Directed Acyclic Graph (DAGs) for trajectories of childhood adversities, biological age, and health in later life.

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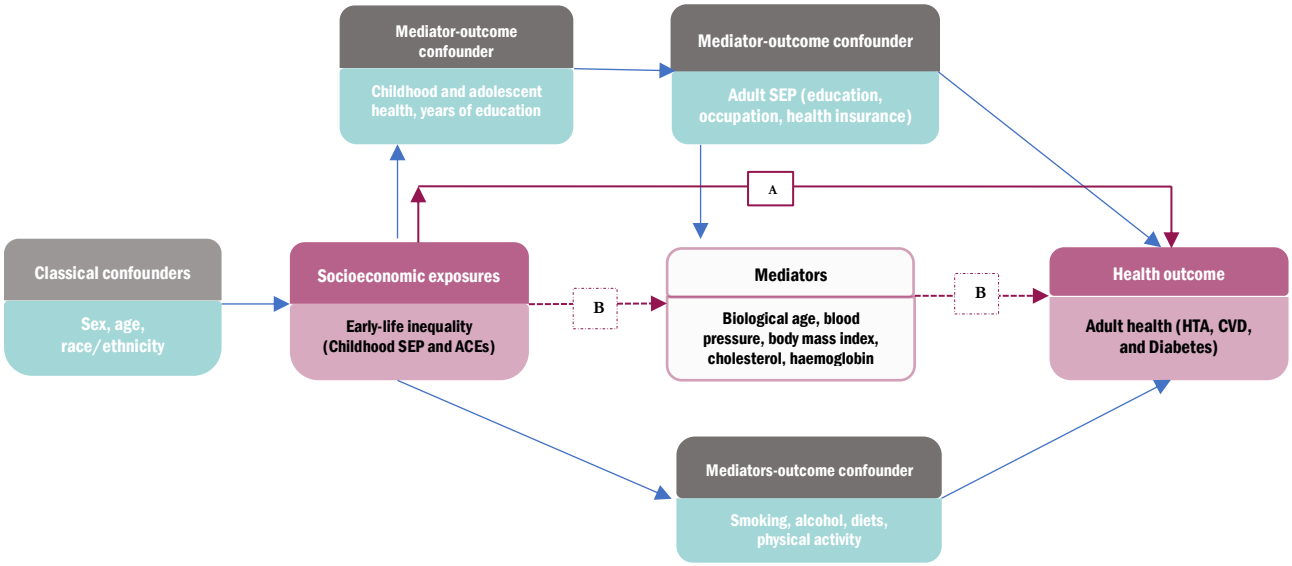
The Direct Acyclic Graph (DAG) is a causal diagram to represent the assumptions about the interrelationships between exposures, outcomes, mediators, and mediator-outcome confounder. A mediator is an intermediate variable on a path between the exposure and outcome. In other words, a mediator is caused by the exposure and in turn causes the outcome. DAGs are useful to select the most appropriate set of variables, avoid overadjustment and maximize model accuracy[1].

Figure 1 illustrates a Directed Acyclic Graph (DAGs) to help to represent the assumptions about the interrelationships between exposures (adverse childhood experiences and childhood SEP), variables of interest or outcomes (adult cardiometabolic diseases), mediators (biological markers and Biological Age), and different mediators-confounders within mechanistic studies of exposures and outcomes. The primary research question of this research is whether early-life inequality is associated with health in later life through biological processes among Colombian population.

Figure 1. Direct effect (A) and indirect effect (B) of childhood socioeconomic exposures on adult health outcomes guides this research.



Adaptation from A. van Zwieten et al. / Journal of Clinical Epidemiology 149 (2022) 127e136.

Briefly explained, the total effects of childhood SEP include the classic potential confounders (age, sex, and race) and mediators-outcome confounders (including childhood and adolescent health, adult SEP, and lifestyle factors). The mediators include biological age, hemoglobin, triglycerides, glucose, cholesterol, blood pressure, waist circumference, and body mass index. We know that lower childhood SEP at one-time point is likely to cause poorer health at the next time point (e.g., adolescence or adulthood), while poorer health at one point is likely to increase socioeconomic inequality at the next stage of the life course. This DAGs allowed delineate between confounders and mediators for appropriate covariate selection and explicitly consider time-evolving versions of SEP and health across sensitive moments of the life course (e.g., microbiome, childhood, adulthood).

In this study, using data from SABE aging survey participants, we investigate the mediating role of biological age behind the relationship between childhood socioeconomic position and adult health. The main purpose is to contribute with evidence of likely or unlikely direct and indirect biological pathways of cardiometabolic diseases in the Colombian population, to inform life-course based interventions to prevent unhealthy aging and contribute to transform debate about exposome within health and social protection systems in the Latin America and Caribbean region.

Social exposures

ACE and childhood SEP were used as measures of exposure to early-life circumstances. ACE and SEP were available in the adverse childhood experience questionnaire of the SABE survey. The ACEs measure was composed of the following dimensions: emotional abuse, poor food environment, poor health status, early chronic infections, domestic violence, and migration due to armed conflict. Low childhood SEP at 15 years old was coded in two categories: exposed (to financial hardship, economic deprivation, or lower family SEP) or not exposed. This approach was validated in previous work using SABE data[2,3] and more generally in surveys of older adults[4].

Mediators-outcome confounders

We assessed seven mediator factors. Socioeconomic strata were coded as low adult SEP in two categories: Yes or no. educational attainment was coded in three categories: low (not schooling, incomplete primary school, completed primary school), intermediate (incomplete high school and finished high school), and high (college or university). Health insurance coverage was coded in two categories: Insured, uninsured. Social policies were based on two questions to explore if older people were exposed to the benefits of the two cash transfer programs" "Have you received the benefits of Colombia Adulto Mayor?" and "Are you beneficiary of the nutrition program?": yes or no. Smoking was regrouped as binary variable indicating if the participant had ever smoked or drunk (yes or no). This variable was filtered by quite smoking age to differentiate between current and former smoker. Alcohol consumption was coded in two groups: non-drinker and drinker (social and moderate drinker). Elevated BMI was calculated from height and weight using the formula: BMI =weight (kg) / height (m) x height (m). BMI was organized into three levels: "below 25 normal", "between 25-30 -Overweigh", and" "above 30-Obesity".

Biological Age and biomarkers

The KDM Biological Age and HD were estimated using a set of eight biomarkers measuring two physiological systems (metabolic and cardiovascular): LDL, HDL, glycated hemoglobin (HbA1C), total cholesterol, fasting glucose, triglycerides, waist circumference, and body mass index.

Outcomes

SABE provides self-reported questions about chronic diseases, treatments, and medications. The cardiometabolic diseases were self-reported during the interview. Self-reported questions concerned whether "you have been diagnosticated or received treatment for x chronic conditions defined diseases status". (a) Cardiovascular diseases (CVD) were coded in the data by any affirmative response to "having had a heart attack", "having had angina" or" "thrombosis"; (b) Diabetes Mellitus (DM); and (c) Hypertension (HTA) were coded by an affirmative response to the question "have you been diagnosticated or received treatment for diabetes/HTA?". Obesity was coded based on BMI >=30 (Yes or no).

Classical confounders

Potential confounding factors were sex, chronological age, and ethnicity. Ethnicity was regrouped into four main groups "indigenous", "white", "mestizo", "afro Colombian", and "other".

References

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