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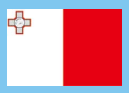

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ORIGINAL ARTICLE

Retrospective Cohort Study

Prevalence of obesity and diabetes in patients with schizophrenia

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Abstract

AIM

To compare the prevalence of diabetes in patients with schizophrenia treated at a community mental health center with controls in the same metropolitan area and to examine the effect of antipsychotic exposure on diabetes prevalence in schizophrenia patients.

METHODS

The study was a comprehensive chart review of psychiatric notes of patients with schizophrenia and schizoaffective disorder treated at a psychosis program in a community mental health center. Data collected included psychiatric diagnoses, diabetes mellitus diagnosis, medications, allergies, primary care status, height, weight, body mass index (BMI), substance use and mental status exam. Local population data was downloaded from the Centers for Disease Control Behavioral Risk Factor Surveillance System. Statistical methods used were χ^2 test, Student's *t* test, general linear model procedure and binary logistic regression analysis.

RESULTS

The study sample included 326 patients with schizophrenia and 1899 subjects in the population control group. Demographic data showed control group was on average 7.6 years older (P = 0.000), more Caucasians (78.7% *vs* 38.3%, P = 0.000), and lower percentage of males (40.7% *vs* 58.3%, P = 0.000). Patients with schizophrenia had a higher average BMI than the subjects in the population control (32.11, SD = 7.72 *vs* 27.62, SD = 5.93, P = 0.000).

Patients with schizophrenia had a significantly higher percentage of obesity (58.5% *vs* 27%, *P* = 0.000) than the population group. The patients with schizophrenia also had a much higher rate of diabetes compared to population control (23.9% *vs* 12.2%, *P* = 0.000). After controlling for age sex, and race, having schizophrenia was still associated with increased risk for both obesity (OR = 3.25, *P* = 0.000) and diabetes (OR = 2.42, *P* = 0.000). The increased risk for diabetes remained even after controlling for obesity (OR = 1.82, *P* = 0.001). There was no difference in the distribution of antipsychotic dosage, second generation antipsychotic use or multiple antipsychotic use within different BMI categories or with diabetes status in the schizophrenia group.

CONCLUSION

This study demonstrates the high prevalence of obesity and diabetes in schizophrenia patients and indicates that antipsychotics may not be the only contributor to this risk.

Key words: Schizophrenia; Antipsychotic; Diabetes; Body mass index; Obesity

Core tip: This study compares obesity and diabetes rates between schizophrenia patients treated in a community mental health center and a local population control. It demonstrates that prevalence of obesity and diabetes is significantly higher in patients with schizophrenia, which is consistent with previous research. In this cross-sectional study, second generation antipsychotic use and antipsychotic dosage were not correlated with obesity categories or diabetes status. This implies that antipsychotics alone may not be responsible for the increased diabetes risk in schizophrenia patients. Many factors may contribute to risk, including an inherent vulnerability to diabetes in schizophrenia patients that has been seen in earlier studies.

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INTRODUCTION

It is now well established that people with serious mental illness (SMI), including schizophrenia, have excess morbidity and mortality leading to a reduced lifespan of 20-25 years compared with the rest of the population[1,2]. The increased mortality is largely attributable to physical illness, including metabolic abnormalities and cardiovascular disease, rather than factors that are directly associated with psychiatric illness such as suicide or homicide.

Schizophrenia is seen in approximately 1% of the population. The rates of obesity and diabetes in patients with schizophrenia are higher than the general population[3]. Obesity is reported in approximately 50% patients, metabolic syndrome is reported in up to 40%, glucose intolerance in up to 25% and diabetes in up to 15% patients with schizophrenia[4]. The cause for the increased prevalence of these conditions is multifactorial. Antipsychotics, a cornerstone of treatment in people with schizophrenia, cause weight gain, glucose intolerance and other metabolic complications. Second generation antipsychotics, notably clozapine and olanzapine, are associated with a 5-fold increase in metabolic syndrome after three years of treatment[5]. Patients with schizophrenia are known to have unhealthy diets and inadequate physical activity[6] due to lower socioeconomic status, lower educational level, and sub-optimal living situations. Symptoms of schizophrenia such as low motivation, apathy and cognitive deficits also could play a role in preventing access to high quality health care.

An additional important contributing factor to the increased prevalence of diabetes in schizophrenia may be an inherent susceptibility to diabetes in people with schizophrenia. Patients with schizophrenia have an increased risk of diabetes in family members[7,8]. Also, parental diabetes is a significant predictor of diabetes in people with psychotic disorders[8]. Inflammatory markers are seen in both schizophrenia and metabolic syndrome and the increased inflammation may explain the association between these conditions[9].

A recent meta-analysis of metabolic parameters in first episode psychosis patients demonstrated increased insulin resistance and impaired glucose tolerance when compared to controls[10]. However, an earlier review of diabetes in first episode patients showed that established diabetes was much less common in first-episode psychosis patients compared to those already on antipsychotics[11]. People with schizophrenia may have increased vulnerability manifesting as pre-diabetes that is compounded by cumulative exposure to antipsychotic medications.

The purpose of this study is to compare the prevalence of obesity and diabetes in patients with schizophrenia treated at a community mental health center with population controls in the same metropolitan area. The authors hypothesized that the prevalence would be higher in patients with schizophrenia. The study also examines the effect of antipsychotic exposure on diabetes prevalence in schizophrenia patients.

MATERIALS AND METHODS

Comprehensive psychiatric review notes of consecutive patients followed at Connecticut Mental Health Center (CMHC) Psychosis Program within a one-year period were audited. The study was approved by the Yale Human Investigations Committee. Inclusion criterion was a chart diagnosis of schizophrenia or schizoaffective disorder verified by the Structured Clinical Interview for

Table 1 Demographic characteristics

	Schizophrenia	Population control
n	326	1899
Age[a]	47.47 (± 26)	55.13 (± 18.21)
Sex (% male)[b]	58.30%	40.70%
Race[c]		
White	38.30%	78.70%
Black	49.70%	9.50%
Hispanic	6.40%	7.90%
Other	1.80%	3.90%
Diagnosis		
Schizophrenia	7%	
Schizoaffective	23.30%	
Antipsychotic medication (*n* = 306)		
First generation	81 (26.5%)	
Second generation	194 (63.4%)	
Both	31 (10.1%)	
Multiple antipsychotic use	59 (2.7%)	
Chlorpromazine equivalent dose	667.0 (± 507.9)	

[a]$P = 0.000$; [b]$P = 0.000$; [c]$P = 0.000$.

Diagnostic and Statistical Manual-IV (SCID for DSM-IV). CMHC Psychosis Program is a diagnosis specific, multidisciplinary outpatient clinic and research program, which serves community dwelling, low-income adult patients diagnosed with a non-affective psychosis. The program is the major point of care for psychotic patients who dwell in the Greater New Haven area, an urban catchment area with an estimated census of 200000 people. The program itself has a census ranging 450 to 500 patients, with about 5% annual turnover rate.

Comprehensive psychiatric review is a 30-50 min full psychiatric examination of established patients by one of four physicians and one advanced practice nurse. Notes are recorded in an institution specific standard form, and requires recording of all diagnoses, all medications, allergies, primary care and physical/gynecological exam status, review of systems, height, weight, body mass index (BMI), substance use, and mental status information. Per Psychosis Program policies, every patient is weighed before the exam with the same scale calibrated regularly and height is measured at least once with the same scale during patients' tenure in the clinic. While waist circumference is a better indicator of abdominal obesity and subsequent cardiovascular risk, it is not clear that it offers additional information for clinical management. Also it is not part of usual clinical care due to provider discomfort[12]. Hence, BMI was used as an index for obesity in this study. Diabetes mellitus (DM) type 2 diagnosis was extracted from the chart by self-report and verified by obtaining primary care records. In addition, patients were screened at least yearly for diabetes by glycosylated hemoglobin (Hba1c) and referred for treatment if they tested positive.

The control group is local population in Greater New Haven metro area and data are downloaded from United States Centers for Disease Control and Prevention (CDC) Behavioral Risk Factors Surveillance System (BRFSS)[13]. BRFSS is an ongoing telephone health survey tracking health conditions and risk behaviors in the United States. Details are described at www.cdc.gov/brfss/. Latest local data was from 2012.

De-identified patient and population data was merged in an SPSS v.22 data file, and corresponding variables recoded for compatibility. Categorical data was compared with χ^2 test, continuous data with Student's *t* test. General linear model (GLM) procedure was utilized to explore the relationship between BMI and schizophrenia while controlling for demographic factors. Binary logistic regression analysis was utilized to calculate adjusted odds ratios.

RESULTS

The study sample included 326 patients with schizophrenia and 1899 subjects in control group of local population. Demographic data for the population control and schizophrenia as well as clinical data for the schizophrenia subjects is presented in Table 1. Control group was on average 7.6 years older ($t = 7.36$, $P = 0.000$), included more subjects that identified themselves as Caucasian (78.7% *vs* 38.3%, $\chi^2 = 228.35$, $P = 0.000$), and had lower percentage of males (40.7% *vs* 58.3%, $\chi^2 = 35.02$, $P = 0.000$).

Subjects with schizophrenia had a higher average BMI (32.11, SD = 7.72) than the subjects in the control group (27.62, SD = 5.93). The difference was highly significant (4.49, 95%CI: 3.75, 5.23; $T = 11.83$, $P = 0.000$). When BMI categories were examined, schizophrenia group had a significantly higher percentage of obesity than the control group (58.5% *vs* 27%), and the control group had a higher percentage of normal and overweight subjects (Figure 1, $\chi^2 = 125.14$, $P = 0.000$). When obesity categories were examined among the obese subjects, schizophrenia group had a higher percentage of Class 2 and 3 obesity (*i.e.*, BMI between 35 to 40 and BMI > 40 respectively) than the control group (Figure 2, $\chi^2 = 6.13$, $P < 0.05$). Within the schizophrenia group, antipsychotic medication dosage was not significantly correlated with BMI either in the entire group or the obese group ($P = 0.93$ and 0.92 respectively). Also, there was no difference in the distribution of second generation antipsychotic use or multiple antipsychotic use within different BMI categories in the schizophrenia group ($P = 20.24$ and 0.19 respectively). Based on these findings, medication variables were dropped out of multivariable tests.

Given the differences between two groups in demographics, a univariate analysis was conducted and GLM procedure used to control for age, sex, and race. After controlling for these demographic variables, schizophrenia group still had a highly significant association with higher BMI ($F = 26.78$, df = 1, $P = 0.003$). None of the other variables, or interactions with demographic variables, were significant. Following this, a binary logistic regression analysis was conducted

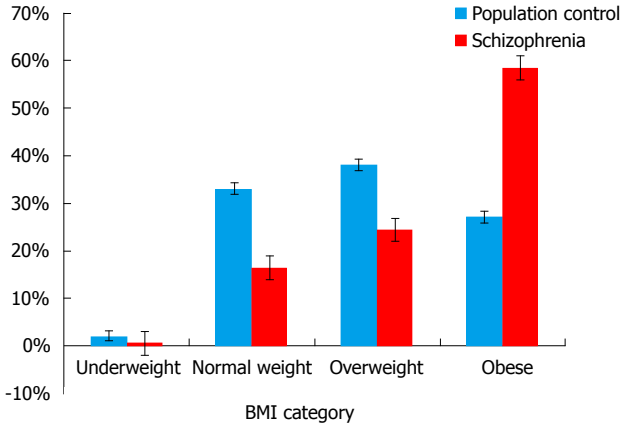

Figure 1 Body mass index categories for schizophrenia patients *vs* population (%). BMI: Body mass index.

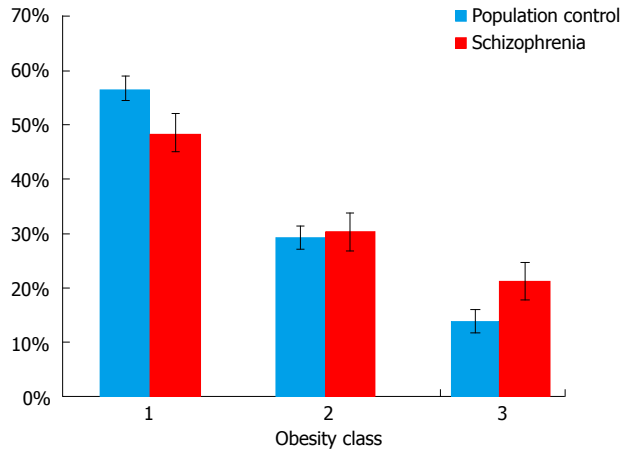

Figure 2 Obesity class categories; schizophrenia patients *vs* population (%).

to calculate predictive value of schizophrenia status for obesity after age, sex and race controlled, and schizophrenia status remained significant with an odds ratio of 3.25 (95%CI: 2.47, 4.29, P = 0.000).

Next, diabetes mellitus status was examined in the sample. Schizophrenia group had a much higher rate of diabetes compared to control group (Figure 3, 23.9% *vs* 12.2%, χ^2 = 31.81, P = 0.000). Within the schizophrenia group, there were no statistically significant differences between diabetics and non-diabetics in rates of second generation antipsychotic use, multiple antipsychotic medication use or chlorpromazine equivalent daily antipsychotic dosage. Based on these findings, medication terms were dropped from multivariable analyses. Following this, a binary logistic regression procedure was conducted to control for demographic variables of age, sex and race to examine the relationship between schizophrenia and diabetes. Higher age (P = 0.000) and non-Caucasian race (P = 0.000) was significantly predictive of diabetes status and male sex approached significance (P = 0.07). After controlling for these demographic factors, schizophrenia remained highly associated with diabetes with an odds

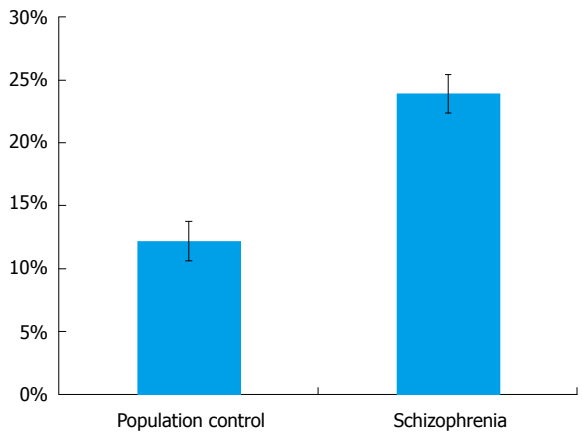

Figure 3 Diabetes mellitus prevalence in schizophrenia *vs* population (%).

ratio of 2.42 (95%CI: 1.75, 3.36, P = 0.000). Since obesity is closely associated with diabetes, one more regression analysis was performed including first BMI, and then obesity status (Table 2) and schizophrenia still remained highly significantly associated with diabetes.

DISCUSSION

In this study, patients with schizophrenia had a significantly higher average BMI, higher percentage of people with class 2 and class 3 obesity and higher percentage of people with diabetes, compared to the general population. The association for both obesity and diabetes remained after controlling for differences in demographic variables between the two groups. Having schizophrenia was associated with more than a 3-fold risk of obesity and more than a 2-fold risk of diabetes.

These results are consistent with what is known about the increased risk for metabolic syndrome in patients with schizophrenia. But a notable finding is that after controlling for BMI and obesity status, the risk of diabetes remained significant, though lower. Though pathways of diabetes development are thought to be the largely the same as those causing obesity, diabetes can occur without weight gain in patients on antipsychotic medications[14]. It is postulated that antipsychotics may to some extent affect glucose regulation independent of their effect on weight.

In this study design, medication variables for the general population were unknown and could not be compared with the schizophrenia group. Within the schizophrenia group, antipsychotic dose, second generation antipsychotics and use of multiple antipsychotic medications did not vary between the different categories of obesity or with diabetes status. It is notable that antipsychotic medication factors did not account for the differences in either obesity or diabetes status within the schizophrenia group. Neither the antipsychotic category nor the medication dose correlated with obesity. The strong risk of obesity and diabetes in schizophrenia coupled with lack of differential effects between antipsychotic medications and persistent risk

Table 2 Adjusted odds of diabetes mellitus in schizophrenia

	B	S.E.	Wald	Df	*P*	Odds ratio	95%CI for Odds ratio	
							Lower	Upper
Age	0.36	0.005	61.88	1	0	1.036	1.027	1.045
Sex (male)	0.34	0.133	6.51	1	0.011	1.405	1.082	1.825
Race (non-white)	0.52	0.156	11.29	1	0.001	1.689	1.224	2.292
Obesity	1.25	0.137	84.61	1	0	3.514	2.689	4.593
Schizophrenia	0.6	0.179	11.31	1	0.001	1.825	1.285	2.59

of diabetes after controlling for obesity in this sample indicates some of the risk may be due to factors other than medications. Many other factors including an innate risk may be responsible for the higher prevalence of obesity and diabetes in the schizophrenia population. An inherent susceptibility to diabetes in schizophrenia patients is supported by studies with medication naive first episode psychosis patients[10]. The inherent risk for diabetes may be mediated in part by elevated levels of inflammatory cytokines seen in both schizophrenia and obesity[9]. On the other hand, cross sectional data may not be sufficient to unravel the complicated relationship between schizophrenia, antipsychotic medications, obesity and diabetes since patients go through medication changes over the course of the disease.

Other factors may affect these results. The survey data from BRFSS is based on self-report by metropolitan area residents. People may have undiagnosed diabetes and tend to underestimate and underreport obesity. Patients with schizophrenia have increased contact with health care leading to higher likelihood of diabetes screening during mental health treatment. However, the increased prevalence of diabetes seen in this study is consistent with earlier reports and is unlikely to result from a screening bias given that historically people with SMI have low rates of screening and treatment for metabolic conditions[15].

This study did not find a correlation between second generation antipsychotics and obesity and diabetes status. It may be that the differential effects of first and second generation antipsychotics on metabolic syndrome are not as different as previously believed. Indeed, the rates of metabolic syndrome between first and second generation antipsychotics are not significant when clozapine and olanzapine are excluded[5]. A meta-analysis of antipsychotic-induced weight gain in first episode psychosis patients showed that most antipsychotic medications, including first generation medications like haloperidol, are associated with some weight gain[16].

An innate predisposition to diabetes, seen in first episode psychosis patients, may be compounded by antipsychotic medications, lower socioeconomic status and decreased access to quality health care. Patients with schizophrenia also are less physically active contributing further to insulin resistance. Antipsychotics alone may not account for the high metabolic burden seen in chronic schizophrenia patients and high mortality rates. In fact, antipsychotic use is associated with overall lower mortality, especially when highly effective medications like clozapine are used for treating schizophrenia[17].

Strengths of this study include the large naturalistic sampling of community dwelling schizophrenia patients as well as a local population control sample in the same geographic area. Patients were not recruited for the study, instead all patients in the Psychosis Program with diagnosis of schizophrenia were included. This study design allows for applicability of results to real world settings. In the community mental health center sample, schizophrenia diagnosis was based on a structured interview and diabetes diagnosis was established based on previous lab diagnosis. A limitation is that the BRFSS survey data was based on self-report. Also the antipsychotic use is cross sectional and results may be confounded by changes in the type of antipsychotic used throughout patients' disease history. Since this was not a controlled study, demographic variables were different between the disease and control groups. While these may confound results, in our study, higher prevalence of obesity and diabetes in schizophrenia persisted after controlling for these variables.

In conclusion, this study is consistent with previous research showing significantly increased prevalence of obesity and diabetes in people with schizophrenia. The risk for diabetes is present even when weight is controlled for as a causative factor. Antipsychotics contribute to the burden of diabetes but may not be the primary cause. Since schizophrenia patients are associated with a very high risk of diabetes, clinicians should be vigilant about screening and monitoring patients for diabetes from the beginning of treatment.

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COMMENTS

Background

People with serious mental illness (SMI), including schizophrenia, have

excess morbidity and mortality compared with the rest of the population, largely attributable to physical illness, including metabolic abnormalities and cardiovascular disease. The rates of obesity and diabetes in patients with schizophrenia are higher than the general population. The cause for the increased prevalence of these conditions is multifactorial. Antipsychotics, unhealthy diets, inadequate physical activity due to lower socioeconomic status, lower educational level, and sub-optimal living situations and symptoms such as low motivation, apathy and cognitive deficits could all play a role in increased metabolic risks in this population. An additional important contributing factor to the increased prevalence of diabetes in schizophrenia may be an inherent susceptibility to diabetes in people with schizophrenia. People with schizophrenia may have increased vulnerability manifesting as pre-diabetes that is compounded by cumulative exposure to antipsychotic medications. This study compares the prevalence of obesity and diabetes in schizophrenia patients treated at a community mental health center with controls in the same metropolitan area. The study also examines the effect of antipsychotic exposure on diabetes prevalence in schizophrenia patients.

Research frontiers

Many studies show there may be an inherent risk for diabetes in schizophrenia patients as evidenced by increased insulin resistance in patients with new onset of psychosis. Inflammatory pathways seen in both schizophrenia and people with obesity and diabetes may mediate some of this risk. The pathways leading to obesity and those leading to diabetes are not well differentiated. All these are important areas for further research. The detrimental effect of antipsychotics on weight and insulin resistance is well known. However, the extent of this risk compared to other factors is not clear. The contribution of various known risk factors on development of metabolic syndrome in people with schizophrenia is an area for further study.

Innovations and breakthroughs

More and more studies are establishing that there is a high prevalence of obesity and diabetes in schizophrenia. There is emerging evidence that some risk of diabetes may be present independent of weight. The present study adds to existing evidence that antipsychotics, while contributing to burden of diabetes, are not the only cause.

Applications

This naturalistic study is consistent with existing research that shows high prevalence of obesity and diabetes in schizophrenia patients. The risk of diabetes appears to be mediated not only by weight gain but other factors. Hence, not only weight but also diabetes screening should be prioritized in schizophrenia populations. Also this should be done regardless of whether they are on antipsychotic medications or not. Clinicians should be vigilant about early detection and treatment. Many studies in people after the first episode of psychosis demonstrate that early detection and treatment of obesity and diabetes may improve morbidity and mortality.

Terminology

First generation antipsychotics refer to a group of antipsychotics used to treat schizophrenia, whose primary mechanism of action is *via* dopamine. Second generation antipsychotics refer to antipsychotics that were developed later and have pharmacologic actions on both dopamine and serotonin. The latter group is generally considered to carry a higher risk for metabolic syndrome.

Peer-review

The manuscript is well written and concise.

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Observational Study

Age-dependent changes in the association between sleep duration and impaired glucose metabolism

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Abstract

AIM

To investigate whether the association between sleep duration and impaired glucose metabolism varies among younger and older populations.

METHODS

We reviewed data of self-reported habitual sleep duration per night, HbA1c levels, and clinically relevant factors in a cross-sectional checkup database of 75472 Japanese from the general population aged 20-79 years (51695 men and 23777 women). Associations of prediabetes (HbA1c $\geqslant$ 5.7% and/or diabetic pharmacotherapy) or diabetes (HbA1c $\geqslant$ 6.5% and/or diabetic pharmacotherapy) with short and long sleep durations compared with a reference sleep duration (7 h) were investigated by multivariate logistic regression analysis. We controlled for potential relevant confounders, including age, sex, and work duration per day according to younger and older subjects.

RESULTS

As age advanced, sleep duration became longer and this increase in the 40s and 50s was two times greater in men than in women. This finding was accompanied by a deterioration in HbA1c levels. In subjects aged younger

than 40 years (n = 32929), HbA1c levels were inversely and linearly correlated with sleep duration in both sexes. However, in subjects aged 40 years or older (n = 42543), HbA1c levels showed a non-linear relationship against sleep duration with a nadir at 7 h. Multivariate logistic regression analysis showed that in younger subjects, short durations of sleep (≤ 5 h and 6 h) were positively associated with prediabetes (both P < 0.001), but a long duration of sleep (≥ 8 h) was inversely associated with prediabetes (P < 0.001). These associations remained significant after adjustment for relevant confounders, including age, sex, and work duration per day (ORs = 1.20, 95%CI: 1.05-1.37, P < 0.001; ORs = 1.12, 95%CI: 1.02-1.24, P < 0.05; and ORs = 0.84, 95%CI: 0.72-0.99, P < 0.05, respectively). In contrast, in older subjects, besides an association of prediabetes with a short duration of sleep (≤ 5 h) (ORs = 1.12, 95%CI: 1.03-1.21, P < 0.01), diabetes was significantly associated with a long duration of sleep (≥ 8 h) (ORs = 1.11, 95%CI: 1.02-1.25, P < 0.05).

CONCLUSION

A short sleep duration may be associated with prediabetes throughout life. However, the association between a long sleep duration and glucose metabolism can change with aging.

Key words: Sleep; Prediabetes; Diabetes; HbA1c; Aging

Core tip: Short and long durations of sleep have been putatively associated with type 2 diabetes. However, whether age affects these associations is unknown, although sleep duration and glucose homeostasis can change with advancing age. Our study demonstrated that a short sleep duration may be associated with prediabetes throughout the lifespan, whereas a long duration of sleep may be inversely associated with prediabetes in younger subjects. Additionally, a long sleep duration was associated with diabetes in older subjects. Therefore, aging may substantially affect the association between a long sleep duration and glucose homeostasis.

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INTRODUCTION

For the last two decades, many clinical studies have shown that shorter and longer durations of sleep are associated with health hazards, including type 2 diabetes, metabolic syndrome, and increased all-cause mortality[1-16]. Although a short sleep duration may be robustly associated with impaired glucose homeostasis, there are conflicting results, especially concerning a long sleep duration[3,5,8,13,15]. Generally, glucose homeostasis is aggravated with aging, probably owing to reduced pancreatic β-cell function and increased insulin resistance[17-19]. In contrast, individual's sleep duration can become longer and its quality can be aggravated (*e.g.*, more fragmented) as people become older[11,20], although it has been shown that objectively measured sleep duration generally decreases with age[21]. Taken together, these findings suggest that glucose homeostasis and sleep duration likely change with advancing age. However, to date, the effect of aging on the association between sleep duration and impaired glucose metabolism is less clear, regardless of accumulated evidence[1-7,9-15].

Based on the findings mentioned above and the worldwide extension of the life span[22,23], we investigated whether the association between self-reported sleep duration and dysglycemia varies among younger and older generations in the general Japanese population who undergo an annual medical checkup.

MATERIALS AND METHODS

This cross-sectional study consisted of data that were recorded in medical checkups of people living or working in Saitama, a suburb of Tokyo, Japan. The original study has been described in more detail elsewhere[24]. The current study involved two institutions in Kanagawa and Saitama, Japan, including Kanagawa University of Human Services and Saitama Health Promotion Corporation, a public interest corporation. The protocol was approved by the Ethics Committee of Kanagawa University of Human Services (No. 10-22). All procedures that were followed were in accordance with the ethical standards of the responsible committee on human experimentation (Kanagawa University of Human Services, Japan) and with the Helsinki Declaration of 1975, as revised in 2008. Informed consent was obtained from all patients for being included in the study.

Subjects

We reviewed the data for 116817 subjects who underwent a medical health checkup at the Saitama Health Promotion Corporation in 2007. Individuals who required immediate treatment for serious conditions, such as suspected cancer, heart failure, atherosclerotic disease, or infectious pneumonia, were not included from the beginning of the study. All recruited subjects, who were free from disability and hemiplegia, answered a questionnaire about their lifestyle characteristics. After exclusion of subjects with incomplete data (n = 41345), 75472 apparently healthy subjects aged 20-79 years were enrolled, without any special selections. Subjects were primarily divided into younger subjects (< 40 years old, n = 32929) and older subjects (≥ 40 years old, n = 42543).

Anthropometric and laboratory tests, and sleep duration

All anthropometric and laboratory tests were carried out in the morning. Body mass index was calculated as weight (kg) divided by height (m^2). Serum parameters were measured using standard methods by the Hitachi autoanalyzer (Tokyo, Japan) at Saitama Health Promotion Corporation. Glycated hemoglobin (HbA1c) was measured in Japan Diabetes Society (JDS) HbA1c units, which were converted to National Glycohemoglobin Standardization Program HbA1c units using the officially certified formula: HbA1c (NGSP) (%) = 1.02 × JDS (%) + 0.25%[25].

Prediabetes (including diabetes) was defined as HbA1c ⩾ 5.7% or any pharmacotherapy for diabetes. Diabetes was defined as HbA1c ⩾ 6.5% or any pharmacotherapy for diabetes[26]. Accordingly, subjects with prediabetes included those with diabetes. We considered the white blood cell (WBC) count, a surrogate marker for inflammation, as an important confounding factor for the association between sleep duration and dysglycemia. However, available data of the WBC count were limited in this study (n = 74837). Self-reported sleep duration per night, which was obtained as a response to a simple question about sleep, was divided into five categories of ⩽ 5, 6, 7, 8, and ⩾ 9 h of sleep duration.

Statistical analysis

Data are expressed as the mean ± SD or median (interquartile range). Differences in continuous variables between men and women were assessed by the *t*-test. In each age group, subjects were divided into four groups according to sleep duration per night: ⩽ 5, 6, 7, and ⩾ 8 h. The percentage of subjects with ⩾ 9 h sleep duration was small (1.1%). Therefore, subjects with an 8-h sleep duration and subjects with ⩾ 9 h of sleep duration were grouped together as subjects with ⩾ 8 h of sleep duration. *P* values for continuous variables were determined using ANOVA and for categorical variables using the χ^2 test. Linear correlations were examined by Pearson's correlation coefficients after coding ⩽ 5, 6, 7, 8, and ⩾ 9 h of sleep duration as continuous values of 5-9, respectively. Multivariate logistic regression models were used to examine the associations between sleep duration and prediabetes or diabetes, compared with a reference sleep duration of 7 h[5,7,8]. These models were used with or without adjustment for relevant confounders, which yielded crude and adjusted odds ratios and 95%CIs. Tests for linear trends (*P* for trend) were calculated by treating sleep duration as a continuous variable (*i.e.*, 1-4 for a sleep duration of ⩽ 5, 6, 7, and ⩾ 8 h, respectively), and the same model analysis was conducted. Statistical review of the study was performed by Dr. Eiichiro Kanda, MD, PhD, MPH, Department of Nephrology, Tokyo Kyosai Hospital, Tokyo, Japan. Statistical analyses were performed using SPSS software version 22.0 (SPSS-IBM, Chicago, IL, United States) and Statview version 5.0 (SAS Institute, Cary, NC, United States). Values of $P < 0.05$ were considered to be statistically significant.

RESULTS

Clinical characteristics of subjects in the younger and older groups are shown in Tables 1 and 2, respectively. Overall, in younger and older subjects, as sleep duration increased, age increased and work duration decreased (both $P < 0.0001$, ANOVA). In older subjects, as sleep duration became longer, most of the parameters became worse (all $P < 0.0001$), except for body mass index (BMI) and the prevalence of regular exercise. In short-duration sleepers, the prevalence of current smokers was higher in younger subjects, whereas it was lower in older subjects. Notably, the rates of current smokers and everyday alcohol drinkers were prevalent in older long sleepers (41.1% and 32.0%, respectively) among the overall subjects (Table 2). Duration of sleep was inversely correlated with the WBC count in younger subjects (r = -0.03, $P < 0.0001$, Pearson's correlation), but it was positively correlated with the WBC count in older subjects (r = 0.02, $P < 0.0001$).

Figure 1 shows overall sleep duration according to age groups and sex. Sleep duration became prolonged as age advanced, and this increase was approximately two times greater in men than in women at middle age (40-59 years) owing to a dip in sleep duration in women. HbA1c levels increased with increasing age in both sexes (Figure 2). In younger subjects, sleep duration was inversely and linearly correlated with HbA1c levels (r = -0.04, $P < 0.0001$), regardless of sex (Figure 3). In older subjects, HbA1c levels showed a non-linear relationship against sleep duration with a nadir 7 h. When subjects were divided by every 10 years, similar results were observed (Figure 4), but the relationship of HbA1c was almost flat against sleep duration in subjects in their 40s (r = -0.006, P = 0.41).

Multivariate logistic regression analysis showed that in younger subjects, short durations of sleep (⩽ 5 h, 6 h) were positively associated with prediabetes compared with the reference duration of sleep (7 h). These findings remained significant after adjustment for relevant confounders (Table 3) ($P < 0.01$ and $P < 0.05$, respectively). In contrast, a long duration of sleep (⩾ 8 h) was inversely associated with prediabetes ($P < 0.05$). Either short or long duration of sleep were not significantly associated with diabetes after full adjustment for relevant confounding factors. In older subjects, a short duration of sleep (⩽ 5 h) was positively associated with prediabetes, which also remained significant after full adjustment (Table 4) ($P < 0.01$). However, a long duration of sleep (⩾ 8 h) was marginally associated with diabetes after full adjustment for relevant confounders ($P < 0.05$). Overall, prediabetes was inversely associated with sleep duration in younger and older subjects ($P < 0.001$ and $P < 0.01$ for linear trend, respectively). However,

Table 1 Characteristics of younger subjects classified by sleep duration

Sleep duration	⩽ 5 h	6 h	7 h	⩾ 8 h	*P* values
n (%)	4110 (12.5)	16265 (49.4)	9377 (28.5)	3177 (9.6)	
Male, *n* (%)	2865 (69.7)	11121 (68.4)	6349 (67.7)	2026 (63.8)	< 0.0001
Age (yr)	30.5 ± 5.5	30.4 ± 5.3	30.7 ± 5.3	31.1 ± 5.3	< 0.0001
BMI (kg/m^2)	23.4 ± 3.9	23.1 ± 3.7	22.8 ± 3.6	23.0 ± 3.8	< 0.0001
Systolic blood pressure (mmHg)	118 ± 14.3	118 ± 14.5	118 ± 14.6	119 ± 14.8	0.58
White blood cell count (× 10^9/L)	6.67 ± 1.8	6.48 ± 1.7	6.46 ± 1.7	6.48 ± 1.9	< 0.0001
Serum triglycerides (mmol/L)	0.9 (0.6-1.5)	0.9 (0.6-1.4)	0.9 (0.6-1.5)	0.9 (0.6-1.5)	0.46
Serum HDL-cholesterol (mmol/L)	1.6 ± 0.4	1.6 ± 0.4	1.6 ± 0.4	1.6 ± 0.4	0.04
HbA1c (NGSP, %)	5.35 ± 0.5	5.32 ± 0.5	5.30 ± 0.4	5.29 ± 0.5	< 0.0001
Work duration (h/d)	9.4 ± 1.5	9.0 ± 1.4	8.6 ± 1.3	8.1 ± 1.4	< 0.0001
Pharmacotherapy for					
Hypertension, *n* (%)	25 (0.6)	73 (0.4)	38 (0.4)	19 (0.6)	0.29
Diabetes, *n* (%)	13 (0.3)	39 (0.2)	22 (0.2)	11 (0.3)	0.83
Dyslipidemia, *n* (%)	11 (0.3)	46 (0.3)	24 (0.3)	22 (0.7)	0.0001
Current smokers, *n* (%)	1791 (43.6)	5980 (36.8)	3221 (34.4)	964 (30.3)	< 0.0001
Everyday alcohol consumers, *n* (%)	353 (8.6)	1386 (8.5)	1022 (10.9)	370 (11.6)	< 0.0001
Regular exercisers, *n* (%)[1]	553 (14.4)	3154 (17.2)	2740 (19.4)	1367 (21.8)	< 0.0001
Past history of					
CVD, *n* (%)	46 (1.1)	129 (0.8)	102 (1.1)	46 (1.4)	0.002

Data are presented as mean ± SD, median (interquartile range), or *n* (%). *P* values were determined by ANOVA and χ^2 tests were used for continuous and categorical variables. Serum triglyceride concentrations were log transformed before parametric analysis. [1]Regular exercise was defined as ⩾ 30 min exercise per session at least twice a week. Values of white blood cell count are only available in 32713 subjects (*n* = 4073, 16171, 9313, and 3156, for ⩽ 5 h, 6 h, 7 h, and ⩾ 8 h sleep duration, respectively). BMI: Body mass index; HDL: High-density lipoprotein; NGSP: National Glycohemoglobin Standardization Program; CVD: Cardiovascular disease.

Table 2 Characteristics of older subjects classified by sleep duration

Sleep duration	⩽ 5 h	6 h	7 h	⩾ 8 h
n (%)	3838 (9.0)	18319 (43.1)	14115 (33.2)	6271 (14.7)
Male, *n* (%)	2197 (57.2)	11630 (63.5)	10399 (73.7)	5108 (81.5)
Age (yr)	49.4 ± 6.9	50.4 ± 6.8	51.8 ± 7.2	54.3 ± 8.4
BMI (kg/m²)	23.9 ± 3.7	23.8 ± 3.5	23.7 ± 3.3	23.7 ± 3.2
Systolic blood pressure (mmHg)	125 ± 18.2	126 ± 18.2	128 ± 18.4	131 ± 19.0
White blood cell count (× 10^9/L)	6.6 ± 1.8	6.5 ± 1.7	6.5 ± 1.7	6.6 ± 1.8
Serum triglycerides (mmol/L)	1.1 (0.7-1.8)	1.2 (0.8-1.8)	1.3 (0.8-1.9)	1.3 (0.9-2.0)
Serum HDL-cholesterol (mmol/L)	1.6 ± 0.4	1.6 ± 0.4	1.6 ± 0.4	1.6 ± 0.4
HbA1c (NGSP, %)	5.69 ± 0.8	5.69 ± 0.8	5.70 ± 0.8	5.77 ± 0.9
Work duration (h/d)	8.9 ± 1.7	8.5 ± 1.5	8.3 ± 1.3	8.1 ± 1.3
Pharmacotherapy for				
Hypertension, *n* (%)	355 (9.3)	1970 (10.8)	1843 (13.1)	1091 (17.4)
Diabetes, *n* (%)	138 (3.6)	633 (3.5)	559 (4.0)	343 (5.5)
Dyslipidemia, *n* (%)	109 (2.8)	621 (3.4)	536 (3.8)	278 (4.4)
Current smokers, *n* (%)	1239 (32.3)	5981 (32.6)	4982 (35.3)	2580 (41.1)
Everyday alcohol consumers, *n* (%)	651 (17.0)	3378 (18.4)	3493 (24.7)	2009 (32.0)
Regular exercisers, *n* (%)[1]	611 (14.9)	2938 (18.1)	1913 (20.4)	617 (19.4)
Past history of				
CVD, *n* (%)	125 (3.3)	620 (3.4)	568 (4.0)	323 (5.2)

Data are presented as mean ± SD, median (interquartile range), or *n* (%). *P* values determined by ANOVA and χ^2 tests for all continuous and categorical variables listed above were < 0.0001 (data not shown). Serum triglyceride concentrations were log transformed before parametric analysis. [1]Regular exercise was defined as ⩾ 30 min exercise per session at least twice a week. Values of white blood cell count are only available in 42124 subjects (*n* = 3809, 18172, 13973, and 6170, for ⩽ 5 h, 6 h, 7 h, and ⩾ 8 h sleep duration, respectively). BMI: Body mass index; HDL: High-density lipoprotein; NGSP: National Glycohemoglobin Standardization Program; CVD: Cardiovascular disease.

a significant association was not observed between diabetes and duration of sleep in both generations.

DISCUSSION

This large, epidemiological study of the general Japanese population showed that a short duration of sleep was robustly associated with prediabetes, but not diabetes, in young and old generations. In contrast, a long duration of sleep was inversely associated with prediabetes in the young generation, but it was positively associated with diabetes in the old generation. Therefore, aging may affect the relationship between a long sleep duration and glucose homeostasis.

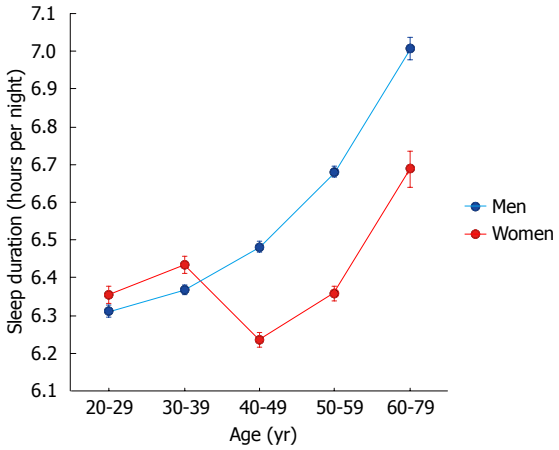

Figure 1 Sleep duration according to age groups and sex. Each point and vertical bar represent the mean ± 1.96 SE. Sleep duration in men and women increased with increasing age (both $P < 0.0001$, ANOVA). Significant differences were observed in sleep duration between men and women in all age groups (all $P < 0.0001$, except for $P = 0.003$ in the 20s, *t*-test). The corresponding number of subjects is shown in the side of the bar.

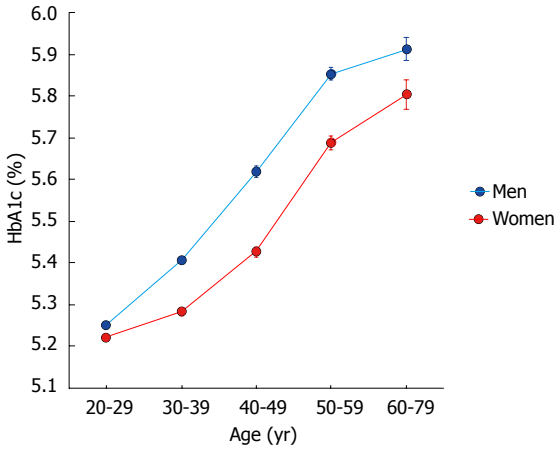

Figure 2 HbA1c levels according to age groups divided by decades. Each point and vertical bar represent the mean ± 1.96 SE. HbA1c levels in men and women increased with increasing age (both $P < 0.0001$, ANOVA). Significant differences were observed in HbA1c levels between men and women in all age groups (all $P < 0.0001$, *t*-test). The corresponding number of subjects is the same as that in Figure 1.

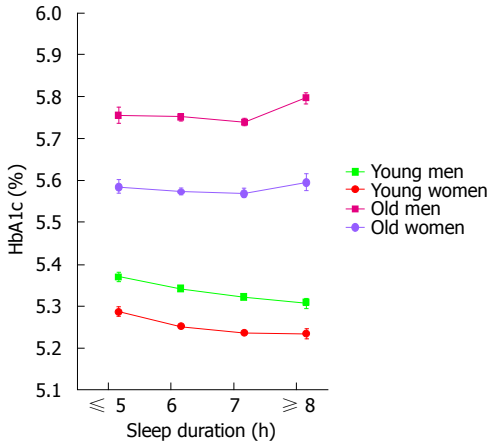

Figure 3 Relationship between HbA1c levels and sleep duration according to age and sex. Each point and vertical bar represent the mean ± SE. *P* values for ANOVA were < 0.0001, 0.0001, 0.002, and 0.56 for young men, young women, older men, and older women, respectively. The corresponding number of subjects is shown in the side of the bar.

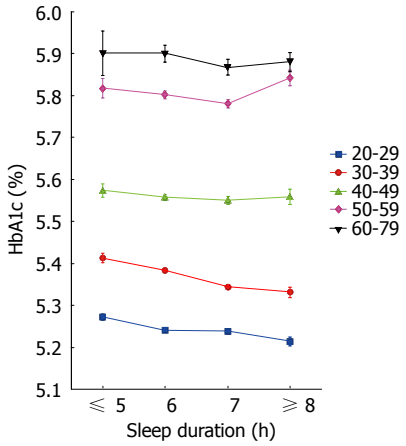

Figure 4 Relationship between HbA1c levels and sleep duration according to age groups divided by decades. Each point and vertical bar represent the mean ± SE. Correlation coefficients and *P* values of Pearson's correlation were $r = -0.03$, $P < 0.0001$ for the 20s, $r = -0.05$, $P < 0.0001$ for the 30s, $r = -0.01$, $P = 0.41$ for the 40s, $r = 0.01$, $P = 0.52$ for the 50s, and $r = -0.01$, $P = 0.32$ for the 60-70s, respectively. The corresponding number of subjects is shown in the side of the bar.

A significant association between a short sleep duration and prediabetes is consistent with many previous studies[1,3,5,6-13,15,16]. This association could be explained by physiological mechanisms, such as insulin resistance[27,28], decreased leptin levels, increased ghrelin levels and inflammation, sympathetic nervous system activation, and oxidative stress[29]. This association could also be explained by behavioral mechanisms, such as increased food intake, and unfavorable lifestyles, such as smoking and sedentary behavior[28]. Long-lasting wakefulness and arousal can increase the level of orexin, a hypothalamic neuropeptide, which is found in the brain and stimulates appetite and food intake[30-32]. Additionally, a short sleep duration can be associated with abnormal eating behavior around sleep (AEBAS), such as breakfast skipping and/or late-night-dinner eating. AEBAS is often observed in younger people[33]. Sleep duration was shorter in younger subjects in our study. Although data for AEBAS was lacking in our study, previous studies have shown that AEBAS is associated with metabolic syndrome and hyperglycemia[33,34]. An elevated WBC and BMI, a higher prevalence of current smokers, and a lower prevalence of regular exercisers in young short-duration sleepers compared with young long-duration sleepers (Table 1) may be compatible with these explanations.

The most plausible explanation for the null association between a short duration of sleep and diabetes, instead of prediabetes, may be partially due to an insufficient number of cases of overt diabetes.

Table 3 Odds ratios (95%CIs) of sleep duration for prediabetes and diabetes in younger subjects *n* (%)

Sleep durations	⩽ 5 h	6 h	7 h	⩾ 8 h	*P* value
Prediabetes					
Cases	418 (10.2)	1463 (9.0)	743 (7.9)	229 (7.2)	
Model 1	1.32 (1.16-1.49)[d]	1.15 (1.05-1.26)[b]	1 (reference)	0.90 (0.77-1.05)	0.88 (0.84-0.92)[d]
Model 2	1.32 (1.16-1.50)[d]	1.18 (1.07-1.29)[b]	1 (reference)	0.89 (0.76-1.04)	0.87 (0.83-0.91)[d]
Model 3	1.20 (1.05-1.37)[b]	1.12 (1.02-1.24)[a]	1 (reference)	0.84 (0.72-0.99)[a]	0.90 (0.86-0.95)[d]
Diabetes					
Cases	58 (1.4)	150 (0.9)	77 (0.8)	27 (0.9)	
Model 1	1.73 (1.23-2.44)[b]	1.12 (0.85-1.42)	1 (reference)	1.04 (0.67-1.61)	0.83 (0.72-0.96)[a]
Model 2	1.72 (1.22-2.43)[b]	1.16 (0.88-1.52)	1 (reference)	1.01 (0.65-1.58)	0.83 (0.72-0.95)[b]
Model 3	1.35 (0.93-1.97)	1.02 (0.76-1.37)	1 (reference)	0.92 (0.58-1.46)	0.90 (0.78-1.04)

Model 1: Unadjusted; Model 2: Adjusted for age and sex; Model 3: Model 2 plus adjustment for current smoking (*vs* non-smoking), daily alcohol consumption (*vs* infrequent/no alcohol consumption), regular exercise (*vs* no regular exercise), pharmacotherapy (hypertension, diabetes, and dyslipidemia), BMI, WBC count, systolic blood pressure, triglycerides, HDL-cholesterol, duration of work (as continuous variables), and past history of CVD (*vs* no history). Triglyceride concentrations were log transformed before analysis. Regular exercise was defined as ⩾ 30 min exercise per session at least twice a week. [a]$P < 0.05$, [b]$P < 0.01$, [d]$P < 0.001$. BMI: Body mass index; HDL: High-density lipoprotein; CVD: Cardiovascular disease; WBC: White blood cell.

Table 4 Odds ratios (95%CIs) of sleep duration for prediabetes and diabetes in older subjects *n* (%)

Sleep duration	⩽ 5 h	6 h	7 h	⩾ 8 h	*P* value
Prediabetes					
Cases	1259 (32.8)	6006 (32.8)	4788 (33.9)	2343 (37.4)	
Model 1	0.95 (0.88-1.03)	0.95 (0.91-0.995)[a]	1 (reference)	1.16 (1.09-1.24)[d]	1.07 (1.05-1.10)[d]
Model 2	1.17 (1.09-1.27)[d]	1.08 (1.03-1.14)[b]	1 (reference)	0.97 (0.91-1.03)	0.94 (0.91-0.96)[d]
Model 3	1.12 (1.03-1.21)[b]	1.04 (0.99-1.11)	1 (reference)	0.97 (0.91-1.04)	0.96 (0.94-0.99)[b]
Diabetes					
Cases	271 (7.1)	1379 (7.5)	1181 (8.4)	702 (11.2)	
Model 1	0.83 (0.73-0.95)[b]	0.89 (0.82-0.97)[b]	1 (reference)	1.38 (1.25-1.52)[d]	1.19 (1.15-1.24)[d]
Model 2	1.10 (0.95-1.26)	1.06 (0.98-1.15)	1 (reference)	1.11 (1.00-1.22)	1.00 (0.96-1.04)
Model 3	1.02 (0.88-1.18)	1.01 (0.93-1.11)	1 (reference)	1.11 (1.02-1.25)[a]	1.03 (0.99-1.08)

Model 1: Unadjusted; Model 2: Adjusted for age and sex; Model 3: Model 2 plus adjustment for current smoking (*vs* non-smoking), daily alcohol consumption (*vs* infrequent/no alcohol consumption), regular exercise (*vs* no regular exercise), pharmacotherapy (hypertension, diabetes and dyslipidemia), BMI, WBC count, systolic blood pressure, triglycerides, HDL-cholesterol, duration of work (as continuous variables), and past history of CVD (*vs* no history). Triglyceride concentrations were log transformed before analysis. Regular exercise was defined as ⩾ 30 min exercise per session at least twice a week. [a]$P < 0.05$, [b]$P < 0.01$, [d]$P < 0.001$. BMI: Body mass index; HDL: High-density lipoprotein; CVD: Cardiovascular disease; WBC: White blood cell.

This occurred because subjects were apparently healthy people who underwent a health screening checkup. Therefore, patients with poor glucose control were unlikely to be enrolled in this study. Before full adjustment for relevant confounding factors, a significant association between a short sleep duration and diabetes was observed with adjustment for age and sex in young subjects (Table 3). However, statistical significance of this association disappeared after full adjustment. This suggests that factors other than age and sex might contribute to the association between poor glucose metabolism and a short sleep duration. Indeed, patients with type 1 diabetes were not excluded in our study. However, most of the subjects who were determined as having diabetes were likely to have type 2 diabetes because of its higher prevalence in the general population (90%-95%)[26].

The reason for the discrepancy in the association between a long sleep duration and glucose metabolism among younger and older generations is unknown. Several studies have shown that a long duration of sleep may reflect underlying inflammatory etiologies in older people[4,35,36]. Pérez de Heredia *et al*[37] showed that sleep duration was negatively associated with the WBC count in adolescents. Consistent with this previous finding, in our study, the duration of sleep was inversely associated with the WBC count in younger subjects, whereas it was positively associated with the WBC count in older subjects. Taken together, in the young generation, a long sleep duration can provide sufficient rest and lead to improvement of metabolic homeostasis and inflammatory status. However, in older people, a long duration of sleep may reflect required long rest because of latent or overt disease[4,12,20]. This situation could simultaneously aggravate glucose homeostasis. Notably, in our study, the relationship between HbA1c levels and the duration of sleep appeared to be flat in subjects in their 40s, and a J-curve relationship gradually occurred after the 40s (Figure 4). This finding indicates that the etiological relation between a long sleep duration and

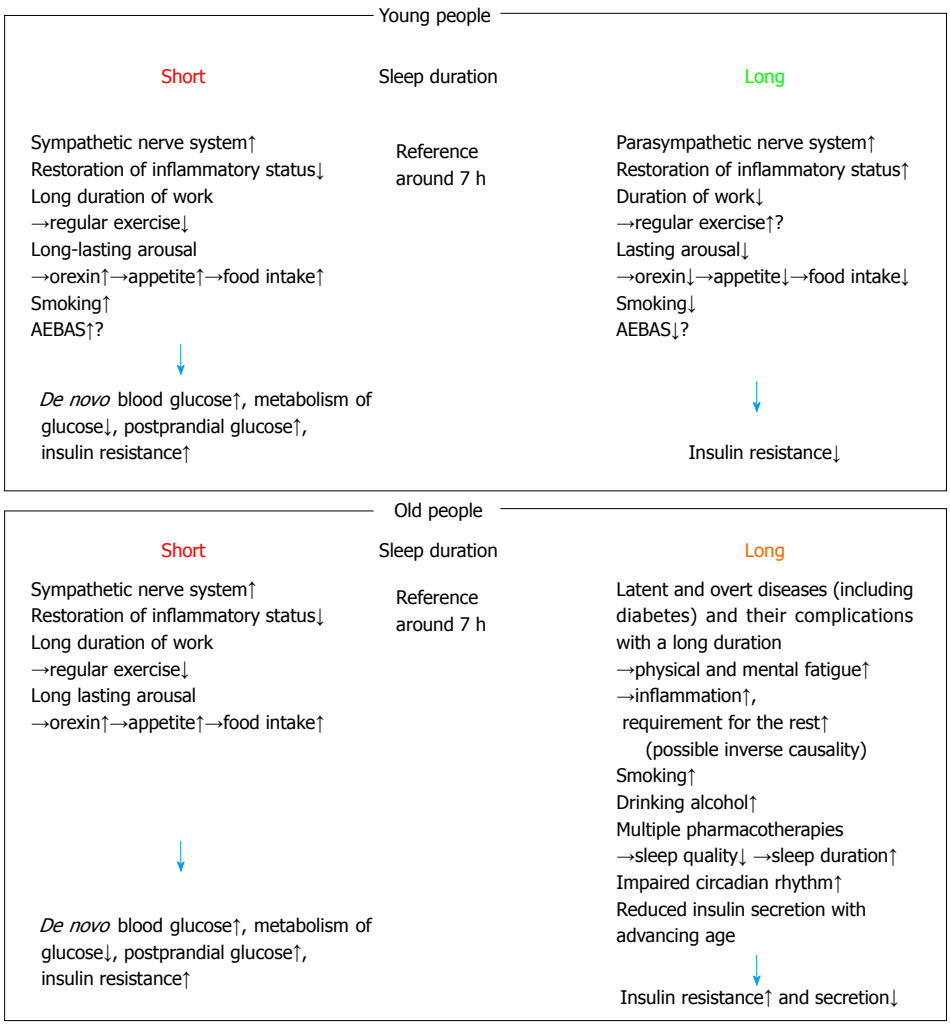

Figure 5 Relationship between sleep duration and impaired glucose metabolism, and plausible underlying mechanisms. AEBAS: Abnormal eating behavior around sleep.

impaired glucose homeostasis may occur approximately in the 40s. Mizukami *et al*[38] studied age-related changes of islet structure in Japanese non-diabetic subjects and showed that the mass of pancreatic β-cells was increased during maturation and slowly decreased after the 40s. Additionally, Uehara *et al*[39] reported in a large-scale Japanese working population that the prevalence of glucose abnormalities increased with advancing age, especially during the mid-40s and 50s. These findings may partly relate to our results regarding the relationship between long sleep duration, prediabetes, and diabetes. Alternatively, an increase in sleep duration rather than a long sleep duration *per se* may be a crucial factor that contributes to development of type 2 diabetes[40]. Among the parameters that were investigated in this study, the duration of work, which was longer in younger than in older subjects in this study, may be a pivotal environmental factor that could restrict the duration of sleep. Therefore, in terms of public health, caution should be exercised in people with a long work duration for preventing a short sleep duration, cardiometabolic disease, and other unfavorable lifestyles.

Currently observed relationships between sleep duration and impaired glucose metabolism in young and older people are summarized in Figure 5. Plausible underlying mechanisms are also described in Figure 5.

Several limitations should be mentioned in this study. First, this study was cross-sectional in nature, and did not allow us to determine the causality between abnormal sleep duration and impaired glucose metabolism. However, the age of subjects in the current study widely varied (20-79 years), which could reflect overall trajectories in sleep duration and glucose homeostasis in the general Japanese population. Second, assessment of sleep duration was self-reported and the quality of sleep was not investigated. In particular, in older people, the time spent in bed can be misinterpreted as sleep duration. Additionally, sleep may be fragmented[20] and actual sleep duration may be less than expected. Therefore, more detailed study is required to confirm the association between sleep duration and metabolic abnormalities, including type 2 diabetes. Third, whether prediabetes with a short sleep duration could lead to diabetes after a certain period during the lifetime is unclear. Long-term, prospective

studies are required to determine this issue. Finally, our study consisted of apparently healthy subjects who underwent an ordinary checkup. As people get older, they usually have more complications and chronic diseases, including cognitive impairment and mental disorders, such as depression. These etiologies often require some pharmacotherapies that predispose to disturbing homeostasis of sleep[41-43]. Prescription for insomnia increases as age advances, which also alters the sleep circadian rhythm[44,45]. Additionally, chronic use of hypnotic might aggravate glucose metabolism, although a conflicting result has been reported[46]. Unfortunately, such pharmacotherapy and sleep medication were not investigated in this study. Therefore, the current findings may not be applicable to other populations who have a different longevity and higher proportions of diabetes and comorbidities.

In conclusion, the current study shows that a short sleep duration may be associated with prediabetes throughout the lifetime, whereas a long sleep duration is inversely associated with prediabetes in younger people. This finding indicates that a long sleep duration leads to better glucose homeostasis. In contrast, a long sleep duration may be associated with diabetes in older people, which might reflect an inverse causality owing to chronic diseases and complications of diabetes. Therefore, aging may be a pivotal factor that affects the association between a long sleep duration and impaired glucose homeostasis. Further large studies are required to confirm the current findings and determine the underlying mechanism(s).

COMMENTS

Background

Many clinical studies have shown that shorter and longer durations of sleep are associated with cardiometabolic diseases including type 2 diabetes and metabolic syndrome. However, there are conflicting results, especially concerning a long sleep duration, albeit a short sleep duration may be robustly associated with impaired glucose homeostasis.

Research frontiers

Although it has been shown that sleep duration generally decreases with age, individual's sleep duration can become longer in the elderly. Therefore, comparison between young and old populations using the same methods and criteria may be important for the research investigating the association between sleep duration and metabolic disease.

Innovations and breakthroughs

The authors investigated the association between sleep duration and impaired glucose metabolism (prediabetes and diabetes) in a large epidemiological study consisting of 75472 apparently healthy subjects with a wide range of age (20-79 years old), which was subdivided into two age groups (young subjects less than 40 years and old subjects aged 40 years or older). In most of previous studies, subjects were limited to patients with type 2 diabetes, middle-aged, or the elderly. By contrast, the authors compared the results of analysis in two age groups, which include not only healthy subjects but also those with diabetes.

Applications

The cause-effect relationship between long sleep duration and impaired glucose metabolism can vary between young and old populations. In brief, long sleep duration may be a cause for the prevention of diabetes in young people, whereas it may be a result that originated from cardiometabolic diseases and their complications. Therefore, when one encounters a patient with diabetes concomitant with long sleep duration, the causality, backgrounds, and confounding factors should be carefully taken into consideration.

Terminology

In this article, the authors use the term, "abnormal eating behavior around sleep (AEBAS)", which the authors made first time based on the current and previous their studies. AEBAS may include overeating at dinner, late-night-dinner eating, eating snack after dinner, skipping breakfast, and their combinations. Such AEBAS can affect the duration of sleep and deteriorate the quality. On the contrary, abnormal durations of sleep likely deteriorate eating behaviors around sleep. The definition of "prediabetes" includes diabetes in this study, which may complicate the relationship between prediabetes and diabetes. It may be appropriate to use the term such as "hyperglycemia" instead of "prediabetes". However, in comparison with diabetes, the authors dared to use the term "prediabetes". Considering these, the current results should be interpreted with care.

Peer-review

The author's purpose of the investigation is very interesting, also for scientists from related research fields.

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ORIGINAL ARTICLE

Observational Study

Clinico-epidemiological factors of health related quality of life among people with type 2 diabetes

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Abstract

AIM

To investigate the quality of life (QOL) and its clinical and epidemiological correlates among people with type 2 diabetes.

METHODS

This cross-sectional study was conducted in Tabriz, Northwest of Iran, including a total of 394 people with type 2 diabetes using convenient sampling method from November 2014 to March 2015. General information including demographic, socioeconomic status and life-style factors were collected by trained interviewers. Clinical information was retrieved from clinic's record and QOL was assessed using the 26-item WHOQOL-BRIFE questionnaire. Univariate and multivariate linear regression were performed to assess the related factors and QOL dimensions.

RESULTS

The mean of overall health related QOL was 52.11 ± 11.53 and the maximum and minimum dimensions were

respectively seen in psychological (60.38 ± 14.54) and social (38.32 ± 16.94) dimensions. The results of multiple linear regression showed a significant overall relationship between HRQOL and age (*b* = -1.48%, 95%CI: -0.03 and -2.93) level of education (*b* = 4.12%, 95%CI: 2.73 and 5.5), number of comorbidities (*b* = -2.41%, 95%CI: -3.89 and -9.41), and level of income (*b* = 1.98, 95%CI: 0.05 and 3.9), functional limitation (*b* = -3.59, 95%CI: -2.26 and -4.92) and psychological distress (*b* = -2.02%, 95%CI: -2.83 and -1.21). Level of education, functional limitation, psychological distress were associated with the score of physical, mental and environmental dimensions, and number of comorbidities was associated with the score of physical and mental dimensions.

CONCLUSION

Based on our findings, lifestyle modification and increasing facilities of clinics providing service can be effective steps to improve the QOL among people with type 2 diabetes.

Key words: Diabetes mellitus; Type 2; Lifestyle; Quality of life; Psychological distress

Core tip: Health related quality of life (HRQOL) is an important outcome measure in chronic diseases. The aim of this study was to assess quality of life and a range of epidemiological and clinical factors among people with type 2 diabetes. The findings of the present study showed that age, level of education, income, body mass index, functional limitation, psychological distress and number of comorbidities have a decisive role on HRQOL of patients with type 2 diabetes. So, it is important to improve the HRQOL by considering above predictors as an appropriate mechanism for public health interventions for type 2 diabetes.

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INTRODUCTION

Diabetes is one of the most common metabolic diseases with increasing prevalence that reduces life expectancy by one third. Diabetes is known as a "silent epidemic" which due to the aging population, changing patterns of life, prevalence of risk behaviors and rapid growth of urbanization has increased around the world[1-3]. It is estimated that 415 million people worldwide and 4.5 million people in Iran had diabetes in 2015. It is predicted that the number rises to more than 642 million worldwide and 4.8 million in Iran by 2040. In addition diabetes caused 4.9 million deaths in 2014 and 48% of deaths occurred in people less than 60 years[4-6].

One of the important issues in the care of chronic diseases such as diabetes is to investigate the quality of their life, which significantly affects one's physical-psychological performance and social communication[7]. As defined by the World Health Organization, quality of life (QOL) refers to "individuals' perception of their position in life in terms of culture, value system where they live, goals, expectations, standards and priorities"[8,9]. In other words, the health related QOL (HRQOL) is a subjective issue that is measured using different dimensions include physical, mental and social functions[10]. HRQOL as a multi-dimensional concept focuses on the impact of health on QOL[11].

There is a mutual relationship between the quality of diabetes care and QOL so that reducing the HRQOL of people with type 2 diabetes leads to poor glycemic control and an increased risk of disease complications. On the other hand, poor quality of care leads to reduced HRQOL[12,13].

Some studies showed that demographic factors, socio-economic status, presence of comorbid conditions, and diabetes control affect HRQOL among people with type 2 diabetes. Results of most studies on this group of patients showed that their HRQOL was not desirable[14-18]. Considering that East Azerbaijan province, is among provinces, in which diabetes is highly prevalent and this disease is among research priorities outlined in the province as well as the different climatic, socio-cultural conditions, lifestyle of the area and the low quality of diabetes care that has been shown in multiple studies[19,20], the present study was designed and implemented in order to investigate the factors affecting the HRQOL of diabetic patients referred to diabetes clinics in Tabriz.

MATERIALS AND METHODS

The present study was a cross-sectional study, which was conducted by trained interviewers on 394 patients with type 2 diabetes referred to diabetes clinics in Tabriz (Imam Reza and Sina Hospitals) in the form of face to face interviews using convenient sampling method from November 2014 to March 2015. Inclusion criteria included the willingness to cooperate and participate in the study, having diabetes type Ⅱ, age group above 25 years, having records of diabetes care in clinics of Tabriz (at least for a year), living in Tabriz and lack of specific (hemophilia, thalassemia, *etc*.) or debilitating diseases leading to hospitalization. Exclusion criteria included death, emigration, or any disability that prevents the provision of information by patients. Information required for the project was collected using a two-part questionnaire.

In the first part of the questionnaire, sociodemographic and clinical characteristics including age, sex, marital status, income, insurance status, education level, type of treatment (diet, oral medications, insulin), having comorbidities (hypertension, depression, kidney

Table 1 Demographic characteristics of diabetic people referring to diabetes clinics of Tabriz, 2015

Variable	Subgroups	*n* (%)
Age[1]	⩽ 49	85 (21.6)
	59-50	147 (37.3)
	⩾ 60	162 (41.1)
Gender	Male	134 (34)
	Female	260 (66)
Level education	Illiterate	143 (36.3)
	Primary school	149 (37.8)
	Secondary school and higher	102 (25.9)
Marital status	Single	45 (11.4)
	Married	349 (88.6)
Occupation	Employed	70 (17.8)
	Housekeeper	252 (63.9)
	Retired/other	72 (18.3)
Health insurance	Yes	378 (95.9)
	No	16 (4.1)
Household monthly income[2]	< 500	25 (6.3)
	1000-500	199 (50.5)
	> 1000	170 (43.1)
Smoking status	Yes	40 (10.2)
	No	354 (89.8)

[1]Mean and standard deviation: 56.67 ± 9.01; [2]Amounts are in 10000 Rials (1 USD equals to 33000 Islamic Republic of Iran's Rials).

disease, cardiovascular disease, cancer and other diseases) complications (retinopathy, neuropathy, nephropathy, cardiovascular complications), duration of diabetes, functional limitation, Kessler psychological distress (K10) and family history as well as anthropometric measures were collected. In the second part, the 26-item WHOQOL-BRIFE questionnaire was used. This questionnaire evaluates four broad areas, including physical health, psychological health, social relationships and environment. This questionnaire contained two questions on the assessment of the overall HRQOL and the level of self-perception of QOL. The 24 the next questions evaluate physical health (7 questions), mental health (6 questions), social relationships (3 questions) and environment (8 questions). The questionnaire was scored using Likert-5 point scale; *i.e.*, every question is assigned five answers (never, low, medium, high, very high), to each of which 1 to 5 points is assigned, respectively. The higher score in each of the dimensions reflects the better QOL. During analysis stage, those questionnaires, more than 20% of questions of which are remained unanswered (6 questions and more), were excluded, After calculating the raw score in each dimension, the scores can be converted and analyzed to 0-100 or 4-20 scale[21,22]. In this study, the 0-100 scale was used to analyze the results. The validity and reliability of the Persian version of the questionnaire, was determined by Nejat *et al*[23] in 2005.

Descriptive statistics [mean, standard deviation and frequency (percent)] was performed and test-*t*, Mann-Whitney, ANOVA, Kruskal Wallis were used and Welch test was employed to analyze the HRQOL according to demographic data and treatment options. Also, the multiple regression models were used to show the association between independent factors with dimensions of QOL. The level of significance of (P = 0.05) was considered in the present study. Data analysis was performed using SPSS 23.

This project was approved by Ethics Committee of Tabriz University of Medical Sciences (Ethic approval numberTBZMED.REC.2015.55). In addition, at the beginning of the study, informed consent was obtained in written forms from all of the participants.

RESULTS

The mean patient age was 56.67 ± 9.01 years. of the majority of participants (66%) were female, and married (88.6%), 36% were illiterate, most of them (96%) had health insurance and 56.8% of them had a monthly income of less than 10 million Rials, respectively. Smokers accounted for 10.2% of the participants and 48.7% of patients suffered complications, in 39.6% of whom the neuropathy was observed. A total of 74.1% of people had comorbidities, the most prevalent of which was high blood pressure (40.4%). A total of 56.9% of them used oral medicine and 55.3% of patients had a family history of diabetes (Table 1).

The mean of overall HRQOL was 52.11 ± 11.53 and the maximum and minimum dimensions of HRQOL were respectively seen in psychological 60.38 ± 14.54 and social dimension 38.32 ± 16.74 (Table 2).

A total of 79.8% of individuals had undesirable BMI (< 25) and HRQOL score was significantly lower in all HRQOL dimensions. The majority (63.5%) of individuals mentioned the disease duration of over 7 years. Also, the association between disease duration and QOL was statistically significant in all dimensions, except in social relations dimensions. HRQOL scores were low in all dimensions in people with functional limitation and those suffering from two or more comorbidities and patients with kidney disease had the lowest HRQOL score in all dimensions but in physical and mental dimensions. Blood biochemical indicators such as levels of HbA1c, cholesterol levels were not significant in each of HRQOL dimensions (P = 0.05) (Table 3).

The results of multiple linear regression showed a significant overall relationship between HRQOL and age (b = -1.48%, 95%CI: -0.03 and -2.93) level of education (b = 4.12%, 95%CI: 2.73 and 5.5), number of comorbidities (b = -2.41%, 95%CI: -3.89 and -9.41), and level of income (b = 1.98, 95%CI: 0.05 and 3.9), functional limitation (b = -3.59, 95%CI: -2.26 and -4.92) and psychological distress (b = -2.02%, 95%CI: -2.83 and -1.21). Also, there was association between the physical (level of education, BMI, functional limitation, psychological distress and number of comorbidities), social (age, level of education and functional limitation), mental (level of education and functional limitation, psychological distress and the number of comorbidities) and environmental dimensions (level of education, functional limitation,

Table 2 The status of different domains of health related quality of life according to the gender of diabetic people referring to diabetes clinics of Tabriz, 2015

HRQOL dimensions	Total		Male		Female		*P*-value
	Mean	SD	Mean	SD	Mean	SD	
Physical health	51.24	13.34	54.97	12.92	49.34	13.18	< 0.001
Psychological health	60.38	14.54	65.26	13.30	57.88	14.54	< 0.001
Social relationship	38.32	16.74	41.96	16.71	36.46	16.48	0.002
Environmental	58.48	10.48	59.64	11.13	57.88	10.10	0.115
Total HRQOL score	52.11	11.53	55.46	11.34	50.39	11.27	< 0.001

HRQOL: Health related quality of life.

Table 3 Different dimensions of health related quality of life according to the clinical aspects of diabetes among diabetic people referring to diabetes clinics of Tabriz, 2015

Variable	Subgroups	*n* (%)	Physical health	Social relationship	Environmental	Psychological health	Total HRQOL
Gender	Male	134 (34)	54.97 (12.92)	41.96 (16.71)	59.65 (11.14)	65.26 (13.30)	55.46 (11.34)
	Female	260 (66)	49.34 (13.18)	36.46 (16.48)	57.88 (10.11)	57.88 (14.54)	50.39 (11.27)
	P-value	-	< 0.001	0.002	0.115	< 0.001	< 0.001
Age	≤ 49	85 (21.6)	58.65 (11.64)	47.8 (17.59)	61.64 (11.14)	64.11 (16.15)	58.8 (11.66)
	59-50	147 (37.3)	52.36 (12.97)	39.68 (15.17)	59.71 (10.9)	61.37 (14.71)	53.28 (11.19)
	≥ 60	162 (41.1)	46.32 (12.53)	32.08 (15.02)	55.68 (9.01)	57.5 (12.91)	47.89 (10.11)
	P-value	-	< 0.001	< 0.001	< 0.001	0.002	< 0.001
Education	Illiterate	143 (36.3)	44.56 (11.04)	29.8 (13.21)	54.34 (8.57)	55.06 (12.25)	45.94 (8.73)
	Primary school	149 (37.8)	51.99 (12.93)	40.25 (16.08)	57.46 (10.13)	59.79 (14.31)	52.37 (10.87)
	Secondary school and higher	102 (25.9)	59.61 (11.92)	47.55 (16.52)	65.83 (9.7)	68.77 (14.15)	60.44 (10.68)
	P-value	-	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001
Income	Low (< 1000)	224 (56.8)	48.43 (12.82)	35.44 (17.47)	56.22 (9.98)	57.9 (14.73)	49.50 (11.39)
	acceptable	170 (43.2)	54.23 (13.27)	41.38 (15.41)	60.86 (10.49)	63 (13.9)	54.86 (11.06)
	P-value	-	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001
Disease duration (yr)	≥ 3 yr	51 (12.9)	56.12 (13.81)	41.88 (16.86)	61.7 (12.31)	65.48 (14.81)	56.29 (12.18)
	4-7	93 (23.6)	51.09 (10.95)	37.3 (16.15)	57.52 (9.29)	59.47 (12.48)	51.34 (10.06)
	≤ 7 yr	250 (63.5)	50.33 (13.89)	38 (16.91)	58.19 (10.43)	59.7 (15.03)	51.55 (11.78)
	P-value	-	0.019	0.26	0.058	0.029	< 0.001
	< 25	72 (20.2)	55.21 (12.90)	42.08 (17.32)	60.77 (12.09)	64.36 (15.85)	55.6 (12.53)
	25-29.9	148 (41.6)	54.2 (13.01)	39.25 (15.68)	59.2 (10.26)	62.15 (14.22)	53.7 (11.66)
	≥ 30	136 (38.2)	47.97 (12.85)	35.27 (17.46)	57.16 (9.98)	58.23 (13.79)	49.66 (11.08)
	P-value	-	< 0.001	0.014	0.052	0.008	0.001
HbA1c	< 7	180 (47.2)	51.11 (12.70)	38.02 (16.02)	57.8 (10.84)	60.1 (14.12)	51.76 (11.07)
	≥ 7	201 (52.8)	51.21 (14.01)	37.96 (17.35)	58.89 (10.25)	60.83 (14.75)	52.22 (12.05)
	P-value	-	0.938	0.969	0.136	0.62	0.696
	NORMAL	195 (49.6)	53.83 (10.78)	38.33 (15.11)	60.4 (9.57)	64.73 (11.81)	54.32 (9.74)
Kessler psychological distress	MILD	72 (18.3)	52.01 (13.65)	41.97 (18.03)	57.47 (10.25)	60.84 (12.61)	53.07 (11.57)
	MODERATE	52 (2.13)	50.96 (14.41)	39.19 (19.07)	58.57 (12.12)	59.76 (16.61)	52.12 (13.91)
	SEVER	74 (18.8)	43.9 (15.76)	34.14 (17.23)	54.33 (66.10)	48.87 (15.22)	45.31 (11.66)
	P-value	-	< 0.001	0.042	< 0.001	< 0.001	< 0.001
Functional limitation	No	106 (26.9)	61.25 (10.89)	47.47 (15.85)	63.05 (11.16)	67.91 (14.37)	59.92 (10.79)
	Moderate	78 (19.8)	54.92 (11.51)	44.34 (18.16)	61.12 (9.62)	64.79 (12.13)	56.29 (10.18)
	Sever	210 (53.3)	44.8 (11.35)	31.44 (13.25)	55.17 (9.26)	54.91 (13.17)	46.58 (9.23)
	P-value	-	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001
Treatment	Oral medication	223 (57.4)	53.57 (12.59)	38.69 (15.71)	58.97 (10.37)	61.69 (14.64)	53.11 (11.09)
	Oral medication + insulin injection	164 (42.2)	48.92 (13.64)	37.82 (17.96)	58.07 (10.55)	58.78 (14.38)	50.9 (11.97)
	P-value	-	0.007	0.883	0.161	0.101	0.12
Comorbidities	No	102 (25.9)	58.93 (11.79)	42.23 (18.29)	63.37 (10.57)	66.51 (14.82)	57.76 (11.75)
	1	207 (52.5)	50.82 (12.07)	38.28 (16.42)	57.56 (10.03)	60.49 (13.19)	51.79 (10.66)
	≥ 2	85 (21.6)	43.05 (12.99)	33.74 (14.41)	54.83 (9.39)	52.75 (13.88)	46.09 (10.09)
	P-value	-	< 0.001	0.002	< 0.001	< 0.001	< 0.001

HRQOL: Health related quality of life.

Table 4 Multivariate linear regression models of significant factors predicting health related quality of life domains among diabetic people referring to diabetes clinics of Tabriz, 2015

HRQOL domains	Variables	B (SE)	Beta	*P*-value	95%CI of B		Adjusted R2
					Lower	Upper	
Physical health	Education	3.35 (0.83)	0.198	< 0.001	1.77	4.93	0.436
	BMI	-1.55 (0.75)	-0.087	0.039	-3.12	0.07	
	Functional limitation	-4.79 (0.77)	-0.229	< 0.001	-6.11	-3.07	
	Kessler psychological distress	-1.98 (0.46)	-0.174	< 0.001	-2.90	-1.06	
	Comorbidies	-4.05 (0.85)	-0.210	< 0.001	-5.73	-2.37	
Social relationship	Age	-4.65 (1.2)	-0.212	< 0.001	-7.01	-2.28	0.279
	Education	5.3 (1.15)	0.246	< 0.001	3.03	7.56	
	Functional limitation	-4.05 (1.11)	-0.208	< 0.001	-6.24	-1.87	
Psychological health	Education	3.52 (0.94)	0.190	< 0.001	1.67	5.38	0.353
	Functional limitation	-3.94 (0.9)	-0.234	< 0.001	-5.72	-2.15	
	Comorbidies	-3.72 (1.0)	-0.176	< 0.001	-5.69	-1.75	
	Kessler psychological distress	-3.96 (0.55)	-0.317	< 0.001	-5.04	-2.88	
Environment	Education	4.3 (0.73)	0.318	< 0.001	2.86	5.75	0.257
	Comorbidies	-2.37 (0.78)	-0.154	0.003	-3.91	-0.83	
	Kessler psychological distress	-1.33 (0.43)	-0.135	0.004	-2.07	-0.38	
	Functional limitation	-1.77 (0.7)	-0.145	0.012	-3.17	-0.38	
	Income	2.13 (1.02)	0.101	0.037	0.12	4.14	
Total HRQOL score	Education	4.12 (0.7)	0.278	< 0.001	2.73	5.5	0.433
	Functional limitation	-3.59 (0.67)	-0.267	< 0.001	-4.92	-2.26	
	Age	1.48 (0.73)	-0.098	0.044	-2.93	-0.03	
	Kessler psychological distress	-2.02 (0.41)	-0.203	< 0.001	2.83	-1.21	
	Income	1.98 (0.97)	0.085	0.044	0.05	3.9	
	Comorbidities	-2.41 (0.75)	-0.143	0.001	-3.89	-9.41	

HRQOL: Health related quality of life.

psychological distress and level of income) (Table 4).

DISCUSSION

HRQOL is one of the most important assessment indices of health cares in chronic disease[24]. In this study, HRQOL based on the WHOQOL-BRIFE and its correlates among people with type 2 diabetes was examined. Based on these findings, the mean of overall HRQOL was 52.11 ± 11.53 which was similar to other studies that have also shown that HRQOL dimensions of diabetes patients was moderate[25-27], while some studies reported the lower score of the mean of overall HRQOL[28-30]. Based on these findings, in all dimensions, men had higher average HRQOL than women (55.46 ± 11.34 and 50.39 ± 11.27 in males and females, respectively), which was consistent with the result obtained in studies conducted by Rasouli *et al*[31], Khalde *et al*[32] and Redekop *et al*[33]. These studies attributed women's low HRQOL score to biological and psychological differences (women's menopause and sensitivity in dealing with the disease). But Saadatjoo *et al*[34] reported that women's HRQOL score obtained in different dimensions was higher than men, which is different from the results obtained in the present research. Some studies also have shown no significant association between gender and HRQOL[35]. In the present study, the lowest and highest HRQOL scores were obtained in mental and social dimensions, respectively. The score was different in other studies due to socioeconomic status and cultural conditions as well as collection tools. The findings of the present study showed a significant association between the HRQOL of patients, and factors including age, income, BMI, level of education, functional limitation, psychological distress, and number of comorbidities which was consistent with the study conducted by Didarloo *et al*[36]. There was a significant relationship between BMI and HRQOL so that by increasing BMI levels, HRQOL level was decreased. The results of regression analysis showed that there was a relationship between BMI and HRQOL in terms of physical dimension (b = -1.5), which were consistent with many studies conducted in this area[30,37,38]. The association between age and HRQOL was consistent with many studies so that the lowest and highest mean HRQOL scores were obtained in young and elderly patients, respectively[19,39,40]. The results of the present study showed that there was a significant relationship between level of education and all HRQOL dimensions so that people with higher education levels also had better QOL, which is consistent with findings obtained in different studies[12,41,42]. Moreover, the findings of the present study indicated that the frequency of comorbidities in patients was associated with a reduced HRQOL and this relationship was significant in the physical, psychological and environmental dimensions based on the results obtained in multiple regression analysis[3,43]. There was a negative correlation between functional limitation and HRQOL among people with type 2 diabetic in the current study. This means that increasing functional limitation score was indicative of the fact that patients faced limitation in doing their daily

activities, which in turn reduced their HRQOL. There were no similar studies for comparison purposes in this context.

The results of the current study showed that the psychological distress had negative effects on the average HRQOL of patients and led to reduced HRQOL in these people. The results of multiple regression analysis were indicative of a significant relationship between psychological distress and all HRQOL dimensions (except social dimension). These findings are consistent with other studies done in this area[24,44]. In the present study, there was a reverse relationship between duration of diabetes, and HRQOL scores; but after adjustment for other variables it was no longer significant in any of HRQOL dimensions. Studies[45,46] also indicated that there was no significant relationship between duration of diabetes and HRQOL, which confirmed the results of the present study.

In conclusion, the findings of the present study showed that age, level of education, income, BMI, functional limitation, psychological distress and number of comorbidities have a decisive role on HRQOL of patients with type2 diabetes. So, it is important to improve the HRQOL by considering above predictors as an appropriate mechanism for public health interventions for type 2 diabetes. Therefore, correcting lifestyle and increasing facilities of clinics providing service can be an effective step to improve the QOL of patients.

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COMMENTS

Background

One of the important issues in the care of chronic diseases such as diabetes is to investigate the quality of their life, which significantly affects one's physical-psychological performance and social communication. Although, some studies showed that demographic factors, socio-economic status, presence of comorbid conditions, and diabetes control affect health related quality of life (HRQOL) among people with type 2 diabetes, a comprehensive assessment of a range of epidemiologic and clinical factors related to the quality of life (QOL) among people with type 2 diabetes in this area is needed.

Research frontiers

Diabetes an emerging health problem in Iran and will continue to rise in the next decades. Considering that East Azerbaijan province, is among provinces, in which diabetes is highly prevalent and the different climatic, socio-cultural conditions, lifestyle of the area as well as the low quality of diabetes care can affect the QOL, a comprehensive assessment of clinical and epidemiological correlates of QOL can provide a more clear picture of the problem in order to implement an appropriate public health interventions.

Innovations and breakthroughs

To the knowledge, limited studies in this area have been conducted to assess QOL and a range of different epidemiological and clinical factors specially there is no information about the association between functional limitation, and psychological distress and QOL in Iran. This study designed to capture a more details about the QOL and its correlates using a valid questionnaires and trained interviewers.

Applications

QOL is considered as an outcome measure therefore identification of any modifiable factor associated with that could be of interest for further intervention. Diabetes will continue to rise; health policy makers need to be updated about the required information in order to implement the new interventional programs and also to enhance the current practice related to diabetes care.

Terminology

QOL: Individuals' perception of their position in life in terms of culture, value system where they live, goals, expectations, standards and priorities; HRQOL: A subjective issue that is measured using different dimensions include physical, mental and social functions; Kessler psychological distress (K10): A 10-item questionnaire intended to measure the level of distress based on questions about anxiety and depressive symptoms over the recent 4 wk.

Peer-review

The paper is interesting and has been developed with appropriate methodology.

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ORIGINAL ARTICLE

Randomized Clinical Trial

Impact on dietary intake of a self-directed, gender-tailored diabetes prevention program in men

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Abstract

AIM

To investigate changes in dietary intake following a 6-mo

randomised controlled trial of the self-directed, gender-tailored type 2 diabetes mellitus (T2DM) Prevention Using LifeStyle Education (PULSE) program in men.

METHODS

Men aged 18-65 years, with a body mass index (BMI) 25-40 kg/m^2, and at high risk for developing T2DM were recruited from the Hunter Region of New South Wales, Australia. Eligible participants were randomised into one of two groups: (1) waitlist control; or (2) PULSE intervention. Dietary intake was assessed at baseline and immediately post-program using the Australian Eating Survey food frequency questionnaire and diet quality measured using the Australian Recommended Food Score (ARFS).

RESULTS

One hundred and one participants (n = 48, control; n = 53, intervention, mean age 52.3 ± 9.7 years, BMI of 32.6 ± 3.3 kg/m^2) commenced the study. Following the active phase, differences between groups were observed for proportion of total energy consumed from healthful (core) foods (+7.6%EI, P < 0.001), energy-dense, nutrient-poor foods (-7.6%EI, P < 0.001), sodium (-369 mg, P = 0.047), and diet quality (ARFS) (+4.3, P = 0.004), including sub-scales for fruit (+1.1, P = 0.03), meat (+0.9, P = 0.004) and non-meat protein (+0.5, P = 0.03).

CONCLUSION

The PULSE prevention program's nutrition messages led to significant improvements in dietary intake in men at risk of T2DM.

Key words: Dietary intake; Diet quality; Men; Diabetes prevention program; Self-directed

Core tip: In the context of type 2 diabetes mellitus (T2DM) prevention programs, only recently has the effect on diet quality been reported. However, no studies have examined the effect on diet of a program designed exclusively for men. This study reports on the dietary outcomes following the self-directed T2DM Prevention Using LifeStyle Education (PULSE) program. Following completion of the PULSE program, men receiving the intervention significantly reduced intake of energy-dense, nutrient-poor foods and portion size. In addition, the intervention group increased overall diet quality and greater variety within healthful food groups.

Rollo ME, Aguiar EJ, Pursey KM, Morgan PJ, Plotnikoff RC, Young MD, Collins CE, Callister R. Impact on dietary intake of a self-directed, gender-tailored diabetes prevention program in men. *World J Diabetes* 2017; 8(8): 414-421 Available from: URL: http://www.wjgnet.com/1948-9358/full/v8/i8/414.htm DOI: http://dx.doi.org/10.4239/wjd.v8.i8.414

INTRODUCTION

Despite concerted public health efforts, the prevalence of diabetes continues to increase worldwide. Between 2013 to 2015, the worldwide prevalence of diabetes increased by 33 million to an estimated 415 million adults[1,2], with the prevalence expected to increase to 642 million in the next 25 years[1]. The economic burden on national health systems attributed to diabetes is significant, with USD 612 billion spent worldwide or 11% of total health expenditure[3]. In higher income countries, approximately 87%-91% of those with diabetes have type 2 diabetes mellitus (T2DM)[1]. Further, global estimates place 318 million adults at risk of developing the condition, with an additional 163 million individuals estimated to have impaired glucose tolerance by 2040[1].

Lifestyle risk factors such as a high body mass index (BMI), sub-optimal diet quality and lack of physical activity are key targets underpinning T2DM prevention programs, such as the Diabetes Prevention Program in the United States[4] and the Diabetes Prevention Study in Finland[5]. In the years following these seminal studies, many diabetes prevention programs have been evaluated including successful adaptations for various populations and different settings[6-8].

These T2DM prevention programs promote moderate weight loss by improving physical activity and dietary behaviours. Programs containing a combination of diet and physical activity components have demonstrated efficacy with regard to weight loss and improvements in glucose regulation[9,10]. Specific dietary changes following the diabetes prevention programs have included a reduction in total energy intake and favourable shifts in macronutrient composition (*e.g.*, reduction in total and saturated fat intake)[9]. Only recently have changes in diet quality or amounts of foods (as opposed to energy or nutrients) been reported both immediately following completion of the intervention[11,12], as well as over the long-term for periods of 5-10 years later[13,14]. To date, no studies have reported the effect on diet of a diabetes prevention program tailored for men. Therefore, this study examines changes in dietary intake, in particular diet quality, among Australian men following the 6-mo randomised controlled trial of the self-directed, gender-tailored Prevention Using LifeStyle Education (PULSE) program.

MATERIALS AND METHODS

The PULSE randomised controlled trial evaluated the efficacy of a self-directed, diabetes prevention program tailored for men at risk of T2DM. The study was conducted in Newcastle, Australia in 2012-2013 after receiving ethical approval (H-2012-0232) from the University of Newcastle Human Research Ethics Committee and registration with

the Australian New Zealand Clinical Trials Registry (ACTRN 12612000721808).

Detailed information regarding the rationale, study design and methods are reported elsewhere[15,16]. Briefly, emerging evidence supports the use of gender-tailored approaches, in particular for weight loss[17,18]. Our previous research has found gender-tailored programs to be effective in producing weight loss in men[19-21]. However, T2DM prevention programs predominantly involve both men and women with results reported collectively[9]. Therefore, the PULSE program aimed to address this gap in the evidence through the evaluation of a T2DM prevention program designed exclusively for men.

Males aged 18-65 years, with a BMI 25-40 kg/m^2 and at high risk for developing T2DM (with a score $\geqslant$ 12 as self-reported *via* the Australian Diabetes risk assessment tool[22]) were recruited. Men with pre-existing diabetes or other serious medical conditions, recent significant weight loss (> 5% in past 6 mo), currently participating in other weight loss programs, and without access to a mobile phone were ineligible. Study recruitment used advertisements across various modes including print and online, workplace emails and research participant registers. Participants were stratified by age and BMI, and randomised to either the intervention group or waitlist control. The active intervention period was 6 mo with the waitlist control group receiving the PULSE program at the completion of active phase.

As previously reported, the program was effective in reducing clinical risk factors of T2DM[16]. In summary, a significant mean difference favouring the intervention group over control was observed for change in body weight (-5.5 kg and -5.3%, both $P < 0.001$), BMI (-1.8 kg/m^2, $P < 0.001$), and waist circumference (umbilicus -5.4 cm, $P < 0.001$; narrowest point -6.2 cm; $P < 0.001$). In addition, significant changes were found for measures of glucose regulation in the intervention group with improvements in HbA1c (-0.2%, $P = 0.002$), fasting insulin (-3.0 mIU/L, $P = 0.002$) and measures of insulin resistance (HOMA-IR; -0.4, $P = 0.002$) and insulin sensitivity (QUICKI; +0.02, $P = 0.006$).

The PULSE program

The current paper reports the secondary dietary outcome data, and therefore the methods focus on the intervention components used to target changes in diet and eating behaviours. Underpinned by Social Cognitive Theory, the PULSE program aimed to promote modest weight loss through changes in key dietary and physical activity behaviours. The program addressed key theoretical constructs relating to goal setting and planning, positive outcome expectations, seeking social support, promoting behavioural self-monitoring, and increasing self-efficacy, as described in detail previously[15,16]. Following randomisation, participants in the intervention group were provided with information and equipment resource packs and briefly orientated to the contents by a research team member[15,16].

The PULSE handbook contained dietary information and focused on four main messages: (1) key nutrients and their role in the body; (2) dietary composition, focusing on amount and quality of carbohydrate [*i.e.*, lower glycaemic index (GI)], fat, protein and fibre, and using the plate model to represent appropriate meal portion sizes; (3) variety within core (healthful) foods, particularly vegetables; and (4) suggestions for the composition (*e.g.*, low-moderate GI) of breakfast, lunch and dinner. In addition, participants were provided with the Self-Help, Exercise and Diet using Information Technology (SHED-IT) program[19,23]. This handbook provided information on general weight loss principles including setting daily energy intake targets, goal setting for eating and activity behaviours, self-monitoring tools for tracking weight, waist circumference and step counts. In addition, participants were provided with a calorie counter[24] and instructions for the accompanying CalorieKing website (www.calorieking.com.au). Participants were encouraged to self-monitor dietary intake and physical activity (both for at least 4 d per week) and weight (once per week).

Outcome measures

Assessments occurred at baseline and following the program (6 mo). Usual dietary intake was assessed using the validated, semi-quantitative food frequency questionnaire, the Australian Eating Survey (AES)[25] at baseline and following the program completion. The AES comprises 120 food items with 15 supplementary questions on food behaviours. Standard adult portion sizes for each food item were derived from National Nutrition Survey data or from the product standard serving size (*e.g.*, slice of bread)[26]. Participants were asked to recall the frequency of food consumption over the past 3 mo, with individual responses for each food or food type. Frequency options ranged from "Never" up to "$\geqslant$ 4 times/d", but varied depending on the food, with some drinks items up to "$\geqslant$ 7 glasses/d". Nutrient intakes were computed from the most current food composition database of Australian foods, the Australian AusNut 1999 database (All Foods) Revision 17, primarily and AusFoods (Brands) Revision 5.

The validated Australian Recommended Food Score (ARFS)[27] assesses diet quality and variety within the food groups relative to the Australian Guide to Healthy Eating within the Australian Dietary Guidelines (ADGs)[28]. The ARFS uses a sub-set of 70 AES food items and comprises eight sub-scales from a range of healthful or core food groups (*e.g.*, vegetables, fruit, grains, meats, non-meat proteins, dairy) with total score ranging from 0 to 73. For most items AES frequency response options are collapsed into two categories "once per week or more" or "less than once per week or never". A higher total score is indicative

Table 1 Baseline dietary intake characteristics (*n* = 101)

	Control (*n* = 48)	Intervention (*n* = 53)	All participants (*n* = 101)
Dietary intake			
EI (kJ/d)	11761 ± 3550	11014 ± 3143	11369 ± 3346
Core foods (%EI)	56.9 ± 9.3	55.8 ± 12.1	56.3 ± 10.8
Non-core foods (%EI)	43.1 ± 9.3	44.2 ± 12.1	43.7 ± 10.8
Protein (%EI)	17.5 ± 2.4	17.3 ± 2.8	17.4 ± 2.6
Carbohydrate (%EI)	45.6 ± 7.1	44.8 ± 5.1	45.1 ± 6.1
Fat (%EI)	30.6 ± 4.6	30.5 ± 5.0	30.6 ± 4.8
Saturated fat (%EI)	12.7 ± 2.2	12.7 ± 2.6	12.7 ± 2.4
Monounsaturated fat (%EI)	11.4 ± 2.1	11.3 ± 2.1	11.4 ± 2.0
Polyunsaturated fat (%EI)	3.8 ± 1.0	3.8 ± 0.9	3.8 ± 0.9
Alcohol (%EI)	6.9 ± 5.9	7.8 ± 7.2	7.4 ± 6.6
Fibre (g/d)	31.5 ± 12.0	29.1 ± 8.9	30.2 ± 10.5
Sodium (mg/d)	2834.3 ± 975.3	2662.1 ± 865.2	2743.9 ± 918.6
ARFS (maximum score)			
Total ARFS (73)	32.2 ± 10.9	30.3 ± 7.8	31.2 ± 9.4
Vegetables (21)	12.1 ± 5.0	11.1 ± 4.2	11.6 ± 4.6
Fruit (12)	4.5 ± 3.2	3.8 ± 2.5	4.1 ± 2.9
Meats (7)	3.1 ± 1.5	2.6 ± 1.3	2.9 ± 1.4
Non-meat protein (6)	2.0 ± 1.1	1.8 ± 1.0	1.9 ± 1.1
Grains (13)	5.1 ± 2.1	5.0 ± 1.7	5.1 ± 1.9
Dairy (11)	4.2 ± 2.0	4.4 ± 1.6	4.3 ± 1.8
Sauces (2)	0.9 ± 0.7	1.1 ± 0.8	1.0 ± 0.7
Water (1)	0.3 ± 0.5	0.4 ± 0.5	0.3 ± 0.5
Portion size			
Potato[1]	1.7 ± 0.5	1.6 ± 0.6	1.7 ± 0.5
Vegetables[3]	1.1 ± 0.6	1.1 ± 0.6	1.1 ± 0.6
Casserole[3]	2.0 ± 0.5	1.9 ± 0.5	1.9 ± 0.5
Steak[2]	1.8 ± 0.6	1.8 ± 0.5	1.8 ± 0.6

Data is presented as mean ± SD. Portion size coded as per Hodge *et al*[31] as follows: Never eat = 0, less than image A = 0.4, equal to image A = 0.5, between images A and B = 0.75, equal to image B = 1.0, between images B and C = 1.5, equal to image C = 2.0, greater than image C = 2.5. [1]*n* = 100 participants; [2]*n* = 97 participants; [3]*n* = 99 participants. EI: Energy intake; ARFS: Australian Recommended Food Score.

of more optimal nutrient intakes[27,29], greater variety within the core food groups and alignment with ADGs.

Portion size for four common foods (potato, vegetables, steak and casserole) was assessed separately using food photographs from the Dietary Questionnaire for Epidemiological Studies, version 2[30,31]. Three photographs are displayed, representing the 25th, 50th (median), and 75th percentiles of portion sizes for adult men and women[31] to indicate the portion size typically consumed, with eight response options ranging from "not eating the food at all" up to "more than the amount represented".

Statistical analysis

Statistical analysis was conducted using Stata version 13. Between group differences in completers (those who did complete all 6-mo follow-up measures) *vs* non-completers (those who did not complete all 6-mo follow-up measures, including those lost to follow-up) were assessed using *t* tests for continuous data and χ^2 tests for categorical data.

Changes in dietary intake over the 6-mo intervention were analysed using linear mixed models according to the intention-to-treat principle. Outcomes were assessed for the impact of treatment (intervention compared to control), time [baseline and immediately post program (*i.e.*, 6 mo)] and group by time interaction. Models were adjusted for participant age and socioeconomic status (SES), which were specified a priori. The coefficient and *P*-value from the mixed model testing the difference between groups in change from baseline to 6 mo was used to determine the effect of the intervention on each outcome (significance level, $P < 0.05$). The statistical methods of this study were reviewed by Daniel Barker from the University of Newcastle.

RESULTS

A total of 101 participants were recruited to the study. Participant baseline dietary intakes are reported in Table 1. Nineteen participants (*n* = 6 control; *n* = 13 intervention) were lost to follow-up (not able to attend the assessment sessions or were unable to be contacted). An additional two participants in the intervention group attended the follow-up session, but did not complete the AES at 6-mo, leaving a total of 21 non-completers and 80 completers from the original 101 participants whom commenced the study. At baseline, non-completers reported lower intakes of total energy, protein and carbohydrates compared to completers. The mean age of the participants was 52.3 ± 9.7 years (range 20-66 years) and the most frequently reported highest education level was a certificate or trade qualification (60%). The mean BMI of the sample was 32.6 ± 3.3 kg/m^2, and ranged from 25.7-41.0 kg/m^2.

Changes in dietary intakes of participants are reported in Table 2. At follow-up, significant mean differences between groups favouring the intervention group were identified for %EI from healthful (core) foods (+7.6%EI; $P < 0.001$), energy-dense, nutrient-poor foods (-7.6%EI, $P < 0.001$), protein (+1.3%EI, $P = 0.03$), and polyunsaturated fat (-0.4%EI, $P = 0.02$), as well as sodium intake (-369 mg, $P = 0.047$). Between group differences were observed in ARFS diet quality, with the intervention group achieving a greater improvement in mean total score (+4.3, $P = 0.004$) and subscales of fruit (+1.1, $P = 0.03$), meat (+0.9, $P = 0.004$) and non-meat protein (+0.5, $P = 0.03$). Greater reductions in portion sizes were achieved in the intervention group for potato (-0.9, $P = 0.002$), steak (-0.9, $P = 0.002$) and casserole (-0.7, $P = 0.01$) compared to controls, however there was no change in vegetable portion size.

DISCUSSION

The PULSE self-directed T2DM prevention program for men resulted in significant improvements in usual

Table 2 Change in dietary intake by group at 6 mo (*n* = 101)

	Change baseline to 6 mo, mean (95%CI)		
	Control (*n* = 48)	Intervention (*n* = 53)	Diff between groups
Dietary intake			
EI (kJ/d)	-315.5 (-1412.9, 781.9)	-1618.1 (-2568.4, -667.9)[b]	-1298.5 (-2737.7, 140.6)
Core foods (% EI)	2.0 (-0.4, 4.5)	9.6 (7.0, 12.3)[d]	7.6 (4.0, 11.2)[d]
Non-core foods (%EI)	-2.0 (-4.5, 0.4)	-9.6 (-12.3, -7.0)[d]	-7.6 (-11.2, -4.0)[d]
Protein (%EI)	0.5 (-0.4, 1.4)	1.9 (1.1, 2.6)[d]	1.3 (0.1, 2.5)[a]
Carbohydrate (%EI)	-0.8 (-2.5, 0.8)	0.1.1 (-2.5, 0.4)	-0.4 (-2.6, 1.9)
Fat (%EI)	-0.5 (-1.9, 1.0)	0.06 (-1.5, 1.4)	0.4 (-1.6, 2.5)
Saturated fat (%EI)	0.004 (-0.7, 0.8)	-0.6 (-1.4, 0.08)	-0.6 (-1.7, -0.4)
Monounsaturated fat (%EI)	-0.2 (-0.8, 0.4)	0.09 (-0.5, 0.7)	0.3 (-1.0, 0.5)
Polyunsaturated fat (%EI)	-0.3 (-0.6, -0.04)[a]	0.1 (-0.1, 0.4)	0.4 (0.1, 0.8)[a]
Alcohol (%EI)	0.7 (-0.5, 1.9)	-0.9 (-2.5, 0.7)	-1.6 (-3.6, 0.4)
Fibre (g/d)	-0.2 (-3.3, 3.0)	-0.1 (-2.6, 2.4)	-0.01 (-4.0, 4.0)
Sodium (mg/d)	-151.3 (-433.2, 130.5)	-519.8 (-753.0, -286.6)[d]	-368.5 (-732.0, -4.9)[a]
ARFS (maximum score)			
Total ARFS (73)	-0.2 (-2.2, 1.7)	4.1 (2.0, 6.3)[d]	4.3 (0.1.4, 7.2)[b]
Vegetables (21)	0.5 (-0.6, 1.5)	2.0 (0.7, 3.3)[b]	1.5 (-0.1, 3.2)
Fruit (12)	-0.08 (-0.8, 0.6)	1.0 (0.3, 1.7)[b]	1.1 (-0.1, 2.1)[a]
Meats (7)	0.3 (-0.7, 0.03)	0.5 (0.1, 1.0)[a]	0.9 (0.3, 1.4)[b]
Non-meat protein (6)	0.07 (-0.3, 0.2)	0.4 (0.05, 0.8)[a]	0.5 (-0.03, 0.9)[a]
Grains (13)	0.07 (-0.5, 0.3)	0.3 (-0.3, 0.8)	0.3 (-0.4, 1.0)
Dairy (11)	-0.2 (-0.6, 0.2)	-0.2 (-0.7, 0.2)	-0.06 (-0.7, 0.5)
Extras (2)	-0.01 (-0.2, 0.2)	-0.06 (-0.3, 0.2)	-0.05 (-0.4, 0.3)
Water (1)	0.04 (-0.07, 0.2)	0.1 (-0.01, 0.3)[a]	0.1 (-0.08, 0.3)
Portion size			
Potato	-0.03 (-0.4, 0.3)	-0.9 (-1.3, -0.4)[d]	-0.9 (-1.4, -0.3)[b]
Vegetable	-0.1 (-0.5, 0.3)	-0.06 (-0.5, 0.3)	-0.04 (-0.5, 0.6)
Steak	-0.2 (-0.5, 0.2)	-1.1 (-1.6, -0.6)[d]	-0.9 (-1.5, -0.3)[b]
Casserole	-0.2 (-0.5, 0.2)	-0.9 (-1.3, -0.5)[d]	-0.7(-1.3, -0.2)[a]

Significant differences within and between groups: [a]$P < 0.05$; [b]$P < 0.01$; [d]$P < 0.001$. Portion size coded as per Hodge *et al*[31] as follows: Never eat = 0, less than image A = 0.4, equal to image A = 0.5, between images A and B = 0.75, equal to image B = 1.0, between images B and C = 1.5, equal to image C = 2.0, greater than image C = 2.5. EI: Energy intake; ARFS: Australian Recommended Food Score.

dietary intake, including a reduction in intakes of energy-dense, nutrient-poor foods and increased overall diet quality and variety within healthful food groups and fruit, non-meat protein and meat ARFS subscales. Of note portion sizes for potatoes, steak and casserole were significantly reduced in the intervention group *vs* the control group. Though not significant, changes in the desired direction were observed for increased vegetable variety and decreased alcohol intake (%EI).

For men in the PULSE program intervention group, the increased diet quality was accompanied by an increased percentage of total energy from healthful foods and a %EI from energy-dense, nutrient-poor foods. Despite a reduction in mean total energy intake of approximately 1300 kJ/d ($P = 0.08$), dietary macronutrient composition remained relatively stable, with a small but significant increase of +1.3% in %EI from protein in the intervention group. This is in contrast to the United States Diabetes Prevention Program which reported a similar reduction in total energy intake among those in the lifestyle intervention group, however total fat intake decreased by 6.6% of total energy intake following the first 6 mo[4]. Similar reductions in total energy were also observed in the Finnish Diabetes Prevention Study following the intensive phase at 1 year[32]. These findings, combined with the increases in diet quality, suggest individuals in the PULSE intervention program replaced energy-dense, nutrient-poor foods with healthful food choices.

Most studies reporting on dietary outcomes immediately following major diabetes prevention program interventions have only reported on changes in total energy and/or nutrient intakes[9]. Few studies have evaluated changes in diet quality as assessed using an a priori defined diet quality index or score, or intakes of individual food groups. Miller *et al*[12] reported significant within group improvements in overall diet quality scores (+4.6, $P < 0.01$) measured using the Alternative Healthy Eating Index following a 4-mo group-based diabetes prevention program. In another study, Block *et al*[11] reported changes in food habits associated with higher diet quality, such as significant changes in the consumption frequency of fruits and vegetables (increases) and sweets and refined carbohydrate foods (decreases) found among those with prediabetes who received a 6-mo automated web-based diabetes prevention program.

Findings from interventions aimed at the prevention of T2DM, including the current PULSE trial, are consistent with meta-analyses[33,34] which support a significant association between higher overall diet quality, as assessed by a score or index, and a decreased risk of T2DM. Specifically in men with a high BMI, diets of higher quality have been associated with a reduction in the incidence of T2DM[35]. Findings from the current study also add to the emerging evidence for a lower risk of developing T2DM in those with a higher diet quality[36,37]. Greater dietary diversity within core food groups has also been associated with a lower risk of metabolic syndrome[38], and to be a predictor of weight loss and reduced waist circumference within a weight loss intervention[39]. In particular, diets that are diverse in the variety of fruits and vegetables consumed are associated with a lower risk of T2DM[37]. Recent meta-analyses on the amounts of fruits and vegetables consumed in relation to T2DM risk confirm the positive relationship between higher intakes of fruits and vegetables and lower risk of developing diabetes[40,41], including a dose-response relationship with a 6% and 13% lower risk for each 1 serve increase in fruit intake and each additional 0.2 serve of green-leafy vegetables, respectively[40].

The changes in diet in those receiving the PULSE intervention program are encouraging, especially given the self-directed nature of the program and compare

favourably to traditional intensive T2DM prevention programs delivered using one-on-one or group or combination approaches. Given the increasing prevalence of T2DM and associated risk factors, such as excess body weight, poor diet and physical inactivity, evidence of the effectiveness of low intensity programs are gaining momentum[7]. However, modifications to the traditional diabetes prevention programs are considered necessary for translation to non-research or "real-world" settings[42] and to promote sustainability of effective programs through delivery of these programs at scale. Delivery of programs using various media and technologies, such as DVD or web- or mobile-based platforms, have demonstrated effectiveness in terms of weight loss[6,11,43], while other diabetes prevention programs have begun to provide higher intensity interventions through the supplementation of mobile applications with remote support from a trained health coach[44,45].

The dietary changes observed by men in the PULSE intervention group support the observed improvements in weight status, waist circumference and measures of glucose regulation[16]. These findings demonstrate that participants adhered to the dietary messages contained in the PULSE program, in particular increasing variety within healthful food groups and reducing portion sizes. This indicates that a gender-tailored, self-directed program can result in desirable dietary changes that reduce T2DM risk. Despite, the benefits demonstrated by the PULSE program immediately following completion, the long-term impact on the maintenance of healthy eating behaviours remain to be established.

Although a validated food frequency questionnaire was used to measure dietary intake, the use of a self-administered measure is subject to inherent errors of self-reported dietary data[46] and is a limitation of the current study. The effect of measurement error in the context of intervention studies is an emerging area of research and recommendations to use a biomarker of dietary intake to calibrate the primary measure of intake[47] were outside the scope of the PULSE pilot study. While the dietary outcome findings should be interpreted in light of this, the use of objective measures for the anthropometric and biochemical outcomes is a strength of the current study, and improvements in these variables are likely to reflect the positive dietary changes observed for the intervention group.

In addition to reductions in anthropometric measures and improved glucose regulation, the self-directed, gender-tailored PULSE program resulted in significant improvements in dietary intake. This included a reduction in intake of energy-dense, nutrient-poor foods and portion size, increased overall diet quality and greater variety of healthful foods, especially within fruit, meat, and non-meat protein food groups.

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COMMENTS

Background

Dietary outcomes following diabetes prevention programs have primarily focused on reporting changes in energy and macronutrient intakes; effects on diet quality have only begun to be investigated. Also, most past programs have included both men and women, were not gender-tailored, and had little or no separate reporting of effects on men and women. This study investigated effects on dietary intakes and diet quality of the self-directed, gender-tailored Prevention Using LifeStyle Education (PULSE) program for type 2 diabetes mellitus (T2DM) prevention in men.

Research frontiers

Emerging evidence supported the use of gender-tailored programs for men in the context of weight loss, however no programs developed for T2DM prevention had been specifically tailored for men. The PULSE program aimed to address this gap.

Innovations and breakthroughs

The PULSE program's nutrition messages led to significant improvements in dietary intake and diet quality, as well as decreasing clinical risk factors for T2DM, in men at risk of T2DM, suggesting that gender-tailoring in this group may be important for achieving healthful dietary behaviour changes in men.

Applications

These findings offer support for the use of gender-tailored dietary messages in the context of dietary advice for the prevention of T2DM, in particular in relation to increasing variety within healthful food groups.

Terminology

Diet quality assessment provides an indication of adherence to dietary guidelines and healthy eating patterns. Diet quality can be assessed *via* indices or scores that evaluate types of foods consumed and variety within food groups, and in some instances, intakes of selected nutrients.

Peer-review

The study is very interesting from a clinical practice point of view.

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