Abstract

Objective: To review the published literature on the effects of telecare intervention in patients with type 2 diabetes and inadequate glycemic control.

Design and methods: A review of randomized controlled trials on telecare intervention in patients with type 2 diabetes, and a search of electronic databases such as The Cochrane Library, PubMed, EBSCO, CINAHL, Science Direct, Journal of Telemedicine and Telecare, and China National Knowledge Infrastructure (CNKI), were conducted from December 8 to 16, 2013. Two evaluators independently selected and reviewed the eligible studies. Changes in HbA1c, fasting plasma glucose (FPG), post-prandial plasma glucose (PPG), BMI, and body weight were analyzed.

Results: An analysis of 18 studies with 3798 subjects revealed that telecare significantly improved the management of diabetes. Mean HbA1c values were reduced by $-0.54$ (95% CI, $-0.75$ to $-0.34$; $P<0.05$), mean FPG levels by $-9.00$ mg/dl (95% CI, $-17.36$ to $-0.64$; $P=0.03$), and mean PPG levels reduced by $-52.86$ mg/dl (95% CI, $-77.13$ to $-28.58$; $P<0.05$) when compared with the group receiving standard care. Meta-regression and subgroup analyses indicated that study location, sample size, and treatment-monitoring techniques were the sources of heterogeneity.

Conclusions: Patients monitored by telecare showed significant improvement in glycemic control in type 2 diabetes when compared with those monitored by routine follow-up. Significant reduction in HbA1c levels was associated with Asian populations, small sample size, and telecare, and with those patients with baseline HbA1c greater than 8.0%.
Telecare intervention with feedback by health professionals could improve the monitoring of glycemic control in patients with type 1 diabetes, which has been demonstrated by a meta-analysis of randomized trials (4). However, there is a paucity of similar data in patients with type 2 diabetes. Previous systematic reviews of telecare intervention in type 2 diabetes have assessed the usage of web-based systems (5, 6) or mobile phones (7, 8) separately to monitor diabetes care. Some of the reviews have considered telecare intervention contents, technologies, and frequencies, but they did not consider adequately the usage of combination technologies in practice, the nature of feedback receipt in telecare, the ethnic differences, etc. Some important issues that require further consideration are as follows: i) the effective feedback receipt mechanism in telecare (human calls, automated calls, or automated text message reminders); ii) the type of diabetes, type 1 or type 2 diabetes, which would benefit more from telecare in terms of the improvement of HbA1C; iii) feasibility among the Asian population. This is especially important in a country like China, with a large population of diabetic patients; however, there are few studies on telecare in the monitoring of diabetes among the Chinese population; and iv) the characteristics of patients with type 2 diabetes who benefit from telecare to a maximum extent.

The objective of this study was to conduct a qualitative and quantitative analysis of randomized controlled trials (RCTs) from published literature to assess the effectiveness of telecare in patients with type 2 diabetes and the effect on HbA1C, to identify effective feedback receiving techniques in telecare, to improve diabetes management, to provide future quantitative analyses, and to establish further research needs.

**Methods**

**Eligibility criteria**

Studies that met the following criteria were included in the meta-analysis: i) RCTs with telecare as an intervention (self-monitored transmission of glucometer data and feedback by health professionals, or automatic medical devices); ii) adult (≥ 18 years) patients with a diagnosis of type 2 diabetes; iii) comparison of standard therapies (conventional outpatient clinic intervention, no special health guidance of diabetes care by health professionals or automatic medical devices); and iv) reported outcome of HbA1C, with mean values and S.D. at baseline and at the end of the study for each group. Only English language papers were reviewed. Studies with mixed patient populations (type 1 and type 2 diabetes) or without diabetes treatment feedback were not included.

**Search strategy and study selection**

We have followed the preferred reporting items for systematic reviews and meta-analyses guidelines (9). The literature search was conducted from December 8 to 16, 2013 and the electronic databases such as The Cochrane Library, PubMed, EBSCO, CINAHL, Science Direct, Journal of Telemedicine and Telecare, and CNKI were searched. For the search string, we have combined ‘telemedicine’ or ‘telecommunications’ or ‘remote consultation’ or ‘telehealth’ or ‘rural health services’ or ‘home care services’ or ‘home nursing’ or ‘home care services’ or ‘home nursing’ or ‘therapy, computer-assisted’ or ‘web-based’ or ‘computer communication networks’ or ‘information technology’ or ‘internet’ or ‘web based’ or ‘remote consultation’ or ‘rural health services’, and ‘diabetes’ in the title, abstract, and keywords. The search was limited to human subjects and English language. Additional strategies included a search of related articles in PubMed and the bibliographies of eligible studies.

**Data extraction**

Titles and abstracts of studies identified by the electronic searches were reviewed independently by two investigators. If potentially eligible, the full text was retrieved for further review. One investigator designed the standardized data extraction form and the other reviewed it for completeness and accuracy. We have included abstracts that described an RCT of telecare intervention in patients with type 2 diabetes, with an outcome of HbA1c level. When both investigators did not agree (e.g. inclusion criteria or quality assessment), conflicts were resolved by discussing with another investigator.

We reported the redundant publications only once. For studies with more than one intervention group, we regarded the most intensive intervention as the experimental one. Intensity was defined by the number of telecommunication modes used, frequency of communication, and duration of intervention.

Extraction of literature and intervention information include: references; country of origin; study duration; number of participants at baseline and follow-up; percentage of women participants; intervention of telecare and control groups; and ways of telecare feedback (e.g. telephone calls, automatic internet-based disease management system, or short message service).
Quality assessment

The quality of data were ensured by selecting RCTs based on randomization procedure and allocation concealment (selection bias); withdrawals, dropouts, and intention-to-treat analysis (attrition bias); and masking of outcome assessors (detection bias), the three main criteria specified by Schulz et al. (10) and Jadad et al. (11) and their colleagues. We have defined three categories as follows: all quality criteria were met with a low risk of bias (A); at least one of the quality criteria was only partly met with a moderate risk of bias (B); and at least one criterion was not met with a high risk of bias (C).

Statistical analyses

Meta-analyses of the primary outcomes (absolute changes in HbA1c before and after interventions) were performed out by the DerSimonian–Laird method, using a randomized effects model, weighted mean difference (WMD). Secondary outcome data, including mean change in the BMI, body weight, fasting plasma glucose (FPG), and 2-h post-prandial plasma glucose (PPG), were pooled in meta-analysis. Heterogeneity was assessed by the Cochran’s \( Q \) and \( I^2 \) statistics, with the Z-score (Q-test) and \( \chi^2 \) statistics set at \( P<0.10 \). \( I^2 \) statistic analysis attributed the percentage variation across studies to heterogeneity rather than chance, and its values of 25, 50, and 75% represented low, moderate, and high heterogeneity respectively (12). Wherever applicable and appropriate (\( I^2 > 50\% \)), efforts were made to explain possible sources of heterogeneity among the studies by subgroup analysis. A funnel plot and the Begg’s adjusted rank correlation test for primary outcomes (HbA1c) assessed publication bias. As overall analysis showed high heterogeneity, sensitivity analyses were conducted by omitting one study and re-evaluating the pooled standardized effect sizes. Meta-analysis was carried out using the Review Manager (RevMan) version 5.2.

The exact effects of some intervention characteristics or demographics on the association with the change in HbA1c level were analyzed through meta-regression. We ran a random-effects meta-regression using the standardized mean difference estimates of HbA1c. For each meta-regression model, the adjusted \( R^2 \) indicated the proportion of between-study variance explained by the covariates. Significant clinical and/or studies variables (\( P<0.05 \)) in univariate models were also combined into multivariate meta-regression analyses. Meta regression was performed using the metan command in STATA version 12.

Results

Study selection

From 1240 citations, 99 publications were identified as potentially eligible studies, and full texts were retrieved and assessed. Out of the 99 identified citations, 18 met the inclusion criteria (Fig. 1).

Study characteristics

All the 18 eligible studies were published between 2000 and 2013, six of which were conducted in the USA, nine in Korea, and one each in Iran, Poland, and Spain. The shortest study lasted 3 months and the longest 60 months; 12 studies were of 6–12 months duration and two lasted > 12 months. The number of subjects in each study ranged from 38 to 1665. To summarize, at baseline 3798 subjects were enrolled through all studies and 2793 subjects completed the studies. All studies shared a completion rate of 73.54% and 72.66% in the telecare groups and 74.43% in the standard care group. The mean age of all participants ranged from 46 to 71 years. Ten studies (13, 14, 15, 16, 17, 18, 19, 20, 21, 22) limited inclusion criteria to participants

Figure 1

Diagram of data extraction.
with baseline HbA1c > 6.5%. The mean baseline HbA1c in the studies included in the meta-analysis ranged from 7.3 to 9.9%. Most studies reported improvement in HbA1c. Four studies (19, 22, 23, 24) scored A for quality, nine (13, 14, 15, 17, 18, 20, 25, 26, 27) scored B, and five (16, 21, 28, 29, 30) scored C. Studies included in the systematic review are listed in Table 1.

**Meta-analysis**

HbA1c at baseline had no significant heterogeneity between the telecare and standard care groups (0.06; 95% CI, −0.03 to 0.15; P=0.25). The telecare groups have demonstrated a significant reduction in HbA1c from baseline to post-intervention (−0.72; 95% CI, −0.81 to −0.63; P<0.05), whereas the standard care groups showed smaller but significant difference (−0.33; 95% CI, −0.62 to −0.04; P=0.03). Telecare was significantly different from standard care (pooled HbA1c change from baseline: (−0.54; 95% CI, −0.75 to −0.34; P<0.05), with statistical heterogeneity to the variability in effect estimate (I² = 76%; Fig. 2).

For PPG, four studies (16, 18, 27, 28) presented outcome data and the meta-analysis showed a significant reduction in telecare group compared with standard care group from baseline (−52.86 mg/dl; 95% CI, −77.13 to −28.58; P<0.05). There were nine studies (13, 16, 18, 21, 23, 27, 28, 29, 30) with FPG data that could be pooled to meta-analysis, which indicated a small but significant difference in FPG decline from baseline, favoring telecare intervention (−9.00 mg/dl; 95% CI, −17.36 to −0.64; P=0.03). The pooled reduction in FPG from baseline in the telecare and standard care groups were −10.23 and 4.51 mg/dl respectively. Outcome data about BMI were provided in four studies (16, 18, 21, 28) and used for meta-analysis, finding no significant difference between telecare and standard care groups (−0.59 kg/m²; 95% CI, −1.52 to 0.34; P=0.21). There were four studies (16, 20, 21, 22) that included weight change data; meta-analysis also showed that the telecare was not significantly different from standard care at endpoint (1.01 pounds; 95% CI, −3.31 to 5.33; P=0.65).

**Adverse effects**

Two studies (15, 16) reported hypoglycemia episodes during the trials. A study by Lim et al. (16) has shown that the hypoglycemia by a minor proportion and hypoglycemic events seemed to be higher in the telecare group than in the standard care group, with no statistical significance, whereas the major and nocturnal hypoglycemia were smaller in the telecare group (P<0.05). The study by Kim et al. (15) has indicated that the total number of symptomatic hypoglycemia episodes, the incidence of asymptomatic hypoglycemia (10.6 vs 11.1%) and nocturnal hypoglycemia (12.8 vs 11.1%) were similar in the telecare and standard care groups.

**Subgroup analyses**

To evaluate the potential source of heterogeneity, we performed subgroup analyses that included feedback

**Table 1** Characteristics of randomized controlled trials included in the meta-analysis.

<table>
<thead>
<tr>
<th>References</th>
<th>Study location</th>
<th>Duration (months)</th>
<th>Recruited/completed</th>
<th>Women (%)</th>
<th>Telecare method</th>
<th>Control</th>
<th>Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>(28) Korea</td>
<td>Poland</td>
<td>6</td>
<td>100/95</td>
<td>46.31</td>
<td>Internet-based</td>
<td>Clinic visit every 2 months</td>
<td>C</td>
</tr>
<tr>
<td>(29) Korea</td>
<td>Korea</td>
<td>30</td>
<td>80/71</td>
<td>38.75</td>
<td>Internet-based</td>
<td>Conventional office visits</td>
<td>C</td>
</tr>
<tr>
<td>(13) Korea</td>
<td>Korea</td>
<td>3</td>
<td>71/64</td>
<td>59.94</td>
<td>Internet-based</td>
<td>General diabetes education</td>
<td>B</td>
</tr>
<tr>
<td>(14) USA</td>
<td>USA</td>
<td>3</td>
<td>120/114</td>
<td>44.54</td>
<td>Automated</td>
<td>Clinic visit every 2–3 months</td>
<td>B</td>
</tr>
<tr>
<td>(30) Korea</td>
<td>Korea</td>
<td>3</td>
<td>73/1</td>
<td>46.57</td>
<td>Internet-based</td>
<td>No scheduled clinic visits</td>
<td>C</td>
</tr>
<tr>
<td>(15) Korea</td>
<td>Korea</td>
<td>3</td>
<td>100/92</td>
<td>50</td>
<td>Internet-based</td>
<td>Clinic visit at 4th and 8th week</td>
<td>C</td>
</tr>
<tr>
<td>(16) Korea</td>
<td>Korea</td>
<td>6</td>
<td>154/144</td>
<td>55.84</td>
<td>Internet-based</td>
<td>No scheduled clinic visits</td>
<td>C</td>
</tr>
<tr>
<td>(17) Iran</td>
<td>Iran</td>
<td>3</td>
<td>61/60</td>
<td>71.67</td>
<td>Telephone</td>
<td>No scheduled clinic visits</td>
<td>B</td>
</tr>
<tr>
<td>(18) Korea</td>
<td>Korea</td>
<td>3</td>
<td>50/38</td>
<td>64</td>
<td>Telephone</td>
<td>Visit every 3 months</td>
<td>B</td>
</tr>
<tr>
<td>(23) USA</td>
<td>USA</td>
<td>12</td>
<td>280/248</td>
<td>58.87</td>
<td>Automated</td>
<td>No scheduled clinic visits</td>
<td>A</td>
</tr>
<tr>
<td>(19) USA</td>
<td>USA</td>
<td>12</td>
<td>213/163</td>
<td>50.31</td>
<td>Internet-based</td>
<td>No scheduled clinic visits</td>
<td>A</td>
</tr>
<tr>
<td>(24) Spain</td>
<td>Spain</td>
<td>12</td>
<td>328/297</td>
<td>48.48</td>
<td>Telephone</td>
<td>No scheduled clinic visits</td>
<td>B</td>
</tr>
<tr>
<td>(25) USA</td>
<td>USA</td>
<td>60</td>
<td>1665/7</td>
<td>62.81</td>
<td>Internet-based</td>
<td>No scheduled clinic visits</td>
<td>B</td>
</tr>
<tr>
<td>(26) Korea</td>
<td>Korea</td>
<td>3</td>
<td>59/49</td>
<td>57.14</td>
<td>Telephone</td>
<td>Monthly care coordination</td>
<td>B</td>
</tr>
<tr>
<td>(20) USA</td>
<td>USA</td>
<td>6</td>
<td>150/137</td>
<td>NR</td>
<td>Telephone</td>
<td>Reminders of laboratory tests</td>
<td>A</td>
</tr>
<tr>
<td>(22) USA</td>
<td>USA</td>
<td>12</td>
<td>415/379</td>
<td>40</td>
<td>Internet-based</td>
<td>No scheduled clinic visits</td>
<td>C</td>
</tr>
<tr>
<td>(21) Korea</td>
<td>Korea</td>
<td>3</td>
<td>114/123</td>
<td>40.35</td>
<td>Internet-based</td>
<td>1 or 2 visits during 6 months</td>
<td>B</td>
</tr>
</tbody>
</table>

NR, not reported; SMS, short messaging service.
text messages in telecare showed no significant difference in technologies, the phone-based SMS and the internet-based indicated that feedback methods of telecare did explain each subgroup when pooling the WMD of HbA1c, which heterogeneity decreased to an insignificant level within calls influenced significantly the pooled results. The sensitivity analysis showed that the studies of automated set studies of automated calls apart from human calls as the (including automated internet text messages and SMS). We voice message from call center); and iii) automated text ii) automated calls (automated telephone of prerecorded i) human calls (interactive telephones with human inter-

methods, duration of follow-up, study location, baseline HbA1c, quality of literature, and sample size (Table 2).

Feedback methods were classified into three categories: i) human calls (interactive telephones with human intervention conducted by a healthcare provider or researcher); ii) automated calls (automated telephone of prerecorded voice message from call center); and iii) automated text (including automated internet text messages and SMS). We set studies of automated calls apart from human calls as the sensitivity analysis showed that the studies of automated calls influenced significantly the pooled results. The heterogeneity decreased to an insignificant level within each subgroup when pooling the WMD of HbA1c, which indicated that feedback methods of telecare did explain the heterogeneity. Despite the usage of different telecare technologies, the phone-based SMS and the internet-based text messages in telecare showed no significant difference in the reduction of HbA1c \( (P = 0.75, I^2 = 0\%) \). The human calls subgroup was associated with the greatest effect size \( (−1.13; 95\% CI, −1.51 to −0.75; P < 0.05) \), whereas the automated calls showed no improvement \( (−0.01; 95\% CI, −0.32 to 0.29; P = 0.94) \). We believed that human calls, by directly communicating with patients, might improve the self-management of diabetes. However, the human calls subgroup had the smallest sample size, which may have emphasized the pooled effect.

We divided HbA1c data acquisition time into 3, 6, 9, 12, and 15 months subgroups, and the differences in subgroup analyses were not significant \( (P = 0.53, I^2 = 0\%) \). These pooled results have suggested that study duration could hardly explain the study heterogeneity. Compared with the standard care groups, the telecare groups attained significant reduction in HbA1c \( (P < 0.05) \) at each time point. A sensitivity analysis of data from the studies by Graziano & Gross (14), Rodriguez-Idigoras et al. (24), and Yoon & Kim (27) altered significantly the pooled estimate of change in HbA1c within the respective subgroups, and hence, they were excluded from subgroup analysis. This could be attributed to the fact that Graziano & Gross (14) have used automated calls to execute telecare intervention and attained few reductions; Rodriguez-Idigoras et al.’s (24) study had low baseline levels of HbA1c values (7.62%), and Yoon & Kim’s (27) study had the smallest sample size with the greatest effect size.

Significant heterogeneity was found among subgroups divided by study location \( (P < 0.05, I^2 = 87\%) \), which was more obvious than that of the total pooled result \( (I^2 = 76\%) \). Although decreased significantly in each subgroup,
heterogeneity was still significant in the Asian population. Asians showed the greatest reduction in HbA1c, which might be associated with three aspects. First, all studies carried out in Asia had smaller samples (38–111 participants, average 68.4 per study) than the other two continents. Second, the studies carried out in Asia had more frequent human calls, once or twice per week, in the telecare groups. Third, the characteristics of different racial groups (North Africans, Asians, and Europeans) might have an impact on the way how people responded to telecare intervention in an unforeseen manner.

We have classified the 18 studies into three subgroups based on their HbA1c levels at baseline (7.0–7.99, 8.0–8.99, and 8.99–10.0%). The pooled effect size was −0.54 (95% CI, −0.75 to −0.34; P<0.05), and there was no significant heterogeneity in subgroup differences (I² = 35.9%). The ‘7.0–7.99%’ group showed the least effect; when we combined the other two subgroups as ‘8.0–10.0%’, the baseline HbA1c level of >8.0% was associated with significant reduction compared with those <8.0% (0.74 vs 0.33), with significant subgroup differences (P<0.05, I² = 70.5%). Our result was comparable with that obtained by Liang et al. (7) (0.6 vs 0.4).

Among the 18 RCTs included, nine that scored B for quality achieved the greatest reduction in HbA1c level, whereas studies that scored A indicated the least reduction. Significant heterogeneity was found in the subgroup of ‘rank B’ (P<0.05, I² = 85%) and among subgroups (P<0.05, I² = 79.9%). It was challenging to interpret this result; we speculated that it was mainly due to a different baseline HbA1c level, ethnicity, feedback method, publication bias, etc.

Significant heterogeneity among subgroups grouped by sample size (≤60 or >60 subjects) has been found (P<0.05, I² = 97.8%), with a pooled estimate of −0.54 (95% CI, −0.75 to −0.34) (P<0.05). Compared with studies with a sample size of more than 60, studies with a smaller sample size achieved greater reduction in the HbA1c level (−1.45 vs −0.33). This difference was greater than that obtained by Liang et al. (7) (−0.8 vs −0.4). However, the meta-analysis by Liang et al. involved patients with types 1 and 2 diabetes, which was a major confounding factor that made our results incomparable. Our results indicated that a small sample size increased the effect size, and we need more RCTs with large samples in the future, especially in Asia.

**Meta-regression analyses**

In addition, the exact effects of feedback ways, duration of follow-up, study location (or continent), baseline HbA1c, quality of literature, and sample size on the association
Asian patients, baseline HbA1c >8.0%, small sample size, and human calls-based intervention; and third, telecare based on automated calls-based showed no positive effect on reducing the HbA1c level.

Compared with the study by Montori et al. (4), meta-analysis of telecare for patients with type 1 diabetes, our study showed greater reduction in HbA1c (−0.54 vs −0.4). Our meta-analysis differed from that by Montori et al. in two aspects: inclusion of different types of diabetes, and inclusion of a small sample size (20–56 subjects) in their studies. This indicated that imbalance among the two groups could easily occur despite the randomization and may have exaggerated the effect. Another similar meta-analysis (31) studied the impact of telemedicine interventions in adolescents with type 1 diabetes, and found that the telecare group had a greater but not significant difference in reduction of HbA1c by −0.12 (95% CI, −0.35 to 0.11) compared with the standard care group. In conclusion, telecare intervention seems to be more useful for patients with type 2 than type 1 diabetes in reducing HbA1c levels.

The meta-analysis by Liang et al. (7) about the effect of mobile phone intervention for type 2 diabetes indicated changes in HbA1c levels of −0.81 (95% CI, −1.11 to −0.50), and our result was −0.67 (95% CI, −0.99 to −0.36). It is necessary to point out that ‘mobile phone intervention’ meant intervention using the mobile phones with or without internet for diabetes self-management, and hence, we pooled data from 12 studies (14, 15, 16, 17, 18, 20, 21, 23, 24, 26, 27, 30) that used a similar intervention. Compared with the study by Liang et al., we consider that our results had several strengths. First, we searched more databases and enrolled only RCTs with more participants. Second, we conducted both subgroup analysis and meta-regression analyses to verify our views. Third, we have identified carefully redundant or duplicate publications (27, 32, 33, 34, 35, 36) and reported them only once. Although telecare communication was conducted using the mobile phones, it is inappropriate to include different feedback ways (human calls, automated calls, and SMS) in the same category of telecare intervention, as the human calls have shown significantly greater pooled reduction in HbA1c than the others.

Our study had the following limitations: i) most of the studies enrolled did not report allocation concealment, due to the nature of the intervention, and it was hard to achieve double blinding, which influenced the assessment of quality evaluation; ii) funnel plots of the studies indicated significant publication bias; iii) most of the studies did not introduce researchers and patient adherence to the telecare.
intervention plan; iv) for subgroups classified by ‘duration of follow-up’, only two studies were of 9 months ‘duration, and the one study of 15 months’ duration, which might have influenced the reliability of the pooled estimate; and v) some studies failed to report the measures of variation for several continuous outcomes (BMI, PPG, body weight, blood pressure, LDL, etc.).

The results of this analysis revealed that patients who will benefit from telecare were as follows. One study (37) indicated that in women a greater frequency of blood glucose transmission resulted in a greater reduction in the HbA1c level. Similar to our results, Salzsieder & Augstein (38) have also suggested that patients with baseline HbA1c greater than 8% achieved a greater reduction in the HbA1c level at the end of the intervention. Bujnowska-Fedak et al. (28) have found that older patients with type 2 diabetes, educated, those with recently detected diabetes, and home-based patients benefited the most from telemonitoring. There was a positive association between education and ability to use the telemonitoring system without help (P=0.045). Our meta-analysis suggests that ethnic variations altered the effect of telecare intervention, and Asian subjects benefited more than North American and European populations in terms of a reduction in the mean HbA1c level. However, this conclusion might be inappropriate because only two studies from Europe were included in contrast with ten from Asia. One systematic review (39) revealed that every 1% absolute reduction in HbA1c required 23.6 h of contact between the diabetes educator and patient. A few studies have reported that telecare intervention can be linked with medical insurance, although the problem that Medicare lags behind Medicaid in reimbursement remains yet to be resolved. More studies of cost-effectiveness analysis of telecare intervention are warranted in the future.

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