

ELECTRONIC SUPPLEMENTARY MATERIAL

‘Obesity Paradox’ and Mortality in Adults with and without Incident Type 2 Diabetes: a matched population-level cohort study

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Literature search

We searched PubMed using the term “type 2 diabetes” AND “mortality” AND “obesity paradox” for articles published in English, from 2000 to September 2016. We cross-referenced with a systematic review published in 2016.[1] We identified eight studies capturing risk data on at least five BMI categories (listed in Table S1),

Table S1 Summary of eight published studies on associations between BMI and all-cause mortality in T2D, which reported risk for at least 5 BMI categories (to allow assessment of the obesity paradox)

Authors, year country	cohort	No. of T2D	Median age	Current smokers %	endpoints	No. of deaths (%)	Median fu (years)	Time to event analysis	Main findings
Khalangot et al. 2009 Ukraine[2]	Patients with known type 2 diabetes from all 25 regions of Ukraine and the city of Kiev were entered into the opulation-based register "System of Diabetes Mellitus Care in Ukraine (SINADIAB)"	89,443	men: approx. 64 yr; women: approx. 66 yr	men: approx. 20%; women: approx. 1%	Total and cardiovascular mortality among diabetes patients	7804 (8.7)	2.7	Cox models plus restricted cubic splines.	"This study indicated a U-shaped association between BMI and total and cardiovascular mortality among diabetic men and women"
Carnethon et al. 2012, USA[3]	Pooled analysis of 5 longitudinal cohort studies.*	2,625	39 to 78	41% to 79% ever smokers	all-cause mortality; cardiovascular mortality	80% survival at 15 years	up to 15 years on K-M curves	K-M curves and Cox models based on cohort entry	"Adults who were normal weight at the time of incident diabetes had higher mortality than adults who are overweight or obese"
Logue et al. 2013 Scotland[4]	Scotland Diabetes registry 2001 to 2007	106,640	59.5 to 62.3	23% to 25%	all-cause mortality and cause-specific mortality	5272 (4.9)	4.6	Associations between BMI and mortality, all-cause and cause-specific, were investigated using Cox proportional hazards regression - by gender	"Results from this large population-based T2DM cohort show that individuals with class II obesity or greater (BMI >35 kg/m ²) and those of normal weight (BMI 20 to <25 kg/m ²), within a year after diagnosis of T2DM have an increased risk of all-cause mortality after ≥2 years compared with people with a BMI in the overweight category (BMI 25 to <30 kg/m ²)."
Thomas et al. 2014 UK[5]	GPRD (General Practice Research Datalink)	47,509	60.0		Primary outcomes were long-term risks of cardiovascular events (CVEs) and all-cause mortality	The mortality rates per 1000 person-years in normal weight, overweight and obese patients among patients without prior CVD were 13.1, 8.6 and 6.0, respectively, during 5 years of median follow-up. Deaths = 6.5%	5.0	To explore the association of BMI at diagnosis with the risk of CVE and all-cause mortality during follow-up, two different stratified Cox regression models were fitted: [1] simple model, adjusted for age, sex, smoking status, systolic blood pressure (SBP), diastolic blood pressure (DBP), HbA1c and BMI categories; [2] extended model included LDL, HDL and triglyceride measures	"Adults with normal weight at the diagnosis of T2DM have significantly higher mortality risk compared to those who are obese"

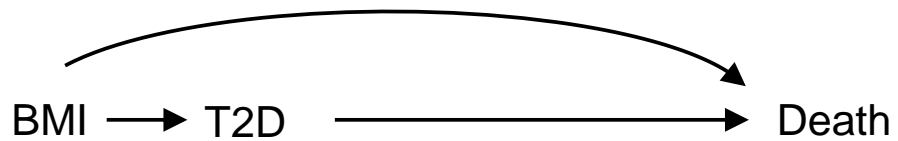
									at diagnosis, apart from the variables included in the simple model.	
Tobias et al. 2014 USA[6]	Nurses' Health Study (8970 participants) and Health Professionals Follow-up Study (2457 participants) who were free of cardiovascular disease and cancer at the time of a diagnosis of diabetes.	11,427	Women: 59.5 to 64.4 Men: 59.7 to 69.2. Overall mean: 62 yr	Never smokers. Women: 43-45.5%. Men: 37.9-45.6%	Primary: overall mortality. Secondary: Cause-specific mortality (CVD, cancer, respiratory diseases, renal disease, suicide, and accidents.	3083 (26.9)	15.8	Multivariable Cox models were used to estimate the hazard ratios and 95% confidence intervals for mortality across BMI categories. Nonlinear trends were assessed with likelihood-ratio tests of restricted cubic splines. Analyses were repeated with stratification according to baseline smoking status and with early deaths (<4 years after diagnosis) excluded.	"We observed a J-shaped association between BMI and mortality among all participants and among those who had ever smoked and a direct linear relationship among those who had never smoked. We found no evidence of lower mortality among patients with diabetes who were overweight or obese at diagnosis, as compared with their normal-weight counterparts, or of an obesity paradox."	
Lajous et al. 2014 France[7]	French women participating in the E3N EPIC study who were free of diabetes in 1990 to 2007: 2421 cases of diabetes were identified and 3750 total deaths occurred	2,421	could not determine	approx. 16%	all-cause mortality	54 (2.2)	16.7	Cox regression models adjusted for baseline covariates (marital status, education, menopause, hormone therapy use, physical activity, smoking, hypertension, cardiovascular disease, and cancer) to estimate hazard ratios (HRs) of mortality for overweight/obesity versus normal weight and for BMI categories	"We found the obesity 'paradox' among women with and without incident diabetes in the same population. Selection bias may be a simple explanation for this "paradox"	
Zhao et al. 2014 USA[8]	Louisiana State University Hospital-Based Longitudinal Study	19478 African American; 15354 Whites	Approximately 49 years in A-A; 51 years in Whites	Never smokers: approx. 55% in A-A; approx. 60% in Whites	all-cause mortality	4042 (11.6)	8.7	Two approaches: standard Cox model adjusted for baseline age, sex, smoking. Then a time-dependent model to account for multiple BMI inputs	"The current study indicated a U-shaped association of BMI (i.e. the obesity paradox) with all-cause mortality risk among African American and white patients with type 2 diabetes"	
Costanzo et al. 2015 UK[9]	Outpatient clinic service for diabetes in Kingston upon Hull (UK), which serves a population of approximately 600 000 persons, were enrolled in a registry between 1995 and 2005	10,568	63 yr	16%	all-cause mortality	3728 (35.3)	10.6	Multivariable Cox regression model for all-cause mortality, adjusting for age, sex, duration of diabetes, smoking history, systolic blood pressure, COPD, cancer, CKD, and previous CVD.	"Being overweight was associated with a lower mortality risk, but being obese was not"	
Present	Salford Integrated Records	10,464	66.0 yr	Ever	all-cause	1175 (11.4)	8.3	Matched analysis.	Demonstrated the obesity	

study	(SIR); New T2M from 1995 to 2012			smokers: 58%	mortality			Cox regression models stratified by smoking status, adjusted for age and sex	paradox in ever smoker for populations with and without T2D
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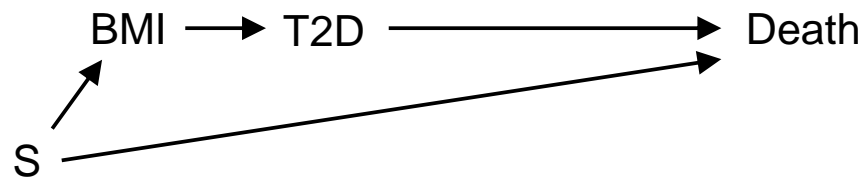
* Atherosclerosis Risk in Communities study, 1990-2006; Cardiovascular Health Study, 1992-2008; Coronary Artery Risk Development in Young Adults, 1987-2011; Framingham Offspring Study, 1979-2007; and Multi-Ethnic Study of Atherosclerosis, 2002-2011.

Figure S1 Simplified causal diagram or direct acyclic graphs (DAGs) for the three hypothesized associations between body mass index (BMI), determined near the time of diagnosis of type 2 diabetes (T2D) and mortality, to explain the obesity paradox. S indicates smoking. The box around T2D in hypothesis C indicates a collider bias.

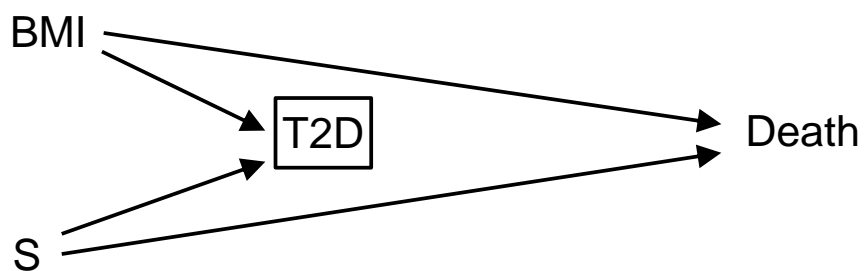
Hypothesis A (obesity paradox is a causal effect)



Hypothesis B (obesity paradox is explained by confounding)



Hypothesis C [obesity paradox is explained by selection (collider) bias]



Matching

We then matched the diabetes cohort 1:3 to the non-diabetes cohort on year of birth, sex and smoking status using the `dmatch` command in R (version 2.7.1, R Foundation, Vienna, Austria). This uses a nearest neighbour approach without replacement. Individuals in the non-diabetes cohort were allocated an index date equivalent to the matched date of the diagnosis of incident T2D. We thank Dr Artur Akbarov for supporting the development of this matching command in R.

```
setwd(dirname(parent.frame(2)$ofile))
rm(list = ls())
library(data.table)
d <- fread("matchingEB.csv")
d <- unique(d)
dmatch <- function(d, n = 3){
  # cases
  cases <- d[which(case == 1), ]
  # controls
  cnts <- d[which(case == 0), ]
  # for printing
  n.cases <- length(unique(cases$patid))
  n.cnts <- length(unique(cnts$patid))
  # combinations of matching values
  b <- expand.grid(sex = unique(d$sex),
                  smoking = unique(d$smoking),
                  yob = unique(d$yob))
  b$CombID <- 1:nrow(b)
  # add combinations IDs
  cases <- merge(cases, b, by = c("sex", "smoking", "yob"))
  cnts <- merge(cnts, b, by = c("sex", "smoking", "yob"))
  # sort cnts by CombID
  setkey(cnts, CombID)
  # randomise and group patid into n groups
  z <- cnts[, list(patid = patid[sample(1:.N, .N)],
                  GroupID = rep(1:.N, length.out = .N, each = n)), by = CombID]
  setkey(z, NULL)
  z <- merge(z, cnts, by = c("patid", "CombID"))
  # add group ID values to cases
  setkey(cases, CombID, patid)
  cases[, GroupID := 1:.N, by = CombID]
  # merge with
  setkey(cases, NULL)
  m <- merge(cases, z, by = c("CombID", "GroupID"),
            suffixes = c("_case", "_cnt"))

  # results details
  cat("Cases :", n.cases)
  cat("\nControls :", n.cnts)
  matched.cases <- length(unique(m$patid_case))
  cat("\nMatched : ", matched.cases, " (",
      round(100 * matched.cases / n.cases, 2), "%)", sep = "")
  cat("\nRatio (n): 1 to ", n)
```

```

cat("\nMatched numbers by n:")
qnt <- m[, list(N = .N), by = patid_case]
print(table(qnt$N))
cat("\nAre matched controls unique? :",
    ifelse(length(unique(m$patid_cnt) == nrow(m)), "Yes", "No"))
cat("\nTest conditions: ")
cols <- c("sex", "yob", "smoking")
for(cl in cols){
  cl1 <- paste0(cl, "_case")
  cl2 <- paste0(cl, "_cnt")
  r <- nrow(m[get(cl1) != get(cl2)])
  cat("\n\t", cl, " : unequal rows =", r)
}
cat("\nResult set size :", nrow(m), "rows")
m
}
m <- dmatch(d)
# write.csv(m, "matched.csv" )

```

Table S2 Hazard ratios (and 95% confidence intervals) of all-cause mortality across BMI categories in individuals with type 2 diabetes, SIR (1995 to 2012) stratified by ever/never smoking status, adjusting for additional covariates (other than age and sex)

	BMI kg/m ² category						Total
	18.5 to 22.49	22.5 to 24.9	25.0 to 29.9	30.0 to 34.9	35.0 to 39.9	40.0 to 59.9	
NEVER SMOKERS							
No. of cases	33	37	118	74	29	31	322
No. of individuals	161	304	1,163	1,084	563	411	3,686
Main model: adjusted for age and sex (95% CIs)*	1.21 (0.75-1.93)	1.00 (referent)	1.01 (0.70-1.47)	0.99 (0.67-1.47)	1.19 (0.73-1.95)	2.55 (1.56-4.19)	
Risk estimates: adjusted for age and sex, with additional adjustment for SBP, DBP, Chol, HbA1c†, metformin and insulin use (95% CIs)*	1.09 (0.68-1.77)	1.00 (referent)	1.03 (0.71-1.50)	1.00 (0.67-1.50)	1.25 (0.75-2.07)	2.82 (1.71-4.65)	
EVER SMOKERS							
No. of cases	48	74	220	141	68	41	592
No. of individuals	216	409	1,721	1,498	741	457	5,042
Main model: adjusted for age and sex (95% CIs)*	1.32 (0.92-1.90)	1.00 (referent)	0.74 (0.57-0.97)	0.77 (0.58-1.02)	1.14 (0.82-1.60)	1.87 (1.26-2.78)	
Risk estimates: adjusted for age and sex, with additional adjustment for SBP, DBP, Chol, HbA1c,† metformin and insulin use (95% CIs)*	1.19 (0.83-1.72)	1.00 (referent)	0.72 (0.56-0.95)	0.77 (0.58-1.03)	1.17 (0.83-1.64)	1.83 (1.22-2.74)	

CI: confidence intervals. SBP: systolic blood pressure; DBP: diastolic blood pressure; chol: serum total cholesterol.

*Note: all analyses are restricted to the T2D population of 8728 with all above measures recorded.

† As a 5 knot splines

Cox model assumptions: We tested the assumptions of proportionality using the Schoenfeld residuals global test option after `stcox` in STATA, for each of the main models: never smokers with and without diabetes and ever smokers with and without diabetes. Because of multiple testing, we took a cut-off p value of 0.01. If the global test returned $p > 0.01$, we assumed that the proportionality assumption had not been broken.

	No. of participants	Global test, p value
Never smokers, diabetes	4398	0.4634
Never smokers, never diabetes	13078	0.2202
Ever smokers, diabetes	6066	0.0194
Ever smokers, never diabetes	17840	0.1785

We additionally assessed for proportionality by visual examination of the K-M curves for all – cause mortality.

Table S3 Hazard ratios (and 95% confidence intervals) for all-cause mortality across BMI categories in individuals with type 2 diabetes and without (never) diabetes, with and without adjustment for smoking status, Salford Integrated Database (1995 to 2012)

	BMI kg/m ²						Total
	18.5 to 22.49	22.5 to 24.9	25.0 to 29.9	30.0 to 34.9	35.0 to 39.9	40.0 to 59.9	
Type 2 diabetes							
No. of deaths	106	151	442	266	126	84	1,175
No. of individuals	468	888	3,513	3,064	1,520	1,011	10,464
HRs: adjusted for age and sex (95% CIs)	1.27 (0.97-1.64)	1.00 (referent)	0.89 (0.73-1.09)	0.90 (0.73-1.11)	1.27 (0.98-1.63)	2.02 (1.51-2.70)	
HRs: adjusted for age, sex, smoking (95% CIs)	1.28 (1.00-1.64)	1.00 (referent)	0.83 (0.69-1.00)	0.83 (0.68-1.02)	1.19 (0.94-1.52)	1.86 (1.41-2.44)	
Never diabetes							
No. of deaths	651	584	868	367	98	45	2,613
No. of individuals	4,777	6,139	12,432	5,426	1,635	611	31,020
HRs: adjusted for age and sex (95% CIs)	1.32 (1.17-1.49)	1.00 (referent)	0.79 (0.71-0.89)	0.92 (0.80-1.06)	1.15 (0.91-1.44)	2.13 (1.55-2.93)	
HRs: adjusted for age, sex, smoking (95% CIs)	1.33 (1.86-1.49)	1.00 (referent)	0.79 (0.71-0.88)	0.95 (0.83-1.08)	1.10 (0.88-1.37)	1.95 (1.44-2.65)	

CI: confidence intervals

Table S4 Testing models with and without interaction terms

Model Letter	Model details	Log likelihood	Likelihood ratio test	P value	Comments
A	Main model: Age, sex, diabetes status, BMI category, smoking status	-33154.452			
B	Age, sex, diabetes status, BMI category, smoking status, [diabetes#BMI category interaction term]	-33152.636	A nested in B	0.6037	
C	Age, sex, diabetes status, BMI category, smoking status, [smoking#BMI category interaction term]	-33146.822	A nested in C	0.0093	We took this as our optimally fitting model
D	Age, sex, diabetes status, BMI category, smoking status, [smoking#BMI category interaction term], plus [diabetes#BMI category interaction term]	-33138.987	A nested in D C nested in D	0.0137 0.1538	

Table S5 Hazard ratios (and 95% confidence intervals) of all-cause mortality across BMI categories in individuals with type 2 diabetes and without (never) diabetes, SIR (1995 to 2012) stratified by ever/never smoking status, excluding the first two years follow-up

	BMI kg/m ² category						Total
	18.5 to 22.49	22.5 to 24.9	25.0 to 29.9	30.0 to 34.9	35.0 to 39.9	40.0 to 59.9	
NEVER SMOKERS							
Type 2 diabetes							
No. of cases	40	44	150	91	40	34	399
No. of individuals	192	352	1,320	1,153	608	435	4,060
Risk estimates: adjusted for age and sex (95% CIs)	1.23 (0.80-1.89)	1.00 (referent)	1.13 (0.81-1.59)	1.16 (0.80-1.66)	1.46 (0.94-2.25)	2.88 (1.81-4.57)	
Never diabetes							
No. of case	164	150	249	102	38	13	716
No. of individuals	1,643	2,437	4,882	2,170	692	257	12,081
Risk estimates: adjusted for age and sex (95% CIs)	1.24 (0.99-1.54)	1.00 (referent)	0.95 (0.78-1.17)	1.01 (0.78-1.30)	2.09 (1.46-3.00)	3.79 (2.14-6.72)	
EVER SMOKERS							
Type 2 diabetes							
No. of cases	56	89	262	157	75	45	684
No. of individuals	237	467	1,942	1,621	763	476	5,506
Risk estimates: adjusted for age and sex (95% CIs)	1.38 (0.99-1.93)	1.00 (referent)	0.78 (0.61-0.99)	0.78 (0.60-1.01)	1.19 (0.87-1.63)	1.72 (1.19-2.51)	
Never diabetes							
No. of cases	400	373	523	221	47	28	1,592
No. of individuals	2,743	3,204	6,483	2,750	797	279	16,256
Risk estimates: adjusted for age and sex (95% CIs)	1.31 (1.14-1.51)	1.00 (referent)	0.74 (0.65-0.85)	0.90 (0.76-1.06)	0.85 (0.62-1.15)	1.63 (1.11-2.04)	

CI: confidence intervals.

Table S6 Hazard ratios (and 95% confidence intervals) of all-cause mortality across BMI categories in individuals with type 2 diabetes and without (never) diabetes, SIR (1995 to 2012) stratified by ever/never smoking status, limiting modelling to age under 65 years

	BMI kg/m ² category						Total
	18.5 to 22.49	22.5 to 24.9	25.0 to 29.9	30.0 to 34.9	35.0 to 39.9	40.0 to 59.9	
NEVER SMOKERS							
Type 2 diabetes							
No. of cases	8	9	42	28	18	22	127
No. of individuals	92	191	839	863	521	404	2910
Risk estimates: adjusted for age and sex (95% CIs)	1.89 (0.73-4.09)	1.00 (referent)	1.13 (0.55-2.32)	1.11 (0.52-2.37)	1.53 (0.68-3.47)	3.41 (1.54-7.55)	
Never diabetes							
No. of case	30	37	64	23	13	7	174
No. of individuals	1,013	1,671	3,545	1,642	578	243	8,692
Risk estimates: adjusted for age and sex (95% CIs)	1.36 (0.83-2.22)	1.00 (referent)	0.87 (0.57-1.33)	0.90 (0.53-1.52)	1.38 (0.71-2.66)	3.71 (1.62-8.49)	
EVER SMOKERS							
Type 2 diabetes							
No. of cases	24	39	102	79	38	34	316
No. of individuals	156	283	1298	1280	640	461	4118
Risk estimates: adjusted for age and sex (95% CIs)	1.18 (0.71-1.97)	1.00 (referent)	0.57 (0.39-0.83)	0.59 (0.40-0.87)	0.82 (0.52-1.30)	1.26 (0.78-2.01)	
Never diabetes							
No. of cases	162	159	216	97	23	16	673
No. of individuals	1,996	2,325	4,845	2,123	669	256	12,216
Risk estimates: adjusted for age and sex (95% CIs)	1.25 (1.00-1.56)	1.00 (referent)	0.65 (0.53-0.80)	0.75 (0.58-0.96)	0.65 (0.42-1.01)	1.54 (0.92-2.58)	

CI: confidence intervals.

Table S7 Hazard ratios (and 95% confidence intervals) of all-cause mortality across BMI categories in individuals with type 2 diabetes and without (never) diabetes, SIR (1995 to 2012) stratified by ever/never smoking status, limiting modelling to age \geq 65 years

	BMI kg/m ² category						Total
	18.5 to 22.49	22.5 to 24.9	25.0 to 29.9	30.0 to 34.9	35.0 to 39.9	40.0 to 59.9	
NEVER SMOKERS							
Type 2 diabetes							
No. of cases	34	38	112	38	25	15	292
No. of individuals	113	183	569	406	146	71	1,488
Risk estimates: adjusted for age and sex (95% CIs)	1.09 (0.68-1.74)	1.00 (referent)	1.09 (0.75-1.57)	1.57 (0.78-1.72)	1.42 (0.85-2.37)	2.41 (1.31-4.43)	
Never diabetes							
No. of case	153	132	206	90	31	6	618
No. of individuals	762	960	1,742	724	173	47	4,408
Risk estimates: adjusted for age and sex (95% CIs)	1.23 (0.97-1.55)	1.00 (referent)	0.94 (0.75-1.17)	1.05 (0.80-1.38)	2.41 (1.59-3.64)	2.76 (1.21-6.28)	
EVER SMOKERS							
Type 2 diabetes							
No. of cases	40	65	186	91	45	13	440
No. of individuals	107	231	807	515	213	75	1,948
Risk estimates: adjusted for age and sex (95% CIs)	1.43 (0.96-2.12)	1.00 (referent)	0.84 (0.63-1.12)	0.80 (0.58-1.10)	1.27 (0.87-1.87)	1.48 (0.81-2.70)	
Never diabetes							
No. of cases	306	256	382	157	31	16	1,148
No. of individuals	1,006	1,183	2,300	935	215	65	5,704
Risk estimates: adjusted for age and sex (95% CIs)	1.38 (1.16-1.64)	1.00 (referent)	0.82 (0.69-0.96)	1.03 (0.84-1.26)	0.98 (0.66-1.45)	1.79 (1.08-2.97)	

CI: confidence intervals.

Table S8 Hazard ratios (and 95% confidence intervals) of all-cause mortality across BMI categories in individuals with type 2 diabetes and without (never) diabetes, SIR (1995 to 2012) stratified by ever/never smoking status, limiting modelling to follow-up \geq 5 years

	BMI kg/m ² category						Total
	18.5 to 22.49	22.5 to 24.9	25.0 to 29.9	30.0 to 34.9	35.0 to 39.9	40.0 to 59.9	
NEVER SMOKERS							
Type 2 diabetes							
No. of cases	37	40	131	78	36	30	352
No. of individuals	166	297	1,063	908	483	322	3,239
Risk estimates: adjusted for age and sex (95% CIs)	1.23 (0.78-1.92)	1.00 (referent)	1.10 (0.77-1.57)	1.11 (0.76-1.64)	1.50 (0.95-2.37)	3.02 (1.85-4.94)	
Never diabetes							
No. of case	142	139	221	90	36	11	639
No. of individuals	1,343	1,962	3,948	1,712	536	191	9,692
Risk estimates: adjusted for age and sex (95% CIs)	1.18 (0.93-1.50)	1.00 (referent)	0.92 (0.74-1.14)	0.99 (0.76-1.30)	2.06 (1.40-3.05)	3.96 (2.13-7.37)	
EVER SMOKERS							
Type 2 diabetes							
No. of cases	48	67	226	126	57	39	563
No. of individuals	195	367	1,586	1,251	551	324	4,274
Risk estimates: adjusted for age and sex (95% CIs)	1.57 (1.09-2.28)	1.00 (referent)	0.88 (0.67-1.16)	0.83 (0.61-1.12)	1.26 (0.88-1.81)	2.05 (1.36-3.08)	
Never diabetes							
No. of cases	347	322	454	180	38	19	1,360
No. of individuals	2,229	2,548	5,089	2,108	586	199	12,759
Risk estimates: adjusted for age and sex (95% CIs)	1.29 (1.10-1.51)	1.00 (referent)	0.74 (0.64-0.86)	0.87 (0.72-1.04)	0.77 (0.54-1.10)	1.37 (0.86-2.18)	

CI: confidence intervals.

Table S9 Hazard ratios (and 95% confidence intervals) of all-cause mortality across BMI categories in individuals with type 2 diabetes and without (never) diabetes, SIR (1995 to 2012) stratified by ever/never smoking status, excluding individuals with CVD or cancer

	BMI kg/m ² category						Total
	18.5 to 22.49	22.5 to 24.9	25.0 to 29.9	30.0 to 34.9	35.0 to 39.9	40.0 to 59.9	
NEVER SMOKERS							
Type 2 diabetes							
No. of cases	27	21	66	38	24	20	196
No. of individuals	150	253	974	898	518	358	3,151
Risk estimates: adjusted for age and sex (95% CIs)	1.19 (0.67-2.11)	1.00 (referent)	0.90 (0.55-1.48)	0.84 (0.49-1.44)	1.34 (0.74-2.44)	2.86 (1.52-5.39)	
Never diabetes							
No. of case	101	70	120	51	19	7	369
No. of individuals	1,397	2,088	4,223	1,873	612	245	10,438
Risk estimates: adjusted for age and sex (95% CIs)	1.60 (1.17-2.12)	1.00 (referent)	1.04 (0.77-1.41)	1.20 (0.83-1.73)	2.47 (1.46-4.21)	4.65 (2.11-10.25)	
EVER SMOKERS							
Type 2 diabetes							
No. of cases	31	49	103	60	26	21	290
No. of individuals	183	347	1,320	1,131	556	379	3,916
Risk estimates: adjusted for age and sex (95% CIs)	1.45 (0.92-2.28)	1.00 (referent)	0.63 (0.45-0.89)	0.60 (0.41-0.88)	0.76 (0.47-1.23)	1.61 (0.94-2.77)	
Never diabetes							
No. of cases	237	188	229	89	24	17	784
No. of individuals	2,243	2,582	5,245	2,250	659	255	13,234
Risk estimates: adjusted for age and sex (95% CIs)	1.41 (1.15-1.71)	1.00 (referent)	0.67 (0.55-0.81)	0.69 (0.53-0.89)	0.83 (0.54-1.29)	1.81 (1.10-2.98)	

CI: confidence intervals.

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