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RESEARCH ARTICLE

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Family size and cardiovascular disease incidence: a population-level association study

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ABSTRACT

Aim: To investigate the population-level association between family size and cardiovascular disease (CVD) incidence, focusing on broad patterns rather than causal mechanisms or individual-level effects.

Methods: Population level correlations of family size to CVD incidence were analyzed with scatter plots, simple regression, partial correlation and multivariate regression separately. Aging, economic affluence, obesity and urbanization were incorporated in models as potential confounders.

Results: Globally, family size negatively correlated to CVD incidence rate. This relationship remained in partial correlation analyses when controlling for confounders. Stepwise multiple regression revealed that family size may be the most significant predictor of CVD incidence.

Conclusions: Large family size is significantly associated with lower cardiovascular disease (CVD) incidence, potentially due to biological, psychological, and social factors. However, as the data are cross-sectional, this relationship should be interpreted as correlational rather than causal. The association appears more pronounced in developing countries, where contextual factors may amplify its effects.

PLAIN LANGUAGE SUMMARY

This study looked at how family size may affect the risk of cardiovascular disease (CVD) worldwide. The researchers analyzed data to see if having more family members is linked to a lower risk of CVD. They also considered other factors that could affect this link, such as aging, income, obesity, and living in urban areas.

The results showed that people in larger families tend to have a lower risk of developing CVD. This connection remained strong even after taking other factors into account. The study found that family size was the most important factor related to CVD risk.

The researchers suggest that larger families may protect against CVD by providing emotional support, reducing stress, and creating stronger social connections. For example, family members often encourage healthy habits, such as eating well and staying active. This protective effect was found to be greater in developing countries, where family ties often play a stronger role in daily life. Overall, the findings highlight the importance of family dynamics in maintaining heart health and reducing the risk of CVD.

ARTICLE HIGHLIGHTS

- This study explores the population-level association between family size and cardiovascular disease (CVD) incidence across countries worldwide.
- A significant negative correlation was found between family size and CVD incidence, suggesting that larger families are associated with lower CVD risk.
- The inverse relationship remained strong after adjusting for confounding variables, including aging, economic affluence, obesity, and urbanization.
- Stepwise multiple regression identified family size as the most significant predictor of CVD incidence among the variables studied.
- The protective effect of larger families was more pronounced in low- and middle-income countries and developing regions.
- Potential mechanisms include enhanced psychological well-being, greater social support, and increased opportunities for health-promoting behaviors in larger families.
- These findings highlight the importance of considering family dynamics in public health planning and CVD prevention strategies.
- Further longitudinal research is needed to explore causal pathways and validate these associations at the individual level.

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1. Introduction

Cardiovascular disease (CVD) is a cluster of health conditions affecting the heart and blood vessels. Worldwide, around 17.9 million people die of CVDs each year [1], which accounts for 32% of global deaths. Globally, CVDs are the leading cause of death and reduced quality of life [1]. CVD burden has been largely attributed to modifiable and preventable behavioral risk factors, which interact with genetic background and external environment [2].

In the past decades, it has been well established that CVD is a condition associated with life-course [3]. Most CVDs are preventable and partially reversible by addressing behavioral risk factors such as physical inactivity [1], unhealthy diet [4] and weight/obesity [5]. These behavioral risk factors have been considered major causes for CVD morbidity and mortality [6]. Family size has been considered vital to providing life-long health promotions to family members by addressing behavioral risks for developing cardiovascular diseases and comorbidities [7,8]. Studies into the protective role of large family size in promoting family members' health share a common interpretation; the correlation between family size and psychosocial support/well-being. Increases in psychological well-being due to larger family size has previously been established a protective factor for diseases such as cancer [9].

Rapid industrialization has seen the human birth rate decline [10]. Therefore, more people grow up in reduced core family sizes (parents only) with no or few siblings and play mates [10]. In retrospect, human cooperative breeding and alloparental care paved the way for the human race to flourish [11]. The discrepancy between how modern humans grow up compared to our evolutionary ancestors (i.e., reduced family sizes) has been considered a risk factor for mental health [12,13] and cancers in the modern population [8].

Total Fertility Rate (TFR), also called sibship size, has been controversially correlated with CVDs in single-parents, both parents and children [14,15]. By measuring the total live births to a female [16,17], TFR has been increasingly used to index family size in demographic studies [18,19]. In this study, the primary aim of this study is to explore the association between family size (indexed by total fertility rate) and CVD incidence at the population level, without attempting to establish causation or individual-level relationships. This aim was examined through analyzing the role of family size in predicting CVD incidence rate with the most recent country level data published by international organizations. Confounding effects of aging, economic affluence, obesity and urban living advantages on the family size-CVD correlation were incorporated while analyzing the statistical independence of family size on CVD incidence.

2. Materials and Methods

2.1. Data selection and data sources

With reference to the previous publications [4,20,21], six variables (independent, dependent and confounders) were chosen for analysis in this observational study:

1. Family size, the independent variable, was represented by Total Fertility Rate (TFR) in 2017, obtained from the World Bank database [22]. In this study, TFR is used as a proxy for family size and is defined as the average number of children born to a woman over her lifetime. TFR was chosen for its widespread availability and consistency across countries, making it a reliable population-level indicator in ecological studies. However, we acknowledge that TFR does not capture all aspects of family dynamics, such as extended family structures or intergenerational interactions.
2. The CVD incidence rate, the dependent variable, was derived from 2017 data published by the Institute for Health Metrics and Evaluation at the University of Washington [23]. It measures the number of new CVD diagnoses per 100,000 people in 2017.
   Previous studies have associated aging, affluence [24], obesity [5,25], and urbanization [26] with CVD. These factors may compete with family size in predicting CVD incidence. Consequently, they were included as confounding factors in this study. The data sources and detailed rationales for incorporating these four variables into the analysis are described below.
3. Aging, indexed with the life expectancy at 65 years old (Life $e_{(65)}$) published by the United Nations Statistics Division [27]
   Aging significantly affects the heart and arterial system, increasing the risk of developing CVDs [28]. For individuals aged 65 and older, age becomes a major risk factor for the onset of CVD [29].

4. Economic affluence was expressed by per capita gross domestic product purchasing power parity (GDP PPP) published by the World Bank [16]
   GDP PPP was recorded in current international $ in 2014 and has been commonly used as the proxy of economic affluence. CVDs have been associated with economic affluence and as such have considered a "Western disease" or a "disease of affluence" [30].
5. Obesity prevalence rate indicated the percentage of the adult population (18+ years) with a Body Mass Index ≥ 30 kg/m^2 in 2014 [31]. Obesity poses multifactorial health challenges which contribute directly (and indirectly) to CVD incidence through shared comorbidities, such as hypertension, type 2 diabetes, dyslipidaemia, and atherosclerosis [5].
6. Urbanization was indexed through the percentage of total populations currently living in urban areas, published by the World Bank [32].

In this study, urbanization refers to the process in which changing to an urban lifestyle leads to a lack of physical exercise and social engagement. In 2014, despite higher levels of education and health care services, global populations increased their intake of less nutritious food, gluten, processed meat, salt, fat, sugar and alcohol. In previous research, an urban lifestyle has been associated with complex risk factors for chronic diseases, including CVD [33].

The whole "country" list, which is comprised of 217 data reporting units, was downloaded from the World Bank database. The most recent "country"-specific CVD incidence rates and TFRs in 2017 were matched to the corresponding country on the World Bank country list. Each "country" is treated as a research subject across the different data analyses. Countries included for analyses with each variable of interest differed slightly due to missing information within the current data available through international agencies.

The confounding variables of aging ($e_{(65)}$), affluence (GDP PPP), obesity and urbanization were backdated to 2014 because of their potentially delayed effect on CVD incidence. The rationale for this decision came from the pathophysiology of CVD as a delayed-onset disorder, in which it may take years for environmental risk factors to affect CVD development. For instance, when a person becomes 65 years old, he/she may not develop CVD immediately. To accurately analyze the independent relationship between family size and CVD incidence, it is essential to consider the time-lag between the impact of confounding factors and the onset of CVD. Therefore, using 2014 data for confounding factors such as aging, GDP, obesity, and urbanization while analyzing 2017 CVD incidence data assumes that these factors require time to affect health outcomes. Although a three-year period may seem short for CVD development, this timeframe aligns with the onset-latency often observed in chronic diseases. Preliminary analyses of 2014 data on confounding variables revealed that each was highly correlated with the same data from other years, indicating that using 2014 data would yield results similar to those obtained using data from different years.

2.2. Data analysis

To examine the role of family size in determining CVD incidence, the analysis proceeded in six steps after referring to the previous quantitative studies [21,34,35]:

1. Bing© within MS Excel® 2016 was used to integrate the countries into a global geographic map where each country was blue-contrasted depending on their family sizes. Countries were also labeled with their ISO codes for ease of identification.
2. Scatter plots were produced in MS Excel® 2016 for exploring and visualizing the correlation between family size and CVD incidence at the country level. Additionally, the scatter plots produced were used to examine data quality and variable distributions.
   Raw data (not log-transformed) were used for geo-mapping family size and generating the scatter plots in Excel (Microsoft® 2016).
   Prior to the analyses of the relationship between family size and CVD incidence rate, all six variables were not log-transformed (ln). However, scatterplots displayed curvilinearity of the data distribution. Accordingly, to increase homoscedasticity, all six variables were log-transformed. The data analyses proceeded with

SPSS v. 28 in four steps; assessing the correlation between family size and CVD incidence rate globally and regionally:

3. Pearson's and Spearman's Rank correlations were used to examine the strength and direction of associations between any pair of the six variables (family size, CVD incidence, aging, economic affluence, obesity prevalence and urbanization).
4. Pearson's partial correlation was performed to explore the independent correlation between family size and CVD incidence rate while controlling for aging, economic affluence, obesity and urbanization.
5. Standard multivariate linear regression (enter modeling) was performed to analyze the respective predictive effects of family size, aging, GDP PPP, obesity and urbanization on CVD incidence. Subsequently, stepwise linear regression was conducted to sort and rank the predictors which significantly predicted CVD incidence.
   To see if and how much family size influenced predictors of CVD incidence in both enter and stepwise models, family size was "added/incorporated" and then "not added/incorporated" as a predicting variable for both the regression analyses.
6. The 217 countries were also grouped by different classification criteria to explore the regional relationship between family size and CVD rate with Pearson's r and Spearman's Rho. Classifier variables were operationalized as follows:

1. The World Bank income classifications: low income, low-middle income, upper middle income and high income;
2. The developed and developing countries defined by the United Nations' common practice;
   To analyze the WHO's statement that low- and middle-income countries (LMIC) take more than 75% of CVD deaths worldwide [1], low- and low-middle and upper-middle- income countries (LMIC) were clustered to create a new country grouping (LIMIC). The coefficients between family size in LMIC and high-income countries were explored separately for coefficient comparison via Fisher's r-to-z transformations. The same comparison approach was also conducted to explore the difference between the coefficients (family size and CVD incidence) in developed and developing countries.
3. The WHO regional classifications: Africa (AFR), Americas (AMR), Eastern Mediterranean (EMR), Europe (EU), South-East Asia (SEAR) and Western Pacific (WPR);
4. "Countries" clustered based on their geographic distributions, economic affluence levels and cultural backgrounds. We analyzed the correlations in the eight country groupings: the Arab World, the Asia-Pacific Economic Cooperation (APEC), Asia Cooperation Dialogue (ACD), English as the official language (government websites), Latin America, Latin America and the Caribbean (LAC), Organization for Economic Co-operation and Development (OECD) and Southern African Development Community (SADC).

The significance of the correlations in the above data analysis models were reported at three levels ($p < 0.05$, $p < 0.01$ and $p < 0.001$).

3. Results

Figure 1 shows global family sizes, with larger families (darker blue contrast in the geo-map) centralized to Africa and some regions of the Middle East. Worldwide, the average family size is 4.7, and the largest and smallest family sizes are in Nigeria (9.1) and British Virgin Island (2.9) respectively (Figure 1).

Scatter plots of the raw data as illustrated in Figure 2, reveal that family size accounts for 52.28% of the variance in CVD incidence ($R^2 = 0.5228$, $r = -0.732$, $n = 186$, $p < 0.001$). The correlation pattern between family size and CVD incidence presents a third-order polynomial relationship, with a strong negative correlation observed ($r = -0.723$, $p < 0.001$, $n = 186$). Notably, the statistical relationship identified in the scatter plots does not significantly differ from any of the family size-CVD correlation coefficients determined in the bivariate correlation analyses using log-transformed data (Table 1).

Table 1 shows that globally family size retains a significant negative correlation to CVD incidence in Pearson's and Spearman's correlation models ($r = -0.809$ and $r = 0.852$ respectively, $p < 0.001$). Table 1 also shows that all four confounding variables of aging, affluence, obesity and urbanization retain moderate to strong correlations to CVD incidence. These relationships establish that the confounding variables are properly selected for this study.

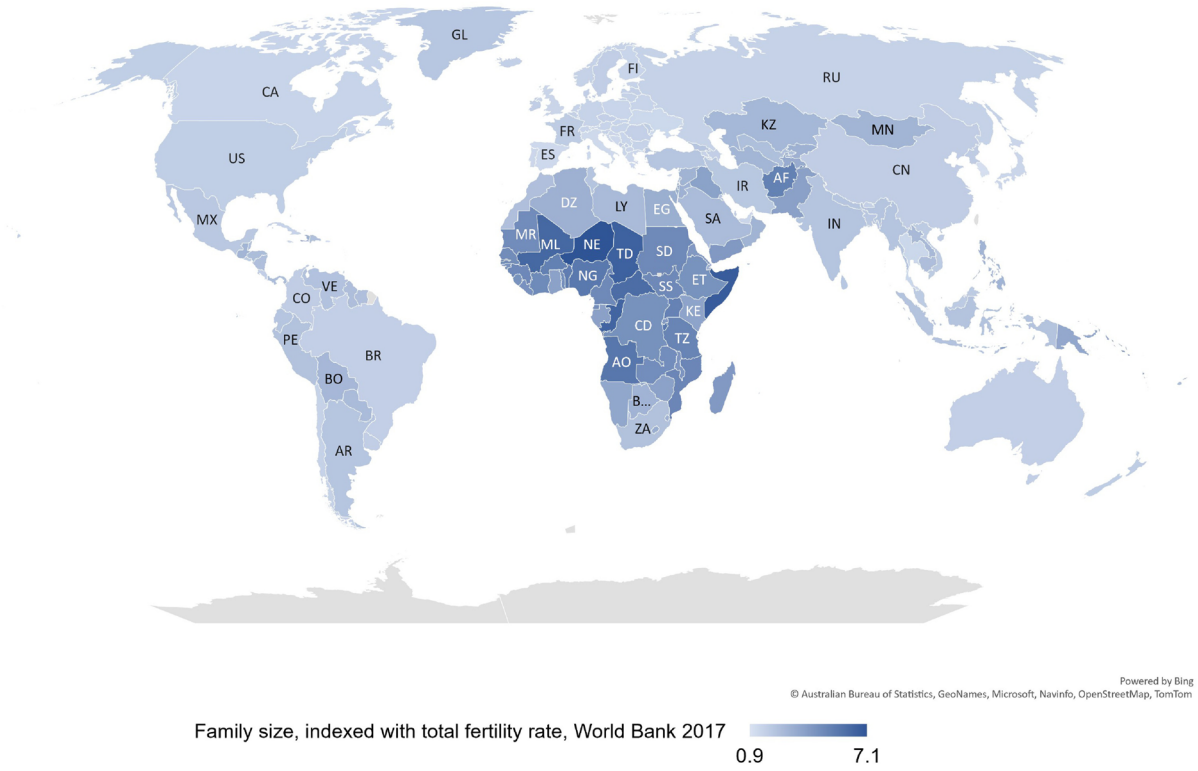

Figure 1. The geographic map to show "country"-specific family sizes worldwide.
Data source & definition: Family size, indexed with total fertility rate (the mean number of children born to a woman in 2017), the World Bank Group.

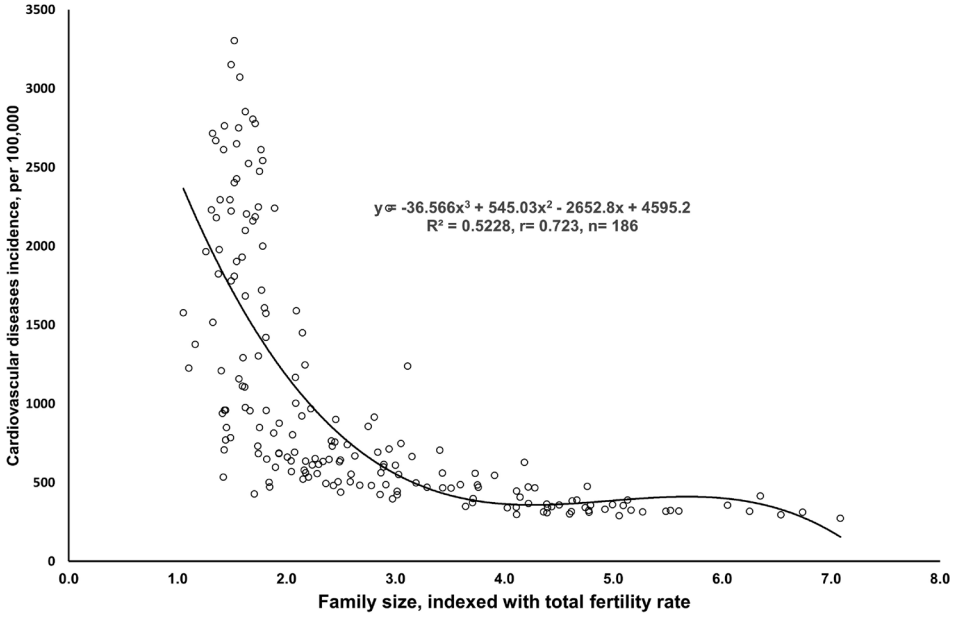

Figure 2. Scatter plots showing the inverse relationship between family size and cardiovascular disease incidence.
Data source & definition: Family size, indexed with total fertility rate (the mean number of children born to a woman in 2017), the World Bank Group; Cardiovascular disease (CVD) incidence, the number of new cases per 100,000, the Institute for Health Metrics and Evaluation 2017.

Partial correlations in Table 2 reveal that when confounders (aging, affluence, obesity and urbanization) are kept constant, family size remains significant to CVD incidence rate (r=-0.459, p<0.001). Conversely, when family size is controlled for; aging, affluence, obesity and urbanization display significant correlations to CVD incidence (r=0.346, p<0.001, r=0.287, p<0.001, r=0.219, p<0.010 and r=0.194, p<0.050). This suggests that family size does not significantly overlap with any of the confounding variables for predicting CVD incidence.

Table 1. Simple regression (Pearson's, nonparametric) to show the relationship between all variables.

	Family size	CVD incidence	Aging $e_{(65)}$	Affluence (GDP PPP)	Obesity %	Urbanization
Family size	1	−0.809***	−0.787***	−0.796***	−0.390***	−0.510***
CVD incidence	−0.852***	1	0.764***	0.734***	0.428***	0.526***
Aging $e_{(65)}$	−0.783***	0.782***	1	0.811***	0.362***	0.556***
Affluence (GDP PPP)	−0.766***	0.775***	0.820***	1	0.502***	0.720***
Obesity %	−0.358***	0.473***	0.388***	0.483***	1	0.546***
Urbanization	−0.510***	0.555***	0.604***	0.757***	0.584***	1

Pearson r (above diagonal) and nonparametric (below diagonal) correlations were reported. Significance levels.
*$P < 0.05$.
***$P < 0.001$.
Number of country range, 179–212.
Data source & definition: Family size, indexed with total fertility rate (the mean number of children born to a woman in 2017), the World Bank Group; Cardiovascular disease (CVD) incidence, the number of new cases per 100,000, the Institute for Health Metrics and Evaluation 2017; Aging indexed with life expectancy at 65 year old in 2014, United Nations; Affluence (Per capita GDP PPP), measured with the per capita purchasing power parity (PPP) value of all final goods and services produced within a territory in a given year, the World Bank 2014; Urbanization, measured with the percentage of population living in urban area, the World Bank 2014; Obesity prevalence, measured with the percentage of population aged 18+ with BMI equal to or over 30 kg/m^2, the World Health Organization 2014.
All the data were log-transformed for correlation analysis.

Table 2. Partial correlations explore the independent role of family size in predicting cardiovascular disease incidence when it is incorporated as an independent and confounding variable.

	Partial correlation to CVDs			Partial correlation to CVDs		
variables	r	p	df	r	p	df
Family size		Predicting variable		–	–	–
CVD incidence	− 0.459	< 0.001	170		Dependent variable	
Aging $e_{(65)}$	–	–	–	0.346	< 0.001	167
Affluence (GDP PPP)	–	–	–	0.287	< 0.001	167
Obesity %	–	–	–	0.219	< 0.010	167
Urbanization	–	–	–	0.194	< 0.050	167

Data source & definition: Family size, indexed with total fertility rate (the mean number of children born to a woman in 2017), the World Bank Group; Cardiovascular disease (CVD) incidence, the number of new cases per 100,000, the Institute for Health Metrics and Evaluation 2017; Aging indexed with life expectancy at 65 years old in 2014, United Nations; Affluence (Per capita GDP PPP), measured with the per capita purchasing power parity (PPP) value of all final goods and services produced within a territory in a given year, the World Bank 2014; Urbanization, measured with the percentage of population living in urban area, the World Bank 2014; Obesity prevalence, measured with the percentage of population aged 18+ with BMI equal to or over 30 kg/m^2, the World Health Organization 2014.
All the data were log-transformed for correlation analysis.
Included as the confounding factor.

Multiple linear regression Table 3 shows that when family size is not added as a predictor variable, aging and affluence (GDP PPP) are the only two variables with significant influence on CVD incidence. When family size is added as a predicting variable, family size and aging are the only two variables which display a significant influence on CVD incidence. Regardless of family size, obesity and urbanization show no significant relationship to CVD incidence. Affluence (GDP PPP) weakly correlates to CVD incidence when family size is not a predictor variable, but the relationship is insignificant when family size is added to the model as a predictor.

In Table 4, stepwise multiple linear regression revealed that aging and GDP PPP are the most influential predictor variables for CVD incidence when family size is removed from the model. When family size is added as a predictor variable, it becomes the most influential variable on the CVD incidence. Aging and obesity are less influential predictors for CVD incidence with reported R^2 values of 0.04 and 0.005 respectively. Similar to the finding in Table 3-1, when family size is removed, affluence (GDP PPP) becomes a significant predictor for CVD incidence. However, this relationship is non-existent when family size is added as a predictor variable to the model.

In both enter and stepwise models, urbanization appeared the least influential in predicting CVD incidence. Unexpectedly in both Table 3-1 and Table 3-2, the role of affluence (GDP PPP) in predicting CVD incidence was statistically explained by family size.

In Table 5, although countries were grouped through various classifiers, family size consistently retains a negative correlation to CVD incidence rate. However, the strengths and significance levels of family size-CVD incidence relationships vary depending on the sample sizes (number of the countries) and homogeneities of grouped countries. It is worth highlighting that family size correlates to CVD incidence in LMIC significantly more strongly than in high-income countries (z= -5.16 and -6.33, $p < 0.001$ in Pearson's r and nonparametric

Table 3. Enter multiple linear regression model to describe the relationship of CVD to each predicting variable.

	Family size not added			Family size added	
Variables entered	Beta	Sig.		Beta	Sig.
Family size	Not added		Family size	−0.489	< 0.001
Aging $e_{(65)}$	0.501	< 0.001	Aging $e_{(65)}$	0.266	< 0.010
Affluence (GDP PPP)	0.334	< 0.001	Affluence (GDP PPP)	0.107	0.270
Obesity %	0.074	0.197	Obesity %	0.079	0.127
Urbanization	−0.056	0.437	Urbanization	−0.018	0.789

Enter multiple linear regression modeling is reported. Contribution of variables is listed in order of how much they contribute to cardiovascular disease incidence.
Data source & definition: Family size, indexed with total fertility rate (the mean number of children born to a woman in 2017), the World Bank Group; Cardiovascular disease (CVD) incidence, the number of new cases per 100,000, the Institute for Health Metrics and Evaluation 2017; Aging indexed with life expectancy at 65 years old in 2014, United Nations; Affluence (Per capita GDP PPP), measured with the per capita purchasing power parity (PPP) value of all final goods and services produced within a territory in a given year, the World Bank 2014; Urbanization, measured with the percentage of population living in urban area, the World Bank 2014; Obesity prevalence, measured with the percentage of population aged 18+ with BMI equal to or over 30 kg/m^2, the World Health Organization 2014.
All the data were log-transformed for correlation analysis.

Table 4. Stepwise linear regression model to sort significant predictors of cardiovascular disease incidence.

	Family size not added			Family size added	
Rank	Variables entered	Adjusted R^2	Rank	Variables entered	Adjusted R^2
	Family size	Not added	1	Family size	0.654
1	Aging $e_{(65)}$	0.591	2	Aging $e_{(65)}$	0.694
2	Affluence (GDP PPP)	0.626	3	Obesity %	0.699
	Obesity	Insignificant		Affluence (GDP PPP)	Insignificant
	Urbanization	Insignificant		Urbanization	Insignificant

Stepwise multiple linear regression modeling is reported. Contribution of variables is listed in order of how much they contribute to cardiovascular disease incidence.
Data source & definition: Family size, indexed with total fertility rate (the mean number of children born to a woman in 2017), the World Bank Group; Cardiovascular disease (CVD) incidence, the number of new cases per 100,000, the Institute for Health Metrics and Evaluation 2017; Aging indexed with life expectancy at 65 years old in 2014, United Nations; Affluence (Per capita GDP PPP), measured with the per capita purchasing power parity (PPP) value of all final goods and services produced within a territory in a given year, the World Bank 2014; Urbanization, measured with the percentage of population living in urban area, the World Bank 2014; Obesity prevalence, measured with the percentage of population aged 18+ with BMI equal to or over 30 kg/m^2, the World Health Organization 2014.
All the data were log-transformed for correlation analysis.

Table 5. Family size determining cardiovascular disease incidence in various country clusters.

Country groupings	Pearson r	p	Nonparametric	p
Worldwide (n = 186)	−0.809***	< 0.001	−0.852***	< 0.001
World Bank income classifications				
High Income, n = 59	−0.326*	< 0.050	−0.271*	< 0.050
Low Income, n = 28	−0.613***	< 0.001	−0.455*	< 0.050
Low Middle Income, n = 48	−0.758***	< 0.001	−0.771***	< 0.001
Upper Middle Income, n = 51	−0.681***	< 0.001	−0.729***	< 0.001
Low- and middle-income countries (LMIC), n = 127	−0.824***	< 0.001	−0.861***	< 0.001
Fisher r-to-z transformation (LMIC vs High)	Z= −5.16, p < 0.001		Z= −6.33, p< 0.001	
United Nations common practice				
Developed, n = 46	−0.599***	< 0.001	−0.190	0.205
Developing, n = 140	−0.769***	< 0.001	−0.811***	< 0.001
Fisher r-to-z transformation (Developing vs developed)	Z= −1.87, p < 0.050		Z= −5.36, p < 0.001	
WHO regions				
Africa, n = 46	−0.839***	< 0.001	−0.650***	< 0.001
Americas, n = 36	−0.622***	< 0.001	−0.724***	< 0.001
Eastern Mediterranean, n = 21	−0.393	0.078	−0.503*	0.020
Europe, n = 51	−0.699***	< 0.001	−0.435***	< 0.001
South-East Asia, n = 10	−0.371	0.292	0.050	0.960
Western Pacific, n = 22	−0.798***	< 0.001	−0.799***	< 0.001
Countries grouped with various factors				
Arab World, n= 21	−0.379	0.090	−0.453*	< 0.050
Asia-Pacific Economic Cooperation, n= 19	−0.706***	< 0.001	−0.818***	< 0.001
Asia Cooperation Dialogue, n = 33	−0.516**	< 0.010	−0.487**	< 0.010
English as Official Language, n = 48	−0.835***	< 0.001	−0.881***	< 0.001
Latin America, n = 21	−0.746***	< 0.001	−0.848***	< 0.001
Latin America and Caribbean, n = 32	−0.678***	< 0.001	−0.749***	< 0.001
Organization for Economic Co-operation and Development, n = 37	−0.504***	< 0.001	−0.495**	<0.010
Southern African Development Community, n= 16	−0.879***	< 0.001	−0.806***	< 0.001

Pearson r and nonparametric correlations within country groupings were reported.
Data source & definition: Family size, indexed with total fertility rate (the mean number of children born to a woman in 2017), the World Bank Group; Cardiovascular disease (CVD) incidence, the number of new cases per 100,000, the Institute for Health Metrics and Evaluation 2017.
All the data were log-transformed for correlation analysis.

respectively). Similarly, family size shows significant strong correlations with CVD incidence in developing countries than in developed countries ($z = -1.87$, $p < 0.050$ and $z = -5.36$, $p < 0.001$ in Pearson's r and nonparametric respectively). This suggests that family size plays a significantly important role in protecting against CVDs in developing/LMIC countries compared to developed countries.

4. Discussion

The findings of this study demonstrate a significant population-level association between family size and CVD incidence. However, as an ecological analysis, this study does not establish causation or examine individual-level relationships. Instead, its primary objective is to explore broad patterns and generate hypotheses for future research. These results highlight the need for longitudinal and experimental studies to validate and further explore the causal mechanisms behind the observed associations.

CVD arises from a variety of causes, and by analyzing the correlation between global family size and CVD incidence rates, this study suggests the following:

1. Worldwide, larger families may be a protective factor against CVD. Scatter plots showed that family size explains 52.28% CVD incidence rate variance globally.
2. Large family size retains a strong protective role in reducing CVD incidence even when confounding effects of aging, affluence, obesity and urbanization are removed.
3. Large family size may be the most influential predictor variable for CVD incidence when family size, aging, affluence, obesity and urbanization are rank-analyzed together in stepwise analyses.
4. The protective role of large family size against CVD incidence appears to be more relevant in LMICs than in high-income countries. Similarly, this protective effect is more pronounced in developing countries compared to developed countries.

Human mental health (mind) and physical health (body) are interconnected and interdependent [36]. The impact of the mind-body connection on human health has been intriguing to academics and clinicians alike since the Chinese medicinal book, *Huangdi Neijing* was compiled and published 2,200 years ago [37]. The mind-heart-body-connection has been well established in academic research and it has been repeatedly reported that positive psychological health is associated with, and can potentially protect, cardiovascular health and decrease CVD initiation [37,38]. The applications of this research have been well-studied and are widely practiced in clinical settings today [39]. Regardless of cultural backgrounds, family can bring stress relief, happiness and a sense of well-being to an individual through core, reliable support networks and close, positive attachments [40]. The impact of family on positive psychological well-being has been scaled with family size and tested in a number of studies [41]. The mechanism for the protecting role of large family size in reducing CVD incidence may include:

1. Large family size may play a biological role in enhancing the mind-heart-body-connection.
   It is well known that oxytocin is also called the "hormone of love" or" hormone of attachment," whose production is associated with positive psychological well-being [42,43]. Therefore, oxytocin may be one of the hormones which underpin the mind-heart-body-connection [44], as it displays therapeutic effects in regulating cardiovascular function and treating cardiovascular pathologies [45].
   A family is a group of individuals sharing strong emotional bonds mediated by behaviors such as identification, loyalty, solidarity, attachment, and reciprocity [46]. Family daily life has been reported as a major factor that can upregulate oxytocin production in the body. Oxytocin release has been previously associated with behaviors in females, such as childbirth [47] and subsequent lactation [48], as well as daily interactions between family members, including interactions between parents [49] and between parents and children [50,51]. Additionally, oxytocin may form a self-reinforcing cycle between its production and family interactions, as it can help maintain monogamous relationships among family members [52].
   Accordingly, studies have revealed that greater family size may create more positive psychological well-being in an individual, leading to more oxytocin release [9,41].

Additionally, from an evolutionary perspective, large family size denotes a high birth rate which provides more opportunity for natural selection to occur [53]. The outcome from the process of natural selection is less CVD genes/mutations accumulated in the population, thus mitigating CVD risk in offspring.

Natural selection acts on each family in our contemporary population [54]. The total opportunity for natural selection to take place in each "country" has been measured with the Biological State Index (I_{bs}) [55]. I_{bs} indexing the opportunity for natural selection in the current global population reveals an inverse correlation to family size [56]. This suggests that populations with larger family sizes may have higher proportions of genetic variation, a precedent to effective natural selection [53]. When natural selective forces occur, individuals with a genetic disposition for increased risk of CVD are limited in their reproductive opportunities [54,57], reducing the likelihood of genes increasing CVD risk being inherited. Therefore, populations with large family size may have higher genetic variation leading to lower CVD incidence rates in offspring.

2. Psychological well-being from family life increases life satisfaction leading to the adoption and maintenance of healthy lifestyle choices.

   Family members from large families have more opportunities for positive interactions with each other, which may assist in maintaining overall life satisfaction within an individual [9,41]. This may psychologically increase the level of life purpose [58]. Large families may offer members more opportunities for social engagement, which can maintain an individual's positive psychological well-being– a protective factor against CVD onset [38]. People with a high level of life satisfaction are more readily optimistic, which in-turn aids them in making and maintaining positive relationships. Through these relationships, individuals create strong support networks which they can rely on in times of stress on hardship [59,60]. Life satisfaction may also help individuals with more positive relationships (such as those in large families) build up cognitive-behavioral mechanisms helping them to more readily follow healthcare advice; previously demonstrated in cardiovascular health promotion [7,61].

3. More social support from family members increases knowledge regarding CVD prevention

   Family is vital for promoting CVD health and preventing CVD progenesis throughout an individual's lifespan [7]. Family members can remind each other to maintain cardioprotective lifestyle choices, such as optimism, physical activity, healthy diet, abstaining from smoking and drinking alcohol, equanimity and medication compliance [62]. Also, family members can recommend and/or remind each other to have necessary medical examinations, especially for those family members exposed to pre-CVD or CVD comorbidities [63]. Pihlman *et al* [18] reported that when compared to children without siblings, children with siblings had reduced exposure to recognized CVD risk factors such as obesity, high LDL-cholesterol and less physical activity. Additionally, this trend was maintained throughout development to adulthood [64].

To compare and highlight the differences between our study and previous studies, we used the phrases "family size and cardiovascular disease," "the number of childbirths and cardiovascular disease" and "parity and cardiovascular disease" for keyword searches in Google Scholar and PubMed. Ten studies were randomly selected and are included in the supplementary file for comparative analysis of study design (SF 1: Comparing Study Designs Between the Current Study and Ten Previously Published Studies).

This study has the following differences from the previous studies, which add to the current study's strengths.

Firstly, a large majority of the previous studies only considered the impact of family size as a potential risk factor for CVD progenesis or mortality in population segments (classified with ages or sexes) within a country [65–69]. Therefore, these studies could not generalize their conclusions among the entire population. Another limitation to this method is that the standard deviations within the individual variables may be too small due to cultural and socio-economical homogeneity within the country. For instance, within Sweden, families share similar culture and economic affluence which influenced smaller family sizes in a large majority of the population [70]. This led to small variance in Swedish family size, making it difficult to observe the inverse correlation of family size to CVD incidence.

Secondly, a common concern with previous studies is that their designs seem to assume that family size was only a risk factor for site-specific CVDs. However, the mechanisms of family size for reducing CVD risk are nonspecific and there have been insufficient studies revealing the etiologies for site-specific CVDs. Previous correlations of family size to site-specific CVDs observed in previous studies may be spurious [70,71]. In this

study, instead of exploring the role of family size in impacting site-specific CVDs, the total CVD incidence was included for quantifying the role of family size in total CVD incidence.

Thirdly, the CVD mortality rate has been used in previous studies as an index to assess the adverse effects of family size on CVDs. This includes two phases of CVD: before diagnosis and the subsequent non-clinical and clinical treatments following diagnosis. Analyzing CVD in two phases implies that the overall measurement of CVD events may not accurately indicate CVD onset, as the impact is confounded by a patient's existing CVDs and subsequent treatments. In contrast, the CVD incidence rate, as included in this study, may serve as a better indicator of CVD risk. It represents the rate of new CVD cases in 2017 for the total population, before patients experienced any significant CVD treatments or effects.

Finally, this study has provided a more comprehensive analysis (on a wider range of variables) exploring the relationship between family size and CVD mortality/incidence compared to previous studies. In this study, several, well-established potential confounding factors (aging [72], GDP PPP [73], obesity [74] and urban living [26,75]) have been included as control variables while analyzing the role of family size in determining CVD incidence. Additionally, the relationship between family size and CVD incidence was quantified at three levels with multiple data analysis models (detailed at the beginning of the Discussion). Although TFR has controversially correlated to CVD risk in previous studies, more siblings can provide a greater source of genetic variation, emotional support and practical aid which may decrease the risk for developing CVDs [40].

This study analyzed multiple datasets using various approaches to examine the relationship between family size and CVD incidence, incorporating key confounders such as aging, economic affluence, obesity, and urbanization. Stepwise linear regression analysis revealed that these five predictive variables collectively accounted for a significant portion of the variance in CVD incidence, with family size, aging, and economic affluence identified as the three most influential contributors, together explaining 69.9 percent of the variance. While the study provides valuable insights, limitations must be acknowledged. Other critical factors, such as healthcare access, dietary habits, genetic predisposition, physical activity, stress levels, and smoking, may also significantly influence CVD incidence [76]. These factors were excluded due to data limitations and potential inconsistencies in international data sources, underscoring the need for cautious interpretation of the findings. Addressing these limitations in future research by including a broader range of confounders and ensuring more reliable data could enhance the understanding of the observed associations and their underlying mechanisms. The inability to include factors such as healthcare access and genetic predisposition represents a key limitation, as these variables could significantly influence cardiovascular disease incidence. Therefore, while the findings offer valuable perspectives, they should be interpreted cautiously, with future research incorporating these additional variables to provide deeper insights into the complex determinants of CVD.

However, CVD has also become a pressing public health concern in low- and middle- income countries, which take up around 80% of all CVD deaths worldwide [5]. The inverse correlation of family size to CVD incidence was also observed in different country groupings. There has been a growing interest in examining the effects of family size on CVDs between LMIC and high-income countries, and between developed and developing countries [1]. In this study, both the bivariate correlations (Pearson's r and Spearman's rho) revealed that family size was significantly weaker in correlations to LMIC CVD incidence compared to high-income countries. This may be explained by emerging economies and a sharp Westernization process in many LMIC and developing countries in the past 30–40 years, which have contributed to reductions in family size and higher levels of CVD diagnoses. In developing countries and LMIC countries, there is a strong correlation between family size and CVD incidence rates. This correlation is even stronger than what is observed in developed and high-income countries. However, it is important to exercise caution when attributing the higher CVD incidence rates in developed or high-income countries solely to smaller family sizes. Other factors, such as urbanization, may complicate the relationship between family size and CVD incidence in our simple regression analyses.

The reliance on TFR as a proxy for family size provides valuable insights at the population level but may oversimplify the complexities of family relationships and their impact on health outcomes [77,78]. While TFR effectively captures the average number of children born to women in a population, it does not account for variations in family structures, such as multigenerational households, single-parent families, or the presence of extended family members. These dynamics can significantly influence emotional support, stress levels, and access to resources, which are crucial factors in cardiovascular health. Additionally, TFR does not reflect the quality or nature of family interactions, such as caregiving roles, communication patterns, or shared

activities, which may play a pivotal role in fostering psychological well-being and healthy behaviors. Expanding future analyses to include more detailed measures of family composition, such as sibling relationships, parental involvement, and intergenerational support, could provide deeper insights into how specific family dynamics contribute to cardiovascular health. Integrating qualitative data, such as interviews or surveys, alongside quantitative metrics could further enrich our understanding of the nuanced ways in which families influence health outcomes. These expanded approaches would allow for a more comprehensive exploration of the protective or risk-modifying effects of family dynamics on cardiovascular health, moving beyond simple numerical proxies to examine the intricate interplay of social and emotional factors within families.

Urbanization influences CVD risk through interconnected pathways, including lifestyle changes, dietary transitions, and reduced physical activity. Rapid urbanization often leads to increased consumption of processed foods high in salt, sugar, and unhealthy fats, along with a sedentary lifestyle, significantly contributing to obesity, hypertension, and diabetes, which are well-established risk factors for CVD. Additionally, urban environments expose individuals to higher levels of air pollution, a recognized contributor to cardiovascular morbidity. While urbanization can improve access to healthcare, its overall impact on CVD risk depends on the balance between positive and negative effects. In regions such as Southeast Asia and Sub-Saharan Africa, rapid urbanization has been associated with dietary shifts toward processed, calorie-dense foods and rising CVD rates [79]. Urbanization also affects mental health, stress levels, and social support networks, indirectly influencing cardiovascular health. Increased social isolation or reduced access to green spaces in urban environments has been linked to poorer cardiovascular outcomes [80]. To better understand these multifaceted effects, future research should employ mixed-methods approaches combining quantitative data with qualitative insights from affected populations, offering a deeper understanding of how urbanization interacts with other factors to influence CVD risk across diverse contexts.

Our findings suggest that larger family sizes may contribute to reduced CVD risk through biological, psychological, and social mechanisms, highlighting the potential value of integrating family dynamics into public health initiatives. Policies supporting strong family networks could include measures such as extended parental leave, affordable childcare, and family-friendly workplace practices, all of which can reduce stress and foster family cohesion. Encouraging multigenerational housing or community-based living spaces can also strengthen intergenerational support systems, offering emotional and practical benefits that mitigate CVD risk. Family planning programs should balance reproductive choices with the promotion of healthy family dynamics by incorporating discussions on the role of social support and psychological well-being in health outcomes. In regions where the protective effects of family size are most pronounced, such as LMICs, culturally appropriate incentives for larger families could be explored. Additionally, integrating cardiovascular health education into family planning initiatives, focusing on stress management, healthy lifestyles, and family-based support, can foster holistic interventions that align family planning policies with cardiovascular disease prevention strategies, promoting both individual and collective health outcomes.

5. Study limitations

Before analyzing the public health implications on CVD prevention with the study's findings, it is necessary to note its limitations below:

Firstly, this is an observational study; therefore, the relationship between family size and CVD incidence should be interpreted as correlational rather than causational. As an ecological analysis, our findings are confined to identifying population-level associations and cannot establish causation or provide insights into individual-level relationships. Future research should adopt longitudinal or experimental designs to explore the causal mechanisms underlying the relationship between family size and CVD incidence more comprehensively.

Secondly, while TFR is a widely used demographic indicator, it may not fully account for the complexities of family dynamics, such as extended family structures, co-residency, and intergenerational interactions, which could influence cardiovascular disease outcomes. Future research should explore additional measures, for example household size of family dynamics to provide a more nuanced understanding of their relationship with CVD incidence.

Secondly, this study only shows a correlation between family size and cardiovascular events at the global, population level, which may not hold true at the individual level. However, to minimize the risk of erroneous correlations, we incorporated a number of control variables for exploring the independent role of family size in predicting CVD incidence.

Thirdly, the observed associations between family size and CVD incidence must be interpreted with caution, given the potential influence of unmeasured confounders such as genetic predisposition, lifestyle factors, and healthcare access. Future studies incorporating these variables could provide a more nuanced understanding of the relationship and its underlying mechanisms.

Fourthly, while this study incorporates key confounders such as aging, economic affluence, obesity, and urbanization, we acknowledge that other critical factors, including healthcare access, dietary habits, genetic predisposition, physical activity, and stress levels, which collectively account for approximately 30 percent of the variance in CVD incidence, may significantly influence cardiovascular disease incidence. These factors were not included in this analysis due to data limitations. Future research should aim to address a broader range of confounders to provide a more comprehensive understanding of the determinants of cardiovascular disease.

Fifthly, this study relies on data sourced from international databases, which may vary in quality and consistency due to differences in data collection methodologies across countries. These variations could introduce biases or inaccuracies in the reported results. While steps were taken to ensure data quality, such as cross-referencing with established sources, future research would benefit from standardized and more granular data to improve reliability.

Finally, data quality could be comprised due to random and human errors made during data collection by the reporting countries. Therefore, the data included in this study may be fairly crude, which may affect the accuracy of our calculations and comparisons.

6. Conclusions

This study reveals a significant negative association between large family sizes and CVD incidence, particularly in LMIC and developing countries. While findings suggest that family-based health promotion offers biopsychosocial benefits, the cross-sectional nature of the data precludes causal inferences. These results highlight the importance of incorporating family dynamics into public health planning. Family planning programs should balance population control with the health benefits of supportive family environments, while CVD prevention strategies could strengthen familial and social support systems to enhance psychological well-being. Future longitudinal research is needed to explore the mechanisms driving these associations and determine if family size directly protects against CVD. Integrating family dynamics into public health initiatives may provide a comprehensive approach to cardiovascular health.

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Authors' contributions

Wenpeng You: Conceptualization; Data Curation; Formal Analysis; Funding Acquisition; Investigation; Methodology; Project Administration; Resources; Software; Supervision; Validation; Visualization; Writing – Original Draft Preparation; Writing – Review & Editing. Jacob Sevastidis: Conceptualization; Data Curation; Formal Analysis; Investigation; Methodology; Project Administration; Resources; Software; Validation; Visualization; Writing – Review & Editing. Maciej Henneberg: Conceptualization; Data Curation; Formal Analysis; Funding Acquisition; Investigation; Methodology; Project Administration; Resources; Software; Supervision; Validation; Visualization; Writing – Review & Editing.

Declaration of generative AI and AI-Assisted technologies in the writing process

The first author utilized ChatGPT during the preparation of this work to improve readability and language while retaining full control over the core authoring tasks. Following its use, the first author and coauthors thoroughly reviewed and revised the content as necessary, assuming complete responsibility for the final version of the publication.

Disclosure statement

The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

Ethical approval and consent to participate

All six variables incorporated into this quantitative study are freely accessible from the official websites of the United Nations (UN) and associated agencies. The ethical approval for analyzing these data in this study was sought from the Office of Research Ethics, Compliance and Integrity (ORECI) of the University of Adelaide (Approval Number: 36289).

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Data availability statement

All the population level variables included our data analyses are freely extracted from the United Nation agencies' online repositories which are open to the public. The sources and rationale for incorporating each variable have been described in the "Materials and Methods." The official permission to extract these data for academic research purposes is not required, as data manipulation was compliant with the data suppliers' terms and conditions.

References

Papers of special note have been highlighted as either of interest (•) or of considerable interest (••) to readers

[1] WHO. C ardiovascular diseases (CVDs); 2021. [December 21 2022]. Available from: https://www.who.int/en/news-room/fact-sheets/detail/cardiovascular-diseases-(cvds).* This reference provides comprehensive global statistics on CVD incidence and prevalence, serving as a foundation for the study's significance and context.

[2] Go AS, Mozaffarian D, Roger VL, et al. Heart disease and stroke statistics—2014 update: a report from the American Heart Association. Circulation. 2014;129(3):e28–e292. doi: 10.1161/01.cir.0000441139.02102.80

[3] Vasan RS, Benjamin EJ. The future of cardiovascular epidemiology. Circulation. 2016;133(25):2626–2633. doi: 10.1161/CIRCULATIONAHA.116.023528

[4] You W, Feng S, Donnelly F. Total meat (flesh) supply may be a significant risk factor for cardiovascular diseases worldwide. Food Sci Nutr. 2023;11(6):3203–3212. doi: 10.1002/fsn3.3300

[5] Powell-Wiley TM, Poirier P, Burke LE, et al. Obesity and cardiovascular disease: a scientific statement from the American Heart Association. Circulation. 2021;143(21):e984–e1010. doi: 10.1161/CIR.0000000000000973

[6] Mozaffarian D, Benjamin EJ, Go AS, et al. Heart disease and stroke statistics—2016 update: a report from the American Heart Association. Circulation. 2016;133(4):e38–e360.

[7] Vedanthan R, Bansilal S, Soto AV, et al. Family-based approaches to cardiovascular health promotion. J Am Coll Cardiol. 2016;67(14):1725–1737. doi: 10.1016/j.jacc.2016.01.036

[8] You W, Rühli FJ, Henneberg RJ, et al. Greater family size is associated with less cancer risk: an ecological analysis of 178 countries. BMC Cancer. 2018;18(1):924. doi: 10.1186/s12885-018-4837-0** This study explores the relationship between family size and health outcomes, offering an ecological perspective that parallels our methodology and supports the hypothesis.

[9] Angeles L. Children and life satisfaction. J Happiness Stud. 2010;11(4):523–538. doi: 10.1007/s10902-009-9168-z

[10] United Nations. Probabilistic projections of total fertility using fertility estimates; 2022 [May 15 2024]. Available from: https://population.un.org/wpp/Graphs/Probabilistic/FERT/TOT/900.

[11] Clark G, Henneberg M. The life history of Ardipithecus ramidus: a heterochronic model of sexual and social maturation. AR. 2015;78(2):109–132. doi: 10.1515/anre-2015-0009

[12] Grinde B. Can the concept of discords help us find the causes of mental diseases? Med Hypotheses. 2009;73(1):106–109. doi: 10.1016/j.mehy.2009.01.030

[13] You W, Henneberg M. Large household reduces dementia mortality: A cross-sectional data analysis of 183 populations. PLoS One. 2022;17(3):e0263309. doi: 10.1371/journal.pone.0263309

[14] Trevisan M, Krogh V, Klimowski L, et al. Absence of siblings–a risk factor for hypertension? N Engl J Med. 1991;324(18):1285. doi: 10.1056/NEJM199105023241813
[15] Eriksson JG, Forsén T, Tuomilehto J, et al. Catch-up growth in childhood and death from coronary heart disease: longitudinal study. BMJ. 1999;318(7181):427–431. doi: 10.1136/bmj.318.7181.427
[16] The World Bank Group. World Bank open data: The World Bank Group; 2016. © 2016; [12.07.2016]. Available from: http://data.worldbank.org/.
[17] United Nations-Department of Economic and Social Affairs-Population Division. World Population Prospects: The 2015 Revision, DVD Edition; 2015.
[18] Australian Bureau of Statistics. Australian Social Trends; 1996. 2006 [03.09.2016].
[19] Hemminki K, Mutanen P. Birth order, family size, and the risk of cancer in young and middle-aged adults. Br J Cancer. 2001;84(11):1466–1471. doi: 10.1054/bjoc.2001.1811
[20] You W, Henneberg M. Prostate cancer incidence is correlated to total meat intake–a cross-national ecologic analysis of 172 countries. Asian Pac J Cancer Prev. 2018;19(8):2229–2239. doi: 10.22034/APJCP.2018.19.8.2229
[21] You W, Henneberg R, Henneberg M. Healthcare services relaxing natural selection may contribute to increase of dementia incidence. Sci Rep. 2022;12(1):8873. doi: 10.1038/s41598-022-12678-4
[22] The World Bank. Fertility rate, total (births per woman): The World Bank Group, © 2016; 2023; [12 December 2024]. Available from: https://data.worldbank.org/indicator/SP.DYN.TFRT.IN.
[23] IHME. Global burden of disease collaborative network. Global burden of disease study 2019 (GBD 2019) results. Seattle, United States: Institute for Health Metrics and Evaluation (IHME); 2020. http://ghdx.healthdata.org/gbd-results-tool.**This dataset supplies the CVD incidence rates used as the dependent variable, forming a critical component of our analysis.
[24] Ezzati M, Vander Hoorn S, Lawes CMM, et al. Rethinking the "diseases of affluence" paradigm: global patterns of nutritional risks in relation to economic development. PLoS Med. 2005;2(5):e133. doi: 10.1371/journal.pmed.0020133
[25] Schwartz MW, Seeley RJ, Zeltser LM, et al. Obesity pathogenesis: an endocrine society scientific statement. Endocr Rev. 2017;38(4):267–296. doi: 10.1210/er.2017-00111
[26] WHO. Diet, nutrition and the prevention of chronic diseases: report of a joint WHO/FAO expert consultation; 2003 (technical report series; 916). Geneva: WHO.
[27] File MORT/05-1: Life expectancy at exact age, e(x), for both sexes combined, by region, subregion and country, annually for 1950-2100 (Estimates, 1950 - 2021) [Internet]; 2021. Online edition The United Nations. Available from: https://population.un.org/wpp/Download/Files/1_Indicators%20(Standard)/EXCEL_FILES/4_Mortality/WPP2022_MORT_F05_1_LIFE_EXPECTANCY_BY_AGE_BOTH_SEXES.xlsx.
[28] North BJ, Sinclair DA. The intersection between aging and cardiovascular disease. Circ Res. 2012;110(8):1097–1108. doi: 10.1161/CIRCRESAHA.111.246876
[29] Chiao YA, Lakatta E, Ungvari Z, et al. Cardiovascular disease and aging. In: Sierra F, Kohanski R, editors. Advances in geroscience. Cham: Springer; 2016. p. 121–160.
[30] Danaei G, Singh GM, Paciorek CJ, et al. The global cardiovascular risk transition: associations of four metabolic risk factors with national income, urbanization, and Western diet in 1980 and 2008 [Research Support, N.I.H., Extramural Research Support, Non-U.S. Gov't]. Circulation. 2013;127(14):1493–1502. 1502e1-8. doi: 10.1161/CIRCULATIONAHA.113.001470
[31] WHO. Global Health Observatory, the data repository: World Health Organization; 2015. [11.26.2015]. Available from: http://www.who.int/gho/database/en/.
[32] The World Bank. Indicators | Data; 2018. Available from: https://data.worldbank.org/indicator.*This reference is essential as it provides the fertility rate data used to quantify family size, a key independent variable in our study.
[33] You W, Donnelly F. Although in shortage, nursing workforce is still a significant contributor to life expectancy at birth. Public Health Nurs. 2023;40(2):229–242. doi: 10.1111/phn.13158
[34] You W, Henneberg R, Saniotis A, et al. Total meat intake is associated with life expectancy: a cross-sectional data analysis of 175 contemporary populations. Int J Gen Med. 2022;15:1833–1851. doi: 10.2147/IJGM.S333004
[35] You W, Henneberg M. Worldwide, economic affluence was in significantly stronger correlation to obesity prevalence rate in males than in females; 2022.
[36] Dunn H. High level wellness. Arlington, Texas: R.W. Beatty, Ltd; 1971.
[37] Huangdi Q. Other ministers. In: Huangdi Q, Huangdi N, editors. Chapter 39 of plain questions: disease prognosis. Wuhan: Wuhan Publishing House; 2013.
[38] Kubzansky LD, Huffman JC, Boehm JK, et al. Positive psychological well-being and cardiovascular disease: JACC health promotion series. J Am Coll Cardiol. 2018;72(12):1382–1396. doi: 10.1016/j.jacc.2018.07.042* This reference highlights the role of psychological well-being in cardiovascular health, supporting our discussion on the protective effects of family size.
[39] Levine GN, Cohen BE, Commodore-Mensah Y, et al. Psychological health, well-being, and the mind-heart-body connection: a scientific statement from the American Heart Association. Circulation. 2021;143(10):e763–e783. doi: 10.1161/CIR.0000000000000947
[40] Rostila M, Saarela J, Kawachi I. The forgotten griever: a nationwide follow-up study of mortality subsequent to the death of a sibling. Am J Epidemiol. 2012;176(4):338–346. doi: 10.1093/aje/kws163
[41] Nan H, Ni MY, Lee PH, et al. Psychometric evaluation of the Chinese version of the Subjective Happiness Scale: evidence from the Hong Kong FAMILY Cohort [Research Support, Non-U.S. Gov't Validation Studies]. Int J Behav Med. 2014;21(4):646–652. doi: 10.1007/s12529-014-9389-3

[42] Magon N, Kalra S. The orgasmic history of oxytocin: Love, lust, and labor. Indian J Endocrinol Metab. 2011;15(Suppl. 3):S156–S161. doi: 10.4103/2230-8210.84851
[43] Insel TR. Oxytocin—a neuropeptide for affiliation: evidence from behavioral, receptor autoradiographic, and comparative studies. Experientia. 1992;17(1):3–35. doi: 10.1016/0306-4530(92)90073-g
[44] Du Vigneaud V. Oxytocin, the principal oxytocic hormone of the posterior pituitary gland: its isolation, structure, and synthesis. Experientia. 1955;(Suppl. 2):9–26.
[45] Jankowski M, Broderick TL, Gutkowska J. The role of oxytocin in cardiovascular protection. Front Psychol. 2020;11:2139. doi: 10.3389/fpsyg.2020.02139**This study discusses the biological mechanisms, particularly oxytocin, that link family dynamics to cardiovascular health, aligning with the hypothesized protective factors in our research.
[46] Medicine Io, Health IoMCo, Practice, et al. Health and behavior: the interplay of biological, behavioral, and societal influences. Washington (DC): National Academies Press (US); 2001.
[47] Takayanagi Y, Yoshida M, Bielsky IF, et al. Pervasive social deficits, but normal parturition, in oxytocin receptor-deficient mice. Proc Natl Acad Sci U S A. 2005;102(44):16096–16101. doi: 10.1073/pnas.0505312102
[48] White-Traut R, Watanabe K, Pournajafi-Nazarloo H, et al. Detection of salivary oxytocin levels in lactating women. Dev Psychobiol. 2009;51(4):367–373. doi: 10.1002/dev.20376
[49] Gordon G, JrBurch RL, Platek SM. Does semen have antidepressant properties? Arch Sex Behav. 2002;31(3):289–293.
[50] Kendrick KM. The neurobiology of social bonds. J Neuroendocrinol. 2004;16(12):1007–1008. doi: 10.1111/j.1365-2826.2004.01262.x
[51] Weisman O, Zagoory-Sharon O, Feldman R. Oxytocin administration to parent enhances infant physiological and behavioral readiness for social engagement. Biol Psychiatry. 2012;72(12):982–989. doi: 10.1016/j.biopsych.2012.06.011
[52] Young LJ, Murphy Young AZ, Hammock EA. Anatomy and neurochemistry of the pair bond. J Comp Neurol. 2005;493(1):51–57. doi: 10.1002/cne.20771
[53] Henneberg M. Natural selection through differential fertility in human populations: Quantitative evaluation of selection intensity. Przeglad Antropologiczny. 1980;46:21–60.
[54] Darwin C. The descent of man, and selection in relation to sex. New ed. London: John Murray; 1901.
[55] You W. Henneberg M. Cancer incidence increasing globally: the role of relaxed natural selection. Evol Appl. 2017;00:1–13.
[56] You W, Henneberg M. Modern medical services, a double-edged sword manages symptoms, but accumulates genetic background of cardiovascular diseases: A cross populational analysis of 217 countries. Health Sci Rep. 2024;7(1):e1828. doi: 10.1002/hsr2.1828
[57] Stephan CN, Henneberg M. Medicine may be reducing the human capacity to survive. Med Hypotheses. 2001;57(5):633–637. doi: 10.1054/mehy.2001.1431
[58] Krause N, Bengston V, Silverstein M, et al. Handbook of theories of aging; 2009.
[59] Brissette I, Scheier MF, Carver CS. The role of optimism in social network development, coping, and psychological adjustment during a life transition. J Pers Soc Psychol. 2002;82(1):102–111. doi: 10.1037/0022-3514.82.1.102
[60] Andersson MA. Dispositional optimism and the emergence of social network diversity. Sociol Q. 2012;53(1):92–115. doi: 10.1111/j.1533-8525.2011.01227.x
[61] Rasmussen HN, Wrosch C, Scheier MF, et al. Self-regulation processes and health: the importance of optimism and goal adjustment. J Pers. 2006;74(6):1721–1747. doi: 10.1111/j.1467-6494.2006.00426.x
[62] Levine GN. The mind-heart-body connection. Circulation. 2019;140(17):1363–1365. doi: 10.1161/CIRCULATIONAHA.119.041914
[63] Bai A, Li H, Huang Y, et al. A survey of overall life satisfaction and its association with breast diseases in Chinese women [Research Support, Non-U.S. Gov't]. Cancer Med. 2016;5(1):111–119. doi: 10.1002/cam4.565
[64] Pihlman J, Magnussen CG, Rovio SP, et al. Association between number of siblings and cardiovascular risk factors in childhood and in adulthood: The Cardiovascular Risk in Young Finns Study. J Pediatr. 2021;237:87–95.e1. doi: 10.1016/j.jpeds.2021.05.058**This reference examines the association between sibling number and cardiovascular risk factors, providing a relevant framework for our study's focus on family size.
[65] Sanghavi M, Kulinski J, Ayers CR, et al. Association between number of live births and markers of subclinical atherosclerosis: The Dallas Heart Study. Eur J Prev Cardiol. 2016;23(4):391–399. doi: 10.1177/2047487315571891
[66] Magnus MC, Iliodromiti S, Lawlor DA, et al. Number of offspring and cardiovascular disease risk in men and women: the role of shared lifestyle characteristics. Epidemiology. 2017;28(6):880–888. doi: 10.1097/EDE.0000000000000712
[67] Gallagher LG, Davis LB, Ray RM, et al. Reproductive history and mortality from cardiovascular disease among women textile workers in Shanghai, China. Int J Epidemiol. 2011;40(6):1510–1518. doi: 10.1093/ije/dyr134
[68] Jacobsen BK, Knutsen SF, Oda K, et al. Parity and total, ischemic heart disease and stroke mortality. The Adventist Health Study, 1976–1988. Eur J Epidemiol. 2011;26(9):711–718. doi: 10.1007/s10654-011-9598-x
[69] Peters SA, Yang L, Guo Y, et al. Parenthood and the risk of cardiovascular diseases among 0.5 million men and women: findings from the China Kadoorie Biobank. Int J Epidemiol. 2017;46(1):180–189. doi: 10.1093/ije/dyw144
[70] Nilsson PM, Sundquist J, Sundquist K, et al. Sibling rank and sibling number in relation to cardiovascular disease and mortality risk: a nationwide cohort study. BMJ Open. 2021;11(6):e042881. doi: 10.1136/bmjopen-2020-042881*This large-scale cohort study directly correlates family size to CVD risk and mortality, making it highly relevant and of considerable interest to our findings.

[71] Parikh NI, Cnattingius S, Dickman PW, et al. Parity and risk of later-life maternal cardiovascular disease. Am Heart J. 2010;159(2):215–221. e6. doi: 10.1016/j.ahj.2009.11.017
[72] Levenson JW, Skerrett PJ, Gaziano JM. Reducing the global burden of cardiovascular disease: the role of risk factors. Prev Cardiol. 2002;5(4):188–199. doi: 10.1111/j.1520-037x.2002.00564.x
[73] Costello A, Abbas M, Allen A, et al. Managing the health effects of climate change: lancet and University College London Institute for Global Health Commission. Lancet. 2009;373(9676):1693–1733. doi: 10.1016/S0140-6736(09)60935-1
[74] Unamuno X, Gómez-Ambrosi J, Rodríguez A, et al. Adipokine dysregulation and adipose tissue inflammation in human obesity. Eur J Clin Invest. 2018;48(9):e12997.
[75] You W, Henneberg M. Meat consumption providing a surplus energy in modern diet contributes to obesity prevalence: an ecological analysis. BMC Nutr. 2016;2(1):1–11.
[76] Ghosh S, Dhar S, Bhattacharjee S, et al. Contribution of environmental, genetic and epigenetic factors to obesity-related metabolic syndrome. Nucleus. 2023;66(2):215–237. doi: 10.1007/s13237-023-00420-y
[77] Brown SL, Manning WD, Stykes JB. Family structure and child well-being: Integrating family complexity. J Marriage Fam. 2015;77(1):177–190. doi: 10.1111/jomf.12145
[78] Härkönen J, Bernardi F, Boertien D. Family dynamics and child outcomes: An overview of research and open questions. Eur J Popul. 2017;33(2):163–184. doi: 10.1007/s10680-017-9424-6
[79] Hugo G. Patterns and trends of urbanization and urban growth in Asia. In: Internal Migration, Urbanization and Poverty in Asia: Dynamics and Interrelationships; 2019. p. 13–45.
[80] Ventriglio A, Torales J, Castaldelli-Maia JM, et al. Urbanization and emerging mental health issues. CNS Spectr. 2021;26(1):43–50. doi: 10.1017/S1092852920001236*[31] The World Bank. Fertility rate, total (births per woman): The World Bank Group. 2017. This reference is essential as it provides the fertility rate data used to quantify family size, a key independent variable in our study.