

ORAL HEALTH STATUS AND ORAL HEALTH-RELATED QUALITY OF LIFE AMONG INSULIN-TREATED AND NON-INSULIN-TREATED DIABETIC PATIENTS IN VISAKHAPATNAM: A COMPARATIVE CROSS-SECTIONAL STUDY

¹Dr Aditya Teja Prasad Pallekonda, MDS, ²Dr Ravada V S S K Kinneresh, MDS, (MBA), ³Dr Divya Nadiminti, MDS, ⁴Dr Likitha Bhumireddy, MDS, ⁵Dr Saripalli Sravya, BDS, MPH, ⁶Dr M Hima Bindu, BDS

¹Department of Public Health Dentistry, Assistant Professor, Meghana Institute of Dental Sciences; Email: Adityateja01@gmail.com

²Department of Public Health Dentistry, Senior Resident, Great Eastern Medical School and Hospital; Email: Rk10121964@gmail.com

³Department of Oral Pathology, Consultant Oral Pathologist; Email: Divyanadiminti9@gmail.com

⁴Department of Oral Medicine and Radiology, Assistant Professor, Meghana Institute of Dental Sciences; Email: likithabhumireddy@gmail.com

⁵Research Officer, Department of Neurovascular Intervention, Medicoover Hospitals; Email: Srays612@gmail.com

⁶Private Practitioner, Indira Multi-Specialty Dental Hospital; Email: Himabindumulumundi2001@gmail.com

Abstract

Background: Oral diseases are highly prevalent in diabetic patients where both the quality of life and patient's perception of their oral health may be affected. **Aim:** The study aims to measure the oral health status and oral health related quality of life among insulin dependent and non-insulin dependent diabetic patients in Visakhapatnam, Andhra Pradesh, India. **Methodology:** This descriptive cross-sectional study was done with a sample of 1019 diabetic patients where 107 patients were insulin dependent diabetic patients and 912 patients were non-insulin dependent diabetic patients conducted in three private diabetic clinics in Visakhapatnam, India to assess their oral health status using WHO 2013 proforma and oral health related quality of life using OHIP-14. The oral health status was compared between the two groups by using chi-square test and OHRQOL by independent t-test. ANOVA test was employed in overall intra group comparison of OHRQOL among the insulin dependent diabetic patients. **Results:** The study showed that higher prevalence of dental caries, periodontal diseases and clinical attachment loss (CAL) in both diabetic groups with periodontal diseases (0.045*) and CAL (0.033*) being significant on comparison between the two groups of diabetics. The oral health related quality of life is comparatively less among the insulin dependent diabetic group and OHRQOL is deteriorated on increase in insulin dosage and age. **Conclusion:** The study results finally conclude that oral health status is poorer among the diabetic patients especially in insulin dependent diabetic patients regarding periodontal diseases and CAL. The deterioration of oral health related quality of life is significantly higher among the insulin dependent patients. The OHRQOL is negatively related to age and increased intake of insulin dosage. So, there is a need for the development of preventive health care interventions that target improvements in oral health status and the oral health related quality of life among the diabetic patients.

Keywords: insulin, diabetes, oral health, periodontal disease, health related quality of life.

1. Introduction

Diabetes is a chronic metabolic condition characterized by hyperglycaemia due to a deficiency in insulin activity, secretion, or both. ^[1] This chronic endocrine condition affects glucose, carbohydrate, protein, and lipid metabolism and is characterized by an inability to create or resist insulin. This noncommunicable illness causes several medical and oral issues. ^[2,3] Diabetes affects around 422 million people globally, primarily in middle- and low-income countries. Diabetes is responsible for 1.6 million fatalities annually. Diabetes incidence and prevalence have gradually increased during the last few decades ^[4]. Diabetes is emerging as a potential epidemic in India, with over 62 million individuals currently diagnosed. In 2000, India had the highest number of diabetes mellitus cases in the world, with 31.7 million affected individuals ^[5]. Along with various systemic adverse effects, diabetic patients also experience a significant prevalence of oral complications, which include oral candidiasis, xerostomia, taste impairment, oral lichen planus, ^[6] and periodontal disease ^[7].

Understanding the connection between diabetes and oral health issues is crucial, especially concerning oral health-related quality of life (OHRQL) for patients with diabetes. The World Health Organization (WHO) defines quality of life as "an individual's perceptions of their position in life in the context of the culture and value system where they live,

and in relation to their goals, expectations, standards, and concerns"^[8]. Research on the health and dental conditions of diabetes individuals may have an impact on how they are managed and ultimately enhance their quality of life.

In 1922, the first insulin was made accessible to humans. Insulin's discovery transformed the management of diabetes and enhanced the quality of life for persons with the disease, particularly those with type 1. Insulin continues to be the cornerstone of care for many individuals with type 2 diabetes^[9], gestational diabetes mellitus, and type 1 diabetes. The effect of insulin on quality of life (QOL) remains unclear. While insulin may enhance QOL by alleviating symptoms of hyperglycaemia and potentially reducing both microvascular and macrovascular complications, as indicated by numerous studies, it can also negatively affect QOL. This negative impact may arise from side effects such as hypoglycaemia and weight gain, as well as psychological distress, stigmatization, and restrictions on social activities^[10]. Based on a study by Shah *et al.*, initiating insulin treatment was associated with improved quality of life (QOL^[11]). However, other research indicates that insulin therapy can negatively affect QOL^[12,13].

Additionally, there is a lack of information in the literature regarding the oral health status and quality of life of both insulin-dependent and non-insulin-dependent diabetes patients. This study was conducted to address the unclear effects of insulin on oral health and its subsequent impact on quality of life.

Materials and methods

Study design and study setting

The present cross-sectional study was conducted on diabetic patients from various diabetic clinics in Visakhapatnam, Andhra Pradesh, India. Of the 1019 subjects in the research, 912 had non-insulin-dependent diabetes mellitus and 107 had insulin-dependent diabetes mellitus. Oral Health Status and Oral Health-Related Quality of Life of the study participants were assessed using a self-administered, pretested proforma, Oral Health Impact Profile (OHIP-14) and WHO oral health assessment form 2013 over a period of two years. Patients with diabetes who were not insulin dependent were split into three groups according to age, while patients with diabetes who were insulin dependent were split into three groups according to their insulin dosage. The patients were selected based on convenience sampling. Those who were present at the day of the study were included. The selected participants are from the community health centre and two private clinics of Visakhapatnam city had confirmed the diagnosis and are under the frequent recall visit.

Ethical clearance and informed consent

The ethical clearance (ANIDS/IEC/2021A013) for the study was obtained from the Institutional Review Board. The permission to conduct the study was obtained from the concerned authorities of the primary health centre and two private clinics and written informed consent was obtained from each of the study subjects after explaining to them the purpose and methodology of the study.

Sample size determination

The sample size for the present study was calculated using G*Power software version 3.1.9.7 (Heinrich Heine University, Düsseldorf, Germany). Since the study aimed to compare the oral health status and oral health-related quality of life between insulin-dependent diabetic mellitus (IDDM) and non-insulin-dependent diabetic mellitus (NIDDM) patients, the sample size estimation was performed using the test family "t-tests" for comparison of means between two independent groups (two-tailed).

The sample size calculation was based on the following statistical assumptions:

- Effect size (Cohen's d) = 0.30
- Alpha error probability (α) = 0.05
- Power of the study ($1 - \beta$) = 0.80 (80%)
- Allocation ratio (N_2/N_1) = 1
- Statistical test = Independent samples t-test (two-tailed)

The effect size of 0.30 was selected based on previous literature and pilot observations, considering a small to moderate clinically significant difference in oral health-related quality of life between the two diabetic groups.

Using the above parameters, the minimum estimated sample size obtained from G*Power analysis was 880 participants. To compensate for possible non-response, incomplete questionnaires, and missing data, an additional 15.8% sample

was included.

The percentage increase was calculated as:

$$\begin{aligned}\text{Percentage Increase} &= \frac{1019 - 880}{880} \times 100 \\ &= \frac{139}{880} \times 100 \\ &= 15.8\%\end{aligned}$$

Accordingly, the final sample size was increased from 880 to 1019 participants to enhance the statistical precision, validity, and reliability of the study findings. The final study population consisted of 107 insulin-dependent diabetic patients and 912 non-insulin-dependent diabetic patients.

Inclusion criteria

The inclusion criteria consist of: a) Patients who were willing to participate in the study. b) Patients who are only above 45 years of age were included in the study population. c) Participants who submitted their informed consent. d) Patients who were diabetic at-least for 5 years are included in the study. e) Patients who were on insulin therapy for at-least one year were included in the insulin dependent diabetic group.

Exclusion criteria

The exclusion criteria consist of: a) patients who are mentally challenged b) patients having chronic systemic illness other than diabetes c) Patients who are not willing to give consent.

Data collection

A self-administered, pretested proforma and Oral Health Impact Profile (OHIP-14) was administered to both insulin dependent and non-insulin dependent diabetes mellitus patients in Visakhapatnam in the English and the local language (Telugu). Information on Socio-demographic details was collected and OHIP-14 was used for assessing their Oral Health-Related Quality of Life. The Oral Health Impact Profile consisted of 14 multiple choice questions assessing oral health-related problems in seven theoretical areas, including functional limitation, pain, physiological discomfort, physical disability, psychological disability, social disability, and handicap. Based on the presence or absence of the problem and its severity, each question had three options each, these options being always, sometimes, and never. The study proforma and OHIP-14 was administered to the participants after providing necessary instructions followed by a clinical examination.

Questionnaire validation: A pilot study was conducted among 100 subjects who were not included in the main study and comprised 10% of the study sample to check for reliability and validity. Reliability was measured through test-retest, and it showed that measured kappa (κ) is 0.88 and weighted kappa (κ) is 0.92. Internal consistency measured through Cronbach's alpha (α) was 0.76. Construct validity was assured using Spearman's correlation coefficient.

Clinical examination

The clinical examination of diabetic patients was carried out to assess their oral health status based on the WHO oral health assessment form 2013. Type III Examination was carried out using a plain mouth mirror and WHO probe to assess their dental caries experience, periodontal status, oral mucosal lesions, dental trauma, dental erosion, dental, and prosthetic status. All protocols and standard procedures were followed to safeguard the infection control during the study.

Training and calibration of examiners

All the examinations were carried out by three qualified examiners. Before the commencement of the study, the examiners were standardized and calibrated in the Department of Public Health Dentistry, by the Head of the Department, to ensure uniform interpretation, understanding, and the application of codes and criteria for the diseases to be observed and recorded and to ensure a consistent examination for assessing the Oral Health Status, and the inter-examiner reliability was 90%. The diagnostic variability was found to be low (Kappa value 0.84).

Statistical analysis

Microsoft Excel was used to tabulate the data, and the Statistical Package for the Social Sciences version 21 program

(SPSS Inc., Chicago, IL, United States) was used for statistical analysis. The t-test was used to compare the mean of the quality of life linked to oral health, and the chi-square test was used to compare the oral health status of diabetes patients who were insulin-dependent and those who were not. For the general intragroup comparison of OHRQOL means among insulin-dependent diabetic patients, Analysis of Variance (ANOVA) was used; a P-value of less than 0.05 was deemed statistically significant.

Results

There are more male patients in both the insulin-dependent and non-insulin-dependent categories. The majority of participants among non-insulin-dependent individuals were between the ages of 45 and 54. Insulin-dependent individuals were most likely to utilize a dose of 20 units, followed by 20–40 units and >40 units, respectively. When comparing the oral health status of insulin-dependent and non-insulin-dependent groups, the oral health condition of insulin-dependent diabetes patients was significantly poor. With the exception of dental fluorosis and oral mucosal lesions, insulin-dependent diabetic patients had higher rates of all other illnesses, including periodontal disease and loss of attachment (p values 0.045 and 0.033, respectively). When comparing the insulin-dependent diabetes group to the non-insulin-dependent diabetic group, the means of all 14 questions in the oral health impact profile questionnaire aside from those from the psychological impairment domain—were higher. When compared to the non-insulin diabetic group, the insulin-dependent diabetes group had significantly higher mean values in the domains of functional limits, physical pain, psychological discomfort, and disability. The comparison of the three insulin dose groups' total mean values for individuals with insulin-dependent diabetes is shown in Table 4. Using an independent t-test, each group of insulin-dependent diabetics was compared separately to the other two dose groups. When the highest dose group (>40 units) was compared to the other two groups, the results were extremely significant. The total comparison of OHRQOL means using the ANOVA test revealed a highly significant difference.

Table 1: Demographic Distribution of the non-insulin dependent diabetic mellitus (niddm) and insulin dependent diabetic mellitus (iddm)

Demographic details	Non-insulin dependent diabetic patients	Insulin dependent diabetic patients
Males	489 (53.6%)	60 (56.07%)
Females	423 (46.4%)	47 (43.93%)
Total	912 (100%)	107 (100%)
Distribution of non-insulin dependent diabetic patients based on age		
45-54 (49.2±2.9)	345 (37.82%)	47
55-64 (58.7±3.6)	316 (34.65%)	39
>65 (67.7±2.2)	251 (27.52%)	21
Total	912 (100%)	107
Distribution of insulin dependent diabetic patients based on dosage		
≤ 20 units	42 (39.3%)	
20-40 units	34 (31.7%)	
>40 units	31 (28.97%)	
Total	107 (100%)	

Table 2: Oral Health Status of non-insulin dependent diabetic mellitus (niddm) and insulin dependent diabetic mellitus (iddm)

Oral Health Status	niddm (%)	iddm (%)	P value
Dental caries	62%	68.2%	0.205
Periodontal status	74.3%	83.2%	0.045*
Loss of attachment	44.3%	55.1%	0.033*

Dental erosion	34.8%	36.4%	0.729
Dental fluorosis	9.5%	9.3%	0.949
Dental trauma	9.4%	9.5%	0.732
Dentures	22.4%	23.4%	0.837
Oral Mucosal Lesions	7.1%	4.7%	0.342

chi-square test. * = P<0.05 is significant

Table 3: OHIP-14 Items among the non-insulin dependent diabetic mellitus (niddm) and insulin dependent diabetic mellitus (iddm)

DOMAINS	OHIP Questions	Niddm	Iddm	P value
Functional Limitation	Have you had trouble pronouncing any words because of problems with your teeth, mouth or dentures?	2.26±0.55	2.48±0.72	0.001**
	Have you felt that your sense of taste has worsened because of problems with your teeth, mouth or dentures?	2.29±0.56	2.54±0.74	0.001**
Physical pain	Have you had painful aching in your mouth?	2.24±0.54	2.56±0.74	0.001**
	Have you found it uncomfortable to eat any foods because of problems with your teeth, mouth or dentures?	2.26±0.547	2.45±0.72	0.01**
Psychological discomfort	Have you been self-conscious because of your teeth, mouth or dentures?	2.17±0.429	3.38±0.660	0.001**
	Have you felt tense because of problems with your teeth, mouth or dentures?	1.28±0.55	2.523±0.72	0.0001**
Physical disability	Has your diet been unsatisfactory because of problems with your teeth, mouth or dentures?	2.26±0.54	2.36±0.66	0.076
	Have you had to interrupt meals because of problems with your	2.24±0.533	2.34±0.64	0.099

	teeth, mouth or dentures?			
Psychological disability	Have you found it difficult to relax because of problems with your teeth, mouth or dentures?	2.26±0.543	2.87±0.57	0.943
	Have you been a bit embarrassed because of problems with your teeth, mouth or dentures?	2.55±0.543	2.16±0.43	0.018*
Social disability	Have you been a bit irritable with other people because of problems with your teeth, mouth or dentures?	2.26±0.54	2.27±0.58	0.904
	Have you had difficulty doing your usual jobs because of problems with your teeth, mouth or dentures?	2.16±0.529	2.46±0.69	0.001*
Handicap	Have you felt that life in general was less satisfying because of problems with your teeth, mouth or dentures?	2.07±0.526	2.52±0.72	0.001**
	Have you been totally unable to function because of problems with your teeth, mouth or dentures?	2.47±0.532	3.72±0.7	0.001**

Independent t-test. * = P<0.05 is significant. **= P< 0.01 is highly significant

Table 4: Comparison of overall means of OHRQOL between the insulin dosage groups of insulin dependent diabetes patients

Overall Means of OHRQOL	Insulin (<=20 units)	Insulin (20-40 units)	Insulin (>40 units)	p-value
	2.32±0.13 ^a	2.38±0.11 ^b	2.78±0.17 ^c	0.001**

ANOVA test. **highly significant

Independent t-test between: a,b (non-significant); b,c (highly-significant); c,a (highly significant)

Discussion

One of the most common chronic illnesses in the world, diabetes mellitus has a significant impact on dental health. As a result, there is more proof that diabetes affects dental health and the quality of life associated with oral health.^[14] Numerous research studies on diabetes patients' oral health status and oral health-related quality of life have been published in the literature. To the best of our knowledge, this study is unique in that it compares the oral health status and oral health-related quality of life between the insulin-dependent and insulin-independent diabetic populations. Additionally, the insulin-dependent diabetic patients' oral health-related quality of life was evaluated based on the population's insulin dosage. With a mean age of 58.5%, the research comprised a greater proportion of individuals who were older than 50. Research by Sadeghi *et al.* (2012) and Nikbin *et al.*^[15] (2015) revealed that the mean age of participation was about the same. The number of insulin-dependent diabetic patients was larger in the dose group of less than 20 units (42 patients) and lower in the dosage group of more than 40 units (31 patients).

The WHO proforma 2013 was used to assess the oral health status of the study population. Patients with periodontal disorders had greater rates of dental cavities and loss of attachment than the entire study group. When comparing the insulin-dependent diabetes group to the non-insulin-dependent diabetic group, there was a significant difference in the periodontal state and attachment loss. Research by Bharateesh *et al.*^[16] (2016), Nadia Khalifa *et al.*^[17] (2017), and S. Azoughi Levy *et al.*^[18] (2018) among the diabetic research populations revealed similar findings on periodontal diseases and attachment loss. With the exception of dental fluorosis and oral mucosal lesions, all disease percentages are greater in insulin-dependent individuals.

The majority of the study populations' oral health-related quality of life is unaffected by the presence of diabetes, according to our examination of OHRQoL using a 14-item OHIP questionnaire. This finding is similar with research by Sadeghi *et al.*², Kumari *et al.*¹⁴, and Allen *et al.*^[19]. "A comparison of oral health-related quality of life (OHRQOL) indicates that insulin-dependent diabetic patients suffer significantly higher rates of deterioration. This trend persists across nearly all metrics, with the notable exceptions of physical disability and specific individual factors within the psychological and social domains." It was discovered that, regardless of insulin usage, the research population's oral health-related quality of life steadily declined as they grew older. This was consistent with research conducted by Kakoei *et al.*^[20]. When comparing the three dosage groups' total averages for oral health-related quality of life in the insulin-dependent diabetic population, there was a very significant difference; however, there was no significant difference when comparing the first two dosage groups. This suggests that when the insulin dose increased, oral health-related quality of life declined. There is evidence to support the theory that stress may contribute to the development of periodontitis in vulnerable patients by altering the host immune response.^[21] In fact, melancholy and stress have been identified as prevalent psychological issues in diabetes patients that may influence the development and course of periodontitis^[22]. Patients with diabetes, who have a disease entity with known impact on both oral and systemic health, represent a population who may benefit from medical and dental integration. The limitation of the study is that there is a large difference of sample size in between insulin dependent and non-insulin dependent diabetic groups that might have affected the results. Despite the limitation, the results of this study can be considered important baseline data for further studies in this area. The significant relation among insulin dosage, OHRQoL and general health in this study needs more attention since it is a relevant topic in the field of both dentistry and general medicine.

Conclusion

The study results finally conclude that oral health status is poorer among the diabetic patients especially in insulin dependent diabetic patients with regard to periodontal diseases and clinical attachment loss. Both insulin-dependent and non-insulin-dependent diabetic patients' OHRQOL has steadily decreased with age. Additionally, there is a negative relation between increasing insulin dose and OHRQOL. Therefore, it is necessary to design preventive health care interventions that aim to promote oral health status and the oral health related quality of life. These interventions should be customized to meet the treatment needs of the particular patient group that is medically challenged. Improving diabetes patients' oral health and understanding of oral disorders and how they affect their quality of life is a major responsibility of dentists and doctors.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. American Diabetes Association. Diagnosis and classification of diabetes mellitus. *Diabetes Care* 2004;27:S5–S10.
2. Sadeghi R, Taleghani F, Farhadi S. Oral health related quality of life in diabetic patients. *J Dent Res Dent Clin Dent Prospects* 2014;8:230-4.
3. Paredes-Rodríguez VM, Torrijos-Gómez G, González-Serrano J, López-Pintor-Muñoz RM, López-Bermejo MÁ, Hernández-Vallejo G. Quality of life and oral health in elderly. *J Clin Exp Dent* 2016;8:e590-6.
4. World Health Organization. (2018) Global report on diabetes. WHO Diabetes
5. Kaveeshwar SA, Cornwall J. The current state of diabetes mellitus in India. *Aust Med J* 2014; 7:45-48.
6. Manfredi M, McCullough MJ, Vescovi P, Al-Kaarawi ZM, Porter SR. Update on diabetes mellitus and related oral diseases. *Oral Dis* 2004;10:187–200.
7. Collin HL, Uusitupa M, Niskanen L, Kontturi-Närhi V, Markkanen H, Koivisto AM, *et al.* Periodontal findings in elderly patients with non-insulin dependent diabetes mellitus. *J Periodontol* 1998;69:962–6.
8. Quality of Life Assessment. The WHOQOL Group, 1994. What Quality of Life? The WHOQOL Group. In: World Health Forum. WHO, Geneva, 1996.
9. Susan Cornell. The Use of Insulin in Diabetes Management: The Next Generation. *Spectrum.diabetesjournals*. 29:(3); 133-134 2016.
10. N. Al-Taie, D. Maftei, A. Kautzky-Willer, M. Krebs, and H. Sting. Assessing the health-related quality of life in type 2 diabetes patients treated with insulin and oral antidiabetic agents. *Wien Klin Wochenschr*. 2019 Nov 18. doi: 10.1007/s00508-019-01573-0.
11. Shah S, Zilov A, Malek R, Soewondo P, Bech O, Litwak L. Improvements in quality of life associated with insulin analogue therapies in people with type 2 diabetes: results from the A1chieve observational study. *Diabetes Res Clin Pract*. 2011;94(3):364–70.
12. Pufal J, Gierach M, Pufal M, Bronisz A, Kiełbasa L, Junik R. The influence of socio-demographic and clinical factors on quality of life of patients with type 2 diabetes. *Diabetol Kliniczna*. 2004;4:137–136.
13. Vijan S, Hayward RA, Ronis DL, Hofer TP. Brief report: the burden of diabetes therapy: implications for the design of effective patient-centered treatment regimens. *J Gen Intern Med*. 2005;20:479–82.
14. Kumari M, Patthi B, Janakiram C, Singla A, Malhi R, Rajeev A. Oral health-related quality of life in well-controlled diabetic patients of Modinagar city: A cross-sectional study. *J Indian Assoc Public Health Dent* 2020;18:54-9.
15. Nikbin A, Bayani M, Jenabian N, Khafri S, Motalebnejad M. Oral health-related quality of life in diabetic patients: Comparison of the Persian version of geriatric oral health assessment index and oral health impact profile: A descriptive-analytic study. *J Diabetes Metab Disord* 2014;13:32.
16. Bharateesh J, Ahmed M, Kokila G. Diabetes and oral health: A case-control study. *Int J Prev Med* 2012;3:806-9.
17. Nadia Khalifa, Betul Rahman, Marianna D. Gaintantzopoulou, Suhail Al-Amad and Manal M. Awad. Oral health status and oral health-related quality of life among patients with type 2 diabetes mellitus in the United Arab Emirates: a matched case-control study. *Health and Quality of Life Outcomes* (2020) 18:182.
18. S Azogui-Levy, R Dray-Spira, S Attal, A Hartemann, F Anagnostou, J Azerad. Factors associated with oral health-related quality of life in patients with diabetes. *Australian Dental Journal* 2018; 63: 163–169.
19. Locker D, Allen PF. Developing short-form measures of oral health-related quality of life. *J Public Health Dent* 2002;62:13-20.
20. Kakoei S, Navabi N, Aghaabbasi S, Hashemipour MA. Oral health related quality of life in patients with diabetes mellitus type 2 in the year 2012. *J Oral Health Oral Epidemiol* 2016; 5(4): 186-91.
21. Doyle CJ, Bartold PM. How does stress influence periodontitis? *J Int Acad Periodontol*. 2012;14:42–9.
22. Novak M, Björck L, Giang KW, Heden-Ståhl C, Wilhelmsen L, Rosengren A. Perceived stress and incidence of type 2 diabetes: a 35-year follow-up study of middle-aged Swedish men. *Diabet Med*. 2013;30:e8–16.