# Thailand Diabetes Registry Project: Glycemic Control in Thai Type 2 Diabetes and Its Relation to Hypoglycemic Agent Usage

Natapong Kosachunhanun MD*, Yupin Benjasuratwong MD**,
Sirima Mongkolsomlit BS***, Petch Rawdaree MD***,
Nattachet Plengvidhya MD****, Rattana Leelawatana MD*****,
Pongamorn Bunnag MD******, Thongchai Pratipanawatr MD*******,
Sirinate Krittiyawong MD********, Sompongse Suwanwalaikorn MD*********,
Chaicharn Deerochanawong MD**********, Thanya Chetthakul MD**********,
Chardpraorn Ngarmukos MD******, Chulaluk Komoltri Ph D**********

** Faculty of Medicine Chiang Mai University, ** Department of Internal Medicine, Phramongkutklao Hospital*
**** BMA Medical College and Vajira Hospital*
***** Department of Medicine, Faculty of Medicine, Siriraj Hospital Mahidol University*
****** Department of Medicine, Faculty of Medicine, Prince of Songkla University*
******* Department of Medicine, Faculty of Medicine, Ramathibodi Hospital Mahidol University*
******** Department of Medicine, Faculty of Medicine, Khon Kaen University*
********* Theptarin General Hospital*
********** Department of Medicine, Faculty of Medicine, Chulalongkorn University*
*********** Rajavithi Hospital, Department of Medicine*
************ Department of Medicine, Maharat Nakhon Ratchasima Hospital*
************* TDR research coordinator, Division of Research and Development, Siriraj Hospital, Mahidol University*

***Objective:*** *To determine the pattern of hyperglycemic agent usage in Thai type 2 diabetics (T2 DM) who attended the diabetes clinic in university and tertiary-care hospitals. The achievement of target glycemic control by various modalities of treatment was also analyzed.*

***Material and Method:*** *A cross-sectional, hospital-based diabetes registry of 8,913 type 2 diabetic patients in 11 tertiary care hospitals and medical schools was carried out from April to December 2003. Demographic data, usage of hypoglycemic agents and level of glycemic control were collected to determine the pattern of use, associated factors, and achievement of glycemic control.*

***Results:*** *Overall, 2,342(26.3%) of T2 DM achieved HbA1C less than 7%. The percentage of patients treated with metformin was 70.8%, sulfonylureas (SU) was 68.7% and insulin was 25.3%. Only 7.0% of patients received alpha-Glucosidase Inhibitor (AGI), 5.7% received ThaiZoliDinediones (TZD), 1.1% received repaglinide, and 3.2% was on diet control alone. Target glycemic control was achieved in 57.6%, 37.1%, 52%, 16.7%, 62.5%, 52% and 16.9% of patients who were on diet control only, monotherapy with SU,metformin, TZD, AGI, repaglinide and insulin,respectively. Sulfonylureas were the most commonly used drug for monotherapy. Metformin with sulfonylurea was the most common combination therapy and was used in 39.5% of patients. More than 60% of the patients treated with metformin monotherapy had body mass index (BMI) of more than 25 kg/m$^2$, as compare to less than half of patient treated with other monotherapy agent. Mean duration of diabetes in the patients treated with metformin alone was 5.9 $\pm$ 5.5 years, less than that in the SU- treated patients (8.3 $\pm$7.1 years) and also in the insulin-treated patients (14.8 $\pm$ 9.0 years). TDZ were commonly prescribed in combination with sulfonylureas and metformin in subjects with relatively longer duration of diabetes.*

***Conclusion:*** *Better treatment strategies for glucose control of diabetic patients on medical treatments should be encouraged to improve glycemic control and reduce long term complications.*

***Keywords:*** *Diabetes registry, Diabetes, Glycemic control, Hypoglycemic agents*

***J Med Assoc Thai 2006; 89 (Suppl 1): S66-71***
***Full text. e-Journal:*** *http://www.medassocthai.org/journal*

*Correspondence to : Kosachunhanun N, Department of Medicine, Faculty of Medicine, Chiang Mai University, Chiang Mai 50200, Thailand. E-mail: nkosachu@mail.med. cmu.ac.th*

Globally, the prevalence of people with diabetes is estimated to be 4.5% and predicted to increase to 6.2% by the year 2030[1]. The estimated national prevalence of diabetes in Thai adults was 9.6%, which included 4.8% previously diagnosed and 4.8% newly diagnosed diabetes[2]. Good glycemic control can prevent microvascular complications in type 2 diabetic patients[3]. Thus, in recent years, clinical recommendations throughout the world have set goals in diabetes care[4-6]. A number of antihyperglycemic agents are available in Thailand. However, there is no systematic study at a national level to evaluate the patterns of prescription of these drugs.

The objective of the present study was to determine the pattern of hypoglycemic agent usage in Thai type 2 diabetes who attended diabetes clinic in 11 university and tertiary-care hospitals nationwide.

## Material and Method

A cross-sectional, hospital-based diabetes registry of 8,913 type 2 diabetic patients in 11 tertiary care hospitals and medical schools was carried out from April to December 2003. The methods of registration and data collection were described in detail in a previous section of this issue[16]. Demographic data, use of hypoglycemic agents and level of glycemic control were collected to determine the pattern of use, associated factors, and achievement of glycemic control. Local laboratory results were used. The study was approved by the ethics committee of each participating hospitals. Written informed consent was obtained from all participants.Only 8913 adults aged 18 years or older with type 2 diabetes were included in the present study. Data were expressed as mean $\pm$ SD and percentage for descriptive analysis. Statistical analyses were performed using STATA version 8.0 (STATA corporation, College Station TX, US).

## Results

The registered number of type 2 diabetic subjects aged 18 years or older was 8,913 (3,012 males and 5,901 females). Baseline characteristics of the subjects were shown in Table 1. Mean age and duration of diabetes were 60.9 $\pm$ 11.5 and 10.5$\pm$ 7.6 years, respectively. Education more than high school was 45% and 62.3% of the patients are part of active work force. The majority of subjects were over weight or obese. Only 30.2% of subjects achieved glycemic control of HbA1c less than 7%. Mean systolic blood pressure was 143.6 $\pm$ 22.4 mmHg while diastolic was 79.1 $\pm$ 11.2 mmHg. The serum triglycerides was 153.1 $\pm$ 105.5 mg/dl, HDL-cholesterol was 53.4 $\pm$ 14.9 mg/dl and LDL-cholesterol levels was 114.4 $\pm$ 35.5 mg/dl. Eight percent of the patients had serum creatinine of more than 2 mg/dl.

The percentage of patients treated with metformin was 70.8%, SU was 68.7% and insulin was 25.3%. Only 7.0% of patients received AGI, 5.7% TZD and 1.1% repaglinide, while 3.2% (285) was on diet control alone. For the 1,506 subjects, target glycemic control was achieved in 57.6% of patients who were on diet control only, 37.1% on monotherapy with SU, 52% on metformin, 16.7% on TZD, 62.5% on AGI, 52% on repaglinide and 16.9% on insulin.

About one-third of the subjects received antihyperglycemic agent monotherapy 31% (1160). Sulfonylureas were the most commonly prescribed monotherapy 42% followed by metformin 29.2% and insulin 27.1%.

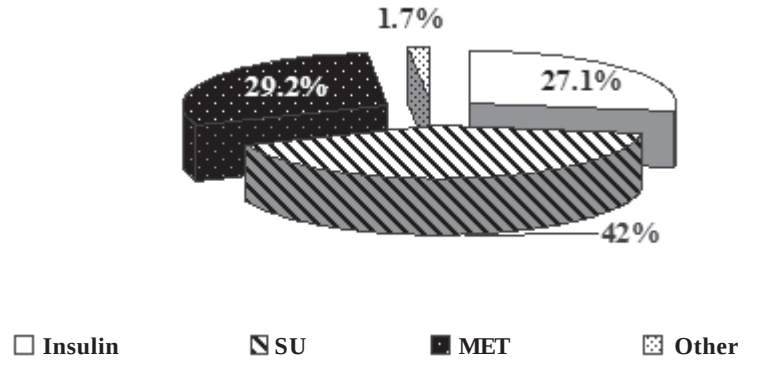
Sixty-nine percent of 6150 subjects received combination therapy. The most commonly prescribed combination therapy was (3702) SU/metformin (60.2%) followed by (640) insulin/metformin (10.4%) and (504) insulin/SU/metformin (8.2%), respectively. The percentage of patients on various antihyperglycemic agent monotherapies and combination therapy are shown in Fig. 2 and Table 3 respectively.

Among the subjects with monotherapy, repaglinide and metformin were used in patients with

**Table 1.** Baseline characteristics of adult type 2 diabetes subjects

| Characteristics | |
|---|---|
| Total number | 8,913 |
| Age (years) | 60.9 $\pm$ 11.5 |
| Male (%) | 33.8% |
| Duration of diabetes (years) | 10.5 $\pm$ 7.6 |
| Employed (%) | 63.2% |
| Educational level higher than high school (%) | 45.0% |
| Systolic blood pressure (mmHg) | 143.6 $\pm$ 22.4 |
| Diastolic blood pressure (mmHg) | 79.1 $\pm$ 11.2 |
| Body mass index (kg/m$^2$) | 25.7 $\pm$ 4.3 |
| Mean HbA1C(%) | 8.1 $\pm$ 1.8 |
| HbA1C >7% (% of patients) | 69.8% |
| Serum creatinine (mg/dl) | 1.2 $\pm$ 0.9 |
| Serum creatinine > 2 mg.dl (% of patients) | 7.8% |
| Total cholesterol (mg/dl) | 197.1 $\pm$ 42.2 |
| Triglycerides (mg/dl) | 153.1 $\pm$ 105.5 |
| HDL-cholesterol (mg/dl) | 3.4 $\pm$ 14.9 |
| LDL-cholesterol (mg/dl) | 114.4 $\pm$ 35.5 |

The data were expressed as mean $\pm$ SD or percentage




SU, sulfonylurea; MET, metformin

**Fig. 1** Percentage of patients on various antihyperglycemic monotherapy

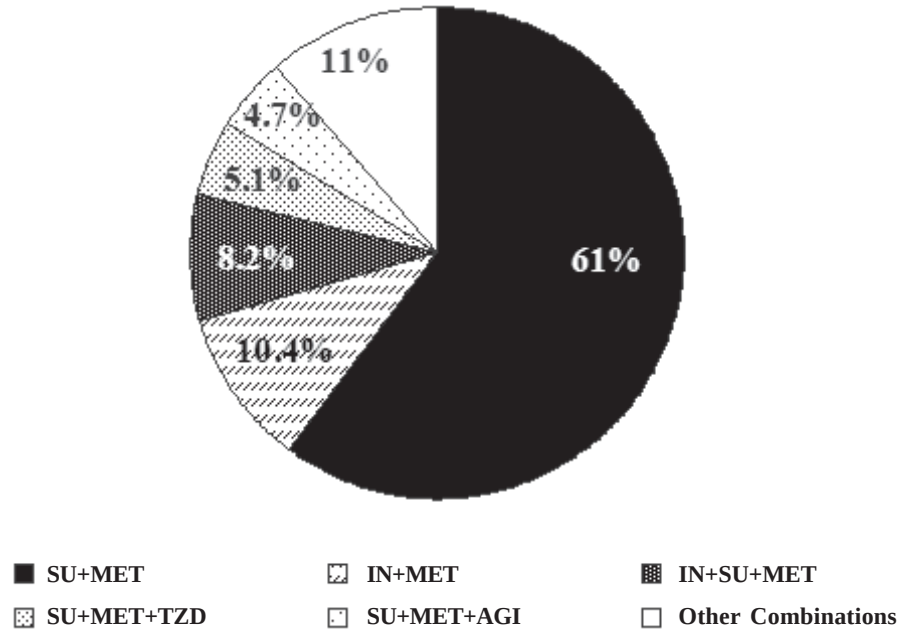



**Fig. 2** Percentage of patients on various antihyperglycemic combination therapy

relatively short duration of diabetes. Insulin was used in subjects with relatively longer duration of diabetes and with less successful diabetes control. Patients who were treated with metformin alone had a relatively higher BMI. Table 2 the shows the mean duration of diabetes, BMI in patients with diet control alone and various monotherapies.

Among subjects with combination therapy, SU and metformin combination were used in patients with the relatively shortest duration of diabetes when compared with the other combinations. The second most commonly prescribed combination was a triple therapy that added TZD to SU and metformin. Like in monotherapy, the combination of oral drugs with insulin was used in the subjects with a relatively longer duration of diabetes and with less successful diabetes control.

Table 3 showed the mean duration of diabetes and HbA1c in patients on various combination therapies.

**Table 2.** Mean duration of diabetes , HbA1c, and body mass index (BMI) in patients with diet control alone and monotherapy

| ModalitiesofTreatment | Duration of DM (years) | HbA1C (%) | BMI (kg/m$^2$) | BMI $\geq$ 25 (%) |
|---|---|---|---|---|
| Diet alone | 6.6 $\pm$ 5.3 | 6.9 $\pm$ 1.2 | 25.2 $\pm$ 3.8 | 49.3 |
| SU alone | 8.3 $\pm$ 7.1 | 7.6 $\pm$ 1.6 | 24.7 $\pm$ 4.0 | 44.8 |
| Metformin | 5.9 $\pm$ 5.5 | 7.1 $\pm$ 1.3 | 26.8 $\pm$ 4.6 | 61.7 |
| TZD | 8.5 $\pm$ 5.4 | 8.2 $\pm$ 1.4 | 26.4 $\pm$ 4.4 | 50 |
| AGI | 9.0 $\pm$ 6.8 | 7.0 $\pm$ 0.9 | 24.4 $\pm$ 4.1 | 43.8 |
| Repaglinide | 6.4 $\pm$ 7.4 | 6.9 $\pm$ 1.0 | 24.8 $\pm$ 4.2 | 56 |
| Insulin | 14.8 $\pm$ 9.0 | 9.0 $\pm$ 2.3 | 25.0 $\pm$ 4.4 | 49 |

SU, sulfonylureas; TZD, thiazolidinediones; AGI, alpha-glucosidase inhibitors

**Table 3.** Mean duration of diabetes, and HbA1c in patients on combination therapy

| Combination Therapy | % of total patients | Duration of DM (years) | HbA1C(%) |
|---|---|---|---|
| SU + MET | 39.5 | 9.7 $\pm$ 6.7 | 7.9 $\pm$ 1.6 |
| SU + MET + TZD | 3.3 | 12.4 $\pm$ 7.0 | 8.5 $\pm$ 1.5 |
| Other oral combination | 6.0 | 12.0 $\pm$ 7.0 | 8.2 $\pm$ 1.6 |
| Insulin + MET | 6.8 | 14.8 $\pm$ 7.5 | 9.2 $\pm$ 2.1 |
| Insulin + SU | 1.3 | 14.2 $\pm$ 9.1 | 9.6 $\pm$ 2.1 |
| Insulin + SU + MET | 5.4 | 12.9 $\pm$ 7.3 | 9.5 $\pm$ 2.0 |
| Other insulin combination | 3.3 | 15.9 $\pm$ 7.8 | 9.3 $\pm$ 1.8 |

SU, sulfonylurea; MET, metformin; TZD, thiazolidinediones; AGI, alpha-glucosidase inhibitors

## Discussion

The present findings showed that only a small percentage of diabetic patients could achieve glycemic target. Metformin was the most common drug used especially among obese patients. However, SUs were most commonly used for monotherapy. The most common combination regimen was SU plus metformin. Insulin therapy was used in patients with relatively longer duration of diabetes with less favorable glycemic control. TZD were commonly used in combination with SU and metformin in the subjects with relatively a longer duration of diabetes and were rarely used as monotherapy.

Evidence from randomized controlled studies shows a relationship between HbA1c and development of microvascular and macrovascular disease[3,7]. The majority of patients involved in the present study had unsatisfactory glycaemic control that may lead to diabetes complications. The gap between guidelines and current practice was similar to earlier findings in other countries[8-10].

The UKPDS[3] reported that glucose lowering with oral drugs was effective in the protection against vascular complications. It also concluded that using metformin in overweight diabetic subjects was associated with better cardiovascular outcomes, supporting the primary use of the drug in overweight people with type 2 diabetes[11], and probably in all people with type 2 diabetes. The common use of metformin, especially in overweight subjects, was probably influenced by the results of UKPDS. However, SUs were still the most commonly prescribed agent for monotherapy in the present study.

With long-term familiarity, proven benefit, known side effects and low cost, sulfonylureas, metformin, and insulin are still the standard treatments of type 2 diabetes in Thailand. Alpha-glucosidase inhibitors and repaglinide may be less efficacious than SUs[12] and are considerably more expensive. The pattern of oral drug use in the present study may be influenced by these factors.

The natural history of type 2 diabetes is progressive islet β-cell failure resulting in worsening glycemic over time despite continuous use of oral antihyperglycemic agents. Insulin remains the only glucose-lowering therapy that can maintain good blood glucose control[13]. However, only a minority of patients with longer duration of diabetes in the present study used insulin therapy. This might reflect the problems of underusage or delay in starting insulin therapy in the authors' practice.

Use of TZDs as monotherapy or as a part of combination therapy could improve glycemic control. TZDs also have been shown to reduce various surrogate markers of macrovascular complications of type 2 diabetes that confer cardiovascular benefit[14]. The earlier use of TZDs in type 2 diabetes has the potential to minimize severe disease sequelaes[15]. However, use of TZDs as monotherapy was rare in the present study. TZDs were commonly used in combination with SU and metformin in subjects with relatively longer duration of diabetes, probably to avoid insulin treatment.

The data presented in the present study had limitations. The subjects of the present study were limited to the patients in diabetes clinics in university and tertiary-care hospitals. Therefore the patterns of antihyperglycemic usage may be different from other settings. In addition, the present study did not address the duration of each antihyperglycemic drugs used. However, this large multicenter study should give some information of glycemic control and patterns of antihyperglycemic drug usage in diabetic patients in Thailand.

Better treatment strategies for glucose control of people with diabetes should be encouraged to improve glycemic control and reduce long term complications.

**Acknowledgement**

This study was supported by the Health Systems Research Institute, Thailand and the Endocrine Society of Thailand. The authors wish to thank staff and nurses in every center for their contribution. Lastly, the authors wish to thank our senior consultants Prof. Sathit Vannasaeng and Prof. Gobchai Puavilai for their invaluable advice.

**References**

1. Wild S, Roglic G, Green A, Sicree R, King H, Wild S. Global prevalence of diabetes: estimates for the year 2000 and projections for 2030. Diabetes Care 2004; 27: 1047-53.
2. Aekplakorn W, Stolk RP, Neal B, Suriyawongpaisal P, Chongsuvivatwong V, Cheepudomwit S, et al. INTERASIA Collaborative Group. The prevalence and management of diabetes in Thai adults: the international collaborative study of cardiovascular disease in Asia. Diabetes Care 2003; 26: 2758-63.
3. Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). UK Prospective Diabetes Study (UKPDS) Group. Lancet 1998; 352: 837-53.
4. IDF Clinical Guidelines Task Force. Global guideline for Type 2 diabetes.Brussels:International Diabetes Federation, 2005.
5. Canadian Diabetes Association Clinical Practice Guidelines Expert Committee.Canadian Diabetes Association 2003 Clinical Practice Guidelines for the Prevention and Management of Diabetes in Canada.Canadian Journal of Diabetes 2003; 27: S37-42.
6. American Diabetes Association. Clinical practice recommendation: standard of medical care in diabetes. Diabetes Care 2005; 28(Suppl 1): S4-36.
7. The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. The Diabetes Control and Complications Trial Research Group. N Engl J Med 1993; 329: 977-86.
8. Beaton S, Nag S, Gunter M, Gleeson J, Sajjan S, Alexander C. Adequacy of glycemic, lipid, and blood pressure management for patients with diabetes in a managed care setting. Diabetes Care 2004; 27: 694-8.
9. Eliasson B, Cederholm J, Nilsson P, Gudbjornsdottir S. for the Steering Committee of the Swedish National Diabetes Register. The gap between guidelines and reality: type 2 diabetes in a national diabetes register 1996-2003. Diabet Med 2005; 22: 1420-6.
10. Chuang LM, Tsai ST, Huang BY, Tai TY. DIABCARE (Taiwan) Study Group. The current state of diabetes management in Taiwan. Diabetes Res Clin Pract 2001; 54: S55-65.
11. Effect of intensive blood-glucose control with metformin on complications in overweight patients with type 2 diabetes (UKPDS 34). UK Prospective Diabetes Study (UKPDS) Group.Lancet 1998; 352: 854-65.
12. Van de Laar FA, Lucassen PL, Akkermans RP, Van de Lisdonk EH,Rutten GE,Van Weel C. Alpha-glucosidase inhibitors for patients with type 2 diabetes: results from a Cochrane systematic review and meta-analysis.Diabetes Care 2005; 28: 154-63.
13. Marre M. Before oral agents fail: the case for starting insulin early. Int J Obes Relat Metab Disord 2002; 26(Suppl 3): S25-30.
14. Viberti G. Rosiglitazone:potential beneficial impact on cardiovascular disease.Int J Clin Pract 2003; 57: 128-34.
15. Zimmet P. Addressing the insulin resistance syn-

drome. A role for the thiazolidinediones. Trends Cardiovasc Med 2002; 12: 354-62.
16. Rawdaree P, Ngarmukos C, Deerochanawong C, Suwanwalaikorn S, Chetthakul T, Krittiyawong S, et al. Thailand diabetes registry project: clinical status and long term vascular complications in diabetic patients. J Med Assoc Thai 2006; 89 (Suppl 1): S1-9.

## *โครงการลงทะเบียนผู้ป่วยเบาหวานในประเทศไทย: การใช้ยาเพื่อควบคุมระดับน้ำตาลของผู้ป่วยเบาหวานชนิดที่สองในประเทศไทยและปัจจัยที่เกี่ยวข้อง*

***ณัฐพงศ์ โฆษชุณหนันท์, ยุพิน เบ็ญจสุรัตน์วงศ์, สิริมา มงคลสัมฤทธิ์, เพชร รอดอารีย์, ณัฐเชษฐ์ เปล่งวิทยา, รัตนา ลีลาวัฒนา, พงศ์อมร บุนนาค, ธงชัย ประฏิภาณวัตร, สิริเนตร กฤติยาวงศ์, สมพงษ์ สุวรรณวลัยกร, ชัยชาญ ดีโรจนวงศ์, ธัญญา เชฏฐากุล, ฉัตรประอร งามอุโฆษ, จุฬาลักษณ์ โกมลตรี***

***วัตถุประสงค์****: เพื่อศึกษารูปแบบของการใช้ยาลดระดับน้ำตาล,การบรรลุเป้าหมายของการรักษาและปัจจัยที่เกี่ยวข้องในผู้ป่วยเบาหวานชนิดที่สองที่เป็นผู้ใหญ่ ที่มารับการรักษาที่คลินิกโรคเบาหวานของโรงพยาบาลมหาวิทยาลัย และโรงพยาบาลศูนย์*

***วัสดุและวิธีการ****: การศึกษานี้เป็นแบบภาคตัดขวางโดยการลงทะเบียนผู้ป่วยเบาหวานชนิดที่สองที่มารับการรักษาที่คลินิกเบาหวานของโรงพยาบาลระดับตติยภูมิทั้งหมด 11 แห่งจำนวนทั้งสิ้น 8,913 คน มีการเก็บข้อมูลด้านประวัติ, การตรวจร่างกาย, บันทึกการใช้ยาและการตรวจเลือดเพื่อนำมาวิเคราะห์หารูปแบบของการใช้ยาลดระดับน้ำตาลที่สัมพันธ์กับระดับการควบคุมระดับน้ำตาลและปัจจัยที่เกี่ยวข้อง*

***ผลการศึกษา****: มีผู้ป่วยเพียง 23%ที่สามารถควบคุมระดับ HbA1c ได้ต่ำกว่า 7% มีจำนวนผู้ป่วยที่ใช้เมทฟอร์มิน, ซัลโฟไนล์ยูเรีย,และ อินสุลิน เป็นจำนวนทั้งสิ้น 70.8%, 68.7%, และ 25.3% ตามลำดับ มีผู้ป่วยเพียง 7.0%, 5.7%, และ 1.1% ที่ใช้อัลฟา-กลูโคสิเดสอินฮิบิเตอร์, ไทเอโซลิดีนไดโอนและเรพาร์กลิไนด์ตามลำดับ มีผู้ป่วย 3.2% ที่ใช้การควบคุมอาหารเพียงอย่างเดียวในการควบคุมโรคเบาหวาน การบรรลุเป้าหมายที่ระดับ HbA1c ได้ต่ำกว่า 7% พบ 57.6%, 37.1%, 52%, 16.7%, 62.5%, 52% และ 16.9% ในผู้ป่วยที่ใช้การควบคุมอาหาร, ใช้เมทฟอร์มิน, ไทเอโซลิดีนไดโอน, อัลฟา-กลูโคสิเดสอินฮิบิเตอร์, เรพาร์กลิไนด์และอินสุลินตามลำดับ ซัลโฟไนล์ยูเรียมีการใช้มากที่สุด (42%) ในผู้ป่วยที่ใช้ยาเพียงชนิดเดียวในการรักษา ในผู้ป่วยที่ใช้ยาร่วมกันในการรักษามีการใช้ซัลโฟไนล์ยูเรียร่วมกับเมทฟอร์มินมากที่สุด (61%) ผู้ป่วยที่ใช้เมทฟอร์มินมักมีดัชนีมวลกายสูงกว่า 25 ก.ก./ม.$^2$ (61.7%) เมื่อเทียบกลุ่มผู้ป่วยที่ใช้ยาลดน้ำตาลตัวอื่น (น้อยกว่า 50%) ค่าเฉลี่ยของระยะเวลาของการเป็นเบาหวานในผู้ป่วยที่ใช้เมทฟอร์มินน้อยกว่าผู้ที่ใช้ซัลโฟไนล์ยูเรียหรืออินสุลิน (5.9 $\pm$ 5.5 ปี เทียบกับ 8.3 $\pm$7.1 ปี,หรือ 14.8 $\pm$ 9.0 ปี) ไทเอโซลิดีนไดโอนมักใช้ร่วมกับยาชนิดอื่นโดยเฉพาะร่วมกับซัลโฟไนล์ยูเรียร่วมและเมทฟอร์มินในผู้ป่วยเบาหวาน ที่เป็นมานาน*

***สรุป****: ควรมีแนวปฏิบัติของการใช้ยาควบคุมระดับน้ำตาลสูงในผู้ป่วยเบาหวานชนิดที่2 ที่ดีกว่า เพื่อปรับปรุงการควบคุมระดับน้ำตาลในเลือดและลดภาวะแทรกซ้อนระยะยาว*