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# Intervention for control of hypertension in Catalonia, Spain (INCOTECA Project): results of a multicentric, non-randomised, quasi-experimental controlled intervention study

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## ABSTRACT

**Objective:** The purpose of this study was to assess the effectiveness of a quality improvement (QI) plan aimed at primary healthcare teams (PHCTs) to optimise hypertension control and to compare it with standard clinical care.

**Methods:**

**Design** Multicentric, non-randomised, quasi-experimental controlled intervention study.

**Setting** 5 PHCTs in the intervention and 13 in the standard care group in the province of Barcelona, Catalonia, Spain.

**Participants** This is a population-based study in which all patients over 18 years of age with a diagnosis of hypertension before 1 January 2006 were included (n=9877 in the intervention group and n=21 704 in the control group).

**Intervention** A QI plan that targeted primary care professionals. The plan included training sessions, implementation of recommended clinical practice guidelines for the management of hypertensive patients and audit and feedback to health professionals.

**Main outcome measure** Prevalence of hypertensive patients with an adequate blood pressure (BP) control.

**Results:** The adjusted difference between intervention and standard care groups in the odds of BP control was 1.3 (95% CI 1.1 to 1.6, p=0.003). Results of the mixed model on repeated measures showed that, on average, an individual in the intervention group had an increase of 92% in the odds of BP control (OR 1.9, 95% CI 1.7 to 2.1).

**Conclusions:** The implementation of a QI plan can improve BP control. This strategy is potentially feasible for up-scaling within the existing PHCTs.

**Trial registration:** ClinicalTrials.gov MS: 1998275938244441.

## ARTICLE SUMMARY

### Article focus

- To assess the effectiveness of a QI programme targeting health professionals to optimise BP control in hypertensive patients. Other factors associated with BP control were analysed.

### Key messages

- The QI plan aimed at PHCTs (doctors, nurses and administrative staff) implemented in our study has proven effective to improve hypertension control.
- A history of a cardiovascular event has a positive effect in BP control.
- The addition of different antihypertensive drugs to the management of hypertensive patients without considering other aggravating factors does not guarantee a better BP control.

### Strengths and limitations of this study

- The population-based design and mixed-effects modelling on repeated measures were the main strengths of this study.
- The mixed models approach is a powerful method for analysing data from longitudinal studies, which include multiple measurements on each participant.
- Most of the intervention effort in this study was implemented with few additional resources.
- The duration of the study can be considered the main limitation of this investigation. Longer term studies that include unmeasured factors are needed to determine the effectiveness and cost-effectiveness of this measure and the impact of a reduction in BP values on cardiovascular morbimortality in the hypertensive population.

## BACKGROUND

High blood pressure (BP) figures among the most common and important health problems in developed countries. Hypertension is an established risk factor for cardiovascular disease, stroke, kidney disease, all-cause mortality and shortened life expectancy.[1 2]

The prevalence of hypertension in Spain ranges from 20% to 47% in the population older than 20 years and up to 65% in the population above 60 years of age.[3] It is one of the main reasons for seeking medical attention in primary care, particularly in the older population.[3]

One in two cardiovascular deaths in Spanish individuals over 50 is attributable to high BP.[4] A number of studies carried out in Europe and in the USA have shown that BP control in hypertensive patients is suboptimal.[3 5–7]

The Catalan Health Department Health Plan for 2007–2010 requires that the health systems implement strategies to help at least 50% control of the hypertensive population achieve good BP control.[8]

Inadequate hypertension control has been associated with various factors such as treatment compliance, diabetes, age, lifestyle, concomitant treatments, the technique and the equipment used to measure BP, etc.[3 6 7 9] Management by primary healthcare teams (PHCTs) is one of the factors that can influence control of hypertensive patients.[5 10–12] Quality improvement (QI) strategies can target health professionals, patients or both, and many QI strategies have focused on improving hypertension control. These interventions can be classified as provider education (materials and instructions given to providers regarding appropriate care for patients), provider reminders (prompts given to providers to perform specific care tasks), provider audit and feedback, patient education, patient reminders, promotion of self-management, team management changes (creation of multidisciplinary teams, addition of new team members, change of roles, case or disease management), financial regulation and incentives or reimbursement changes.[12]

Previous studies have shown the positive impact of multifaceted QI interventions on BP control. However, few of these studies have been analysed using the appropriate methodology or have been designed as population based. We believe therefore that the evaluation of the effectiveness of a programme to improve healthcare quality that targets primary healthcare professionals with the aim to optimise BP control in the whole hypertensive population is warranted.[5 10–12]

We hypothesised that a plan for QI at the primary healthcare level addressed to primary healthcare professionals would improve the management and control of hypertensive patients. Our primary aim was to assess the effectiveness of a QI programme targeting health professionals to optimise BP control in hypertensive patients. Other factors associated with BP control were analysed.

## METHODS

The study protocol received institutional review board approval (IDIAP Jordi Gol Clinical Ethics Committee) and conforms to the principles embodied in the Declaration of Helsinki. The detailed methods and the study protocol have been described elsewhere.[13]

### Recruitment and assignment

The study took place from January 2006 to April 2008. All hypertensive patients diagnosed and registered in the electronic medical records of 18 PHCTs (405 232 inhabitants) in the Barcelona province (Catalonia, Spain) were included in this population-based study. All the Catalan Institute of Health PHCTs invited to take part in this study accepted.

Inclusion criteria: patients eligible to be enrolled in the study were over 18 years of age and with a hypertension diagnosis before 1 January 2006. A diagnosis of hypertension was considered when the doctor had entered in the patient's clinical record the relevant ICD-10 code (I10), following the recommendations of the European Hypertension Guidelines.[14] Exclusion criteria: we excluded patients whose electronic medical records contained no BP measurements in the year previous to the study.

The non-random allocation to the control or intervention group was decided on the basis of the PHCTs administrative area. Each administrative area has its own training and tasks strategies. The study design was therefore not randomised by PHCT to reduce the possibility of contamination between the PHCTs of the same administrative area.

The intervention group consisted of five PHCTs in the Cerdanyola-Ripollet area with a catchment population of 135 505 at the onset of the study. The standard care group (control group) consisted of 13 PHCTs in the Sabadell area with a catchment population of 269 727 inhabitants. Both primary healthcare areas are comparable in terms of population characteristics and socio-economic level. The study was fully explained to health professionals in both the standard care and intervention groups, and verbal consent to participate was obtained.

### Quality improvement intervention

The study intervention consisted in the implementation of a QI plan targeted at all health professionals (approximately 430 physicians, nurses and administrative staff) working in PHCTs in the Cerdanyola-Ripollet administrative area. In the Sabadell administrative area, the number of professionals was approximately 600. Briefly, the QI plan was divided in four phases:

1. Pre-intervention: non-validated BP monitors were removed from the PHCTs examination rooms and replaced by the digital OMRON M6 BP monitor.[15] The BP measurement technique was standardised in both groups following the Clinical Practice Guidelines recommendations.[14 16] The software used to store computerised clinical records was modified to permit health professionals to enter specific data related to hypertensive patients following the Catalan Institute of Health guidelines on hypertension.[16]

2. Second phase (intervention group): a programme was designed to train PHCTs' doctors and nurses. Posters and leaflets with specific educational contents were made available to participants. A total of eight workshops at each of the participating PHCTs took place in three stages (mean attendance rate at workshops was 65% with 6.59 mean assessment points over a 10-points range):
   - Year 2006: three sessions to introduce the QI plan and review the criteria for diagnosis of hypertension, BP measurement method and criteria for entering data in the computerised clinical record.
   - Year 2006–2007: three sessions to discuss issues such as the implementation of the QI plan, hypertension treatment and approaches to poor compliance.
   - Year 2008: two sessions to present the interim results of the QI plan and the comprehensive management of hypertensive patients.
3. Third phase (intervention group): from April 2007 to April 2008 the interventions focused on the identification of patients with uncontrolled hypertension and the improvement of their management. The applied measures were: 6-month feedback to professionals; audits to evaluate the implementation of the QI plan and a reference team (a doctor and a nurse) assigned to each PHCT.
4. Fourth phase: evaluation of the effectiveness of a QI plan.

Professionals allocated to the standard care group followed the standard clinical management based on the Catalan Institute of Health hypertension guidelines.[16]

### Masking

The study was not blinded at the PHCT or patient level because of the nature of the intervention. The analyst was unaware of the group allocation.

### Data collection

Primary care professionals regularly enter the results and activities of their work in the e-CAP (in English, electronic Primary Care Centre) database. The data collection procedure involved the reading of this computerised clinical records database approximately every 4 months from April 2007 to April 2008.

### Outcomes and other variables

Control of hypertension based on the average systolic blood pressure (SBP) and diastolic blood pressure (DBP) readings recorded over the previous 12 months was considered a dichotomous outcome variable (yes/no). The median number of BP readings was three (IQR: 2–5). SBP and DBP were evaluated as dependent continuous variables.

Control was defined as SBP <140 mm Hg and DBP <90 mm Hg. In patients with diabetes, heart failure or renal failure, control values were defined as SBP <130 mm Hg and DBP <85 mm Hg. Other variables considered were age (continuous); sex (male/female); number of antihypertensive drugs as categorical (0/1/2/3 or more); comorbidities as presence of diabetes mellitus type I or II, heart failure or renal failure (yes/no); cardiovascular events as presence of acute myocardial infarction, angina or stroke (yes/no).

### Analysis

Data were reported according to the standard published by the TREND group.[17] Descriptive statistics were used to describe the study population.

Differences between groups at baseline and at follow-up times were assessed by comparing means, medians or percentages, depending on the type of variable.

The analysis was performed at the individual level using clustered data methods (grouping factor: PHCT)[18] and based on the intention-to-treat principle.

The following time points were considered for data collection: baseline, 4, 9 and 12 months. Patients were included in the analysis if data were available for at least one follow-up time point in addition to the baseline data. To address potential biases due to incomplete follow-up data, we imputed missing values using the last known value carried forward.

The intervention effect was assessed through observed change and standardised effect size (SES).[19–21] For between-group comparisons, SES were calculated following the Kazis *et al* method.[20]

For within-group comparisons, we used the longitudinal form of SES, also known as the standardised response mean (SRM).[19 20 22] Cohen's rule of thumb for interpreting the effect size index, which considers a value of 0.2 as small, 0.5 as moderate and 0.8 or greater as large, can be applied to the SRM.[19]

Linear and logistic mixed-effects models with PHCT as random effect were used to allow for within-PHCT correlation to assess the effect of the intervention at 1-year follow-up, adjusted for baseline measurement and for differences between groups in the individual variables. The OR for the logistic model was estimated as the exponential function of the regression coefficient, exp (coefficient).

The individual variables considered were age, sex, number of antihypertensive drugs, comorbidity and cardiovascular event.

We examined the effects of intervention over all time points using mixed-effects models on repeated measures.[23 24] Level 1 covariables varied by measurement occasion and included time (age centred at 1-year follow-up), number of antihypertensive drugs, comorbidity and cardiovascular event. Level 2 covariables varied by subject and included sex and group. Interactions between covariables and the covariable 'group' were assessed.

All models were compared by the partial likelihood ratio test and Akaike information criterion. All results are shown with their 95% CIs. Statistical significance was set at $p<0.01$ (two tailed).

Stata SE V.11.0 (StataCorp LP) and SAS statistical software V.9.1 (SAS Institute Inc.) were used for all analyses.

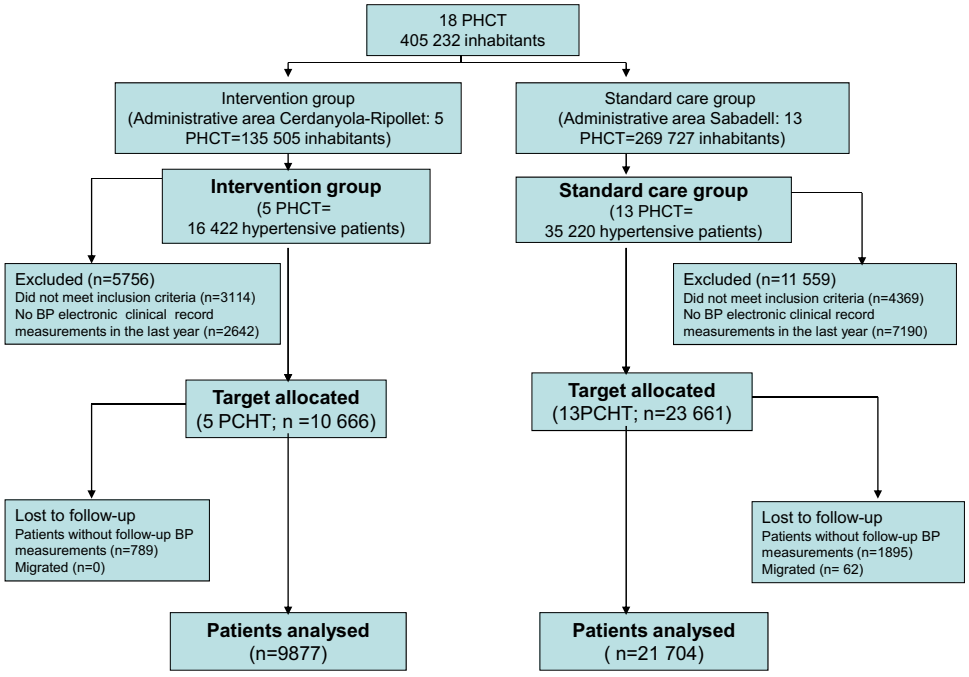


**Figure 1** Flow chart of study. BP, blood pressure; PHCT, primary healthcare teams.

## RESULTS

A total of 51 642 people were included in the study; 16 422 (5 PHCTs) were allocated to the intervention and 35 220 (13 PHCTs) to the standard care group. The exclusion rate was 33.5% (17 315 patients). Follow-up data were available for 92% of the patients. The final analysis included 31 581 patients, 9877 (5 PHCTs) in the intervention arm and 21 704 (18 PHCTs) in the standard care arm (figure 1).

The mean age of the standard care group was slightly higher and presented a higher proportion of cardiovascular events than the patients in the intervention group. Otherwise the groups were clinically comparable (table 1).

A faster increase in the percentage of BP control was observed in the intervention group during the follow-up period. In the intervention group, BP was 1.3 times more likely to be controlled than in the standard care group (adjusted OR: 1.3, 95% CI 1.1 to 1.6, p=0.003) (table 2).

The mean differences and SRM for within-group comparisons of SBP and DBP were larger in the intervention group than in the standard care group. A larger mean difference and SRM were detected in SBP and DBP at 1-year follow-up, with slightly higher values for DBP. According to the Cohen guidelines,[19] only this change in DBP can be considered a relevant change, and even so it represents a small effect size (SRM=0.21).

The larger significant differences between intervention and standard care group were found at 1-year follow-up in favour of the intervention for SBP and DBP. However, the SES did not reach even a small effect.

In the repeated measures analysis, the proportion of patients who maintained BP control during follow-up was 38.4% (95% CI 38.1% to 38.7%) (intervention group: 40%, 95% CI 39.4% to 40.5%; standard care group: 37.7%, 95% CI 37.3% to 38.1%) and the proportion of patients that improved over time (ie, achieved BP control) was 6.6% (95% CI 6.4% to 6.7%) (intervention group: 7.4%, 95% CI 7.1% to 7.7%; standard care group: 6.2%, 95% CI 6% to 6.4%). The difference between the intervention and standard care groups in the percentage of patients who maintained BP control was 2.3% (95% CI 1.6% to 3.0%) and the difference in those who improved was 1.2% (95% CI 0.8% to 1.5%). The global trend showed a highly significant change in BP control over time (p<0.001).

In phases 2, 3 and 4, the percentage of patients who were not taking antihypertensive drugs (BP drugs) at baseline and remained free of BP drugs was 79.5%, 72.9% and 66.4% in the intervention group and 66.0%, 58.1% and 54.1% in the standard care group, respectively.

In the multilevel analysis, we found that after 1 year of follow-up, an individual in the intervention group was expected on average to have an increase of 92% (OR: exp (0.65)=1.9, 95% CI 1.7 to 2.1) in the odds of BP control, a reduction of 1.77 mm Hg on the SBP (95% CI −2.10 to −1.45) and of 0.78 mm Hg in DBP (95% CI −0.98 to −0.57). The effect of time showed that a patient in the intervention group experienced an increase in BP control together with a reduction in SBP and DBP over time (table 3).

At 1 year of follow-up, another associated factor that increased the probability of BP control was the presence of a cardiovascular event, also significantly associated with a reduction in SBP and DBP. Furthermore, the presence of comorbidity was associated with lower DBP but with a worse BP control and higher SBP. The use of two or more antihypertensive drugs was associated with

**Table 1** Patient characteristics

| | Total | Standard care group | Intervention group | p Value* |
|---|---|---|---|---|
| No. of PHCTs | 18 | 13 | 5 | |
| No. of patients | 31 581 | 21 704 | 9877 | |
| Demographic/clinical variables | | | | |
| Age, years (mean (SD)) | 68.6 (11.6) | 69.1 (11.5) | 67.6 (11.6) | <0.001 |
| Sex, female | 18 825 (59.6) | 12 914 (59.5) | 5911 (58.8) | 0.562 |
| No. of BP drugs (mean (SD); median (IQR)) | 1.4 (0.8); 1 (1–2) | 1.4 (0.9); 1 (1–2) | 1.5 (0.9); 1 (1–2) | 0.028† |
| Patients with antihypertensive drugs, n (%) | | | | |
| 0 | 3315 (10.5) | 2319 (10.7) | 996 (10.1) | 0.031 |
| 1 | 15 209 (48.1) | 10 501 (48.4) | 4708 (47.7) | |
| 2 | 9068 (28.7) | 6212 (28.6) | 2856 (28.9) | |
| 3 or more | 3989 (12.6) | 2672 (12.3) | 1317 (13.3) | |
| Comorbidity‡ | 9490 (30.0) | 6584 (30.3) | 2906 (29.4) | 0.101 |
| Diabetes mellitus | 8309 (26.3) | 5720 (26.3) | 2589 (26.2) | 0.79 |
| Renal failure | 1022 (3.2) | 721 (3.3) | 301 (3.1) | 0.201 |
| Heart failure | 862 (2.7) | 648 (2.9) | 214 (2.2) | <0.001 |
| CV event§ | 3839 (12.2) | 2928 (13.5) | 911 (9.2) | <0.001 |
| Outcome characteristics¶ | | | | |
| BP control | 14 195 (44.9) | 9854 (45.4) | 4341 (43.9) | 0.016 |
| SBP, mm Hg (mean (SD)) | 138.3 (13.6) | 138.1 (13.6) | 138.7 (13.7) | <0.001 |
| DBP, mm Hg (mean (SD)) | 79.5 (8.5) | 79.4 (8.3) | 79.5 (8.9) | 0.231 |

Note. The diseases considered in the CV risk calculation tables in the ICS clinical practice guideline used in this study, as well as other international guidelines,[14 16] are heart failure, kidney failure and diabetes mellitus. Hypertension was defined as SBP ≥140 mm Hg and DBP ≥90 mm Hg of clinical BP measurements. In patients with diabetes, heart failure or renal failure (code ICD-10: E10–E11–N17–N18–N19–I50), hypertension was defined as SBP ≥130 mm Hg and DBP ≥85 mm Hg. BP control was defined as SBP <140 mm Hg and DBP <90 mm Hg. In patients with diabetes, heart or renal failure, control values were defined as SBP <130 mm Hg and DBP <85 mm Hg.
*p Values were calculated from a Student t test, the $\chi^2$ test or medians' test as appropriate, by comparing the different intervention groups.
†p Value for median comparison.
‡Comorbidity: presence of diabetes mellitus type I or II, heart failure or renal failure.
§CV: patient's clinical history of ICD-10 codes of acute myocardial infarction, angina or stroke.
¶BP was calculated from the mean of 3.5 (SD: 2.2) (median (IQR: 3 (2–5))) BP readings obtained during 1 year.
BP, blood pressure; CV, cardiovascular; DBP, diastolic blood pressure; SBP, systolic blood pressure; PHCTs, primary healthcare teams.

a significantly decreased BP control and higher SBP, but lower DBP compared with patients using one antihypertensive drug. In all three models, there was strong evidence of variation in the outcomes between participants, as indicated by the random intercepts (table 3).

## DISCUSSION

### Principal findings of the study

Our results show a significant improvement in the intervention compared with the standard care group, consistent across all assessed outcomes. The different models used to analyse the data from our study indicate that the implementation of a QI plan is effective in increasing BP control and decreasing both SBP and DBP. The analysis adjusted by baseline data shows that patients in the intervention group had 30% more probability of an adequate BP control after 1-year follow-up. In the intervention group, mean SBP and DBP values decreased 2.1 mm Hg and 0.9 mm Hg, respectively, compared with the patients from the standard care group.

The patients in the intervention group had a higher probability of an adequate BP control (OR 1.9), as shown by the repeated measures analysis. The percentage of patients that maintained a good BP control or that changed from poor to adequate BP control was larger in the intervention (2.3%) than in the standard care group (1.2%).

### Comparison with other studies

Various reviews and meta-analyses on the effectiveness of QI strategies to improve BP control have been published.[5 10–12] In general, QI interventions on BP control are considered effective, although the results are variable and difficult to compare. For instance, the change in SBP and DBP values in QI interventions that included monitoring and feedback for providers was 1.5/0.6 mm Hg,[12] a result similar to the current study. There is also a recent study that evaluated the effectiveness of a continuing medical education programme to train primary care providers in evidence-based guidelines for hypertension prevention and control.[25] The change in BP was 1.99 mm Hg in SBP and 1.49 mm Hg in DBP. This intervention was a cost-effective strategy to address hypertension.[26] The study reported by Landon and colleagues[27] was carried out in asthmatic and diabetic patients. Despite the lack of differences between groups, in the hypertension subgroup, the percentage of adequate control was similar to ours.

**Table 2** Changes in BP control, SBP and DBP within and between intervention and standard care groups with missing data replaced using last value carried forward

| | Standard care group (n=21 704) | | | Intervention group (n=9877) | | | Difference (95% CI) between groups (intervention group − control group) | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | n (%) or mean (SD) | Difference* (95% CI) | SRM† | n (%) or mean (SD) | Difference* (95% CI) | SRM† | Unadjusted difference | p Value | SES‡ | Adjusted difference§ | p Value |
| BP control | | | | | | | | | | | |
| Baseline | 9854 (45.4) | | | 4341 (43.9) | | | | | | | |
| 4 months | 9657 (44.5) | −0.9 (−1.5 to −0.3) | | 4547 (46.0) | 2.1 (1.2 to 2.9) | | 1.5 (0.4 to 2.7) | 0.011 | | | |
| 9 months | 9469 (43.6) | −1.8 (−2.4 to −1.2) | | 4614 (46.7) | 2.8 (1.9 to 3.6) | | 3.1 (1.9 to 4.3) | <0.001 | | | |
| 1 year | 9457 (43.6) | −1.8 (−2.5 to −1.1) | | 4880 (49.4) | 5.5 (4.4 to 6.5) | | 5.8 (4.6 to 7.0) | <0.001 | | 1.3 (1.1 to 1.6)¶ | 0.003 |
| SBP (mm Hg) | | | | | | | | | | | |
| Baseline | 138.1 (13.6) | | | 138.7 (13.7) | | | | | | | |
| 4 months | 138.3 (13.6) | 0.3 (0.1 to 0.4) | −0.03 | 138.3 (13.7) | −0.4 (−0.5 to −0.2) | 0.04 | 0.0 (−0.3 to 0.3) | 0.95 | 0.00 | | |
| 9 months | 138.5 (13.1) | 0.4 (0.3 to.0.5) | −0.04 | 137.9 (13.1) | −0.8 (−1.0 to −0.6) | 0.09 | −0.6 (−0.9 to −0.3) | <0.001 | 0.05 | | |
| 1 year | 138.6 (13.8) | 0.5 (0.3 to 0.7) | −0.04 | 136.7 (13.3) | −2.0 (−2.3 to −1.8) | 0.16 | −1.9 (−2.2 to −1.6) | <0.001 | 0.14 | −2.1 (−3.3 to −0.8) | 0.001 |
| DBP (mm Hg) | | | | | | | | | | | |
| Baseline | 79.4 (8.3) | | | 79.5 (8.9) | | | | | | | |
| 4 months | 78.9 (8.3) | −0.4 (−0.5 to −0.4) | 0.07 | 78.7 (9.0) | −0.8 (−0.9 to −0.7) | 0.14 | −0.2 (−0.4 to −0.0) | 0.023 | 0.03 | | |
| 9 months | 78.0 (8.1) | −0.4 (−0.5 to −0.3) | 0.07 | 78.6 (8.7) | −0.9 (−1.0 to −0.8) | 0.15 | −0.4 (−0.6 to −0.2) | <0.001 | 0.05 | | |
| 1 year | 78.6 (8.5) | −0.7 (−0.8 to −0.6) | 0.09 | 77.9 (9.0) | −1.6 (−1.7 to −1.4) | 0.21 | −0.7 (−0.9 to −0.5) | <0.001 | 0.08 | −0.9 (−1.3 to −0.5) | <0.001 |

*Mean differences are shown for quantitative outcomes and percentage differences for dichotomous outcomes. Differences were calculated between follow-up measurements and baseline measurements.
†SRM: standardised response mean was calculated as the mean change by the SD of the change.
‡SES: standardised effect size was calculated as the mean difference between intervention and control groups divided by the SD of the control measurement. A positive SRM or SES denotes improvement; a negative one denotes worsening of some clinical measurements.
§Estimated with a mixed-effects model considering primary healthcare team as random effect. Mean differences are shown for quantitative outcomes and ORs for dichotomous outcomes. Adjusted for age at baseline, sex, number of antihypertensive drugs, comorbidity, cardiovascular event and baseline measurement.
¶Value is OR (95% CI).
BP, blood pressure; DBP, diastolic blood pressure; SBP, systolic blood pressure.

**Table 3** Effects of covariables on BP control, SBP and DBP (N=31 581)

| | BP control* | | | SBP† | | | DBP† | | |
|---|---|---|---|---|---|---|---|---|---|
| | Adjusted β | SE | p Value | Adjusted β | SE | p Value | Adjusted β | SE | p Value |
| Fixed effects | | | | | | | | | |
| Final status | | | | | | | | | |
| Intercept | 0.54 | 0.05 | <0.0001 | 137.93 | 0.14 | <0.0001 | 80.01 | 0.09 | <0.0001 |
| Group (ref. control) | 0.65 | 0.06 | <0.0001 | −1.77 | 0.17 | <0.0001 | −0.78 | 0.10 | <0.0001 |
| Gender (ref. male) | 0.14 | 0.05 | 0.006 | −0.11 | 0.14 | 0.434 | −0.60 | 0.09 | <0.0001 |
| Number of antihypertensive drugs (ref. 1 drug) | | | | | | | | | |
| 0 drugs | 0.16 | 0.08 | 0.049 | −0.53 | 0.18 | 0.004 | 0.01 | 0.11 | 0.898 |
| 2 drugs | −0.44 | 0.05 | <0.0001 | 0.89 | 0.12 | <0.0001 | −0.31 | 0.08 | <0.0001 |
| ≥3 drugs | −0.69 | 0.07 | <0.0001 | 1.49 | 0.17 | <0.0001 | −0.79 | 0.10 | <0.0001 |
| Comorbidity (ref. no) | −3.92 | 0.06 | <0.0001 | 1.49 | 0.13 | <0.0001 | −1.42 | 0.08 | <0.0001 |
| Cardiovascular event (ref. no) | 0.51 | 0.06 | <0.0001 | −1.05 | 0.16 | <0.0001 | −2.01 | 0.10 | <0.0001 |
| Rate of change | | | | | | | | | |
| Time | −0.21 | 0.04 | <0.0001 | 0.93 | 0.11 | <0.0001 | −0.29 | 0.07 | <0.0001 |
| Time × group | 0.80 | 0.06 | <0.0001 | −2.51 | 0.15 | <0.0001 | −0.78 | 0.09 | <0.0001 |
| Time × number of antihypertensive drugs (ref. 1 drug) | | | | | | | | | |
| 0 drugs | −0.12 | 0.10 | 0.217 | 0.30 | 0.24 | 0.206 | 0.31 | 0.14 | 0.028 |
| 2 drugs | 0.26 | 0.06 | <0.0001 | −0.92 | 0.16 | <0.0001 | −0.52 | 0.09 | <0.0001 |
| ≥3 drugs | 0.34 | 0.09 | <0.0001 | −2.09 | 0.21 | <0.0001 | −1.04 | 0.12 | <0.0001 |
| | **BP control*** | | | **SBP†** | | | **DBP†** | | |
| | **Variance** | **SE** | **p Value** | **Variance** | **SE** | **p Value** | **Variance** | **SE** | **p Value** |
| Random effects | | | | | | | | | |
| Level 1 | | | | | | | | | |
| Within-person (residual) | | | | 26.65 | 0.15 | <0.0001 | 9.65 | 0.05 | <0.0001 |
| Level 2 | | | | | | | | | |
| In final status (intercept) | 12.64 | 0.24 | <0.0001 | 165.83 | 1.48 | <0.0001 | 67.20 | 0.59 | <0.0001 |
| In rate of change (time) | | | | 104.35 | 1.26 | <0.0001 | 36.14 | 0.44 | <0.0001 |
| Covariance | | | | 53.74 | 1.06 | <0.0001 | 20.30 | 0.40 | <0.0001 |
| Goodness of fit | | | | | | | | | |
| Deviance | 115 503 | | | 906 066.8 | | | 780 098.3 | | |
| AIC | 115 531 | | | 906 100.8 | | | 780 132.3 | | |
| BIC | 115 648 | | | 906 243.0 | | | 780 274.4 | | |

Mixed-effects models of repeated measures (phases 1–4). Time was patient's age centred at 1-year follow-up (final status).
*SAS Proc NImixed.
†SAS Proc mixed, full ML.
AIC, Akaike's Information Criterion; BIC, Bayesian Information Criterion; BP, blood pressure; DBP, diastolic blood pressure; ref., Reference; SBP, systolic blood pressure.

Effectiveness varies according to the study. BP control and reduction in SBP and DBP values are analysed in two studies in relation to the type of intervention carried out: an educational intervention aimed at patients and general practitioners,[28] and a qualitative intervention aimed at general practitioners,[29] very similar to our study. The results related to the general practitioners differed from the results of our investigation. In the first study cited, effectiveness was evaluated after 2 years and no improvement in BP control was observed. However, they obtained a more significant reduction in SBP and DBP values (5 and 4 mm Hg, respectively). This could be explained by their very low levels of BP control (27.8%) at the onset of the study, their very high SBP and DBP means (153.3 mm Hg and 92.9 mm Hg, respectively) and the health infrastructure of a developing country (Pakistan). Therefore, even if SBP and DBP values improved significantly, BP control was below the target of the BP Control Clinical Practice Guidelines.[28]

In the second study cited, SBP reduction after 6 months was 0.3 mm Hg (95% CI −1.5 to 2.2, p=0.76).[29] The following reasons may account for this lack of effect: (1) the intervention was addressed only to physicians; (2) the analysis was based on the patients that had completed follow-up and (3) the study population represented a relatively healthy cohort with high rates of BP control at baseline.

On the other hand, in a study similar to ours with the aim to reduce cardiovascular risk in hypertensive patients, Gomez Marcos and colleagues[30] showed that the differences between the intervention and control groups in SBP and DBP values were larger, −9.0 mm Hg (95% CI −11.3 to −6.7) and −3.9 mm Hg (95% CI −5.4 to −2.4), respectively. The greater reduction of BP values in this

study compared with our analysis of an entire hypertensive population could be explained by their recruitment of only 849 hypertensive patients with a long-term regular follow-up in the PHCTs. Although such studies allow health professionals to focus on the follow-up of these patients to achieve better results, the lower patient numbers limit their external validity. The impact of a previous cardiovascular event on BP control in these studies is not known.[27–30]

Despite the small impact of our intervention on SBP and DBP, we consider these results clinically relevant because several studies have shown that small reductions in SBP and DBP in the general population are associated with a decrease in the number of cardiovascular events: a 10% reduction in stroke mortality and around 7% reduction in mortality due to cardiovascular disease in the middle-aged population have been associated to a 2 mm Hg decrease in SBP.[31 32]

It is important to emphasise that other factors influencing poor BP control are the presence of comorbidities and treatment with two or more antihypertensive drugs. Following the recommendations in the clinical guidelines, it is sometimes necessary to increase the number of drugs to improve BP control.[14 16 33 34] However, this was not a finding of our study, a difference that might be explained by unknown or unmeasured confounding factors that we did not analyse, such as the patient's treatment compliance.

## Strengths and weaknesses of the study

The population-based design and mixed-effects modelling on repeated measures were the main strengths of this study. The extensive catchment population included in the investigation reinforces the external validity of our findings. Most studies on similar QI strategies have been carried out in samples of hypertensive patients.[27–29 35]

The mixed models approach is a powerful method for analysing data from longitudinal studies, which include multiple measurements on each participant.[24 36] This approach allows the use of all available data and explicit modelling of the within- and between-person variation in the outcome while taking into account the correlation between measurements obtained from the same individual, which other classical models of analysis cannot explore.

We would like to emphasise that most of the intervention in this study was implemented with few additional resources since the QI plan was carried out with the usual human and financial resources allocated to the health area of the intervention group. Only the publication of the training material in the form of posters and leaflets and the replacement of sphygmomanometers with digital equipment involved additional costs. Sometimes the main difficulty of improving care lies in the feasibility of including in the PHCT routine and at low cost simultaneous strategies that have an impact on every hypertensive patient.

The duration of the study can be considered the main limitation of this investigation. We have not been able to determine if the improvements are sustainable after the intervention was finalised, though a study carried out in Spain suggested that the effects of quality interventions on hypertension tend to decrease over time.[30] Also, we do not know if a better hypertension control in the intervention group is related to a decrease in cardiovascular morbimortality.

The impossibility of randomising by PHCT is another limitation of the study, partially compensated by selecting two different administrative health areas as the control and intervention groups to prevent contamination issues among PHCT professionals of the same area.

The BP measurements used in the study were obtained as part of routine care and were therefore subjected to error and variability between professionals, as reflected in the electronic medical record (EMR). To minimise variability, training workshops on BP measurement methods and proper data entry in the clinical records took place throughout the 1-year project period.

## Policy implications, future research and conclusions

The results of this study show that in our setting, it is feasible to implement a QI plan for the improvement of hypertension control in the PHCTs. The design of this QI plan that will permit its integration in the regular clinical care of the PHCT professionals (doctors, nurses and administrative staff) without a significant increase in workload or cost is its main (and important) advantage. Longer-term studies that include unmeasured factors are needed to determine the effectiveness and cost-effectiveness of this intervention and the impact of a reduction in BP values on cardiovascular morbimortality in the hypertensive population.

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**Contributors** RV-F contributed to conception and design of study and analysis and interpretation of data, and drafting and revising of the article and gave final approval. TR-B and MR-M contributed to analysis and interpretation of data and drafting and revising of article and gave final approval. MR-M, LM-M,

GP-DL and AF-S contributed to conception and design of study. LM-M, FM-F, SM-M, EB-S, AA-L, JCM-V, MSA-O and IO-M contributed to acquisition of data. JMB-S contributed to drafting and revising of the article.

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**Competing interests** None.

**Ethical approval** The study protocol received institutional review board approval (IDIAP Jordi Gol Ethical Clinical Committee).

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**Data sharing statement** No additional data available.

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## APPENDIX 1

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**STROBE 2007 (v4) checklist of items to be included in reports of observational studies in epidemiology***

**Checklist for cohort, case-control, and cross-sectional studies (combined)**

| Section/Topic | Item # | Recommendation | Reported on page # |
|---|---|---|---|
| **Title and abstract** | 1 | (*a*) Indicate the study's design with a commonly used term in the title or the abstract | 1 |
| | | (*b*) Provide in the abstract an informative and balanced summary of what was done and what was found | 4,5 |
| **Introduction** | | | |
| Background/rationale | 2 | Explain the scientific background and rationale for the investigation being reported | 7-8 |
| Objectives | 3 | State specific objectives, including any pre-specified hypotheses | 8 |
| **Methods** | | | |
| Study design | 4 | Present key elements of study design early in the paper | 8-12 |
| Setting | 5 | Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection | 8-9 |
| Participants | 6 | (*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up<br>*Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls<br>*Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants | 8-9 |
| | | (*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed<br>*Case-control study*—For matched studies, give matching criteria and the number of controls per case | |
| Variables | 7 | Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable | 11 |
| Data sources/ measurement | 8* | For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group | *10* |
| Bias | 9 | Describe any efforts to address potential sources of bias | 9 |
| Study size | 10 | Explain how the study size was arrived at | 8 |
| Quantitative variables | 11 | Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why | 11 |
| Statistical methods | 12 | (*a*) Describe all statistical methods, including those used to control for confounding | 11,12 |
| | | (*b*) Describe any methods used to examine subgroups and interactions | 11,12 |
| | | (*c*) Explain how missing data were addressed | 11 |

| | | | |
|---|---|---|---|
| | | (*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed<br>*Case-control study*—If applicable, explain how matching of cases and controls was addressed<br>*Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy | |
| | | (*e*) Describe any sensitivity analyses | 11,12 |
| **Results** | | | |
| Participants | 13* | (a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed | 12,13 |
| | | (b) Give reasons for non-participation at each stage | 12 |
| | | (c) Consider use of a flow diagram | 12 (figure 1) |
| Descriptive data | 14* | (a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders | 13 (table 1) |
| | | (b) Indicate number of participants with missing data for each variable of interest | |
| | | (c) *Cohort study*—Summarise follow-up time (eg, average and total amount) | |
| Outcome data | 15* | *Cohort study*—Report numbers of outcome events or summary measures over time | |
| | | *Case-control study*—Report numbers in each exposure category, or summary measures of exposure | |
| | | *Cross-sectional study*—Report numbers of outcome events or summary measures | 13 (table 1) |
| Main results | 16 | (*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included | 14,15,16 |
| | | (*b*) Report category boundaries when continuous variables were categorized | 13 (table 1) |
| | | (*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period | 14,16 (table 2 and 3) |
| Other analyses | 17 | Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses | 15,16 (table 3) |
| **Discussion** | | | |
| Key results | 18 | Summarise key results with reference to study objectives | 17 |
| Limitations | 19 | Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias | 19,20 |
| Interpretation | 20 | Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence | 17-20 |
| Generalisability | 21 | Discuss the generalisability (external validity) of the study results | 20,21 |
| **Other information** | | | |
| Funding | 22 | Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based | 22 |

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.