Digital redesign of hypertension management with practice and patient apps for blood pressure control (PIA study): A cluster-randomised controlled trial in general practices

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Summary

Background Long-term hypertension control prevents heart attacks and other cardiovascular diseases, yet implementation is insufficient worldwide. The redesign of hypertension management by information and communication technology (ICT) improved hypertension control, e.g., by transmission of blood pressure (BP) measurements to a central webspace. However, an easy-to-use secure patient app connected with a practice management centre is lacking. This study evaluates the effectiveness of the newly developed PIA (PC-supported case management of hypertensive patients to implement guideline-based hypertension therapy using a physician-defined and -supervised, patient-specific therapeutic algorithm) intervention with PIA-ICT and eLearning for general practices.

Methods The effectiveness of the PIA intervention was evaluated in a cluster-randomised study. Practices were randomly allocated (1:1) to the intervention or the control group (usual care). Group allocation was unmasked for participants and researchers. The primary outcome was the BP control rate (BP < 140/90 mmHg) after 6–12 months. Secondary outcomes included BP changes and satisfaction with PIA-ICT. The trial is registered in the German Clinical Trials Register (DRKS00012680).

Findings Starting from December 1, 2019, 64 general practices were recruited over 1 year during the COVID-19 pandemic. Overall, 848 patients were enrolled between April 15, 2020 and March 31, 2021. The study was completed Sept 30, 2021. At baseline, 636 patients (intervention: 331; control: 305) of 50 general practices met the inclusion criteria. The final dataset for analyses comprised 47 practices and 525 patients (intervention 265; control 260). In the adjusted hierarchical model, the PIA intervention increased the BP control rate significantly by 23.1% points (95% CI: 5.4–40.8%): intervention 59.8% (95% CI: 47.4–71.0%) compared to 36.7% (95% CI: 24.9–50.3%) in the control group. Systolic BP decreased by 21.1 mmHg in the intervention and 15.5 mmHg in the control group.

Interpretation The PIA redesign of care processes improved BP in an outcome-relevant way. Prospectively, it may constitute an important model for hypertension care in Germany.

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benefit of blood pressure control by widely available antihypertensives is well documented: in a meta-analysis of randomised controlled trials, each 10 mmHg reduction in systolic blood pressure (SBP) resulted in significant risk reductions of major cardiovascular events (~20%), coronary heart disease (~17%), stroke (~27%), heart failure (~28%) and all-cause mortality (~13%). However, routine implementation remains a challenge with improvement shown by IT-supported strategies.

In eight studies with ICT (information and communication technology)-supported hypertension management, BP was reduced significantly by ~6.0 to ~21.4 mmHg systolic and ~2.3 to ~9.4 mmHg diastolic after 6 months. The ICT systems studied differ in their degree of ICT support for the complex care processes of hypertension management. All systems operate with an IT-based case management and a secure webspace/application with central data collection of patients’ BP measurements, while other aspects vary considerably, e.g., access for care providers and/or patients, delegation models, modes of physician-patient communication and integration into the electronic health record (EHR). A 2013 landmark study by Margolis et al. showed a significant BP improvement (71.8% controlled BP in the telemonitoring group and 45.2% in the usual care group after 6 months) using a delegation model to a clinician pharmacist who evaluated BP readings of 380 US patients, uptitration medications following a written algorithm and informed patients of medication changes by phone. In a 2013 study by McKinstry et al. with 401 Scottish patients, practices and patients had access to a secure webspace, which sent automated responses (SMS) to patients depending on BP results. If medications needed to be optimised, the system suggested contacting the general practitioner (GP) with whom patients communicated by email or SMS outside the ICT. A system used by McManus et al., 2018 provided an automated weekly message to the participating 393 patients depending on BP readings. Practices were asked to log into the platform monthly to adjust medications; any changes could be communicated to patients from within the system by text messages (SMS). In two studies the same research group, patients received paper-based algorithms for medication self-titration if the electronic platform told them to do so, with physician contact at the latest after two adjustments. All described BP monitoring systems lack easy patient-practice chat communication on BP readings, well-being and medication plans. Also, most systems require additional input outside the EHR, resulting in double documentation of medication adjustments. To facilitate care, there is a need for ICTs that simplify more steps of the complex hypertension management tailored to practices’ and patients’ needs.

Similar to other countries, BP control in German GP patients is poor (prevalence of uncontrolled BP 49%) and no ICT-supported hypertension management is available. This cluster-randomised, controlled study describes the effectiveness of the PIA-ICT for BP control in German general practices. The acronym PIA refers to a PC-supported case management of hypertensive patients to implement guideline-based hypertension therapy using a physician-defined and -supervised, patient-specific therapeutic algorithm. Following above mentioned international experiences, the IT solution was developed in a participatory approach with patients, GPs and practice assistants (PrA). It allows for a highly secure, electronic communication of blood pressure readings, medication plans and chats between patients (PIA app for smartphone/tablet) and practices (PIA practice management centre, PIA-PrMC). Physician-defined medication electronic algorithms are implemented stepwise by trained
PrAs under physician supervision. Medication plans from the practice’s EHR are electronically transmitted to the PIA app via the PIA-PrMC.

The main study objective was to investigate whether the PIA intervention improves BP control (BP ≤ 140/90 mmHg) after 6–12 months in patients with uncontrolled hypertension at baseline.

Methods

Study design
The study was designed as a cluster-randomised controlled trial (cRCT) in 60 German GP practices from the Greater Bonn region which were randomised 1:1 to an intervention group (PIA-ICT) and a waiting-list control group (usual care). The waiting list control group obtained access to PIA-ICT for 3 months after the collection of follow-up data (see Figure 1 in study protocol15). Further information is published in the study protocol.15 Ethics approval was obtained from the Ethics Committee of the Medical Faculty of the University of Bonn (reference number: 156/18, date of approval: 02/08/2018). An advisory and review board with three international researchers in the field and one national GP specialist was implemented.

Participants
Board-certified GPs accredited for the statutory health insurance system were eligible to participate in the study. Patients were eligible if they had an uncontrolled practice BP (≥140/90 mmHg). The exclusion criteria for age are based on the European Guidelines for the Management of Hypertension (ESH/ESC): patients younger than 40 years need routine evaluation for potential secondary hypertension; for patients older than 80 years higher target values are recommended.16 For details on the inclusion and exclusion criteria, see Table 1. All participants (GPs, PrA, patients) provided written informed consent. Recruitment of practices followed a multi-stage procedure (mail, fax, and/or email, phone). Participating general practices recruited patients.

Randomisation and masking
Randomisation took place at the practice level, i.e., all patients of a practice were assigned to either the intervention or the control group. Randomisation was conducted by the independent trial centre. The allocation sequence was based on computer-generated random numbers. Stratified block randomisation (1:1) was used to ensure a balanced distribution of urban and rural practices in the intervention and control arms. Masking of involved scientists, practice personnel and patients was not possible due to the ICT-based intervention, which was offered to the intervention group only. Data analysts followed predefined standard operating procedures for analysis to avoid bias.

Procedures
PIA is a complex intervention comprising two elements: the PIA-ICT (PIA app and PIA-PrMC) and the PIA education (eLearning/on-site training for practice teams and patients).15

The following features characterise the electronic PIA intervention:

1. PIA communication: Highly secure communication between patients (PIA app) and practices (PIA-PrMC):
   a. PIA app for patients: transmission of BP measurements, graphic display of BP over time with individual target range, medication plan, ordering of prescription refills, video education and links to BP related information;
   b. PIA-PrMC with delegation model: recall and step-wise medication adjustments, predefined and guideline-oriented algorithms for

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Table 1: Inclusion and exclusion criteria.

| Practice level | Inclusion criteria | Exclusion criteria |
|---------------|--------------------|--------------------|
| Inclusion criteria | Certified GP accredited for the statutory health insurance system | GP has an additional qualification in hypertensiology |
| Practice level | Practice computer with internet access (Windows 7 or higher) | GP/practice participated in the development of the intervention |
| Inclusion criteria | Participation of at least one GP and up to three practice assistants per practice | |

Table 1: Inclusion and exclusion criteria.
medication regimens, graphic display of BP over time with individual target range, electronic transmission of medication plan to PIA app, predefined process with colour scheme for delegation to PrAs, option to export data from the PIA-PrMC to the EHR for documentation.

2. PIA medication plan transfer: electronic transmission from the EHR to the PIA-PrMC and the PIA app;

3. PIA medication safety: the GP signs each medication plan electronically (required by German law as PrAs have no prescribing privileges);

4. PIA eLearning for GPs and PrAs: videos present evidence-based information on hypertension management including medication classes, how to use the PIA-PrMC and the PIA app, how to obtain valid BP measurements in the practice and at home, and the study details. PrAs complete a short, written exam to qualify as a PIA-PrA.

After randomisation, all practices received information on the patient recruitment procedure and standardised blood pressure measurements. Practices in the intervention group received access to eLearning, on-site training if needed, and the PIA-PrMC.

In each practice, patients were approached and recruited using pre-specified criteria. The practices created lists of patients with the ICD diagnosis hypertension who were eligible for the study. By protocol, the practices were asked to approach patients on this list consecutively as they visited the practice. Due to the pandemic, not all practices followed this approach rigidly. However, a comparison of patients' characteristics (age groups, sex, history of coronary disease/myocardial infarction) with national data suggests that this did not lead to a systematic error.

Recruited patients received two blood pressure measurements in the office (5 min rest, then two measurements taken with 1-min in-between). In addition to an automatic upper arm blood pressure monitor (Boso® medicus family 4), patients in the intervention group received access to the PIA app and training on its use and blood pressure measurement.

The PIA intervention used repetitive cyclic communication: Patients measure their resting blood pressure daily at home two times in the morning and in the evening, each time with an interval of 1-min in-between, and manually entered the readings into the PIA app. These BP values are transmitted to the PIA-PrMC in real time. The PIA-PrA analyses the values on a weekly basis and makes medication suggestions based on the physician’s instructions. The suggestions are supervised by the physician and signed with an electronic PIN. Modified medication plans are automatically sent to the PIA app. The patient receives a push message when new information is available in the PIA app. The practice and patients can exchange information electronically via the PIA-ICT. After patients reached the target value, the practices defined an individual interval for further blood pressure measurements. For the follow up survey, blood pressure measurements were performed according to the same scheme at baseline.

Outcomes
The primary outcome was the BP control rate (% of patients with BP < 140/90 mmHg). BP was defined as “controlled” if the second of two resting practice BP was within the target range. The mean of a second and third BP reading was initially used to define the outcome, but practices refused a third reading to decrease contact times during the COVID pandemic. A literature review showed a difference of 0–1 mmHg between these approaches, which we deemed acceptable as it systematically affected both study arms. Additional sensitivity analyses were performed using the mean of two BP measurements. In addition, the following secondary outcomes are reported for both groups: changes in systolic and diastolic blood pressures (SBP, DBP) between baseline and follow up; medication changes; frequency of cardiovascular events, emergency treatments and hospitalisations; patients’ satisfaction with hypertension treatment by their GP practice. For the intervention group only, the number of contacts between the practice and the patients via PIA-ICT, as well as the satisfaction with PIA-ICT among GPs, PrAs and patients were obtained. For details see the study protocol.

Statistical analysis
As detailed in the study protocol, it was estimated that 600 patients from 40 GP practices (300 patients from 20 GP practices per study arm) would be required to detect a 15% difference in control rates between the groups with 80% power. The sample size calculation respected for the clustered design.

The confirmatory analysis for the primary endpoint was based on a generalized linear mixed model (GLMM) with a significance level of 95% (2-sided). The model included relevant patient covariates (four age groups, sex, history of coronary disease/myocardial infarction). The recruitment period was included as covariate because the COVID-19 pandemic delayed patient recruitment. To account for the clustered structure of the data, the patients’ practice was entered as a random effect. The null hypothesis (no difference in blood pressure control rate) was rejected if the p-value for the Wald test for the intervention effect was <0.05. The adjusted odds ratio (OR) and associated 95% confidence interval are reported. The secondary outcomes addressing blood pressure measurements (changes in systolic and diastolic BP) were evaluated using GLMM with random effects to account for the clustered design of the data. All other secondary analyses were performed in an exploratory
fashion using adequate standard statistical procedures (Mann–Whitney U test, chi-square-test ($\chi^2$), Z statistics). A significance level of 95% was assumed for all statistical analyses which were performed using IBM SPSS 27 on Windows and R 3.6 (GLMM model: lme4 [1.1-26]).

**Role of the funding source**

The funder had no role in the study design, data collection, data analysis, data interpretation, writing of the report, or the decision to submit for publication. All authors had access to dataset and decided to submit the publication.

**Results**

A total of 64 practices and 848 patients were recruited for the study. Study participants were recruited during the COVID-19 pandemic with three lock-downs in Germany (February 2020 up until March 2021). The recruitment rate was 3.6% which is in line with recruitment rates from other studies. At baseline, 50 primary care practices and 636 patients participated. Reasons for study withdrawal were pandemic-related burden and/or non-compliance with the inclusion criteria for the practice and/or patients. A total of 47 general practices with 525 patients, 51 GPs and 61 PrAs completed the follow up (final study cohort). The details are outlined in the CONSORT flowchart (Fig. 1).

In the baseline evaluation, 50 practices with 636 patients met the study criteria (28 intervention practices with 331 patients; 22 control practices with 305 patients). On average, 12.7 patients were recruited per practice (intervention 11.8 patients [SD 9.9]; control 13.9 [SD 11.2]). At follow up, 525 (82.3%) of these patients from 47 practices (intervention: 26; control: 21) had provided complete datasets with an average of 11.2 patients per practice [SD 10.3].

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**Fig. 1:** CONSORT flowchart.
A comparison between the intervention and control groups at baseline showed no significant differences except that control group participants were 2.3 years older on average. In the final study population, the control group was 0.9 years older on average. The final model controlled for this difference. There were no further significant differences between study participants with complete datasets at baseline (Table 2).

Table 3 presents the BP measurements at follow up. Unadjusted results showed significantly lower first and second SBPs as well as significantly higher control rates for SBP and DBP in the intervention compared to the control group. 62.6% of the patients in the intervention compared to only 44.6% of patients in the control arm reached the BP target range (p < 0.001).

The GLMM model for the primary endpoint is detailed in Table 4. The odds ratio for the influence of the intervention versus the control group was 2.57 (95% CI: 1.23–5.37, p = 0.012), so that the null hypothesis (intervention has no influence) can be rejected with a probability of error of 5% (2-sided test). The population-adjusted proportion of patients with controlled blood pressure at the end of the study was 59.8% (95% CI: 47.4–71.0%) in the intervention group and 36.7% (24.9–50.3%) in the control group. This result in a difference of 23.1 percentage points (95% CI: 5.4–40.8 percentage points), which is markedly higher for the PIA intervention than the estimated difference of 15% used a priori to calculate the number of cases. The covariates age, sex, and concomitant disease (coronary disease/myocardial infarction) had no influence. Additional analysis showed that BP control rates at follow-up did not differ between urban and rural practices. A bootstrapping with 1000 replications for the systolic SBP (control group) showed a minimum difference in standard errors of the means between the descriptive data and the bootstrapping sample (0.96 vs. 0.98). The bootstrapping confidence interval ranged from 135.86 to 139.67 and did not include the mean of 134.28 from the intervention group.

In a sensitivity analysis, the mean of the results of both BP measurements instead of the results of the second BP measurement alone was in line with the prior result: the odds ratio for the intervention arm was 2.59 (95% CI: 1.35–4.96, p = 0.004). For details, see Table 5.

The validity of the practice BP readings was ensured by comparing the second home and the second practice BP readings at follow up (intervention group only). The measured difference in SBP of 4.85 mmHg (mean home: 129.45 [SD 12.27]; mean practice: 134.3 [SD 14.5]) is in agreement with the expected difference between home and practice readings of 5 mmHg reflected in the target values for home and office readings. The difference for the second DBP was 0.34 mmHg (mean home: 82.76 [SD 9.26]; mean practice: 83.1 [SD 9.7]).

At baseline, the mean SBP was 155.4 mmHg in the intervention group and decreased to 134.3 mmHg at follow up. In the control group, baseline SBP was 153.3 mmHg and follow up SBP was 137.8 mmHg. SBP decreased by 21.1 mmHg in the intervention and 15.5 mmHg in the control group.

There were no differences in the frequencies of hospital and/or emergency department and/or emergency service visits between the study arms. Also, the number of serious cardiovascular events (stroke, myocardial infarction, heart failure, renal failure, death) with a need for hospital or emergency service did not differ. For details, see Table 6. Patients receiving the PIA intervention were significantly more satisfied with their BP treatment than patients in the control arm: in the intervention arm, 89.4% of patients rated it as good to excellent, while in the control arm this was significantly lower at 79.5% (χ²: p < 0.001).

Medication changes: The number of drugs and drug categories did not differ significantly between intervention and control group at baseline, but at follow up. The number of patients with a thiazide antihypertensive was significantly higher in the intervention than the control group at follow up (p = 0.001). For details, see Table 7.

Utilization of PIA-ICT: The PIA communication tool was frequently used by patients and practices. On average, 10.59 medication plans were transferred to patients (SD 11.25; median 8; min–max 0–48). A mean of 249.79 blood pressure readings were transmitted from patients to practices (SD 228.90; median 164.0; min–max 0–1138). On average 3.71 chats were sent from patients to practices (SD 7.95; median 1.0; min–max 0–91), while practices sent 6.93 messages (SD 8.87; median 3.0, min–max 0–49). These messages included automated ones indicating a new medication plan. For details, see Table 8.

Satisfaction with the PIA-Intervention: Patients scored their satisfaction with the PIA app as 1.76 (SD: 2.00) on a five-point scale (1 = very good to 5 = poor). GPs rated the PIA-PrMC as 1.88 (SD: 0.50) and the PrAs as 1.98 (SD: 0.66) using the same scoring system.

Discussion

This cluster-randomised controlled trial of the PIA-ICT for hypertension management showed a significant improvement of BP control rates after 6–12 months (adjusted: +23.1%). The finding of this complex intervention is in line with prior studies of various IT-supported hypertension management systems. However, our PIA system differs from the other systems in several features. First, the IT set-up was developed with the participation of the end users (GPs, PrAs, patients) which led to a thorough understanding and design of the IT-supported care processes, e.g., electronic transmission of the full medication plan from the EHR with antihypertensives and all other

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medications, use of different colours for GPs’ and PrAs’ tasks, options for individual adjustments by GPs on all levels (BP targets, medication algorithms, medication dosing), easy to use app design manageable also by the elderly. Following Yardley’s framework for person-based approaches to intervention development, the three user groups (patients, GPs, PrA) were involved repetitively in intervention development.19 This participatory approach

| Social demographic characteristics | Baseline | Baseline with complete follow-up data |
|-----------------------------------|----------|---------------------------------------|
|                                   | All (N = 636) | Intervention group (n = 331) | Usual care group (n = 305) | All (N = 525) | Intervention group (n = 265) | Usual care group (n = 260) |
| **Sex, N (%)**                    |           |                                      |                            |              |                                      |                            |
| Women    | 301 (47.3%) | 159 (46.3%) | 151 (49.5%) | 124 (54.4%) | 66 (49.6%) | 68 (52.9%) |
| Man      | 335 (52.7%) | 181 (53.7%) | 154 (50.5%) | 101 (45.6%) | 69 (50.4%) | 67 (47.1%) |
| **Age, mean (SD)**                | 58.0 (9.2) | 56.9 (8.7) | 59.2 (9.7) | 59.4 (9.7) | 57.7 (8.7) | 58.6 (9.2) |
| **Marital status, N (%)**         |           |                                      |                            |              |                                      |                            |
| Married or cohabiting             | 411 (64.7%) | 213 (64.4%) | 198 (64.9%) | 178 (67.2%) | 169 (65.0%) |                            |
| Divorced or separate living       | 84 (13.2%) | 43 (13.0%) | 41 (13.4%) | 32 (12.1%) | 40 (15.4%) |                            |
| Widowed                            | 38 (6.0%) | 17 (5.1%) | 21 (6.9%) | 35 (6.7%) | 17 (6.4%) | 18 (6.9%) |
| Single                             | 69 (10.8%) | 38 (11.5%) | 31 (10.2%) | 26 (9.8%) | 24 (9.2%) |                            |
| Missing data                       | 34 (5.3%) | 20 (6.0%) | 14 (4.6%) | 21 (4.0%) | 12 (4.5%) | 9 (3.5%) |
| **School graduation, N (%)**      |           |                                      |                            |              |                                      |                            |
| No school graduation              | 26 (4.1%) | 13 (3.9%) | 13 (4.3%) | 23 (4.4%) | 11 (4.2%) | 12 (4.6%) |
| Finished 9th grade                 | 206 (32.3%) | 98 (29.5%) | 108 (35.5%) | 185 (35.2%) | 89 (33.6%) | 96 (36.9%) |
| Finished 10th grade                | 178 (28.0%) | 103 (31.0%) | 75 (24.7%) | 147 (28.0%) | 81 (30.6%) | 66 (25.4%) |
| Finished 12th grade                | 50 (7.9%) | 25 (7.6%) | 25 (8.2%) | 38 (7.2%) | 21 (7.9%) | 17 (6.5%) |
| High school diploma               | 126 (19.6%) | 63 (19.0%) | 63 (20.7%) | 103 (19.6%) | 48 (18.1%) | 55 (21.2%) |
| Graduated from other schools       | 14 (2.2%) | 8 (2.4%) | 6 (2.0%) | 6 (1.1%) | 2 (0.8%) | 4 (1.5%) |
| Missing data                       | 36 (5.7%) | 20 (6.0%) | 16 (5.2%) | 23 (4.4%) | 12 (4.5%) | 11 (4.2%) |
| **General health status, N (%)**  |           |                                      |                            |              |                                      |                            |
| Excellent                          | 6 (0.9%) | 2 (0.9%) | 4 (1.3%) | 5 (1.0%) | 1 (0.4%) | 4 (1.5%) |
| Very good                         | 53 (8.3%) | 25 (8.3%) | 27 (8.9%) | 45 (8.6%) | 21 (7.9%) | 24 (9.2%) |
| Good                               | 347 (54.4%) | 175 (54.8%) | 172 (56.5%) | 290 (55.2%) | 142 (53.6%) | 148 (56.9%) |
| Less good                         | 155 (24.3%) | 91 (24.4%) | 64 (21.0%) | 129 (24.6%) | 74 (27.9%) | 55 (21.2%) |
| Bad                                | 25 (3.9%) | 12 (3.6%) | 13 (4.3%) | 22 (4.2%) | 10 (3.8%) | 12 (4.6%) |
| Missing data                       | 36 (5.7%) | 20 (6.0%) | 16 (5.2%) | 23 (4.4%) | 12 (4.5%) | 11 (4.2%) |
| **Blood pressure, mean (SD)**     |           |                                      |                            |              |                                      |                            |
| SBP (mmHg), M1                     | 156.9 (14.8) | 157.8 (16.2) | 155.9 (13.1) | 156.9 (14.5) | 158.5 (16.4) | 155.2 (12.2) |
| DBP (mmHg), M1                      | 93.7 (9.6) | 94.8 (9.8) | 92.5 (9.3) | 93.6 (9.7) | 94.5 (10.1) | 92.6 (9.3) |
| SBP (mmHg), M2                      | 154.1 (14.1) | 154.7 (15.7) | 153.5 (12.1) | 154.4 (13.8) | 155.4 (15.7) | 153.3 (11.5) |
| DBP (mmHg), M2                      | 93.1 (9.6) | 94.6 (9.8) | 91.5 (9.1) | 93.0 (9.8) | 94.4 (10.2) | 91.6 (9.1) |
| **Coronary heart disease and/or myocardial infarction, N (%)** |           |                                      |                            |              |                                      |                            |
| Without coronary heart disease or myocardial infarction | 529 (83.2%) | 280 (84.5%) | 249 (81.6%) | 429 (81.7%) | 217 (81.9%) | 212 (81.5%) |
| With coronary heart disease and/or myocardial infarction | 107 (16.8%) | 51 (18.4%) | 56 (18.4%) | 96 (18.3%) | 48 (18.1%) | 48 (18.5%) |
| Current smoker, N (%)              | 160 (25.2%) | 86 (26.0%) | 74 (24.3%) | 131 (25.0%) | 68 (25.7%) | 63 (24.2%) |

Table 2: Patient characteristics at baseline (n = 636) and at baseline with complete follow-up data (n = 525).

BP M1 = first measurement after 5 min rest; BP M2 = second measurement after 1 min; DBP = Diastolic blood pressure; SBP = Systolic blood pressure.
is reflected in the high acceptance of the system as indicated by the high frequencies of use as well as all users’ evaluations. To our knowledge, the publication of such data on utilisation is new and not available for the other IT-supported hypertension management systems. Second, the PIA setup with the secure communication between the patients’ PIA app and the PIA-PrMC is novel and much easier for practices and patients to use than logins onto separate platforms. Hammerslay et al., 202013 partially addressed this issue by implementing an automated import of BP results into EHRs from the third-party website. Third, we did not use automated BP transmission from the BP monitor device to the electronic platform (e.g., by Bluetooth) as nicely used in the studies of Margolis,6 McKinstry10 and McManus,8 because such BP monitors are more costly and not financed by the statutory health insurance in regular care, which we aimed to reflect as closely as possible. However, the proximity of the first and the second BP measurements in our study indicates that the documentation in the PIA app were easily manageable for patients. Fourth, both the standardisation and individualisation of hypertension management is a challenge for the design of clinical IT systems. To decrease

|                         | All (N = 525) | Intervention group (n = 265) | Usual care group (n = 260) | P value* |
|-------------------------|--------------|-----------------------------|---------------------------|----------|
| SBP (mmHg), M1, mean (SD) | 138.6 (17.3) | 136.0 (16.4) | 141.3 (17.8) | <0.001 |
| Controlled SBP (mmHg), M1, N (%) | 282 (53.7%) | 173 (65.3%) | 109 (41.9%) | <0.001 |
| DBP (mmHg), M1, mean (SD) | 84.5 (11.0) | 84.1 (10.9) | 84.9 (11.1) | 0.40    |
| Controlled DBP (mmHg), M1, N (%) | 361 (68.8%) | 194 (72.2%) | 167 (64.2%) | 0.03    |
| SBP (mmHg), M2, mean (SD) | 136.0 (15.1) | 134.3 (14.5) | 137.8 (15.5) | 0.01    |
| Controlled SBP (mmHg), M2, N (%) | 323 (61.5%) | 192 (72.5%) | 131 (50.4%) | <0.001 |
| DBP (mmHg), M2, mean (SD) | 83.3 (10.1) | 83.1 (9.7) | 83.4 (10.6) | 0.73    |
| Controlled DBP (mmHg), M2, N (%) | 387 (73.7%) | 206 (77.7%) | 181 (69.6%) | 0.04    |
| BP, M1, N (%) | 242 (46.1%) | 149 (56.2%) | 93 (35.8%) | <0.001 |
| Primary endpoint: BP M2, N (%) | 282 (53.7%) | 166 (62.6%) | 116 (44.6%) | <0.001 |

BP M1 = first measurement after 5 min rest; BP M 2 = second measurement after 1 min; DBP = Diastolic blood pressure; SBP = Systolic blood pressure.az-Test.

Table 3: BP measurements at follow-up (unadjusted) (n = 525).

|                         | Odds ratio | 95%-CI       | P value |
|-------------------------|------------|--------------|---------|
| (Intercept)             | 0.38       | 0.17-0.81    | 0.01    |
| Study arm               |            |              |         |
| Usual care arm (reference) |          |              |         |
| Intervention arm        | 2.57       | 1.23-5.37    | 0.01    |
| Age                     |            |              |         |
| 40-49 years (reference) |           |              |         |
| 50-59 years             | 1.16       | 0.66-2.03    | 0.61    |
| 60-69 years             | 1.09       | 0.59-2.03    | 0.73    |
| 70-79 years             | 1.38       | 0.69-2.97    | 0.34    |
| Sex                     |            |              |         |
| Women (reference)       |           |              |         |
| Man                     | 1.07       | 0.67-1.84    | 0.78    |
| Comorbidities           |            |              |         |
| Without coronary heart disease and/or myocardial infarction (reference) | | | |
| With coronary heart disease and/or myocardial infarction | 0.78 | 0.45-1.34 | 0.36 |
| Recruiting duration     |            |              |         |
| Recruiting (first quarter to fourth quarter in 2020) (reference) | | | |
| Recruiting (first quarter in 2021) | 1.67 | 0.97-2.88 | 0.07 |
| Blood pressure (Baseline, M2) | | | |
| SBP, mmHg               | 0.98       | 0.96-0.99    | 0.00    |
| DBP, mmHg               | 0.99       | 0.97-1.02    | 0.57    |

BP M 2 = second measurement after 1 min; DBP = Diastolic blood pressure; SBP = Systolic blood pressure. Statistical measures: Variance of random effects (practice ID) τ_00 = 0.86 (SD: 0.88). Intra-cluster correlation coefficient IIC = 0.21.

Table 4: GLMM model of primary endpoint.
|                          | Odds ratio | 95%-CI    | P value |
|--------------------------|------------|-----------|---------|
| (Intercept)              | 0.40       | 0.2-0.81  | 0.01    |
| Study arm                |            |           |         |
| Usual care arm (reference)|           |           |         |
| Intervention arm         | 2.59       | 1.35-4.96 | 0.00    |
| Age                      |            |           |         |
| 40–49 years (reference)  |            |           |         |
| 50–59 years              | 1.12       | 0.66-1.91 | 0.67    |
| 60–69 years              | 1.01       | 0.56-1.81 | 0.98    |
| 70–79 years              | 1.1        | 0.55-2.19 | 0.78    |
| Sex                      |            |           |         |
| Women (reference)        |            |           |         |
| Man                      | 1.09       | 0.74-1.6  | 0.66    |
| Comorbidities            |            |           |         |
| Without coronary heart disease and/or myocardial infarction (reference) | 0.89 | 0.53-1.49 | 0.66 |
| With coronary heart disease and/or myocardial infarction |           |           |         |
| Recruiting duration      |            |           |         |
| Recruiting (first quarter to fourth quarter in 2020) (reference) | 1.58 | 0.95-2.62 | 0.08 |
| Recruiting (first quarter in 2021) |           |           |         |
| BP (Baseline), mean M1/M2|            |           |         |
| SBP, mmHg                | 0.98       | 0.96-0.99 | 0.00    |
| DBP, mmHg                | 0.99       | 0.97-1.01 | 0.48    |

BP M1 = first measurement after 5 min rest; BP M2 = second measurement after 1 min; DBP = Diastolic blood pressure; SBP = Systolic blood pressure. Statistical measures: Variance of random effects (practice ID) $\tau_00 = 0.66$ (SD: 0.81). Intra-cluster correlation coefficient ICC = 0.17.

Table 5: Sensitivity analysis: GLMM model of the primary endpoint using the mean of the first and second BP readings.

|                                | All (N = 525) | Intervention group (n = 265) | Usual care group (n = 260) | P value<sup>a</sup> |
|--------------------------------|---------------|------------------------------|---------------------------|---------------------|
| Number of inpatient treatments, n (%) | 58 (11.0%)    | 23 (8.7%)                   | 35 (13.5%)                | 0.10               |
| One hospital treatment          | 45 (8.6%)     | 19 (7.2%)                   | 26 (10%)                  |                     |
| Two hospital treatments         | 9 (1.7%)      | 3 (1.1%)                    | 6 (2.3%)                  |                     |
| Three hospital treatments       | 3 (0.6%)      | 0 (0.0%)                    | 3 (1.2%)                  |                     |
| Inpatient treatment without frequency indication | 1 (0.2%) | 1 (0.4%) | 0 (0.0%) | |
| Number of emergency treatments, n (%) | 39 (7.4%)    | 16 (6.0%)                   | 23 (8.8%)                 | 0.21               |
| One emergency treatment         | 32 (6.2%)     | 13 (4.9%)                   | 19 (7.2%)                 |                     |
| Two emergency treatments        | 4 (0.8%)      | 3 (1.1%)                    | 1 (0.4%)                  |                     |
| Emergency treatment (without frequency indication) | 3 (0.6%) | 0 (0.0%) | 3 (1.2%) | |
| Number of major cardiovascular events (hospitalizations), n (%) | 21 (4.0%) | 12 (4.5%) | 9 (3.5%) | 0.14 |
| Myocardial infarction           | 4 (0.8%)      | 1 (0.4%)                    | 3 (1.2%)                  |                     |
| Stroke                          | 3 (0.6%)      | 3 (1.1%)                    | 0 (0.0%)                  |                     |
| Other cardiovascular events     | 14 (2.6%)     | 8 (3.0%)                    | 6 (2.3%)                  |                     |
| Cardiovascular events (emergency treatment), n (%) | 12 (2.3%) | 9 (3.4%) | 3 (1.2%) | 0.45 |
| Myocardial infarction           | 1 (0.2%)      | 1 (0.4%)                    | 0 (0.0%)                  |                     |
| Stroke                          | 3 (0.6%)      | 3 (1.1%)                    | 0 (0.0%)                  |                     |
| Blood pressure derailing        | 4 (0.8%)      | 2 (0.8%)                    | 2 (0.8%)                  |                     |
| Other cardiovascular events     | 4 (0.8%)      | 3 (1.1%)                    | 1 (0.4%)                  |                     |

SD = standard deviation. <sup>a</sup>Chi-Square-Test.

Table 6: Treatments in hospital and/or emergency department or emergency service: frequency of treatments and number of serious cardiovascular events (stroke, myocardial infarction, heart failure, renal failure, death) with inpatient or emergency outpatient treatment at follow up.
the number of antihypertensives according to guidelines, we had initially restricted the list to the 98% most frequently prescribed antihypertensive drugs. However, the reactions of the GPs led us to include even rarely used drugs. Thus, our system was designed to guide an evidence-based path but was simultaneously open fully to adjustments, e.g., in BP targets, medications used and uptitration steps. In contrast to studies by McManus who used paper-based, self-uptitration of BP medication with GP contact after two changes,8,9 we continuously used physician-initiated uptitration via the ICT. Fifth, our ICT successfully realized a delegation model to PrAs who have a certified vocational training without prescribing privileges, while nurses and clinician pharmacists were involved in care processes from the US, England and Scotland.6,9,13 Sixth, the transfer of medication plans from the EHR is an important step towards the safe digitalisation of care processes as it prevents transcription errors; this was not applied in prior studies. However, further developments towards even better IT support of hypertension care processes are needed, e.g., artificial intelligence (AI)-supported management including a substitution of delegation models by AI-supported processes, block chain technologies for large scale data protection, full integration of data and processes in EHRs.13,20 Given the magnitude of the care problem presented by uncontrolled hypertension, systems need to be as simple and reliable as possible to address the populations in need of better care.

This cluster-randomised controlled trial was successfully conducted during the pandemic, although follow up and support of practices and patients required additional time and effort of the study team. The primary outcome was initially based on the mean of the second and third standardised BP reading, but the pandemic forced us to rely on the second measurement only to reduce contact times. Although this approach differs from other studies, the difference is 0–1 mmHg according to an analysis of the NHANES data.17 As this systematic bias applies to both the intervention and the

| Drug classes | Baseline (N = 492) | P value<sup>a</sup> | Follow-up (N = 501) | P value<sup>a</sup> |
|--------------|------------------|-----------------|--------------------|-----------------|
|              | Intervention (n = 248) | Usual care (n = 244) | Intervention (n = 244) | Usual care (n = 257) |
| Number of antihypertensives, mean (SD) | 2.09 (1.07) | 2.04 (1.15) | 0.37 | 2.42 (1.26) | 2.19 (1.19) | 0.05 |
| Number of prescribed drug classes, mean (SD) | 1.75 (0.94) | 1.65 (0.88) | 0.34 | 2.42 (1.14) | 2.20 (1.09) | 0.04 |
| Without antihypertensives, N (%) | 13 (5.3%) | 15 (6.1%) | 1 (0.4%) | 3 (1.2%) | 2 (0.8%) | 1 (0.4%) |
| One drug class, N (%) | 98 (39.5%) | 101 (41.4%) | 54 (22.1%) | 78 (30.4%) |
| Two drug classes, N (%) | 87 (35.1%) | 87 (35.7%) | 79 (32.4%) | 73 (28.4%) |
| Three drug classes, N (%) | 39 (15.7%) | 36 (14.8%) | 64 (26.2%) | 72 (28.0%) |
| Four drug classes, N (%) | 11 (4.4%) | 5 (2.0%) | 34 (13.9%) | 24 (9.3%) |
| Five drug classes, N (%) | 0 (0.0%) | 0 (0.0%) | 10 (4.1%) | 6 (2.3%) |

<sup>a</sup>Mann-Whitney U-Test.

Table 7: Medication changes.

| Articles |
|--------------------------|
| <ref>6</ref> www.thelancet.com Vol 55 January, 2023 |
control arm, it does not impair the study results. Our sensitivity analyses indicate that patients reliably used a resting position even when the first reading was taken. As 2/3 of smart devices in Germany are android based, the PIA app was developed for this operating system.46 However, a PIA app for iOS devices is currently being developed. For long-term benefit, the development of the PIA app for iOS devices is currently in the planning process. Although patients self-recording of BPs in the app has the potential for errors, the closeness of the first and second readings recorded does not indicate a problem. Long-term success will need to be evaluated. It is difficult to determine which components of the complex PIA intervention contributed to the final result.

The planned case number for the analyses of 600 patients (300 per study arm) was just not achieved. The recruitment period actually coincided with the outbreak of the Corona pandemic, resulting in a significant burden on GP practices caused by uncertainty and increased workload. This was compounded by patient fears that led to routine visits to the primary care physician’s office being avoided. Nevertheless, 525 patients could be included in the analyses. Although the target sample size was not fully reached due to the pandemic, the improved BP can be considered an effect of the intervention but not chance as shown by the additional bootstrapping analysis. The PIA intervention lowered SBP by 6.1 mmHg systolic which is outcome-relevant according to large cohort studies with decreased morbidity and mortality already after SBP reductions of 3 mmHg.22,23

Our IT-supported hypertension management PIA with several novel features significantly improved BP control rates and was well accepted by professionals and patients.

Contributors
B.W. had the study idea. B.W., A.K., and F.L. developed the study protocol, detailed the methodology and administrated the project. B.W., A.K. and F.L. developed the intervention materials supported by F.D. und K.K.A.K., F.L., F.D. and K.K. conducted the intervention. T.G. and T.B. verified and analysed the data. A.K., F.L. and B.W. drafted the first version of the manuscript. All authors provided feedback on the manuscript and approved the version of the manuscript. All authors provided feedback on the manuscript and approved the version of the manuscript.

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Appendix A. Supplementary data
Supplementary data related to this article can be found at https://doi.org/10.1016/j.remlre.2022.101712.

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