How to reduce hypoglycemia in treating patients with diabetes

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Iatrogenic hypoglycemia

- It is a problematic obstacle to treat diabetes mellitus both in type 1 and type 2
- The rate of hypoglycemia
  - DCCT (Type 1)
    - Severe hypoglycemia : 65 % patients over 6.5 yrs
    - Other studies: Symptomatic hypoglycemia-twice per week, severe hypoglycemia-at least once per yr
  - UKPDS (Type 2)
    - 3.3 % in SU group vs. 11.2% in insulin Tx over 6 yrs
    - Roughly 10% of T1DM from many studies

Hypoglycemia related micro- and macro-vascular complications

UKPDS f/u: Legacy effect

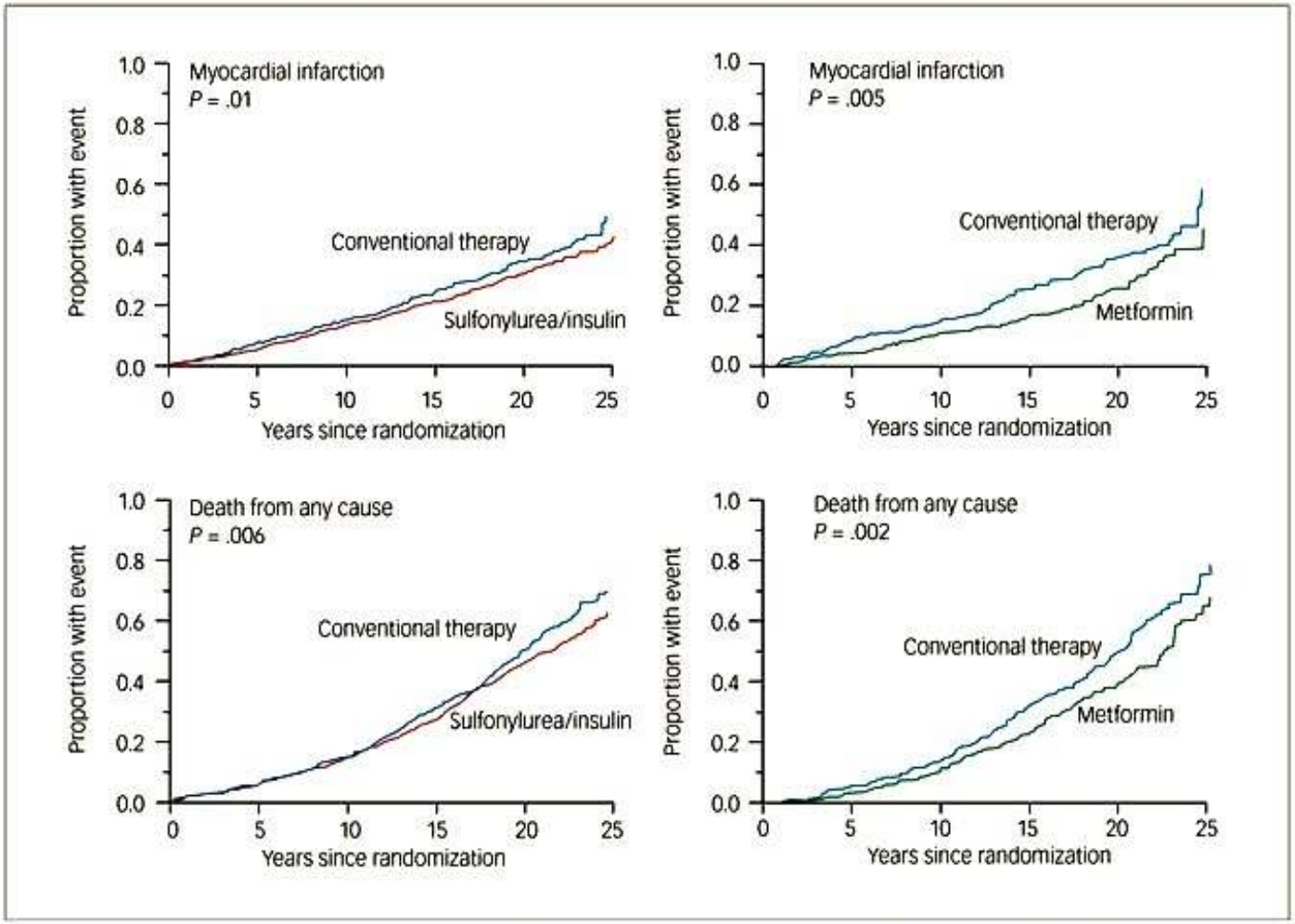


Figure 1. MI and mortality outcomes by glucose-lowering treatment assignment in the long-term follow-up of the UKPDS (United Kingdom Prospective Diabetes Study). Adapted with permission from: Holman RR, Paul SK, Bethel MA, Matthews DR, Neil HA. 10-year follow-up of intensive glucose control in type 2 diabetes. *N Engl J Med.* 2008;359(15):1577-1589.[18]

ACCORD, ADVANCE, VADT 연구

	ACCORD[1]	ADVANCE[2]	VADT[3]
디자인	정상 당화혈색소 6.0%미만을 목표로 하는 엄격한 혈당 조절(엄격한 치료군)이 당화혈색소 7.0-7.9%를 치료 목표로 하는 환자(고식적 치료군)보다 심혈관질환의 발생을 감소시킬 수 있는가를 결정하기 위한 임상연구	당화혈색소를 6.5% 이하로 엄격히 조절하는 것이 주요 혈관질환에 어떠한 영향을 미치는 지를 평가하기 위한 임상연구	7.5년간 미국에서 시행된 임상연구로 고위험군 환자 (심혈관질환 병력이 있는 환자 40% 포함)의 엄격한 혈당관리가 심혈관질환 위험을 낮출 수 있는지 관찰
결과	**고식적 치료군에 비해, 3.5년간 당화혈색소 정상범위로 조절한 엄격한 치료군의 사망률이 증가하였으며, 주요 심혈관질환 발생에 유의한 감소가 없었음**	**엄격한 당화혈색소 조절은 주요 대혈관질환 발생위험도에 유의한 영향을 미치지 않음**	**엄격한 혈당관리가 심혈관질환 발생률에는 유의한 감소효과를 나타내지 못했음**

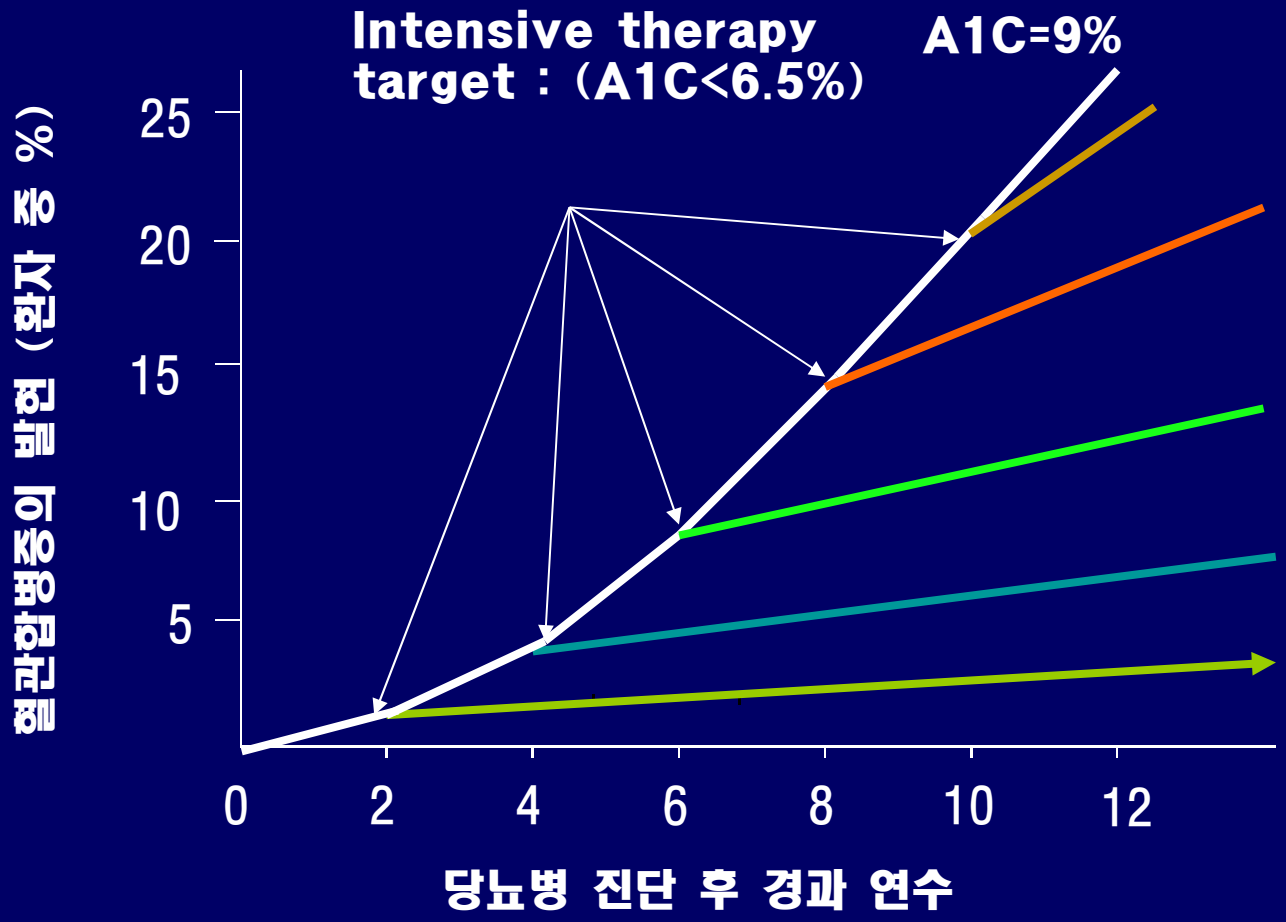
1. The Action to Control Cardiovascular Risk in Diabetes Study Group. N Engl J Med 2008;358(24):2545-59.
2. The ADVANCE Collaborative Group. *N Engl J Med* 2008;358(24):2560-72.
3. Duckworth W et al. N Engl J Med 2009;360:129-139

ACCORD: severe hypoglycemia (%)

	Intensive therapy N (%)	Conventional therapy N (%)	p
Need assistance	830 (16.2)	261 (5.1)	<0.001
Need medical intervention	538 (10.5)	179 (3.5)	<0.001

집중치료군 (2.8 *vs* 1.3%/ yr) 과 전통치료군 (4.9 *vs* 1.1%/ yr) 모두에서, **중증 저혈당이 발생한 환자는 그렇지 않은 환자와 비교하여 사망률의 증가**가 나타남

Intensive glycemic control & Macrovascular complication



Lebovitz HE. J Indian Med Assoc 2008;106(11):724-26.

How to reduce hypoglycemia ?

- Behavioral approach : Detection
  - Frequent glucose monitoring
    - SMBG
    - Continuous glucose monitoring system
- Life style modification
  - Eating habit
  - Time of exercise
- U health care system : integration
- Consider changing treatment options
  - Sulfonylurea based regimen
  - Insulin based regimen

Behavioral approach : Detection

- Self Monitoring Blood Glucose
- Continuous Glucose Monitoring System
  - Glucose variability control

- In T1DM: SMBG 3 or more times per day for type 1 diabetes
- In T2DM: no specific recommendation

By ADA guideline

- Forearm glucose rises more slowly and less high after a small meal
- Thigh and forearm glucose levels fall lower than does fingertip glucose after exercise

Self-monitoring Blood Glucose (SMBG)

Association of SMBG and glycemic control in diabetic patients from an integrated health plan (Kaiser Permanente Northern California)

Observational study involving two large cohorts of patients:

16,091 patients initiating SMBG

15,347 ongoing users of SMBG

Greater SMBG frequency among new users was associated with a decrease in HbA_1c (0.23% to 0.42%) regardless of diabetes therapy ($p<0.0001$) with diminishing returns after ≈ 3 strips per day

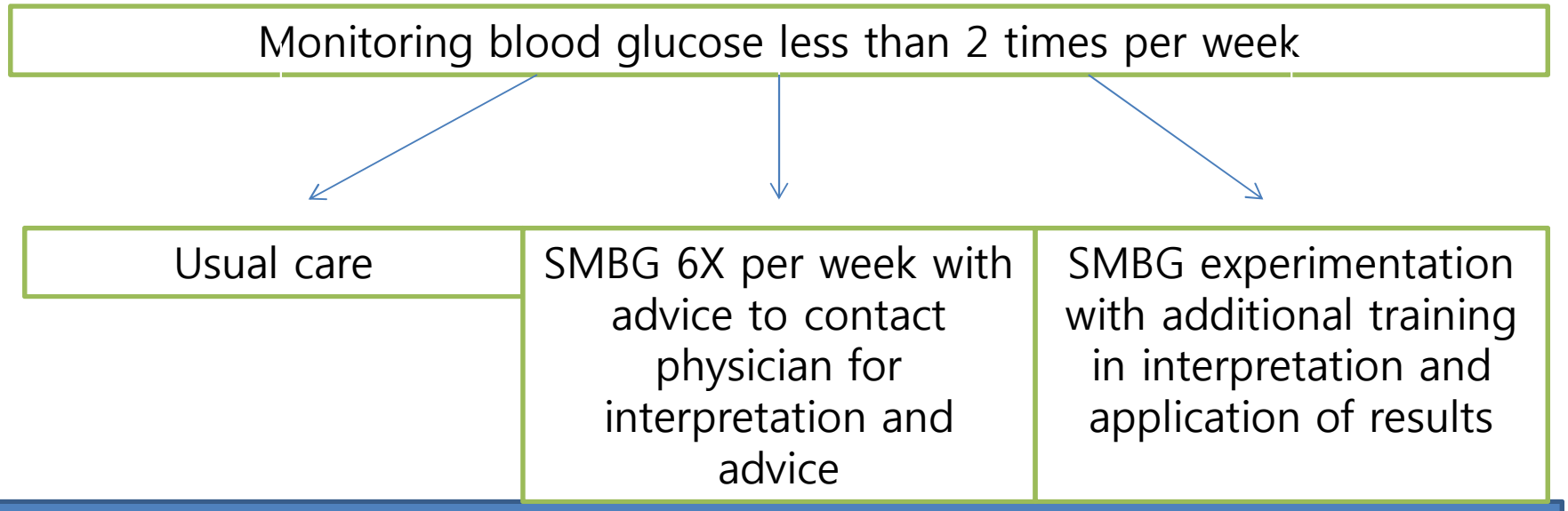
Among prevalent users, HbA_1c improved by only 0.16% and 0.12% among OHA-only and insulin-treated patients respectively ($p<0.0001$) over 3 years by increasing SMBG by one strip per day with diminishing returns with changes larger than 2 to 3 strips per day

Karter AJ, et al. *Diabetes Care* 2006;29:1757-1763

Self-monitoring Blood Glucose (SMBG)

Impact of self monitoring of blood glucose in the management of patients with non-insulin treated diabetes: open parallel group randomized trial Farmer A, et al. *BMJ* 2007

453 patients with non-insulin treated type 2 diabetes for median duration of 3 years with mean hemoglobin A_1c of 7.5%



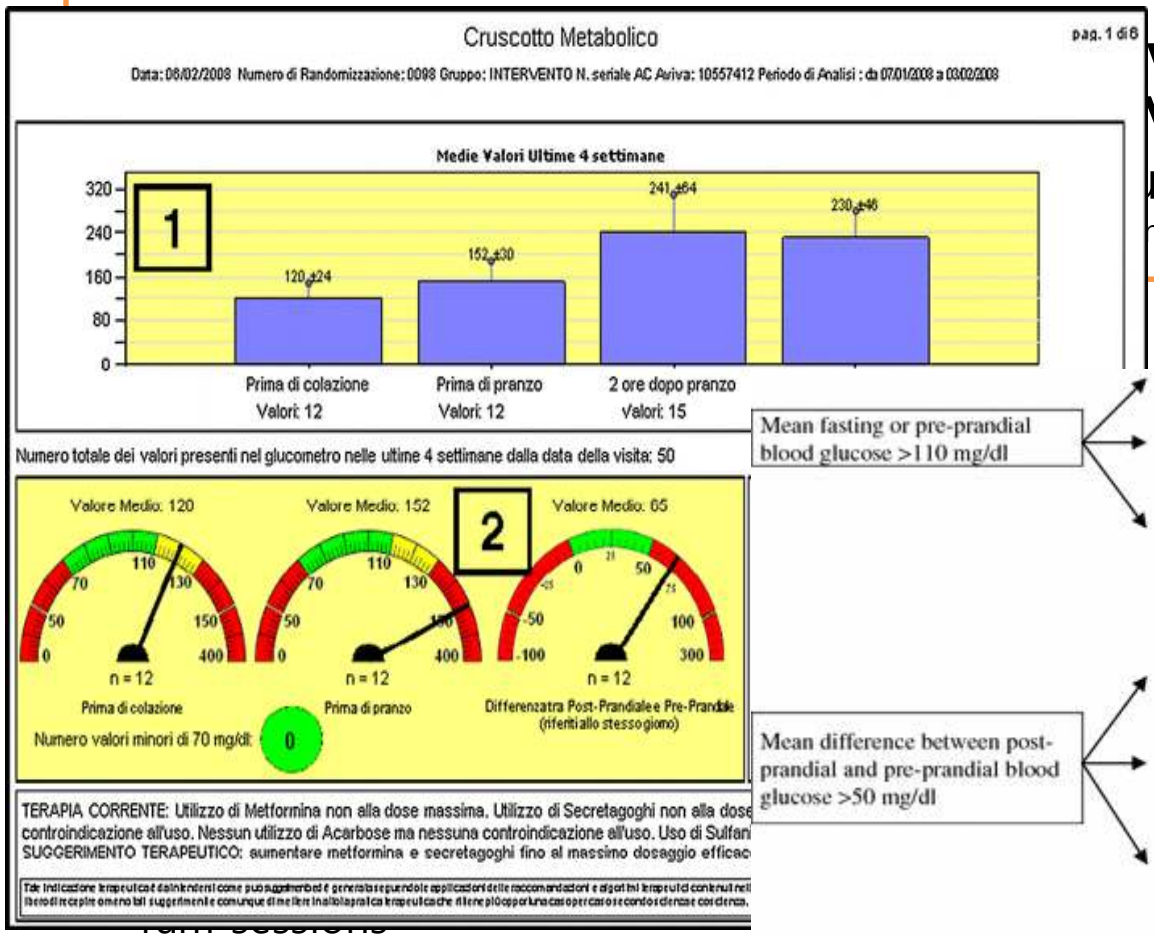
At 12 months the differences in HbA_1c level between the three groups were not statistically significant (p=0.12): 0.14% vs. 0.17%

Prospective, randomized trial on intensive SMBG management added value in non-insulin-treated T2DM patients (PRISMA): a study to determine the effect of a structured SMBG intervention

Marina Scavini[1], ,,,,,,,,Domenico Cucinotta[12]

	ISM group	AC group
Measurements of capillary glucose at fixed times	12 Measurements per week for 1 year (i.e., 4-point daily profile, 3 times per week for 1 year)	12 Measurements during the week before V3 and V5 (i.e., 4-point daily profile, 3 times during the week before V3 and V5)
Additional discretionary capillary glucose measurements	50 every 3 months	26 for one year
Standard educational program sessions	Yes	Yes
Structured SMBG data available to the patient to guide lifestyle changes	Yes	No
Structured SMBG data available to the investigator to adjust diabetes medications	HbA1c *and* SMBG data	HbA1c *only*

ve SMBG management
M patients (PRISMA): a
ured SMBG intervention
hotta[12]



AC group

Mean fasting or pre-prandial blood glucose >110 mg/dl

- If not treated with Metformin → Metformin
- If treated with Metformin → Intensify Metformin treatment to 2-2.5 g/day
- If already treated with maximum dose of Metformin (or this is contraindicated or not tolerated) → Add a Thiazolidinedione (TZD) up to the maximum dose

Mean difference between post-prandial and pre-prandial blood glucose >50 mg/dl

- If not treated with Repaglinide or a Sulfonylurea (SU) → Add Repaglinide or SU
- If treated with Repaglinide or a SU → Intensify Repaglinide or SU up to the maximally effective dose
- If already treated with maximum dose of Repaglinide or SU (or these are contraindicated or not tolerated) → Acarbose or TZD according to their tolerability

Yes

More than 3 blood glucose values <70 mg/dl

A mean negative difference between post-prandial and pre-prandial blood glucose values

- If treated with a SU → Reduce the dose of the SU by 50% **or** Stop the SU **or** Switch from SU to Repaglinide

Hb

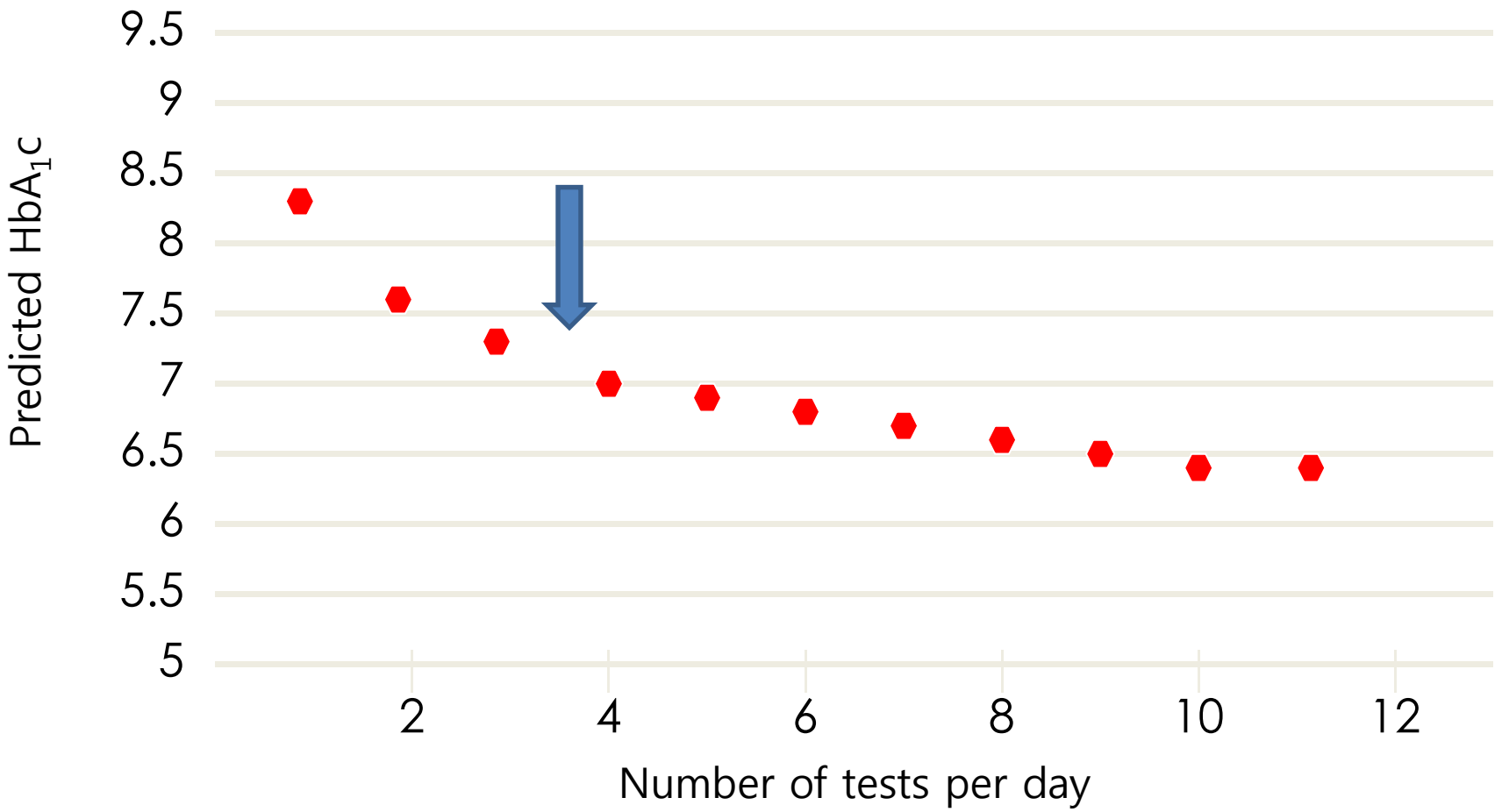
Hypoglycemic episodes reported

- If treated with Repaglinide → Reduce the dose of Repaglinide by 50% **or** Stop Repaglinide

Structured SMBG data avai lable to the patient to gui de lifestyle changes

Structured SMBG data avai lable to the investigator to adjust diabetes medication s

Statistically-Fitted Curve for A_1c as a Function of the SMBG Tests Per Day (Intensive Insulin Therapy)



Davidson PC, et al. Abstracts from the 64th Scientific Sessions of the American Diabetes Association; June 4-8, 2004; Orlando, Florida. Abstract 430-P

COMMENTARY

Self-monitoring of Blood Glucose in Individuals with Type 2 Diabetes Not Using Insulin: Commentary

Table 1. SMBG guideline recommendations

Organization	*Recommendations*
American Diabetes Association (31)	1. SMBG should be carried out three or more times daily for patients using multiple insulin injections or insulin pump therapy. 2. For patients using less frequent insulin injections, noninsulin therapies or medical nutrition therapy alone, SMBG may be useful as a guide to the success of therapy. 3. To achieve postprandial glucose targets, postprandial SMBG may be appropriate. 4. When prescribing SMBG, ensure that patients receive initial instruction in, and routine follow-up evaluation of, SMBG technique and their ability to use data to adjust therapy.
Canadian Diabetes Association (30)	1. For individuals treated with oral antihyperglycemic agents or lifestyle alone, the frequency of SMBG should be individualized depending on glycemic control and type of therapy and should include both pre- and postprandial measurements. 2. In many situations, for all individuals with diabetes, more frequent testing should be undertaken to provide information needed to make behavioural or treatment adjustments required to achieve desired glycemic targets and avoid risk of hypoglycemia. 3. In order to ensure accuracy of BG meter readings, meter results should be compared with laboratory measurement of simultaneous venous FPG at least annually and when indicators of glycemic control do not match meter readings.
Diabetes Australia (32)	1. SMBG should be considered in all people with type 2 diabetes but the decision to perform SMBG, and the frequency and timing of testing, should be individualized.

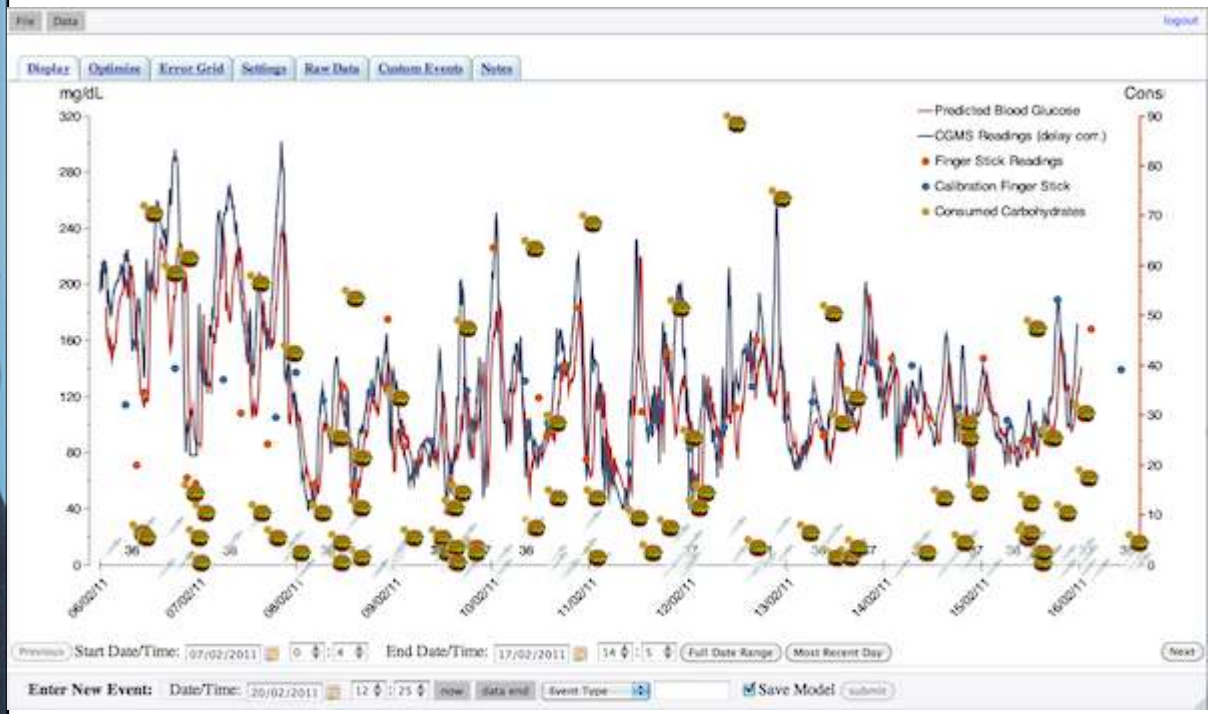
International Diabetes Federation (33)	1. SMBG should be considered at the time of diagnosis to enhance the understanding of diabetes as part of their education and to facilitate timely treatment initiation and titration optimization. 2. SMBG should also be considered as part of ongoing diabetes self-management education to assist people with diabetes to better understand their disease and provide a means to actively and effectively participate in its control and treatment modifying behavioural and pharmacologic interventions as needed. 3. SMBG should be used when individuals with diabetes and/or their healthcare providers have the knowledge, skills and willingness to incorporate SMBG and therapy adjustment into their care plan in order to attain agreed treatment goals. 4. SMBG protocols (intensity and frequency) should be individualized to address each individual's specific educational/behavioural/clinical requirements (identify/prevent/manage acute hyper- and hypoglycemia) and provider requirements for data on glycemic patterns and monitor impact of therapeutic decision making. 5. The purpose(s) for performing SMBG should be agreed between the person with diabetes and the healthcare provider. These agreed upon purposes/goals and actual review of SMBG data should be documented. 6. An easy procedure for patients to regularly check on their glucose meter performance should be a requirement for SMBG use.
National Institute for Health and Clinical Excellence, United Kingdom (34)	1. Offer SMBG to a person newly diagnosed with type 2 diabetes only as an integral part of his or her self-management education. Discuss its purpose and agree how it should be interpreted and acted upon. 2. SMBG should be available: • to those on insulin treatment • to those on oral glucose lowering medications to provide information on hypoglycemia • to assess changes in glucose control resulting from medications and lifestyle changes • to monitor changes during intercurrent illness • to ensure safety during activities, including driving. 3. Assess at least annually and in a structured way: • self-monitoring skills • quality and appropriate frequency of testing • use made of the results obtained • impact on quality of life • continued benefit • equipment used.

SMBG guideline summary in T2DM

- 처음 당뇨병을 진단 받은 사람들에게는 혈당 측정이 약물, 운동, 음식과 어떻게 연계되는지 교육적인 측면에서 꼭 권고된다
- 인슐린이나 인슐린 펌프를 사용하는 사람들에게서는 측정이 자주 (3회 이상) 추천된다
- 잦은 저혈당, 조절되지 않는 고혈당이 생기는 경우 개인의 측정가능 정도에 따라 SMBG를 시행하여 치료방법을 조절한다
- 식후 혈당 상승이 의심되는 경우 식후 SMBG도 권고된다
- 새로운 약물 투여, 치료 방법을 바꾼 경우 혈당 조절의 정도를 모니터하기 위해 SMBG를 식전, 식후로 권고한다
- 운동방법의 효율성을 체크할 때 운동 전 후, 또한 긴 운전이 예상되는 경우 SMBG를 권고한다
- **2형 당뇨병환자에서의 환자의 지식 수준, 정확한 SMBG 측정법, 환자의 혈당 측정 가능 시간, 치료법 등 모든 것을 고려하여 개별적인 횟수 제안이 필요하다**

Clinical Evidence

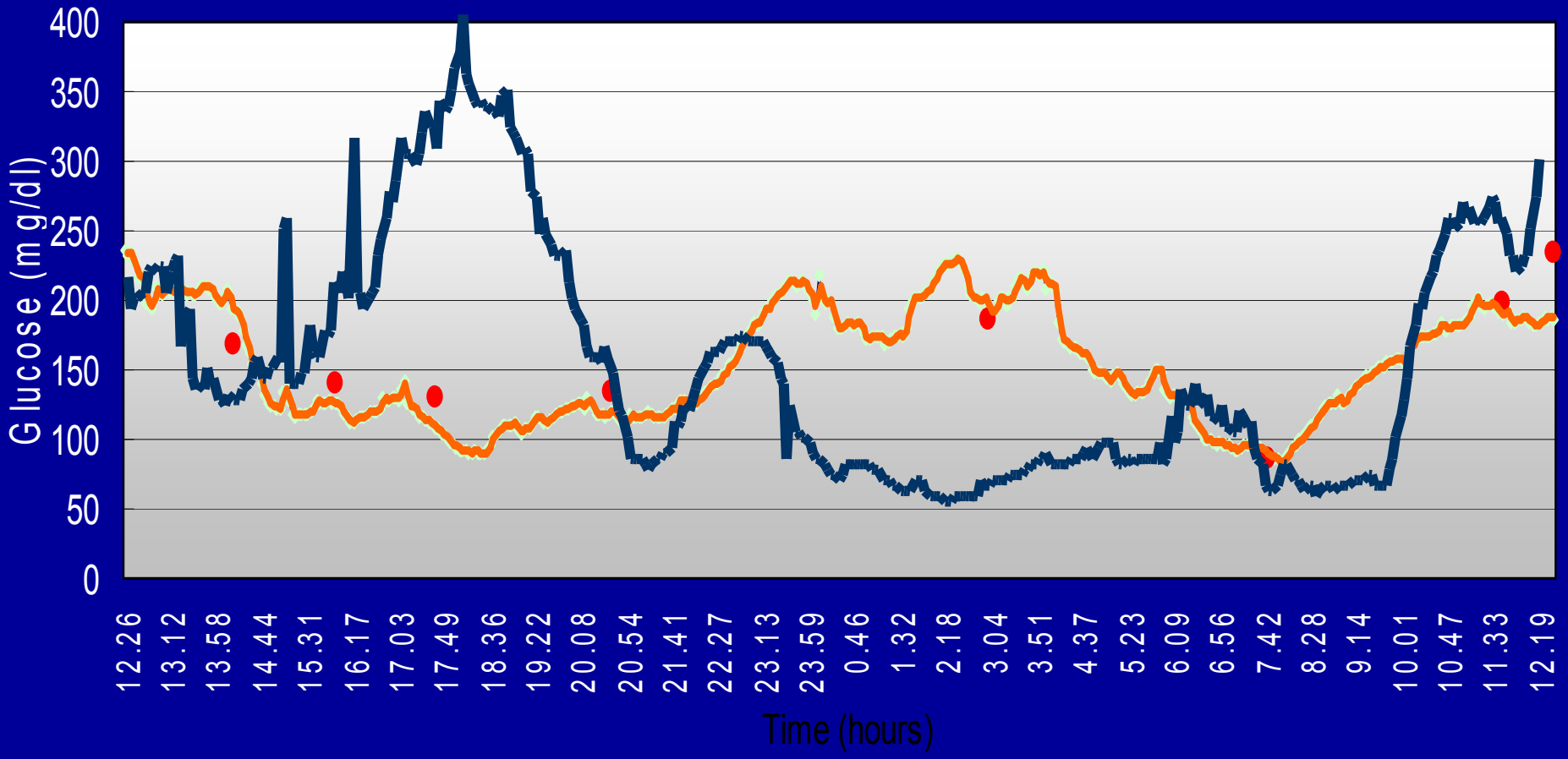
Continuous Glucose Monitoring System



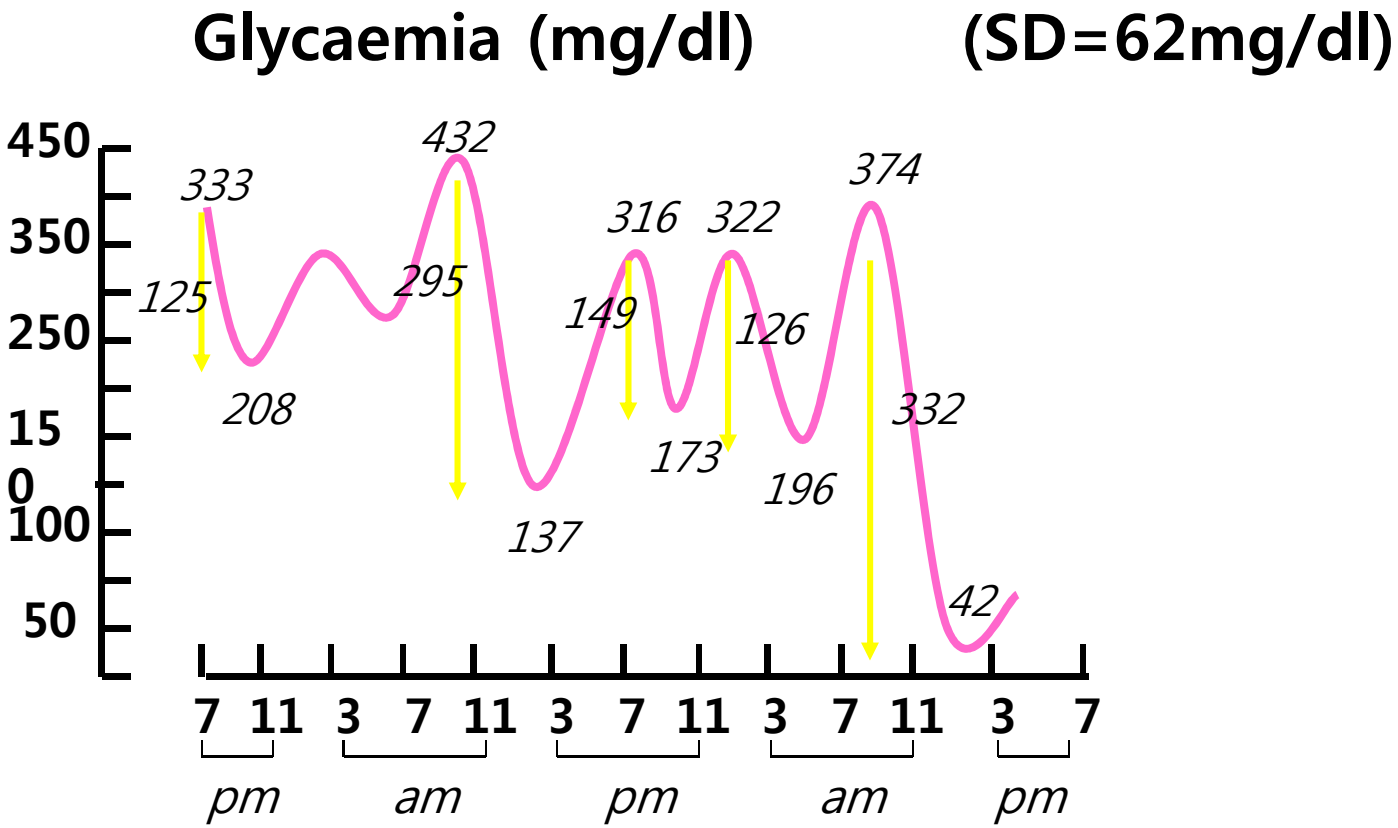
Continuous glucose monitoring

C.M. (F), 28 y.o.
HbA1c =8.2%

S.M. (M), 58 y.o.
HbA1c =8.2%



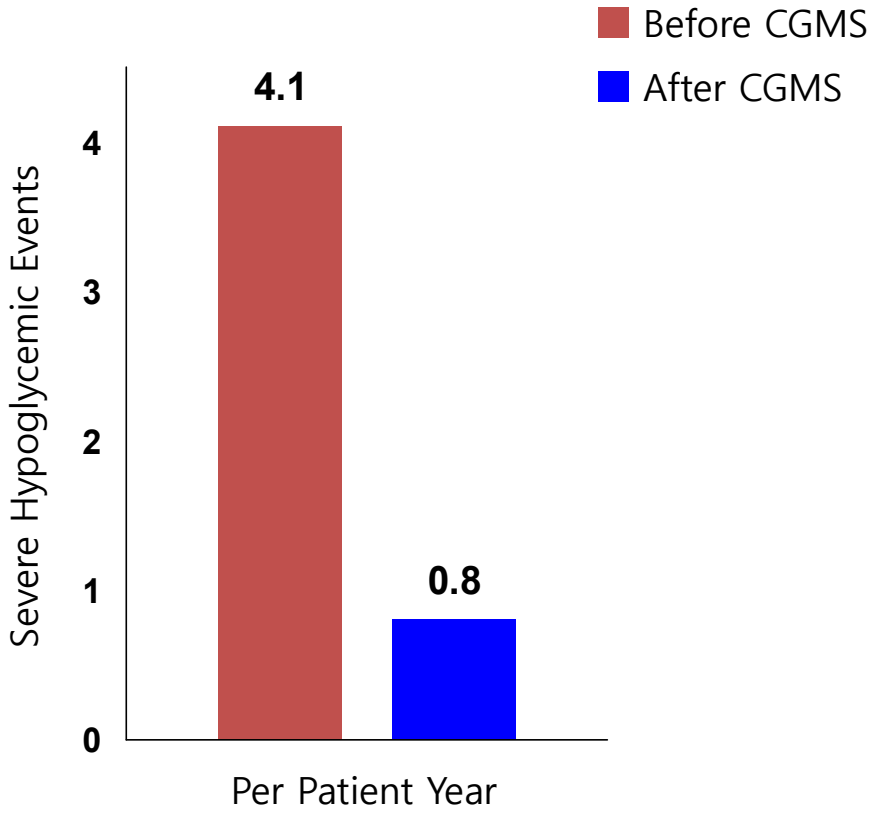
Courtesy of A. Maran, University of Padova, Italy



Principle of MAGE: [mean amplitude of glycemi excursion] assessment (from Molnar et Service)

Leads to a Reduction in Severe Hypoglycemic Events

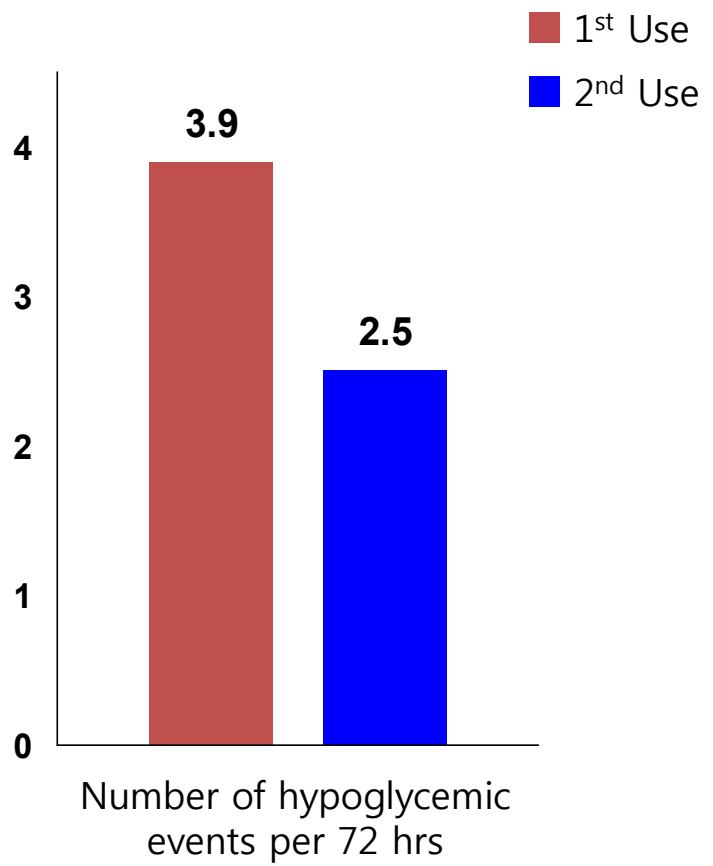
- 10 patients with a history of severe hypoglycemia
- CGMS profiles reviewed and therapy adjustments made: mainly time adjust
- No Change in HbA1c (7.2 +/- 0.8)
- No Change in total daily insulin dose



Sabbah et al., *Diabetes,* 2001 50 (suppl. 2):1877-PO.

Decreases Hypoglycemic Events in Type 1 Pediatric Patients

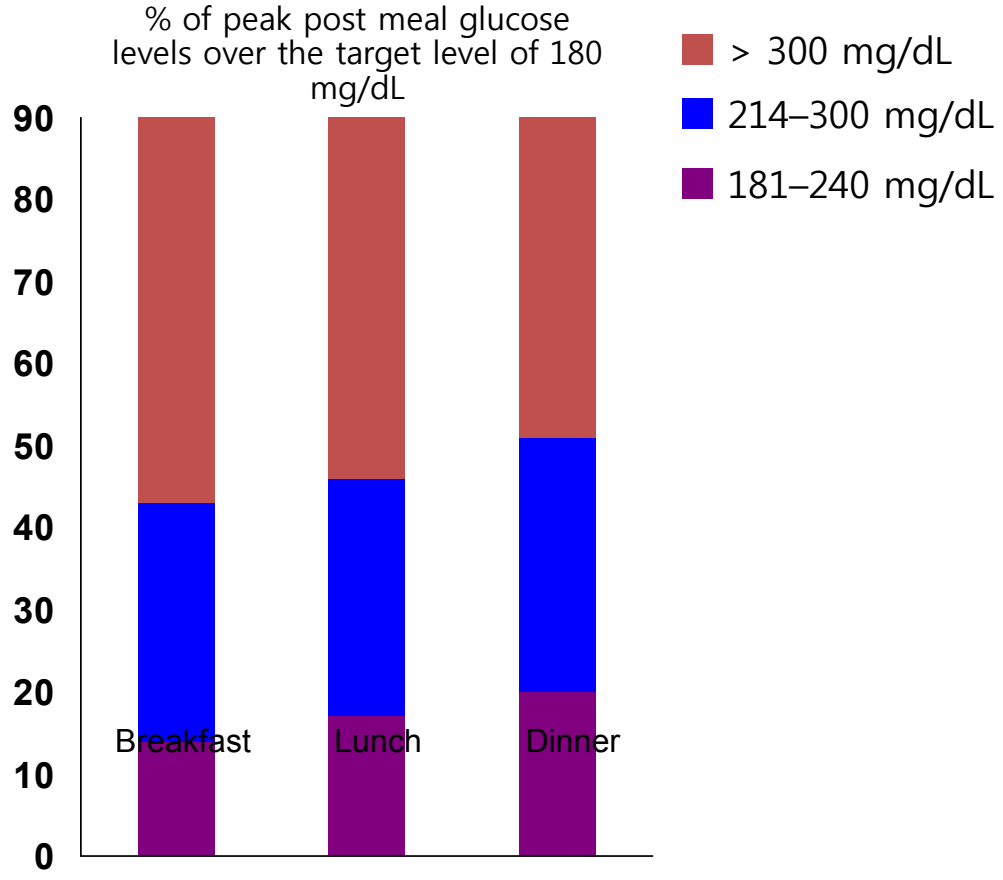
- 27 Type 1 Pediatric Patients (6–13 yrs), with a mean HbA1c of 7.6% on MDI therapy
- CGMS profiles reviewed and therapy adjustments made
- Hypoglycemic Events Reduced
  - Hypoglycemia defined at 55 mg/dl



Adapted from Schiaffini et al., *Diabetes* Metab Res Rev 2002; 18:324-9.

Reveals Postprandial Hyperglycemia Previously Hidden With Fingersticks

- 56 Type 1 Pediatric patients with HbA1c 7.7% and near target pre-meal glucose
  - 90% experienced glucose levels of > 180 mg/dl after meals
  - Almost 50% experienced glucose levels of > 300 mg/dl after meals

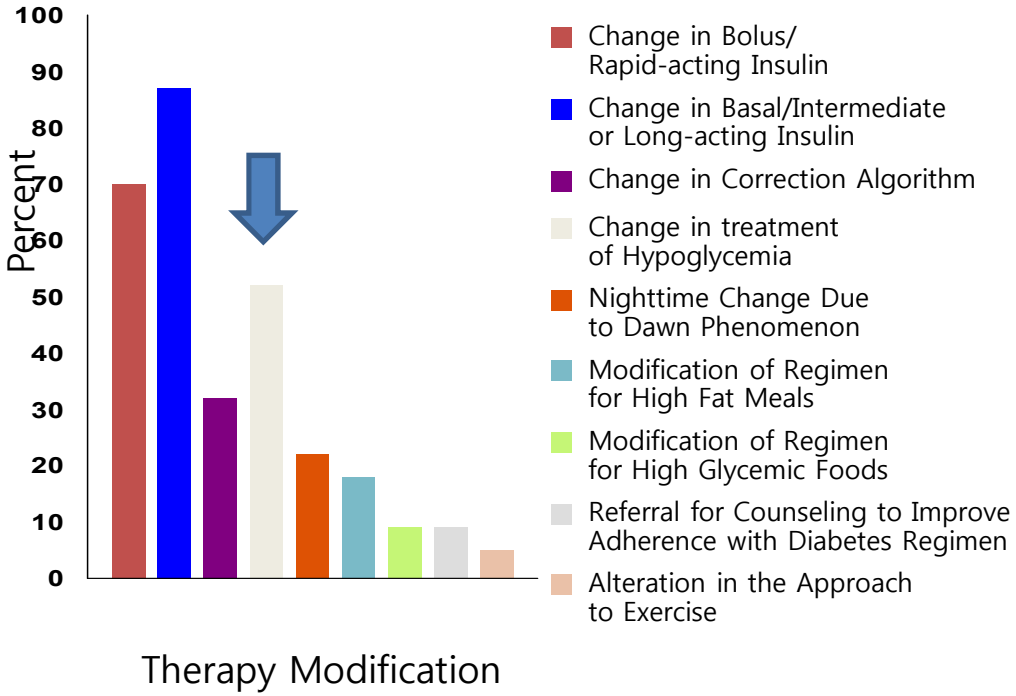


Normal A1C and Target Ranges May Not be Enough Overall Glycemic Control

Boland E, et al. *Diabetes Care* 2001;24:1858-1862.

Determines Bolus / Basal Therapy Modification

- 35 Type 1 Pediatric patients with poor compliance
- Investigators were surprised by the number of therapy modifications
  - **50% inappropriately managed hypoglycemia**
  - 30% did not re-check SMBG post-hypoglycemia



Adapted from Kaufman F et al; *Diabetes Care* 2001; 24(12): 2030-2034.

Diet tips for preventing hypoglycemia

1. 적어도 하루에 4번 이상 단백질, 섬유소를 포함한 음식을 3끼 식사 보다 적은 양으로 자주 먹는 것이 저혈당 예방에 도움이 된다.
2. 오트밀, 통곡물 등의 복합 탄수화물과 단백질을 주로 먹고, 단순당을 피한다.
3. 섬유질을 식단에서 늘려라. gastric emptying time 을 늘려주고, 단순당의 흡수율을 저하시켜 급격한 고혈당을 막아주고, 식간 사이의 저혈당 위험성을 감소시켜 줄 수 있다.
4. 단순당과 당질의 섭취를 줄여라. 특히 음식 성분 표시를 주의 깊게 살피고 설탕, 옥수수당 등의 성분을 포함한 음식을 피해라. 아직까지 인공감미료에 대한 안정성은 확보되지 않았다.
5. 지방질의 섭취는 가급적 총 열량의 30% 이내로 줄여라. 가급적 오메가-3 등의 불포화지방산류를 섭취하여야 한다.
6. 술은 피하라. 칼로리는 높고 많은 양의 섭취는 저혈당을 유발할 수 있다. 또한 혈당 조절폭을 불규칙하게 만든다.
7. 카페인을 피하라. 카페인의 과량 섭취는 아드레날린 및 교감신경계 활성화를 통해 저혈당 증상을 더욱 유발할 수 있다.
8. 운동과 연계된 저혈당: 운동 전, 후로 탄수화물 섭취를 고려하라

Exercise Benefits

- 50-80% VO2 Max
- 4 days a week
- 30 – 60 min
- Overall rate reduction for CAD and diabetes
- Moderate intensity
  - at least 30 minutes per day,
  - most days of the week

- Decrease pre-exercise meal insulin by 30-50%
- Decrease basal insulin by 30-50%
- Increase in insulin sensitivity, adjust insulin:BS
- Don't use insulin for pre-exercise carbs or carbs during exercise
- Avoid exercise during peak insulin actions
- Don't inject in working muscle

U health care system

Diabetes Care. 2011 Feb;34(2):308-13.

Improved glycemic control without hypoglycemia in elderly diabetic patients using the ubiquitous healthcare service, a new medical information system.

Lim S, Kang SM, Shin H, Lee HJ, Won Yoon J, Yu SH, Kim SY, Yoo SY, Jung HS, Park KS, Ryu JO, Jang HC.

Source

Department of Medical Informatics, Seoul National University Bundang Hospital, Seongnam, Korea.

Abstract

OBJECTIVE:

To improve quality and efficiency of care for elderly patients with type 2 diabetes, we introduced elderly-friendly strategies to the clinical decision support system (CDSS)-based ubiquitous healthcare (u-healthcare) service, which is an individualized health management system using advanced medical information technology.

RESEARCH DESIGN AND METHODS:

We conducted a 6-month randomized, controlled clinical trial involving 144 patients aged >60 years. Participants were randomly assigned to receive routine care (control, n = 48), to the self-monitored blood glucose (SMBG, n = 47) group, or to the u-healthcare group (n = 49). The primary end point was the proportion of patients achieving A1C <7% without hypoglycemia at 6 months. U-healthcare system refers to an individualized medical service in which medical instructions are given through the patient's mobile phone. Patients receive a glucometer with a public switched telephone network-connected cradle that automatically transfers test results to a hospital-based server. Once the data are transferred to the server, an automated system, the CDSS rule engine, generates and sends patient-specific messages by mobile phone.

RESULTS:

After 6 months of follow-up, the mean A1C level was significantly decreased from 7.8 ± 1.3% to 7.4 ± 1.0% ($P < 0.001$) in the u-healthcare group and from 7.9 ± 1.0% to 7.7 ± 1.0% ($P = 0.020$) in the SMBG group, compared with 7.9 ± 0.8% to 7.8 ± 1.0% ($P = 0.274$) in the control group. The proportion of patients with A1C <7% without hypoglycemia was 30.6% in the u-healthcare group, 23.4% in the SMBG group (23.4%), and 14.0% in the control group ($P < 0.05$).

CONCLUSIONS:

The CDSS-based u-healthcare service achieved better glycemic control with less hypoglycemia than SMBG and routine care and may provide effective and safe diabetes management in the elderly diabetic patients.

Background

- Ubiquitous [yoo-bik-wi-tuhs]
  - ***Adjective***
    existing or being everywhere, esp. at the same time
  - ***Origin:***
    1830–40; ubiquit(y) + -ous

- Ubiquitous (U)-healthcare
  - Telemedicine, e-health, connected health
  - Provides real-time individualized medical treatment using internet and wireless technology
  - Disease treatment and continuous follow-up, prevention, and early diagnosis

Naseer A, *IEEE Trans Inf Technol Biomed* 2010
Alasaarela E et al, *Technol Health Care* 17:353-367, 2009
Perez-Ferre N et al, *Diabetes Care* 33:602-604, 2010

Methods

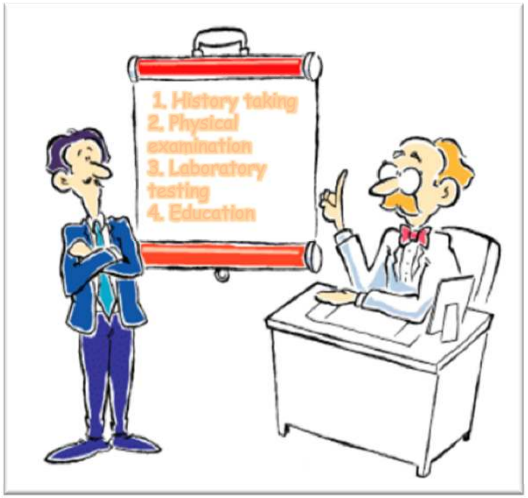
- Study participants
  - Patients with type 2 diabetes aged 60 years or older
  - three groups (50 in each group);

    1) routine care (control group),

    2) self monitoring blood glucose (SMBG) group,

    3) u-healthcare group with public switched telephone network (PSTN)-connected glucometer plus mobile phone (u-healthcare) group.

- Primary endpoint
  - The proportion of patients achieving **A1C level of < 7% without hypoglycemia** at 6 months



Patient

Doctor

Baseline data
Prescription

Nurse & Dietitian

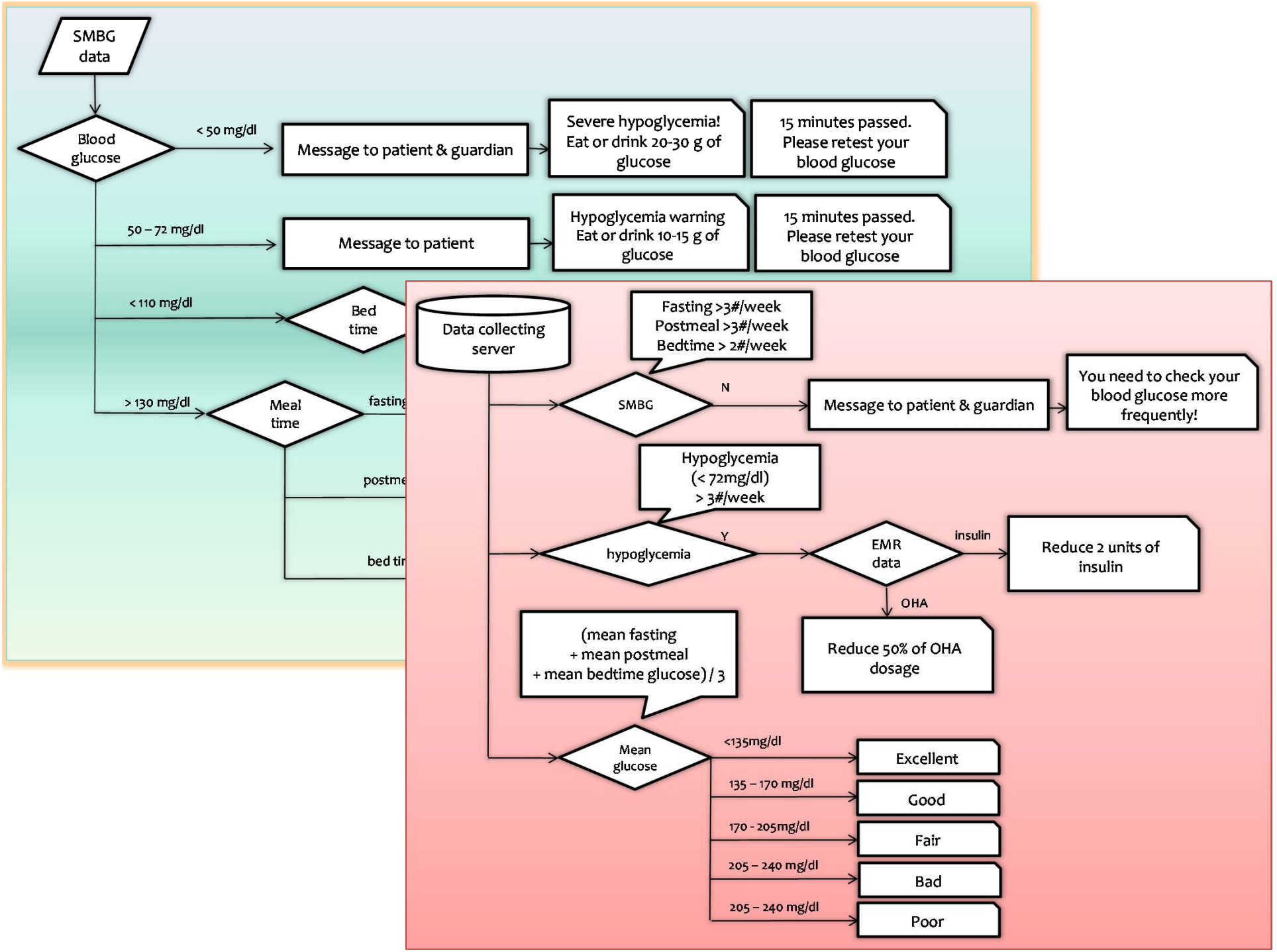
Lifestyle
Nutritional status

U-healthcare Server

SNUBH EMR

CDSS rule engine

Message generation


SMBG data
Blood glucose
< 50 mg/dl
Message to patient & guardian
Severe hypoglycemia! Eat or drink 20-30 g of glucose
15 minutes passed. Please retest your blood glucose
50 – 72 mg/dl
Message to patient
Hypoglycemia warning Eat or drink 10-15 g of glucose
15 minutes passed. Please retest your blood glucose
< 110 mg/dl
Bed time
> 130 mg/dl
Meal time
fasting
postme
bed tir
Data collecting server
Fasting >3#/week
Postmeal >3#/week
Bedtime > 2#/week
SMBG
N
Message to patient & guardian
You need to check your blood glucose more frequently!
Hypoglycemia (< 72mg/dl) > 3#/week
hypoglycemia
Y
EMR data
insulin
Reduce 2 units of insulin
OHA
Reduce 50% of OHA dosage
(mean fasting + mean postmeal + mean bedtime glucose) / 3
Mean glucose
<135mg/dl
Excellent
135 – 170 mg/dl
Good
170 - 205mg/dl
Fair
205 – 240 mg/dl
Bad
205 – 240 mg/dl
Poor

- 혈당측정기
  - 고령자 사용 편이성이 증대된 무선통신 혈당 측정기 개발
  - Code-free : 사용자가 코드를 입력할 필요 없음
  - Voice 기능 : 측정 과정 및 측정 결과의 음성 안내
  - 식사 상황 입력 기능 : 식전/식후/ 취침전 체크
  - Bluetooth (BT HDP)를 이용한 혈당측정값 자동 전송
  - 국제 통신 표준(IEEE 11073-10417) 탑재
  - 기기 원격 제어 기능 : 기기의 설정을 서버에서 원격 관리

Results Baseline characteristics

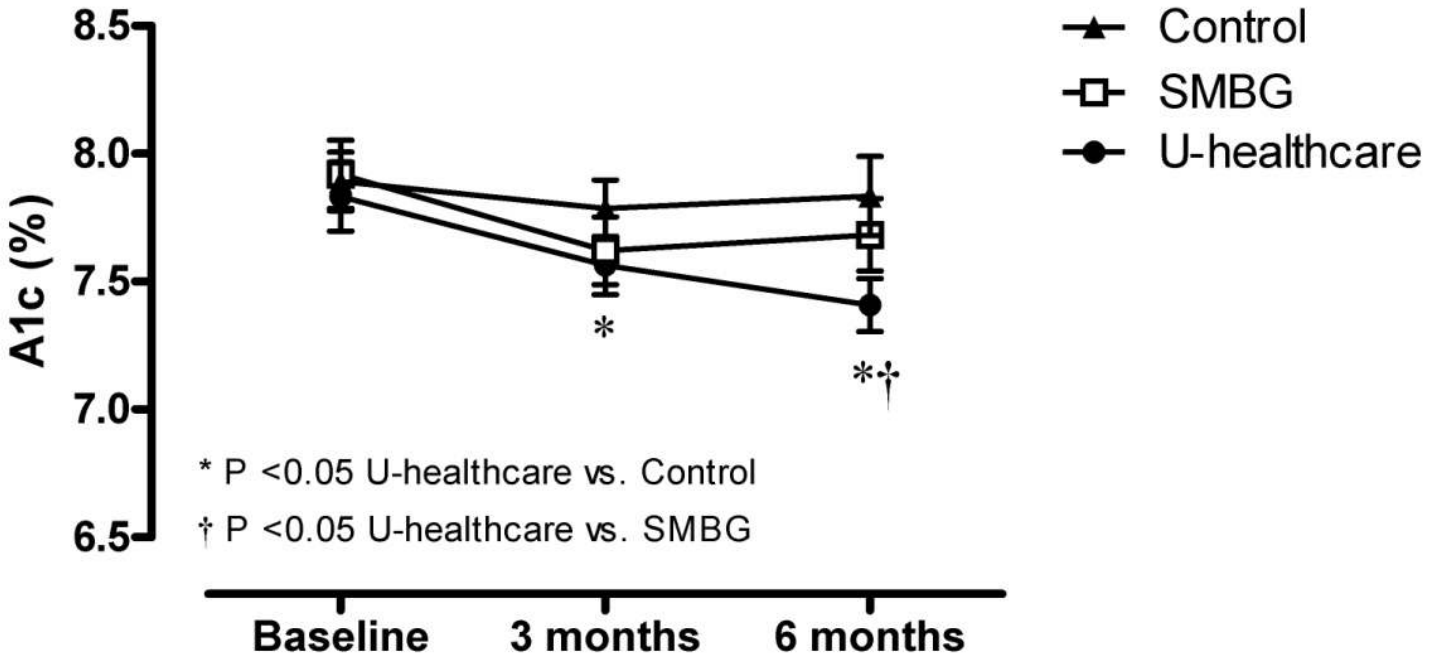
Characteristics	U-healthcare group ($n = 51$)	SMBG group ($n = 51$)	Control group ($n = 52$)	p
Age, years	67.2 (4.1)	67.2 (4.4)	68.1 (5.5)	0.542
Male/female	23/27	22/28	19/31	0.706
Duration of diabetes, years	14.1 (10.1)	15.4 (8.3)	15.8 (10.7)	0.695
Height, cm	161.0 (8.2)	161.6 (10.4)	158.5 (8.4)	0.191
Weight, kg	64.0 (8.5)	65.3 (11.5)	63.8 (9.5)	0.739
Body mass index, kg/m^2	24.7 (2.3)	24.9 (3.0)	25.4 (3.3)	0.408
Systolic blood pressure, mmHg	129.8 (18.2)	127.9 (16.1)	129.2 (17.1)	0.856
Diastolic blood pressure, mmHg	73.2 (10.3)	72.7 (10.3)	74.2 (11.1)	0.778
Fasting plasma glucose, mg/dL	137.3 (34.4)	137.8 (40.1)	141.6 (43.0)	0.828
Postprandial 2h glucose, mg/dL	242.5 (64.7)	242.6 (50.1)	246.3 (55.7)	0.982
A1C, %	7.8 (1.0)	7.9 (0.9)	7.9 (0.8)	0.884
Total cholesterol, mg/dL	173.7 (34.7)	175.3 (28.2)	169.1 (30.0)	0.602
Triglyceride, mg/dL	144.4 (53.0)	151.5 (66.2)	164.2 (84.6)	0.685
HDL cholesterol, mg/dL	49.1 (9.9)	48.0 (10.4)	51.9 (16.4)	0.640
LDL cholesterol, mg/dL	110.4 (28.6)	92.9 (22.9)	101.5 (25.3)	0.104
AST, IU/L	20.9 (6.8)	22.3 (9.1)	22.3 (8.5)	0.644
ALT, IU/L	22.3 (9.9)	26.7 (20.9)	24.9 (15.4)	0.425
Creatinine, mg/dl	1.06 (0.19)	1.11 (0.34)	1.16 (0.26)	0.211
Medication for glucose control				
Sulfonylurea, n (%)	29 (58.0)	24 (56.0)	28 (48.0)	0.317
Metformin, n (%)	34 (68.0)	30 (65.2)	28 (56.0)	0.216
Thiazolidinedione, n (%)	4 (8.0)	8 (16.0)	3 (6.0)	0.740
DPP4 inhibitor, n (%)	6 (12.0)	11 (22.0)	6 (12.0)	0.999
α-glucosidase inhibitor, n (%)	9 (18.0)	13 (26.0)	12 (22.7)	0.475
Insulin, n (%)	12 (24)	12 (24)	19 (38)	0.123

Changes of anthropometric, biochemical parameters and frequency of SMBG by the groups after 6 months

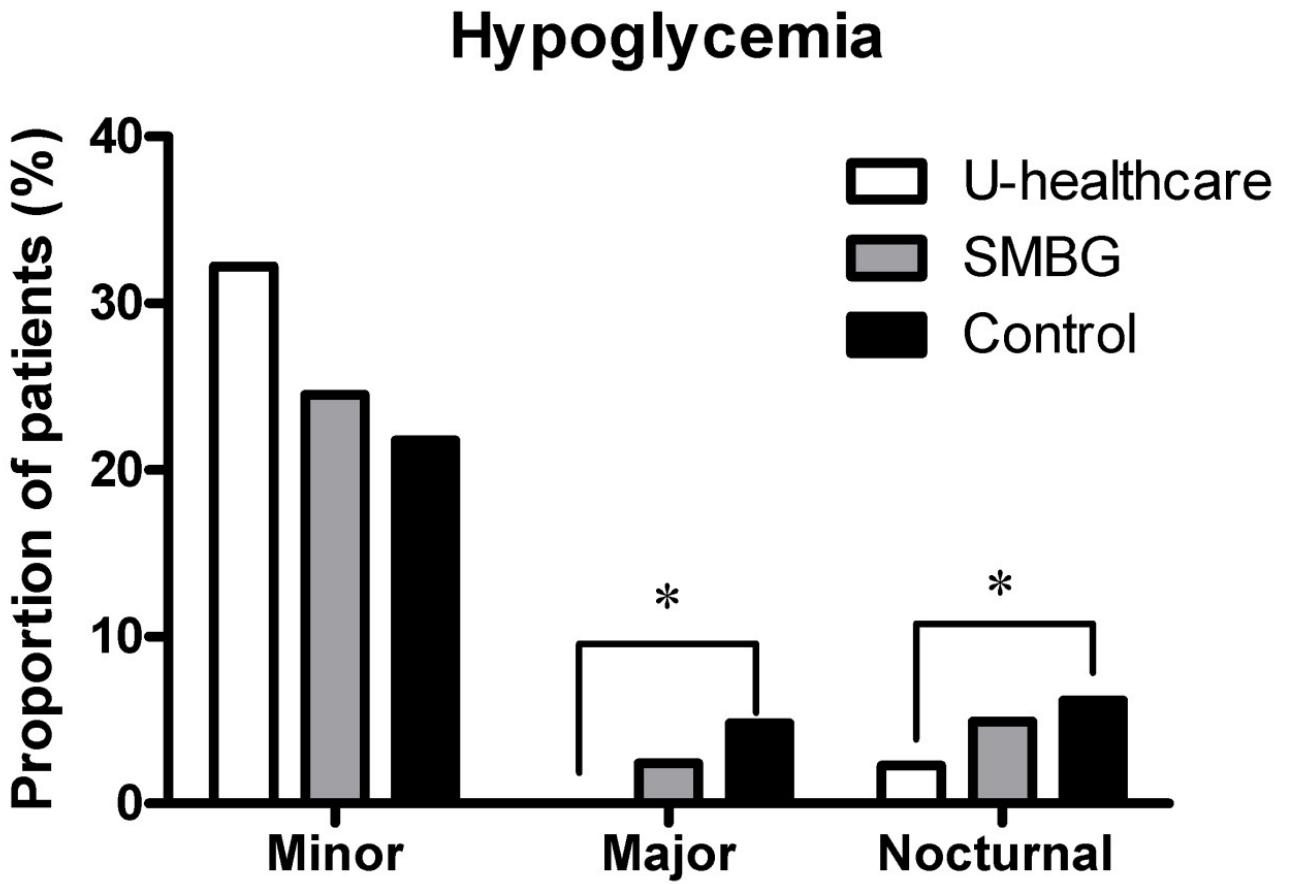
	U-healthcare group (*n*=49)			SMBG group (*n*=47)			Control group (*n*=48)		
	Baseline	6 months	p	Baseline	6 months	p	Baseline	6 months	p
Weight, kg	64.3 (8.5)	63.5 (8.5)	0.001	66.8 (11.5)	66.4 (11.6)	0.310	63.6 (9.9)	64.2 (9.4)	0.074
BMI, kg/m^2	24.7 (2.4)	24.4 (2.5)	0.009	25.1 (2.9)	25.0 (3.2)	0.303	25.5 (3.5)	25.8 (3.4)	0.005
Fasting glucose, mg/dL	137.3 (32.7)	124.3 (29.7)	0.054	137.6 (40.5)	132.2 (15.6)	0.403	146.8 (48.8)	152.6 (58.0)	0.388
Postprandial glucose, mg/dL	250.1 (68.0)	210.1 (49.0)	0.077	239.3 (42.5)	229.80 (65.2)	0.592	259.1 (64.5)	291.1 (77.9)	0.212
A1C, %	7.9 (1.0)	7.4 (0.7)	< 0.001	7.9 (1.0)	7.6 (1.0)	0.016	8.2 (1.2)	8.2 (1.3)	0.982
A1C < 7%, (%)*	15 (30.6)	17 (34.7)	0.415	11 (23.4)	15 (31.9)	0.245	7 (14.0)	10 (20.4)	0.282
Frequency of SMBG, N/week	3.2 (3.5)	10.5 (5.1)	< 0.001	3.1 (2.7)	8.2 (4.2)	< 0.001	2.7 (4.4)	2.4 (3.3)	0.664
Total cholesterol, mg/dL	174.8 (36.0)	171.8(34.0)	0.490	177.2 (27.1)	183.4 (28.7)	0.242	169.1 (30.0)	174.1 (30.0)	0.168
Triglyceride, mg/dL	150.1 (58.2)	138.8 (56.5)	0.278	175.8 (71.7)	149.9 (85.0)	0.275	135.2 (45.5)	130.1 (69.5)	0.911
HDL cholesterol, mg/dL	51.6 (11.8)	47.7 (8.1)	0.043	43.8 (9.2)	46.2 (10.2)	0.421	43.8 (10.9)	45.0 (9.4)	0.750
LDL cholesterol, mg/dL	115.1 (27.8)	95.6 (26.4)	0.038	92.8 (23.7)	100.8 (31.3)	0.302	109.8 (20.5)	93.2 (15.0)	0.099

Data are presented as mean (SD) or n (%)*.
BMI, body mass index; SMBG, self monitoring of blood glucose; HDL, high-density lipoprotein; LDL, low-density lipoprotein

A1C change after 6 months

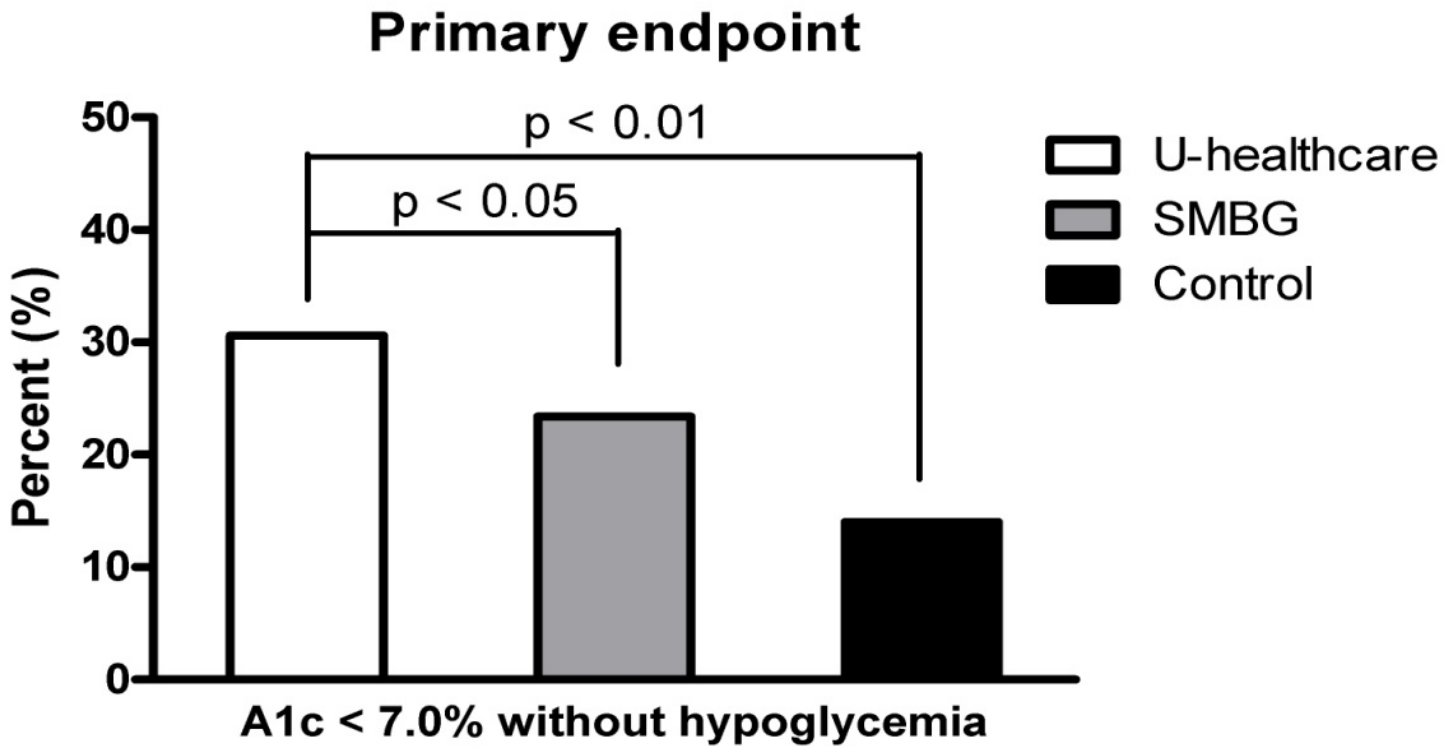


Hypoglycemia over 6 months of study



Primary endpoint

A1C <7% without hypoglycemia



운동량모니터

- 매 1시간마다 운동량 측정, 저장, 표시
  측정 시각, 측정 기간, 걸음 수 활동량, 소모 칼로리
- 측정/저장 주기, 전송 주기 설정 가능
- 측정 데이터 무선 전송
- 국제 통신 표준 적용: IEEE 11073-10441
- 충전용 배터리 (5일 이상)
- 의류 고정 방식: 클릭을 사용, 과격한 운동에도 탈락하지 않도록 설계됨
- 고령자임을 감안하여 버튼에 돌기 구현

U-헬스케어 시스템

일상 생활

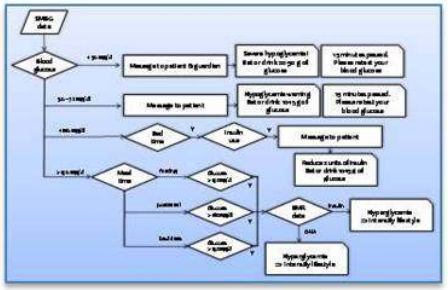
혈당측정

운동측정

식사입력

병원 서버

환자의 병력에
의거한 맞춤형 평가



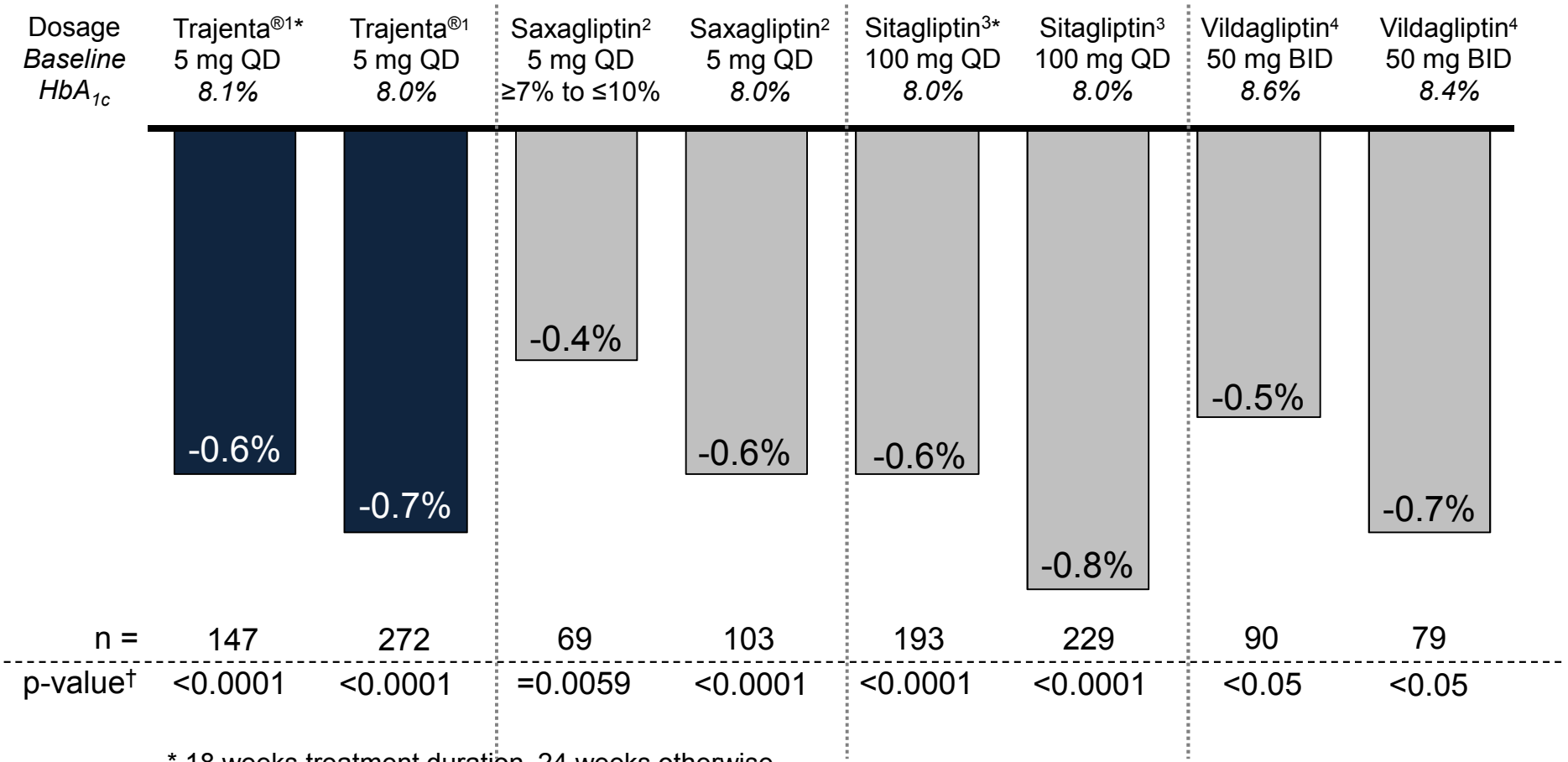
포털과 실시간
메시지 전송

Treatment

- OHA
  - DPP4 inhibitor 유용성, especially in the elderly
- Insulin 요법시 고려 사항
  - basal insulin based regimen
    - Glargine 사용 그룹 -> Determir 사용으로 전환하면 저혈당의 발생률이 유의하게 감소
    - 새벽에 basal insulin 을 사용하던 사람을 식사 패턴을 고려하여 아침/점심으로 이동 시 저혈당 감소
    - 특히 MDI를 사용하는 사람들은 하루 3차례 이상의 SMBG를 하여 혈당을 monitoring 하는 것이 도움

Efficacy of DPP-4 inhibitors in monotherapy trials

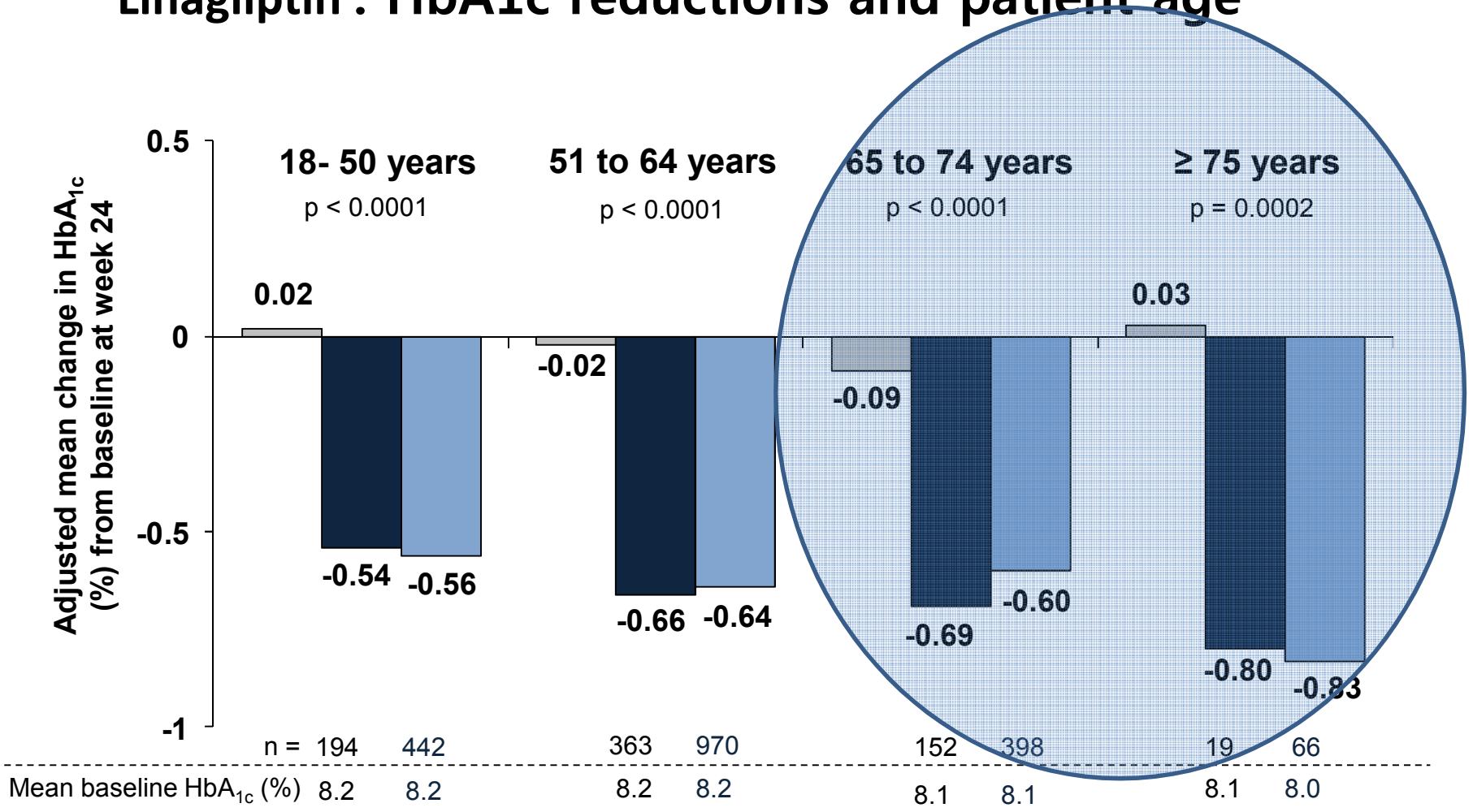
Placebo-corrected, adjusted mean change from baseline HbA_{1c}



* 18 weeks treatment duration, 24 weeks otherwise
† Between group difference versus placebo

Sources: 1– 4, EU SmPC for Trajenta® , saxagliptin, sitagliptin and vildagliptin

Linagliptin : HbA1c reductions and patient age



Pre-specified sub-group analysis on pooled data from four pivotal phase III randomized placebo-controlled trials: treatment in monotherapy, add-on to metformin, add-on to metformin + SU, initial combination with pioglitazone. p-values for between-group difference (versus placebo)

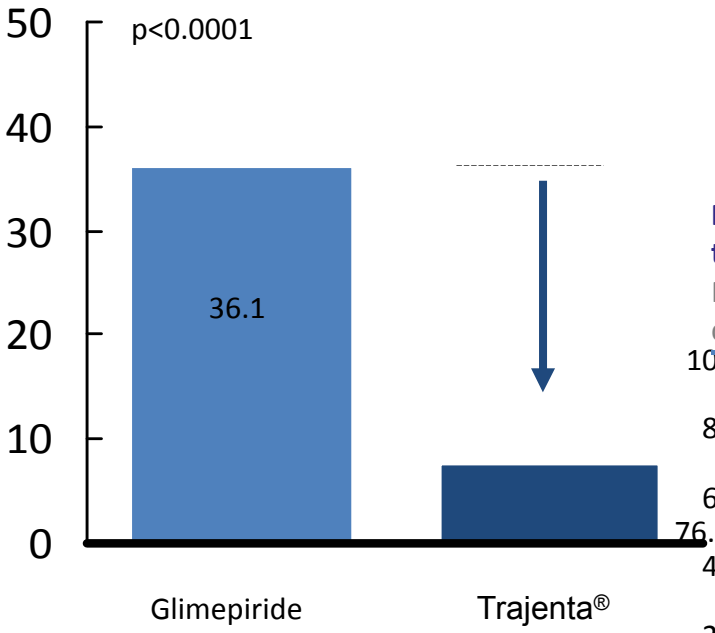
Source: Patel 2011 EASD Poster P-832

Placebo
Trajenta®
Trajenta® placebo-corrected

DPP4 inhibitor compared to glimepiride – incidence of hypoglycemia, weight change and rate of patients achieving HbA1c target <7%

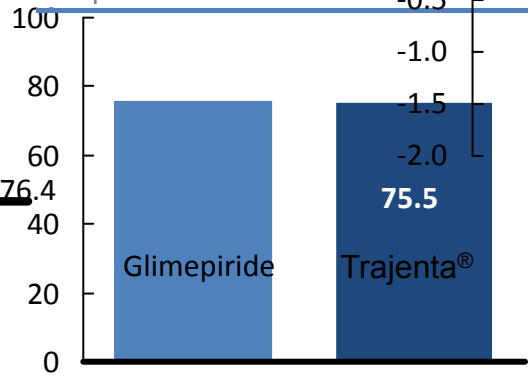
Incidence of hypoglycemia

Percent of patients - Treated set[1]



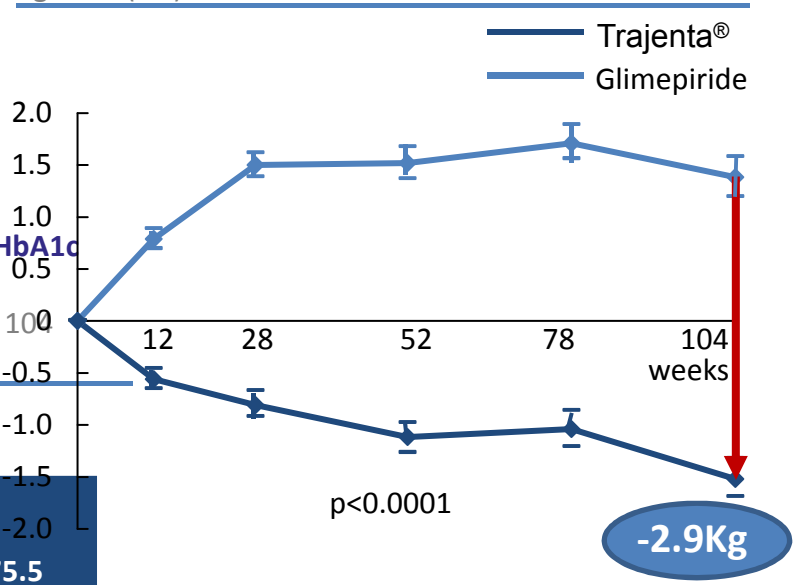
Rate of patients achieving HbA1c target <7%

Percent of patients at week 104 completers cohort[2]



Adjusted3 means for body weight change from baseline ± SE

Kg - FAS (OC)



Trajenta® brings patients to target (HbA1c <7%) with significantly less hypoglycemia and relative weight loss compared to glimepiride

1 Treated Set: Trajenta® n=776, glimepiride n=775
2 Completers cohort: Trajenta® n=233, glimepiride n=271
3 Model includes baseline HbA1c, baseline weight, no. prior OADs, treatment, week repeated within patients and week by treatment interaction

Source: Gallwitz et al. American Diabetes Association, 71th Scientific Sessions, San Diego, CA, June 24-28, 2011; 39-LB

Summary

- **Tailored management for considering patient's life style and glucose pattern is the most important factor to reduce iatrogenic hypoglycemia**
  - Structured SMBG : new onset diabetes, T1DM, and intensified insulin user
  - CGMS: adjustment therapy, reduce glycemic variability
  - U health care : ideal but dependent on patient intelligence, cost?
  - Diet & exercise adjustment needed
  - The role of DPP4 inhibitor : non-inferior to SU & glucose dependent manner, safe in the elderly