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Intentional weight loss as a predictor of type 2 diabetes occurrence in a general adult population

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ABSTRACT

Introduction Observational and intervention studies have verified that weight loss predicts a reduced type 2 diabetes (T2D) risk. At the population level, knowledge on the prediction of self-report intentional weight loss (IWL) on T2D incidence is, however, sparse. We studied the prediction of self-report IWL on T2D incidence during a 15-year follow-up in a general adult population.

Research design and methods The study sample from the representative Finnish Health 2000 Survey comprised 4270 individuals, aged 30–69 years. IWL was determined with questions concerning dieting attempts and weight loss during the year prior to baseline. Incident T2D cases during a 15-year follow-up were drawn from national health registers. The strength of the association between IWL and T2D incidence was estimated with the Cox model.

Results During the follow-up, 417 incident cases of T2D occurred. IWL predicted an increased risk of T2D incidence (HR 1.44; 95% CI 1.11 to 1.87, p=0.008) in a multivariable model. In interaction analyses comparing individuals with and without IWL, a suggestively elevated risk emerged in men, the younger age group, among less-educated people and in individuals with unfavorable values in several lifestyle factors.

Conclusions Self-report IWL may predict an increased risk of T2D in long-term, probably due to self-implemented IWL tending to fail. The initial prevention of weight gain and support for weight maintenance after weight loss deserve greater emphasis in order to prevent T2D.

Significance of this study

What is already known about this subject?

- Successful weight loss reduces the risk of type 2 diabetes (T2D).
- At population level, weight loss tends to fail, and intentional weight loss (IWL) and dieting attempts have been shown to associate with subsequent weight gain.

What are the new findings?

- At population level, self-initiated IWL seems to be associated with higher risk of developing T2D in long term.
- It appears that among individuals with IWL, elevated risk of developing T2D is indicatively pronounced in certain subgroups including those with unfavorable lifestyle habits.
- It seems that among individuals with overweight, IWL is associated with higher risk of developing T2D regardless of initial health conditions.

How might these results change the focus of research or clinical practice?

- Information on self-report IWL can be used to identify individuals potentially at elevated risk of gaining weight and developing T2D in the future.
- Special focus and support to learn healthy lifestyle should be targeted to individuals with IWL behavior in order to prevent future weight gain and development of T2D.

INTRODUCTION

Consistent evidence suggests that overweight/obesity is a major risk factor of type 2 diabetes (T2D).[1] A cohort study estimated that 77% of all T2D cases were attributable to overweight.[2] Accordingly, in clinical practice, weight loss is used as the main preventive factor against T2D occurrence. However, weight loss attempts are not limited to individuals with genuine medical weight loss needs. Over 40% of adults report having tried to lose weight at some point in life.[3]

Systematic reviews, based on several intervention studies, in which participants receive support on weight loss and lifestyle change (ie, healthy diet and physical activity (PA)), have shown that weight loss predicts lowered risk of T2D compared with not losing weight.[4 5] In these studies, mostly including participants with overweight, obesity or other initial risk factors of T2D, active intervention periods have ranged between 0.5 and 6 years (mean 2.6, SD 1.7 years).[4] In one of the seminal intervention studies, the Finnish Diabetes Prevention Study, the individuals in the intervention group had 58% smaller risk of developing T2D during a mean intervention period of 3.2 years than the individuals in the control group,[6] and the risk remained decreased during a 13-year total follow-up

(HR of intervention group vs control group 0.61; 95% CI 0.48 to 0.79; p<0.001).[7] These findings are supported in part[8–12] but not all[13–16] cohort studies with weight loss without information on intentionality (WLW) as an exposure. In these WLW studies, as no information exists on the intentionality of weight loss, the weight-losers may also include individuals with unintentional weight loss. It would appear, however, that only three cohort studies (and all in the same cohort including individuals with overweight and obesity) have so far been performed on the prediction of intentional weight loss (IWL) on T2D occurrence[17–19] and only one study on the prediction of weight control by dieting on T2D occurrence.[20] The results of these observational studies acknowledging the intentionality aspect in weight loss were in line with the results of WLW and intervention studies.

The majority of epidemiological follow-up studies have suggested that dieting predicts weight gain.[21–23] Some studies have indicated the association to be accentuated in individuals with normal weight.[22 23] It has been suggested that dieting attempts may act as a proxy for susceptibility to gain weight.[24] This finding may also be due to weight loss induced autoregulated metabolic changes (eg, lowering of energy expenditure, hyperphagia), which contribute to weight regain and possible fat overshooting.[25] Failed dieting attempts often lead to a subsequent attempt, and repeated attempts lead to weight cycling. Weight cycling, however, is not a new phenomenon, but already in 1962 Neel[26] suggested that a 'thrifty genotype', originally beneficial for hunter-gatherers during cycles of feast and famine, predisposes its carriers to increased risk of diabetes through efficient utilization of food and, thus, development of obesity. The evidence for weight cycling causing adverse metabolic changes is, however, inconsistent.[27] Nevertheless, weight cycling seems to play a role in the development of chronic diseases such as T2D.[28]

As only a few studies exist on associations between IWL and T2D, and none conducted in a representative adult population, but in populations with overweight or obesity, and as the associations between dieting and weight gain suggest that dieting may also have adverse metabolic consequences, the present study aimed to investigate the prediction of IWL on subsequent T2D incidence during a 15-year follow-up in a general adult population.

RESEARCH DESIGN AND METHODS

Study population

The cohort sample used was based on the Health 2000 Survey (BRIF8901) collected in 2000–2001.[29] The nationally representative adult population sample was drawn from the Finnish Population Information System with a two-stage stratified cluster sampling design and included 8028 men and women aged 30 years and over. Of the original sample, 6771 (84% of the sample) participated in a health examination (see online supplementary figure S1). We excluded those with previously diagnosed diabetes or myocardial infarct, not within age range of 30–69 at baseline, pregnant at baseline or with missing information in the variables included in the analyses (see online supplementary figure S1). We tested whether the exclusion of those having recently given birth (during 2, 3 or 4 years before baseline) and, thus, possibly losing 'baby weight' would affect the results by excluding such individuals from the study sample. As this did not make any difference, we included these women in the sample. After the exclusions, the study sample included 4270 individuals (2308 women and 1962 men).

Methods

Information on variables used in this study was collected during a field phase including a health examination, interviews, and self-administered questionnaires. Moreover, information was drawn from national health registers.

IWL was defined by combining questions concerning dieting attempts during the year prior to baseline (no/yes) and weight loss during the year prior to baseline (no/yes) from a self-administrative questionnaire. The questionnaire included a question concerning the amount of weight loss during the year prior to baseline (among those with weight loss: range 1–38 kg, mean 5.2, SD 4.0), but, in line with previous studies on self-report IWL, individuals who had attempted to lose weight and had lost any amount of weight were considered as satisfying the IWL criteria, irrespective of the amount of weight lost during the year prior to baseline.[17–19 30]

Data on sex and age were obtained from the sampling frame. Educational attainment and smoking habits were asked about during an interview. Education was divided into a three-class variable including categories: low (did not graduate from upper secondary school or vocational school), intermediate (graduated from upper secondary school or vocational school) and high (graduated from university or university of applied sciences). Individuals were categorized according to their smoking status as never-smokers, former smokers and current smokers.

A self-administered questionnaire was used to measure leisure-time PA, alcohol consumption (g ethanol/week) and habitual sleep duration during 24 hours. PA was categorized in three levels: not physically active ('low'), regularly engaging in light PA such as walking or cycling ('moderate') and exercising for 3 hours or more per week or training for competitive sports ('regular vigorous training'). Individuals were categorized according to their alcohol consumption (g ethanol/week) as non-users, moderate users (1–199 for male or 1–99 for female) and heavy users (200 or over for male or 100 or over for female). Sleep duration was divided into a three-class variable including the categories: '≤6 hours', '7–8 hours' and '≥9 hours'.

A self-administered Food Frequency Questionnaire assessing habitual food intake during the last 12 months[31 32] was used to measure energy intake and quality of diet. Average daily intakes of food groups,

energy and nutrients were calculated using The National Food Composition Database (Fineli) and in-house software (Finessi).[33] Quality of diet was measured with The Alternate Healthy Eating Index (AHEI).[34] In this study, the AHEI was constructed to suit the Finnish food culture while imitating the original AHEI as closely as possible.[35]

Data for body mass index (BMI) and metabolic factors was collected during a health examination. Height and weight were measured by trained study nurses, with the participants only wearing light clothing and no shoes, and BMI was calculated. Normal weight was defined as BMI <25 kg/m^2, overweight as 25 ≤BMI <30 kg/m^2 and obesity as BMI ≥30 kg/m^2. As the proportion of individuals with underweight was small (n=29), they were included in the group with normal weight. Waist circumference was measured and abdominal obesity was, in accordance with the International Diabetes Federations (IDF) metabolic syndrome (MetS) criteria, defined as a waist circumference of ≥80 cm for women and ≥94 cm for men.[36]

Blood pressure was measured twice using a standard mercury manometer, with 2 min intervals (Mercuro 300; Speidel & Keller, Jungingen, Germany). The mean of the two measurements was used. The use of antihypertensive medication was asked about during the interview. The IDF's definition of elevated blood pressure was used: systolic pressure ≥130 mm Hg or diastolic pressure ≥85 mm Hg, or use of antihypertensive medication.[36]

Concentrations of serum triglycerides (automated enzymatic method, Olympus system reagent, Germany), serum HDL cholesterol (enzymatic method, Roche Diagnostics, Mannheim, Germany) and serum fasting glucose (hexokinase, Olympus System Reagent, Germany) were determined from frozen (−70C) serum samples. Categorization of these variables was conducted according to threshold values for the MetS: serum triglycerides (mmol/L) <1.7 and ≥1.7, serum HDL cholesterol (mmol/L) ≥1.03 in men or ≥1.29 in women and <1.03 in men or <1.29 in women and fasting serum glucose (mmol/L) <5.6 and ≥5.60.[36] MetS was defined as having a waist circumference of ≥80 cm in women or ≥94 cm in men and meeting two or more of the aforementioned unfavorable values of serum triglycerides, serum HDL cholesterol, fasting serum glucose and blood pressure.[36]

Four variables representing different indicators of poor health were formed. Severe MetS was defined as an unfavorable value in each MetS component. Mental health status was determined with a self-administered questionnaire, including the General Health Questionnaire (GHQ).[37] Individuals with a GHQ score >2 were categorized as having poor mental health. Self-perceived health was determined during an interview with a five-category question including the options: good, quite good, mediocre, quite poor, poor. Additionally, a two class-variable was formed including categories: 1) good, quite good and mediocre and 2) quite poor and poor. Specially trained physicians diagnosed osteoarthritis in the knee and hip joints during the health examination on the basis of physical status, symptoms and medical history, according to detailed written instructions with uniform diagnostic criteria.[29]

The study was conducted using a cohort study design with T2D incidence as the outcome. The T2D cases occurring during a 15-year follow-up were identified from nationwide registers covering information on medication use, hospitalization and cause of death, with the presence of any of the International Classification of Diseases, Tenth Revision codes E10–E14 (see online supplementary file S1). In Finland, under the Health Insurance Act, the costs of diabetes medication are reimbursed for patients with diabetes with a diagnosis from an attending physician.[38] In order to receive the medication allowance, the physician must provide a certificate describing the diagnostic criteria applied for T2D diagnosis and the certificate must be checked and accepted by special advisers at the Social Insurance Institution of Finland (Kela). The nationwide register of patients receiving diabetes medication reimbursement is maintained by Kela. Moreover, information from the Finnish Hospital Discharge Register[39] and the National Causes of Deaths Register were used. Study participants were linked to these registers with a unique social security number identifying each Finnish citizen. During the 15-year follow-up, 417 individuals (241 men and 176 women) developed T2D.

Statistical methods

Cox's proportional hazards model[40] was used to estimate the HR and its 95% CI of T2D in relation to the different predictors considered. The follow-up time was defined as the number of days from the baseline examination to the date of T2D occurrence, death or end of follow-up, whichever came first. Statistical significance was tested using the likelihood ratio test. Potential confounding factors were first selected based on the literature, and the variables which satisfied criteria for confounding in this data were included in the models.[41] Since it is not easy to draw the line between confounding factors and mediators, four main effects models and one interaction model were defined. The first model included age, sex and an exposure variable in question. The second model included age, sex, waist circumference and IWL. The third model included age, sex, IWL, education (low, intermediate, high), alcohol consumption (none, moderate, heavy), leisure time PA (low, moderate, regular vigorous training), smoking status (never, past, current), AHEI (quintiles), energy intake (quintiles), BMI (continuous) and sleep duration (<6, 7–8, ≥9 hours/day). The fourth model included the variables of the third model and the variables of the MetS, that is, waist circumference (continuous), blood pressure (raised, normal), serum glucose (continuous), serum triglycerides (continuous) and serum HDL cholesterol (continuous). Finally, possible modification by sex, age, leisure time PA, body mass index, energy intake, AHEI, sleep duration and MetS on the prediction of the IWL on T2D risk was studied by including an interaction term between IWL

Table 1 Characteristics of the participants by IWL during the year prior to baseline (n=4270)

	IWL		
	No (n=3712)	Yes (n=558)	P value for heterogeneity
	Mean (SD) or %*	Mean (SD) or %*	
Sociodemographic factors			
Sex (% male)	47.4	35.7	<0.001
Age (years)	47.5 (10.6)	45.9 (9.93)	<0.001
High education (%)	33.5	39.1	0.008
Lifestyle factors			
BMI (kg/m^2)	26.3 (4.43)	28.7 (5.05)	<0.001
Regular vigorous training (%)	19.6	22.1	0.16
Alcohol consumption (g ethanol/week)	81.9 (145)	86.6 (126)	0.44
Current smoking (%)	29.9	29.3	0.76
Energy intake (kcal/day)	2314 (785)	2242 (751)	0.04
AHEI (score) (range 7–35)	20.9 (4.87)	22.4 (4.96)	<0.001
Sleep duration (hours)	7.45 (1.01)	7.42 (1.05)	0.59
Metabolic factors			
Waist circumference (cm)	90.7 (12.9)	96.8 (14.4)	<0.001
Elevated blood pressure (%)	55.0	58.7	0.08
Serum triglycerides (mmol/L)	1.51 (1.02)	1.65 (0.98)	0.002
Serum HDL cholesterol (mmol/L)	1.36 (0.38)	1.26 (0.35)	<0.001
Fasting serum glucose (mmol/L)	5.34 (0.54)	5.40 (0.94)	0.01
MetS (IDF definition) (%)	34.8	48.5	<0.001
Indicators of poor health			
Severe MetS† (%)	4.49	5.42	0.33
Poor mental health‡ (%)	21.6	23.6	0.28
Poor or quite poor self-perceived health (%)	6.65	6.87	0.85
Osteoarthritis (%)	4.38	5.88	0.11

*Adjusted for age and sex.
†Fulfillment of each MetS precondition (according to IDF definition).
‡General Health Questionnaire score >2.
AHEI, Alternate Healthy Eating Index; BMI, body mass index; HDL, high-density lipoprotein; IDF, International Diabetes Federation; IWL, intentional weight loss; MetS, metabolic syndrome; n, number of subjects in respective category.

and the potential effect modifying factor considered in the fourth model.

The calculations were performed using SAS (V.9.3, SAS Institute, Cary, North Carolina, USA).

RESULTS

IWL was more common in women, younger individuals, persons with a high level of education, persons with higher BMI, persons with lower energy intake, persons with higher diet quality persons with pathological values in metabolic factors (table 1).

A strong and consistent association between potential risk factors of diabetes and T2D incidence was seen: practically all baseline variables considered concerning sociodemography, lifestyle, metabolism and health significantly predicted T2D occurrence after adjustment for sex and age (table 2). The only exceptions were energy intake and quality of diet (AHEI score).

The individuals with IWL showed a statistically significant elevated risk of T2D occurrence, with an HR of 1.58 (95% CI 1.23 to 2.03) after adjustment for sociodemographic status and lifestyle, including BMI (model 3, table 3). The significance still remained after further inclusion of the metabolic factors in the model (model 4, table 3; HR 1.44; 95% CI 1.11 to 1.87). Examination of the association by length of follow-up showed no significant association during the first 5 years of follow-up (model 4, table 3; HR 0.94; 95% CI 0.48 to 1.84) and a significant association (HR 1.70; 95% CI 1.28 to 2.25) during the remaining part of the follow-up.

Study of interactions between IWL and potential effect modifying factors showed significance for age, alcohol consumption and AHEI (table 4). The increased risk of

Table 2 Risk of type 2 diabetes incidence during a 15-year follow-up between categories of selected variables

	n of cases (n=417)	N at risk (n=4270)	%	HR*	95% CI
Sociodemographic factors					
Sex					
Women	176	2308	54.1	1	
Men	241	1962	45.9	1.77	1.46 to 2.16
Age (years)					
30–39	42	1215	28.5	1	
40–49	109	1287	30.1	2.58	1.81 to 3.68
50–59	175	1083	25.4	5.23	3.74 to 7.33
60–69	91	685	16.0	4.62	3.21 to 6.67
Education					
Low	179	1285	30.1	1	
Intermediate	151	1523	35.7	0.91	0.72 to 1.14
High	87	1462	34.2	0.59	0.45 to 0.77
Lifestyle factors					
BMI (kg/m^2)					
<25	44	1704	39.9	1	
25–29.9	172	1704	39.9	3.33	2.38 to 4.65
≥30	201	862	20.2	8.59	6.18 to 11.9
Physical activity					
Low	123	1018	23.8	1	
Moderate	232	2403	56.3	0.71	0.57 to 0.89
Regular vigorous training	62	849	19.9	0.56	0.41 to 0.76
Alcohol consumption					
No	111	1048	24.5	1	
Moderate	211	2531	59.3	0.82	0.64 to 1.03
Heavy	95	691	16.2	1.35	1.01 to 1.79
Smoking					
Never	172	2139	50.1	1	
Former smoker	110	872	20.4	1.37	1.07 to 1.76
Current smoker	135	1259	29.5	1.57	1.24 to 1.98
Energy intake quintiles† (kcal/day)					
First (lowest)	100	853	20.0	1	
Second	74	854	20.0	0.75	0.55 to 1.01
Third	75	854	20.0	0.75	0.56 to 1.01
Fourth	72	854	20.0	0.77	0.57 to 1.04
Fifth	96	855	20.0	1.05	0.79 to 1.39
AHEI quintiles‡					
First (lowest)	65	780	18.3	1	
Second	88	861	20.2	1.16	0.84 to 1.60
Third	100	995	23.3	1.09	0.80 to 1.49
Fourth	83	800	18.7	1.16	0.84 to 1.60
Fifth	81	834	19.5	0.95	0.69 to 1.33
Sleep duration (hours)					
≤6	74	587	13.7	1	

Continued

Table 2 Continued

	n of cases (n=417)	N at risk (n=4270)	%	HR*	95% CI
7–8	297	3239	75.9	0.77	0.59 to 0.99
≥9	46	444	10.4	0.93	0.64 to 1.34
Metabolic factors					
Waist circumference (cm)					
<80 cm for women or <94 cm for men	43	1531	35.9	1	
≥80 cm for women or ≥94 cm for men	374	2739	64.1	4.57	3.32 to 6.29
Blood pressure					
Normal	94	1901	44.5	1	
Elevated	323	2369	55.5	2.07	1.62 to 2.65
Serum triglycerides (mmol/L)					
<1.7	189	2993	70.1	1	
≥1.7	228	1277	29.9	2.54	2.08 to 3.10
Serum HDL cholesterol (mmol/L)					
≥1.29 for women or ≥1.03 for men	186	2857	66.9	1	
<1.29 for women or <1.03 for men	231	1413	33.1	2.75	2.27 to 3.34
Fasting serum glucose (mmol/L)					
<5.6	151	3041	71.2	1	
≥5.6	266	1229	28.8	3.99	3.24 to 4.92
MetS (IDF definition)					
No	100	2708	63.4	1	
Yes	317	1562	36.6	5.07	4.02 to 6.39
Indicators of poor health					
Severe MetS§					
No	336	4073	95.4	1	
Yes	81	197	4.61	4.75	3.70 to 6.10
Mental health¶					
Good	314	3328	78.1	1	
Poor	103	931	21.9	1.26	1.01 to 1.58
Self-perceived health					
Good, quite good or mediocre	366	3980	93.3	1	
Quite poor or poor	51	285	6.68	1.74	1.30 to 2.34
Osteoarthritis					
No	373	4043	95.4	1	
Yes	42	194	4.58	1.68	1.21 to 2.34

*Adjusted for age and sex.
†Energy intake quintile ranges (kcal): first 732–1755 for male, 593–1613 for female; second 1756–2113 for male, 1614–1946 for female ; third 2114–2478 for male, 1947–2285 for female; fourth 2479–3022 for male, 2286–2677 for female; fifth 3023–6413 for male, 2678–6495 for female.
‡AHEI quintile ranges (points): first 7–16 for male, 7–16 for female; second 17–19 for male, 17–19 for female; third 20–22 for male, 20–22 for female; fourth 23–25 for male, 23–25 for female; fifth 26–34 for male, 26–35 for female.
§Fulfillment of each MetS precondition (according to IDF definition).
¶General Health Questionnaire score >2.
AHEI, Alternate Healthy Eating Index; BMI, body mass index; HDL, high-density lipoprotein; IDF, International Diabetes Federation; MetS, metabolic syndrome; n, number of subjects in respective category.

T2D in those with IWL was concentrated to the younger age group (HR 1.95; 95% CI 1.35 to 2.81), individuals not using alcohol (HR 1.57; 95% CI 1.00 to 2.47) or using it moderately (HR 1.71; 95% CI 1.22 to 2.41), and to those with the lowest quality diet (HR 2.76; 95% CI 1.51 to 5.04). Moreover, despite the lack of significant interaction, a

Table 3 Risk of type 2 diabetes incidence by IWL during a 15-year follow-up and during different lengths of follow-up

			Model 1*		Model 2†		Model 3‡		Model 4§	
IWL	**n of cases**	**N at risk**	**HR**	**95% CI**	**HR**	**95% CI**	**HR**	**95% CI**	**HR**	**95% CI**
	Total follow-up									
No	328	3712	1		1		1		1	
Yes	89	558	2.18	1.73 to 2.77	1.48	1.16 to 1.88	1.58	1.23 to 2.03	1.44	1.11 to 1.87
P value for heterogeneity				<0.001		0.002		<0.001		0.008
	0–5 years follow-up									
No	60	3712	1		1		1		1	
Yes	18	558	2.39	1.41 to 4.06	1.46	0.85 to 2.51	1.46	0.83 to 2.57	0.94	0.48 to 1.83
P value for heterogeneity				0.003		0.19		0.21		0.84
	6–10 years follow-up									
No	147	3587	1		1		1		1	
Yes	42	533	2.26	1.60 to 3.20	1.50	1.05 to 2.14	1.68	1.16 to 2.41	1.74	1.20 to 2.53
P value for heterogeneity				<0.001		0.03		0.008		0.005
	11–15 years follow-up									
No	121	3354	1		1		1		1	
Yes	29	485	1.98	1.32 to 2.98	1.48	0.97 to 2.24	1.56	1.02 to 2.39	1.63	1.06 to 2.49
P value for heterogeneity				0.002		0.08		0.05		0.03

*Adjusted for sex and age.
†Adjusted for sex, age and waist circumference.
‡Adjusted for sex, age, education, BMI, physical activity, alcohol consumption, smoking, energy intake, AHEI and sleep duration.
§Adjusted for sex, age, education, BMI, physical activity, alcohol consumption, smoking, energy intake, AHEI, sleep duration, waist circumference, elevated blood pressure, serum HDL cholesterol, serum triglycerides and fasting serum glucose.
AHEI, Alternate healthy eating index; BMI, body mass index; HDL, high-density lipoprotein; IWL, intentional weight loss; n, number of subjects in respective category.

Table 4 Risk of type 2 diabetes incidence during a 15-year follow-up between those with and without IWL during the year prior to baseline in categories of effect modifying factors

Variable	Number of individuals				HR*	95% CI	P for interaction
	No IWL (ref.)		IWL				
	Cases	At risk	Cases	At risk			
Sociodemographic factors							
Sex							0.38
Women	138	1950	38	358	1.28	0.88 to 1.86	
Men	190	1762	51	200	1.60	1.13 to 2.27	
Age (years)							0.03
30–49	108	2140	43	362	1.95	1.35 to 2.81	
50–69	220	1572	46	196	1.12	0.78 to 1.59	
Education							0.11
Low	144	1148	35	137	1.70	1.15 to 2.51	
Intermediate	117	1334	34	189	1.60	1.07 to 2.39	
High	67	1230	20	232	0.89	0.51 to 1.54	
Lifestyle factors							
BMI† (kg/m^2)							0.54
<25	40	1561	4	143	1.32	0.47 to 3.70	
25–29.9	142	1463	30	241	1.36	0.90 to 2.05	
≥30	146	688	55	174	1.79	1.28 to 2.49	
Physical activity							0.22
Low	102	905	21	113	1.94	1.20 to 3.16	
Moderate	183	2080	49	323	1.20	0.85 to 1.69	
Regular vigorous training	43	727	19	122	1.72	0.97 to 3.06	
Alcohol consumption							0.05
No	84	904	27	144	1.57	1.00 to 2.47	
Moderate	166	2211	45	320	1.71	1.22 to 2.41	
Heavy	78	597	17	94	0.74	0.39 to 1.41	
Smoking							0.35
Never	136	1885	36	254	1.76	1.20 to 2.59	
Former smoker	79	729	31	143	1.13	0.70 to 1.84	
Current smoker	113	1098	22	161	1.39	0.87 to 2.21	
Energy intake quintiles (kcal/day)							0.09
First (lowest)	71	723	27	122	2.00	1.26 to 3.16	
Second–fifth	257	2989	62	436	1.25	0.92 to 1.70	
AHEI quintiles							0.03
First (lowest)	51	712	14	68	2.76	1.51 to 5.04	
Second–fifth	277	3000	75	490	1.27	0.95 to 1.68	
Sleep duration (hours)							0.37
≤6	57	510	17	77	1.82	1.05 to 3.15	
7–8	235	2815	62	424	1.28	0.93 to 1.75	
≥9	36	387	10	57	1.96	0.96 to 3.99	
Metabolic factors							
MetS (IDF definition)‡							0.46
No	81	2404	19	304	2.20	1.33 to 3.64	
Yes	247	1308	70	254	1.77	1.35 to 2.32	

*Total model: sex, age, education, BMI, physical activity, alcohol consumption, smoking, energy intake, AHEI, sleep duration, waist circumference, elevated blood pressure, serum HDL cholesterol, serum triglycerides, fasting serum glucose and interaction variable in question.
†Not adjusted for waist circumference.
‡Not adjusted for BMI, waist circumference, elevated blood pressure, serum HDL cholesterol, serum triglycerides or fasting serum glucose.
AHEI, Alternate healthy eating index; BMI, body mass index; HDL, high-density lipoprotein; IDF, International Diabetes Federation; IWL, intentional weight loss; MetS, metabolic syndrome; n, number of subjects in respective category.

Table 5 Risk of type 2 diabetes incidence during a 15-year follow-up between those with and without IWL during the year prior to baseline in categories of different indicators of health in subjects with BMI ≥25 kg/m^2 (n=2484)

	Number of individuals						
	No IWL (ref.)		IWL				
Variable	Cases	At risk	Cases	At risk	HR*	95% CI	P for interaction
Severe MetS†‡							0.37
No	216	1925	65	373	1.87	1.41 to 2.48	
Yes	63	160	16	26	2.79	1.59 to 4.90	
Mental health§							0.74
Good	207	1638	59	305	1.57	1.14 to 2.16	
Poor	72	447	22	94	1.76	1.08 to 2.86	
Self-perceived health							0.25
Good, quite good or mediocre	243	1909	68	370	1.48	1.11 to 1.99	
Quite poor or poor	36	176	13	29	3.05	1.60 to 5.80	
Osteoarthritis							0.78
No	248	1955	73	372	1.66	1.25 to 2.21	
Yes	31	130	8	27	1.30	0.59 to 2.85	

*Adjusted for sex, age, education, physical activity, alcohol consumption, smoking, energy intake, AHEI, sleep duration, elevated blood pressure, serum HDL cholesterol, serum triglycerides and fasting serum glucose.
†Fulfillment of each MetS precondition (according to IDF definition).
‡Not adjusted for elevated blood pressure, serum HDL cholesterol, serum triglycerides and fasting serum glucose.
§General Health Questionnaire score >2.
AHEI, Alternate healthy eating index; BMI, body mass index; HDL, high-density lipoprotein; IDF, International Diabetes Federation; IWL, intentional weight loss; MetS, metabolic syndrome; n, number of subjects in respective category.

statistically significantly increased risk in those with IWL could be seen in the subgroups of men, individuals with low or intermediate education, individuals with obesity, individuals with low PA, never-smokers, individuals with the lowest energy intake and individuals with short sleep.

Further study of the interaction between IWL and indicators of poor health in persons with an elevated T2D risk (BMI ≥25 kg/m^2) showed no significant effect modification (table 5). With only one exception regarding one indicator (ie, osteoarthritis), a significantly elevated risk of T2D was seen for IWL both among individuals having and not having poor health.

DISCUSSION

Findings

In this representative sample of the Finnish population, IWL predicted an elevated risk of T2D. This finding was relatively consistent. It was found in the total population and in several categories of the known T2D risk factors considered. Elevated T2D risk in individuals with IWL was indicatively pronounced in men, younger persons, less educated persons, persons with obesity, persons with low PA, non-alcohol and moderate alcohol consumers, never-smokers, persons with low energy intake, persons with low quality of diet and persons with short sleeping duration. Furthermore, the association was present in overweight persons irrespective of health status (ie, severe MetS, mental health or self-perceived health). The elevated risk was also seen during the different time intervals of the 15-year follow-up. Thus, our results can be generalized to a wide variety of subpopulations.

Interpretation

There are several potential explanations for our findings. It is well known that overweight/obesity is a major risk factor of T2D and it has been reported to explain 77% of T2D incidence.[2] Even though several randomized controlled trials on behavioral/lifestyle interventions for diet and PA have shown successful weight loss and T2D risk reduction,[4 5] weight loss and especially weight maintenance has appeared to be difficult for the majority of individuals with weight regain after weight loss.[42] Accordingly, large population studies have shown that IWL or dieting attempts predict subsequent weight gain.[21–23] A previous study, conducted with the same but somewhat smaller population as used in this study, showed that dieting attempts and weight loss during the year prior to baseline were associated with increase in BMI and waist circumference during an 11-year follow-up.[23] Hence, it can be assumed that weight regain occurs among those with IWL and developing T2D as well.

In addition to potential straightforward weight gain after weight loss, a further potential metabolic pathway between IWL and increased risk of T2D may be related to weight cycling, which often results from repeated weight loss efforts. It has been suggested that weight cycling may increase the risk of T2D via subsequent weight gain[23 27] or, specifically, because of accumulation of abdominal

obesity,[27] which is known to associate with insulin resistance.[26 43] Alternatively, weight cycling may affect metabolic factors and, consequently, elevate the risk of T2D.[44] Although the mechanisms between weight cycling and the development of T2D remain partly uncertain,[27] evidence suggesting an association between weight cycling and T2D occurrence is relatively consistent.[28] Thus, the possibility of weight cycling acting as a mediator between IWL and T2D cannot be ruled out. Hence, when considered together, the possibility cannot be excluded that, especially in general population like ours, the harmful effects of IWL may predominate and lead to excess T2D occurrence.[45]

In accordance with the findings from the randomized controlled trials,[4 5] the results from the majority of previous cohort studies[8–12 17–20] have differed from those of our own. The only findings from cohort studies so far published on the prediction of IWL on T2D occurrence were based on individuals with overweight in three substudies from the American Cancer Society's Cancer Prevention Study, conducted in 1959–1972. A total of 43 457 women[18] and 49 337 men[19] aged 40–64 years considered the T2D-related mortality, and 180 768 men and women aged 30 years and older[17] the incidence of T2D during a mean follow-up of 12 years. All three substudies suggested IWL to predict a lowered risk of T2D. Accordingly, an 8-year follow-up study of 844 Mexican-Americans from the San Antonio Heart Study suggested self-report weight control by dieting (without information on the successfulness of weight loss) to be associated with a decreased risk of T2D in women.[20]

The results of cohort studies on WLW are inconsistent. Approximately half of the studies reported that WLW is related to a reduced T2D incidence.[8–12] These studies were all based on large samples (n=1929–114 281) from established cohort studies, for example, Nurses' Health Study,[8] The Health Professionals Follow-up Study,[10] National Health and Nutrition Examination Survey[12] and The British Regional Heart Study.[11] Other studies have failed to find any association between WLW and T2D.[13–16]

Potential reasons for the discrepant results in this study and those of other studies may be a lack of reliability and/or of validity of the IWL measure we used or of differences between IWL and the measures of weight loss and dieting used in the other studies. The overall agreement between the IWL used and an intended weight loss of ≥5%, a measure of weight loss suggested,[46] considered sufficient for diabetes prevention,[47] and commonly used,[48] was relatively good. The intraclass correlation coefficient between these measures, estimated as kappa, was 0.66 (95% CI 0.63 to 0.70). A sensitivity analysis showed a non-significant difference between the prediction of the IWL used and the intended weight loss of ≥5% on diabetes outcome (p=0.10), the HRs being 1.44 (95% CI 1.11 to 1.87) and 1.65 (95% CI 1.21 to 2.25), respectively. These results thus suggest that the IWL used (ie, any IWL during the year prior to baseline) is a reliable measure for use as a predictor of diabetes occurrence.

Other potential reasons explaining the discrepant results include differences in study populations, length of follow-up, control for confounding and definition of T2D. These questions are evaluated in the online supplementary file S1. The evaluation showed that despite differences in several study characteristics considered, the discrepant results appear to be potentially explained by two factors. First, the group with IWL may, due to higher incidence of obesity, poor health, potentially higher genetic predisposition to obesity and T2D or pronounced health consciousness, have been over-represented by individuals with an elevated risk of T2D or an elevated risk of being diagnosed with T2D. Second, self-implemented IWL during the short, 1-year period may not have worked properly for all individuals, resulting in weight regain or weight cycling and, later, in an elevated risk of T2D. To get a deeper understanding on these potential reasons, the IWL/T2D association was studied in subgroups of the population.

Effect modification

To the best of our knowledge, this is the first study to investigate the modifying effects of different health, sociodemographic and lifestyle factors on the association between IWL and T2D incidence in a general population. As literature on effect modifiers between IWL and T2D is almost non-existent, we selected a priori variables for which it was plausible, based on their known associations with exposure and outcome variables, that the strength of association may vary from one subgroup to another.

We found some indicators of poor health, such as the presence of MetS predicting T2D occurrence, and to be more common in individuals with IWL. It is possible that individuals with IWL already have an elevated risk of T2D at baseline and try to lose weight in response to that. This is supported by the fact that even after adjustment for age and sex the amount of IWL was greater in individuals later developing T2D (mean 7.16, SD 5.33 kg) than in individuals not developing T2D (mean 5.44, SD 4.12 kg) during the follow-up (p=0.0009). Also the finding that inclusion of the components of the MetS in the model attenuated the association into non-existent during the first 5 years of the follow-up implies that individuals with IWL indeed may initially have an elevated risk that explains the association in short-term. In long-term, however, adjustment for the components of MetS did not notably alter the primary results. Furthermore, in the interaction analyses no differences in the risk of T2D emerged between those with IWL and different aspects of poorer health and those with IWL and no such health conditions. It is, therefore, unlikely that poorer health at baseline entirely could explain the results.

Even though most of the interactions for sociodemographic and lifestyle risk factors remained non-significant, several suggestive associations, based on statistically significant differences between those with IWL and without IWL in certain subgroups, emerged. Moreover, these tentative associations seemed plausible

and conformed to associations between such sociodemographic and lifestyle risk factors as exposures and T2D as an outcome found in this study and in the literature. We found that IWL was indicatively associated with an elevated risk of T2D in men, in younger persons and in less educated persons. It is possible, that men or younger persons do not take their IWL as seriously as women or older persons and regain the weight more often. Men with IWL may also initially be at greater risk of T2D, as previous findings indicate that men do not attempt dieting unless they become affected by overweight[49 50] or develop an actual disease.[50] The indicative association found in less educated individuals with IWL may be due to more unfavorable lifestyle[51] or a lack of positive interpersonal and intrapersonal resources[52] that possibly lead to poorer strategies for trying to lose and maintain weight.

Furthermore, an indicative association was observed in individuals with IWL and lifestyle risk factors of T2D: obesity, low PA, low-quality diet and short or long sleep duration. Conversely, smoking or heavy alcohol consumption did not show such associations. Those with obesity are initially at greater risk of T2D and the consequences of failed IWL may be decisive in the development of the disease. Poor lifestyle while trying to lose weight may predispose individuals to eventually failing in weight loss and regaining the weight. Moreover, an indicative association emerged in individuals with IWL and the lowest energy intake. Indeed, it is possible that too drastic a reduction of energy intake predisposes to relapses in dieting regimen.

It is thus possible that in subgroups with IWL in men, in younger individuals, in less educated, and in individuals with unfavorable lifestyle factors long-term success in IWL is poorer and weight regain and weight cycling are more common than in those who pursue weight loss with healthy lifestyle, better strategies or otherwise more earnestly. Hence, it is plausible that poor implementation of the IWL is the leading explanation for the results found.

Strengths and limitations

The strengths of the current study are the representative population sample, the prospective study design and the comprehensive set of potential risk factors of T2D considered, which enabled extensive control for confounding factors and the opportunity to study versatile interactions. The major limitations were the lack of repeatability data on the IWL measure, the uncertainty related to the validity of the measure, incomplete diagnosis and lack of information on amount of weight change during the follow-up. A significant association between IWL and T2D incidence was found in subgroups of several potential effect-modifying factors. Since a significant interaction, possibly due to skew distributions, was confirmed only for some of these variables, no firm conclusions about the presence of effect modification can be made.

Generalization of the results

Even though findings of this study on general adult population imply that self-initiated and self-reported IWL is associated with subsequently increased risk of developing T2D, this result should not be used as an advice not to lose weight among individuals with obesity and medical reasons for weight loss. Weight loss, and especially weight maintenance are difficult, but results of several lifestyle intervention studies have proved that with lifestyle changes and support, they are possible. Thus, special emphasis should be placed on weight loss and weight maintenance that are conducted with proper lifestyle changes that can be applied to for life. Healthy eating and enough PA are the cornerstones of the process, but the key is to find an individually suited, yet flexible, weight loss and weight maintenance supporting lifestyle that does not lead into total relapses and weight regain. For many individuals, seeking assistance from professionals or participating in a structured weight loss program can also be of help.

CONCLUSIONS

During a 15-year follow-up, IWL consistently, after exclusion of the first 5 years of follow-up, predicted an elevated risk of T2D. This is the first cohort study on this subject conducted in a representative sample of a general adult population. In addition to the whole sample, an elevated risk was tentatively accentuated in certain subgroups, for example, in those with IWL and with less education or unfavorable lifestyle factors, which implies that poorly conducted IWL may be, in particular, a risk factor of T2D. The increased risk may derive from weight gain that occurs after IWL or from weight fluctuation resulting from IWL and inducing unfavorable changes in metabolic values. On the other hand, it cannot fully be excluded that the increased risk observed is partly due to an initially higher risk of T2D among individuals with IWL or due to methodological factors such as more frequently diagnosed T2D in those with IWL.

Despite the associations found in the present study, dieting should not be avoided by individuals with severe obesity or with unfavorable metabolic values, but the sustainability of the weight loss should be underlined. Since failed weight loss seems to result in disadvantageous consequences, dieting should be conducted carefully and, in the absence of medical reasons for weight loss, it should be avoided. These findings call for an emphasis on the prevention of weight gain, throughout learning about healthy and weight-maintenance-supportive lifestyle, and, in clinical settings, on the long-term follow-up and support provided after IWL in order to hinder weight regain and weight cycling and, thus, possibly reduce the risk of T2D. The novel information provided by this study, on individuals with IWL being at higher risk of developing T2D in the future, can also be applied, in addition to the more traditional risk factors, to identify high-risk individuals of T2D in public healthcare. Further cohort

studies with repeated measurements on dieting behavior and changes in weight, and samples large enough to properly enable the examination of effect modifying factors are needed.

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