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Effects of type 2 diabetes behavioural telehealth interventions on glycaemic control and adherence: a systematic review

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Running head: Internet video-calls

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Summary
We reviewed the effect of behavioural telehealth interventions in type 2 diabetes on glycaemic control and diabetes self-management. The databases CINAHL, Medline and psychINFO were searched in August 2012. Peer-reviewed journal articles that were published in English with a randomised controlled trial design using a usual care comparison group, and in which the primary intervention component was delivered by telehealth, were selected. Relevant outcome measures were glycaemic control and one or more diabetes self-care area of: diet, physical activity, blood glucose self-monitoring (BGSM) or medication adherence. Interventions were excluded if they were primarily based on a telemonitoring. The search retrieved 1027 articles, from which 49 were selected based on their title and abstract. Fourteen articles (reporting 13 studies) met the eligibility criteria for inclusion. Four studies reported significant improvements in glycaemic control. Five of eight studies on dietary adherence reported significant treatment effects, as did five of eight on physical activity, four of nine on blood glucose self-monitoring, and three of eight on medication adherence. Overall, behavioural telehealth interventions show promise in improving the diabetes self-care and glycemic control of people with type 2 diabetes.

Introduction

Diabetes is responsible for the eighth-highest burden of disease in Australia. Type 2 diabetes accounts for 92% of the burden due to diabetes,[1] and affects 3.8% of Australians.[2] Glycaemic control is strongly associated with diabetes-related morbidity and mortality,[3] with higher glycaemia predicting increased physical, mental, psychological and psychosocial comorbidities. Improvements in glycaemia to the recommended glycosylated haemoglobin (HbA_{1c}) level of ≤7%[4] are significantly related to a reduced risk of micro- and macro-vascular complications.[5] Maintaining essential diabetes self-care practises that include regular physical activity, healthy eating, blood glucose self-monitoring (BGSM) and medication adherence is integral to achieving this.[4] However the majority of diabetes patients remain poorly controlled (HbA_{1c}≥8%), which indicates that regular, accessible and effective type 2 diabetes self-management support is required.

Telehealth may assist type 2 diabetes patients by improving accessibility to health care services. This may be of particular importance in rural and regional areas. Currently 26% (230,700) of Australians with diabetes live in inner regional, and 12% (110,400) in outer regional or remote areas.[6] Whilst general practitioners (GPs) are the primary care providers for patients with type 2 diabetes, only 20% of all GPs are based outside metropolitan city areas.[7] Telehealth also presents a convenient, cost-effective way for patients with mobility or motivational problems to receive regular support, including the elderly and patients with complicated diabetes.

Telehealth applications including telephone counselling, videoconferencing and educational telephone-based interventions have been favourably received with good acceptability and uptake by type 2 diabetes patients.[8] Telehealth interventions have also shown efficacy in improving psychosocial, psychological and clinical outcomes in diabetes.[9] Previous reviews of diabetes self-management telehealth interventions have reported the effect of both isolated telephone support[10] and multi-component interventions. Whilst behavioural interventions and ongoing support are acknowledged as being cornerstones for effective type 2 diabetes self-management,[11] the efficacy of behavioural telehealth interventions specifically aimed at improving glycaemic control and diabetes self-care remains unexplored.

We have therefore conducted a systematic literature review of the effects of behavioural type 2 diabetes telehealth interventions.

Methods

The EBSCOHOST research databases CINAHL (Cumulative Index to Nursing and Allied Health Literature), Medline and psychINFO were searched using the terms: (diabet* and random*) and (tele* or mobile or SMS or smart phone or video* or ehealth). There was no limit on the date of publication.

Eligible studies were peer-reviewed journal articles published in the English language that reported evaluating the effects of telehealth interventions on glycaemic control and at least one diabetes self-care outcome out of: physical activity, diet, blood glucose self-monitoring, and medication adherence. Studies had to be randomised controlled trials and included either a usual care comparison, or an active treatment control (where the telehealth condition received the same treatment). Included studies had a sample comprising adults (≥18 years) with the majority having type 2, rather than type 1 diabetes. The intervention could not primarily be telemonitoring, and must have been exclusively for diabetes management. Studies where medication titration was a major component were excluded, as intensive medication therapy would confound the effects of behavioural change on glycaemic control. Abstracts and titles were screened, and those that appeared to fulfil the eligibility criteria were retrieved (as were ones where eligibility was not able to be determined from the abstract). Backward and forward searches of retrieved articles and relevant systematic reviews were performed to identify additional potentially eligible studies.

The Cochrane Collaboration's tool for assessing risk of bias[12] was used as a marker for each study's internal validity. Assessments were performed by indicating a yes/no judgement on each of the six domains of validity, and studies deemed to have a high risk of bias were excluded from the review. Data from each study was abstracted and stored in a spreadsheet that included the study's purpose, nature of the intervention, study conditions, outcomes and results.

Results

A total of 49 full papers were examined for eligibility, and 14 articles reporting on 13 studies were included in the review. The study processes and outcomes of the included studies are summarised in Table 1.

Interventions

The majority of study interventions involved participants receiving regular telephone calls from trained staff (mainly study nurses,[13-18] but also psychologists/social workers,[19] PhD[20] and Master's[21] students). An exception was the study by Bell *et al.*[22] in which each participant was sent 30- to 60-second video messages via their mobile phone every 24 hours on diabetes self-care topics. Two studies[16,23] involved participants receiving automated telephone disease management (ATDM) calls to supplement nurses' follow-up calls. All interventions included diabetes education.

The active intervention period ranged from 5 weeks[14,18] to 12 months,[13,16,17,24] and periods for final outcome assessments ranged from 3 months[15,20,21] to 12 months post-baseline.[13,15-17,22,24] In most studies (69%), endpoint measures were taken directly post-intervention. Five studies assessed short-term maintenance,[14,15,18,22,25] with the longest interval between post-intervention and final assessments being 6 months.[22]

Glycaemic control
Four[20-22,24] of thirteen studies reported significant treatment effects on glycaemic control. Three also reported significant treatment effects on diabetes self-care.[20,21,24] Two[20,21] assessed all four self-care outcomes in addition to glycaemic control, and reported significant improvements in them all. The majority of significant results for glycaemic control were measured directly following the active intervention period, at 3 months[20,21] or 12 months.[24] In Bell *et al*.'s study,[22] significant improvements in HbA_{1c} were seen 3 months into the 6-month intervention, but were not maintained at the 6-month post-baseline assessment.

Whilst five studies reported on the dosage of intervention received by intervention group participants,[14,16,17,22,24] only two of them evaluated dosage relationships with glycaemic outcomes.[22,24] Both reported significant intervention dosage effects on glycaemic improvements. Walker *et al*.'s study[24] -- a telephone intervention offering ≥10 calls over a year -- indicated that intervention group participants completing more than five telephone calls had a significantly greater reduction in HbA_{1c}. Bell *et al*.[22] found significant between-group interactions for HbA_{1c} at the 3-month post-baseline follow-up, but no differences at 12 months post-baseline, which was 6 months post-intervention. However, further analyses revealed that "persistent viewers" (who viewed >10 video messages a month) experienced a significant reduction in HbA_{1c} of 0.6% over 12 months, compared with "early cessation" participants who did not view the videos or stopped viewing videos within 2 months post-enrolment.

Dietary adherence
Five of eight studies (63%) that assessed the effects of interventions on dietary adherence reported significant improvements.[13,20,21,24,26] In four of these, dietary improvements were found directly following the active intervention.[20,21,24,26] There was no notable distinction between the type of dietary and lifestyle intervention offered by studies reporting significant improvements in diet and ones where no significant effect was found.[14,18,25] While Kim & Oh's positive study[20] included dietitian reviews of patient meal plans, Trief *et al*.[25] used dietary goal setting as the primary focus of their telephone counselling intervention, but found no significant dietary improvements. Differences in the study populations may have accounted for the difference in results: in Trief *et al*.'s study,[25] most participants were obese, and dietary changes may have presented a significant motivational hurdle.

Physical activity
Statistically significant treatment effects were reported in five of eight studies (63%) that assessed physical activity participation.[14,19,21,24,26] Three of these[14,19,26] did not find improvements in glycaemic control. Sustained exercise can reduce insulin resistance and improve glycaemic control,[27] and most studies only tested for effects on glycaemic control immediately post-intervention. A delayed effect of increased physical activity on glycaemic control may have occurred, provided that behavioural changes were maintained. Furthermore, different types of physical activity (e.g. resistance vs. aerobic) has differential

impacts on glycaemia.[28] Measures that are sensitive to specific activity changes would help to determine the clinical value of reported improvements.

Blood glucose self-monitoring

Four of nine studies (44%) that measured BGSM found significant improvements in frequency.[16,17,20,21] Studies reporting significant effects required participants to regularly self-report their blood glucose levels to the researcher or nurse, indicating possible effects of accountability on monitoring. However, the findings should be interpreted with caution, as self-report surveys rather than objective assessments were used both for regular BGSM reports during the study and study outcome measures. Only one study[22] provided diabetes supplies at no cost to participants. The cost of increased BGSM may have been a deterrent to increasing self-monitoring in some participants.

Medication adherence

Eight studies assessed medication adherence, with only three[17,19,21] (38%) reporting significant improvements. In Walker *et al*.'s study,[24] significant improvements in medication adherence were reported on ASK-20 items, but not on items from the Morisky Adherence Scale. Only one study reported the intervention group experiencing significant improvements in glycaemia as well as medication adherence.[21] However, significant improvements in three other diabetes self-care outcome measures relevant to the present review also occurred, and those changes may have collectively influenced glycaemic improvements. The study of Walker *et al*.[24] was the only one to compare medication adherence in insulin-dependent compared with non-dependent type 2 diabetes: It found no significant difference between these sub-groups. Future studies should include analyses of changes in medication adherence within diabetes treatment sub-groups to detect any mediating effects of treatment burden.

Study quality and validity

Overall, improvements in study quality and validity of reporting are required, with internal validity being moderate at best amongst the studies. In five studies, it was unclear whether allocation was concealed,[15,19,20,21,25] presenting a risk of exaggerated treatment effects.[12] Most studies used relatively small sample sizes,[18-22,25,26] which may have resulted in difficulties detecting significant treatment effects. Trief *et al*.[25] cited individual differences between study conditions as a potential source of bias in their results. Most studies used samples comprised mainly of ethnic and socioeconomic minorities,[13,14,16,17,19,20-22,24] presenting problems for external validity.

Discussion

Considerable heterogeneity between study processes and outcomes meant that it was difficult to draw firm conclusions. However, the present review demonstrated that behavioural telehealth interventions can significantly improve both glycaemic and diabetes self-care outcomes in type 2 diabetes patients. Of the diabetes self-care outcomes that were examined, physical activity and dietary adherence most commonly demonstrated improvements in response to telehealth.

The longest study post-intervention follow-up period was only 6 months.[22] Longer intervals between post-intervention and final endpoint follow-up measures would provide a better indication of the longevity of treatment effects and enable detection of "sleeper" (delayed) effects. This may also assist with determining optimum times for booster appointments in real-world implementations of telehealth interventions.

In order to optimise the effect of telehealth for type 2 diabetes, systematic evaluations of different dosages and durations of interventions are also needed, as are studies of specific subgroups of patients (e.g. insulin dependent/non-dependent). Only two studies in the present review reported relationships between intervention exposure and clinical improvements, with both revealing stronger effects from more substantial interventions.[22,24]

The studies reviewed typically had samples of poorly controlled type 2 diabetes patients. Whilst that allows significant treatment effects to be detected, it excludes participants who may benefit from a behaviourally focused telehealth intervention. As shown in Piette *et al*.[16] and Wolever *et al*.,[19] sub-group analyses according to HbA_{1c} allow the detection of treatment effects in cohorts of participants within higher baseline HbA_{1c} ranges. Undertaking sub-group analyses may be a solution for including individuals with reasonable glycaemic control in behavioural telehealth trials for diabetes. Furthermore, a focus on community sampling, rather than recruiting primarily from diabetes outpatient clinics and/or from minority groups, would enable greater generalisability of results.

Finally, research in this field requires substantial improvements in study methodology, including blind assessment and allocation concealment. Clearer reporting of study processes and outcomes would enable methodological quality and more confident conclusions to be drawn from reviews.

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Table 1. Study characteristics [Production -- this table for the online archive]

Study	Sample characteristics (No; mean age; % female; mean baseline HbA_{1c}; mean y since diagnosis; population type)	Study conditions (1) Control condition (2) Intervention condition 1 (3) Intervention condition 2	Duration, intensity and follow-up times	Reported outcomes (relevant to review) and associated measures	Effects of interventions
Anderson, D.R. (2010)	295 (149 Usual care; 146 Intervention); NR; 58%; 8.0%; NR; mostly Hispanic or African American; Type 2 diabetes	(1) TAU (2) Unscripted calls from nurse - brief clinical measures, self-care education, BGSM review, mailed educational materials.	(2) 12 months Call intensities: (i) HbA1c ≥ 9%: weekly, (ii)<9%: biweekly, (iii)≤ 7%: monthly. Follow-up: 6 & 12 months	HbA1c: NR Diet: Brief Dietary Assessment survey (fruit and vegetable intake) Physical activity: Rapid Assessment of Physical Activity (RAPA)	**HbA1c** **NS**. 6 & 12 months post-baseline - Group x Time. **NS**. Within-group. **Diet** **N.S**. 6 & 12 months post-baseline – Group x Time. **NS**. Within-group.
Bell, A.M. (2012)	64 (33 Usual care; 31 Intervention); 58y; 45%; 9.3%; NR; mostly African American, obese; Type 1 or 2 diabetes	(1) TAU: Received glucose meter and strips, broad-band enabled cell phone and services for 6 months. (2) TAU + 30 – 60-sec video SMS's on diabetes self-care topics.	(2) 6 months SMS's: 24-hourly. Follow-up: 3, 6, 9 & 12 months	HbA1c: High performance liquid chromatography (HPLC; COBAS C 111 Analyzer) BGSM: Data upload frequency.	**HbA1c** *****3-months post-baseline – Group x time (P=.02). **NS**. 6-, 9- & 12-months post-baseline. **NS**. Within-group. **BGSM** **NS**. Group x Time. **NS**. Within-group.
Frosch, D.L. (2011)	201 (100 Usual care; 101 Intervention); 55.5y; 48.5%; 9.6%; 10y; mostly African American or Latino & obese; Type 2 diabetes	(1) TAU: Received 20-page diabetes education brochure. (2) TAU + 24-minute DVD program; booklet "Living with Diabetes" + phone coaching sessions	(2) 5 weeks ≤ five phone sessions. Session 1: ≤60 min; 2 & 3:≤30 min; 4 & 5:≤15 min.	HbA1c: HPLC Diet, exercise, BGSM, medication: Summary of Diabetes Self-Care Activities (SDSCA) Survey	**HbA1c** **NS**. Group x Time. *****Time effects across groups (P<.001). **Diet** **NS**. Group x time. *Time effects across groups (P<.001). **Exercise** ***** 6 months post-baseline – Group x Time (P=.04).

		with diabetes nurse.	Follow-up: 1 & 6 months		**NS**. Time effects across groups. **BGSM** **NS**. Group x Time. ***Time effects across groups (P=.03). **Medication** **NS**. Group x Time: (i) taking most medications, (ii) all medications. * 1 & 6 months post-baseline - Time effects across groups, (i) (P=.01), (ii) (P<.001).
Kim, H. (2003)	50 (25 control; 25 intervention); 60.3y; 70%; 8.5%; 13.7y; South Koreans, half < middle school; Type 2 diabetes	(1) TAU (2) Diabetes care booklet & daily diet log; phone calls from PhD student - continuing education, reinforcement of diet & exercise; medication recommendations & frequent BGSM. Diet recommendations mailed from Dietitian after daily diet log review.	 (2) 3 months Calls ≥ twice/wk for 1 mth; weekly for months 2 & 3. Calls, *M*=25 min. Follow-up: 3 months	HbA1c: HPLC (Variant II, Bio-Rad Hercules) Diet, exercise, blood glucose testing, medication-taking: Self-Reported Adherence Questionnaire (Kim, 1999)	**HbA1c** ***Group x Time (P=.0001). *** Within-group: intervention decline (P<.05); control increase (P<.05). **Diet** ***Group x time (P=.006). ***Within-group improvement - intervention (P<.05). **Exercise** **NS**. Group x time. **NS**. Within-group. **BGSM** ***Group x time (P=.024). ***Within-group improvement - intervention (P<.05). **Medication** **NS**. Group x time. **NS**. Within-group.
Maljanian, R. (2005)	336 (160 control, 176 intervention); 58y; 53.3%; 7.9%; NR; mostly Caucasian, overweight; Type 1 or 2 diabetes	(1) TAU: 3 diabetes education classes; individual visits with Registered Nurse & Nutritionist; collaborative care management with written evaluations and recommendations for Primary Care Provider. (2) TAU + phone calls from Research	(1) Classes= 4 hours each (2) 3 months Calls: weekly. Call 1, *M*=15-20 min; other calls, *M*=5-7 min. Follow-up: 3 & 12 months	HbA1c: HPLC (Bayer DCA 2000 Analyzer) or collected from participant's Physician BGSM: Diabetes Quality Improvement Project (DQIP) items	**HbA1c** **NS**. Group x time. **NS**. Within-group. **BGSM** **NS**. Group x time. **NS**. Within-group.

		Nurse - education & self-management skills reinforcement.			
Nesari, M. (2010)	61 (31 control; 30 intervention); 51.6y; 71.7%; 9.0%; NR; mostly Iranian, overweight; Type 2 diabetes	(1) TAU: 3-day diabetes self-care education program. (2) TAU + phone calls from Master's nursing student on health behaviours, education, & medication adjustment according to glucose levels.	(1)Each session =60 min (3/day) (2) 3 months Calls: twice/wk for 1 mth; weekly for months 2 & 3. Calls, *M*=20 min. Follow-up: 3 months	HbA1c: HPLC (Pars Azemoo) Diet, exercise, BGSM, medication-taking: Level of adherence; Self-reported questionnaire (developed by research staff)	**HbA1c** *****3 months post-baseline – intervention better. (P<.001). * Within-group decline - intervention (P<.001). **Diet** *****3 months- intervention better (P<.001). *Within-group improvement – both groups (P<.001). **Exercise** *****3 months post-baseline – intervention better (P<.001). *****Within-group increase - intervention (P<.001). **BGSM** *****3 months post-baseline – intervention better (P<.001). **NS**. Within-group. **Medication** *****3 months post-baseline – intervention better. (P=.001). *****Within-group increase – intervention (P<.001)
Piette, J.D. (2001)	272 (140 control; 132 intervention); 60.5y; 28.65%; 8.1%; NR; department of veterans affairs patients, overweight; Type 1 or 2 diabetes	(1) TAU (2) Outbound automated telephone disease management (ATDM) calls with self-assessments (BGSM readings, self-care activities, symptoms, medical care use); health promotion messages (optional) + nurse follow-up	 (2) 12 months ATDM calls: biweekly, *M*= 5- 8 min (+ promotion messages); nurse calls: weekly, *M*=29 min. Follow-up:12 months	HbA1c: NR BGSM, medication-taking (problems): NR (phone interview)	**HbA1c** **NS**. Between-groups. *****12 months post-baseline – Baseline HbA1c ≥8.0% - intervention better (P=.04); Baseline HbA1c ≥9.0% - intervention better (P=.04). **BGSM** *****12 months post-baseline – intervention better (P=.05). **N.S**. Within-group. **Medication** **NS**. Between-groups. **NS**. Within-group.
Piette, J.D. (2000)	280 (124 control; 124 intervention); 54.5y; 73%; 8.7%; NR; mostly Hispanic or Caucasian, overweight; Type 1 or 2 diabetes	(1) TAU (2) Outbound ATDM calls with self-assessments	 (2) 12 months ATDM calls:	HbA1c: NR BGSM, medication: Self-report survey questions	**HbA1c** **NS**. Group x time. **BGSM** *****12 months post-baseline - intervention better (P=.03).

		(BGSM readings, self-care, symptoms, medical care use); "health tips", diet & exercise self-care module (optional) + nurse follow-up	biweekly, *M*=5-14 min; nurse calls: weekly, *M*=20 min. Follow-up:12 months		**NS**. Within-group. **Medication** ***12 months post-baseline – intervention better (P=.003).
Sacco, W.P. (2011), Sacco, W.P. (2009)	62 (31 control; 31 intervention); 52y; 58%; 8.5%; 9.5y; mostly Caucasian, obese; Type 2 diabetes	(1) TAU (2) Phone coaching - BGSM review to identify causes of "out of range" readings; help translating broad goals into weekly implementation intentions; problem-solving; reinforcement of positive changes.	 (2) 6 months Weekly calls – 3 months; biweekly – 3 months. Initial intake call, *M*= 53.63 min; other calls, *M*= 17.38 min. Follow-up: 6 months	HbA1c: Baseline - medical records (majority HPLC; Bayer DCA 2000 Analyzer); follow-up – lab values Diet, exercise, BGSM, medication: SDSCA Survey	**HbA1c** **NS**. Group x time. **Diet** ***Group x time (P<.05). **Exercise** ***Group x time (P<.001). **BGSM** **NS**. Group x time. **Medication** **NS**. Group x time.
Sigurdardottir, A.K. (2009)	53 (25 control; 28 intervention); 60.7y; 32%; 8.0%; 8.7y; mostly overweight; Type 2 diabetes	(1) TAU (2) One face-to-face session with Nurse Educator - diabetes knowledge, dietary & exercise behaviour survey items; guided goal-setting; discussed obstacles to change; then five phone coaching sessions.	 (2) 5 weeks Face-to-face session = 1-2 h; five calls, *M*= 15-20 min. Follow-up: 3 & 6 months	HbA1c: NR Diet, exercise, BGSM: 12 Items from SDSCA Survey	**HbA1c** **NS**. Group x time. ***3 months baseline – within-group decline – both (P<.05). **NS**. 6 months post-baseline – within-group. **Diet** **NS**. Group x time. ***6 months post-baseline – within-group – intervention (P=.027). **Exercise** **NS**. Group x time. ***6 months post-baseline – within-group – intervention (P=.045). **BGSM** **NS**. Group x time. ***6 months post-baseline – within-group – intervention (P=.013).
Trief, P. (2011)	44 (13 control; 12 individual intervention; 12 couples intervention); 59.9y; 63.6%; 8.3%; 13.4y; mostly obese, all couples – 1 partner with T2D	(1) TAU: Two diabetes education sessions & meal		HbA1C: HPLC (DCA 2000 A1C Analyzer) Diet, BGSM: SDSCA Survey	**HbA1c** **NS**. Group x time. **NS**. Within-group.

		plan review by phone. (2) Individual: TAU + phone sessions on dietary goal-setting, two on emotions re. Diabetes (3) Couples: TAU + phone sessions including partner on collaborative problem-solving.	(2 & 3) 3 months Nine phone sessions. Follow-up: 3 & 6 months		**Diet** **NS**. Group x time. **NS**. Within-group. **BGSM** **NS**. Group x time. **NS**. Within-group.
Walker, E.A. (2011)	526 (264 control; 262 intervention); 55.5y; 67.1%; 8.6%; 9.2y; mostly Black and Hispanic, overweight; Type 2 diabetes	(1) TAU: Diabetes education materials mailed after randomisation. (2) TAU + phone calls from Health Educator - medication adherence, problem-solving, goal-setting, communication, planning medical visits, diet, physical activity.	(2) 12 months ≥10 calls, 4- to 6-week intervals, *M*=14.1 min. Follow-up: 12 months	HbA1c: “Dry-dot” Method (mail-out kits) Diet (number days/week following healthy eating plan); exercise (number days ≥30 min exercise); self-care: SDSCA survey; medication: Morisky Adherence Scale	**HbA1c** ***Group x time (P=.009). **Diet** ***Group x time (P<.05). **Exercise** ***Group x time (P<.05). **Medication** **NS**. Group x time.
Wolever, R.Q. (2010)	56 (26 control; 30 intervention); 53y; 77%; 8.0%; 11y; mostly African American; Type 2 diabetes	(1) TAU (2) Integrative Health coaching by phone with trained social worker/ psychology graduate coaches. Guided in creating vision of health and long-term goals. Wheel of Health used to guide conversations; received educational materials.	(2) 6 months 8 weekly calls; 4 biweekly. Final call 1 mth later. Calls, *M*=30 min. Follow-up: 6 months	HbA1c: lab values Exercise - (How many times/week exercised ≥ 15-20 minutes in past mth)” Medication: Morisky Adherence Scale, ASK-20 items.	**HbA1c** **NS**. Group x time. ***6 months post-baseline – within-group – intervention HbA1c≥7% (P=.03). **Exercise** ***Group x time (P=.026). **Medication** ***Group x time, ASK-20 survey (P=.036). **NS**. Group x time – Morisky Adherence Scale ***6 months post-baseline – within-group – intervention (ASK-20, P=.001; Morisky, P=.004)

NR, not reported
NS, not significant (*P*≥0.05)
**P*<0.05
TAU, treatment as usual