Association between lifestyle factors and the incidence of multimorbidity in an older English population

Running title: lifestyle factors and multimorbidity

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ABSTRACT

Background: Evidence on the role of lifestyle factors in relation to multimorbidity, especially in elderly populations, is scarce. We assessed the association between five lifestyle factors and incident multimorbidity (presence of ≥2 chronic conditions) in an English cohort aged ≥50 years.

Methods: We used data from wave 4, 5 and 6 of the English Longitudinal Study of Ageing. Data on smoking, alcohol consumption, physical activity, fruit and vegetable consumption and BMI were extracted and combined to generate a sum of unhealthy lifestyle factors for each individual. We examined whether these lifestyle factors individually or in combination predicted during the subsequent wave. We used marginal structural Cox proportional hazard models, adjusted for both time-constant and time-varying factors.

Results: A total of 5,476 participants contributed 232,749 person-months of follow-up during which 1,156 cases of incident multimorbidity were recorded. Physical inactivity increased the risk of multimorbidity by 33% (adjusted Hazard Ratio (aHR) 1.33, 95% CI 1.03-1.73). The risk was about two-three times higher when inactivity was combined with obesity (aHR 2.87, 95% CI 1.55-5.31) or smoking (aHR 2.35, 95% CI 1.36-4.08) and about four times when combined with both (aHR 3.98, 95% CI 1.02-17.00). Any combination of 2, 3 and 4 or more unhealthy lifestyle factors significantly increased the multimorbidity hazard, compared to none, from 42% to 114%.

Conclusion: This study provides evidence of a temporal association between combinations of different unhealthy lifestyle factors with multimorbidity. Population level interventions should include reinforcing positive lifestyle changes in the population to reduce the risk of developing multimorbidity.

Keywords: multimorbidity, physical activity, obesity, smoking, nutrition, alcohol

INTRODUCTION

Multimorbidity has now become the clinical norm in primary care and has led to deterioration in the quality of life,[1] higher health care costs[2] and an increased burden on health care systems.[3] This is more pronounced in older adults, with prevalence of over 50% in those above 50 years[4-7]. In order to tackle the multimorbidity challenge, it is not only important to design effective interventions but also to focus on primary prevention. The role of lifestyle factors has been extensively studied in relation to the prevention of individual chronic conditions[8] but evidence on the causal association of these lifestyle factors on the incidence of multimorbidity, especially in geriatric population, is very limited. The studies conducted so far are mostly cross-sectional,[9-12] based on small sample sizes[10,12] or included only women[10,12] and examined single lifestyle factors.[10-14] Only one study from Finland has assessed the longitudinal association of lifestyle risk factors and incident multimorbidity, finding physical inactivity, body mass index (BMI) and smoking to be significantly associated with incident multimorbidity. This study only included five chronic conditions to define multimorbidity in people aged 25-64 years, and did not account for possible behaviour changes during the study period.[15] We used a cohort of English population aged ≥50 years to assess the longitudinal association between five lifestyle factors and multimorbidity.

METHODS

Data source and study population

The English Longitudinal Study of Ageing (ELSA) is an ongoing study of a nationally representative of the English population aged ≥50 years. Participants were recruited from households that were included in the Health Survey for England in 1998, 1999, 2001 and then followed up every two years with detailed health examinations taking place every four years.[16] Ethical approval for ELSA was obtained from NHS Research Ethics Committees under the National Research and Ethics Service (NRES) and participants gave full informed written consent for participation.[17] Since fruit and vegetable consumption was only recorded wave 3 onwards and BMI measurements were only conducted in every even wave, our study population included ELSA participants from waves 4 (2008/09), 5 (2010/11) and 6 (2012/13) with no evidence of multimorbidity at baseline (the first wave when patient contributed data out of the included waves).

Lifestyle factors

Smoking: Participants were categorised as smokers (smoking at the time of the interview) and non-smokers (not smoking at the time of the interview).

Alcohol: Participants were asked for the number of pints of beer, glasses of wine and measures of spirit consumed in the last seven days and converted into units based on the Office for National Statistics guidelines.[18] Total weekly units of alcohol were calculated by adding the units of beer, wine and spirit, divided by the number of days the participants consumed alcohol out of the last seven days to obtain total daily units of alcohol. Excess alcohol consumption was defined as ≥4 alcohol units/day for males and ≥ 3 alcohol units/day for females.[19]

Physical activity (PA): At each wave participants were asked about the frequency of vigorous, moderate and mild PA (more than once/week, once/week, 1-3 times/month, or hardly ever) using show cards to help classify the intensity of each activity.[17] We categorised PA into physically inactive and physically active (mild, moderate and high physical activity at least once/week) as in addition to moderate and vigorous PA, engagement in even mild PA has been associated with lower cardiovascular risk and mortality, especially in older adults.[20,21]

Fruit/vegetable consumption: Participants were asked about the number of small, medium fruits, slices of large and very large fruits, tablespoons of dried fruit and vegetables and bowls of salad eaten. These were converted to portions of fruits and vegetables, using 5-a-day portion sizes.[22] This was then dichotomised to indicate whether participants ate <5 portions/day or ≥5.

BMI: BMI was measured during the nurse visits at wave 4 and 6 and categorised as underweight (<18.5 kg/m^2), normal (≥18.5 and <25 kg/m^2), overweight (≥25, <30 kg/m^2), obese (≥30 kg/m^2) and missing. For wave 5 an average of BMI recording from wave 4 and 6 was used. BMI was also categorised as a binary variable as non-obese (normal and overweight) and obese. We used this classification versus combining overweight and obese categories together as the risk of mortality in overweight categories in older adults has previously been demonstrated to be protective.[23] Since <1% of the participants were categorised as underweight, we excluded these individuals from our analyses.

Multimorbidity

ELSA collects self-reported information on doctor-diagnosed diabetes, hypertension, stroke, myocardial infarction, congestive heart failure, angina, lung disease, chronic obstructive

pulmonary disease, asthma, arthritis, osteoporosis, cancer, hearing problems, Parkinson's, Alzheimer's, dementia, macular degeneration and glaucoma. We defined multimorbidity as presence ≥2 of the above conditions.

Statistical Analysis

We described baseline characteristics using medians, interquartile ranges and proportions. Data on alcohol, fruit/vegetable intake and BMI was missing for 12.7%, 29.3% and 16.8% participants, respectively. Therefore, we imputed missing data using chained equations with a logit function to create five imputed datasets and used Rubin's rules to combine the effect estimates from the imputed datasets. We modelled the incident multimorbidity hazard ratio (adjusted hazard ratio (aHR)) associated with five individual lifestyle factors first, followed by different combinations of these factors in dyads, triads and tetrads, using marginal structural models (MSM) to control for time-varying factors.[24] For all different combinations of these lifestyle factors, participants with no reported unhealthy lifestyle factors were taken as the reference group. MSMs were estimated with pooled logistic regression to accommodate the discrete time data structure, using sampling weights to account for the survey design. Each observation corresponded to the wave when multimorbidity status was reported, linked to the lifestyle factors and participant age in the preceding interview wave and baseline measurements on these lifestyle and sociodemographic factors. Time-constant variables included ethnicity (white, non-white), sex (male, female), total non-pension net wealth in quintiles and education (as proxy measurements of socioeconomic status) and presence of a chronic condition at baseline as we believed these to be closely associated with each lifestyle factor and multimorbidity.[25,26] We applied stabilised inverse probability weights to account for time-varying confounding. For each individual at each follow-up, we

estimated the probability of having the exposure, conditional on the observed fixed and time-varying covariates up to that time. Participants were then weighted by the inverse of their predicted probability of exposure. Participants who dropped out or died during follow up were censored at the last wave of data contribution. We also calculated the probability of remaining uncensored until the outcome wave, given the observed and fixed time-varying covariates at the preceding waves. Similar to the exposure weights, participants were weighted by the inverse of their predicted probability of being censored. The final weights in the model were the product of the stabilised inverse probability of exposure weight, stabilised inverse probability of censoring weight and the sampling weights. Using inverse probability weighting creates a 'pseudopopulation' which has a balanced distribution of potential confounders across exposure levels and can be used to estimate unconfounded causal association between exposure and outcome under study.[27,28] All analyses were conducted in STATA 13 MP.[29]

RESULTS

A total of 10,518 participants contributed data between waves 4 and 6 out of which 4,288 participants had multimorbidity at baseline and 436 only had baseline data. The remaining 5,476 participants contributed 232,749 person-months of follow-up during which 1,156 cases of incident multimorbidity were recorded, giving an incidence rate of 5.9 per 100 person-years. The median age of participants at baseline was 61 years (interquartile range 57-68 years) (Table 1). The study population comprised of more females than males (53% vs. 47%) with majority of the participants being white (96.9%). 19.5% participants belonged to the richest quintile of the total non-pension net wealth compared to 20.4% in the poorest quintile; 640 (11.7%) of the participants had a degree level qualification compared to 921 (16.8%) with no qualification.

When each lifestyle factor was assessed independently, the hazard of multimorbidity increased by 33% for physical inactivity (aHR 1.33, 95% CI 1.03-1.73). Smoking and excess alcohol consumption were not associated with a statistically significant increase in the risk of multimorbidity. There was a statistically significant effect modification by sex on the association between inadequate fruit/vegetable intake and incident multimorbidity (p=0.005) such that inadequate fruit and vegetable consumption paradoxically resulted in a 40% reduced risk of incident multimorbidity in males (aHR 0.60, 95% CI 0.43-0.86) whereas it increased the hazard of multimorbidity by 65% in females (aHR 1.65, 95% CI 1.17-2.34). Obesity was associated with a 28% non-significant increase in the risk of multimorbidity (aHR 1.28, 95% CI 0.85-1.91) (Table 2).

Compared to having no risk factors, having 2, 3 and 4 or more unhealthy lifestyle factors was associated with a greater multimorbidity hazard, from 42% to 114% (Table 3).

For specific dyads (physical inactivity and smoking, smoking and obesity, physical inactivity and obesity, and smoking with inadequate fruit/vegetable intake), the increased risk of multimorbidity was two to three times higher (physical inactivity and obesity: aHR 2. 87, 95% CI 1.55-5.31; obesity with inadequate fruit and vegetable consumption: aHR 1.76 , 95% CI 1.26-2.44) compared to the reference group (Table 4).

The risk of multimorbidity in the participants with a combination of physical inactivity, obesity and smoking was about 4 times higher (aHR 3.98, 95% CI 1.02-17.00) and about 6 times higher in participants with low fruit/vegetable intake, excess alcohol consumption and smoking (aHR 5.91, 95% CI 1.70-20.70) compared to the reference group. The risk of multimorbidity for smoking and inadequate fruit/vegetable intake along with both physical inactivity and obesity was over 3 times higher compared to the reference group (Supplementary Table 2).

Physical inactivity, obesity and smoking combined with both excess alcohol consumption and inadequate fruit/vegetable intake resulted in a statistically significant increase in the risk of multimorbidity (aHR 7.22, 95% CI 1.38-37.72 and 10.21, 95% CI 2.57-40.50 respectively) compared to the reference group (Supplementary Table 3).

DISCUSSION

Principal findings

We found a dose response association between unhealthy lifestyle factors and multimorbidity. Physical inactivity increased the risk of multimorbidity by 32% on its own and inadequate fruit and vegetable intake increased the risk by 65%. When physical inactivity was combined with obesity or smoking the risk increased to by two-three times and over four times more when combined with both smoking and obesity.

Strengths and limitations

Using a large prospective cohort, we were able to examine the longitudinal relationship between lifestyle factors and incident multimorbidity, which has been a limitation of previous studies.[9,10,12] We only included data from the three most recent ELSA waves for this analysis in order to capture all five lifestyle factors; we still had a large number of people in the study with over 100,000 person-months of follow-up, however when assessing different triads and tetrads of unhealthy lifestyle factors the number of people with specific combinations of unhealthy lifestyle factors was quite low as depicted by the small number of people in some triads and tetrads (Supplementary Table 1) and wide confidence intervals of the estimates. Consequently, it is difficult to distinguish true negative findings from the negative findings associated with low statistical power; therefore the findings should be interpreted with caution. Chronic disease diagnoses in ELSA are based on self-reports of physician diagnoses and participants with cognitive or physical impairments were eligible for a proxy interview, to get ensure optimal accuracy of the information provided including the reporting of chronic conditions.[30] Furthermore, chronic conditions such as diabetes have been validated in ELSA using objective biomedical data collected as part of the nurse visits.[31] We further compared some of the individual chronic disease estimates from ELSA to other

national estimates[32] and reports[33] and found good agreement. Our multimorbidity definition relied on the number of conditions with no account of disease severity. Nonetheless, in light of the lack of a standard definition of multimorbidity[34], we used the most common definition used in epidemiological studies.[34] The information on all lifestyle factors, apart from BMI, is self-reported in ELSA. Nevertheless previous studies have found good agreement between self-reported smoking status and cotinine levels, with only 1.9% discrepancy between the two measures in people ≥65 years.[35,36] Physical activity has been validated in ELSA itself for a subset of population using accelerometer data where self-reported physical activity was found to be moderately correlated with objectively assessed hours per day of moderate-to-vigorous physical activity.[37] The proportion of people in the inactive category in our study population was lower than the national estimates for older adults (~26%)[38]; however our population was restricted to people aged ≥50 with ≤1 chronic condition at baseline, considering that about half the UK population is likely to be multimorbid by 50 years,[39] our study population was healthier than the average UK population. Furthermore, our definition of inactivity was different from the one used for the national statistics (< 30 mins of moderate PA per week or <15 mins of vigorous PA per week) potentially explaining the difference in the proportion of inactive people between the two sources. Assessment of dietary intake is inherently difficult and dietary intake questions in ELSA have not been validated, hence there is a potential for measurement error which may also potentially explain the paradoxical reduction in the risk of multimorbidity in males. Since BMI recording was only available for every even wave, we imputed BMI for wave 5 as the average of the BMI in wave 4 and 6. We believe that we closely predicted the BMI for wave 5 using this method as the mean difference in BMI between wave 4 and wave 6 was 0.5kg/m^2 and >70% of people in the normal, overweight and obese categories in wave 4

remained in the same category in wave 6. We adjusted our analysis for indicators of socioeconomic status like quintiles of wealth and education status; however, the analysis did not take into account other social factors (e.g. access to health care, social support, social isolation etc.) which may affect the reporting of chronic conditions and consequently the incidence of multimorbidity. Lastly, some of the changes in lifestyle factors may be due to underlying conditions which may be diagnosed at a later stage, and therefore reverse causation cannot be completely ruled out.

Comparison with current literature

The incidence of multimorbidity in our study was about 6 per 100 person-years which is considerably lower than the incidence in a Swedish sample of 418 participants (12.6 per 100 person-years for participants with no disease at baseline).[40] However, the participants in this study were 75 and older compared to 50 and older in our study, which may potentially explain the difference in the incidence rates. Smoking and excess alcohol consumption were not found to increase the risk of multimorbidity in this cohort of older English adults. This is in contrast with the Finnish study, which found a 2.5 fold increase in the risk of multimorbidity associated with smoking in initially-disease free men and women. However, when the analysis was restricted to people with cardiovascular disease at baseline no significant association between smoking and multimorbidity was found (HR 1.23, 95% CI 0.77-1.96).[15] Our study included people both with and without one existing condition, more conditions to define multimorbidity and slightly shorter follow-up time compared with the Finnish study, which may explain the contrasting findings. Furthermore, the median age of our study population was 61 years with no or one chronic condition at baseline; given that heavy smokers die younger, there may be a healthy survivor effect in that our sample, resulting in dilution of the effects of smoking. A secondary cross-sectional analysis of the

PRECISE cohort from Canada did not find a significant association between high risk drinking and multimorbidity (odds ratio (OR) 0.94, 95% CI 0.43-2.03 for men and OR 0.83, 95% CI 0.31-2.23 for women), which is in line with our findings.[9] We found a 32% increase in the multimorbidity hazard in association with physical inactivity. This is consistent with the results of the previous prospective Finnish study which found a 34% increase in the risk of multimorbidity in men and 62% in women with physical inactivity who were initially disease-free.[15] We found a 63% increase in the risk of multimorbidity associated with inadequate fruit/vegetable intake in women and a paradoxical reduction of multimorbidity risk by 39% in males. A recent study using the Jiangsu Longitudinal Nutrition Study from China showed a statistically significant association between high levels of fruit/vegetable intake and healthier stages in the evolution of multimorbidity.[13] Previous studies have also reported differences in the association of fruit/vegetable intake and chronic conditions and mortality by gender. A population-based study from Japan found a reduced risk of cardiovascular mortality associated with vegetable intake in women but not men.[41] However, considering the inherent limitations of dietary assessment and a lack of validity measures in ELSA, the results should be interpreted with caution. Our study has shown that accumulating unhealthy lifestyle factors corresponds to an increasing risk of multimorbidity with stronger associations with some factors compared to others. Obesity and smoking, although not significant individually, had the strongest association with incidence of multimorbidity in combination with other factors. Therefore, the overall risk may be more dependent on which specific combination of unhealthy lifestyle factors one accumulates rather than the quantity.

Conclusion

This study provides a strong evidence for a temporal association of unhealthy lifestyle factors and multimorbidity. The increase in the risk of multimorbidity associated with certain lifestyle factors and their combinations indicates that a healthy lifestyle would reduce several clustered diseases, offering an alternative and cost-effective approach to reducing the burden of multiple diseases that are still approached as single entities in clinical practice. Hence, there is a need of population-based interventions potentially including brief consultation and advice and wider public health campaigns to focus on primary prevention of multimorbidity by encouraging healthy lifestyle in the population.

COMPETING INTERESTS

Khunti has acted as a consultant and speaker for Astra Zeneca, Novartis, Novo Nordisk, Sanofi-Aventis, Lilly, Merck Sharp & Dohme, Janssen and Boehringer Ingelheim. He has received grants in support of investigator and investigator initiated trials from Astra Zeneca, Novartis, Novo Nordisk, Sanofi-Aventis, Lilly, Janssen, Boehringer Ingelheim and Merck Sharp & Dohme and Roche. Khunti has served on advisory boards for Astra Zeneca, Novartis, Novo Nordisk, Sanofi-Aventis, Lilly, Merck Sharp & Dohme, Janssen and Boehringer Ingelheim, Roche. Yates has have received grant funding from the Medical Research Council and the National Institute for Health Research that broadly investigate the impact of lifestyle behaviours and the risk of chronic disease. Davies has acted as consultant, advisory board member and speaker for Novo Nordisk, Sanofi-Aventis, Lilly, Merck Sharp & Dohme, Boehringer Ingelheim, AstraZeneca and Janssen and as a speaker for Mitsubishi Tanabe Pharma Corporation. She has received grants in support of investigator and investigator initiated trials from Novo Nordisk, Sanofi-Aventis and Lilly. Dhalwani, Zaccardi, O'Donovan, Carter and Hamer have nothing to disclose.

AUTHOR CONTRIBUTIONS

Dhalwani and Khunti conceived the idea of the study; Dhalwani and Zaccardi designed the study; Dhalwani acquired the data; carried out the statistical analysis; interpreted the data; and drafted the manuscript. O'Donovan, Zaccardi, Carter and Khunti provided input in the analysis and interpretation of the findings; O'Donovan, Zaccardi, Carter, Hamer, Yates, Davies and Khunti critically reviewed the manuscript and Dhalwani revised the manuscript for final submission.

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Table 1 - Baseline characteristics of the study population

	All participants	Incident Multimorbidity	
	N=5,476	Yes (n=1,156)	No (n=4,320)
	n(%)	n(%)	n(%)
Age in years			
50-59	2,077 (37.9)	285 (24.6)	1792 (41.5)
60-69	2,137 (39.0)	446 (38.6)	1691 (39.1)
70-79	991 (18.1)	312 (27.0)	679 (15.7)
80-89	245 (4.5)	99 (8.6)	146 (3.4)
90+	26 (0.5)	14 (1.2)	12 (0.3)
Male	2,575 (47.0)	542 (46.9)	2,033 (47.0)
Ethnicity: White	5,307 (96.9)	1,122 (97.1)	4,185 (96.9)
Total non-pension net wealth (Quintile)			
Quintile 1 ≤126,000 (poorest quintile)	1,115 (20.4)	294 (25.4)	821 (19.0)
Quintile 2 (126,001-210,599)	1,091 (19.9)	267 (23.1)	824 (19.1)
Quintile 3 (210,600-318,399)	1,088 (19.9)	214 (18.5)	874 (20.2)
Quintile 4 (318,400-511,299)	1,072 (19.6)	190 (16.4)	882 (20.4)
Quintile 5 ≥511,300 (richest quintile)	1,068 (19.5)	185 (16.0)	883(20.4)
Missing	42 (0.8)	6 (0.5)	36 (0.8)
Highest Education Qualification			
NVQ4/NVQ5/ Degree or equivalent	640 (11.7)	131 (11.3)	509 (11.8)
Higher education below degree	542 (9.9)	111 (9.6)	431 (9.9)
NVQ3/GCE A level or equivalent	283 (5.2)	55 (4.8)	228 (5.3)
NVQ2/ GCE O level or equivalent	724 (13.2)	168 (14.5)	556 (12.9)
NVQ1/CSE other grade equivalent	135 (2.5)	28 (2.4)	107 (2.5)
Foreign/Other	411 (7.5)	94 (8.1)	317 (7.3)
No qualification	921 (16.8)	246 (21.3)	675 (15.6)
Not known	1,820 (33.2)	323 (27.9)	1,497 (34.6)
Chronic Disease at Baseline	2,905 (53.0)	964 (83.4)	1,941 (44.9)
Smoking	835 (15.2)	186 (16.1)	649 (15.0)
↑Alcohol	1,535 (28.0)	290 (25.1)	1,245 (28.8)
Physical Inactivity	315 (5.8)	107 (9.3)	208 (4.8)
IFV	2,045 (37.3)	402 (34.8)	1,643 (38.0)
Obesity	1,212 (22.1)	327 (28.3)	885 (20.5)

↑ Alcohol= Excess alcohol consumption, IFV=Inadequate fruit and vegetable intake, NVQ=National Vocational Qualification, GCE=General Certificate of Education, CSE=Certificate of Secondary Education

Table 2 - Adjusted Hazard Ratios for Incident Multimorbidity by individual lifestyle factors among ELSA participants (2008-2013)

	n(%)* N=5476	Adjusted Hazard Ratio**(95% CI)	p-value for interaction with sex
Smoking	776 (14.2)	1.21 (0.65-2.27)	0.663
↑ Alcohol	1,994 (35.5)	1.15 (0.92-1.43)	0.407
Physical Inactivity	300 (5.5)	1.33 (1.03-1.73)	0.804
IFV Male	1,327 (51.5)	0.60 (0.43-0.86)	0.005
IFV Female	1,135 (39.1)	1.65 (1.17-2.34)	
Obesity	1,466 (26.8)	1.28 (0.85-1.91)	0.741

↑ Alcohol= Excess Alcohol consumption, IFV=Inadequate Fruit & Vegetable consumption

*sum of all columns is greater than the total participants as one participant can have more than one unhealthy lifestyle factor, n(%) based on the latest observations of lifestyle factors

****** Adjusted for sex, wealth quintiles, education level, ethnicity, age at baseline, calendar time, age at exposure wave, presence of chronic disease at baseline and the other four lifestyle factors at exposure wave and baseline

Table 3 - Adjusted Hazard Ratios for Incident Multimorbidity by the number of unhealthy lifestyle factors among ELSA participants (2008-2013)

	n(%)* N=5,476	Adjusted Hazard Ratio**	95% Confidence Interval	p- for trend
0	1,269 (23.2)	Reference	-	
1	2,143 (39.1)	1.17	0.97-1.40	
2	1,459 (26.6)	1.42	1.16-1.74	0.001
3	536 (9.8)	1.75	1.32-2.30	
4-5	69 (1.3)	2.16	1.29-3.64	

p-for gender interaction=0.05

*n(%) based on the latest observations of lifestyle factors

**Adjusted for sex, wealth quintiles, education level, ethnicity, age at baseline, calendar time, age at exposure wave, presence of chronic condition at baseline

Table 4 - Adjusted Hazard Ratios for Incident Multimorbidity by dyads of unhealthy lifestyle factors among ELSA participants (2008-2013)

	n	Adjusted Hazard Ratio**	95% Confidence Interval
Physical Inactivity + Obesity	104	2.87	1.55-5.31
↑ Alcohol + Obesity	499	1.45	0.78-2.69
Smoking + Obesity	162	2.65	1.75-3.99
IFV + Obesity	647	1.76	1.26-2.44
IFV + Physical Inactivity	156	1.48	0.71-3.05
Smoking + Physical Inactivity	73	2.35	1.36-4.08
↑ Alcohol + Physical Inactivity	94	0.81	0.34-1.94
Smoking + ↑ Alcohol	329	1.61	0.78-3.30
Smoking + IFV	502	2.84	1.34-6.06
↑ Alcohol + IFV	927	1.35	0.92-1.96

↑ Alcohol= Excess Alcohol consumption, IFV=Inadequate Fruit & Vegetable consumption

***** n based on the latest observations of lifestyle factors. 1269 participants did not have any unhealthy lifestyle factors

****** Adjusted for sex, wealth quintiles, education level, ethnicity, age at baseline, calendar time, age at exposure wave, presence of chronic disease at baseline and the other three lifestyle factors at baseline