Improved blood pressure control using an interactive mobile phone support system

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This explorative, longitudinal study evaluated the effect of the daily use of a mobile phone-based self-management support system for hypertension in reducing blood pressure (BP) among 50 primary care patients with hypertension over 8 weeks. The self-management system comprises modules for (1) self-reports of BP, pulse, lifestyle, symptoms, and well-being; (2) delivery of reminders and encouragements; and (3) graphical feedback of self-reports. Daily use of the support system significantly reduced BP (systolic BP −7 mm Hg, diastolic BP −4.9 mm Hg) between baseline and week 8, with daily improvements leveling off as the study progressed. Three homogenous subsets of patients were identified who, despite different initial BP levels, showed similar decreases in BP during the study, indicating that patients benefited irrespective of baseline BP. In showing significant reductions in BP, our results suggest that the self-management support system may be a useful tool in clinical practice to help patients self-manage their hypertension.
(2) to examine BP change trajectories over the course of the 56-day study period; and (3) to identify subsets of patients who benefit most from the self-management support system.

METHODS

Recruitment and Participants
Based on data from earlier studies, a sample size was estimated based on a standard deviation (SD) of 12 for systolic BP (SBP) and 7 for diastolic BP (DBP). For detecting a difference of 8 mm Hg SBP and 5 mm Hg DBP with 90% power and at a 5% significance level, the sample size was estimated to 50 patients. Seventy-three patients located at four different primary healthcare centers and meeting the criteria of being currently medically treated for hypertension, older than 30 years, and able to understand and read Swedish were asked to participate by their treating healthcare professional, either through a phone call or at a regularly scheduled consultation. In addition, participants needed to have access to a mobile phone with Internet access and to agree to allow access of their data at the National Prescription Repository (NPR) to verify medication adherence. The NPR stores all prescriptions dispensed at Swedish pharmacies during the last 15 months. Data from the NPR may be used to reliably estimate refill adherence. All patients who were asked to participate were informed about the study both in writing and orally, and were ensured confidentiality before giving their written informed consent. In total, 54 patients subsequently agreed to participate, of whom three withdrew before study start because their mobile phones did not have Internet access. Hence, 51 patients started the study. Data were collected from February until June 2012.

The Intervention

Interactive Self-Management Support System. The self-management support system was developed in collaboration with researchers, patients, and clinicians and was evaluated for content validity, reliability, and usability through focus group interviews, cognitive interviews, and piloting. Detailed descriptions of the development and validation process are provided elsewhere. The communication platform for the system was developed by Circadian Questions (CQ), 21st Century Mobile (http://www.cqmobil.se). Briefly, the system includes several components that have not been integrated in the same intervention for supporting self-management of hypertension: (1) questions on well-being, symptoms, lifestyle, medication intake, and side effects; (2) daily home BP and pulse measurements with an automatic and validated BP monitor; (3) weekly motivational messages to encourage patients to maintain lifestyle changes; and (4) graphical feedback to patients and healthcare professionals of patient self-reports and BP.

Study Procedures. Start-up meetings were held where a healthcare professional instructed the patients on how to use the system and tailored it to the wants and needs of individual patients, such that drug side-effect items were selected according to the patient’s antihypertensive medication (twice weekly); motivational messages were chosen according to patients’ preferences (twice weekly); and timing of daily BP measurements, self-reports, and reminders were decided by the patient. No individual target BP levels were specified.

Thereafter, patients used the interactive self-management support system and self-reported once daily during 8 weeks. The patients first answered items and then directly thereafter measured their BP and pulse rate and reported it in the system through their mobile phone. These took on average 12 minutes to complete. The reported data were automatically registered in the database.

Self-reports of medication intake (“Taken your antihypertensive medication today?” with a response of “yes,” “partly,” or “no”) were manually checked for consistency with the NPR registry, i.e., if prescription fill rates corresponded with reported intake.

BP Self-Monitoring. Patients received instructions on how to measure their BP, following the European Society of Hypertension practice guidelines for home BP monitoring (HBPM). A home BP monitor (Microlife BP A200 AFIB, Widnau, Switzerland), validated according to the International Protocol of the European Society of Hypertension, was used. Pre-trial BP values, representing the four most recent BP checkups prior to the start of the intervention, were extracted from patient journals for each patient.

Data Analysis

Before and After Group Level Analyses. Descriptive statistics were used to characterize patient demographics and clinical variables. Comparisons between the means of the four pre-trial SBP and DBP measurements with those of the last 7 days of the study were carried out using a paired-samples t test and statistical significance was set to a P value of <.05. These analyses were performed with SPSS version 19 for Windows (SPSS Inc, Chicago, IL).

Plots of the estimated probability density functions of the SBP and DBP were produced to illustrate differences between the pre-trial BP measurements (190 values) vs the last 7 days of the study (278 values). The units in the plot are mm Hg and %/mm Hg at x- and y-axes, respectively (the integral of each curve is dimensionless and equals one). Mathematica version 9.0 for Mac (Wolfram Research, Champaign, IL) was used. Each data set was smoothed using a Gaussian kernel with the SD of the corresponding data.

Latent Class Growth Modeling. Trends in change in BP during the course of the 8-week intervention period were examined by means of latent class growth modeling (LCGM) using Mplus version 7.1 (Muthén & Muthén, 1998–2010, Los Angeles, CA).
As heterogeneity in response to treatment is common in clinical trials,39,40 we further sought to identify homogenous subgroups of patients who respond differently to the intervention.

Latent class growth models were conducted to identify latent subgroups with different profiles of change in terms of BP across time. In LCGM, latent classes (unobservable subgroups) are created with different profiles of change and stability. LCGM are a special type of Growth Mixture Models41 where individuals within each class are assumed to be homogenous, and the variances of starting point (intercept), change (linear slope), and change in change (nonlinear change or quadratic slope) are therefore fixed to zero. Several different criteria were used to determine the number of classes to select.42 These criteria included Bayesian Information Criterion (BIC), Sample Size–Adjusted Bayesian Information Criterion (SSABIC), entropy (posterior probabilities of group membership ranging from 0 to 1, where values closer to one indicate better classification, as well as substantive interpretation. In addition, the Adjusted Lo-Mendell-Rubin likelihood ratio test43 was used to test whether the k class model significantly improved in fit compared with the k–1 class model, as described below.

We based the LCGM analyses on the first 14 days of measurement, excluding day 1, in addition to one occasion per week from day 14 to day 56 (ie, 19 waves of data). Excluding values from day 1 is common and acknowledged in guidelines for HBPM,36 since these values are normally higher than the patients’ normal BP. This was in line with the day 1 values in our study.

An initial one-class model (ie, similar to a general latent growth model) was run to examine patterns of trajectories in the whole sample across 55 days. This model included both linear and quadratic slope. A series of LGCMs, with increasing numbers of classes, were then tested, and each new model, including one less class (ie, the k–1 class model), was compared with the previous one to identify the number of classes that best represented data. Subsequently, the best fitting model was used to describe the patterns of BP (intercept, linear slope, and quadratic slope) of the different classes across the 55-day period.

The study was approved by the regional ethics board in Gothenburg, Sweden (study code 551-09 and T-100-12) and was conducted in accordance with the Declaration of Helsinki.44 The study was registered in the Clinical Trial Protocol Registration System (ClinicalTrials.gov NCT01510301), under the acronym MIHM (Mobile Phone in Hypertension Management). Data were anonymized and the study was monitored by an independent monitoring board to ensure that data were entered accurately.

RESULTS
A total of 50 of 51 recruited patients completed the study. One patient dropped out 4 weeks into the study after having registered his/her self-reports sporadically.

All data from this person were excluded from the analyses. The proportion of men was slightly higher than women (not significant) as is the case in the middle-aged hypertensive population,45 and other demographics were also comparable with the general hypertensive population in Sweden.30 Patient characteristics, comorbidities, and medication are shown in Table I.

| TABLE I. Patient Characteristics (N=50) |
|-----------------------------------------|
| Women, No. (%)                          | 24 (48) |
| Mean age (range), y                     | 59.5 (33–81) |
| Mean SBP (range), mm Hg                 | 142 (115–195) |
| Mean DBP (range), mm Hg                 | 84 (61–113) |
| Mean years with hypertension (range)    | 8.5 (1–32) |
| Comorbidity, No. (%)b                   | 22 (52) |
| Cardiovascular disease                  | 3 (14) |
| Decreased renal function                | 2 (9) |
| Diabetes                                | 7 (32) |
| Musculoskeletal disorder                | 3 (14) |
| Other                                   | 7 (32) |
| Antihypertensive medication, No.        |
| Diuretics                               | 12 |
| Potassium-sparing diuretics             | 4 |
| β-blockers                              | 18 |
| Calcium channel blockers                | 22 |
| ACE inhibitors                          | 11 |
| Angiotensin II receptor antagonists     | 21 |
| ACE inhibitors + diuretic               | 1 |
| Angiotensin II receptor antagonist + diuretic | 5 |
| Antihypertensive drugs, No.             |
| One                                     | 19 |
| Two                                     | 19 |
| Three                                   | 11 |
| Four                                    | 1 |
| Marital status, No. (%)                 |
| Married                                 | 39 (78) |
| Unmarried                               | 10 (20) |
| Widow/widower                           | 1 (2) |
| Education, No. (%)                      |
| Compulsory school (<9 y)                | 5 (10) |
| High school (9–12 y)                    | 22 (44) |
| University                              | 22 (44) |
| Missing                                 | 1 (2) |
| Employment status, No. (%)              |
| Employed                                | 28 (56) |
| Long-term sick leave                    | 1 (2) |
| Retired                                 | 19 (38) |
| Missing                                 | 2 (4) |

Abbreviations: ACE, angiotensin-converting enzyme; DBP, diastolic blood pressure; SBP, systolic blood pressure. *Mean of patients’ three or four baseline blood pressure measurements (n=49).

bInformation provided by patients; eight missing.
adherence to medication and was validated against NPR data, which showed that 46 of 50 patients had filled their prescriptions, corresponding to at least 80% of the prescribed dose during the study period.

Before and After Analyses on a Group Level
Statistically significant decreases in both SBP and DBP were found between mean pre-trial BP measurements and mean week 8 values (SBP, 7 mm Hg; SD, 18; 95% confidence interval [CI], 1.94–12.25; \( t \) [48]=2.77 [\( P=.008 \)] and DBP, 4.9 mm Hg; SD, 10; 95% CI, 1.95–7.8; \( t \) [48]=3.35 [\( P=.002 \)].

The characteristics of the four sampled data sets (SBP and DBP from the pre-trial BP measurements and week 8 values) are illustrated in Figure 1. The figure shows the smoothed histograms of the data sets where each curve is an estimation of the corresponding probability density function.

Latent Class Growth Modeling
The average SBP and DBP at the first day of the study was 140.34 (standard error [SE]=2.16) mm Hg and 81.78 mm Hg (SE=1.05), respectively. The average change (average linear slope) was significant and negative for SBP (\( M=-0.32 \), SE=0.11) and DBP (\( M=-0.17 \), SE=0.06), indicating that SBP decreased by an average of 0.32 mm Hg per day and DBP decreased by 0.17 mm Hg per day during the course of the study period. In addition, the quadratic slope was significant and positive for both SBP (0.004; SE=0.002) and DBP (0.002; SE=0.001), indicating that the average decline in BP flattened out over time. The patterns of trajectories for SBP and DBP are illustrated in Figure 2a,b.

The Three Latent Classes
For both SBP and DBP, the three class models demonstrated the best fit to data and were retained (Table II). The parameter estimates of the selected three-class models for SBP and DBP are presented in Table III. Regarding SBP, the first latent class (n=5) demonstrated a higher average SBP at the start of the study (168.81 mm Hg) and had a nonsignificant decrease (–0.42 mm Hg) and a nonsignificant quadratic effect (0.003). The second and largest class (n=30) had a substantially lower average SBP at the start of the study (143.40) and a significant average decrease of –0.28 and a nonsignificant positive quadratic effect (0.003). Finally, the third class (n=15) had an even lower SBP at the start of the study (124.71 mm Hg) that also significantly decreased (–0.46 mm Hg). This decline leveled off, as indicated by a positive and significant quadratic slope (0.08). Trajectories for SBP for the three groups are shown in Figure 2c.

For DBP, the first class (n=15) had a starting DBP of 91.27 mm Hg and a significant average decrease of –0.21 mm Hg and a nonsignificant quadratic effect (0.002). The second class (n=29) had a starting DBP of 79.33 mm Hg and a significant decrease of –0.19 mm Hg and a positive and significant quadratic effect (0.004). Finally, the third class (n=6) had a lower DBP at the start (71.63 mm Hg) and a significant decrease (–0.20) and significant positive quadratic effect (0.003). Trajectories for DBP for the three groups are shown in Figure 2d.

DISCUSSION
This explorative study showed that the daily use of a mobile phone–based self-management support system for hypertension significantly reduced BP over the course of 8 weeks. Statistically and clinically important improvements were noted between baseline and week 8 in both SBP (7 mm Hg) and DBP (4.9 mm Hg). Significant improvements were also seen over the course of the 8 weeks; however, average daily improvement was not uniform but rather leveled off as the study progressed. Furthermore, we were able to identify three homogenous subsets/latent classes of patients who differed from each other with respect to level of BP at baseline. Despite distinct baseline BP levels, all groups responded similarly to the intervention, showing substantial decreases in BP. The decreases were statistically significant except in SBP class 1, which may be a result of the small size of this group (n=5). By the same logic, the statistical significance regarding DBP class 3 (n=6) may be uncertain. Nonetheless, the magnitudes of absolute change observed in these two classes may still reflect important clinical changes regarding atypical groups of patients who would otherwise be handled as outliers in more traditional analyses. Although the greatest improvements were seen in patients with BP >140/90 mm Hg, even the subset of patients with relatively controlled BP showed significant improvements. These results indicate that the system is effective and efficient in reducing BP, particularly in patients with high to moderate BP.

This study is unique in capturing daily BP assessments over an 8-week period, in addition to four pre-trial, baseline measurements. Although our initial before and after comparison revealed statistically and clinically significant declines in SBP and DBP between baseline
and 8 weeks, such an analysis does not fully exploit the potentials of this rich data set. We therefore applied LCGM, which is a relatively new yet increasingly common method for analyzing longitudinal data in clinical trials. LCGM enabled us to examine and analyze trends in change in BP over the full 8 weeks. Results from this analysis mirrored those from the before and after analysis, showing significant declines in BP during the study period; however, they also showed that the declines leveled off over the course of the 8 weeks. Inspection of the LCGM trajectory plots indicated that initial BP improvements peaked after about 2 weeks and then stabilized, suggesting that a relatively short intervention period may be required to attain optimal BP effects.

Interestingly, the two sets of analyses had different initial BP measurement periods and procedures, where the first were conducted pre-trial, in-office by a physician or nurse, and the second were performed by the patients at home as part of the trial. After excluding BP measurements taken day 1 of the trial from analyses as recommended in guidelines for HBPM, no significant differences were found between the average of the four pre-trial BP measurements and that of week 1 of the trial, suggesting that the measurements yield comparable results. On the other hand, if a white-coat effect was in operation and our baseline values were hence inflated, then by extension it may take longer than has been suggested for patients to familiarize themselves with HBPM. Sebo and colleagues recently concluded

Figure 2. Between-person heterogeneity in systolic (a) and diastolic (b) blood pressure for all participants (1-class model) and description of the classes in the best-fitting three-class models for systolic (c) and diastolic (d) blood pressure.

Table II. Fit Indices, Entropy, and Model Comparisons for Estimated Latent Class Growth Models for 56 Days of Data

| Models          | Log Likelihood | BIC   | SSABIC | Entropy | Adjusted LRT |
|-----------------|----------------|-------|--------|---------|--------------|
| **Systolic**    |                |       |        |         |              |
| One class       | -3838.60       | 7767.17| 7694.98| 1.00    |              |
| Two classes     | -3641.81       | 7389.24| 7304.49| .99     | 369.94*      |
| Three classes   | -3518.07       | 7157.42| 7060.12| .99     | 232.61*      |
| Four classes    | -3489.11       | 7115.14| 7005.29| .95     | 54.44        |
| **Diastolic**   |                |       |        |         |              |
| One class       | -3272.36       | 6634.70| 6562.51| 1.00    |              |
| Two classes     | -3064.66       | 6234.94| 6150.19| .98     | 390.46*      |
| Three classes   | -3005.48       | 6132.24| 6034.94| .99     | 111.24*      |
| Four classes    | -2987.11       | 6111.14| 6001.27| .93     | 34.55        |

Abbreviations: BIC, Bayesian Information Criterion; LRT, likelihood ratio; SSABIC, Sample Size-Adjusted Bayesian Information Criterion. *P<.05.
that BP measurements performed by primary care physicians are often inaccurate and with low specificity to diagnose hypertension. Instead, automated office BP is now recommended globally in guidelines and has been shown to be consistent with HBPM.\textsuperscript{48} Nonetheless, HBPM may provide more accurate groundwork for diagnosing hypertension or detecting treatment effects and eliminating the white-coat effect due to in-office measurements.\textsuperscript{36}

A second advantage to LCGM is that it offers possibilities to examine heterogeneity in treatment response.\textsuperscript{39} Clearly, patients do not respond to treatment equally and it is important to identify patients who benefit or benefit most from any particular treatment or intervention. Our analyses yielded three relatively homogenous (with respect to initial BP values) subgroups of patients who benefitted differentially from the intervention. Although all three subgroups showed significant decreases in BP after 2 weeks, only those with moderate to high BP had maintained these improvements at 8 weeks, whereas the subgroup of patients with BP in the normal range (<140/90 mm Hg) had returned to nearly initial BP levels. Hence, the system seems to be most beneficial for patients with the greatest margin for improvement and also at greatest risk for developing CVD, which is similar to results presented in a recent study by McManus and colleagues,\textsuperscript{49} where self-monitoring of BP and self-titration of medication significantly lowered systolic BP in high-risk patients. However, it has been proposed that lowering BP even in the normal range has heart protective effects\textsuperscript{15,50} and hence the small gains manifested in the patient group with normal BP may be advantageous.

Research on interventions aimed at improving BP has thus far shown that BP self-monitoring in conjunction with education and/or counseling is most effective in reducing BP.\textsuperscript{24} Our mobile phone self-management support system thus incorporated HBPM together with several other components, suggested by patients to aid in self-managing their BP.\textsuperscript{22,23,34} The system was intended to help patients gain awareness of and insight into the importance of controlling their BP by not only taking their BP medication, but also maintaining a healthy lifestyle and avoiding stress. As such, the system was conceived as a self-learning tool whereby patients themselves could, by means of a feedback module, examine interplays between their BP, adherence to various aspects of their treatment regimen, and general well-being, through graphs. Moreover, the system included tailored reminders and motivational messages to encourage patients in their self-management efforts. Our study was not designed with the intention of distinguishing which components of the system are effective in helping patients to self-manage, but rather to evaluate whether the system as a whole contributed to lower BP in our patients. More research is needed to evaluate the contributions of the various components of the system.

Given the proven efficacy of hypertension treatment strategies in clinical trials, intentional and unintentional nonadherence to treatment is generally considered the main reason for poor control rates among patients undergoing treatment. The evidence supporting adherence-promoting interventions over the past decade has been weak.\textsuperscript{51} Moreover, many of these interventions are complex and labor-intensive and may therefore not be feasible in clinical settings in the current era of cost-containment. Our point of departure in designing our system was to develop a tool to aid patients in their efforts to self-manage their hypertension by empowering and engaging them in their treatment. By enabling patients to gain firsthand insight into how health-promoting behaviors, including taking medications, can affect their BP and well-being, the system may serve to prompt them to be more adherent—not because they are advised to do so but because they have gained an understanding for why they should. A shift in focus from adherence to self-management might be a path in the right direction. However, more studies, in particular randomized controlled studies that include patients with resistant hypertension and/or lack of motivation to follow treatment, are needed to further assess the effectiveness of the intervention.

### Limitations and Methodological Considerations

There are several limitations to this study. First, sample bias has to be considered. Although we tried to minimize this by recruiting a demographically diverse and representative sample of the target population,\textsuperscript{30,45} the sample nonetheless included only one participant of non-Swedish origin. Furthermore, our sample had a higher adherence rate (80%) at outset compared with earlier research on adherence to hypertension medication.\textsuperscript{9} It is noteworthy that despite good adherence to medication, our patient group still significantly decreased their BP. This suggests the importance of supporting lifestyle modifications in addition to medication adherence for controlling BP. Nonetheless, the support system needs to be evaluated among patients who are less adherent to medication. Second, a controlled design would naturally have strengthened our results and conclusions; however, all patients in

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**TABLE III. Parameter Estimates of Latent Growth Factors in the Selected Three Class Latent Class Growth Models**

| Models       | Intercept (Standard Error) | Linear Slope (Standard Error) | Quadratic Slope (Standard Error) |
|--------------|----------------------------|-------------------------------|---------------------------------|
| **Systolic** |                            |                               |                                 |
| Class 1 (n=5)| 168.81 (4.61)              | -0.42 (0.41)                  | 0.003 (0.006)                   |
| Class 2 (n=30)| 143.40 (1.50)              | -0.28 (0.14)*                 | 0.003 (0.003)                   |
| Class 3 (n=15)| 124.71 (2.32)              | -0.46 (0.14)*                 | 0.008 (0.003)*                  |
| **Diastolic**|                            |                               |                                 |
| Class 1 (n=15)| 91.27 (1.14)               | -0.21 (0.09)*                 | 0.002 (0.002)                   |
| Class 2 (n=29)| 79.33 (0.73)               | -0.19 (0.08)*                 | 0.004 (0.002)*                  |
| Class 3 (n=6) | 71.63 (0.99)               | -0.20 (0.07)*                 | 0.003 (0.002)*                  |

\*p<.05.
the study had a long history of hypertension and the observed BP decreases were substantial during the intervention. Third, long-term follow-up was not performed; hence, we do not know whether the BP improvements manifested during the intervention are sustainable. Our rationale for using LCGM was to enable analysis of large numbers of measure points, which, in our study, included 55 days. However, these analyses in fact comprised 19 measurement points (13 of the 14 first 2 weeks plus day 1 of each of the following 6 weeks) due to analytical and interpretive constraints related to the complexity of models.

PRACTICAL IMPLICATIONS
The self-management support system was conceived as a tool to help patients gain an understanding of the interrelationships between BP, medication intake and side effects, symptoms, well-being, and lifestyle, thereby motivating them to engage in health-promoting behaviors. It was also designed to serve as a source of comprehensive and structured patient-generated health data in consultations with healthcare professionals about the management of their condition. The system may thus act as a mediator for improving patient participation in clinical consultations and as a facilitator for a person-centered approach in hypertension care.

CONCLUSIONS
The study showed that daily use of a mobile phone–based self-management support system for hypertension: (1) significantly reduced BP over the course of 8 weeks; (2) that optimal effects appeared to be achieved after a relatively short period of use of the system; and (3) that patients benefiting most were those with moderate to high BP at study start. Our results are promising and suggest that the self-management support system may be a useful tool to help patients self-manage their hypertension.

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