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1	TEN-YEAR INCIDENCE OF HYPERTENSION IN A SWISS POPULATION-					
2	BASED SAMPLE					
3	Incidence of hypertension in Switzerland					
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Abstract 27

28 Few studies assessed incidence and determinants of hypertension. We assessed the incidence and 29 determinants of hypertension in a cohort of healthy adults aged 35 to 75 years living in Lausanne, 30 Switzerland. Baseline data was collected from 2003 to 2006. Follow-ups were conducted in 2009-2012 31 and 2014-2017. Incident hypertension, defined as a systolic BP \geq 140 mm Hg or a diastolic BP \geq 90 mm 32 Hg or anti-hypertensive medication, was assessed at 1) second follow-up only; 2) first and/or second 33 follow-up. After 10.9 years, incident hypertension was 26.8% (analysis 1, N=3299) and 30.3% (analysis 34 2, N=3728). After multivariate adjustment, the variables associated with increased hypertension 35 incidence were male gender [incident-rate ratio (IRR) and (95% confidence interval)]: 1.20 (1.07-1.35) 36 and 1.24 (1.13-1.37) for analyses 1 and 2, respectively; increasing age (p for trend < 0.001) and body 37 mass index (p for trend <0.001) and history of cardiovascular disease (CVD). Being physically active was 38 negatively associated with incident hypertension: 0.88 (0.78-0.98) and 0.92 (0.83-1.01) for analyses 1 39 and 2, respectively. Except for male gender, these associations remained after adjusting for baseline 40 BP levels, with incident rate ratios for physical activity of 0.86 (0.77-0.96) and 0.91 (0.83-0.99) for 41 analyses 1 and 2, respectively. No association was found for education, alcohol consumption or smoking status. We conclude that over 10.9 years, between 1/4 and 1/3 of the Swiss population aged 42 43 35 to 75 developed hypertension. Male gender, history of CVD, increasing age and higher BMI increase 44 the risk of hypertension, while being physically active reduces the risk.

- 45 Abstract word count: 250

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Keywords: prospective study; hypertension; incidence; Switzerland.

47 Introduction

Hypertension is a major public health challenge given its involvement in cardiovascular diseases (CVD). Hypertension is one of the main causes of disability-adjusted life years (DALY) worldwide ¹ and ranks second in Switzerland ². Over 1 billion people have hypertension worldwide, and the prevalence is increasing ³. Hypertension is a major risk factor for cardiovascular diseases, renal failure, and retinal disorders. Several different guidelines have been published regarding the prevention and management of hypertension ^{4, 5}.

The strongest determinants of hypertension incidence are aging and obesity. Nevertheless, the importance of individual factors such as smoking ⁶, alcohol ⁷, physical activity ⁸ and socioeconomic status such as education ⁹ is less well characterized. Such information is important both from a public health and individual perspective. Furthermore, although many studies have assessed the incidence of hypertension in several countries, none has been performed in Switzerland.

59 The aim of this study was thus to assess the incidence of hypertension and to identify the 60 socio-demographic and clinically-actionable risk factors of hypertension, in a sample of healthy adults 61 aged 35 to 75 years living in Lausanne (Switzerland).

62 **Participants and methods**

63 Recruitment

The CoLaus Study (www.colaus-psycolaus.ch) is a prospective study aimed to assess the prevalence and determinants of cardiovascular risk factors in participants aged 35 to 75 years living in the city of Lausanne (Switzerland). The sampling procedure of the CoLaus study can be found elsewhere ¹⁰. Participants were included if they provided (a) written informed consent; (b) willingness to take part in the examination and to provide blood samples.

69 Recruitment began in June 2003 and ended in May 2006, enrolling 6733 participants who 70 underwent an interview, a physical exam, and a blood analysis. The first and second follow-ups were 71 performed between April 2009 and September 2012 and between May 2014 and April 2017,

respectively, corresponding to an average of 5.6 and 10.9 years after the collection of baseline data,

respectively. Data collected in the follow-ups was similar to the baseline examination.

74 Blood pressure measurement

At baseline and follow-ups, blood pressure (BP) and heart rate were measured thrice on the left arm after a 10 minutes rest in the seated position. A clinically validated automated oscillometric device (Omron® HEM-907, Matsusaka, Japan) was used with a standard cuff. In the case of an arm circumference ≥33 cm, a larger cuff was used. The average of the last two BP readings was used. Hypertension was defined as a systolic BP (SBP) ≥140 mm Hg or a diastolic BP (DBP) ≥90 mm Hg or presence of anti-hypertensive medication. Incident hypertension was defined as presence of hypertension at first or second follow-up among participants devoid of hypertension at baseline.

82 Other variables

83 All participants were examined in the morning after a fast of at least 8 hours. Personal and 84 family history of CVD, CVRFs, and cardiovascular treatment were assessed by questionnaire. Smoking 85 was categorized into never, former (irrespective of the time since quitting) and current. Education was 86 categorized according to the highest educational level completed into low (primary), middle 87 (apprenticeship), upper middle (high school), and high (university). Self-reported alcohol consumption 88 during the previous week was based on the number of units (i.e. a glass of wine, a can of beer or a shot 89 of liquor) and categorized as none, 1-13, 14-34 and 35+/week. Physical activity was defined if the 90 participant exercised at least twice per week for at least 20 minutes per session. Participants also 91 indicated all medicines they were taking, prescribed or obtained over the counter.

Body weight and height were measured using Seca® equipment (Hamburg, Germany) to the
nearest 100 g and 5 mm, respectively, while participants stood shoeless in light indoor attire.

94 Inclusion and exclusion criteria

95 Participants were excluded if they: 1) presented with hypertension at baseline; 2) did not
96 participate in the follow-up; and 3) had missing covariates.

97 Ethical considerations

98 The institutional Ethics Committee of the University of Lausanne, which afterwards became 99 the Ethics Commission of Canton Vaud (www.cer-vd.ch) approved the baseline CoLaus study and 100 subsequent follow-ups. The study was performed in agreement with the Helsinki declaration and its 101 former amendments. Informed consent was obtained from all participants.

102 Statistical analysis

Statistical analyses were conducted using Stata version 14.2 (Stata Corp, College Station, Texas,
USA).

105 Two analyses were performed focusing on incident hypertension between baseline and 1) 106 second follow-up only, or 2) first and/or second follow-up. In each analysis, the following clinical and 107 lifestyle determinants of incident hypertension were analyzed: gender, age, BMI, smoking, alcohol 108 consumption, education, and physical activity.

109 Participants characteristics were expressed as number (percentage) for categorical variables 110 or as average ± standard deviation for continuous variables. Between-group comparisons were 111 performed using chi-square or Fisher's exact test for categorical variables and student's t-test for 112 continuous variables. As the incidence of hypertension was high (>20%), Poisson regression with 113 robust confidence intervals was preferred to logistic regression for multivariable analysis, as the results from logistic regression might be overestimated ¹¹. Results of the multivariable analysis were 114 expressed as incidence rate ratio and (95% confidence interval). As some studies did ^{9, 12} and others 115 did not ^{13, 14} adjust for baseline blood pressure, two multivariable models were used: with and without 116 117 adjusting for baseline blood pressure.

A sensitivity analysis was performed to take into account the fact that excluded and included participants differed significantly regarding several clinical and demographic characteristics. First, and for each analysis as defined previously, the probability of nonparticipation was computed using a lostic model with gender, age, BMI, smoking, alcohol consumption, education, physical activity, personal and

122 family history of CVD as the independent variables. The inverse of the probability of nonparticipation

123 was used for weighting ¹⁵. Statistical significance was considered for p<0.05 (two-sided test).

124 **Results**

125 Characteristics of the sample

The selection procedures for the two analyses are presented in **Figure 1**. Respectively 3299 (49.0%) and 3728 (55.4%) participants were included in the first and in the second analysis. The characteristics of the included and excluded participants are provided in **supplemental tables 1 and 2** for the first and second analysis, respectively. Overall, excluded participants were older, more frequently men, with lower education, higher alcohol consumption, higher BMI and no physical activity. Excluded participants also had a higher prevalence of personal and family history of CVD.

132 Incidence and determinants of incident hypertension

After an average follow-up of 10.9 years, 883 (26.8%) and 1128 (30.3%) participants developed hypertension in the first and second analysis, respectively. The analysis of factors associated with incident hypertension is summarized in **tables 1** (bivariate), **2** (multivariable, not adjusted for baseline blood pressure) and **3** (multivariable, adjusted for baseline blood pressure).

As alcohol consumption was not associated with incident hypertension in the bivariate analysis, it was not introduced in the multivariable model. Overall, male gender, increasing age, higher BMI and personal or family history of CVD were positively associated, while being physically active was inversely associated with incident hypertension (**table 2**), and most of the associations remained after adjusting for baseline blood pressure (**table 3**).

The results of the sensitivity analyses taking into account non-participation in the follow-up are summarized in **supplemental tables 3 and 4**. Again, male gender, increasing age, higher BMI and personal or family history of CVD were positively associated, while being physically active was inversely associated with incident hypertension (**supplemental table 3**). The associations for age, BMI, personal 146 history of CVD and physical activity remained after adjusting for baseline blood pressure147 (supplemental table 4).

148 **Discussion**

To our knowledge, this is the first study to assess incidence of hypertension in a Swiss population. Our results indicate that, over a period of 10.9 years, between one fourth and one third of the population aged 35 to 75 develops hypertension. Our results also indicate that male gender, increasing age, higher BMI and history of CVD (personal or familial) increase the risk of developing hypertension, while being physically active reduces the risk.

154 *Prevalence of hypertension*

One-third (35.4%) of participants was excluded at baseline due to hypertension. This prevalence is almost identical to the one found in the Bus Santé study of Geneva (34.4%) ¹⁶ and in another multi-cantonal cohort study (34.9%) ¹⁷. Overall, the prevalence of hypertension in our sample agrees with other existing data for Switzerland.

159 Incidence of hypertension

160 Between one fourth (26.8%) and one third (30.3%) of the sample developed hypertension after 10.9 years of follow-up. Those values are comparable or lower to those reported in studies conducted 161 for a shorter period in France (19.6% after 3 years) ¹⁴, Portugal (23.2% after 3.8 years) ⁹, and China 162 (38.9% after 3.5 years) ¹⁸. Possible explanations are the rather low prevalence of obesity in the Swiss 163 population ¹⁹ and a differing dietary intake ²⁰ relative to other European countries, which might reduce 164 the incidence of hypertension. Another explanation is the different economic status of the country, as 165 166 it has been shown that developing countries are more affected by emerging risk factors than 167 developed ones due to societal changes in diet and physical activity²¹. Overall, our results indicate that 168 the incidence of hypertension in the Swiss population appears to be lower than in other countries.

169 Determinants of incident hypertension

170 Male gender was positively associated with incident hypertension, a finding also reported 171 elsewhere ^{5, 13}. Possible explanations include the protective effect of hormonal status among 172 premenopausal women ²², a less healthy dietary intake and a lower health consciousness among men 173 ²³.

174 Increasing age was positively associated with incidence of hypertension, a finding in agreement 175 with the literature ⁵. Possible explanations are lower physical activity levels and increasing BMI, 176 although in this study the association between age and hypertension remained after adjusting for BMI 177 categories and physical activity status. Other explanations include differences in dietary intake, or an 178 age-dependent hardening of the vascular system ²⁴ or worsening of kidney function ²⁵. Overall, our 179 results stress the need for adequate prevention of hypertension among elderly subjects.

Increasing BMI was associated with increased incidence of hypertension. Indeed, several
 studies have shown that weight loss, either via diet or bariatric surgery, leads to a decrease in BP levels
 ⁵. Hence, our results indicate that overweight or obese subjects should be motivated to lose weight, as
 it will reduce the risk of developing hypertension.

184 Personal and familial history of CVD were positively associated with incident hypertension, 185 independently of other cardiovascular risk factors such as smoking, obesity or physical activity. These 186 findings are partly in agreement with the literature, where subjects with a family history of 187 hypertension also had a higher risk of developing hypertension ^{26, 27}. Possible explanations include other cardiovascular risk factors not accounted for such as dyslipidemia and diabetes ⁶. Alternatively, 188 genetic markers associated with both conditions (i.e. CVD and hypertension) might also play a role ²⁸. 189 190 Our results thus suggest that subjects with personal or family history of CVD are at a higher risk of 191 developing hypertension.

Being physically active was inversely associated with incident hypertension, a finding in agreement with the literature ⁸. Several mechanisms have been put forward to explain this effect, such as a decrease in heart rate and in systemic vascular resistance. Our results thus stress the need ofregular physical exercise to prevent incidence of hypertension.

Former smoking was associated with increased incidence of hypertension on bivariate analysis, but this association disappeared after multivariate adjustment, namely by the inclusion of BMI. This suggests that the effect of quitting smoking on incidence of hypertension is due to the frequent increase in weight after quitting smoking. Hence, subjects who quit smoking without increasing BMI have a triple benefit: no increase of body weight, no increase of BP, and no deleterious effects of smoking.

202 Contrary to other studies ⁷, no association was found between alcohol consumption and 203 incidence of hypertension. A likely explanation is the small proportion of excessive alcohol consumers 204 in the sample, making the analyses underpowered to detect such associations. Also contrary to other 205 studies ⁹, no association was found between educational level and incidence of hypertension, 206 suggesting that, at least in this setting, the impact of education is modest.

207 Implications for clinical practice and public health

208 From a clinical perspective, prevention of hypertension should focus on men, the elderly and 209 overweight/obese subjects. Subjects with personal of family history of CVD should also be 210 recommended to regularly monitor their blood pressure levels. Measures aimed at losing weight, 211 quitting smoking and increasing physical exercise, together with an improvement in dietary intake by 212 reducing alcohol consumption ⁵ should be performed. From a public health perspective, general 213 measures to promote healthy eating, a physically active friendly environment, and health education 214 should be strengthened. Still, as our findings are based on observational and not on interventional 215 data, our conclusions should be interpreted with caution.

216 Strengths and limitations

To our knowledge, this is the first ever study assessing the incidence and socio-demographic determinants of hypertension in Switzerland. It is also based on a relatively long follow-up time (10.9 years on average) while most studies relied on a 5-year follow-up ^{9, 14}.

220 This study has several limitations: firstly, it was based on an urban, French-speaking sample of 221 Switzerland. Hence, it might not reflect the status of the other linguistic parts of the country. Still, both 222 the prevalence rates and the determinants identified were in agreement with the literature, and 223 similar findings might be expected in the other parts of Switzerland. Still, it would be interesting that 224 such a study be conducted in the German or Italian speaking parts of Switzerland. Secondly, as the 225 original sampling database was no longer available, we cannot compare the characteristics of 226 responders and non-responders. Even though, only gender and age were available in the population 227 register, so comparisons regarding socio-demographic determinants would have been limited. Thirdly, 228 participation rate was low (6733 participants out of 19,830 invited, 34%) but in line with other 229 European surveys (participation rates ranging between 16% and 57% for men and 31% and 74% in 230 women)²⁹. Participation rate was lower than for a comparable study conducted in the canton of Geneva (55% to 65%) ¹⁶ but higher than or comparable to other Swiss national surveys that also 231 232 included physical examinations: 9.7% for the Swiss Survey on Salt Intake ³⁰ and 38% for the Swiss National nutrition survey ³¹. Fourthly, sample size was rather small, which might have reduced 233 234 statistical power and precluded the identification of some associations such as with alcohol 235 consumption. Still, most of the existing associations were identified. Fifthly, more women than men 236 accepted to participate in the study, a finding in agreement with the literature ²⁹. This might have 237 reduced the incidence of hypertension, as women have a lower risk of developing hypertension than 238 men ^{6, 9}. Still, most associations remained after inverse probability weighting, suggesting that the 239 higher prevalence of women in our sample did not distort the findings.

240	Conclusion
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After a follow-up of 10.9 years, between one fourth and one third of the Swiss population aged 35 to 75 developed hypertension. Male gender, increasing age and higher BMI increase the risk of developing hypertension, while being physically active reduces the risk.

244 **Conflict of interest**

245 The authors report no conflict of interest.

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255 **References**

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379 Figure legends

Figure 1: selection procedure for the two analyses.



Tables

Table 1: comparison between participants who developed/did not develop hypertension between the baseline and 1) the second follow-up only or 2) the first or the second follow-up and participants who remained free of the condition, CoLaus study, Lausanne, Switzerland

	Between baseline and second FU only			Between baseline and first or second FU		
	Normotensive	Hypertensive	P-value	Normotensive	Hypertensive	P-value
Sample size	2416	883		2600	1128	
Women	1474 (61.0)	480 (54.4)	<0.001	1575 (60.6)	590 (52.3)	<0.001
Age (years)	48.1 ± 9.1	52.6 ± 10.1	<0.001	47.9 ± 9.0	52.7 ± 10.3	<0.001
Age groups			<0.001			<0.001
[35-44[1058 (43.8)	233 (26.4)		1162 (44.7)	300 (26.6)	
[45-54[796 (33.0)	295 (33.4)		851 (32.7)	368 (32.6)	
[55-64[445 (18.4)	246 (27.9)		471 (18.1)	308 (27.3)	
[65+	117 (4.8)	109 (12.3)		116 (4.5)	152 (13.5)	
BMI (kg/m²)	24.1 ± 3.7	25.6 ± 3.8	<0.001	24.1 ± 3.7	25.8 ± 4.0	<0.001
BMI categories			<0.001			<0.001
Normal	1585 (65.6)	403 (45.6)		1708 (65.7)	506 (44.9)	
Overweight	674 (27.9)	384 (43.5)		729 (28.0)	488 (43.3)	
Obese	157 (6.5)	96 (10.9)		163 (6.3)	134 (11.9)	
Smoking categories			<0.001			<0.001
Never	1028 (42.6)	331 (37.5)		1089 (41.9)	433 (38.4)	
Former	704 (29.1)	331 (37.5)		744 (28.6)	406 (36.0)	

Current	684 (28.3)	215 (24.4)		767 (29.5)	289 (25.6)	
Alcohol consumption			0.051			0.055
None	648 (26.8)	252 (28.5)		712 (27.4)	321 (28.5)	
1-13/week	1483 (61.4)	504 (57.1)		1563 (60.1)	639 (56.7)	
14-34/week	262 (10.8)	121 (13.7)		298 (11.5)	160 (14.2)	
35+/week	23 (1.0)	6 (0.7)		27 (1.0)	8 (0.7)	
Education categories			<0.001			<0.001
Basic	360 (14.9)	166 (18.8)		412 (15.9)	219 (19.4)	
Apprenticeship	764 (31.6)	322 (36.5)		821 (31.6)	399 (35.4)	
High School	673 (27.9)	216 (24.5)		709 (27.3)	278 (24.7)	
University	619 (25.6)	179 (20.3)		658 (25.3)	232 (20.6)	
Physical activity			<0.001			0.016
No	1016 (42.1)	421 (47.7)		1120 (43.1)	534 (47.3)	
Yes	1400 (58.0)	462 (52.3)		1480 (56.9)	594 (52.7)	
Personal history of CVD			<0.001			<0.001
No	2374 (98.3)	840 (95.1)		2557 (98.4)	1070 (94.9)	
Yes	42 (1.7)	43 (4.9)		43 (1.7)	58 (5.1)	
Family history of CVD			0.002			<0.001
No	1833 (75.9)	622 (70.4)		1993 (76.7)	796 (70.6)	
Yes	583 (24.1)	261 (29.6)		607 (23.4)	332 (29.4)	

BMI, body mass index; CVD, cardiovascular disease; FU, follow-up. Results are expressed as number (percentage) for categorical variables or as average ± standard deviation for continuous variables. Between-group comparisons performed using chi-square for categorical variables and student's t-test for continuous variables.

Table 2: Multivariable analysis without adjusting for baseline blood pressure of the factors associatedwith incident hypertension at 1) the second follow-up only or 2) at the first or the second follow-up,CoLaus study, Lausanne, Switzerland.

	Between baseline and second FU	Between baseline and first or
	only	second FU
Sample size	3299	3728
Gender		
Woman	1 (ref.)	1 (ref.)
Man	1.22 (1.08 - 1.36)	1.25 (1.13 - 1.38)
Age groups		
[35-44[1 (ref.)	1 (ref.)
[45-54[1.43 (1.23 - 1.66)	1.40 (1.23 - 1.60)
[55-64[1.83 (1.57 - 2.14)	1.80 (1.58 - 2.06)
[65+	2.45 (2.04 - 2.96)	2.53 (2.17 - 2.95)
p-value for trend	<0.001	<0.001
BMI categories		
Normal	1 (ref.)	1 (ref.)
Overweight	1.57 (1.39 - 1.77)	1.55 (1.39 - 1.72)
Obese	1.58 (1.32 - 1.89)	1.70 (1.47 - 1.98)
p-value for trend	<0.001	<0.001
Smoking categories		
Never	1 (ref.)	1 (ref.)
Former	1.17 (1.03 - 1.33)	1.11 (0.99 - 1.23)
Current	0.95 (0.82 - 1.10)	0.95 (0.84 - 1.07)
p-value for trend	0.521	0.418
Education categories		
University	1 (ref.)	1 (ref.)
High school	1.04 (0.88 - 1.23)	1.04 (0.90 - 1.20)
Apprenticeship	1.15 (0.99 - 1.35)	1.11 (0.97 - 1.26)
Basic	1.18 (0.99 - 1.42)	1.12 (0.96 - 1.31)
p-value for trend	0.035	0.102
Physically active		
No	1 (ref.)	1 (ref.)
Yes	0.87 (0.78 - 0.98)	0.92 (0.83 - 1.01)
Personal hist. of CVD		
No	1 (ref.)	1 (ref.)
Yes	1.51 (1.21 - 1.90)	1.45 (1.21 - 1.74)
Family history of CVD		
No	1 (ref.)	1 (ref.)
Yes	1.17 (1.04 - 1.32)	1.19 (1.08 - 1.32)

BMI, body mass index; CVD, cardiovascular disease; FU, follow-up. Results expressed as multivariable adjusted incident rate ratio and (95% confidence interval). Statistical analysis conducted using Poisson regression adjusting for all the variables in the table.

Table 3: Multivariable analysis with further adjustment for baseline systolic and diastolic bloodpressure of the factors associated with incident hypertension at 1) the second follow-up only or 2) atthe first or the second follow-up, CoLaus study, Lausanne, Switzerland.

-	Between baseline and second FU	Between baseline and first or
	only	second FU
Sample size	3299	3728
Gender		
Woman	1 (ref.)	1 (ref.)
Man	0.94 (0.84 - 1.05)	0.98 (0.89 - 1.08)
Age groups		
[35-44[1 (ref.)	1 (ref.)
[45-54[1.28 (1.11 - 1.47)	1.24 (1.10 - 1.40)
[55-64[1.41 (1.21 - 1.65)	1.38 (1.21 - 1.58)
[65+	1.74 (1.44 - 2.11)	1.81 (1.55 - 2.11)
p-value for trend	<0.001	<0.001
BMI categories		
Normal	1 (ref.)	1 (ref.)
Overweight	1.33 (1.19 - 1.50)	1.32 (1.19 - 1.45)
Obese	1.19 (1.00 - 1.42)	1.30 (1.13 - 1.50)
p-value for trend	0.049	<0.001
Smoking categories		
Never	1 (ref.)	1 (ref.)
Former	1.18 (1.05 - 1.33)	1.13 (1.02 - 1.25)
Current	1.09 (0.95 - 1.25)	1.06 (0.95 - 1.19)
p-value for trend	0.239	0.302
Education categories		
University	1 (ref.)	1 (ref.)
High school	1.04 (0.89 - 1.22)	1.04 (0.91 - 1.19)
Apprenticeship	1.10 (0.95 - 1.27)	1.07 (0.95 - 1.21)
Basic	1.12 (0.94 - 1.33)	1.08 (0.93 - 1.25)
p-value for trend	0.167	0.270
Physically active		
No	1 (ref.)	1 (ref.)
Yes	0.86 (0.77 - 0.95)	0.9 (0.82 - 0.99)
Personal hist. of CVD		
No	1 (ref.)	1 (ref.)
Yes	1.62 (1.31 - 1.99)	1.60 (1.35 - 1.90)
Family history of CVD		
No	1 (ref.)	1 (ref.)
Yes	1.12 (1.00 - 1.25)	1.14 (1.03 - 1.25)

BMI, body mass index; CVD, cardiovascular disease; FU, follow-up. Results expressed as multivariable adjusted incident rate ratio and (95% confidence interval). Statistical analysis conducted using Poisson regression adjusting for all the variables in the table.