



Lifetime employment, tobacco use, and alcohol consumption trajectories and cardiovascular diseases in old age

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ABSTRACT

Despite the great advances of life course epidemiology studies during the last decade in understanding the general health effects of employment trajectories, research has yet to evaluate the effects of employment trajectories along with other major risk factors, such as tobacco and alcohol consumption, on cardiovascular diseases (CVDs)—the main cause of deaths worldwide. This is highly relevant, since health advantages in one domain (e.g., being a permanent formal full-time worker) may offset health disadvantages in other domains (e.g., being a regular smoker or alcohol consumer); conversely, disadvantages in both domains may interact, leading to even greater health risks. Considering these knowledge gaps, this research has two main objectives: (1) to reconstruct simultaneous employment, tobacco use, and alcohol consumption trajectories over the life course (from birth to old age) and (2) to measure the association between these trajectories and CVD in old age. Drawing on a rich and comprehensive life history dataset and using multichannel sequence and regression analyses, we analyzed a cohort of individuals aged 65–75 in Chile, a Latin American country with high social inequalities and scarce research on this matter. Our study shows that following a trajectory of formal employment together with no tobacco and alcohol use reduces CVD risk by 36 percentage points relative to a similar employment trajectory but with regular tobacco and alcohol use. Even with an employment trajectory characterized by constant informal employment or permanent inactivity, a life course free of regular tobacco and alcohol use shows protective effects against CVD. This study stresses the importance of health policies that consider CVD as a condition that strongly depends on individual experiences in multiple life domains and across different life stages.

Introduction

During the last decade, multiple life course epidemiology studies have examined the association between employment conditions and health, stressing that health conditions cannot be attributable to work status at a specific life point but stem from exposure to work-related advantages and disadvantages across several life stages (Carmichael & Ercolani, 2016; Di Gessa, Corna, Price, & Glaser, 2020; McDonough et al., 2015, 2017). Thus, these life course studies show that health conditions are the result not only of traditional health-related risks but also of a variety of individual experiences in other life domains (e.g., the work domain) to which individuals are exposed at different points in life and across different time spans (Ben-Shlomo & Kuh, 2002; Bernardi,

Huinink, & Settersten, 2019; Settersten et al., 2020). These individual experiences, in turn, tend to progressively accumulate during the life course as either advantages or disadvantages for subsequent health statuses (Corna, 2013; Dannefer, 2003).

Research has provided robust evidence on the ways in which different long-term employment trajectories affect individuals' prospective health status. Studies have shown that employment patterns characterized by continuous, formal, full-time, and stable jobs that provide an income that allows people to meet their basic needs lead to a better quality of life in late adulthood and old age, including greater pleasure, autonomy, self-realization, and sense of control (Di Gessa et al., 2020; Wahrendorf, 2015); better self-rated health (Carmichael & Ercolani, 2016; McDonough et al., 2015, 2017); higher subjective

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well-being (Ponomarenko, 2016); fewer functional limitations (Tosi & Grundy, 2019; Wahrendorf, Hoven, Goldberg, Zins, & Siegrist, 2019); better oral health (Ramsay et al., 2018); lower mortality risk before age 75 (Sabbath, Guevara, Glymour, & Berkman, 2015); lower markers of stress and inflammation (Lacey, Sacker, et al., 2016); better metabolic markers, including waist circumference, blood pressure, lipoprotein cholesterol density, triglycerides, and glycated hemoglobin (Lacey, Kumari, et al., 2016; McMunn et al., 2016); better mental health, including less mental illness and fewer depressive symptoms (Arpino, Gumà, & Julià, 2018; Engels et al., 2019; Giudici & Morselli, 2019); and lower levels of frailty after age 60 (Lu et al., 2017).

Scholars have argued that these positive health effects can be explained by the fact that employment trajectories in better working conditions allow individuals throughout their lives to accumulate advantages in multiples domains of life, such as better housing conditions, better medical care and health services, and access to a more adequate financial status. Such employment trajectories also enable individuals to perceive greater control over the development of their individual and family lives, lower their stress levels (especially in jobs with a high sense of control and sense of belonging), and make them feel less socially excluded—all factors associated with better health conditions (Benach et al., 2014; Giudici & Morselli, 2019; Wahrendorf, 2015).

While an increasing number of studies have adopted a life-course perspective to analyze the determinants of noncommunicable diseases (NCDs; Ben-Shlomo & Kuh, 2002), to the best of our knowledge, only three studies have examined the influence of employment trajectories on NCDs (Madero-Cabib, Azar, & Pérez-Cruz, 2019; Madero-Cabib, Corna, & Baumann, 2020; van Hedel et al., 2016). These studies show the protective effects of formal and continuous employment trajectories against NCDs, except in the case of single mothers (van Hedel et al., 2016). However, they either focus on employment trajectories in later life, analyze only female samples, or use aggregated measures of NCDs. Therefore, the association between long-term employment trajectories and specific NCDs across a general population remains largely unexplored.

Cardiovascular diseases (CVDs), such as myocardial infarction, coronary thrombosis, and congestive heart failure, are among the most prevalent NCDs worldwide (Balakumar, Maung-U, & Jagadeesh, 2016). According to the World Health Organization (World Health Organization, 2018), NCDs accounted for 71% of all deaths (41 million) in 2018, 17.9 millions of which were caused by CVDs—the most prevalent cause of death. Only one study has examined the association between employment trajectories and CVDs; this study found that single mothers who work continuously throughout their lives have the highest CVD risk (van Hedel et al., 2016).

Several epidemiological studies have pointed out that employment-related experiences and modifiable health risk behaviors, such as regular tobacco use and harmful alcohol consumption, are crucial factors in the development of CVD (Knott, Bell, & Britton, 2018; Mayyas & Alzoubi, 2018; Parry, Patra, & Rehm, 2011). The vast majority of these findings come from cross-sectional analyses conducted at a single time point. However, over the last decade, increasing evidence has shown how long-term tobacco and alcohol consumption patterns influence CVDs. In addition, a number of sociodemographic and health variables that might act as confounders of these associations have been identified, such as age, sex, educational level, and health behaviors (Britton, Ben-Shlomo, Benzeval, Kuh, & Bell, 2015; Gémes, Moeller, Engström, & Sidorchuk, 2019; Jandackova, Scholes, Britton, & Steptoe, 2019).

Studies that analyzed the alcohol consumption trajectories of individuals over 6 years (Bell et al., 2017), 10 years (O'Neill, Britton, Brunner, & Bell, 2017; Ruidavets et al., 2010), 20 years (Britton et al., 2016), 25 years (O'Neill et al., 2017), and 35 years (Romelsjö, Allebeck, Andréasson, & Leifman, 2012) concluded that consumption patterns have either a U- or J-shape association with the risk of CVD, meaning that people who never drank and permanent heavy drinkers were more likely to develop CVD. Also, people who started follow-up periods as

nondrinkers and then became moderate drinkers showed the lowest risk of CVD. However, the findings of these studies are highly sensitive to the cardiovascular outcome evaluated (see, e.g., Bell et al., 2017), as well as to the type of alcoholic beverage measured and the individuals' gender, educational level, and ethnic background. More importantly, recent research has shown that drinking has either a nonsignificant or no protective effect on all-cause mortality and cardiovascular outcomes, emphasizing that alcohol use, regardless of amount, leads to health loss across populations (Global Burden of Disease Alcohol Collaborators, 2018; Ortolá et al., 2019).

Regarding studies on the health effects of long-term tobacco use patterns, one of the key findings is that people following smoking trajectories characterized by late cessation, as well as those who stop smoking earlier in life and experience weight gain afterward, are at higher risk of CVD (Chen et al., 2019; Hu et al., 2018; Liu et al., 2020; Mayyas & Alzoubi, 2018).

Despite the great advances of this body of life course research in understanding long-term patterns of tobacco use and alcohol consumption and their effects on CVDs, no studies have examined the associations of simultaneous long-term patterns of smoking and drinking with CVD. This is highly relevant, since health advantages in one life domain (e.g., being a permanent nonsmoker) may offset health disadvantages in the other life domain (e.g., being a permanent heavy alcohol drinker); conversely, disadvantages in both life domains may interact, leading to even higher health risks. Most notably, no research has evaluated the health impact of trajectories in different life domains—for example, in the employment domain and the health risk behavior domain. While multiple combinations of life domains could be studied, employment, tobacco use, and alcohol consumption have shown significant associations with each other and with health outcomes. Specifically, cross-sectional studies have shown that both tobacco and alcohol consumption are associated with a loss of income and loss of productivity, leading to the impoverishment of individuals and their families (Ciapponi & World Health Organization, 2014). On the other hand, people with a lower income, education, or occupational status are much more likely to become ill or die prematurely from a disease related to their tobacco or alcohol use (Jones & Sumnall, 2016, pp. 9–17).

This led us to hypothesize that the health advantages of having a strong attachment to the labor market through a full-time, stable, and formal job throughout life might be different for individuals who report being regular smokers and drinkers during long periods in adulthood. By contrast, having a weak attachment to the labor market during adulthood or working permanently in informal jobs might not necessarily be harmful for health if individuals experienced simultaneous trajectories as nondrinkers and nonsmokers.

Drawing on a life course approach, the analysis of the health effects of simultaneous employment, tobacco use, and alcohol consumption trajectories is relevant for two reasons: First, it is possible to focus on the duration of exposure to different employment, smoking, and drinking statuses across different life spans. Second, it is possible to estimate whether the time point or the timing of the life course at which individuals are in different statuses in these three domains plays an important role in the likelihood of contracting CVD. In concrete terms, simultaneously being a permanent full-time worker, a nondrinker, and a nonsmoker might affect the likelihood of experiencing CVD differently if these statuses are experienced in early or late adulthood and if they are maintained over different stages of the life course.

Considering these knowledge gaps, this paper has two main objectives: (1) to reconstruct simultaneous employment, tobacco use, and alcohol consumption trajectories over the life course (from birth to old age) and (2) to measure the association between these trajectories and CVDs in old age. We examine the differences in the effects of the duration of exposure to different employment, smoking, and drinking statuses throughout life and the timing of these statuses on CVD risk. We draw on a rich and comprehensive life history dataset and analyze a cohort of individuals born between 1944 and 1954 (i.e., those 65–75

years old at the time of the interview) in Santiago, Chile.

Most of the evidence about CVDs and their association with either employment or health behavior trajectories comes from studies conducted in developed and high-income countries. We conducted an in-depth review of multiple databases but could not find a single longitudinal study on these topics from developing countries, such as those from Latin America. Chile has multiple characteristics that make it a particularly interesting case study for the international audience interested in the determinants of CVDs related to employment, smoking, and drinking. Chile is a developing Latin American country with a comparatively high income (GDP per capita, PPP, in 2018 = US\$25,222) but a highly unequal distribution of wealth (Gini coefficient = 0.55). It has a relatively large informal labor sector and a strong male-breadwinner culture that restricts the labor force participation of about half of the female population (Madero-Cabib, Undurraga, & Valenzuela, 2019). It has nearly universal health coverage (Frenz, Delgado, Kaufman, & Harper, 2014). NCDs account for 85% of all deaths among adults in the country (World Health Organization, 2017). According to the National Health Survey (Ministerio de Salud de Chile, 2017, 2018), 73.3% and 10.0% of people aged 65+ have high blood pressure and have suffered a heart attack, respectively. The majority of the population (74.2%) are overweight or obese—the highest among all countries in the Organization for Economic Co-operation and Development (OECD), surpassing even the United States.

Regarding the use of alcohol and tobacco in Chile, 37.8% of men and 29.1% of women are current smokers (Ministerio de Salud de Chile, 2017), and the average annual consumption of pure alcohol is 7.9 L (28th among OECD countries; OECD, 2020). Given these high figures, Chile has implemented tobacco control policies since 2005, such as protecting smoke-free environments, marketing regulations, and tax increases on tobacco products. These policies will contribute to decreasing the prevalence of smoking among the Chilean population, particularly among the youth, who will grow up in an environment where smoking is more expensive, less marketed, less accessible, and less socially accepted (Bambs, Bravo-Sagua, Margozzini, & Lavandero, 2020). However, the same is not true for alcohol regulation policies and alcohol intake. There is a lack of marketing regulations, and aggressive marketing campaigns for alcohol products are targeted at young people; moreover, alcohol is readily available and cheaper than in other countries (Bambs et al., 2020). Finally, most of the literature that has addressed the relationship between employment trajectories and well-being has done so in contexts where informal employment is not a major feature of the labor market (McDonough et al, 2015, 2017; Wahrendorf, 2015). Examining the case of Chile allows us to expand on this literature by adding an extra layer of complexity to this association, particularly by studying the importance of informal employment trajectories.

The main purpose of this research is therefore to examine the relationship between employment, tobacco use, and alcohol consumption trajectories and CVDs in Chile.

Materials and methods

Data

We used data from a population-representative and longitudinal survey entitled “Life Course and Vulnerability Among Older People in Santiago, Chile.” This is the first survey in Chile to collect retrospective annual information on multiple dimensions of the life course, such as residential histories, educational and occupational trajectories, lifetime behavioral risk factors, marital and fertility patterns, work and financial vulnerabilities, and health status in old age. This representative survey collected life course information on 802 people born between 1944 and 1954 (currently aged 65–75) living in Santiago, Chile’s capital city, which represents approximately 40.5% of Chile’s population. The survey was conducted between March and August 2019 and followed the latest quality standards defined by the American Association for Public

Opinion Research (2016).¹

To ensure that our results were not affected by potential sample selection bias, the study sample was weighted to provide representative results for older adults aged 65–75 in the city of Santiago. The data collection process involved the use of two types of questionnaires: First, to explore current work and financial and health conditions, we used a traditional cross-sectional questionnaire. Second, to reconstruct long-term trajectories in different life domains, we used a retrospective life-history-calendar questionnaire, which helped respondents remember and chronologically organize various episodes throughout their lives, along with the approximate dates of occurrence (Morselli, Goff, & Gauthier, 2019). There were only two missing observations in our data for the heart attack variable. Because of this small number, no further robustness analyses regarding missing data were conducted.

Variables

Lifetime employment, tobacco use, and alcohol consumption trajectories

Our study is divided into two phases: First, we identified patterns in lifetime trajectories. Second, we estimated associations between these patterns and CVD measures after the age of 65. We measured life trajectories in three dimensions: employment, tobacco use, and alcohol consumption. Using the retrospective life-history-calendar questionnaire described earlier, participants were asked, on an annual basis, when they had a job-related change and whether they smoked and drank alcohol occasionally or regularly or did not consume them at all. With this information, we were able to build a life history dataset in which each individual was observed every year since birth until the time of the interview, repeatedly recording the same state for each dimension until there was a change in their status.

To reconstruct employment trajectories, three categories were considered: (1) “formal employment,” which includes the self-employed and those employed in jobs from which they contribute to their individual retirement accounts, a key indicator of work formality in Chile (for an in-depth discussion, see Madero-Cabib, Biehl, Sehnbruch, Calvo, & Bertranou, 2019); (2) “informal employment,” which refers to those who are employed (either as employees or self-employed) but not contributing to individual retirement accounts, and (3) “out of the labor force,” which indicates individuals without a paid work.

To reconstruct tobacco use trajectories, three smoking categories were considered: (1) “does not smoke”; (2) “smokes occasionally,” which refers to people who smoked only a few times a year; and (3) “smokes regularly,” referring to people who reported smoking on a daily basis. Finally, to reconstruct alcohol consumption trajectories, three categories were used: (1) “does not drink alcohol”; (2) “drinks alcohol occasionally,” referring to people who drank only a few times a year; and (3) “drinks alcohol regularly,” which refers to people who reported drinking at least once a week. Regular tobacco use and regular alcohol consumption used different time frames because those were the categories best understood by the respondents, as shown in the pilot cognitive interviews and usability tests conducted in the early phase of the retrospective data collection process (see Supplemental Material, pp. 1–3). In other words, participants were able to remember properly whether they smoked on a daily basis and drank alcohol on a weekly basis in a given year. Unfortunately, we were not able to include aspects such as the number of cigarettes or alcoholic drinks consumed per occasion and the presence of dependence symptoms.

Cardiovascular disease

Two cardiovascular outcomes were measured in the cross-sectional questionnaire and included as the dependent variables of the second stage of our study: having ever experienced a heart attack and having

¹ For an in-depth explanation of the data used in this study, please refer to Supplemental Material, pp. 1–3.

ever been diagnosed with high blood pressure. Based on international survey standards, both indicators were derived from a question asking whether a medical doctor had ever told the participant that they had had or currently had that condition.

Control variables: Sociodemographics and health risks

Based on studies conducted in developed countries, we adjusted our analyses for the traditional risk factors of CVDs. These indicators came from the cross-sectional questionnaire. Specifically, all models were adjusted for three sociodemographic variables: age, gender, and self-reported educational level (“primary or none,” “secondary,” “technical college,” and “college”). Additionally, all models included controls for measures of three health risks: (1) body mass index (BMI), measured in four categories: “underweight,” “normal weight,” “overweight,” and “obese”; (2) physical activity, measured by a question on how much physical activity people perform during the week, considering sports, heavy home-related duties, or something else that requires physical effort (“more than once a week” and “once a week or less”); and (3) food frequency, indicating how frequently people consume (i) milk and dairy; (ii) legumes, beans, or eggs; (iii) beef, fish, or chicken; and (iv) fruits and vegetables (“two times a week or less” and “three to six times a week or more”). Finally, considering studies stressing the relevance of childhood health for later-life health (Haas, 2008), we also included summative indicators of childhood health status (based on international survey standards), namely the number of illnesses experienced at or before age 15 (polio, tuberculosis, allergies, asthma, respiratory problems other than asthma, acute diarrhea, meningitis/encephalitis, chronic ear problems, speech problems, vision problems even with glasses, and infectious diseases, such as measles, rubella, chickenpox, mumps, diphtheria, and scarlet fever).²

Statistical methods

Our analytical approach had two stages. First, we conducted multichannel sequence analysis (MCSA) and cluster analysis to reconstruct simultaneous employment, tobacco use, and alcohol consumption trajectories throughout the life course. Second, we estimated logistic regression models predicting the association between the identified trajectories and the probability of ever experiencing a heart attack or being diagnosed with high blood pressure.

To reconstruct the types of lifetime trajectories in the three domains of interest, we used MCSA (Gauthier, Widmer, Bucher, & Notredame, 2010), an extension of traditional sequence analysis (see MacIndoe & Abbott, 2011), and cluster analysis (see Supplemental Material, pp. 4–5, for an in-depth explanation of this longitudinal technique). An important decision in MCSA concerns the selection of a more robust cluster solution that will better summarize the diversity of trajectory types followed by individuals in the domains of interest.

We employed four selection criteria: average silhouette width (ASW), point biserial correlation (PBC), Hubert’s gamma (HG), and Hubert’s C (HC). We used normalized scores because some of these criteria have an index that ranges from -1 to 1, while others have an index ranging from 0 to 1. Furthermore, while a higher measure in the ASW, PBC, and HG indices means a better cluster solution, a lower HC

² We also estimated models that instead of including a summative indicator of illnesses, considered a summative of the following conditions experienced at or before age 15: severe headaches or migraines; epilepsy, fits or seizures; emotional, nervous or psychiatric problems; broken bones; appendicitis; childhood diabetes or blood sugar levels; heart problems; leukemia or lymphoma; and cancer or malignant tumor, excluding minor skin cancers. When including the latter instead of the former summative indicator, the effect of our main independent variable (employment, tobacco use, and alcohol consumption trajectory types) on the two CVD outcomes, slightly changed. Results available upon request.

measure indicates a better solution (see Studer, 2013). However, in any cluster analysis, there is no rule of thumb for this selection process, in part because there is no null hypothesis regarding the number of clusters that should exist (Dubes & Jain, 1980). In most cluster analyses within the sequence analysis framework, most researchers have reached solutions between three and a dozen clusters (Cornwell, 2015), avoiding very few clusters that hide variability and a too large number of groups that overcomplicates the classification scheme. In our case, most indicators used for cluster selection indicate that an ideal solution—maximizing between-cluster differences and minimizing within-group differences—would be between 6 and 11 clusters. However, the six-cluster solution offered too little variability, and the groups were hard to classify. Also, any solution between 7 and 10 did not perform well according to our indicators. Based on these selection criteria (see Fig. 1), our final lifetime trajectory solution considers 11 types.

To identify possible effects of attrition in our life trajectories given that individuals are observed at different ages, making life trajectories end at different time points, we compared our 11-type solution to one that considered only individuals’ states up to age 65, independent of their age at the time of the interview. No significant differences were observed, and most individuals were classified in the same group as in the original classification (results not shown but available upon request).

Finally, once we identified the clusters of lifetime trajectory types, these became the main independent variable in two sets of logistic regression models: one predicting heart attacks and another predicting high blood pressure. We estimated all regression models in Stata using survey weights, and we calculated the average marginal effects for our main variable of interest to simplify the interpretation of our results. Additionally, multichannel sequence and cluster analyses were conducted in R using the TraMineR package (Gabadinho, Ritschard, Muel-ler, & Studer, 2011).

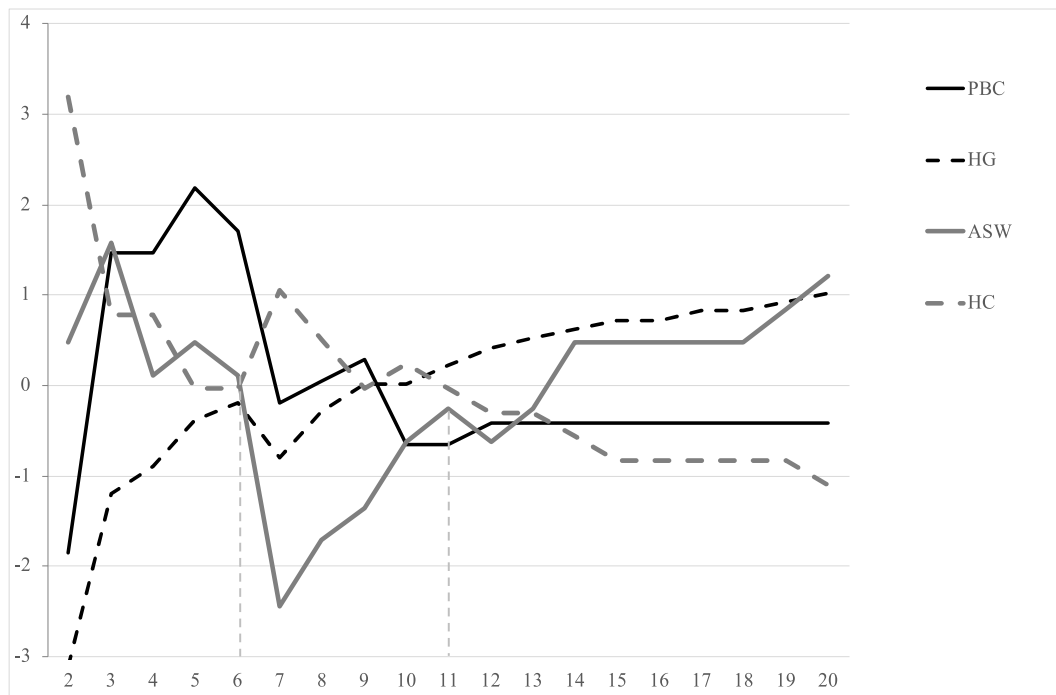
Results

Lifetime employment, tobacco use, and alcohol consumption trajectories

Table 1 shows the weighted distribution of our sample across our dependent variables, and the sociodemographic and health risks variables. The people sample is majority women around 70 years old in average, with relatively low levels of education and with a low average number of illnesses during childhood. Most people are overweight or obese and make some kind of physical activity more than once a week. Our sample’s diet includes high levels of legumes, beans or egg, and high levels of fruits and vegetables. The consumption of beef, fish, or chicken and of milk and dairy is relatively lower. As far as the dependent variables are concerned, we observe that 17.34% and 66.00% have been diagnosed by a medical doctor of a heart attack and high blood pressure, respectively.

Figs. 2 and 3 show a chronogram plot and a sequence index plot for the 11 types of lifetime trajectories identified in the multichannel sequence and cluster analyses. Chronogram plots show the proportion of people in each status at each age, while sequence index plots display one line for each trajectory of each individual from age 1 to 65–75 (depending on the respondent’s age at the interview), where a change of color symbolizes a change in status for that specific trajectory. All percentages displayed in the figures are weighted.

Type 1, “mostly formal, regular smoker-drinker,” represents 10.9% of our study sample and is characterized by people following a formal employment trajectory, with a few individuals transitioning between formal and informal employment throughout their lives. The main distinctive feature of this type is that all members drank and smoked regularly during long periods of adulthood, starting to drink and smoke, on average, at ages 22 and 20, respectively. Type 2 (“formal, mostly nonsmoker, occasional drinker,” 13.6%) and Type 3 (“formal,



Note: All measures are standardized. PBC: Point Biserial Correlation. HG: Hubert's Gamma. ASW: Average Silhouette width. HC: Hubert's C coefficient.

Fig. 1. Cluster cut-off criteria

Note: All measures are standardized. PBC: Point Biserial Correlation. HG: Hubert's Gamma. ASW: Average Silhouette width. HC: Hubert's C coefficient.

Table 1
Weighted univariate descriptive statistics.

Variable		Mean (SD)	Min	Max	
Age		69.83 (3.14)	65	75	
Number of illnesses at age 15		0.32 (0.58)	0	4	
Variable		%	Variable	%	
Heart attack	Presence	17.34	High blood pressure	Presence	66.00
	Absence	82.65		Absence	34.00
Gender	Female	56.77	Physical activity	1 or less a week	35.97
	Education	Male		43.23	>1 a week
Primary or none		38.58		3+ times a week	35.76
Secondary		38.77		<3 times a week	64.24
	Technical college	10.06	Legumes, beans, or egg	3+ times a week	69.10
	College	12.58		<3 times a week	30.90
BMI	Underweight	1.22	Beef, fish, or chicken	3+ times a week	43.55
	Normal	27.02		<3 times a week	56.45
	Overweight	41.56	Portion of fruits or vegetables	3+ times a week	6.17
	Obese	30.20		<3 times a week	93.83

N = 800.

nonsmoker, nondrinker," 11.3%) are composed of people following stable formal employment trajectories who did not smoke for most of their lives, although some individuals under Type 2 smoked in early periods of adulthood. People under Type 2 started drinking occasionally at around 20 years of age, while people under Type 3, in general, did not drink.

Type 4 ("informal, midlife smoker, occasional drinker"), representing 7.7% of our sample, is characterized by individuals with stable informal employment trajectories, occasional alcohol use, and regular or occasional tobacco use until their mid-40s. Type 5 ("mostly informal, nonsmoker, nondrinker," 7.7%) represents people with an employment trajectory mostly in the informal labor market (with some individuals showing transitions between informal and formal employment in early adulthood) who mostly did not drink or smoke throughout their lives.

Type 6 ("formal/informal, regular smoker, occasional drinker," 9.0%) and Type 7 ("formal/informal, regular smoker, nondrinker," 7.5%) are characterized by constant transitions between formal and informal jobs in adulthood and by regular smokers who started using tobacco roughly in their early 20s. However, they differ in their alcohol consumption trajectory, as people under Type 6 drank occasionally while those under Type 7 did not drink for most of their lives.

Type 8 ("formal/informal, occasional smoker, nondrinker") represents a small proportion of people (2.7%) with employment and alcohol consumption patterns very similar to those of Type 7 but with occasional rather than regular tobacco use. Type 9 ("either formal/informal, mostly nonsmoker, regular drinker," 5.8%), in contrast to the three previous types, is not composed of people moving between formal and informal job positions but of individuals who were either formally or informally engaged with the labor force throughout their lives. Type 9 is also characterized by people who smoked only during early adulthood and drank regularly starting at around age 25.

Finally, Type 10 ("mostly inactive, nonsmoker, occasional drinker," 8.8%) and Type 11 ("mostly inactive, nonsmoker, nondrinker," 15.2%) are characterized by people mostly out of the labor force who did not smoke throughout their entire lives. Type 10 is characterized by people who occasionally drank in their mid-20s, whereas Type 11 is composed of people who did not drink.

Table 2 shows the distribution of the 11 trajectory types across educational levels and gender. Types 2, 3, and 9 have the highest

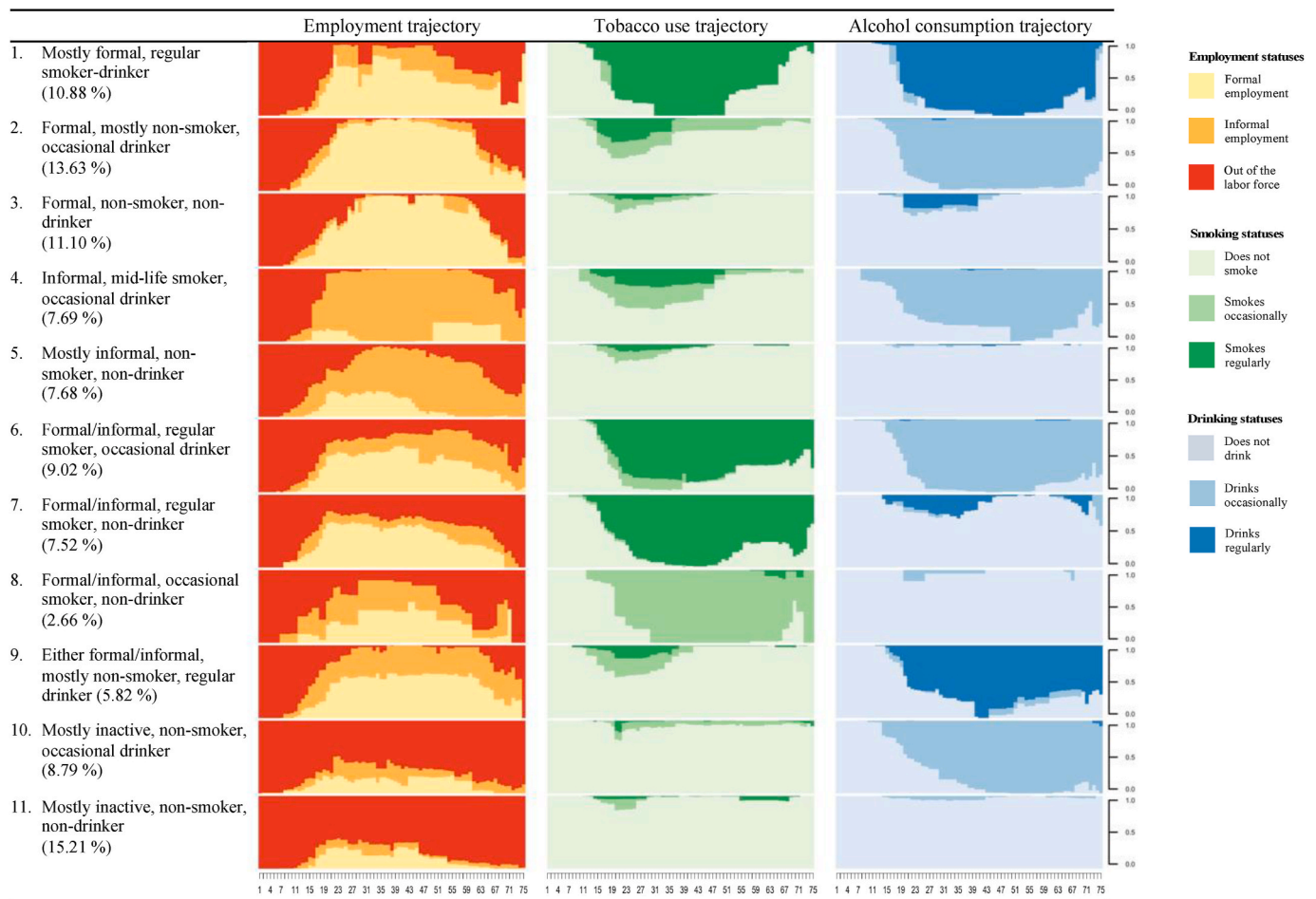


Fig. 2. Chronogram plots of 11 types of weighted lifetime employment, tobacco use and alcohol consumption trajectories.

proportion of college-educated people, while Types 5, 6, 7, 10, and 11 are the most disadvantaged in terms of educational level. More than 90% of the people under Types 10 and 11 are women, while Types 1 and 9 have the highest proportion of men. Table 2 also shows two key variables that might be confounding the studied associations: BMI and childhood health. There are no statistically significant differences in BMI between the trajectory types, although Type 10 has a slightly higher average BMI. Some differences emerge when we observe the number of illnesses that people experienced at age 15. For instance, Type 10 shows a significantly higher average number of illnesses (0.38) compared to Type 8 (0.06).

Lifetime employment, tobacco use, and alcohol consumption trajectories and CVD

The second stage of our analysis tested the association between the lifetime trajectory types and two indicators of CVD: having ever experienced a heart attack and having ever been diagnosed with high blood pressure. Fig. 4 shows the prevalence of both conditions across the types of trajectories. As expected, the general prevalence of heart attacks is significantly lower than that of high blood pressure diagnoses. The most disadvantaged trajectory is Type 1 (“mostly formal, regular smoker-drinker”), which has a high prevalence of both indicators. Types 3 (“formal, nonsmoker, nondrinker”) and 6 (“formal/informal, regular smoker, occasional drinker”) have the lowest prevalence of heart attacks. Type 8 (“formal/informal, occasional smoker, nondrinker”) has the lowest proportion of people ever diagnosed with high blood pressure.

Table 3 shows two weighted logistic regression models: one for the

probability of experiencing a heart attack and one predicting the probability of experiencing high blood pressure. The models included the main independent variable of interest—the 11 trajectory types—and all sociodemographic and health-risk control variables. Results show that all types have a negative association with the probability of experiencing a heart attack. As expected from the bivariate analysis, Type 1 has the highest likelihood of having heart attacks. Types 3 (“formal, nonsmoker, nondrinker”) and 6 (“formal/informal, regular smoker, occasional drinker”) show the largest and most significant associations, reducing the odds of experiencing a heart attack by over 90% relative to those following the Type 1 trajectory. Types 2 (“formal, mostly nonsmoker, occasional drinker”), 5 (“mostly informal, nonsmoker, nondrinker”), 9 (“either formal/informal, mostly nonsmoker, regular drinker”), 10 (“mostly inactive, nonsmoker, occasional drinker”), and 11 (“mostly inactive, nonsmoker, nondrinker”) also have a lower likelihood of having a heart attack. These results show the importance of following a trajectory with no or short use of tobacco throughout one’s life; such a trajectory is even more protective when accompanied by some kind of attachment to the labor force.

Regarding high blood pressure, the largest association was observed for Type 8 (“formal/informal, occasional smoker, nondrinker”), which reduced the odds of being diagnosed with this CVD by 89%. Types 2, 3, 7, 9, and 11 also show protective effects against high blood pressure. All the trajectory types that have a protective health effect are characterized by the nonregular use of alcohol, except Type 9, which has the smallest significant association. The same is true for tobacco use; except Type 7, trajectory types with a protective effect show patterns of little or no tobacco use. It is worth noting that these protective health effects of little alcohol and tobacco use are always accompanied by employment

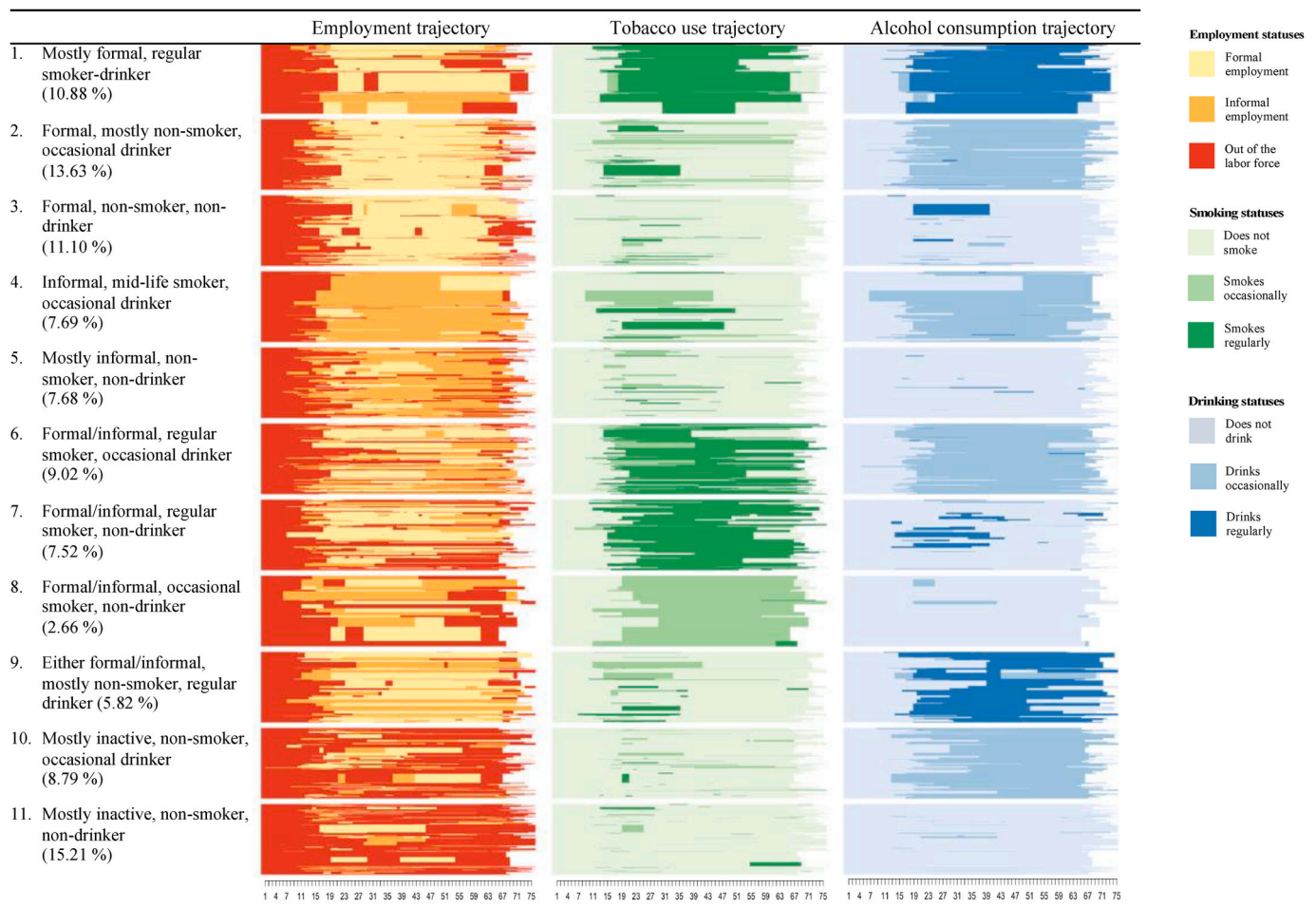


Fig. 3. Sequence index plots of 11 types of weighted lifetime employment, tobacco use and alcohol consumption trajectories.

trajectories with some kind of attachment to the labor market.

For both outcomes, all control variables showed effects in the expected direction: Older age increased the likelihood of heart attacks and high blood pressure, men suffered less high blood pressure and heart attacks after controlling for other factors, a higher educational level reduced the probability of having a heart attack and high blood pressure, and being overweight or obese increased the probability of suffering a heart attack or high blood pressure. Not consuming fruits and vegetables increased the likelihood of being diagnosed with high blood pressure, and consuming little beef, fish, or chicken reduced the probability of having a heart attack.

To make our results more intuitive, we estimated the average marginal effects for each trajectory type over the probability of having experienced a heart attack or being diagnosed with high blood pressure relative to Type 1 (see Fig. 5). As expected from the odds ratio results, Type 3 (“formal, nonsmoker, nondrinker”) had the largest protective effect on the probability of experiencing a heart attack, reducing this probability by 36 percentage points on average (AME = -0.36, $p < .001$). Type 2 (“formal, mostly nonsmoker, occasional drinker”) reduced the probability of experiencing a heart attack by 29 percentage points, all else being equal (AME = -0.29, $p < .005$). This is a relatively large effect compared to, for example, the average marginal effect of being obese (BMI ≥ 30) relative to having a normal weight (BMI = 18.5–24.9) which is, on average, 12 percentage points (AME = 0.12, $p < .007$). Therefore, a formal employment trajectory accompanied by relatively low tobacco use and occasional or no alcohol consumption has a high protective health effect relative to a similar employment trajectory but with regular tobacco and alcohol use.

Types 4 and 5, characterized by a relatively long-term informal employment trajectory, had protective health effects only when there was no alcohol or tobacco use throughout the life course (Type 5). Interestingly, the nonsignificant result of Type 4 suggests that the detrimental effect of informal employment relative to formal employment remains even when a person drinks occasionally and does not smoke. Types 6 and 9, with relatively similar employment trajectories to Type 1, had protective health effects driven by lower alcohol use in the case of Type 6 (AME = -0.36, $p < .000$) and lower tobacco use in the case of Type 9 (AME = -0.28, $p < .009$). Finally, trajectory types characterized by individuals who were inactive for most of their lives (Types 10 and 11), a labor force status known to be detrimental to health (Madero-Cabib et al., 2020), also show protective effects driven by the low tobacco and alcohol use relative to Type 1.

Types 2 and 3 still had protective effects against high blood pressure, reducing the probability of ever being diagnosed with high blood pressure by 30 and 22 percentage points, respectively. However, Types 5 and 6 marginally lost their protective power. It is interesting to note that while Types 7 and 8 were not significantly different from Type 1 with regard to their effect on heart attacks, they significantly reduced the probability of being diagnosed with high blood pressure by 25 (AME = 0.25, $p < .002$) and 39 (AME = 0.39, $p < .007$) percentage points, respectively. Type 10 also lost its protective effect on the likelihood of experiencing heart attacks. Given the associations observed for Types 7 and 8, the distinct alcohol trajectory of these two types relative to Type 1 seems to be driving their protective effect on health.

Table 2
Weighted distribution of education, gender, BMI and Number of Illnesses at 15, by lifetime trajectory type.

Lifetime trajectories types	Education								Female	Total	
	Primary or none		Secondary		Technical College		College				
1. Mostly formal, regular smoker-drinker	12.65	(5.76)	47.71	(16.80)	39.28	(19.31)	0.37	(0.29)	12.71	(5.28)	10.88
2. Formal, mostly non-smoker, occasional drinker	30.44	(7.26)	38.82	(8.45)	3.72	(1.66)	27.02	(12.70)	43.06	(11.08)	13.63
3. Formal, non-smoker, non-drinker	36.80	(9.23)	28.13	(10.83)	4.49	(1.90)	30.58	(12.60)	45.36	(11.07)	11.10
4. Informal, mid-life smoker, occasional drinker	35.33	(10.09)	61.61	(10.84)	2.57	(2.62)	0.50	(0.52)	37.23	(14.98)	7.69
5. Mostly informal, non-smoker, non-drinker	45.86	(7.47)	34.92	(7.18)	10.13	(6.65)	9.09	(5.72)	73.26	(7.48)	7.68
6. Formal/informal, regular smoker, occasional drinker	46.14	(8.18)	40.30	(6.72)	13.17	(8.82)	0.38	(0.39)	57.33	(9.49)	9.02
7. Formal/informal, regular smoker, non-drinker	54.28	(9.68)	36.85	(8.41)	4.26	(2.66)	4.61	(3.19)	56.30	(9.56)	7.52
8. Formal/informal, occasional smoker, non-drinker	22.99	(12.79)	52.97	(16.42)	10.29	(7.37)	13.76	(12.46)	79.48	(11.06)	2.66
9. Either formal/informal, mostly non-smoker, regular drinker	30.76	(8.53)	36.84	(9.39)	5.96	(5.39)	26.44	(11.23)	22.34	(7.85)	5.82
10. Mostly inactive, non-smoker, occasional drinker	48.93	(11.27)	34.23	(8.52)	16.04	(11.37)	0.80	(0.81)	99.78	(0.24)	8.79
11. Mostly inactive, non-smoker, non-drinker	51.22	(8.34)	31.43	(10.44)	1.74	(1.19)	15.61	(11.80)	94.70	(3.02)	15.21
Total	38.58	(3.24)	38.77	(3.01)	10.06	(2.95)	12.58	(3.81)	56.77	(4.25)	100.00

Lifetime trajectories types	BMI		Average Number of Illnesses at 15		Total
	1. Mostly formal, regular smoker-drinker	27.07	(5.10)	0.25	
2. Formal, mostly non-smoker, occasional drinker	27.01	(4.03)	0.21	(0.45)	13.63
3. Formal, non-smoker, non-drinker	27.82	(4.14)	0.15	(0.44)	11.10
4. Informal, mid-life smoker, occasional drinker	28.32	(3.97)	0.26	(0.53)	7.69
5. Mostly informal, non-smoker, non-drinker	27.90	(4.38)	0.31	(0.65)	7.68
6. Formal/informal, regular smoker, occasional drinker	27.63	(4.38)	0.20	(0.53)	9.02
7. Formal/informal, regular smoker, non-drinker	26.90	(4.89)	0.30	(0.60)	7.52
8. Formal/informal, occasional smoker, non-drinker	26.80	(4.99)	0.06	(0.24)	2.66
9. Either formal/informal, mostly non-smoker, regular drinker	27.21	(3.99)	0.22	(0.62)	5.82
10. Mostly inactive, non-smoker, occasional drinker	29.07	(5.87)	0.38	(0.69)	8.79
11. Mostly inactive, non-smoker, non-drinker	27.76	(4.65)	0.23	(0.50)	15.21
Total	27.67	(4.59)	0.24	(0.54)	100.00

Note: Standard errors in parentheses.

Discussion and conclusion

Adopting a life course approach, this study examined the associations of simultaneous employment, tobacco use, and alcohol consumption trajectories with the development of CVDs. Our results highlight the need to move beyond the analysis of the effects of single-point measurements of employment, smoking, or drinking status on CVDs and toward the study of long-term life trajectories in these domains. By examining such trajectories, we were able to evaluate the divergent health effects of different trajectory types, which reflect longer or shorter exposure to formal or informal employment, as well as regular versus occasional tobacco use and alcohol consumption. The focus on long-term trajectories instead of single-point statuses also allowed us to observe whether employment, smoking, and drinking statuses across different stages of the life course (especially in adulthood) have different impacts on CVDs.

Our results are consistent with those of previous studies on the association between CVD and long-term experiences in the single domains of employment (van Hedel et al., 2016), tobacco use (Chen et al., 2019), and alcohol consumption (Ortolá et al., 2019). Our findings also reveal that simultaneous experiences in these domains have different effects on the cardiovascular outcomes evaluated. Specifically, the health advantage of being strongly attached to the labor market through a full-time stable and formal job across adulthood was not able to offset the risk of being a regular smoker or drinker during long periods of adult life. Moreover, our results show that maintaining simultaneous trajectories as nonsmokers and nondrinkers was associated with greater health benefits despite a weak attachment to the labor market during adulthood or having worked permanently in informal jobs.

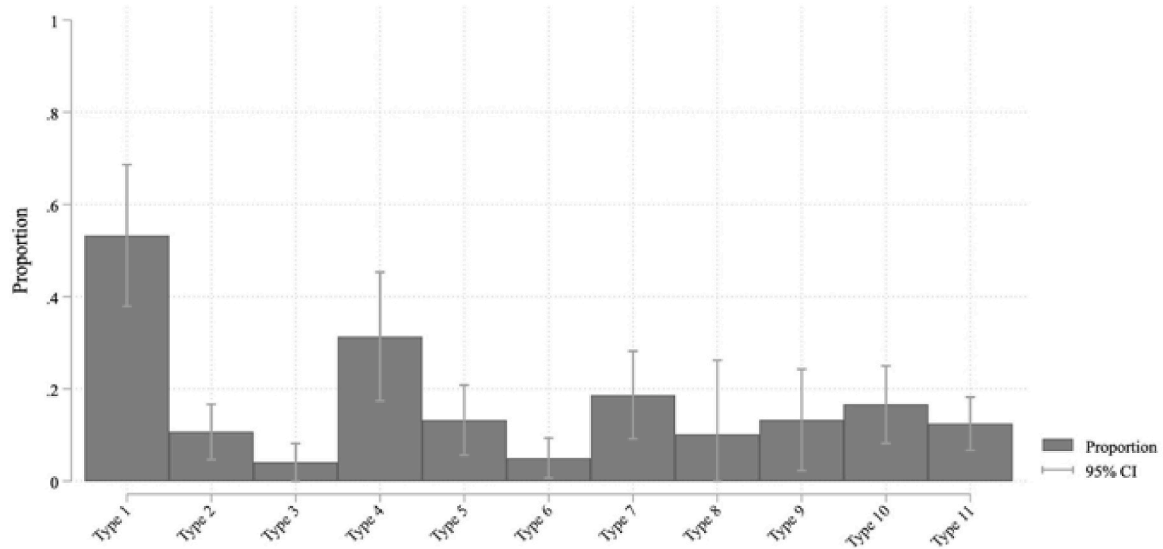
Our study shows consistent results across CVD outcomes. However, as suggested by Bell et al. (2017), researchers should be cautious when evaluating different CVDs for which different mechanisms might explain the relationship with employment, tobacco use, and alcohol use trajectories or that might be more or less sensitive to changes in these life domains. For example, we found that formal/informal employment

trajectories accompanied by tobacco use seem to matter more for high blood pressure than for heart attacks, but being permanently out of the labor force with low alcohol and tobacco use and being attached to the labor force with high tobacco use seem to matter more for heart attacks than for high blood pressure. Compared to hypertension, the diagnosis of heart attacks might be more accurate and depend less on factors such as access to health care. Since 2006, nevertheless, hypertension has been covered by the Chilean universal health care system, which provides access to diagnosis and treatment for all Chilean citizens. However, we acknowledge that participants with informal or no employment are less likely to be diagnosed with hypertension.

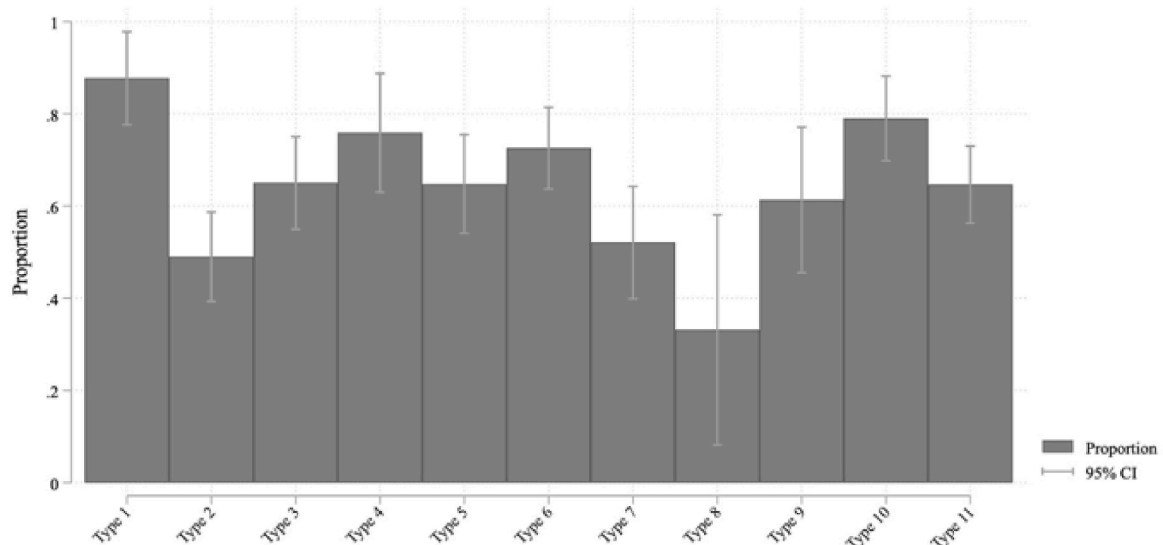
Our findings have important implications for both individual and population strategies to prevent CVDs. In terms of individual strategies, these results might be useful for health professionals in discussing the benefits of a tobacco- and alcohol-free life with their patients. These findings can also contribute to improving cardiovascular health policies that take into account the fact that CVDs are chronic conditions that strongly depend on previous individual experiences in multiple life domains from infancy until old age. In particular, population-wide interventions that affect price, marketing, and physical availability are the most cost-effective measures for controlling both tobacco and alcohol consumption in the general population and have been listed by the WHO as among the “best buys” for middle- and low-income countries (Bambas et al., 2020; WHO, 2017). Future research should address how current and prospective changes in the prevalence of tobacco use and alcohol consumption, as well as in the structure of the labor market in Chile, are able to modify the effect of the examined lifetime trajectories on CDV among younger cohorts. In this way we could understand how these relationships vary across generations.

Public health policies have a key role in influencing both the duration of exposure and the timing of the life course in which individuals are exposed to different employment, smoking, and drinking statuses. Our results suggest that renewed efforts to prevent CVDs in the population could focus on health policies encouraging people to abstain from tobacco and alcohol throughout their adult life while maintaining

(A) Heart attacks



(B) High blood pressure



Note: Lifetime trajectory types names: Type 1=‘Mostly formal, regular smoker-drinker’; Type 2=‘Formal, mostly non-smoker, occasional drinker’, Type 3 Formal, non-smoker, non-drinker’; Type 4=‘Informal, mid-life smoker, occasional drinker’; Type 5=‘Mostly informal, non-smoker, non-drinker’; Type 6=‘Formal/informal, regular smoker, occasional drinker’; Type 7=‘Formal/informal, regular smoker, non-drinker’; Type 8=‘Formal/informal, occasional smoker, non-drinker’; Type 9=‘Either formal/informal, mostly non-smoker, regular drinker’, Type 10=‘Mostly inactive, non-smoker, occasional drinker’, Type 11=‘Mostly inactive, non-smoker, non-drinker’.

Fig. 4. Weighted distribution of CVD across types of lifetime employment, tobacco use, and alcohol consumption trajectories

Note: Lifetime trajectory types names: Type 1 = ‘Mostly formal, regular smoker-drinker’; Type 2 = ‘Formal, mostly non-smoker, occasional drinker’, Type 3 Formal, non-smoker, non-drinker’; Type 4 = ‘Informal, mid-life smoker, occasional drinker’; Type 5 = ‘Mostly informal, non-smoker, nondrinker’; Type 6 = ‘Formal/informal, regular smoker, occasional drinker’; Type 7 = ‘Formal/informal, regular smoker, non-drinker’; Type 8 = ‘Formal/informal, occasional smoker, non-drinker’; Type 9 = ‘Either formal/informal, mostly non-smoker, regular drinker’, Type 10 = ‘Mostly inactive, non-smoker, occasional drinker’, Type 11 = ‘Mostly inactive, nonsmoker, non-drinker’.

Table 3
Weighted logistic regression models over the probability of experiencing CVD (odds ratios).

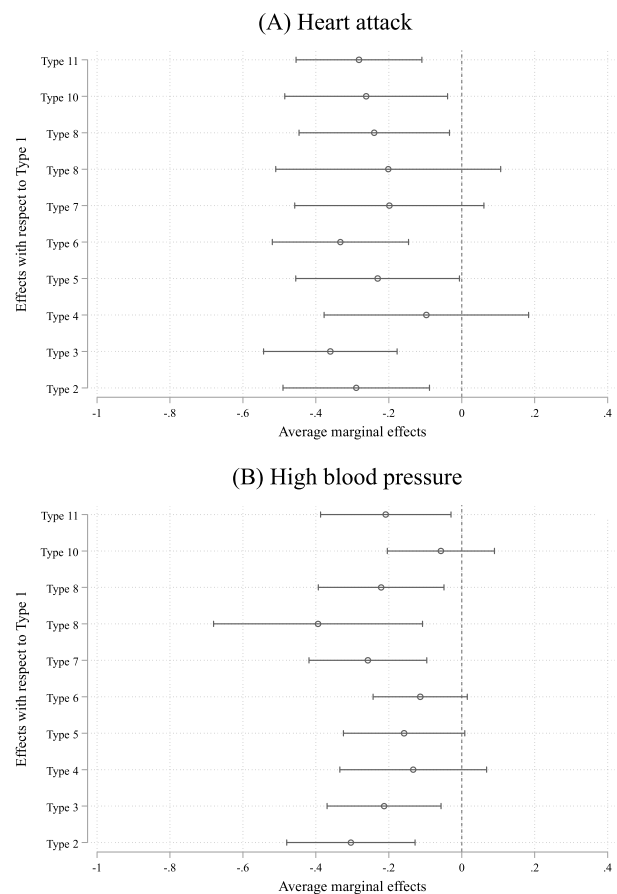
	Heart attack		High blood pressure	
	Coef.	SE	Coef.	SE
Lifetime trajectories types (ref = Type 1. Mostly formal, regular smoker-drinker)				
Type 2. Formal, mostly non-smoker, occasional drinker	0.14**	(0.09)	0.17**	(0.09)
Type 3. Formal, non-smoker, non-drinker	0.05***	(0.03)	0.26*	(0.14)
Type 4. Informal, mid-life smoker, occasional drinker	0.59	(0.46)	0.41	(0.26)
Type 5. Mostly informal, non-smoker, non-drinker	0.24*	(0.17)	0.35	(0.20)
Type 6. Formal/informal, regular smoker, occasional drinker	0.08***	(0.05)	0.45	(0.22)
Type 7. Formal/informal, regular smoker, non-drinker	0.31	(0.24)	0.21**	(0.11)
Type 8. Formal/informal, occasional smoker, non-drinker	0.31	(0.31)	0.11**	(0.08)
Type 9. Either formal/informal, mostly non-smoker, regular drinker	0.23*	(0.16)	0.25**	(0.13)
Type 10. Mostly inactive, non-smoker, occasional drinker	0.19*	(0.14)	0.65	(0.37)
Type 11. Mostly inactive, non-smoker, non-drinker	0.15**	(0.09)	0.27*	(0.15)
Socio-demographics				
Age	1.07	(0.06)	1.05	(0.06)
Gender (ref = Women)				
Men	0.86	(0.40)	0.70	(0.20)
Educational level (ref = primary or none)				
Secondary	0.57	(0.19)	0.65	(0.19)
Technical college	0.92	(0.65)	1.00	(0.50)
College	0.93	(0.61)	0.52	(0.23)
Health risks				
Body mass index (ref = normal)				
Underweight	0.29	(0.37)	0.22	(0.20)
Overweight	3.11*	(1.46)	2.04*	(0.70)
Obese	4.05**	(1.99)	2.66*	(1.07)
Physical activity (ref = more than once a week)				
Once a week or less	0.82	(0.30)	0.97	(0.20)
Food frequency (ref = three times a week or more)				
Milk and dairy two times a week or less	1.89	(0.74)	0.68	(0.19)
Legumes, beans, or egg two times a week or less	0.85	(0.32)	0.89	(0.25)
Beef, fish, or chicken two times a week or less	0.26***	(0.09)	0.77	(0.20)
One portion of fruits or vegetables two times a week or less	0.58	(0.34)	3.02**	(1.17)
Number of illnesses at age 15	1.52*	(0.27)	2.13***	(0.40)
N	800			

Note: *p < .05, **p < .01, ***p < .001. Standard errors in parentheses.

formal employment.

Our study is the first to examine the simultaneous association of lifetime employment, tobacco use, and alcohol consumption trajectories with the development of CVDs in the context of a high level of informal employment and using high data collection standards. We used a comprehensive life history dataset and a sampling method that provides representative results for older adults aged 65–75 in the city of Santiago. We adjusted the results for sociodemographic, lifestyle, and clinical variables, which added robustness to our statistical models.

However, our study is not without limitations. Notably, exposure to smoking and alcohol consumption might have been insufficiently measured because its indicator was based on frequency questions and did not include aspects such as the number of cigarettes or amount of alcoholic drinks consumed per occasion and the presence of dependence symptoms. Nevertheless, the same questions and field protocols were



Note: 95% confidence intervals are displayed. Average marginal effects estimates based on models shown in Table 2. Lifetime trajectory types names: Type 1=‘Mostly formal, regular smoker-drinker’; Type 2=‘Formal, mostly non-smoker, occasional drinker’; Type 3=‘Formal, non-smoker, non-drinker’; Type 4=‘Informal, mid-life smoker, occasional drinker’; Type 5=‘Mostly informal, non-smoker, non-drinker’; Type 6=‘Formal/informal, regular smoker, occasional drinker’; Type 7=‘Formal/informal, regular smoker, non-drinker’; Type 8=‘Formal/informal, occasional smoker, non-drinker’; Type 9=‘Either formal/informal, mostly non-smoker, regular drinker’, Type 10=‘Mostly inactive, non-smoker, occasional drinker’, Type 11=‘Mostly inactive, non-smoker, non-drinker’.

Fig. 5. Weighted average marginal effects over the probability of experiencing CVD across types of lifetime employment, employment, tobacco use, and alcohol consumption trajectories

Note: 95% confidence intervals are displayed. Average marginal effects estimates based on models shown in Table 2. Lifetime trajectory types names: Type 1 = ‘Mostly formal, regular smoker-drinker’; Type 2 = ‘Formal, mostly nonsmoker, occasional drinker’; Type 3 = ‘Formal, non-smoker, non-drinker’; Type 4 = ‘Informal, mid-life smoker, occasional drinker’; Type 5 = ‘Mostly informal, non-smoker, nondrinker’; Type 6 = ‘Formal/informal, regular smoker, occasional drinker’; Type 7 = ‘Formal/informal, regular smoker, non-drinker’; Type 8 = ‘Formal/informal, occasional smoker, non-drinker’; Type 9 = ‘Either formal/informal, mostly non-smoker, regular drinker’, Type 10 = ‘Mostly inactive, non-smoker, occasional drinker’, Type 11 = ‘Mostly inactive, non-smoker, non-drinker’.

used for all participants, which leads us to conclude that any measurement errors are mostly nondifferential—that is, they occurred proportionally the same for all. This type of error might lead our results toward the null hypothesis or bias our results toward an underestimation of the

true effects of the association. This might be important for the types in which we obtained results with borderline or no statistical significance.

Our results must be interpreted in the context of the epidemiological stages of the tobacco epidemic. In Chile, the prevalence of cigarette smoking is still higher among more educated people (Bambas & Alcántara, 2016, pp. 137–147), but we expect this to change in the near future. Thus, it is important to repeat and validate analyses like this over time. Moreover, our measurement of diet and physical activity included a limited set of questions that might not capture dimensions that are known to be associated with CVDs (e.g., energy intake, consumption of olive oil and nuts, and sedentary time); therefore, our results can be subject to residual confounding. Additionally, these indicators, together with BMI, were measured cross sectionally and not as time-varying variables. This could affect our results as we are not able to capture changes in these health risks longitudinally. However, as previous research has shown in different populations, BMI, diet, and physical activity trajectories are pretty stable among older adults (Dhana et al., 2016; Mok, Khaw, Luben, Wareham, & Brage, 2019). Future research with rich longitudinal data could explore cooccurring trajectories for these health risks, assessing their association with CVD later in life.

Also, although the retrospective life-history-calendar questionnaire used in this study addresses different key biases of autobiographical memory (see Supplemental Material, pp. 2–3), this longitudinal survey is always less reliable than a panel survey. Also, self-reports of tobacco use and alcohol consumption might be subject to social desirability bias. Finally, the sample used in this study is representative of older individuals aged 65–75 in Santiago, which is an urban area. Thus, our sample is not representative of individuals older than 75 or the elderly living in rural geographical areas in Chile.

Further research is needed to expand these analyses to other chronic conditions, such as diabetes, cancer, and musculoskeletal diseases. Future investigations can evaluate the population impact of current and future public policies that affect employment, tobacco use, and alcohol consumption at different moments of the life course, putting especial emphasis on how the timing of certain events or behaviors at specific stages throughout the life course matter for CVD. Here, we mostly explore long-term trajectories throughout a long-life sequence. Looking at trajectories during specific life stages might help to better elucidate how timing matters.

Overall, our results stress the importance of a life course approach in improving the understanding and prevention of CVDs and their determinants.

Ethical statement

We, the authors of this manuscript, certify that we do not have any actual or potential conflict on ethical standards, financial and non-financial interests and compensations, ethical approvals, personal relationships with people or organizations, which could inappropriately influence, or be perceived to influence, our work.

Declaration of interest

Declarations of interest: None.

Author contributions

Ignacio Madero-Cabib, Ariel Azar, and Claudia Bambas planned the study and wrote the paper. Ignacio Madero-Cabib and Ariel Azar performed the data analysis.

CRedit authorship contribution statement

Ignacio Madero-Cabib: Conceptualization, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Visualization, Writing - review & editing. **Ariel Azar:**

Conceptualization, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Visualization, Writing - review & editing. **Claudia Bambas:** Conceptualization, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Visualization, Writing - review & editing.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.ssmph.2021.100737>.

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