

Association of glucagon-like peptide-1 receptor agonists with suicidal ideation and self-injury in individuals with diabetes and obesity: a propensity-weighted, population-based cohort study.

Electronic Supplementary Material

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ESM Table 1. International Classification of Diseases, Ninth and Tenth Revision (ICD-9 and ICD-10) codes for comorbidities, exclusion criteria, lifestyle variables and outcomes.

Heart Failure	ICD9 428.xx, 398.91, 402.01, 402.11, 402.91, 404.01, 404.11, 404.03, 404.13, 404.91, 404.93, 425.4x ICD10 I50.x, I11.0, I13.0, I13.2, I42.0
Dementia	ICD9 290.xx, 294.xx, 330.xx, 331.xx ICD10 F00.x- F03.x, G30.x, G31.x
Hypertension	ICD9 401.xx-405.xx, 437.2 ICD10 I10.x-I13.x, I15.x, I67.4
Liver disease	ICD9 070.0, 070.2x, 070.4x, 070.6x, 070.71, 570.xx- 573.xx, 782.4x, 789.1x, 789.5x, 790.4x, 790.5x, 794.8x ICD10 B19.11, B15.0x, B16.0, B16.2, B19.0, I85.x, K70.x-K77.x, R17.x, R18.x, R74.x, R94.5, Z94.4
Renal disease	ICD9 403.x, 404.x, 580.x-589.x, 590.1, 753.x, 792.5, V42.0, V45.1, V56.x ICD10 I12.x, I13.x, N00.x-N05.x, N07.x, N11.x, N14.x, N17.x-N19.x, Q61.x, Z49.x, Z94.0, Z91.15, Z99.2
Coronary heart disease	ICD9 410.xx-414.xx ICD10 I20.x-I25.x
Chronic Obstructive Pulmonary Disease	ICD9 491.xx, 492.xx, 496.xx, 493.20, 493.21, 493.22 ICD10 diagnosis J41.x- J44.x
Malignancies	ICD9 140.xx-208.xx ICD10 C00.x-C96.x
Obesity	ICD9 278.8, 278.00, 278.01, 278.03, E66.8, E66.9, V85.3, V85.4 ICD10 Z68.3, Z68.4
Suicidal ideation or self- injury	ICD9 E95.x, V62.84, 300.9 ICD10 T36.92X, T37.92X, T39.92X, T41.42X, T42.72X, T43.92X, T45.92X, T47.92X, T49.92X, T51.92X, T52.92X, T53.92X, T54.92X, T56.92X, T57.92X, T59.92X, T60.92X, T61.92X, T62.92X, T63.92X, T65.92X, X71.x-X83.x, T58.02X, T58.03X,

	T58.04X , T58.05X , T58.06X , T58.07X , T58.08X, T58.09X , T58.10X , T58.11X , T58.12X, T61.02X , T61.03X , T61.04X, T61.05X, T61.06X , T61.07X , T61.08X), T61.09X , T61.10X , T61.11X , T61.12X, T64.02X , T64.03X , T64.04X , T64.05X , T64.06X , T64.07X , T64.08X, T64.09X , T64.10X , T64.11X , T64.12X, R45.851 T14.91X, Z91.5,T14.91, T36–T65 with the 6th character of 2 (except for T36.9, T37.9, T39.9, T41.4, T42.7, T43.9, T45.9, T47.9, T49.9, T51.9, T52.9, T53.9, T54.9, T56.9, T57.9, T58.0, T58.1, T58.9, T59.9, T60.9, T61.0, T61.1, T61.9, T62.9, T63.9, T64.0, T64.8, and T65.9, which are included if the 5th character is 2)
Anxiety	ICD9 300.x, 308.x ICD10 F40.x-F48.x
Depression	ICD9 296.2x, 296.3x, 298.0, 300.4x, 301.12, 311.xx ICD10 F32.x-F33.x; F34.1
Alcohol use	ICD9 291.xx, 303.xx, 305.0x, 571.0x, 571.1x, 571.2x, 571.3x, 357.5x, 425.5x, E860.0x ICD10 F10.x; K70.x; G62.1; I42.6
Tobacco use	ICD9 305.1,989.84,V15.82 ICD10 F17.x,T65.2
Drug use	ICD9 292.xx, 304.xx, 305.2x-305.9x ICD10 F11.x-F16.x; F18.x-F19.x
Personality disorders	ICD9 301.xx ICD10 F60.x
Sleep disorders	ICD9 307.4x, 327.xx, 780.5x, 347.xx ICD10 G47.x; F51.x; Z72.82x
Psychotic disorders	ICD9 290.x-299.x ICD10 F20.x-F29.x
Other psychiatric disorders	<u>Bipolar disorders</u> ICD9 296.0x, 296.1x, 296.4x, 296.5x, 296.6x, 296.7x, 296.8x, 296.99 ICD10 F31.x <u>Disturbance of conduct</u> ICD9

309.x; 312.x

ICD10

F91.x

Hyperkinetic syndrome of childhood

314.xx

ICD10

F90.x

ESM Table 2. Anatomical Therapeutic Chemical classification of study drugs

Sodium-glucose cotransporter 2 inhibitors (SGLT-2i)	A10BK. Combination with metformin: A10BD15, A10BD16, A10BD20, A10BD23
Glucagon-like peptide 1 receptor (GLP-1RA) agonists	A10BJ, A10AE54, A10AE56, A10BX04, A10BX07, A10BX10, A10BX13, A10BX14
Metformin monotherapy	A10BA02

ESM Table 3. Code employed for analysis.

```
*****

*PRINCIPAL ANALYSIS - PER PROTOCOL*

*****

use "Q:\ANTIDIABETICOS_suicide\3-
ANALISIS\FINAL_CONJUNTO\cohorte_final_censura_sinunderlyover.dta",clear

*COVARIATES SETUP

global cov_prop_scores sex i.income i.cat_age c_heart_f c_dementia c_hyperte c_liv ///
c_kidney c_ethanol c_depression c_chd c_codp c_smoke c_sleepdisord c_anxiety c_otherabuse
c_persondis c_otherpsych c_psychotic c_cancer c_suicide i.imc_bis

*GENERATE IPTW

logit clas_bi $cov_prop_scores
predict ps_clas_bi
propwt clas_bi ps_clas_bi, ipt smr

*CALCULATE P FOR INTERACTION BETWEEN GROUPING VARIABLE AND SOME COVARIATES

logit o_suicide clas_bi sex b(first).clas_bi#b(first).sex
logit o_suicide c.cat_age##i.clas_bi
logit o_suicide c.income##i.clas_bi
logit o_suicide c.imc_bis##i.clas_bi
logit o_suicide clas_bi c_depression b(first).clas_bi#b(first).c_depression
logit o_suicide clas_bi c_sleepdisord b(first).clas_bi#b(first).c_sleepdisord
logit o_suicide clas_bi c_anxiety b(first).clas_bi#b(first).c_anxiety

*COX MODEL

*Define censoring date and fix outcome variable

replace o_suicide=0 if censor_date<suicide_date & suicide_date!=.
replace censor_date=suicide_date if suicide_date!=. & censor_date>suicide_date & o_suicide==1

stset censor_date [pweight=ipt_wt], failure(o_suicide) origin(index_date) id(sip) scale(365.25)

stdes
```

```
stcox clas_bi $cov_prop_scores
```

```
*****
```

```
*WITHOUT UNKNOWN BMI*
```

```
*****
```

```
use "Q:\ANTIDIABETICOS_suicide\3-  
ANALISIS\FINAL_CONJUNTO\cohortes_final_censura_sinunderyover.dta",clear
```

```
*DROP THE PATIENTS WITH UNKNOWN BMI
```

```
drop if imc_bis==9
```

```
*COVARIATES SETUP
```

```
global cov_prop_scores sex i.income i.cat_age c_heart_f c_dementia c_hyperte c_liv ///  
c_kidney c_ethanol c_depression c_chd c_codp c_smoke c_sleepdisord c_anxiety c_otherabuse  
c_persondis c_otherpsych c_psychotic c_cancer c_suicide i.imc_bis
```

```
*GENERATE IPTW
```

```
logit clas_bi $cov_prop_scores  
predict ps_clas_bi  
propwt clas_bi ps_clas_bi, ipt smr
```

```
*COX MODEL
```

```
*Define censoring date and fix outcome variable
```

```
replace o_suicide=0 if censor_date<suicide_date & suicide_date!=.  
replace censor_date=suicide_date if suicide_date!=. & censor_date>suicide_date & o_suicide==1
```

```
stset censor_date [pweight=ipt_wt], failure(o_suicide) origin(index_date) id(sip) scale(365.25)
```

```
stdes
```

```
stcox clas_bi $cov_prop_scores
```

```
*****
```

```
*STRATIFIED ANALYSIS*
```

```
*****
```

*SEX

stcox clas_bi if sex==1

stcox clas_bi if sex==2

*OBESITY

stcox clas_bi if imc_bis==3

stcox clas_bi if imc_bis==4

stcox clas_bi if imc_bis==5

*DEPRESSION

stcox clas_bi if c_depression==0

stcox clas_bi if c_depression==1

*SLEEP DIS

stcox clas_bi if c_sleepdisord==0

stcox clas_bi if c_sleepdisord==1

*ANXIETY

stcox clas_bi if c_anxiety==0

stcox clas_bi if c_anxiety==1

*GLOBAL

stcox clas_bi

INTENTION TO TREAT

use "Q:\ANTIDIABETICOS_suicide\3-
ANALISIS\FINAL_CONJUNTO\cohorte_final_censura_sinunderlyover.dta",clear

*COVARIATE SETUP

global cov_prop_scores sex i.income i.cat_age c_heart_f c_dementia c_hyperte c_liv ///

```
c_kidney c_ethanol c_depression c_chd c_codp c_smoke c_sleepdisord c_anxiety c_otherabuse  
c_persondis c_otherpsych c_psychotic c_cancer c_suicide i.imc_bis
```

```
*GENERATE IPTW
```

```
logit clas_bi $cov_prop_scores
```

```
predict ps_clas_bi
```

```
propwt clas_bi ps_clas_bi, ipt smr
```

```
*COX MODEL
```

```
*Define censoring date and fix outcome variable
```

```
drop censor_date
```

```
gen censor_date=mdy(12,31,2021)
```

```
replace censor_date=def_date if def_date<=censor_date & def_date>index_date
```

```
replace o_suicide=0 if censor_date<suicide_date & suicide_date!=.
```

```
replace censor_date=suicide_date if suicide_date!=. & censor_date>suicide_date & o_suicide==1
```

```
stset censor_date [pweight=ipt_wt], failure(o_suicide) origin(index_date) id(sip) scale(365.25)
```

```
stdes
```

```
stcox clas_bi $cov_prop_scores
```

```
*****
```

```
*MULTIPLE IMPUTATION PER PROTOCOL*
```

```
*****
```

```
use "Q:\ANTIDIABETICOS_suicide\3-  
ANALISIS\FINAL_CONJUNTO\cohorte_final_censura_sinunderyover.dta",clear
```

```
*RECODE TO MISSING
```

```
recode imc_bis (9=.)
```

```
*IMPUTATION OF BMI BY ICE PROTOCOL
```

```
ice imc_bis clas_bi sex i.income i.cat_edad c_heart_f c_dementia c_hyperte c_liv ///
```

```
c_kidney c_ethanol c_depression c_chd c_codp c_smoke c_sleepdisord c_anxiety c_otherabuse  
c_persondis c_otherpsych c_psychotic c_cancer c_suicidio o_suicidio_periodo,
```

```

cmd(imc_bis:ologit)seed(1001) m(5) saving("Q:\ANTIDIABETICOS_SUICIDIO\3-
ANALISIS\multiple.dta",replace)

use "Q:\ANTIDIABETICOS_SUICIDIO\3-ANALISIS\multiple.dta",replace

mi import ice

*COVARIATE SET UP

global cov_prop_scores sex i.income i.cat_age c_heart_f c_dementia c_hyperte c_liv ///
c_kidney c_ethanol c_depression c_chd c_codp c_smoke c_sleepdisord c_anxiety c_otherabuse
c_persondis c_otherpsych c_psychotic c_cancer c_suicide i.imc_bis

*GENERATE IPTW

mi estimate, saving("Q:\ANTIDIABETICOS_SUICIDIO\3-ANALISIS\imput_imc_ice.ster",replace): logit
clas_bi $cov_prop_scores

mi predict ps_clas_bi using "Q:\ANTIDIABETICOS_SUICIDIO\3-ANALISIS\imput_imc_ice.ster"

quietly mi xeq: generate ps_clas_bi_t = invlogit(ps_clas_bi)

gen iptw=1/ps_clas_bi_t if clas_bi==1

replace iptw = 1 / (1 - ps_clas_bi_t) if clas_bi==0

sort sip iptw

by sip: replace iptw=iptw[1] if iptw==.

*COX MODEL

*Define censoring date and fix outcome variable

replace o_suicide=0 if censor_date<suicide_date & suicide_date!=.

replace censor_date=suicide_date if suicide_date!=. & censor_date>suicide_date & o_suicide==1

mi stset censor_date [pweight=iptw] , failure(o_suicide) origin(index_date) id(sip) scale(365.25)

mi estimate,hr : stcox clas_bi $cov_prop_scores

```

ESM Fig. 1. Forest plot for stratified analyses per sex, obesity, depression, sleep disorders and anxiety, plotted in logarithmic scale. P values for interaction, number of events and hazard ratios for each group are shown.

