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Effectiveness of a patient-centred complex intervention to improve Initial Medication Adherence to cardiovascular disease and diabetes treatments in primary care (the IMA-cRCT study): a pragmatic cluster randomised controlled trial using real-world data

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ABSTRACT

Introduction Non-adherence to cardiovascular disease and diabetes treatments contributes to suboptimal clinical outcomes and higher cost. The initial medication adherence (IMA) intervention is a multidisciplinary primary care (PC) intervention based on shared decision-making (SDM). The IMA-cluster-randomised controlled trial (cRCT) study evaluated the impact of the IMA intervention on medication initiation, secondary adherence and clinical outcomes compared with usual care (UC).

Methods This was a pragmatic cRCT with a hybrid effectiveness-implementation design which randomised 24 PC centres in Spain to intervention or UC. Patients receiving a new prescription of antihypertensive, lipid-lowering, antiplatelet and/or oral/injectable antidiabetic medication at the intervention centres (March 2022–September 2022) were attended by general practitioners (GPs), nurses and community pharmacists who had been trained in SDM and given decision aids (leaflets and website). Real-world data from prescription and dispensing records—used to assess medication initiation and secondary adherence (correct dosing and continued use)—and clinical outcome data from electronic health records were collected up to 18 months after initial prescription and analysed using multilevel regression models.

Results Overall, 4910 prescriptions were issued to 3629 patients (Intervention=2148; UC=1481) by 150 GPs (Intervention=91; UC=59). No differences were detected between groups in medication initiation or secondary adherence. Among clinical outcomes, only blood pressure outcomes favoured the IMA intervention, reflecting a small but clinically meaningful improvement.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Evidence on the impact of shared decision-making (SDM) on adherence and clinical outcomes for cardiovascular disease and diabetes pharmacological treatments remains limited and mixed, coming mostly from the USA and often associated with a high risk of bias.

WHAT THIS STUDY ADDS

⇒ The IMA-cRCT represents a large, pragmatic trial based on real-world data (RWD) that provides robust evidence on the effectiveness of SDM with high internal and external validity.

⇒ This study contributes to SDM research by focusing on medication adherence as a primary outcome—a rarely prioritised behavioural outcome in SDM trials—and by using RWD rather than self-reported measures to assess impact, while highlighting the inherent complexity of working with routinely collected data.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Further evidence is needed to understand for which patients and in which contexts SDM can positively affect health outcomes.

⇒ This study promotes a debate on the intrinsic value of SDM (improving patient and professional experience) irrespective of direct patient health outcomes.

Conclusions The IMA intervention had limited overall impact, with no effect on adherence, but showed potential benefits in blood pressure. However, SDM, as an ethically grounded approach, may enhance patients and professional experiences, supporting its consideration for broader implementation. Future efforts should prioritise these benefits by investing in professional training and patient support, addressing implementation challenges and deepening understanding of SDM effects, which would warrant further evaluation.

Trial registration number NCT05026775.

INTRODUCTION

Cardiovascular diseases (CVDs) and diabetes are major contributors to non-communicable disease morbidity and mortality.[1] Adherence to pharmacological treatments to control these conditions remains low; between 2% and 40% of prescribed medications are never initiated, and poor secondary adherence and discontinuation are common.[2–4] This results in worse disease control, higher morbidity and mortality and increased healthcare costs,[5–10] highlighting the need for effective interventions to improve adherence.

Patient-centred care interventions are increasingly being implemented across healthcare systems to enhance quality of care[11–13] and are particularly important for individuals with chronic conditions who face a succession of health-related decisions.[14 15] Shared decision-making (SDM) is a benchmark for quality care, and its inclusion in clinical prescribing guidelines has been advocated.[16 17] However, evidence regarding its effectiveness in improving medication adherence or clinical outcomes remains inconclusive.[18–22] The initial medication adherence (IMA) intervention is a theory-based[23 24] multidisciplinary patient-centred intervention designed to improve primary (medication initiation) and secondary adherence (correct dosing–medication implementation–and continued use over time–persistence) to CVD and diabetes pharmacological treatments prescribed in primary care (PC). It promotes health literacy and SDM at the time of a new prescription. Care is standardised among general practitioners (GPs), nurses and community pharmacists.

The IMA intervention was developed within the Medical Research Council Framework for complex interventions as part of the non-initiation project.[3 23–28] This paper presents Phase III, or the evaluation phase, a pragmatic effectiveness-implementation type I hybrid trial based on real-world data (RWD). Hybrid trials are essential for evaluating interventions in real-world contexts and facilitating the translation of research, not only by assessing effectiveness but also by understanding its implementation, how it works and the interaction of context with trial outcomes.[29 30] RWD has considerable potential for pragmatic trials, provides real-world outcomes, facilitates monitoring and follow-up, reduces costs and enables larger-scale trials with less involvement from researchers, eliminating the Hawthorne effect.[31 32] However, RWD presents challenges as it is not intended for research, leading to potential variability in data quality and consistency.[31 32]

This study aims to evaluate the effectiveness of a quality care-enhancing intervention, the IMA intervention, in comparison to usual care (UC) in improving initial and secondary medication adherence and clinical outcomes in patients with new pharmacological prescriptions for CVD or diabetes in PC using a cluster-randomised controlled trial (cRCT) based on RWD.

METHODS

Trial design

The IMA-cRCT is an effectiveness-implementation type I hybrid trial; a 7-month pragmatic cRCT (March 2022–September 2022) with an embedded process evaluation and economic modelling.[27 28] Patient follow-up was between 12 and 18 months depending on the specific outcome (online supplemental file 1). 24 PC teams were assigned to two parallel arms; 12 to UC and 12 to the IMA intervention group. See study protocol for further details on design and trial methods[27] (ClinicalTrials.gov trial registration n° NCT05026775).

This study is reported according to the CONSORT (Consolidated Standards of Reporting Trials) 2010 statement: extension to cRCTs.[33]

Setting

The trial was conducted in urban and rural PC centres and community pharmacies in Catalonia, Spain. The Spanish National Healthcare System provides universal coverage, is tax-funded and services are free of charge, although pharmaceutical prescriptions are co-paid by patients based on employment and household income status.[34 35] PC is the access point to the healthcare system where most pharmacological prescriptions are managed. Generally, GPs carry out early detection, diagnosis and treatment of the most prevalent CVD and diabetes, and nurses monitor adherence and assess treatment results.[34] Medications can only be obtained at community pharmacies, which are considered private establishments of public interest. Pharmacists serve as dispensers and health agents by providing information and early detection of side effects.[34 36] Patients are free to choose any community pharmacy within or without their PC centre catchment area.

Study population

PC centre based teams are groups of GPs, nurses and other healthcare professionals that attend specific populations by area. All Catalan Health Institute PC centres were assessed for eligibility (n=287), randomly selected and paired according to location and non-initiation predictors.[25 27] The selected PC centres and healthcare professionals were invited to participate if inclusion criteria were fulfilled; (1) the manager agreed to participate and guarantee ethical standards; (2) at least five GPs in urban or two GPs in rural PC centres agreed to participate; and (3) GPs and nurses signed informed consent, were willing to attend intervention training and did not anticipate employment termination or interruption during the study period.

All community pharmacies located within the intervention PC centres catchment areas were invited to participate if inclusion criteria were fulfilled; (1) the manager agreed to guarantee ethical standards; (2) at least one pharmacist agreed to participate in the trial; and (3) pharmacists signed informed consent and were willing to attend intervention training. Pharmacies located within the catchment areas of the UC PC centres were neither contacted nor involved. In the intervention areas, the proportion of pharmacies that agreed to participate ranged from 10% to 100%.

To avoid contamination between both PC centres and community pharmacies, a maximum of one PC centre was selected per municipality if ≤100 000 inhabitants, or per neighbourhood (if municipality >100 000 inhabitants). At least 3 km between PC centres was ensured to prevent contamination.

All patients over 18 years old, who received a new lipid-lowering, antihypertensive, antiplatelet and antidiabetic medication prescription from a participating GP between March 2022 and September 2022, were identified from electronic health records (EHR) and included in the study. Patients' informed consent was obtained through simplified means.[27 37]

A prescription was considered new if a patient had no prescription/dispensation record of the same pharmacotherapeutic group in the previous 6 months. Each new prescription was considered the index prescription and patients were included as often as pharmacotherapeutic groups were prescribed. Pharmacotherapeutic groups were aggregated by pharmacological treatment; lipid-lowering medication, antihypertensive medication, antiplatelet medication and antidiabetic medication (online supplemental file 2). For this study, we refer to prescription as individual index prescriptions and to treatment as the aggregation of index prescriptions by pharmacological treatments.

Intervention

The IMA intervention is a patient-centred intervention aiming to improve medication initiation, secondary adherence and ultimately patient clinical outcomes by promoting SDM and standardising clinical practice among healthcare professionals (GPs, nurses and community pharmacists). Training was provided to all professionals on medication adherence, the principles of SDM and use of decision aids. GPs were trained to apply SDM during the consultation by informing the patient about their disease and available treatment options using decision aids (leaflets and a website[38]), and by exploring patient's perspective and questions before prescribing new pharmacological treatments for CVD or diabetes.[16 39] Nurses and pharmacists were encouraged to reinforce the information provided by GPs by addressing patients' questions and using decision aids. A full description of the intervention, its logic model and implementation strategy is described elsewhere.[28 40]

Usual care

Healthcare professionals in UC centres received no training or access to study decision aids. The prescription process is not standardised in Spain, nor is patient involvement in the decision-making process guaranteed when being prescribed a new treatment. Each GP decides how to provide disease and treatment-option information, and in some situations, it is the nurse who gives this information to the patient during a follow-up consultation. Nurses usually promote adherence by exploring any potential side-effects of prescribed treatments and monitoring clinical parameter results. Community pharmacists are expected to explore patients' information and queries about the medication during drug dispensing; however, this is not standardised.

Sample size

A proportion of 10% non-initiation for CVD and diabetes medications in Catalonia was assumed for sample size calculations.[3] To detect a 3% reduction in non-initiation with 80% power and 5% significance, given an intracluster correlation coefficient of 0.01, assuming that on average each GP issues 30 new prescriptions every 6 months, and estimating losses of 10% (incomplete EHR), 3878 prescriptions and 130 GPs were required. Therefore, 24 PC centres were contacted to reach the sample needed for both groups.

Randomisation

First, PC centres were matched in pairs (1:1) based on key characteristics of the PC teams—rurality/urbanity, area socioeconomic status, size of the population served, proportion of immigrant population and number of GPs in the team. For each pair, an ordered list of replacement centres with the same characteristics was randomly generated, to account for non-participation or ineligibility. Second, consent for participation was obtained. Finally, paired centres were randomised into UC or intervention groups using a computerised random number generator, ensuring allocation concealment at the cluster level.

Concealment of allocation for patients was unfeasible due to intrinsic cluster-design characteristics.

Blinding

Owing to the nature of the intervention, healthcare professionals and patients could not be blinded.

Data collection

All data were collected from the EHR (SIDIAP (Sistema d'Informació per al desenvolupament de la Investigació en Atenció Primària) database[41]), including patients' sociodemographic and clinical data, and information on dispensed medications at any Catalan community pharmacy (March 2021–December 2023). This database was encrypted, anonymised and provided RWD for research purposes under a legal and regulatory framework, following ethical principles and maintaining transparency.[41]

Outcomes

Baseline sociodemographic characteristics

Sociodemographic characteristics were collected at baseline (first index prescription): patient (sex, age, nationality, socioeconomic[42] and pharmacy copayment status, tobacco use and diagnoses (based on International Classification of Diseases-10 code)); prescribing GP (sex, age, population assigned and covered and care quality standards[43 44]); and PC centre (rurality and area socioeconomic status, size of the population served, proportion of immigrant population, number of GPs in the team and training centre).

Impact on adherence

Prescription and dispensation data from EHRs were compared to assess prescription adherence. The absence of data implies a non-existent prescription or dispensation. Data on the prescribed dose were unavailable. Most studied treatments involve a single daily dose, and medicine boxes generally contain 28 pills, therefore assumed to last 28 days.

Primary adherence or initiation (primary outcome measure): Prescriptions were considered initiated if obtained at any community pharmacy in Catalonia within 3 months after index prescription.[45] 1-month initiation, late initiation or initiation at any time after index prescription, and single prescription dispensation (only for initiated prescriptions with an active period >45 days) were also estimated.

Secondary adherence: For initiated treatments lasting ≥6 months, 6-month and 12-month secondary adherence was estimated. The level of adherence in terms of medication implementation, or correct dosing, was based on the *proportion of days covered (PDC)*; the number of days for which the prescription was available divided by the number of days from initiation to end of active prescription period.[45] Treatment PDC was estimated as a continuous measure and dichotomised as implemented if PDC ≥80%. *Persistence* was based on the time from initiation to discontinuation of treatment,[45] accepting a maximum gap of 2 months and classified as persistent if ≥1 prescriptions were not discontinued within each treatment. Finally, *total adherence* was estimated by combining the dichotomised PDC and persistence variables.

Impact on clinical outcomes

Clinical parameter observations from EHR were dated and could have been repeatedly registered for one patient at different time points during follow-up, from 12 months before the index prescription by treatment up to 18 months afterwards.

The impact on clinical outcomes was assessed per treatment as per clinical guidelines[46–48]; Antihypertensive: systolic and diastolic blood pressure; Antidiabetic: glycated haemoglobin and impaired fasting blood glucose; Lipid-lowering: total cholesterol, high-density lipoprotein (HDL), low-density lipoprotein (LDL) and triglycerides. Cardiovascular risk (CVR) was assessed using the Framingham Risk Score, calculated per patient based on clinical outcomes (diabetes diagnosis, total cholesterol, HDL, systolic and diastolic blood pressure) and sociodemographic variables (age, sex and tobacco use). It was only calculated for patients aged 35–74 years, free of CVD or event, diabetes mellitus type I and familial hypercholesterolaemia as per the score authors and clinical guidelines.[48 49]

Statistical methods

Main analyses followed the intention-to-treat (ITT) principle (all patients treated by GPs who fulfilled inclusion criteria—signed an informed consent, were willing to attend intervention training and did not anticipate employment termination or interruption during the study period) and the per protocol (PP) principle (only patients who received a prescription by GPs who completed the training in the intervention group and visited a participating GP or nurse at least 7 days before or after the index prescription in both groups). The basic units of analysis were either prescriptions, patients or GPs based on the outcome (online supplemental file 3), and were performed using multilevel techniques clustered by PC centre and GP.

A descriptive analysis of baseline sociodemographic characteristics was performed at all levels to summarise differences between groups. Continuous variables were described using means and standard deviations (SD), and categorical variables using counts and percentages. Multiple imputation using chained equations (MICE) was applied to handle missing values for nationality and pharmacy copayment, which were required for covariate adjustment.

Impact on adherence

Intervention impact on adherence was assessed for prescriptions overall and for each aggregated treatment, estimated using multilevel logistic regression

models (linear regression when considering mean PDC) in which the dependent variable was adherence and the independent variable the group. Models were adjusted for randomisation matching variables and adherence predictors (age, nationality, teaching centre status and pharmacy copayment as a proxy for socioeconomic status[3 25]).[50 51] To account for missing data in nationality and pharmacy copayment, the models were run across imputed data sets and the results were combined following Rubin's rules.

Impact on clinical outcomes

The range and completion of clinical parameters on EHRs were assessed by summarising the data and identifying missing values. All values were within feasible ranges and completion rates ranged from 65% to 90% (online supplemental file 4). The differences between groups in the proportion of missing data were explored using logistic regression models. A missing at random pattern was assumed.

Multilevel linear repeated measures models gauged the impact of the intervention on clinical outcomes.[52] These allowed us to include varying numbers of observations and time points, account for within-patient correlation over time, consider the interaction between group and time and avoid excluding patients with partial measurements.

CVR was the clinical outcome with the highest proportion of missing data required for its calculation. Therefore, two imputation strategies were tested: multilevel repeated measure models and MICE (online supplemental file 5). CVR calculations estimated from the two strategies were very similar and the results presented are based on the more restrictive one: MICE.

Intervention impact was estimated per treatment on all clinical outcomes but CVR, which was estimated per patient using multilevel linear repeated measure models adjusted for randomisation matching variables and baseline covariates known to influence clinical outcomes (age, sex, nationality, tobacco use and pharmacy copayment as a proxy for socioeconomic status).[50 51] CVR and triglycerides were transformed to logarithmic scale to achieve a normal distribution. These observations were considered several times at diverse time points during follow-up, and the interaction 'time x group' as the independent variable. Time was measured in days, with index prescription time=0. All models were run across imputed databases to account for missing data, and Rubin's rules were used to combine the results.

Taking into account the maximum fraction of missing information, a total of 90 imputed data sets were generated for all the analyses.

Sensitivity analysis

Complete case analyses (patients attended by GPs who completed the 7-month study period and had 12-month follow-up) and model outputs without controlling for baseline characteristics to assess uncertainty were performed. A secondary analysis was performed by stratifying all the outcomes by sex (online supplemental file 9).

To assess the potential impact of the small number of clusters (n=24), we conducted additional sensitivity analyses applying small-sample corrections to those outcomes that showed statistically significant effects by applying Satterthwaite degrees-of-freedom corrections.[53]

Deviations from study protocol

There were deviations from the study protocol:[27] (1) Visits with participating GPs or nurses at least 7 days before or after the index prescription were included as PP cohort criteria; (2) Secondary adherence was calculated only for initiated treatments from initiation and not from the moment of prescription; (3) CVR was only calculated for 35–74 year-old patients, free of CVD, diabetes mellitus type I and familial hypercholesterolaemia as per the score authors and clinical guideline recommendations[48 49]; (4) Intervention impact on cardiovascular events was not explored due to follow-up duration constraints; (5) A secondary analysis limited to lipid-lowering prescriptions for secondary prevention was conducted, as these treatments are primarily recommended for such cases[48] (online supplemental file 10); (6) Following the recommendations of an external expert reviewer, two key adjustments were made: (a) statistical models were adjusted for prespecified randomisation matching variables and outcome baseline predictors identified in the literature,[50 51] rather than variables showing baseline significant differences, as originally outlined in the study protocol, and (b) small-cluster sample corrections were applied as sensitivity analyses for outcomes with statistically significant effects; (7) Based on the preliminary results, a post hoc exploratory hypothesis was formulated to explore whether the IMA intervention could have influenced *professionals' prescribing behaviour*—whether GPs in the intervention group issued fewer prescriptions following SDM implementation. The prescription monthly ratio (new IMA pharmacological treatments or otherwise) per 30 visits (mean visits per shift) made by participating GPs was compared between groups 12 months prior to and during the 7-month trial. The impact was estimated through multilevel repeated measure models which considered the ratio as the dependent variable and the interaction 'time x group' as the independent variable (online supplemental file 11); (8) Trial effectiveness results were shared in a focus group with professionals (online supplemental file 12) and, together with the process evaluation findings,[40] the opinions gathered on clinical implications and the intervention logic model were integrated to facilitate interpretation of trial outcomes and inform the discussion.

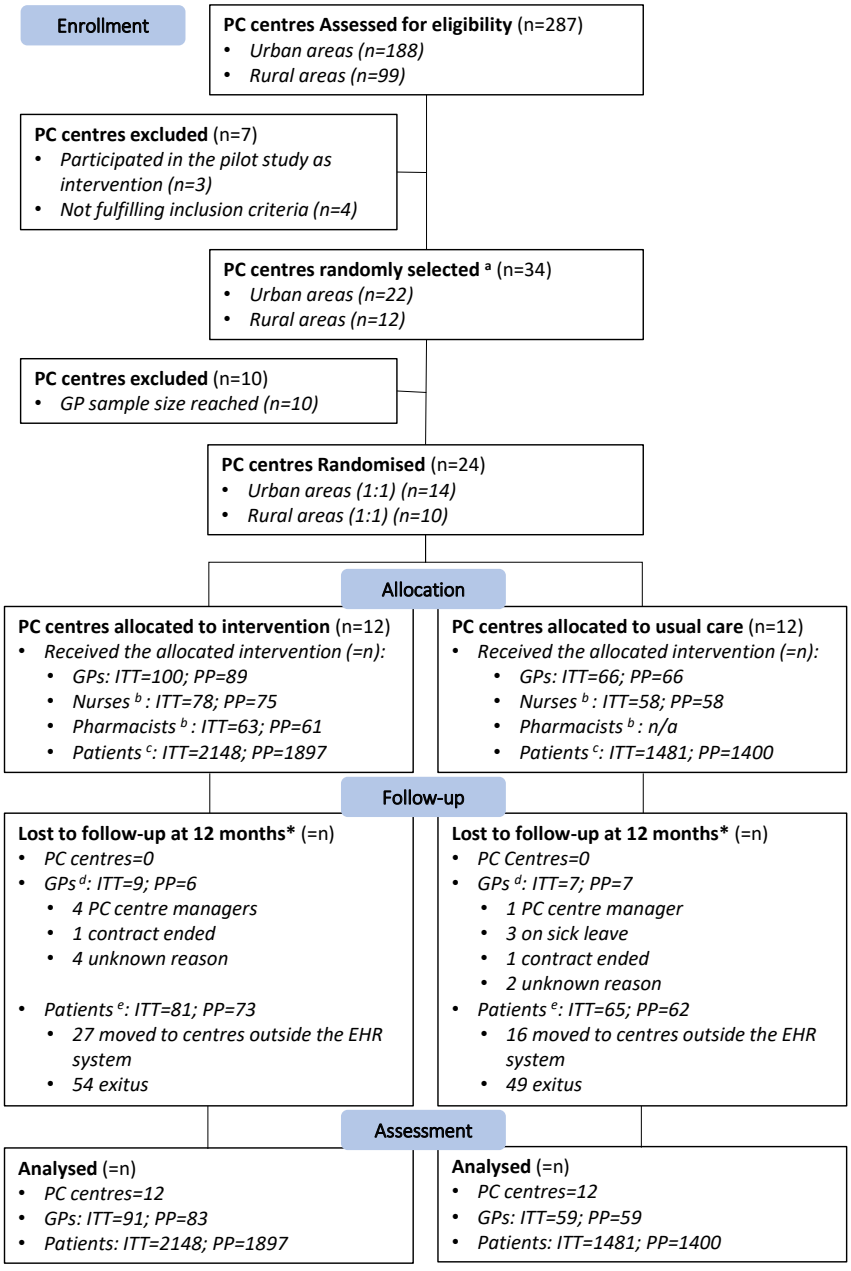

Figure 1 CONSORT flow diagram of participants. (a) Three centres declined to participate and their replacements were selected instead. (b) Nurses and pharmacists from the enrolled PC centres were allocated, they supported GPs but did not include patients in the trial. Data on these professionals were not available in the EHR and they were not included in the analysis. (c) Each patient can have >1 pharmacological treatment prescribed and/or >1 prescription per pharmacological treatment. (d) GPs were lost to follow-up when they were not identified in the EHR database. (e) Patients lost to follow-up were included in the analysis until their discharge date in the EHR. *42% of patients with antihypertensive treatments, 58% of patients with antidiabetic treatments and 42% of patients with lipid-lowering treatments were followed up >12 months (data used only for clinical parameters and cardiovascular risk impact evaluation). CONSORT, Consolidated Standards of Reporting Trials; GPs, general practitioners; ITT, intention-to-treat; PC, primary care.

RESULTS

Figure 1 shows the study flowchart. 24 PC centres, 150 GPs and 3629 patients (receiving 4910 prescriptions) were included and analysed. 16 included GPs (Intervention=9; UC=7) had no follow-up data in the EHR: 5 were managers with no prescription history, 3 were on sick leave, 2 had contract termination and 6 had no records for unknown reasons. Given the intrinsic RWD study characteristics, all patients were included in the analysis until their EHR discharge date; 103 patients died and 43 moved to centres outside the EHR system before follow-up completion. Nurses and pharmacists did not include patients in the study and were not identified in the EHR; therefore, no data on

these professionals were available, and they were not included in the statistical analyses.

Almost 95% of GPs and 91% of patients were included in the PP analyses. There were no relevant differences between ITT and PP analyses (online supplemental file 6) nor in any sensitivity analysis, including when small-cluster sample corrections were applied (analysis available on request), therefore only ITT main analysis results are reported and discussed in the main text.

Baseline characteristics of patients, GPs and PC centres are presented in table 1.

Impact on adherence

No differences were detected between groups in medication initiation (at 1 or 3 months), late initiation or single prescription dispensation or in PDC, persistence or total adherence at 6–12 months (table 2; by aggregated treatment see online supplemental file 7). Although persistence at 6 months reached statistical significance (p=0.043), the absolute difference was small. Similarly, in the stratified sex analysis, some statistically significant differences at 6 months were found in the male subgroup against the intervention, but these were also minor in magnitude (online supplemental file 9).

Impact on clinical outcomes

Tables 3 and 4 present the results of the multilevel repeated measures model and the model-based mean values for each group at baseline and 12 months postintervention (online supplemental file 8 shows raw clinical data). Statistically significant group and 'time x group' interaction in favour of the IMA intervention was observed for blood pressure. Based on model-based estimates, the mean extra 12-month reduction in the intervention group was 9.0 mm Hg for systolic and 3.7 mm Hg for diastolic blood pressure. When stratified by sex, this difference was observed only among females (online supplemental file 9). Statistically significant 'time x group' interactions were also observed for total cholesterol, LDL, HDL and triglycerides. However, these interactions favoured UC, and the overall 12-month differences between groups were small.

Impact on professionals' prescription behaviour (post hoc exploratory hypothesis)

No differences were detected between groups in GP new prescriptions/visits ratio for all prescriptions, although intervention GPs issued 0.3 more IMA study prescriptions per one shift (30 visits) 6 months postintervention (online supplemental file 11).

DISCUSSION

This study evaluated a patient-centred SDM intervention in PC to improve adherence to CVD and diabetes treatments, presenting a methodology for evaluating complex behavioural interventions in real-world settings using RWD. The IMA intervention had no impact on medication initiation or secondary adherence, with only a slight effect on blood pressure.

Our large-scale pragmatic trial used adherence (medication initiation) as the primary outcome, measured using robust RWD rather than self-reported methods. Most studies evaluating SDM interventions primarily focus on psychosocial or clinical outcomes, while behavioural outcomes like adherence are often treated as secondary, with small samples and methodological limitations leading to low-to-moderate evidence quality.[20 21 54–56] SDM research is primarily conducted in the USA or northern Europe, with few studies conducted in Spain and none targeting adherence as a primary outcome.[57–59] Few of these trials integrated process evaluations, limiting understanding on outcome mechanisms.

Consistent with prior studies on SDM's effects on adherence to diabetes or CVD treatments, the IMA intervention had no impact on adherence.[20 58 60–63] Overall, both groups improved clinical outcomes at 12 months, although clinically relevant between-group differences were observed in blood pressure, with a reduction shifting classification from hypertension to normal.[46] Total cholesterol, HDL, LDL and triglycerides showed clinically insignificant 12-month differences.[48] The impact of SDM interventions on clinical outcomes reported in the literature is inconclusive, with most studies showing no effect.[60 61 63] Previous SDM interventions failed to improve blood pressure[56 63] but showed positive effects on glycaemic control.[56 64] Notably, one study supported SDM's potential to improve the reach of treatment goals for blood pressure and glycated control.[62] These differences reflect SDM's contradictory evidence, with stronger effects on knowledge, trust, decisional conflict or satisfaction (typically primary outcomes) compared with adherence and clinical outcomes (often secondary) for which the evidence remains limited and generally of low-to-moderate quality.

The impact observed on clinical outcomes was not mediated by improved adherence. Therefore, we tested an exploratory hypothesis that SDM training might have led to fewer new treatments being indicated and accepted (ie, prescribed). However, analysis showed no change in overall prescription trends. In fact, GPs in the intervention group issued slightly more IMA prescriptions 6 months postintervention.

Adherence, as a dynamic behaviour, requires more than a single intervention to sustain long-term change, despite the importance of the moment of the initial prescription.[65] Although SDM can positively impact satisfaction, knowledge, communication and decision involvement,[21] it did not impact adherence, and its slight effect on blood pressure and mechanisms driving this change remain uncertain. Focus group feedback on clinical implications and intervention logic model

Table 1 Sample baseline characteristics: patient, professional and PC centre level

	Intervention	Usual care
Patient level	**n=2148**	**n=1481**
Sex % (N)		
Female	51.7 (1110)	48.5 (718)
Male	48.3 (1038)	51.5 (763)
Age mean (SD)	61.2 (13.9)	62.7 (13.8)
Nationality % (N)		
Spain	75.1 (1612)	61.6 (912)
Other	16.5 (355)	17.1 (254)
Missing	*8.4 (181)*	*21.3 (315)*
Postal code area % (N)		
Urban	77.2 (1659)	64.5 (955)
Rural	11.9 (255)	19.8 (294)
Missing	*10.9 (234)*	*15.7 (232)*
Socioeconomic deprivation* % (N)		
Low	14.5 (311)	11.4 (169)
Low intermediate	27.5 (590)	21.9 (324)
Intermediate	27.9 (600)	29.2 (433)
High intermediate	16.5 (355)	21.7 (322)
High	4.6 (99)	1.7 (25)
Missing	*9.0 (193)*	*14.0 (208)*
Pharmacy copayment % (N)		
Low-income population (0%)	17.0 (365)	17.6 (260)
Low–middle-income pensioners (10%)	32.2 (692)	32.3 (479)
Low-income non-pensioners (40%)	28.0 (602)	28.4 (421)
Middle–high-income non-pensioners (>50%)	21.1 (454)	19.5 (288)
Missing	*1.6 (35)*	*2.2 (33)*
Tobacco % (N)		
Non-smoker	64.3 (1382)	65.5 (970)
Smoker	29.1 (625)	27.2 (403)
Missing	*6.6 (141)*	*7.3 (108)*
Diagnosis records % (N)		
Lack of record	10.9 (234)	10.0 (148)
Record	89.1 (1914)	90.0 (1333)
Diabetes mellitus type 2 (E10–E14)	28.0 (602)	29.9 (443)
Dyslipidaemia (E70–E90)	47.9 (1029)	50.5 (748)
Hypertensive diseases (I10–I15)	60.0 (1288)	57.4 (850)
Coronary heart diseases (I20–I25)	4.8 (103)	5.7 (85)
Other heart diseases (I50–I52)	3.4 (72)	4.9 (72)
Cerebrovascular diseases (I60–I69)	5.4 (115)	5.1 (75)
Arterial diseases (I79–I79)	5.4 (115)	5.3 (78)
Acute and chronic kidney failure (N17–N19)	6.8 (145)	5.9 (88)
General Practitioner level	**n=91**	**n=59**
Sex % (N)		
Female	72.5 (66)	72.9 (43)
Male	27.5 (25)	27.1 (16)
Age % (N)		
18–45	36.3 (33)	37.3 (22)
45–55	42.9 (39)	40.7 (24)
≥55	20.9 (19)	22.0 (13)
Population assigned mean (SD)	1338.4 (346.7)	1333.7 (329.7)
Proportion of population covered mean (SD)	67.7 (10.8)	67.3 (10.1)
Healthcare quality standard in 2022 % (N)		
Low/intermediate	8.8 (8)	17.0 (10)
High	82.4 (75)	78.0 (46)

Continued

Table 1 Continued

	Intervention	Usual care
Missing	*8.8 (8)*	*5.0 (3)*
Pharmacological prescription quality standard in 2022% (N)		
Low	13.2 (12)	16.9 (10)
Intermediate	34.1 (31)	32.2 (19)
High	48.3 (44)	42.4 (25)
Missing	*4.4 (4)*	*8.5 (5)*
Primary care centre level	**n=12**	**n=12**
Area socioeconomic deprivation † % (N)		
Rural	41.7 (5)	41.7 (5)
Urban 1	16.7 (2)	8.3 (1)
Urban 2	8.3 (1)	16.7 (2)
Urban 3	16.7 (2)	8.3 (1)
Urban 4	16.7 (2)	25.0 (3)
Size of the population mean (SD)	18 640.5 (10 336.5)	18 195.9 (9598.0)
Proportion of immigrant population mean (SD)	16.6 (12.9)	13.7 (4.1)
Number of GPs mean (SD)	13.6 (5.5)	11.9 (6.1)
Training centre‡ % (N)	66.7 (8)	25.0 (3)

*Deprivation Index 2011 of the Spanish Society of Epidemiology (IP2011).[42]
†Area socioeconomic deprivation: four urban categories based on quartiles from low (urban 4) to high (urban 1) socioeconomic deprivation and a rural category.
‡Training centre: PC centres that host university students and clinical residents and have trained professionals as student supervisors.
GPs, general practitioners; N, number; PC, primary care; SD, standard deviation.

revealed professionals were surprised by the lack of adherence impact but improved blood pressure. They attributed this to increased awareness leading to better adherence to non-pharmacological measures, despite acknowledging these are usually harder for patients to follow (further details in online supplemental file 12). A complementary process evaluation study similarly found increased patient awareness, although it could

Table 2 Intervention impact on adherence: prescription level

	Intervention	Usual care	
Primary adherence	**n=2856**	**n=2054**	**P value**
Initiation % (N)			
1-month initiation	86.6 (2473)	85.8 (1762)	0.646
3-month initiation	91.3 (2607)	91.3 (1876)	0.708
Late initiation	94.2 (2689)	95.0 (1951)	0.857
Single prescription dispensation*	7.0 (182)	7.5 (141)	0.315
Secondary adherence by treatment†			
6-month secondary adherence	**n=2003**	**n=1415**	**P value**
Proportion of days covered (PDC)			
PDC ≥80% % (N)	49.4 (990)	48.2 (682)	0.121
PDC mean (SD)	73.8 (26.5)	72.6 (27.1)	0.082
Persistence % (N)	73.7 (1477)	72.2 (1022)	0.043
Total adherence % (N)	49.3 (988)	48.1 (681)	0.112
12-month secondary adherence	**n=2038**	**n=1432**	**P value**
Proportion of days covered (PDC)			
PDC ≥80% % (N)	48.8 (994)	47.2 (676)	0.341
PDC mean (SD)	70.9 (28.9)	69.5 (29.3)	0.205
Persistence % (N)	62.5 (1273)	60.2 (862)	0.186
Total adherence % (N)	47.0 (958)	45.5 (651)	0.304

All intraclass correlation coefficients (ICCs) indicate minimal variability across GPs and PC centres.
P values estimated by multilevel logistic regression models in all but PDC-mean (multilevel linear regression model).
*Single prescription dispensation in 3-month initiators sample (Intervention=2607; UC=1876).
†Secondary adherence was calculated by aggregating prescriptions by pharmacological treatment and considering 3-month initiators with an active prescription period of ≥6 months from the first pharmacy refill at 6 and 12 months.
GPs, general practitioners; N, number; PC, primary care; SD, standard deviation; UC, usual care.

Table 3 Multilevel model b-coefficients (95% CI) and p values of clinical outcomes impact models: prescriptions aggregated by pharmacological treatment

	b-coefficients (95% CI)	P value
Antihypertensive*		
Systolic blood pressure (mm Hg)		
Constant	139.81 (134.36 to 145.25)	0.000
Group		
Usual care	Ref	
Intervention	−6.09 (−7.13 to −5.06)	0.000
Time (days)	−0.01 (−0.01 to −0.008)	0.000
Time (days) × group interaction	−0.008 (−0.01 to −0.004)	0.000
Diastolic blood pressure (mm Hg)		
Constant	101.48 (97.65 to 105.31)	0.000
Group		
Usual care	Ref	
Intervention	−2.22 (−2.85 to −1.58)	0.000
Time (days)	−0.006 (−0.008 to −0.005)	0.000
Time (days) × group interaction	−0.004 (−0.006 to −0.002)	0.001
Antidiabetic*		
Blood glucose (mg/dL)		
Constant	158.91 (131.89 to 185.93)	0.000
Group		
Usual care	Ref	
Intervention	−21.76 (−28.56 to −14.97)	0.000
Time (days)	−0.02 (−0.03 to −0.007)	0.001
Time (days) × group interaction	0.004 (−0.02 to 0.03)	0.663
Glycated haemoglobin (%)		
Constant	8.15 (7.31 to 8.98)	0.000
Group		
Usual care	Ref	
Intervention	−0.32 (−0.55 to −0.09)	0.006
Time (days)	−0.0009 (−0.001 to −0.0005)	0.000
Time (days) × group interaction	−0.0004 (−0.001 to 0.0003)	0.250
Lipid–lowering*		
Total cholesterol (mg/dL)		
Constant	248.21 (224.83 to 271.58)	0.000
Group		
Usual care	Ref	
Intervention	−46.89 (−52.84 to −40.94)	0.000
Time (days)	−0.06 (−0.07 to −0.05)	0.000
Time (days) × group interaction	0.07 (0.05 to 0.09)	0.000
High-density lipoprotein (mg/dL)		
Constant	42.16 (34.52 to 49.81)	0.000
Group		
Usual care	Ref	
Intervention	−2.71 (−3.94 to −1.48)	0.000
Time (days)	0.0007 (−0.001 to 0.003)	0.490
Time (days) × group interaction	0.005 (0.001 to 0.009)	0.011
Low-density lipoprotein (mg/dL)		
Constant	142.68 (121.69 to 163.67)	0.000
Group		
Usual care	Ref	
Intervention	−44.55 (−49.82 to −39.28)	0.000
Time (days)	−0.05 (−0.06 to −0.04)	0.000
Time (days) × group interaction	0.06 (0.05 to 0.08)	0.000
Triglycerides (mg/dL)		
Constant	140.77 (124.42 to 159.26)	0.000
Group		
Usual care	Ref	
Intervention	0.82 (0.78 to 0.87)	0.000
Time (days)	0.9998 (0.9997 to 0.9999)	0.000
Time (days) × group interaction	1.0002 (1.00006 to 1.0004)	0.007
Cardiovascular risk†		
Constant	3.65 (3.45 to 3.87)	0.000
Group		
Usual care	Ref	
Intervention	0.94 (0.92 to 0.97)	0.000
Time (days)	0.9998 (0.9997 to 0.9998)	0.000
Time (days) × group interaction	0.99990 (0.9998 to 1.00003)	0.137

All intraclass correlation coefficients (ICCs) indicate minimal variability across GPs and PC centres.
P values estimated by multilevel repeated measures models.
Coefficients are presented as mean differences in the dependent variable (beta).
*Prescription level by pharmacological treatment:(1) Antihypertensive: Intervention=1135; UC=784; (2) Antidiabetic: Intervention=414; UC=303; (3) Lipid-lowering: Intervention=765; UC=521.
†Patient level from 35 to 74 years old and free of CVD, DM 1 and familial hypercholesterolaemia: Intervention=1490; UC=987.
CVD, cardiovascular disease; DM 1, diabetes mellitus type 1; GPs, general practitioners; PC, primary care; UC, usual care.

not confirm an influence on non-pharmacological measures.[40] Adherence behaviour includes pharmacological and non-pharmacological treatment components, and the former, along with refilling medication, includes correct dosing and regularity.[66] While the method used to measure adherence in this study is consistent and widely used, and medication collection was similar across groups, we cannot determine if more precise adherence in the intervention group contributed to clinical changes.

When exploring sex differences, the blood pressure decrease was only observed in females. While no direct evidence links SDM interventions to gender-specific effects, research suggests that female physician–female patient interactions can enhance patient-centred care and health outcomes.[67–69] Since most GPs in this study were women, this finding might align with previous research but requires further investigation.

In the context of a type I effectiveness-implementation hybrid trial, a process evaluation was conducted to help interpret the trial findings.[40] Triangulating results from the effectiveness and process evaluations provided insights into the observed lack of effect. Findings from the process evaluation showed that although professionals valued the training, many felt it was insufficient, highlighting the need for ongoing training.[40] Although patients reported feeling engaged and most

Table 4 Multilevel model-based clinical outcomes mean (SE) at baseline and 12 months follow-up: prescriptions aggregated by pharmacological treatment

	Intervention	Usual care	
Antihypertensive*	**n=1135**	**n=784**	**P value**
Systolic blood pressure (mm Hg)			
Baseline	133.7 (2.8)	139.8 (2.8)	0.000
12 months	127.1 (2.8)	136.1 (2.8)	0.000
Diastolic blood pressure (mm Hg)			
Baseline	99.3 (1.9)	101.5 (1.9)	0.000
12 months	95.5 (1.9)	99.1 (1.9)	0.000
Antidiabetic*	**n=414**	**n=303**	**P value**
Blood glucose (mg/dL)			
Baseline	137.1 (14.1)	158.9 (13.8)	0.000
12 months	132.5 (13.9)	152.5 (13.9)	0.000
Glycated haemoglobin (%)			
Baseline	7.8 (0.4)	8.1 (0.4)	0.006
12 months	7.4 (0.4)	7.8 (0.4)	0.000
Lipid-lowering*	**n=765**	**n=521**	**P value**
Total cholesterol (mg/dL)			
Baseline	201.3 (12.3)	248.2 (11.9)	0.000
12 months	206.1 (12.1)	226.3 (12.3)	0.000
High-density lipoprotein (mg/dL)			
Baseline	39.5 (3.9)	42.2 (3.9)	0.000
12 months	41.6 (3.9)	42.4 (3.9)	0.214
Low-density lipoprotein (mg/dL)			
Baseline	98.1 (11.0)	142.7 (10.7)	0.000
12 months	102.8 (10.8)	124.5 (10.8)	0.000
Triglycerides (mg/dL)			
Baseline	115.8 (7.8)	140.8 (8.9)	0.000
12 months	117.0 (7.5)	130.6 (8.5)	0.000
Cardiovascular risk†	**n=1490**	**n=987**	**P value**
Baseline	3.5 (0.1)	3.7 (0.1)	0.000
12 months	3.0 (0.1)	3.3 (0.1)	0.000

P values estimated from linear combination of estimates following multilevel repeated measures models.
*Prescription level by pharmacological treatment.
†Patient level from 35 to 74 years old and free of CVD, DM 1 and familial hypercholesterolaemia.
CVD, cardiovascular disease; DM 1, diabetes mellitus type 1.

professionals indicated that they had integrated SDM into routine practice, some perceived no difference between the intervention and UC.[40] This highlights the challenge of promoting behavioural change when professionals believe they are already implementing SDM. While attitudes towards SDM and its perceived benefits improved, implementation was inconsistent due to time constraints and ingrained habits that often exclude patients from decision-making.[40] Furthermore, patients appreciated involvement but noted it did not always influence their decision to start medication.[40] Despite these challenges, both professionals and patients reported an overall positive experience with the intervention, suggesting it might add value beyond clinical outcomes.

While the impact on adherence or clinical outcomes may be limited, SDM enhances the experiences of patients and healthcare professionals.[40] Within value-based healthcare, its ability to endorse quality of care and patient engagement warrants discussion on its broader implementation. Rooted in ethical principles, SDM respects patients' right to informed choices as the foundation of professional practice.[70] It promotes autonomy and active participation, while repeated SDM practice enhances professionals' communication skills and the quality of health information provided.[70 71] Beyond individual interactions, SDM can foster a culture of collaboration, encouraging patients to critically evaluate decisions, weigh benefits and harms and ultimately share responsibility in healthcare.[13]

Nevertheless, implementing SDM is complex and requires sustained efforts to achieve and maintain its adoption. It involves behavioural changes among professionals, patients and the healthcare system. While rooted habits in healthcare and organisational

constraints pose challenges, addressing these barriers and promoting SDM offers the opportunity to build a more inclusive, patient-centred healthcare system.

Strengths and limitations

The IMA-cRCT is a large, methodologically robust study designed to ensure reliable and reproducible results. Its cRCT design minimised bias, achieved statistical power, employed rigorous analysis for accurate finding interpretation and ensured representativeness through random sampling of the centres. By using a hybrid effectiveness-implementation approach, the trial enhanced pragmatism, addressing both dimensions and providing comprehensive insights for clinical decision-making and research translation.

The use of RWD as part of the pragmatic trial enabled a large sample size, reduced researcher involvement and improved transferability, but presented challenges. These were addressed through tailored analytical strategies, but assumptions and imputation methods were necessary.[72] For instance, measuring adherence through pharmacy dispensation may have overestimated adherence, as refilling medication does not guarantee it was taken. Clinical parameter observations, based on guideline recommendations, were not always followed in practice, and variations in measurement time points and missing data were observed.

The pragmatic nature of the study hampered identification of which professionals actually delivered the intervention in the PP analysis. Additionally, while RWD offered valuable insights into adherence and clinical outcomes unattainable with traditional trials, it may not capture specific behaviours potentially influenced by SDM affecting clinical outcomes, indicating a need for further research. Notably, no direct, proximal measures of SDM uptake or professional behaviour were included, limiting the understanding of the intervention mechanisms. This was a deliberate trade-off to maintain the trial's pragmatism, while exploring insights into the intervention mechanisms through the complementary process evaluation.[40] A further contextual limitation relates to the pharmacy component as patients are free to use any pharmacy, and dispensing data are not linked to specific establishments. As a result, actual exposure to this component of the intervention could not be assessed through RWD.

CONCLUSIONS

This study indicates that the IMA intervention, based on SDM models, does not improve medication adherence in the current context. While a modest positive effect in blood pressure was observed, the mechanisms of action underlying this effect remain unclear. Future efforts should balance the benefits of enhanced patient and professional experiences with the resource implications of SDM implementation and additional care costs. Continued investment in professional training, patient support and research to address implementation challenges is essential to fully understand and enhance the benefits of SDM, which would warrant further evaluation.

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Ethics approval This study involves human participants and was approved by the Drug Research Committee (CEIm) at IDIAP Jordi Gol, codeCEIm 21/051-P. Informed consent from the patients was obtained by simplified means in the cRCT. The IMA-cRCT is a low-intervention clinical trial where groups of subjects are allocated to the intervention groups and which satisfies all the conditions described in paragraphs 2 and 3 of article 30 of EU regulation Nº 536/2014. Informed consent was obtained by displaying posters in prominent locations of the participating PC centres notifying people that a clinical trial was being conducted in the centre and that patients could be part of this comparative study. The posters contained information on how and why the trial was being conducted and what the implications of participating in the study were. It was clearly stated that patients could request extra information and decline to participate in the study. Professionals in the intervention and usual care PC centres

were trained to deal with patients' queries regarding the study. If patients declined to participate, this information was documented by physicians in the electronic health records and data from those patients was not used for the trial. Furthermore, patients could withdraw at any time from the clinical trial without any detriment.Healthcare professionals' participation was entirely voluntary. All healthcare professionals participating in the study signed an informed consent at the time of the first training session. They had the right to refuse to participate and to withdraw from the study at any time.The electronic health records database used met all legal requirements and it was encrypted and pseudonymised so that researchers did not have access to data that identified the patients or professionals.

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