retention Can all 6 practices be retained in the study until completion?	≥ 5 retained	≥ 4 retained	≤ 3 retained
4. Feasibility of patient retention ^a Can at least 90% of recruited patients be retained in the study until completion?	> 9 patients (90%) retained per practice	7–8 patients (70–80%) retained per practice	< 7 patients (< 70%) retained per practice
5. Intervention feasibility	Delivery of intervention judged strongly feasible by qualitative data	Delivery of intervention judged mainly feasible by qualitative data	Delivery of intervention judged problematic by qualitative data

^a Retention defined as availability of primary outcome at follow-up

systolic BP. In order to achieve 80% power (at a significance level α of 0.05) with an average cluster size of 30, a minimum of 6 clusters of size 30 in both the intervention and control arms (i.e. 360 in total) is required.

To allow for a loss to follow-up of up to 20% of participants, an additional cluster in each arm should be recruited.

Health economics analysis

The methods developed and implemented for the conduct of the pilot health economics analysis proved to be feasible and acceptable to study patients. In terms of the cost data generated in the pilot, the implementation cost of the MIAMI intervention was estimated at €490 per participant (see Appendix 2). The summary statistics for the usage and costs of the other healthcare resources for the intervention arm and the control arm are presented in Table 8. In terms of health outcomes, summary statistics for the EQ-5D-5L raw data are presented in Appendix 2 and the utility scores and QALYs at twelve weeks are presented in Table 8. The mean QALYs gained per patient at twelve-week follow-up was estimated at 0.19 (SD: 0.05) for the intervention arm and 0.19 (SD: 0.07) the control arm. The key issue of concern for the health economics analysis was missing data arising from non-response or misreporting of responses (e.g., qualitative rather than quantitative responses) to the self-report questionnaires (see Table 7). In planning for a future definitive trial, careful consideration of how best to capture the health economic data, informed by patient feedback, is needed.

Intervention fidelity

Fidelity was assessed through a checklist for GPs and explored in the qualitative interviews. Adherence to protocol was generally good but three deviations from protocol were identified. The first was the use of the pre-consultation tool, which did not always happen. Qualitative interviews identified that this was because patients did not bring it in with them. The second of these was advice on habit formation, which GPs did not always give to patients. Checklists revealed that this occurred when GPs felt that patients already had a strong habit in place. Finally, the results of the urine test of adherence were not always given to patients. This was due to logistical issues, which are explored further in the next section.

Intervention acceptability

Overall, the intervention was viewed positively by both patient and GP participants; however, there were some issues with some individual intervention components.

Acceptability of MIAMI to patient participants

Patient participants were generally very happy to take part in the study and could see the benefit of the MIAMI intervention to their medication management. Patients were often grateful to have their blood pressure checked and an extra consultation with their GP. Wearing an ABPM before the consultation was not a problem, as most participants had worn one in the past and were familiar with the process. All patients were also happy to consent to their urine being tested for the presence of their medication and did not report any difficulties with their GP having access to this result. One participant in particular was quite appreciative, as the 'non-detected' result from the urine test corrected a problem with her medication-taking.

"The thing that I really appreciated about it, and I thought was very beneficial, was when [GP name] called me in to go through all the readings of the monitor, and she said that on the morning I gave the urine test, there was no trace of my blood pressure tablet in the urine. That was the most beneficial thing I found, simply because I have a tablet for my bladder, which is Betmiga, and it's similar in colour to the blood pressure one. Obviously, I was taking more of the Betmiga instead of taking the one for the blood pressure. So that to me, I thought, 'well, this is just brilliant that this can be detected.'" (Female, age 76, intervention arm).

As mentioned previously, while patients appreciated the idea of the pre-consultation plan, many did not use it in practice.

"The consultation tool is probably not something I would [use], to be honest, because I tend to just go and ask and not bother writing stuff down." (Male, age 65, intervention arm).

Similarly, while many of the patients appreciated the GP signposting information on blood pressure at the Croí website, many did not avail of it.

"She [GP] sent me an email, and would you believe it, I haven't looked at it yet to be totally honest with you." (Male, age 79, intervention arm).

Acceptability of MIAMI to GP participants

GPs similarly could see the benefit of the MIAMI intervention for medication management. They were universally positive about both the booklet and consultation guide. They liked the online training, particularly its short nature (30 minutes) and focus on shared decision-making.

"I mean it did give me pause for thought around the whole negotiation side of things in terms of the patient and involving patients in their own care." (GP, male, intervention arm).

They also liked having the Croí website as a resource for patients.

"You know those type of online resources are I think really helpful because you have limited time in the consultation, so it's great to be able to refer people to those types of resources." (GP, male, intervention arm).

The urine test of medication adherence presented some logistical challenges, which sometimes meant that it was difficult to use in practice. The first issue was the length of time it took for results to come back, which ranged between three and 10 weeks, which led to one GP describing the results as *"historical data."* Another issue was the delivery of results, which happened both electronically and by paper. Due to the novel nature of the test, the electronic messaging system from lab to GP practice did not always convey the full set of results, meaning that GPs received conflicting results in electronic and paper formats, with the correct results on paper only. This issue was resolved once identified but did present a *"hiccup"* to GPs involved. Finally, there was some confusion about the *"not detected"* result, with GPs feeling that they had not been given enough information about the possibility of false negatives.

"I thought, if I'm honest with you, there was some level of lack of clarity around, if the drugs weren't in the urine sample, does it absolutely mean that they hadn't taken them?" (GP, female, intervention arm).

Despite these challenges, GPs could appreciate the benefit of this kind of testing and if results delivery could be improved, were keen to incorporate it into routine practice.

"We all know the rule of thirds, that a third of the people take medication as prescribed, a third take it but not as prescribed, and then a third don't take it. So it's the first thing that pops into your mind so having that sort of reassuring data, particularly in terms of the urine testing is very reassuring in terms of your management of somebody like this. And I think it's also reassurance for the patient because I think a lot of people, when they think, 'is it actually working?' I think you're showing them metabolising the urine, that it's some a little bit of extra evidence that, yeah, this is going through your system and doing what it's supposed to do." (GP, male, intervention arm).

Stop/go criteria

Table 8 illustrates how study results map to each criterion.

ADePT process

Table 9 presents the fourteen methodological issues used to inform the ADePT process [38, 39] and a mapping of these to the research questions and relevant findings.

Discussion

The MIAMI study was, overall, implemented as planned and was well-received by practitioners and patients alike. Medication adherence in this primary care population, aged over 65 years and on at least two blood pressure lowering medications, was found by urine analysis to be high at 97-99%, although somewhat more variable according to prescription refill (85-88%) and self-report methods (33/52 i.e. 63% reported a maximum adherence score of 5 at baseline). It appears both feasible and worthwhile to proceed to a full definitive trial. However, two important issues, focused on patient selection and conduct of the urine analyses, were identified and will need to be modified and managed for any full trial.

Recruitment

Practice recruitment, utilising practices that had previously expressed an interest in hypertension research, was straightforward. The initial random sampling strategy for patient recruitment, which involved a combination of electronic and manual record searching against the inclusion and exclusion criteria by practice staff, was found to be both cumbersome and time consuming by GP participants. After a review of procedures, it was abandoned and a prospective case finding approach was adopted, which utilised patients who were booked in for routine ABPMs. Such patients usually have some concerns regarding their hypertension management. It was quite straightforward to then review, using the inclusion and exclusion criteria, the records of these patients booked in for an ABPM. If eligible, the patients were then contacted to determine their interest in study participation.

Study recruitment achieved 52 of a planned 60 patients (87%) with three practices recruiting to target, two just below target, and one less than 50%. The criterion that patients had to be older than 65 years significantly reduced the eligible number of patients. For the full definitive trial, this age bar could be removed. Younger patients may have the potential for comparatively more health gain from the intervention [40, 41].

Our non-adherence rate by urine analysis ranged from 1-3%, and is comparable to the 4.7% rate found by Sheppard et al. [42] for 191 patients attending five English

Table 9 Summary of findings for the decision-making after pilot and feasibility trials (ADePT) process [27]

Methodological issue	Objective	Findings
1. Did the study allow a sample size calculation for the definitive trial?	5	Yes, in order to achieve 80% power (at a significance level a of 0.05) with an average cluster size of 30, a minimum of 6 clusters of size 30 in both the intervention and control arms (i.e. 360 in total) is required.
2. What factors influenced eligibility and what proportion of those approached were eligible?	2	All GP practices approached were eligible. Initially all patients who met the inclusion criteria were eligible, however after the introduction of case-finding to the recruitment strategy patients who met the inclusion criteria and were booked for recent or future ABPMs at the practice were eligible.
3. Was recruitment successful?	2	In five sites, over 80% of the target recruitment was achieved. However, in one site just 40% of the target was met.
4. Did eligible participants consent?	2	Consent was obtained successfully in all sites.
5. Were participants successfully randomised and did randomisation yield equality in groups?	2	This was a cluster RCT and randomisation was successful.
6. Were blinding procedures adequate?	2	Not applicable to current study.
7. Did participants adhere to the intervention?	1	GPs filled in a checklist after each consultation. In general adherence was good but some deviations were identified, see text for details.
8. Was the intervention acceptable to participants?	1	Patients – yes, although many did not use the pre-consultation plan in practice. GPs – yes but many identified the logistical challenges with the urine test to be a challenge. See text for details.
9. Was it possible to calculate intervention costs and duration?	4	Yes. The MIAMI intervention was estimated at €490 per participant (see Appendix 2). When other healthcare resources are included, the mean total healthcare cost per patient was estimated at €654 (SD: 123).
10. Were outcome assessments completed?	3	Yes. 100% of the self-reported outcomes were completed at baseline and 90% at follow up.
11. Were outcomes measured the most appropriate outcomes?	3	Yes, the outcomes used are common outcomes used in blood pressure and medication taking research. Participants had positive feedback on completing the study questionnaire.
12. Was retention to the study good?	2	Yes, there was a 92.31% patient retention rate and 100% for practices.
13. Were the logistics of running a multicentre trial assessed?	2	Yes. Patient recruitment was identified as being resource intensive. The logistics of the urine test also need streamlining to work in a multicentre context.
14. Did all components of the protocol work together?	2	Yes, but some modifications are required to move forward to definitive RCT.

practices who were aged over 65 years, with hypertension and on at least one antihypertensive medication. It is much lower than the 26% partial or full non-adherence rate by urine analysis we previously reported for 235 patients from fifteen Irish general practices [24]. These patients all had apparent treatment resistant hypertension, that is, uncontrolled BP in patients taking ≥ 3 differing groups of antihypertensive medications (one of which must be a diuretic-type medication) or patients who are taking ≥ 4 medications regardless of type and BP level. It therefore seems reasonable to suggest that, for a full trial, patient eligibility should be simply targeted at patients with apparent treatment resistant hypertension. These patients, by definition, need additional clinical consideration, and participation in a MIAMI full trial could provide practitioners with a structured, efficient, and evidence-based approach to their management.

Randomisation and intervention components

Cluster randomisation worked successfully with similar patient characteristics in intervention and control groups (Table 5).

The complex intervention, for both GP and patient participants, worked well with two important exceptions. For practitioners, the online training, particularly the videos, were commended for their brevity and acuity. The drop-down consultation menus helped to structure the consultation. The ability to copy-and-paste relevant websites to be texted to patients also received positive feedback. Written background information regarding available single pill combinations was also reported to encourage practitioners to prescribing these.

The largest area of concern was the logistics of urine testing. The significant delays in practices receiving results impeded efficient patient management. This was

compounded by having paper and electronic records, which sometimes differed in their results. These logistical issues can be avoided with appropriate pre-planning with the local laboratory. In future studies, streamlining this process by establishing more efficient communication pathways between the lab and GP—could improve the timeliness of patient management. These quicker feedback loops would enable more responsive and informed clinical decision-making. GPs also requested specific written information regarding patient communication when prescribed medications were not found in urine tests. A summary sheet was then developed in consultation with colleagues at the University of Leicester and was subsequently found to be helpful.

For patients, as in previous studies in general practice [24, 42], acceptability of the urine testing was very high. The pre-consultation tool, whilst considered useful in theory, was not widely used by patients. Qualitative interviews revealed that patient participants could see in the value in it, but often just did not bring it with them to their GP appointments. This underuse may have been due to a lack of familiarity with the process or other practical barriers. This lack of use diminished the anticipated benefits, as fewer patients engaged in reflective preparation, potentially limiting the depth of conversations around medication taking and reducing opportunities for GPs to provide tailored care. Future adaptations of the intervention may consider simplifying the tool, offering more guidance to patients on its use, integrating its completion more closely with routine clinical workflows to improve adherence and uptake or replacing it entirely. There appeared to be variable uptake among patients regarding accessing relevant websites sent to them by text by practitioners.

Retention and outcome measures

The three-month retention of practices (100%) and patients (92%) was satisfactory. Outcome measures seemed acceptable with completion rates of 90% for the six self-report outcomes and 92.3% for completion of an ABPM at follow up.

Strengths and limitations

Our intervention was developed according to the MRC Framework [43] with a very strong multidisciplinary theoretical framework [20]. PPI was also incorporated at all stages. Incorporation of health economic analyses and a sample size calculation enables a future trial to determine both outcomes and costs. Salient issues for consideration before proceeding to a full trial have been found and potential remedial actions identified.

Regarding recruitment, there was a strong response from practices which had previously been involved in hypertension research. Such practices may not be representative of practices generally.

The original patient search strategy had the advantage of estimating the total number of patients eligible in each practice and then producing a random sample. It was not feasible, however. The alternative case finding approach worked well but has the disadvantage of not determining the total number of eligible patients and potentially excluding participants who find alternatives to ABPM more acceptable for out of office assessment of BP [44]. Another disadvantage is that it targeted patients who are already engaged in care, and not those who may have most to gain from the intervention.

Conclusions and future directions

We have described the successful piloting of a novel collaborative intervention intended to maximise blood pressure control for persons with uncontrolled blood pressure and on at least two medications. The trial progression criteria facilitated the identification of limitations and potential modifications for a full definitive trial.

Appendix 1

CONSORT 2010 checklist of information to include when reporting a pilot or feasibility trial

Section/Topic	Item no	Checklist item	Reported on page no
Title and abstract			
	1a	Identification as a pilot or feasibility randomised trial in the title	1
	1b	Structured summary of pilot trial design, methods, results, and conclusions (for specific guidance see CONSORT abstract extension for pilot trials)	2, 3
Introduction			
Background and objectives	2a	Scientific background and explanation of rationale for future definitive trial, and reasons for randomised pilot trial	4, 5
	2b	Specific objectives or research questions for pilot trial	5
Methods			
Trial design	3a	Description of pilot trial design (such as parallel, factorial) including allocation ratio	7
	3b	Important changes to methods after pilot trial commencement (such as eligibility criteria), with reasons	9

Section/Topic	Item no	Checklist item	Reported on page no	Section/Topic	Item no	Checklist item	Reported on page no
Title and abstract				Title and abstract			
Participants	4a	Eligibility criteria for participants	7	Results			
	4b	Settings and locations where the data were collected	14–16	Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were approached and/or assessed for eligibility, randomly assigned, received intended treatment, and were assessed for each objective	24 & Fig. 3
	4c	How participants were identified and consented	8, 9		13b	For each group, losses and exclusions after randomisation, together with reasons	24 & Fig. 3
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	10–12	Recruitment	14a	Dates defining the periods of recruitment and follow-up	8, 9
Outcomes	6a	Completely defined prespecified assessments or measurements to address each pilot trial objective specified in 2b, including how and when they were assessed	14–16		14b	Why the pilot trial ended or was stopped	n/a
	6b	Any changes to pilot trial assessments or measurements after the pilot trial commenced, with reasons	n/a	Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	Table 5
	6c	If applicable, prespecified criteria used to judge whether, or how, to proceed with future definitive trial	19, 20	Numbers analysed	16	For each objective, number of participants (denominator) included in each analysis. If relevant, these numbers should be by randomised group	Tables 6 and 7
Sample size	7a	Rationale for numbers in the pilot trial	8	Outcomes and estimation	17	For each objective, results including expressions of uncertainty (such as 95% confidence interval) for any estimates. If relevant, these results should be by randomised group	Tables 6 and 7
	7b	When applicable, explanation of any interim analyses and stopping guidelines	n/a	Ancillary analyses	18	Results of any other analyses performed that could be used to inform the future definitive trial	22–36
Randomisation:				Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms)	n/a
Sequence generation	8a	Method used to generate the random allocation sequence	9		19a	If relevant, other important unintended consequences	n/a
	8b	Type of randomisation(s); details of any restriction (such as blocking and block size)	9	Discussion			
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	n/a	Limitations	20	Pilot trial limitations, addressing sources of potential bias and remaining uncertainty about feasibility	39, 40
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	8, 9	Generalisability	21	Generalisability (applicability) of pilot trial methods and findings to future definitive trial and other studies	37–40
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how	n/a	Interpretation	22	Interpretation consistent with pilot trial objectives and findings, balancing potential benefits and harms, and considering other relevant evidence	37–40
	11b	If relevant, description of the similarity of interventions	n/a		22a	Implications for progression from pilot to future definitive trial, including any proposed amendments	37–40
Statistical methods	12	Methods used to address each pilot trial objective whether qualitative or quantitative	19	Other information			
				Registration	23	Registration number for pilot trial and name of trial registry	7
				Protocol	24	Where the pilot trial protocol can be accessed, if available	7

Section/Topic	Item no	Checklist item	Reported on page no
Title and abstract			
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	42
	26	Ethical approval or approval by research review committee, confirmed with reference number	21

Appendix 2: Health economics

Table 10 Categories of unit cost estimates in 2022(€) prices

Resource Item	Activity	Unit Cost €	Source
Healthcare Resources			
GP Visits:	Per Visit	€53	(Smith et al., 2021)
Practice Nurse Visit	Per Visit	€45	Study Records
Outpatient Visits	Per Visit	€146	HPO
Inpatient Days	Per Day	€771	HPO
Inpatient Night	Per Night	€994	HPO
A&E visits	Per Visit	€300	HPO
ICU night	Per night	€2,662	(McLaughlin et al., 2009)

Unit costs in €2022 prices. Where necessary unit costs were inflated using the health component of the consumer price index from the Central Statistics Office. HPO Healthcare Pricing Office, GP General practitioner, A&E Accident and emergency, ICU Intensive care unit

Table 11 MIAMI intervention costing

Resource item	Total Cost	Total Cost Per Patient
Training		
Video	€221	€9
GP Time Input, Educational Materials.	€745	€30
Intervention Delivery		
Healthcare Professional Time Input	€4,813	€193
Consumables and Tests	€2,475	€99
ABPMs	€4,000	€160
MIAMI Intervention Cost	€12,254	€490
Sensitivity Analysis 1 + 10%	€13,480	€539
Sensitivity Analysis 2 + 50%	€18,382	€735
Sensitivity Analysis 3 - Low cost	€11,530	€471

Table 12 Proportion of responses by level of severity for EQ-5D-5 L dimensions at baseline and at follow-up Time point 1 by intervention arm

Dimensions	Levels	Intervention			Control		
		Baseline	Follow-up	Difference Baseline to Follow-up Time 1	Baseline	Follow-up	Difference Baseline to Follow-up Time 1
		Time 1			Time 3		
		N=23	N=22		N=26	N=23	
		%	%		%	%	
Mobility							
	None	65.22	77.27	12.05	65.38	56.52	-8.86
	Slight	26.09	4.55	-21.54	11.54	21.74	10.20
	Moderate	4.35	13.64	9.29	7.69	8.70	1.01
	Severe	4.35	4.55	0.20	15.38	13.04	-2.34
	Unable	0.00	0.00	0.00	0.00	0.00	0.00
Self-care							
	None	86.96	85.71	-1.25	88.46	86.96	-1.50
	Slight	4.35	9.52	5.17	7.69	13.04	5.35
	Moderate	8.70	0.00	-8.70	3.85	0.00	-3.85
	Severe	0.00	4.76	4.76	0.00	0.00	0.00
	Unable	0.00	0.00	0.00	0.00	0.00	0.00
Usual activities							
	None	54.55	54.55	0.00	65.38	60.87	-4.51
	Slight	22.73	18.18	-4.55	19.23	21.74	2.51
	Moderate	22.73	18.18	-4.55	7.69	8.70	1.01
	Severe	0.00	9.09	9.09	7.69	8.70	1.01
	Unable	0.00	0.00	0.00	0.00	0.00	0.00
Pain/Discomfort							
	None	34.78	31.82	-2.96	38.46	34.78	-3.68
	Slight	34.78	36.36	1.58	26.92	30.43	3.51
	Moderate	21.74	27.27	5.53	23.08	26.09	3.01
	Severe	4.35	4.55	0.20	11.54	8.70	-2.84
	Extreme	4.35	0.00	-4.35	0.00	0.00	0.00
Anxiety/Depression							
	None	56.52	54.55	-1.97	73.08	78.26	5.18
	Slight	30.43	31.82	1.39	15.38	8.70	-6.68
	Moderate	13.04	9.09	-3.95	7.69	4.35	-3.34
	Severe	0.00	4.55	4.55	0.00	8.70	8.70
	Extreme	0.00	0.00	0.00	3.85	0.00	-3.85

Smith S, Jiang J, Normand C, O'Neill C. Unit costs for non-acute care in Ireland 2016—2019. HRB Open Res. 2021;4

McLaughlin AM, Hardt J, Canavan JB, Donnelly MB. Determining the economic cost of ICU treatment: a prospective “micro-costing” study. Intensive Care Med. 2009;35:2135–40

Abbreviations

ABPM	Ambulatory Blood Pressure Monitor
ADEPT	A process for Decision-making after Pilot and feasibility Trials
A&E	Accident and Emergency
GP	General Practitioner
ICU	Intensive Care Unit
PPI	Public and Patient Involvement
QALY	Quality Adjusted Life Year
RCT	Randomised Controlled Trial
SWAT	Study Within A Trial

Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s12875-024-02635-7>.

Supplementary Material 1.

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Consortium list: MIAMI PPI Panel

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Authors' contributions

ECM: conceptualisation, methodology, formal analysis, investigation, data curation, writing – original draft preparation, project administration, funding acquisition. LOG: investigation, writing – review & editing, project administration. PJM: conceptualisation, methodology, supervision, writing – review & editing, funding acquisition. MB: conceptualisation, writing – review & editing, funding acquisition. MC: conceptualisation, methodology, writing – review & editing, funding acquisition. HDY: investigation, resources, writing – review & editing. ED: conceptualisation, writing – review & editing, funding acquisition. SD: conceptualisation, methodology, writing – review & editing, funding acquisition. HDd: conceptualisation, writing – review & editing, funding acquisition. PG: conceptualisation, methodology, supervision, writing – review & editing, funding acquisition. PH: conceptualisation, methodology, writing – review & editing, funding acquisition. AH: conceptualisation, methodology, formal analysis, writing – original draft preparation. LH: conceptualisation, writing – review & editing. JWME: conceptualisation, writing – review & editing, funding acquisition. JN: conceptualisation, methodology, formal analysis, writing – original draft preparation, funding acquisition. DB: investigation, resources, writing – review & editing. HG: investigation, resources, writing – review & editing. PG: investigation, resources, writing – review & editing. PPI: conceptualisation, writing – review & editing. AWM: conceptualisation, methodology, supervision, writing – review & editing, funding acquisition. GJM: conceptualisation, methodology, supervision, writing – review & editing, funding acquisition.

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Data availability

The materials and datasets generated and/or analysed during the current study are available in the OSF repository, <https://osf.io/xusby/>

Declarations

Ethics approval and consent to participate

The study was conducted in accordance with the Declaration of Helsinki. Ethical approval was granted by the Irish College of General Practitioners (ICGP_REC_22_014). An amendment was sought and approved for the change to recruitment strategy. All participants gave explicit written consent for participation.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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References

- Zhou B, Perel P, Mensah GA, Ezzati M. Global epidemiology, health burden and effective interventions for elevated blood pressure and hypertension. *Nat Rev Cardiol*. 2021;18(11):785–802.
- Zhou B, Carrillo-Larco RM, Danaei G, Riley LM, Paciorek CJ, Stevens GA, et al. Worldwide trends in hypertension prevalence and progress in treatment and control from 1990 to 2019: a pooled analysis of 1201 population-representative studies with 104 million participants. *Lancet*. 2021;398(10304):957–80.
- Mancia G, Kreutz R, Brunström M, Burnier M, Grassi G, Januszewicz A, et al. 2023 ESH guidelines for the management of arterial hypertension the Task Force for the management of arterial hypertension of the European Society of Hypertension: endorsed by the International Society of Hypertension (ISH) and the European Renal Association (ERA). *J Hypertens*. 2023;41(12):1874–2071.
- Whelton PK, Williams B. The 2018 European society of cardiology/European society of hypertension and 2017 American college of cardiology/American heart association blood pressure guidelines: more similar than different. *JAMA*. 2018;320(17):1749–50.
- Suchard MA, Schuemie MJ, Krumholz HM, You SC, Chen R, Pratt N, et al. Comprehensive comparative effectiveness and safety of first-line antihypertensive drug classes: a systematic, multinational, large-scale analysis. *Lancet*. 2019;394(10211):1816–26.
- Lane D, Lawson A, Burns A, Azizi M, Burnier M, Jones DJL, et al. Nonadherence in hypertension: how to develop and implement Chemical Adherence Testing. *Hypertension*. 2022;79(1):12–23.
- Burnier M, Egan BM. Adherence in hypertension: a review of prevalence, risk factors, impact, and management. *Circ Res*. 2019;124(7):1124–40.
- Vrijens B, De Geest S, Hughes DA, Przemyslaw K, Demonceau J, Ruppert T, et al. A new taxonomy for describing and defining adherence to medications. *Br J Clin Pharmacol*. 2012;73(5):691–705.
- Corrao G, Zambon A, Parodi A, Poluzzi E, Baldi I, Merlino L, et al. Discontinuation of and changes in drug therapy for hypertension among newly-treated patients: a population-based study in Italy. *J Hypertens*. 2008;26(4):819–24.
- Glynn LG, Murphy AW, Smith SM, Schroeder K, Fahey T. Self-monitoring and other non-pharmacological interventions to improve the management of hypertension in primary care: a systematic review. *Br J Gen Pract*. 2010;60(581):e476–88.
- McManus RJ, Little P, Stuart B, Morton K, Raftery J, Kelly J et al. Home and online management and evaluation of blood pressure (HOME BP) using a digital intervention in poorly controlled hypertension: randomised

- controlled trial. *BMJ*. 2021;372. <https://www.bmj.com/content/372/bmj.m4858.abstract>.
12. Morrissey EC, Durand H, Nieuwlaat R, Navarro T, Haynes RB, Walsh JC, et al. Effectiveness and content analysis of interventions to enhance medication adherence and blood pressure control in hypertension: a systematic review and meta-analysis. *Psychol Health*. 2017;32(10):1195–232.
 13. Conn VS, Ruppap TM, Chase JAD, Enriquez M, Cooper PS. Interventions to improve medication adherence in hypertensive patients: systematic review and meta-analysis. *Curr Hypertens Rep*. 2015;17:1–15.
 14. Kassavou A, Mirzaei V, Brimicombe J, Edwards S, Massou E, Prevost AT, et al. A highly tailored text and voice messaging intervention to improve medication adherence in patients with either or both hypertension and type 2 diabetes in a UK primary care setting: feasibility randomized controlled trial of clinical effectiveness. *J Med Internet Res*. 2020;22(5):e16629.
 15. Bobrow K, Farmer AJ, Springer D, Shanyinde M, Yu LM, Brennan T, et al. Mobile phone text messages to support treatment adherence in adults with high blood pressure (SMS-Text adherence support [StAR]): a single-blind, randomized trial. *Circulation*. 2016;133(6):592–600.
 16. Hayes P, Casey M, Glynn LG, Molloy GJ, Durand H, O'Brien E, et al. Prevalence of treatment-resistant hypertension after considering pseudo-resistance and morbidity: a cross-sectional study in Irish primary care. *Br J Gen Pract*. 2018;68(671):e394.
 17. Durand H, Hayes P, Morrissey EC, Newell J, Casey M, Murphy AW, et al. Medication adherence among patients with apparent treatment-resistant hypertension: systematic review and meta-analysis. *J Hypertens*. 2017;35(12):2346–57.
 18. Durand H, Hayes P, Harhen B, Conneely A, Finn DP, Casey M, et al. Medication adherence for resistant hypertension: assessing theoretical predictors of adherence using direct and indirect adherence measures. *Br J Health Psychol*. 2018;23(4):949–66.
 19. Durand H, Casey M, Glynn LG, Hayes P, Murphy AW, Molloy GJ. A qualitative comparison of high and low adherers with apparent treatment-resistant hypertension. *Psychol Health Med*. 2020;25(1):64–77.
 20. Morrissey EC, Harney OM, Hogan MJ, Murphy PJ, O'Grady L, Byrne M, Casey M, Dunae S, Durand H, Hayes P, Panel MIAMIPPI, Murphy AW, Molloy GJ. Supporting General practitioners and people with hypertension to maximise medication use to control blood pressure: the contribution of collective intelligence to the development of the 'Maximising Adherence, Minimising Inertia' intervention. *Health Psychol Behav Med*. 2024. <https://doi.org/10.1080/21642850.2024.2404038>.
 21. Morrissey E, Murphy A, Murphy P, O'Grady L, Byrne M, Casey M et al. Supporting GPs and people with hypertension to maximise medication use to control blood pressure: Protocol for a pilot cluster RCT of the MIAMI intervention [version 1; peer review: awaiting peer review]. *HRB Open Res [Internet]*. 2023;6(6). Available from: <https://hrbopenresearch.org/articles/6-6/v1>.
 22. Socrates. [Internet]. [cited 2024 Mar 1]. Socrates | Clanwilliam Group | Healthcare Management Software. <https://www.socrates.ie/>
 23. McEvoy JW, McCarthy CP, Bruno RM, Brouwers S, Canavan MD, Ceconi C, Christodorescu RM, Daskalopoulou SS, Ferro CJ, Gerdtz E, Hanssen H. 2024 ESC guidelines for the management of elevated blood pressure and hypertension: developed by the task force on the management of elevated blood pressure and hypertension of the European Society of Cardiology (ESC) and endorsed by the European Society of Endocrinology (ESE) and the European Stroke Organisation (ESO). *Eur Heart J*. 2024 Aug;30:ehae178.
 24. Hayes P, Casey M, Glynn LG, Molloy GJ, Durand H, O'Brien E, et al. Measuring adherence to therapy in apparent treatment-resistant hypertension: a feasibility study in Irish primary care. *Br J Gen Pract*. 2019;69(686):e621.
 25. Larvin H, Peckham E, Prady SL. Case-finding for common mental disorders in primary care using routinely collected data: a systematic review. *Soc Psychiatry Psychiatr Epidemiol*. 2019;54:1161–75.
 26. Whelton PK, Carey RM, Aronow WS, Casey DE, Collins KJ, Dennison Himmelfarb C, DePalma SM, Gidding S, Jamerson KA, Jones DW, MacLaughlin EJ. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA guideline for the prevention, detection, evaluation, and management of high blood pressure in adults: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *J Am Coll Cardiol*. 2018;71(19):e127–248.
 27. Tomaszewski M, White C, Patel P, Masca N, Damani R, Hepworth J, et al. High rates of non-adherence to antihypertensive treatment revealed by high-performance liquid chromatography-tandem mass spectrometry (HP LC-MS/MS) urine analysis. *Heart*. 2014;100(11):855–61.
 28. Chan AHY, Horne R, Hankins M, Chisari C. The Medication Adherence Report Scale: A measurement tool for eliciting patients' reports of nonadherence. *Br J Clin Pharmacol*. 2020;86(7):1281–8.
 29. Horne R, Weinman J, Hankins M. The beliefs about medicines questionnaire: the development and evaluation of a new method for assessing the cognitive representation of medication. *Psychol Health*. 1999;14(1):1–24.
 30. Moss-Morris R, Weinman J, Petrie K, Horne R, Cameron L, Buick D. The revised illness perception questionnaire (IPQ-R). *Psychol Health*. 2002;17(1):1–16.
 31. Gardner B, Abraham C, Lally P, de Bruijn GJ. Towards parsimony in habit measurement: testing the convergent and predictive validity of an automaticity subscale of the self-report habit index. *Int J Behav Nutr Phys Act*. 2012;9(1):20.
 32. Wensing M, van Lieshout J, Jung HP, Hermsen J, Rosemann T. The patients Assessment Chronic Illness Care (PACIC) questionnaire in the Netherlands: a validation study in rural general practice. *BMC Health Serv Res*. 2008;8(1):182.
 33. Sandelowski M. Whatever happened to qualitative description? *Res Nurs Health*. 2000;23(4):334–40.
 34. Braun V, Clarke V. Reflecting on reflexive thematic analysis. *Qual Res Sport Exerc Health*. 2019;11(4):589–97.
 35. Hobbins A, Barry L, Kelleher D, Shah K, Devlin N, Goni JMR, et al. Utility Values for Health States in Ireland: a Value Set for the EQ-5D-5L. *Pharmacoeconomics*. 2018;36(11):1345–53.
 36. Campbell MJ, Walters SJ. How to design, analyse and report cluster randomised trials in medicine and health related research. Wiley; 2014.
 37. Hemming K, Eldridge S, Forbes G, Weijer C, Taljaard M. How to design efficient cluster randomised trials. *BMJ*. 2017;358. <https://www.bmj.com/content/358/bmj.j3064.abstract>.
 38. Bugge C, Williams B, Hagen S, Logan J, Glazener C, Pringle S, et al. A process for decision-making after pilot and feasibility trials (ADePT): development following a feasibility study of a complex intervention for pelvic organ prolapse. *Trials*. 2013;14(1):353.
 39. Shanyinde M, Pickering RM, Weatherall M. Questions asked and answered in pilot and feasibility randomized controlled trials. *BMC Med Res Methodol*. 2011;11(1):1–11.
 40. Sagara K, Goto K, Maeda M, Murata F, Fukuda H. Medication adherence and associated factors in newly diagnosed hypertensive patients in Japan: the life study. *J Hypertens*. 2024;42(4):718–26.
 41. Lee H, Yano Y, Cho SMJ, Heo JE, Kim DW, Park S, et al. Adherence to antihypertensive medication and incident cardiovascular events in young adults with hypertension. *Hypertension*. 2021;77(4):1341–9.
 42. Sheppard JP, Albasri A, Gupta P, Patel P, Khunti K, Martin U, et al. Measuring adherence to antihypertensive medication using an objective test in older adults attending primary care: cross-sectional study. *J Hum Hypertens*. 2022;36(12):1106–12.
 43. Skivington K, Matthews L, Simpson SA, Craig P, Baird J, Blazeby JM, et al. A new framework for developing and evaluating complex interventions: update of Medical Research Council guidance. *BMJ*. 2021;374:n2061.
 44. Kitt J, Fox R, Tucker KL, McManus RJ. New approaches in hypertension management: a review of current and developing technologies and their potential impact on hypertension care. *Curr Hypertens Rep*. 2019;21:1–8.
 45. Michie S, Van Stralen MM, West R. The behaviour change wheel: a new method for characterising and designing behaviour change interventions. *Implement Sci*. 2011;6:1–2. <https://doi.org/10.1186/1748-5908-6-42>.

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