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# Clinical outcomes and resource use after 24 months of insulin therapy in Turkish patients with type 2 diabetes: subgroup analysis of the TREAT study

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**Disclosure**
None.

**SUMMARY**

**Purpose:** This study evaluated levels of metabolic control, resource use and quality of life in Turkish patients with type 2 diabetes initiated on insulin in routine care. **Patients and methods:** The prospective, observational TREAT study evaluated patients from five different countries who were initiated on insulin and followed for 24 months. In this paper, we present the results of a cohort analysis specific to Turkish patients from the study. **Results:** A total of 211 patients in the Turkish multicenter cohort [male patients 50.2%, age 56.5 year ± 8.9 SD, body mass index (BMI) 30.6 kg/m$^2$ ± 5.4 SD, diabetes duration 9.7 year ± 5.9 SD] initiated insulin at baseline. Oral antidiabetic drugs had been used by 93.4% of patients prior to insulin initiation, and 65.9% had used more than one regimen. Pre-existing metformin therapy was continued by 68.7% of patients after insulin initiation. In the three most common insulin regimens, glycosylated haemoglobin ($HbA_{1C}$) declined over 24 months from 10.27% to 7.82% (long/intermediate acting), from 10.82% to 7.52% (premixed) and from 10.42% to 7.67% (basal-bolus). Less than 25% achieved a glycaemic goal of $HbA_{1C} \leq 7.0\%$ and changes in insulin dose or regimen rarely occurred. Premixed insulin regimens were associated with greatest weight gain. Hypoglycaemic episodes were reported by more patients at 3, 6 and 12 months than at baseline or at 18 or 24 months. Healthcare use increased over baseline levels in the first 6 months, but was closer to baseline levels at subsequent assessments.Patient recorded health profiles improved after initiating insulin, particularly quality of life scores related to psychological distress and pain/discomfort. Morisky scores predictive of medication adherence and treatment persistence also improved. **Conclusions:** In Turkish patients with type 2 diabetes, metabolic control remained suboptimal after initiating insulin as part of routine care even after 24 months of insulin treatment. Apparent shortcomings in routine care in most patients included a high baseline $HbA_{1C}$ because of delayed insulin initiation and an unwillingness to individualise insulin regimens.

**What's known**
The incidence of type 2 diabetes in Turkey has increased considerably over the past 10–20 years. Diabetes care is often inadequate, which is partly because of suboptimal use of insulin therapy.

**What's new**
*Post hoc* analysis of a Turkish subset of patients in the TREAT study reveals that insulin initiation is frequently delayed, by which time many patients' $HbA_{1C}$ levels greatly exceed goal levels. Within the 2-year follow-up, few patients underwent insulin titration or changes in insulin regimen.

## Introduction

The past 15 years has seen an alarming increase in the prevalence of diabetes in Turkey. The first Turkish Epidemiology Survey of Diabetes, Hypertension, Obesity and Endocrine Disease (TURDEP-I) revealed a 7.2% prevalence of diabetes in a nationally representative population in 1997–1998 (1). Although the prevalence increased to 16.5% in the 2012 successor TURDEP-II study (2), using the same diabetes definition and age composition as the original TURDEP-I study would have lowered the prevalence to 11.4% (2). The 2012 survey confirms reports of increasing diabetes prevalence by other health surveys in Turkey (3, 4). Significant policy changes with regard to diabetes management have been made in recent years in the Turkish healthcare system, including an increased emphasis on effective glycaemic control in patients and improved diabetes awareness, screening and prevention in the general population (5).

Effective control of blood glucose levels, cardiovascular risk factors and microvascular complications has been shown to be an effective means of reducing the burden of type 2 diabetes from both societal and healthcare system perspectives (6–9). This evidence has shaped the development of treatment guidelines



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and policy statements (10, 11). Control of blood glucose in type 2 diabetes is usually initiated with oral antidiabetic drugs (OADs) combined with changes in diet and physical activity (lifestyle changes). Insulin treatment is an important intervention in managing type 2 diabetes given that single-agent or combination treatments with OADs can lose effectiveness over time. The decision to initiate insulin is significant one in diabetes management and has been shown to be associated with increased healthcare expenditure on drugs, supplies, consultations and patient education (12). However, insulin initiation in patients with type 2 diabetes is often unnecessarily delayed, even when clearly indicated, resulting in suboptimal glycaemic control (13, 14). Delayed initiation of insulin has been linked to worsening diabetes complications (15, 16) and reduced effectiveness of insulin therapy (17).

The TREAT study (Treatment Factors and Costs Associated with Insulin Therapy in Patients with Type 2 Diabetes) was a prospective, observational study in patients from five countries who initiated insulin therapy as part of the normal course of care. The study was designed to investigate treatment choices, metabolic outcomes and resource use during 24 months after initiating insulin therapy (18). The study also investigated the effects of disease, region, type of care and socio-demographic variables on diabetes control and treatment choices. Clinical results from the entire cohort (18) and associated findings regarding treatment costs and resource use (19) have been previously published.

This study focuses specifically on clinical outcomes and resource use in patients from the Turkey cohort of the TREAT study, the largest regional subgroup. A single country analysis may reveal additional information to that already obtained in the main study.

## Methods

The TREAT study design was previously reported (18). Briefly, insulin-naive patients presenting within the routine course of care were initiated on insulin therapy at the time of enrolment. The aim of the study was to assess factors associated with different types of insulin therapy at baseline and subsequent changes in insulin regimens and metabolic control ($HbA_{1C}$) at 24 months. The study was conducted in Greece, Portugal, Romania, Sweden and Turkey in order to obtain a better understanding of insulin therapy across different cultural settings. Patients started insulin therapy at the time of enrolment. At intervals of 3, 6, 12, 18 and 24 months, patient data were collected according to common clinical practices in type 2 diabetes treatment, including changes in diabetes management (other than dose titrations or medication changes within the same therapeutic drug class). Use of healthcare resources [e.g. medication, self-monitoring of blood glucose (SMBG) supplies, contact with healthcare professionals or hospital admission] was also recorded. Study sites in Turkey were chosen if they treated a large number of patients, and this treatment included initiation of insulin therapy. All patients at a site that initiated insulin or who were referred to another physician for insulin initiation were invited to enrol. Because this was an observational study, insulin initiation and all subsequent treatments and observations were provided in the normal course of care. Regulatory approvals for an observational study were obtained and the protocol was reviewed by an independent ethics committee. All patients gave informed consent at the time of enrolment for the release of information. This study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki.

Patient reported outcomes based on the Morisky, Diabetes Health Profile-18 (DHP-18) and EQ5D-3L questionnaires were recorded to gain additional insight into treatment choices and outcomes. The 4-item Morisky questionnaire is designed to predict patient behaviour regarding taking medication (20) and can be used to measure attitudes that encourage adherence to insulin regimens. Morisky scores have been shown to be associated with favourable metabolic control (21, 22). The 18-item DHP-18 questionnaire assesses the following three domains: psychological distress, barriers to activity and disinhibited eating (23). The standardised health profile ED5D-3L was used to measure overall health states (24).

## Results

### Patient characteristics

Secondary and tertiary healthcare centres in Istanbul and other regions in Turkey were included in the study. Table 1 shows the characteristics of 211 patients from Turkey who enrolled in the TREAT study. Mean age was 56.5 years $\pm$ 8.9 SD and duration of diabetes was 9.7 years $\pm$ 5.9 SD. Mean body mass index (BMI) was 30.6 kg/m$^2$ $\pm$ 5.4 SD, The most common diabetes-related complications were diabetic neuropathy (37.0%) and diabetic retinopathy (30.8%). The most common macrovascular complication was coronary heart disease (25.6%). Other risk factors were common in the patient cohort, including hypertension (66.4%; defined as systolic BP $\geq$ 140 mmHg or diastolic BP $\geq$ 85 mmHg or receiving antihypertensive therapy) and hyperlipidaemia

**Table 1** Patient characteristics and significant baseline diagnoses ($n$ = 211)

| | *n* | % |
|---|---|---|
| Age, year (SD) | 56.5 (8.9) | |
| Sex (male/female) | 106/105 | 50.2/48.8 |
| Time since diagnosis of diabetes (SD) | 9.7 (5.9) | |
| Body mass index, kg/m$^2$ (SD) | 30.6 (5.4) | |
| **Macrovascular diagnoses** | | |
| Coronary heart disease | 54 | 25.6 |
| Previous myocardial infarction | 9 | 4.3 |
| Transient ischaemic attack | 4 | 1.9 |
| Peripheral arterial occlusive disease | 2 | 0.9 |
| **Microvascular diagnoses** | | |
| Diabetic neuropathy | 78 | 37.0 |
| Diabetic retinopathy | 65 | 30.8 |
| Diabetic nephropathy | 20 | 9.5 |
| **Other diagnoses** | | |
| Hypertension | 140 | 66.4 |
| Hyperlipidaemia | 131 | 62.1 |
| Previous coronary artery bypass graft | 5 | 2.4 |
| Chronic heart failure | 4 | 1.9 |
| Depression | 56 | 26.5 |
| Erectile dysfunction | 20 | 9.5 |
| Cancer | 2 | 0.9 |
| Other significant comorbidities | 7 | 3.3 |

(62.1%). More than half of the patients were taking one or more antihypertensive agents, with angiotensin receptor blockers being the most frequent (40.3%). One or more lipid-lowering agents were reported in 55.5% of patients, with statins as the most frequent class (47.4%). Antiplatelet therapy with aspirin was reported in 60.7% of patients.

## Previous diabetes control

The majority of patients had been treated with OADs at some point since diagnosis (93.4%) or had followed a diet and exercise regimen to control diabetes (72.5%). One previous treatment regimen using OADs was reported by 27.5% of patients, and 65.9% reported using more than one OAD. Metformin plus sulfonylurea was the most widely used two-agent combination [120/161 (74.5%)] and metformin plus sulfonylurea plus thiazolidinedione [38/78 (48.7%)] was the most widely used triple combination. As shown in Figure 1, most patients were still on treatment within 4 weeks of initiating insulin. Metformin was the most commonly used agent during a 2-week time interval before initiating insulin [164 (77.7%)], and 145 (68.7%) of all patients continued on metformin after initiating insulin. Sulphonylureas were the

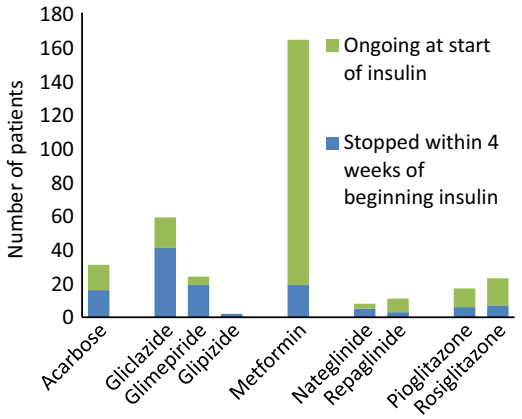


**Figure 1** Oral antidiabetic drugs used immediately before and during insulin therapy

second most widely used OAD class, but were less likely to be continued after insulin initiation. Eighty-five patients (40.3%) were taking a sulfonylurea prior to insulin and 23 (10.9%) continued the treatment in combination with insulin. The most commonly used sulfonylurea was gliclazide (28.0% before and 8.5% after initiating insulin). Patients who initiated a basal-bolus insulin regimen were less likely to remain on OAD therapy (54.5%) compared with those initiating with long/intermediate acting (86.4%) or premixed (75.7%) insulin regimens.

## Insulin regimens and metabolic control

Insulin was initiated as a premixed regimen in 115 patients (54.5%), generally on a twice-daily schedule. A long/intermediate acting regimen was used by 59 patients (28.0%), and a basal-bolus regimen was used by 33 patients (15.6%). In addition, three patients (1.4%) were initiated on insulin as a short acting only regimen, and one patient used a combination of long acting and premixed insulin formulations (Table 2). Logistic regression analysis conducted as part of the original TREAT study found no effect in Turkish patients of gender, diabetes duration, BMI, or baseline $HbA_{1C}$ on the choice of regimen (long/intermediate vs. premixed), although waist circumference had a small effect (odds ratio 1.04, p = 0.0167). Most patients had relatively poor metabolic control before initiating insulin, which improved over the 24 months of insulin therapy. The largest 24-month mean $HbA_{1C}$ reduction from baseline occurred in patients on premixed regimens (10.82–7.52%). $HbA_{1C}$ declined from 10.27% to 7.82% in patients receiving long/intermediate acting insulin and 10.42–7.67% in patients receiving basal-bolus insulin (Figure 2). $HbA_{1C}$ declined from 11.53% to 8.11% in the three patients receiving short acting insulin. Mean fasting plasma glucose levels for

**Table 2** Insulin use by regimen at study baseline ($n$ = 211)

| Insulin preparation and regimen | Number of patients, $n$ (%) | | Doses/day baseline | Mean dose (IU) baseline | Doses/day final | Mean dose (IU) final |
|---|---|---|---|---|---|---|
| Long/intermediate acting only | 59 | 28.0 | 1.1 | 21.6 | 1.2 | 22.6 |
| Premixed only | 115 | 54.5 | 2.0 | 34.5 | 2.0 | 34.3 |
| Basal-bolus | 33 | 15.6 | 4.0 | 54.5 | 4.0 | 54.6 |
| Short acting only | 3 | 1.4 | 2.7 | 39.7 | 2.5 | 51.5 |
| Other* | 1 | 0.5 | 3.0 | 60.0 | 3.0 | 60.0 |

$n$ = number of patients in study (baseline); $n$ = number of patients on each regimen. *Lantus, Humalog Mix 25.

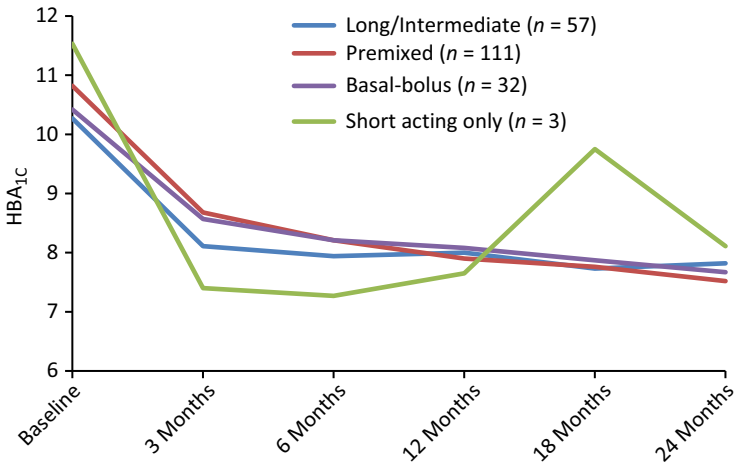


**Figure 2** $HbA_{1C}$ according to insulin regimen. $n$ = number of patients with an $HbA_{1C}$ result at baseline

the entire cohort decreased from 14.01 mmol/l (252.18 mg/dl) at baseline to 8.86 mmol/l (159.48 mg/dl) at 24 months, an improvement of −5.15 mmol/l (−92.7 mg/dl). Other factors affecting $HbA_{1C}$ at 24 months included baseline $HbA_{1C}$ and insulin dose at 24 months. Patients with $HbA_{1C}$ < 7.5% at the end of the study had a lower baseline $HbA_{1C}$ (10.12 ± 2.69 SD vs. 11.39 ± 2.77 SD) and lower insulin dose (31.7 IU ± 14.6 SD vs. 37.5 IU ± 17.3 SD) than those with $HbA_{1C} \geq 7.5\%$.

Despite the improvement in metabolic control, most patients irrespective of regimen did not attain ≤ 7.0% $HbA_{1C}$. Eight (20%), 17 (19.1%) and 6 (25%) patients who received long/intermediate acting, premixed and basal-bolus regimens, respectively, were at this goal after 24 months of insulin therapy. Withdrawal rates from the study (four patients) and loss to follow-up did not appear to differ between insulin regimens. At insulin initiation, 59, 115, 3 and 33 patients were administering, long/intermediate acting, premixed, short acting and basal-bolus regimens, respectively. At 24 months, 46, 93, 2 and 30 patients remained in the study and reported using these regimens. The four withdrawals (discontinuing insulin completely) all occurred prior to the 6-month time point and comprised three patients on premixed and one on long/intermediate acting insulin. Reasons included lack of compliance and patient decision. Only one patient changed regimens, switching from the premixed regimen to basal–bolus prior to the 12-month follow-up because of lack of efficacy. Higher mean initial daily doses were used in the basal-bolus regimens (54.5 IU ± 17.65 SD; 0.623 IU/kg ± 0.1871 SD) compared with premixed insulin only (34.5 IU ± 10.60 SD; 0.420 IU/kg ± 0.1280 SD), long/intermediate acting (21.6 IU ± 11.07 SD; 0.250 IU/kg ± 0.1096 SD) or short acting regimens (39.7 IU ± 20.79 SD; 0.571 IU/kg ± 0.3285 SD). Insulin dose changes were minimal over 24 months. No consistent changes were seen in total insulin dose or dose per body weight for any of the regimens. Mean weight gain over 24 months was greater with short acting insulin and premixed insulin (7.6 and 4.5 kg, respectively) than with long/intermediate acting or basal-bolus insulin (2.0 and 1.9 kg, respectively).

Hypoglycaemic episodes increased in frequency after beginning insulin therapy and were more frequent in the 12 months after insulin initiation than at later time points (Table 3). Overall, hypoglycaemic events were reported in 19.0% of patients at baseline, increasing to 35.9% at 3 months and decreasing over the remaining 21 months of the study. At 24 months, 22.7% of patients reported one or more hypoglycaemic episodes. Hypoglycaemic events requiring assistance were reported in 5.7% of patients at baseline, 12.6% at 3 months and 7.0% at 24 months. Hypoglycaemic events requiring hospitalisation were reported in very few patients and only during the first 6 months of therapy.

Mean values for total and LDL cholesterol decreased by 0.38 and 0.13 mmol/l from baseline to 24 months. Triglycerides were reduced by 0.32 mmol/l. There was an increase in serum creatinine from 75.83 to 84.71 μmol/l (0.857–0.957 mg/dl). There were no discernible changes in blood pressure. At baseline, 60% of patients used lipid-lowering drugs, such as statins, and up to 76% used antiplatelet medications and most continued with these after insulin initiation.

### Resource use

Initiation of insulin therapy had an effect on resource use during the study. Healthcare visits increased from baseline for various healthcare specialties (Figure 3). The frequency of healthcare visits was greatest in the first 12 months and returned to near baseline levels during the remaining 12 months. This pattern was most evident for primary care physicians and internal medicine specialists. Increased visits to nurses, dieticians, and endocrinologists were also more frequent at 3 and 6 months than at other time points. Use of SMBG test strips increased from a mean of 2.64 per week to 5.53 per week in the first 3 months of insulin therapy, with a slight decrease thereafter. Interquartile ranges suggest that most patients did not self-monitor blood glucose more than once per day (Table 4). Hospital admissions peaked in frequency during the first 6 months after initiating insulin, with a mean 0.20 visits per patient. This compares with 0.12 admissions per patient at baseline and 0.08–0.12 visits per patient at time points after 12 months (Figure 3). The increase in hospital admissions during the first 12 months was mainly because of the need for inpatient insulin titration. Hospital stays caused by long-term diabetes complications, which can include limb complications, coronary artery disease, or stroke, were longer during the 6-month baseline pretreatment period than at any time during insulin therapy.

### Patient reported outcomes

Scores from the 4-item Morisky questionnaire at each time point are shown in Figure 4A. One-third of patients at baseline had Morisky scores predictive of high adherence to insulin therapy, which increased to more than half after 3 months of insulin therapy. At 18 and 24 months, approximately two-thirds of patients had scores suggesting high levels of regimen adherence. DHP-18 standardised scores are shown in Figure 4B. Small, gradual improvements were observed in the disinhibited eating and psychological distress domains. The percentage of patients indicating the best possible score for the individual EQ5D items pain/discomfort (no pain) and anxiety/depression (not anxious) increased by up to 30% after 24 months on insulin (Figure 4C). Smaller increases were apparent in the number of patients reporting that they had no problems with usual activities and mobility. Patients' self-reported health status determined using the visual analogue scale increased by 10.6% (from 68.1% to 78.7%) after 24 months.

## Discussion

This country-specific report on the Turkish patients enrolled in the TREAT study describes further details

**Table 3** Patients with episodes of hypoglycaemia

| | Baseline | | 3 months | | 6 months* | | 12 months | | 18 months | | 24 months | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | *n* | % | *n* | % | *n* | % | *n* | % | *n* | % | *n* | % |
| Number of patients | 211 | 100.0 | 198 | 100.0 | 186 | 100.0 | 177 | 100.0 | 173 | 100.0 | 172 | 100.0 |
| **With one or more episodes** | 40 | 19.0 | 71 | 35.9 | 56 | 30.1 | 53 | 29.9 | 41 | 23.7 | 39 | 22.7 |
| Resolved alone | 39 | 18.5 | 68 | 34.3 | 55 | 29.6 | 53 | 29.9 | 41 | 23.7 | 38 | 22.1 |
| Resolved with assistance (without a hospital visit) | 12 | 5.7 | 25 | 12.6 | 22 | 11.8 | 15 | 8.5 | 9 | 5.2 | 12 | 7.0 |
| Required a hospital visit | 1 | 0.5 | 4 | 2.0 | 1 | 0.5 | 0 | | 0 | | 0 | |

*10 patients with missing data at this time point.

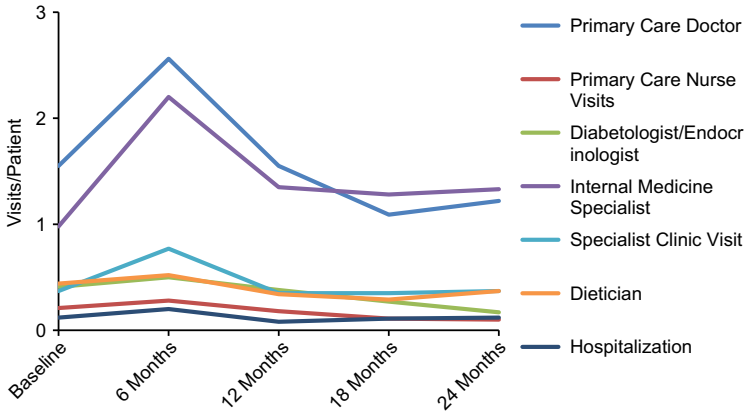


**Figure 3** Healthcare visits per patient in the Turkish cohort during the 24 months of the TREAT study. Rates are shown for the 6-month period prior to each time point

**Table 4** Frequency of self-monitoring blood glucose

| Months | Baseline | 3 | 6 | 12 | 18 | 24 |
|---|---|---|---|---|---|---|
| *n* | 210 | 197 | 186 | 177 | 173 | 172 |
| Mean | 2.64 | 5.53 | 4.22 | 3.92 | 4.51 | 4.27 |
| SD | 4.82 | 4.85 | 3.58 | 3.43 | 4.58 | 3.29 |
| Min | 0 | 0 | 0 | 0 | 0 | 0 |
| Q1 | 0 | 3 | 2 | 1 | 1 | 2 |
| Median | 1 | 4 | 4 | 4 | 4 | 5 |
| Q3 | 3 | 7 | 5 | 5 | 5 | 6 |
| Max | 35 | 30 | 20 | 20 | 30 | 20 |

to those previously reported for the entire TREAT cohort. As an observational study, TREAT was designed to record outcomes of insulin therapy in clinical practice, which may include a more representative range of patients than would be recruited to participate in a randomised controlled trial. Insulin regimens included long/intermediate acting, premixed (usually administered twice daily), basal-bolus and short acting.

Because type 2 diabetes is a progressive disease, intensification of therapy may be required if $HbA_{1C}$ exceeds target levels. Most evidence-based guidelines recommend an $HbA_{1C}$ goal of either $\leq 6.5\%$ or $\leq 7.0\%$ to allow for individualised treatment (11, 25, 26). The Society of Endocrinology and Metabolism of Turkey (SEMT) guidelines for diabetes mellitus recommend an $HbA_{1C} \leq 6.5\%$ in most patients (26). Less stringent goals, such as 7.5% or 8.5%, may be appropriate for patients with comorbidities and a limited life expectancy. In this cohort, the mean $HbA_{1C}$ at baseline was 10.6%, and most patients had likely exceeded the target $HbA_{1C}$ for a prolonged period of time before study entry. Diabetes complications, especially retinopathy and neuropathy, were also common at baseline, which suggests a significant duration of hyperglycaemia. Poor metabolic control at initiation of insulin therapy was observed in patients from other countries, who participated in the TREAT and INSTIGATE studies (18, 27) and other prospective and retrospective studies (28–35).

Insulin therapy lowered $HbA_{1C}$, and the effect was sustained over 24 months. The mean $HbA_{1C}$ at 24 months remained above the target range of $< 7\%$ appropriate for most patients. Twenty-five per cent of patients attained this goal with basal-bolus insulin, although success rates were lower with long/intermediate acting and premixed insulin. Mean $HbA_{1C}$ at 24 months was lowest in patients treated with premixed insulin (7.52%) compared with those receiving basal-bolus (7.67%) or long/intermediate acting (7.82%) insulin. In comparison, a cross-sectional survey in Turkey showed a mean $HbA_{1C}$ of 8.5% in patients treated with varying durations of insulin (36), with a similar mean duration of diabetes as patients in the cohort. Patients with type 2 diabetes treated with insulin alone included in the 2007–2010 National Health and Nutrition Examination Surveys (NHANES) in the US achieved $< 7\%$ $HbA_{1C}$ at a rate of 30.3%, compared with 25.8% reported in the 1999–2002 survey. For patients combining insulin and an OAD therapy the respective rates were 22.5% and 24.2%(37).

In the Turkish patients in the TREAT study the mean insulin dose remained little changed and only one patient switched regimens (from premixed to basal-bolus insulin). This contrasts with other countries, particularly Sweden and Portugal, where the mean dose increased over 24 months and there was a clear tendency to switch insulin regimens from long/intermediate acting to premixed or basal-bolus. In the Turkish cohort, most patients self-monitored once a day or less, suggesting that they were not trained in insulin titration or were unwilling to do

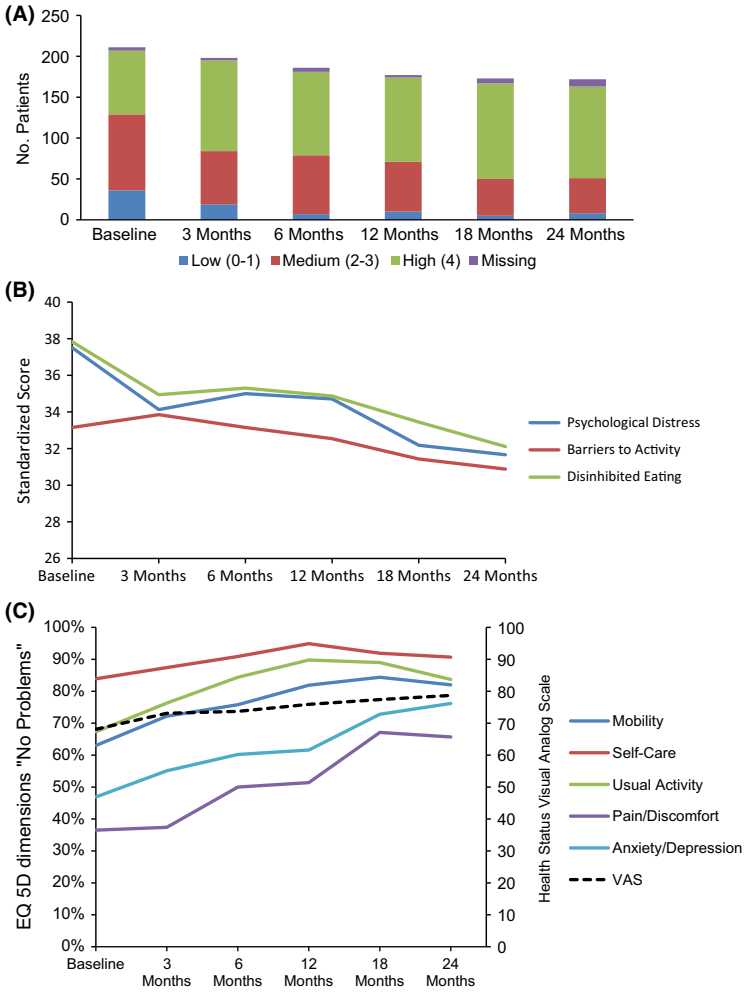


**Figure 4** Patient reported outcomes in the Turkish cohort of the TREAT study. (A) Morisky scores indicative of medication compliance; (B) Standardized Diabetes Health Profile-18 scores; (C) Percentage of patients who indicated 'No Problems' for EQ5D dimensions Mobility, Self-care, Usual Activity, Pain/Discomfort and Anxiety/Depression. Mean Visual Analog Scale (VAS) health status is also shown

so. Insulin dose titration over time has been shown to improve glycaemic control and reduce the incidence of diabetes complications (38, 39). The SEMT guidelines for type 2 diabetes recommend dose intensification and switching between regimens to maintain goal $HbA_{1C}$ (26). An American Diabetes Association and European Association for the Study of Diabetes consensus statement recommends progression of treatment if $HbA_{1C}$ remains $\geq 7\%$ after 3 months of basal insulin therapy (40). Reasons for lack of dose titration and individualisation of treatment are complex and suggest a deficiency in resources, such as an adequate number of physician visits and patient training in self-monitoring and dose titration.

Basal-bolus regimens or frequent use of postprandial short acting insulin can achieve better glycaemic control but require more frequent SMBG. As previously reported, once-daily SMBG appears to have been the practice in other countries, with the exception of the German cohort in the INSTIGATE study, where many of the patients used prandial insulin with SMBG under the direction of diabetologists (41, 42). In addition to insulin and OADs, the majority of patients in the Turkish cohort used one or more medications for risk factor reduction, including antihypertensives, lipid-lowering medications or aspirin.

Resource use, including medication, SMBG supplies and visits and telephone contacts with healthcare professionals, was generally greatest at 3 and 6 months post initiation and declined thereafter. Several patients required hospital admission for insulin titration, which resulted in an increase in the overall hospitalisation rate in the first 6 months of insulin therapy. A temporary increase in resource use or treatment costs after initiating insulin has been

widely reported in the literature. In this study, SMBG, insulin and short-term patient education costs would have likely increased resource use. Nevertheless, cost effectiveness studies have shown that adherence to treatment guidelines for glycaemic control reduces the burden of diabetes complications.

Patient reported outcomes for psychological and behavioural function and quality of life are important when determining overall treatment success and can predict a patient's willingness to begin and persist with insulin therapy. Lower Morisky scores caused by unfamiliarity with injection, doubts over treatment efficacy or other misconceptions appeared to be more prevalent at the time of insulin initiation. Morisky scores increased over the course of the study, and the absolute number of patients with responses predicting good treatment compliance was greatest at 24 months. DHP-18 psychological distress and disinhibited eating domain scores improved by several percentage points with use of insulin up to 24 months. EQ5D scores also improved, with the greatest improvements in the pain/discomfort and anxiety/depression domains. The visual analogue score of self-rated health improved by approximately 10% and was greatest after 24 months of insulin therapy.

One advantage of the TREAT study is the observational design that included type 2 diabetes patients who initiated insulin with few restrictions on eligibility, which is more representative of patients in clinical practice. However, an unknown number of patients would have had individualised glycaemic goals (10) that were less stringent than the $HbA_{1C}$ of $\leq 7.0\%$ assumed in this analysis. Adjustments for missing data were not made for patients lost to follow-up, and the possibility exists that these patients had poorer outcomes than those who remained in the study. Nevertheless, in many instances, the absolute number of patients with favourable outcomes increased over the course of the study, suggesting that missing data would not have affected the conclusions.

## Conclusions

In this representative cohort of patients with type 2 diabetes who initiated insulin therapy in the Turkish healthcare system, most did not attain metabolic control, although $HbA_{1C}$ levels remained consistently lower than at the time of insulin initiation. High baseline levels suggested that insulin therapy had been unnecessarily delayed in most patients and that the majority did not use dose titration or prandial insulin, which might have enabled more to attain goal $HbA_{1C}$. Self-rated measures of overall health, especially psychological and emotional domains, showed gradual improvement, suggesting that adherence to insulin therapy is likely to be maintained over the long term.

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