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Smoking cessation and the incidence of pre-diabetes and type 2 diabetes: a cohort study

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Abstract

Aims: Smoking cessation has been suggested to increase the short-term risk of type 2 diabetes mellitus (T2DM). This study aimed at assessing the association between smoking cessation and incidence of T2DM and impaired fasting glucose (IFG).

Methods: Data from participants in the CoLaus study, Switzerland, aged 35-75 at baseline and followed for 5·5 years were used. Participants were classified as smokers, recent (≤5 years), long-term (>5 years) quitters, and non-smokers at baseline. Outcomes were IFG (fasting serum glucose (FSG) 5·6-6·99 mmol/l) and T2DM (FSG ≥7·0 mmol/l and/or treatment) at follow up.

Results: 3,166 participants (63% women) had normal baseline FSG, of whom 26·7% were smokers, 6·5% recent quitters, and 23·5% long-term quitters. During follow-up 1,311 participants (41·4%) developed IFG (33·6% women, 54·7% men) and 47 (1·5%) developed T2DM (1·1% women, 2·1% men). Former smokers did not have a statistically significant increased odds of IFG compared with smokers after adjustment for age, education, physical activity, hypercholesterolemia, hypertension and alcohol intake, with OR of 1·29 [95% confidence interval 0·94-1·76] for recent quitters and 1.03 [0·84-1·27] for long-term quitters. Former smokers did not have significant increased odds of T2DM compared with smokers with multivariable-adjusted OR of 1·53 [0·58-4·00] for recent quitters and 0·64 [0·27-1·48] for long-term quitters. Adjustment for body-mass index and waist circumference attenuated the association between recent quitting and IFG (OR 1·07 [0·78-1·48]) and T2DM (OR 1·28 [0·48-3·40].

Conclusion: In this middle-aged population, smoking cessation was not associated with an increased risk of IFG or T2DM.

Keywords: Smoking cessation, pre-diabetes, diabetes

Table of abbreviations:

FSG	Fasting serum glucose
IFG	Impaired fasting glucose
IQR	Inter Quartile Range
T2DM	Type two diabetes mellitus
US	United States of America

1. Introduction

Smoking is as an established risk factor for type 2 diabetes (T2DM) (1, 2) and increases the risk of micro- and macro-vascular complications (3-5). The increased risk is due to different mechanisms: smoking is toxic on the pancreatic beta cells(6), acts on inflammatory pathways(7), induces oxidative stress, and favours central obesity(8) and insulin resistance(4, 9). As a consequence, to quit smoking should reverse or at least lower this increased metabolic risk. However, the reversible character of the pro-diabetogenic effects of smoking has not yet been proven. Besides, smoking cessation is associated in most cases with weight gain(10), which is a known risk factor for T2DM. Weight gain is also an important barrier to smoking cessation in many smokers (11).

Studies on metabolic risk after smoking cessation show controversial results. A meta-analysis estimated that the risk of developing T2DM for ex-smokers was not as high as that of smokers, but was still 23% higher relatively to non smokers(1). The incidence of T2DM after smoking cessation has been investigated in six prospective studies (12-17) and all showed an increased risk in the first years following smoking cessation.

The development metabolic risk goes through a continuum from normoglycemic to impaired fasting glucose (IFG), a pre-diabetic state, and T2DM. IFG is the key state in which life style measures are effective to prevent disease(18). Though, few studies considered the risk of developing impaired fasting glucose following a smoking quit attempt and most focused on established T2DM.

Furthermore gender/sex disparities might exist concerning metabolic risk after smoking cessation. Studies suggest that women might gain more weight at smoking cessation(19) and the effect of smoking on their health also differs from men(8, 20).

Our study aimed at assessing whether the incidence of T2DM as well as IFG increases after smoking cessation in a middle-aged European population and test for an interaction with gender.

2. Subjects, Material and Methods

2.1 CoLaus study

Data from a Swiss prospective observational cohort study (CoLaus) were used. The CoLaus study has been accepted by the Ethics Committee of the Canton Vaud. The sampling procedure of the CoLaus study has been described previously(21). Recruitment began in June 2003 and ended in May 2006. The following inclusion criteria were applied: (i) written informed consent; (ii) age 35–75 years; (iii) willingness to take part in the examination and to have a blood sample drawn. Participation rate was 41% and 6,733 participants (3,544 women and 3,189 men) were recruited. A follow up interview at 5·5 years was completed in 2012.

2.2 Participants

For the present study, 5,064 participants who completed follow-up were selected. Ninety of them (0·8%) were further excluded because of missing data for smoking status, fasting serum glucose (FSG), treatment for T2DM, body-mass index (BMI) or waist circumference at baseline or follow up. Participants with T2DM (n=278) or IFG (n=1530) at baseline were also excluded, leaving 3,166 participants with FSG ≤5·6mmol/l and no treatment for T2DM.

2.3 Variables

2.3.1 Impaired fasting glucose and T2DM

The primary outcomes were the cumulative 5·5-year incidences of IFG and of T2DM. Serum glucose was measured at baseline and 5·5-year follow-up from blood samples drawn after an 8-hours fasting. T2DM was defined as FSG ≥7 mmol/l or presence of an oral anti-diabetic or

insulin treatment. IFG was defined as FSG between 5·60 and 6·99 mmol/l and no treatment for T2DM.

2.3.2 Smoking status

Smoking status and years since quitting were self-reported. Participants were categorised in four groups: current smokers if they reported smoking ≥1 cigarette/day or ≥1 pipe or cigar/day at baseline; recent quitters if they reported quitting smoking ≤5 years before baseline; long-term quitters if they reported quitting >5 years before baseline, and as never smokers otherwise. We considered pipe and cigar smoking as equivalent to cigarette smoking because they represented a minority of smokers (7%) and because all types of tobacco combustion are harmful (22).

Exposure of interest was smoking cessation > 5 years or ≤ 5 years before baseline, with smokers as the control group.

2.3.3 Other variables

BMI was calculated based on weight and height measured at baseline. Waist circumference was measured at a level midway between the lower rib margin and the iliac crest.

Baseline BMI (kg/m^2) and weight gain during follow up (weight at follow up minus weight at baseline in kilograms) was calculated in women and men.

We defined participants as physically active if they exercised at least 20 minutes of leisure time physical activity per week (23, 24). Alcohol consumption was defined as reported standard units consumed per week. High level of education was defined as having completed at least secondary school (>9 years of school)(21). As participants were included from an urban area, they were mainly with middle to high socio-economic status. Hypercholesterolemia was defined as LDL cholesterol ≥4·1mmol/l or taking a lipid lowering treatment; hypertension was defined as a systolic blood pressure >140 mmHg and/or diastolic blood pressure >90 mmHg and/or taking an antihypertensive drug treatment.

2.4 Statistical analysis:

2.4.1 Basis analysis

Statistical analysis was conducted using Stata version 12·0 (StataCorp, College Station, Texas). Descriptive results were presented as number of participants (percentage) or as mean ± standard deviation. Between-group comparisons were performed using Student t-test for continuous variables and Fischer's exact tests for proportions.

Analyses were stratified by sex. The associations between smoking status and incidence of IFG and T2DM were assessed separately. We used logistic regressions to estimate the Odd Ratios (ORs) and 95% confidence intervals (CI) of developing IFG or T2DM in recent quitters, long-term quitters and never smokers compared with smokers. Three levels of adjustment were performed: age only (model 1); age, education, leisure-time physical activity, alcohol consumption, hypercholesterolemia, and hypertension (model 2), and all variables in model 2 plus BMI, and waist circumference (model 3). We adjusted for waist circumference and BMI in a separate model because they might be mediators rather than confounders in the relationship between smoking cessation and development of IFG or T2DM.

Finally, we tested the interaction for sex in the association between smoking status and IFG or T2DM incidence using an interaction term in the fully adjusted non-stratified model.

A two-sided p-value <0·05 was considered as statistically significant.

2.4.2 Sensitivity analyses:

We tested whether participants with inconsistent smoking status during the 5·5 years of follow-up influenced results. These participants (n=343, 10·8%) were excluded, and the association between smoking status and IFG or T2DM by smoking status was assessed in the remaining 2823 (89·2%) participants using the fully adjusted model (model 3). We also repeated the analyses without excluding participants with IFG at baseline (n=1,530, 30·8%). This was done to test whether

selecting participants with normal FSG introduced a bias towards T2DM resistant smokers and ex-smokers.

We also adjusted the multivariate analysis to weight change defined as weight at follow up minus weight at baseline.

Finally, in post-hoc analyses we analysed the change in glycaemia as a continuous variable between baseline and follow up in each smoking category by Wilcoxon Ranksum test and between categories by Kruskall Wallis test.

3. Results

3.1 Subjects

The baseline characteristics of the participants free from IFG and T2DM are summarized in Table 1. There were 63% of women, mean age was 50·7 years and the majority had a high educational level. There were 846 smokers (26·7%), 207 recent quitters (6·5%), 743 long-term quitters (23·5%) and 1370 never smokers (43·3%). Men presented significantly higher levels of cardiovascular risk factors and were more frequently current or former smokers than women.

3.2 Weight gain during follow-up

Weight gain during follow up according to smoking status can be found in Table 2. Overall, women gained slightly less weight than men over the 5.5 years of follow-up with a median of 1·2 kg (interquartile range (IQR)-0·9-3·7) compared with 1·6 kg (IQR -0·8-4·2) in men (p= 0·048). Among women, recent quitters gained the most weight with a median of 1·6 kg, followed by smokers (1·5 kg), long-term quitters (1·3 kg) and never smokers (1·1 kg). Among men, smokers gained the most weight with a median of 2 kg, followed by never smokers (1·5 kg), long term quitters (1·4 kg), and recent quitters (1·3 kg).

3.4 Association between smoking status and incidence of IFG or T2DM

During follow-up, 1,311 participants (41·1%) developed IFG and 47 (1·5%) T2DM. The unadjusted cumulative incidences of IFG and T2DM according to baseline smoking status, stratified by sex are shown in Figure 1. Women had a lower cumulative incidence of IFG than men (33·6% versus 54·7%, p<0·001). Similarly women also had a lower incidence of T2DM than men (1·1% versus 2·1%, p=0·032).

The results of the minimal-adjusted and multivariable-adjusted analyses of the associations between incidence of IFG or T2DM and smoking status are summarized in Table 3. No statistically significant association was found between smoking and the incidence of IFG or T2DM. Former smokers did not have a statistically significant increased odds of IFG compared with smokers with multivariable-adjusted OR, adjusted for age, education, physical activity, hypercholesterolemia, hypertension and alcohol intake, of 1·29 [0·94-1.76] for recent quitters and 1.03 [0·84-1·27] for long-term quitters. Further adjustment for body-mass index and waist circumference attenuated the association for recent quitters (OR 1.07 [0·78-1.48]) and to a lesser extent for long-term quitters (OR 0.96 [0·78-1.19]). Similarly, former smokers did not have a statistically significant increased odds of IFG compared with smokers with multivariable-adjusted OR of 1·53 [0·58-4.00] for recent quitters and 0.64 [0·27-1·48] for long-term quitters. Further adjustment for body-mass index and waist circumference attenuated the association for recent quitters (OR 1.28 [0·48-3·40]). The sex×smoking status interaction was non-significant.

3.5 Sensitivity analyses

The analyses were repeated using the fully adjusted model after excluding participants who changed their smoking status during follow-up: 204 (10·2%) women and 139 (11·8%) men. Again, no significant association was found between the incidence of IFG or T2DM and

smoking status but the association was somewhat stronger for recent quitters (supplementary table 1).

A second sensitivity analysis was performed using the fully adjusted model and including 1,530 participants with IFG at baseline (and who initially excluded in the main analyses, total N=4696). Never smokers had a significantly lower likelihood of developing T2DM compared with smokers (OR 0·67 [0·49-0·94]), while recent quitters and long-term quitters did not have statistically different odds of developing T2DM compared with smokers.

The adjustment for weight change between baseline and follow up did not change the main results, as there was no significant increase in IFG en T2DM incidence after smoking cessation when adjusted for this factor either (Table 3, Model 4).

Finally analysis of change in glycaemia between baseline and follow-up showed no statistically significant difference (P=0·16) between smokers and those who had stopped smoking or never smoked (Supplementary table 2).

4. Discussion

In this study, we found no significant association between smoking cessation and the incidence of IFG or type 2 T2DM. On average men were at higher metabolic risk at baseline and also gained more weight during follow up than women, but there was no interaction between sex and metabolic risk after smoking cessation.

Smoking cessation and risk of T2DM

In a meta-analysis including 25 cohort studies not specifically designed to assess the relationship between smoking cessation and the incidence of T2DM, former smokers had on average a lower risk of developing T2DM compared with current smokers on the long term (1).

Nevertheless, six studies specifically designed to assess T2DM after smoking cessation showed an increased risk in the short term after cessation(13-17); Will et al. showed an increased risk of T2DM in the ten first years after smoking cessation for men and in the five first years for women in a US population(17). No specific data were given regarding weight gain. Wannamathee and colleagues reported a higher risk of T2DM for smokers who had quit for less than five years compared with smokers who continued to smoke in British men(12). In this study participants gained between 3·2 and 4·3 kg and recent quitters gained more weight than continuing smokers and long-term quitters (4·3 vs. 3·8 vs. 3·2 kg). In Korea, Hur et al. reported a significantly increased risk of T2DM for men who had quit for two to four years compared with non-smokers (13). No specific data were given regarding weight gain. In 2010 Yeh et al. showed an increased risk of T2DM in American men and women in the first six years after smoking cessation compared with smokers(14). Recent quitters gained significantly more weight (3·8 kg) compared to continuing smokers (0·6 kg) and longer term quitters (1·2 kg). In Japan, Oba showed an increased risk of T2DM among male former smokers who had quit for less than five years compared with never smokers but former smokers who had quit for longer than five years did not have an increased risk(15). Recent quitters gained more weight (1·3 kg) than continuing smokers (0·2 kg) and long-term quitters (0·2 kg). In this same study among women, the risk of T2DM was increased to a greater extend, and for all former smokers, even those who had quit for a longer period. A recent study, conducted in the US among women, also showed an increased risk of T2DM in the first ten years after quitting (16). In this study recent quitters gained more weight (2·9 kg) than all other groups (0·3-0·5 kg). None of these studies specifically tested the risk for IFG development.

Our study does not confirm these findings. Several hypotheses can explain the discrepancy. First, weight gain after smoking cessation was rather limited in our cohort particularly among recent quitters. This may explain the lower incidence of T2DM and IFG after smoking cessation

compared with other cohorts. Surprisingly, recent quitters did not gain more weight than the continuing smokers in our study. In most studies described earlier, recent quitters gained more weight over time than continuing smokers (with differences in weight gain ranging from 0·5 to 3·2 kg) and this might in part explain the lack of association between smoking cessation and T2DM or IFG in our study.

Second, the association between smoking cessation and T2DM probably draws an inverse U-shaped curve (25) with an increased risk of T2DM in the short term, followed by a decrease after several years of abstinence. Based on the six prospective studies, it takes between two to ten years for a former smoker to have a risk of T2DM similar to that of someone who has never smoked. In our population, recent quitters had quit for 2·6 years but former smokers were abstinent for 19·5 years on average. We might have measured the incidence of T2DM at a moment when the risk was already decreasing, explaining the absence of positive association for former smokers.

Another hypothesis is that the population we followed might not be comparable to that of the other studies. Our sample was rather homogenous, including an urban population with middle to high socio economic status. Our population had a standard prevalence of T2DM for Europe (5·6%), but great differences between men and women for IFG and T2DM incidence and a low prevalence of obesity (12%). Indeed, in Europe there is an estimated prevalence of 6% of diabetes (in adults, type 1 and 2 together) as compared with 11·1% in North America (26), and the prevalence of obesity in Europe is around 10-30% (27) as compared with 34·9% in the US(28). These particularities have to be taken into account, and our results cannot be generalized to other populations.

Supplementary analyses showed that change in glycaemia was similar in the different smoking categories. This strengthens our results and the hypothesis that higher weight gain in quitters than

in smokers might explain the increased risk of diabetes after smoking cessation found in other studies.

Our study speaks against an increase in metabolic risk after smoking cessation, in an urban normal weight European setting with overall low weight gain.

Limitations and strengths

The study has a number of limitations that need to be acknowledged. First, since this is an observational prospective study, associations were measured but there is no proof that they are causal. Some potential confounders such as diet were not included in our models. Second, variables were measured at baseline and five-year follow-up only. Smoking habits might have changed during this period. However we conducted a sensitivity analysis excluding participants with inconstant smoking behaviour over follow-up, which showed no significant influence on the analyses. Additionally, other studies have used similar timeframes and found valid results (12, 15, 29). Third, smoking status and duration of smoking abstinence were self-reported. There might be a difference between the actual duration of smoking abstinence and the reported years, and we had no biological validation of smoking abstinence. People usually remember well when they quit smoking and self-reported smoking status is considered as trustworthy in this kind of population(30). Another limitation is the exclusion of participants with pre-diabetes at baseline. We therefore conducted another sensitivity analysis, in which we included people with IFG at baseline. We observed a significantly lower risk of T2DM in never smokers. We might have underestimated the increased risk in smokers and ex-smokers by selecting only baseline participants with normal glycaemia. This has to be taken into account when generalizing our results to global population. Furthermore, the number of events is quite low in our population, especially the incidence of new T2DM. As observed by the large confidence intervals for the incidence of T2DM in multivariate analysis (Table 3), lack of power might explain the non

significant results. Finally we have used impaired fasting glucose and not impaired glucose tolerance because only a minority of participants had an oral glucose tolerance test. Impaired glucose tolerance test is a better predictor for cardiovascular disease than impaired fasting glucose (31).

Several strengths deserve to be mentioned. Our study is based on prospective data, representative of real life conditions. We used data from an initial population of over 5,000 participants followed over a 5·5-year period and randomly selected. The sample we studied is representative of an urban middle-aged population of European decent. Numerous life styles, as well as anthropometric and biologic variables, were reliably collected, allowing for an extensive adjustment for potential confounders. We have especially been able to measure fasting serum glucose levels, which is a major strength of this study.

5. Conclusion and implication

In an urban population of European decent, smoking cessation is not associated with an increased risk of pre-diabetes or T2DM, compared with smoking continuation or not smoking. Health professionals should strongly recommend smoking cessation with focus on limiting weight gain after quitting.

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Contribution statement

Study concept and design: Le Boudec, Clair. *Acquisition of data:* CoLaus team *Analysis and interpretation of data:* Le Boudec, Clair, Marques-Vidal. *Drafting of manuscript:* Le Boudec. *Critical revision of the manuscript for important intellectual content:* Clair, Marques-Vidal, Cornuz. *Statistical analysis:* Le Boudec, Clair, Marques-Vidal *Administrative, technical and material support:* Cornuz *Study supervision:* Clair

Conflict of interest:

Joana Le Boudec declares that she does not have a conflict of interest; Carole Clair declares that she does not have a conflict of interest; Pedro Marques-Vidal declares that he does not have a conflict of interest; Jacques Cornuz declares that he does not have a conflict of interest.

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Figure legend

Figure 1: Unadjusted five years incidence of IFG and T2DM according to baseline smoking status, stratified by gender.

Table 1: baseline characteristics of 3166 participants with normal FSG at baseline*

	Total N=3166	Women N=1993	Men N=1173	*P value*
Mean age at baseline, years	50·7±0·2	51·5±10·5	49·3±10·2	*<0·001*
Higher educational level (Secondary school or University)	1579 (49·9)	945 (47·4)	634 (54·1)	*<0·001*
BMI at baseline, kg/m²	24·6±0·1	24·1±4·1	25·5±3·4	*<0·001*
Waist circumference at baseline, cm	84·9±0·2	80·4±10·6	92·6±9·9	*<0·001*
Hypercholesterolemia**	705 (22·3)	381 (19·1)	324 (27·6)	*<0·001*
Low HDL (<1.03 mmol/l)	469 (14·8)	124 (6·2)	345 (29·4)	*<0·001*
Hypertension***	808 (25·5)	447 (22·4)	361 (30·8)	*<0·001*
Alcohol consumption, standard units/week	5.6 ± 0·1	3·7±5·1	8·8±10·0	*<0·001*
Higher leisure time physical activity (≥ 20 min/week)	2124 (67·1)	1330 (66·7)	794 (67·7)	*0·60*
Positive family history of diabetes	622 (19·6)	417 (20·9)	205 (17·5)	*0·06*
Baseline cardiovascular disease****	131 (4·1)	74 (4·0)	57 (5·3)	*0·06*
Smoking status				*<0·001*
Never smokers	1370 (43·3)	932 (46·8)	438 (37·3)	
Long term quitters (>5 years)	743 (23·5)	454 (22·8)	289 (24·6)	
Recent quitters (≤5 years)	207 (6·5)	111 (5·6)	96 (8·2)	
Smokers	846 (26·7)	496 (24·9)	350 (29·8)	

* Results are expressed as number of subjects (percentage) or as means ±standard deviation. ** defined as LDL >4·1 mmol/l or hypolipidemic treatment. *** defined as systolic blood pressure >140 mmHg and/or diastolic blood pressure >90 mmHg and/or antihypertensive drug treatment. ****defined as coronary heart disease present at baseline. BMI: body mass index.

Table 2: Body mass index* at baseline and weight gain** between baseline and follow up according to baseline smoking status

	Total		Women		Men		*P-value****
	BMI *	**Weight gain ****	**BMI***	**Weight gain ****	**BMI ***	**Weight gain ****	
Never smokers	24·7±0·4	1.2 (-0.8-3.7)	24·4±4·2	1·1 (-0·9-3·4)	25·2±3·4	1·5 (-0·7-4·1)	*0·047*
Long term quitters	24·9±0·6	1.3 (-0.9-3.4)	24·2±4·1	1·3 (-0·9-3·4)	25·9±3·6	1·4 (-1·1-3·4)	*0·682*
Recent quitters	25·2±0·9	1.5 (-1-4.7)	24·3±3·6	1·6 (-1·0-4·9)	26·2±3·1	1·3 (-0·7-4·6)	*0·940*
Smokers	24·1±0·5	1.7 (-1-4.7)	23·2±4·0	1·5 (-1·0-4·5)	25·4±3·3	2·0 (-0·9-4·9)	*0·185*
All subjects	24·6±0·1	1.3 (-0.9-3.9)	24·1±4·1	1·2 (-0·9-3·7)	25·5±3·4	1·6 (-0·8-4·2)	*0·048*

*Mean+/- SD, kg/m² ** Median (IQR), kg. *** P-value for differences in weight gain between men and women using Wilcoxon ranksum test. BMI = Body-mass index, SD = standard deviation, IQR = Interquartile range.

Table 3: Multivariate analysis of the associations between incidences of **IFG** and **T2DM** and smoking status

	Smokers	**Recent quitters**	**Long-term quitters**	**Never smokers**
IFG (N=3,166)	**N=846**	**N=207**	**N=743**	**N=1370**
Nº of events	*349*	*92*	*317*	*553*
Model 1	1	1·20 (0.88-1.64)	0·94 (0·77 - 1·11)	0·93 (0·78 – 1·12)
Model 2	1	1·29 (0·94 - 1·76)	1·03 (0·84 - 1·27)	1·08 (0·90 - 1·30)
Model 3	1	1·07 (0·78 - 1·48)	0·96 (0·78 - 1·19)	1·05 (0·87 - 1·27)
Model 4	1	1·12 (0·80-1·55)	0·97 (0·78-1·21)	1·09 (0·90-1·32)
T2DM (N=3,166)	**N=846**	**N=207**	**N=743**	**N=1370**
Nº of events	*17*	*6*	*9*	*15*
Model 1	1	1·50 (0·58 - 3·87)	0·56 (0·24 - 1·27)	0·53 (0·26 - 1·06)
Model 2	1	1·53 (0·58 - 4·00)	0·64 (0·27 - 1·48)	0·58 (0·28 - 1·21)
Model 3	1	1·28 (0·48 - 3·40)	0·57(0·24 - 1·38)	0·57(0·27 - 1·20)
Model 4	1	1·33 (0·50-3·53)	0·57 (0.24-1·34)	0·57 (0·27-1·19)

Results are expressed as Odds ratio (OR) and 95% confidence interval relative to current smokers. Statistical analysis by logistic regression. **Model 1**: adjusted for age. **Model 2**: adjusted for age, education, physical activity, hypercholesterolemia, hypertension and alcohol intake. **Model 3**: adjusted for age, education, physical activity, hypercholesterolemia, hypertension, alcohol intake, body mass index and waist circumference. **Model 4:** adjusted for age, education, physical activity, hypercholesterolemia, hypertension, alcohol intake, body mass index, waist circumference and weight gain.

Supplementary tables

Supplementary table 1: Sensitivity analyses: Multivariate analysis of the associations between incidence of IFG and T2DM and smoking status excluding participants who changed their smoking status, and in non-diabetic participants at baseline (adjustment model 3)

	Smokers	**Recent quitters**	**Long-term quitters**	**Never smokers**
		Participants with constant smoking status only		
IFG				
N=2,763	**N=589**	**N=134**	**N=742**	**N=1358**
Model 3	1	1·22 (0·82 – 1·81)	0·98 (0·77 - 1·25)	1·07 (0·86 - 1·33)
T2DM				
N=2,763	**N=589**	**N=134**	**N=742**	**N=1358**
Model 3	1	1·73 (0·56 – 5·40)	0·68 (0·26 - 1·79)	0·72 (0·30 - 1·70)
		Incidence of T2DM in all non-diabetic participants, including participants with IFG at baseline		
N=1696	**N=1261**	**N=340**	**N=1154**	**N=1941**
Model 3	1	1·09 (0·69 – 1·74)	0·77 (0·55 - 1·08)	0·67 (0·49 – 0·94)

Results are expressed as Odds ratio (OR) and 95% confidence interval relative to current smokers. Statistical analysis by logistic regression. Model 3: adjusted for age, education, physical activity, hypercholesterolemia, hypertension, alcohol intake, body mass index and waist circumference.

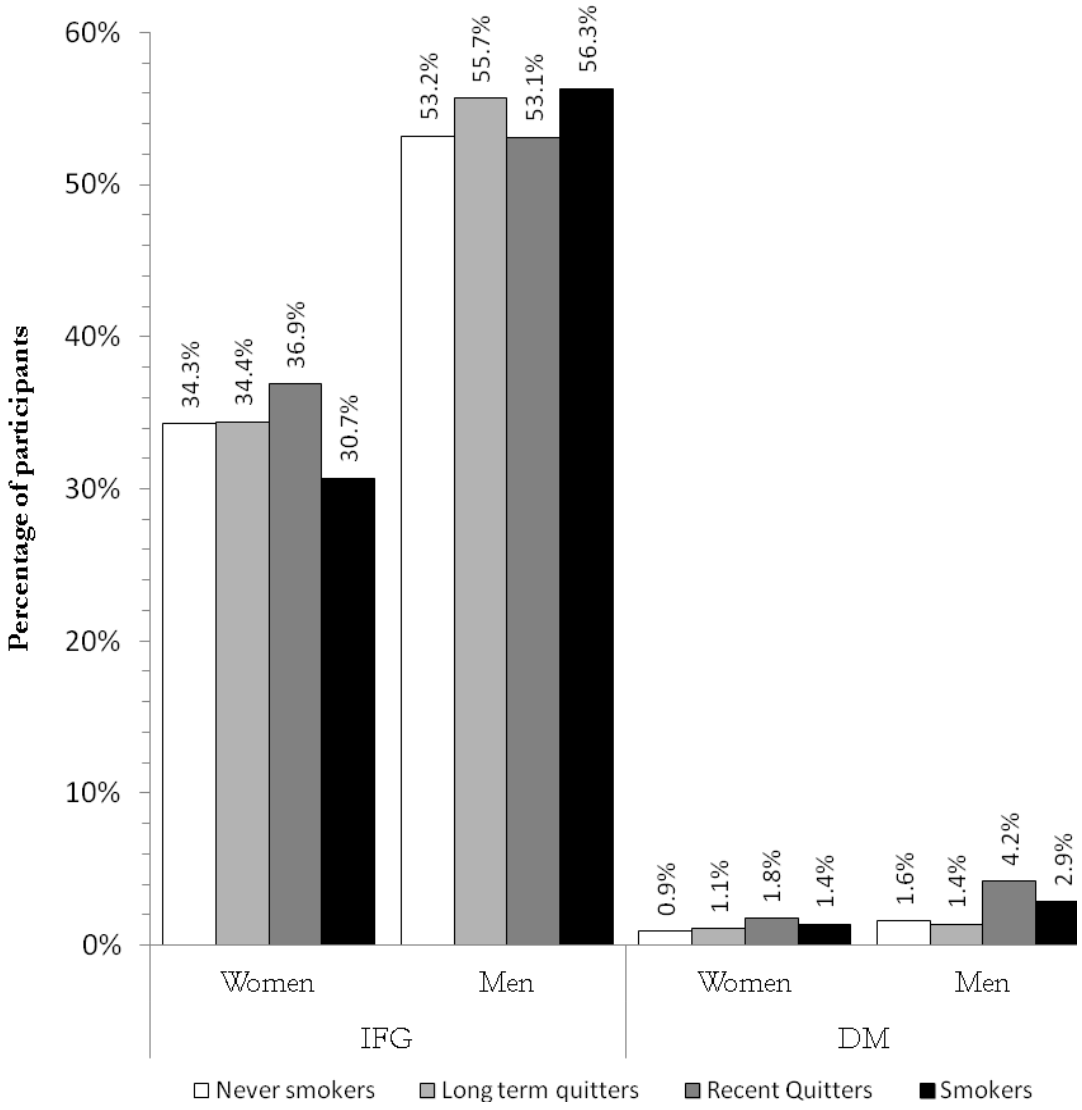
Supplementary table 2: Changes in glycaemia and weight gain by smoking category

	Total	**Smokers**	**Recent quitters**	**Long-term quitters**	**Never smokers**
	N=3,166	*N=846*	*N=207*	*N=743*	*N=1370*
Change in glycaemia*	0·4 (0·4-0·4)	0·4 (0·4-0·5)	0·4 (0·3-0·5)	0·4 (0·4-0·5)	0·4 (0·4-0·4)
P value**			0.26	0.29	0.23
Weight gain***	1·3 (-0·9-3·9)	1·7 (-1-4·7)	1·5 (-1-4·7)	1·3 (-0·9-3·4)	1·2 (-0·8-3·7)
P value**			0.97	0.01	0.02

*Median (IQR) change in glycaemia in mmol/l between baseline and follow up **P value for difference between non smoker category and smokers (Wilcoxon Ranksum test) ***Median (IQR) weight gain in kg between baseline and follow up

Figures

Figure 1



IFG, Impaired fasting glucose (Fasting serum glucose 5·60 - 6·99 mmol/l and no treatment for diabetes)

DM = type 2 diabetes (Fasting serum glucose ≥ 7mmol/l and/or treatment)