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Automated Symptom and Treatment Side Effect Monitoring for Improved Quality of Life among Adults with Diabetic Peripheral Neuropathy in Primary Care: A Pragmatic, Cluster, Randomized, Controlled Trial

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Abstract

Aims: To evaluate the effectiveness of automated symptom and side effect monitoring on quality of life among individuals with symptomatic diabetic peripheral neuropathy.

Methods: We conducted a pragmatic, cluster randomized controlled trial (July 2014 through July 2016) within a large health care system. We randomized 1,834 primary care physicians and prospectively recruited 1,270 of their patients newly prescribed medications to treat neuropathy symptoms. Intervention participants received automated telephone-based symptom and side effect monitoring with physician feedback over six months. The control group received usual care plus 3 non-interactive diabetes educational calls. Our primary outcomes were quality of life (EQ-5D) and

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Conflicts of Interest Disclosures

The authors report no conflicts of interest and that the results of this paper have not been previously published. A brief abstract of the study findings is available on the PCORI webpage at pcori.org/Adams071.

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select symptoms (e.g., pain) measured 4-8 weeks after starting medication and again 8 months after baseline. Process outcomes included receiving a clinically effective dose and patient-provider communication over 12 months. Interviewers collecting outcome data were blinded to intervention assignment.

Results: 1,252 participants completed baseline [mean age [st. dev.]: 67 [11.7], 53% female, 57% white, 8% Asian, 13% black, 20% Hispanic]. 1,179 participants (93%) completed follow up (619 control, 560 intervention). Quality of life scores [intervention: 0.658[0.094]; control: 0.653[0.092]] and symptom severity were similar at baseline. The intervention had no effect on primary [EQ-5D: −0.002 (−0.01, 0.01), p=0.623; pain: 0.295 (−0.75, 1.34), p=0.579; sleep disruption: 0.342 (−0.18, 0.86), p=0.196; lower extremity functioning: −0.079 (−1.27, 1.11), p=0.896; depression: −0.462 (−1.24, 0.32); p=0.247] or process outcomes.

Conclusions: Automated telephone monitoring and feedback alone was not effective at improving patient quality of life or symptoms for individuals with symptomatic diabetic peripheral neuropathy.

Trial Registration: ClinicalTrials.gov (NCT02056431)

Keywords

diabetes; peripheral neuropathy; automated monitoring

INTRODUCTION

An estimated 5.5 million people with diabetes have symptomatic diabetic peripheral neuropathy (1). Characterized by pain, burning, tingling, and electric shock sensations in the extremities, neuropathic pain can negatively impact individuals' quality of life and is responsible for nearly one-third of all diabetes related health care costs, approximately $5-14 billion per year (1–3). Although diabetic peripheral neuropathy is not curable, its development can be slowed via improved glycemic control and long-term impact may be moderated by effective symptom treatment, particularly pain (2–6). However, there is increasing evidence that diabetic peripheral neuropathy is underdiagnosed and treated in primary care (7,8).

Clinical guidelines recommend starting patients on select medications (e.g., tricyclic antidepressants, gabapentinoids) and gradually titrating the dose to balance symptom relief and side effects (4–6). For the estimated 50% of individuals with active symptoms, frequent patient-provider communication may facilitate early diagnosis and treatment of neuropathy (2). However, there are numerous barriers to effective patient-provider communication, including low health literacy, language barriers and patient reluctance to discuss symptoms (9,10). Additionally, the limited time available during primary care visits can hamper discussion of patient reported concerns about diabetic peripheral neuropathy symptoms and their treatment.

To address these patient, provider, and temporal barriers to effective treatment of neuropathy symptoms, the Diabetes Telephone Study (11) was designed as a cluster randomized controlled trial to test whether automated monitoring of participants' treatment experiences

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and feedback to physicians using interactive voice response technology and an electronic health record could support patient-provider communication, facilitate guideline consistent care, and result in improvements in individuals' quality of life and symptoms compared to usual care.

METHODS

Design Overview

We conducted a pragmatic, cluster randomized controlled trial in primary care clinics within the Kaiser Permanente Northern California health system between July 2014 and July 2016 (11). The clusters were primary care physicians treating patients with diabetes. We designed the intervention to work under usual clinical conditions, minimize exclusions, and employ technologies routinely used in clinical practice, i.e., interactive voice response technology which allows individuals to interact with a computerized voice, and the electronic health record (12).

The intervention was designed and evaluated in close collaboration with three individuals with neuropathy being cared for in our settings and three clinician stakeholders who were active members of the research team (11). In addition, we received ongoing feedback from two community-based neuropathy support groups. The Kaiser Permanente Northern California Institutional Review Board approved all research procedures and the study is registered at ClinicalTrials.gov (CE-1304-7250). Consent was waived for physicians and written consent was waived for patients in lieu of phone consent.

Study Setting and Participants

Kaiser Permanente Northern California is a multi-specialty health care system with 21 medical centers that serve more than 4 million people in northern California. Usual care for people with diabetes includes a robust panel management approach that leverages performance feedback, system-wide efficiencies, disease registries and evidence-based practice leveraging an integrated electronic health record (13).

All primary care physicians treating at least one patient enrolled in the Kaiser Permanente Northern California Diabetes Registry in the prior year were eligible for randomization. People with diabetes were potentially eligible for the study if they were 18 years old when they started a neuropathy medication, screened positive for neuropathy symptoms (according to brief questionnaire administered during routine primary care visits and available for more than 85% of all people with diabetes), continuously enrolled in our setting during the 12 months prior to starting study medications, and spoke English or Spanish. We excluded individuals who had a diagnosis of gestational diabetes, dementia or substance abuse disorder during the previous 12 months as medication strategies may differ for these patients. In addition, we excluded individuals who had any opioid use during the 90 days prior to starting first-line diabetic peripheral neuropathy treatment as opioid use in the near-term may indicate prior treatment failures (4).

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Randomization and Participant Recruitment

We randomized 1,834 Kaiser Permanente Northern California primary care physicians treating adults with diabetes in the ratio of one to one to the intervention and control groups on July 11, 2014. Of those randomized, 1,714 physicians had patients who met the initial study criteria. In October 2014, we notified these physicians that their patients might be approached about the study and invited the physicians to opt out any patient due to illness or other factors that would make them ineligible for participation. We then used the electronic health record to prospectively identify individuals who met the above inclusion criteria and who were newly prescribed (i.e., no use in the previous 12 months) one of 10 medications commonly used to treat neuropathy symptoms in this setting (amitriptyline, nortriptyline, imipramine, desipramine, duloxetine, paroxetine, citalopram, pregabalin, venlafaxine, or gabapentin) during the last 2 weeks. The total enrollment period was September 2014 through November 2015.

Recruitment letters in English and Spanish were sent to 5,716 people identified by a computer algorithm as possibly having diabetic peripheral neuropathy symptoms and who started a study medication within the past two weeks. Interviewers, blinded to treatment assignment, called individuals approximately one week later to assess eligibility for the trial and, among those deemed eligible, to obtain phone consent and to conduct the baseline interview. Patients and providers were unaware of their treatment status during recruitment. Within the study team, only the main analyst, the research assistant charged with entering patient data into the electronic health record, and the individual responsible for scheduling the interactive voice response calls, were aware of the participants' treatment status.

English and Spanish speaking interviewers were able to reach and screen 2,203 people with diabetes to confirm eligibility. In addition, the interviewers excluded individuals based on other factors that may have impeded participation in the study (e.g., rotary phone). Individuals who could not be contacted within 56 days of starting treatment (maximum of 10 call attempts) were excluded from further recruitment calls. Specific reasons for ineligibility are described in Figure 1.

The Intervention

Participants in the intervention arm received all usual care, plus three five-minute interactive voice response calls spaced two months apart over the six months following DPN treatment start. [Figure 2] These interactive calls systematically collected information on symptom relief, medication use, titration, discontinuation and side effects. Participant responses were then manually entered into the electronic health record by a trained research assistant. We created an algorithm to 'alert' physicians via secure staff message when their patients reported specific problems identified by our clinician partners as requiring physician intervention (i.e., dissatisfaction with symptom relief, side effects, discontinuation (or failing to start)). No specific follow-up protocol was imposed for physician response at the request of these clinician partners to minimize disruptions in usual care. Responses from participants who reported none of these problems were entered into the EHR with no physician alert.

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Control Arm

Participants in the control arm received all usual care for diabetes and neuropathy, plus three non-interactive 2-3 minute educational calls (i.e., physical activity, dietary changes, foot checks) in English and Spanish delivered over the same time intervals as the intervention calls. The goal of providing these non-interactive calls was to isolate the marginal impact of receiving an automated, diabetes-related phone call in the intervention arm.

Outcomes and Follow Up

The primary outcome for this study was quality of life, a patient reported outcome that is highly associated with DPN symptoms, but rarely studied in drug trials (14) We calculated quality of life using the Global Health Scale (e.g., general health status, social functioning), a 10-item PROMIS® (Patient-Reported Outcomes Measurement Information System) questionnaire developed and validated in individuals with neuropathy (15). We converted the Global Health Scale into the EQ-5D, a standardized instrument developed by the European Quality of Life (EuroQol) Group as a measure of health-related quality of life, using previously validated methods to ensure comparability with other studies (16).

In addition to quality of life, we also evaluated changes in DPN symptoms, including pain interference (range=40.7-77.0; 77 indicates maximum interference), sleep disruption (range: 32-84.2; higher score indicates maximum disruption), lower extremity functioning (range: 16.5-58.6; 58.6 indicates best possible functioning) and depressive symptoms (range:38.2-81.3; 81.3 indicates worst possible symptoms). These measures were assessed using the NeuroQOL measurement system instruments that have been previously validated in individuals with diabetic peripheral neuropathy (17).

All patient-reported outcomes were collected by trained interviewers during 20-minute phone interviews at approximately 2 months (baseline) and again 8 months (follow up) following treatment start. We hypothesized that automated monitoring and feedback of information on patient symptoms and side effects would result in clinically significant improvements in quality of life (EQ-5D=0.074) and DPN symptoms (16,17).

In addition, we evaluated two process measures to assess changes in patient-provider communication and dosing. We used the six-item Doctor Communication Composite questionnaire from the Consumer Assessment of Health Plans (CAHPS) Survey (min=4; max=24; 24 indicates best communication) to assess patient satisfaction with the quality of communication with their primary care provider over the last 12 months (18). To evaluate medication dosing, we used EHR data to calculate whether the participant ever received the minimum effective dose of DPN medication (7,8). Specifically, for each medication, we assessed whether the maximum daily dose ever reached or surpassed the dose found to be therapeutically effective in clinical trials (7). This measure was assessed only for the 12 months following the first observed prescription.

Sub-Group Analyses

Variation in Treatment Effect by Level of Shared Decision Making—Our protocol included a preplanned analysis of differences in effect of the intervention by the level of

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shared decision making at baseline, measured using the 9-Item Shared Decision Making Questionnaire (SDM-Q-9) [6 point scale: completely disagree (0); completely agree (5)] (19). We hypothesized that the intervention would be more effective in participants who perceived a high level of shared decision making between themselves and their physician.

Statistical Analysis

The unit of analysis in this cluster randomized trial is the primary care physician. On average, physicians had fewer than two patients enrolled in the study.

Nevertheless, to formally account for the dependence of patient measurements clustered within physicians and because our main analysis was conducted at the patient level, we employed generalized estimating equations (GENMOD procedure in SAS®) (20) with robust standard errors and an independent correlation structure to estimate intervention effects. Our models estimated the change from baseline in each of the patient-reported outcomes of interest. The resulting treatment effects provided an estimate of the difference in the change (i.e., the difference in difference) between individuals in the treatment group relative to controls. Unlike random effects models, GEE does not require a normality assumption and these regression models therefore provide valid estimation of treatment effects and associated standard errors even when the assumptions about the correlation structure are wrong. In sensitivity analyses, the estimates of treatment effects and associated standard errors were robust to changes in the choice of correlation structure, level of analysis (physician vs patient) and whether the outcome was treated as a change from baseline or a repeated measure. While the trial took part in multiple medical centers, patients and physicians can receive care and practice across in multiple medical centers. Therefore, we did not adjust for medical center in the analysis.

No additional covariates were included in the main GEE analyses due to the high degree of similarity between the treatment and control groups with respect to baseline characteristics following randomization. Models estimating heterogeneity in treatment effects included the shared decision making score as a continuous variable and an interaction between this measure and the treatment indicator for the primary outcomes of interest. [Table 1]

The analyses were based on the intent-to-treat and complete case analysis principles, using only data from participants with complete baseline and follow up outcome measurements regardless of whether they completed all three intervention calls (22). A two-sided test of each null hypothesis that the mean change in outcomes in the treated arm is equal to that of the control arm was derived from the test that the slope of each linear model is equal to zero.

All participants were required to complete the quality of life and sleep disruption surveys. However, to minimize participant burden, we only administered the pain, depressive symptom and lower extremity functioning reports to individuals who indicated problems with these symptoms in the quality of life survey. To account for this intentional skipping pattern in the statistical analysis, we imputed the data by setting outcomes to their best possible value by subtracting 0,1 from the minimum value for pain interference, lower extremity functioning and depressive symptoms.

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Contextual Considerations

We conducted a limited survey with physicians to assess awareness and acceptance of the intervention. We also assessed physicians' perception of the intervention's potential utility to aid decision making related to DPN care, as well as its use for other conditions. We randomly selected 50 physicians in the intervention arm who received at least one alert during the study to receive an email from the PI. We aimed to recruit 30 physicians to participate in the follow up survey. This survey group was not planned as a representative sample, but as a brief assessment of physician attitudes toward their experience of intervention.

Role of the Funding Source

This work was supported through a Patient-Centered Outcomes Research Institute (PCORI) Assessment of Prevention, Diagnosis, and Treatment Options Program Award (CE-1304-7250). The sponsor had no role in the study design, data collection, analysis and interpretation of data, writing of the manuscript, or in the decision to submit the article for publication.

Power

With a type I error alpha of 0.05 and a type II error beta of 0.20, we estimated that the minimum detectable effect (i.e., the difference in EQ-5D change from baseline to end of study between the two arms, was 0.017. This calculation was conservative in the sense that it concerned an analysis in which only outcomes from the first patient of each randomized physician would be considered (cluster of size 1). The calculation assumed that a minimum of 118 eligible participants would be enrolled per month with a drop-out rate of 40% (min 850 participants; 425 per arm), and a standard deviation for the outcome of 0.143. Thus, we anticipated having more than 80% power to detect an effect that was smaller than the published clinically meaningful differences in EQ-5D change of 0.074. (16,23)

Results

Participants

Of the 5,716 individuals contacted, 2,203 were screened for eligibility. Compared to those who were screened, those who were not screened were slightly younger (66.3 (12.2) vs 67.0 (11.8); p=0.051), more likely to be Asian (16% vs. 8%) and less likely to be white (46% vs. 57%) (p<0.0001). Among the 2,203 who were screened, we identified 1,535 people with diabetes who were eligible for participation in the main study, 83% (1,270) of whom consented to participate. [Figure 1] Reasons for declining consent could be multiple and included: lack of interest (173), being too busy (44), and being too sick to participate (52). Our retention rate (proportion completing follow up) was 93%. Compared to participants who dropped out, participants with complete data were more likely to be female (54% versus 41%; p=0.299), slightly higher baseline quality of life (mean Eq-5D: 0.657 ± 0.092 versus 0.634 ± 0.100; p=0.0437) and had slightly higher average lower extremity functioning scores (48.359 ± 11.439 vs. 45.660 vs. 12.598; p=0.0519. [Supplemental Table S1]

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Baseline characteristics of the study sample are presented in Table 1. The mean age was 67 (standard deviation: 11.7) and female (53%). The sample was racially and ethnically diverse (57% white, 8% Asian, 13% black, 20% Hispanic) and 17% were living in economically depressed areas. Fifteen percent of participants had an A1c above 74 mmol/ml (>9%). There were no statistically significant differences in baseline characteristics between the intervention and control groups.

Intervention Uptake and Fidelity

Of the 1,252 participants who completed the baseline assessment, 1,248 completed the first call (100% control; 98% intervention). Only 53% of the intervention participants completed all three calls compared to 60% of control participants. More than 80% of participants completed at least one post-baseline call (85% control; 83% intervention). The average intervention call lasted five minutes, compared to four minutes for the control calls. [Supplemental Table S2]

Trial Outcomes

The intervention was not effective in improving quality of life [Estimated difference in change between treatment and control of −0.002 (standard error 0.005; p=0.623], DPN symptoms, effective dosing [53% treatment compared to 48% control (−0.11 to 0.38)] or communication [−0.45 (−0.97 to 0.07)]. [Table 2] In the subgroup analyses, no significant interactions related to shared decision making were observed. [Supplemental Table S3] The independent safety monitor reported no adverse events or unintended effects attributable to the trial.

Participant Experiences with DPN Medications

Among participants in the intervention group, seventy-four percent reported side effects, medication discontinuation or dissatisfaction with treatment during the first IVR call, triggering a physician alert. Side effects were the most common problem reported (<50%). Among participants who were actively using the medication at the time of the first call, more than 95% reported taking it once a day and 33% reported self-titrating the medication dose.

Clinical Context for the Intervention

We successfully recruited 31 of 50 physicians who received an alert to report on their experiences with the intervention. Only 7 recalled seeing the electronic patient reports, though 13 reported being aware or very aware of the study. Of those who recalled seeing the reports, most did not think the information was actionable, would change how they provided care or could not have been obtained directly from the patient. Most (23/31) of the physicians surveyed reported that the automated monitoring strategy could be useful for other conditions where “answers are black and white” such as diabetes and hypertension and for medications “with serious side effects” such as warfarin.

DISCUSSION

In this pragmatic randomized trial, automated monitoring and feedback of patient-reported symptoms and side effects related to DPN treatment was not effective in improving

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outcomes. Our study findings are in conflict with prior studies demonstrating positive effects of automated monitoring in diabetes and chronic pain (non-DPN pain) using IVR (24–28). One possible explanation for this difference is that compared to prior interventions, our intervention did not dictate a specific protocol for physicians and was less intensive (three calls over six months). Our effort to minimize physician burden may have weakened the potential impact of the intervention. However, it is also important to note that while participant reports triggered an alert in 74% of all calls, most physicians only had one patient enrolled in the trial. Therefore, it is not surprising that individual physicians did not recall this specific alert among the many they receive on a daily basis. Further, low intervention fidelity (~50% completed all three calls) may have contributed to the lack of intervention effect. In addition, this intervention was conducted within a system with a high functioning diabetes management program (13), which may have made it harder to have a clinically important impact over and above usual care.

Our findings suggest that in cases like DPN where outcomes related to the natural progression of the disease (e.g., symptoms) are considered more acceptable than outcomes that are induced by treatment (e.g., side effects), physicians may tend toward more conservative treatment strategies or intentional under dosing (29–32). In the absence of highly effective treatments, the impact of interventions to improve use of existing treatments on physician prescribing is likely to be limited. Research is needed to identify treatment pathways that yield greater efficacy with reduced side effects, including nonpharmacologic treatments (33–35).

Our findings related to patient-reported experiences with treatment are, to our knowledge, the first published evidence regarding rates of self-titration of DPN medication. We found that approximately 30% of participants reported self-titrating, which may indicate a potential opportunity for patient-focused interventions to improve dosing (36,37). This may be especially important given the challenges we observed with physician recall of patient-reported data within the context of EHR data overload and alert fatigue. However, high rates of side effects and recent reports of the potential for abuse of gabapentinoids suggest such interventions in DPN would need to first identify which individuals are most likely to benefit from and not be harmed by these treatments (38).

Our study has several limitations that deserve consideration. First, our findings may not extend to other types of delivery systems or to patient subgroups that we explicitly excluded from participation (e.g., dementia). We endeavored to include a diverse cohort of people with diabetes and the technologies we employed are widely available across diverse systems of care (27,28), though we did not include an assessment of participants' satisfaction with the IVR system, and how it might be improved for future interventions. In addition, some participants may have been taking study medications for conditions other than DPN, which may have diluted the impact of the DPN-focused intervention. Further, we assessed quality of communication over the prior 12 months and may have captured aspects of patient-physician interactions that are not specific to the 8-month intervention period. Additionally, given physicians' general lack of recall of the study EHR messages, a more intensive roll-out of the study would have been advisable. Lastly, we conducted an intent to treat analysis,

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which risks underestimating treatment effects by not accounting for partial compliance with the intervention.

Our study had several strengths that contributed to the validity of study results, including the large sample size, the high response rate and low rates of drop outs and missing data. Also, this study demonstrated the feasibility of automated monitoring of treatment effects using IVR and feedback to providers via an EHR, which can be tested for other types of interventions (e.g., patient activation) and clinical goals (e.g., medication safety).

Conclusions

Symptomatic DPN is one of the most common complications of diabetes and one of the most difficult to treat due to the variable efficacy and tolerability of available treatments (4–6, 10). As one of the first studies to employ automated monitoring to improve outcomes for patients with DPN, this study is an important step in developing new ways to address the unmet needs of this patient population. While IVR technology is widely available within health systems (28), it may be more effective if focused on patient activation (e.g., self-titration) or coupled with provider education about which individuals are most likely to benefit from available treatments and safe prescribing practices. In addition, our study demonstrates the challenges in finding a balance between intervention intensity and acceptance and adoption in real world settings. Given the high costs of under-treatment of DPN symptoms for individuals and health systems (1–3), inaction is not an option and evidence-based strategies are needed to help people with DPN and clinicians to balance the potential benefits and harms of treatment.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Novelty Statement

- Frequent patient-provider communication about symptoms and medication side effects is critical to optimizing mediation dosing to treat painful diabetic peripheral neuropathy. Yet, there are considerable barriers to effective communication.
- This cluster randomized controlled trial found that a brief intervention to automatically monitor patient-reported data on symptoms and side effects and provide the information to physicians via an electronic health record was not effective in improving patient-valued outcomes.
- Alerts alone are unlikely to change provider behavior related to treatment intensification. More intensive interventions focused on patient activation or provider education may be more effective in changing prescribing behavior and patient-valued outcomes.

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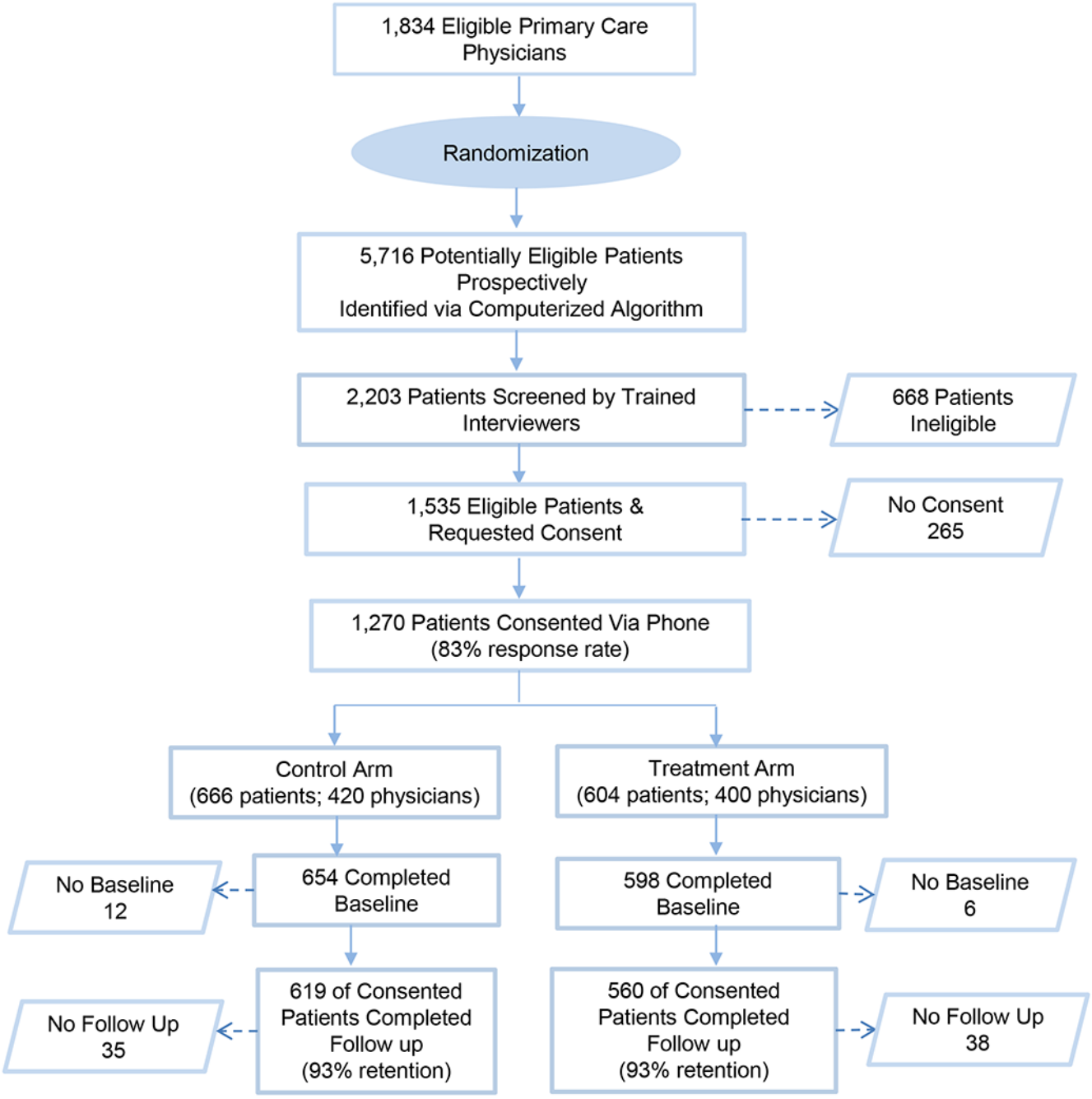

Figure 1: Clinical Trial Flowchart

Reasons for ineligibility (patients could have more than one): patient did not recall being prescribed a new medication (193), had no symptoms (152), denied having diabetes (2), had only a rotary phone and unable to receive IVR calls (1), was on the no contact registry (1), was no longer a KP member (16), was prescribed a study drug for a condition other than DPN (290), was unable to communicate in English or Spanish (1), or was unreachable or unavailable during the length of the study (3).

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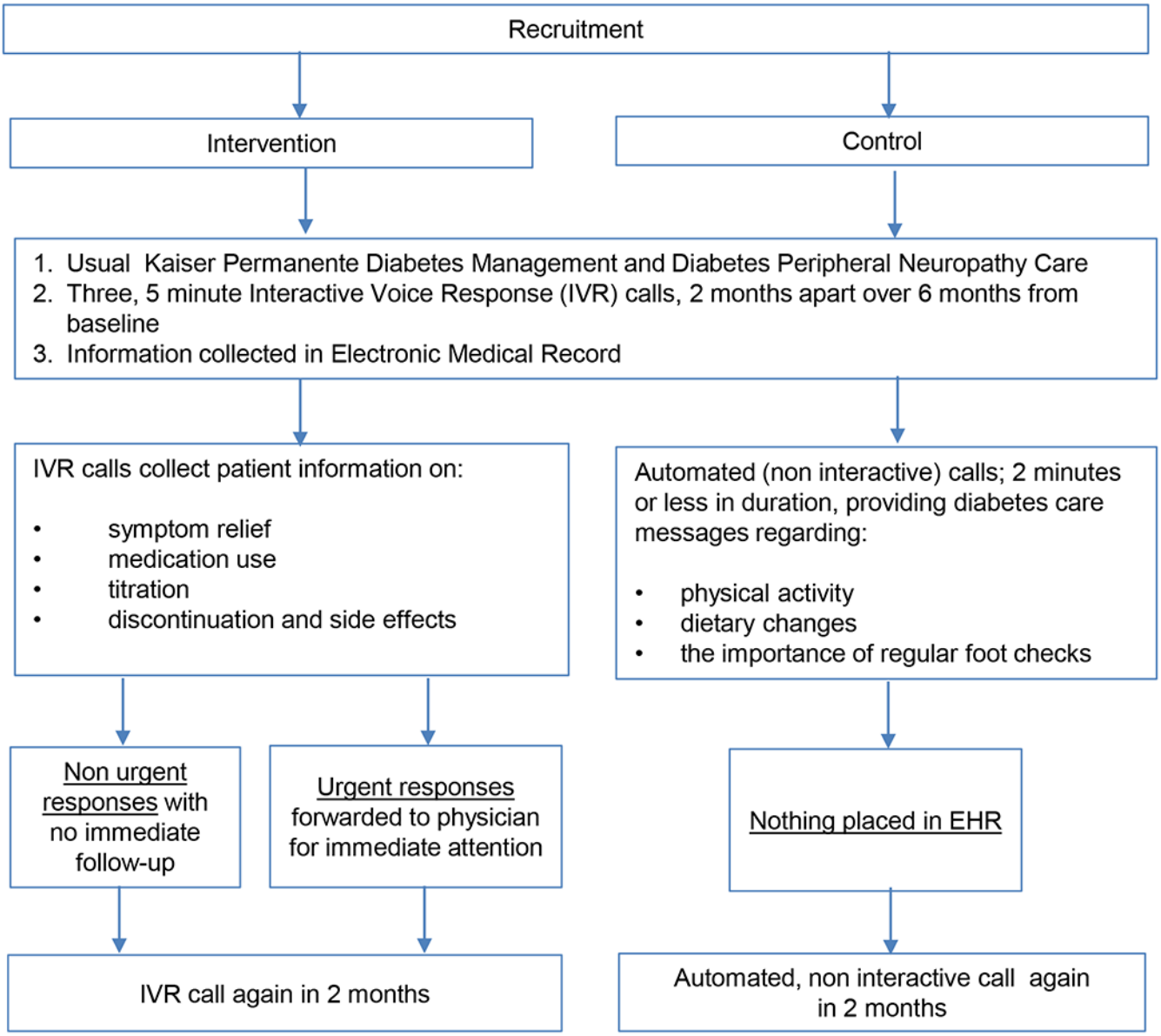

Figure 2:
Description of Study Arms

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Table 1.

Baseline Characteristics of 1,252 Patients with Complete Baseline Data

	All (N=1,252)	Control Group (N=654)	Treatment Group (N=598)	P value
Demographics				
Age (Mean ± Standard Deviation)	67.0 ± 11.7	67.1 ± 11.5	67.1 ± 12.0	0.938
Gender [N(%)]				0.497
Female	670 (53.5)	344 (52.6)	326 (54.5)	
Male	582 (46.5)	310 (47.4)	272 (45.5)	
Race/Ethnicity [N(%)]				0.541
White	709 (56.6)	368 (56.3)	341 (57.0)	
Asian	102 (8.2)	47 (7.1)	55 (9.2)	
Black	167 (13.3)	90 (13.8)	77 (12.9)	
Hispanic	246 (19.7)	132 (20.2)	114 (19.1)	
HI/PI/NA	14 (1.1)	10 (1.5)	4 (0.7)	
Unknown	14 (1.1)	7 (1.1)	7 (1.1)	
Spanish Speaker [N(%)]				0.958
Yes	77 (6.1)	40 (6.1)	37 (6.2)	
No	1,175 (93.8)	614 (93.9)	561 (93.8)	
Standardized Neighborhood Deprivation Index [N(%)]				0.810
1st quartile - least deprived (−1.45 to −0.75)	255 (20.4)	129 (19.7)	126 (21,0)	
2nd quartile (−0.74 to −0.20)	374 (29.9)	190 (29.1)	184 (30.8)	
3rd quartile (−0.19 to 0.53)	342 (27.3)	180 (27.5)	162 (27.1)	
4th quartile - most deprived (0.54 to 4.19)	267 (21.3)	147 (22.5)	120 (20.1)	
Unknown	14 (1.1)	8 (1.2)	6 (1.0)	
Diabetes Management				
Total count of A1c tests (Mean ± Standard Deviation)	2.2 ± 1.2	2.2 ± 1.2	2.2 ± 1.2	0.777
Most recent A1c prior to baseline assessment in IFCC units (mmol/mol) and DCCT units (%)				0.469
<53 (<7%)	438 (35.0)	225 (34.4)	213 (35.6)	
53-63 (7 – 8%)	420 (33.5)	232 (35.5)	188 (31.4)	
63-74 (8-9%)	170 (13.6)	83 (12.7)	87 (14.6)	
>=74 (>= 9%)	188 (15.0)	93 (14.2)	95 (15.9)	
Unknown	36 (2.9)	21 (3.2)	15 (2.5)	
Calf Pain [N(%)]				0.549
Yes	469 (37.5)	253 (38.7)	216 (36.1)	
No	698 (55.7)	355 (54.3)	343 (57.4)	
Unknown	85 (6.8)	46 (7.0)	39 (6.5)	
Shared Decision Making (range: 0-100; higher score indicates highest level of shared decision making) [N(%)]				0.945
1st quartile - low level (0.00 to 24.44)	160 (12.8)	85 (13.0)	75 (12.6)	
2nd quartile (26.67 to 48.89)	303 (24.2)	161 (24.6)	142 (23.8)	

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	All (N=1,252)	Control Group (N=654)	Treatment Group (N=598)	P value
3rd quartile (51.11 to 73.33)	326 (26.1)	166 (25.4)	160 (26.8)	
4th quartile - high level (75.56 to 100)	462 (36.9)	242 (7.0)	220 (36.9)	
Outcomes (mean + standard deviation)				
Quality of Life (range=0-1; 1 indicates best possible health)	0.655 ± 0.093	0.653 ± 0.092	0.658 ± 0.094	0.335
Pain Interference 8-Item Short Form (range=40.7-77.0; higher score indicates maximum interference)	57.3 ± 8.8	57.4 ± 8.7	57.2 ± 8.9	0.682
Sleep Disruption (range: 32-84.2; higher score indicates maximum disruption)	57.6 ± 4.1	57.6 ± 4.0	57.7 ± 4.2	0.610
Lower Extremity Functioning (range: 16.5-58.6; higher score indicates better functioning)	48.2 ± 11.5	48.1 ± 11.5	48.3 ± 11.6	0.850
Depressive Symptoms (range:38.2-81.3; higher score indicates worse symptoms)	40.0 ± 6.9	39.8 ± 6.6	40.2 ± 7.3	0.288
Patient-Provider Communication Score (CAHPS Health Plan Survey: 7 items rated on a 6-point scale, ranging from: “never” (1) to “Always” (6)): min=4; max=24; higher score indicates better communication)	20.9 ± 4.4	20.8 ± 4.4	20.9 ± 4.4	0.620

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Table 2.

Results of Primary and Secondary

Outcome Measures	Control Group		Treatment Group		Difference in Change		
Patient Reported Outcomes (Mean/%, sd)	**Baseline**	**Change from Baseline**	**Baseline**	**Change from Baseline**	**Intervention Effect (SE)**	**95% CIl**	**p value**
Change in EQ-5D[a]	0.65 + 0.1	0.024 ± 0.078	0.66 + 0.1	0.022 ± 0.080	−0.002 (0.005)	−0.01, 0.01	0.623
Change in Pain Interference	57.4 ± 8.7	−2.816 ±8.950	57.2 ± 8.9	−2.521±9.246	0.295 (0.531)	−0.75, 1.34	0.579
Change in Sleep Disruption	57.6 ± 4.0	0.470 ± 4.249	57.7 ± 4.2	0.812 ± 4.577	0.342 (0.264)	−0.18, 0.86	0.196
Change in Lower Extremity Functioning[a]	48.1 ± 11.5	1.751±10.526	48.3 ± 11.6	1.671±9.994	−0.079 (0.606)	−1.27, 1.11	0.896
Change in Depressive Symptoms	39.8 ± 6.6	−0.442±6.737	40.2±7.3	−0.904±6.634	−0.462 (0.399)	−1.24, 0.32	0.247
Clinical Care							
Change in Communication Score[b]	20.8 + 4.4	−0.006 (4.440)	20.9 ± 4.4	−0.456 (4.665)	−0.450 (0.266)	−0.97, 0.07	0.091
% Ever Achieved Minimum Effective Dose (post only, 12-months)		48%		52%	0.033 (0.031)	−0.28, 0.094	0.289

[a]Increase=improvement for EQ-5D and Lower Extremity Functioning; Increase=worsening symptoms for pain interference, sleep disruption, and depressive symptoms

[b]Increase=Improvement for Communication Measure