Research Square

Preprints are preliminary reports that have not undergone peer review.
They should not be considered conclusive, used to inform clinical practice,
or referenced by the media as validated information.

Population Attributable Fraction of Coronary Heart Disease and Stroke Due to Insufficient Physical Activity in Iranian Adults: Evidence from the STEPS 2021 Survey

Mohammadamin Sabbagh Alvani
Non-Communicable Diseases Research Center, Endocrinology and Metabolism Population Sciences Institute, Tehran University of Medical Sciences, Tehran, Iran

Keyvan Karimi
Non-Communicable Diseases Research Center, Endocrinology and Metabolism Population Sciences Institute, Tehran University of Medical Sciences, Tehran, Iran

Sepehr Khosravi
Non-Communicable Diseases Research Center, Endocrinology and Metabolism Population Sciences Institute, Tehran University of Medical Sciences, Tehran, Iran

Mohammadreza Naderian
Non-Communicable Diseases Research Center, Endocrinology and Metabolism Population Sciences Institute, Tehran University of Medical Sciences, Tehran, Iran

Yosra Azizpour
Non-Communicable Diseases Research Center, Endocrinology and Metabolism Population Sciences Institute, Tehran University of Medical Sciences, Tehran, Iran

Ali Golestani
Endocrinology and Metabolism Research Center, Endocrinology and Metabolism Clinical Sciences Institute, Tehran University of Medical Sciences, Tehran, Iran

Moloud Payab
Non-Communicable Diseases Research Center, Endocrinology and Metabolism Population Sciences Institute, Tehran University of Medical Sciences, Tehran, Iran

Maryam Selk-Ghaffari
Sports Medicine Research Center, Neuroscience Institute, Tehran University of Medical Sciences, Tehran, Iran.

Hanieh-Sadat Ejtahed
Obesity and Eating Habits Research Center, Endocrinology and Metabolism Clinical Sciences Institute, Tehran University of Medical Sciences, Tehran, Iran.

Amirhossein Takian
Centre of Excellence for Global Health (CEGH), Department of Global Health, School of Public Health, Tehran University of Medical Sciences (TUMS), Tehran, Iran

Afshin Ostovar
Osteoporosis Research Center, Endocrinology and Metabolism Clinical Sciences Institute, Tehran University of Medical Sciences, Tehran, Iran
Rajabali Daroudi
Department of Health Management, Policy and Economics, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran
Elham Ahmadnezhad
National Institute of Health Research, Tehran University of Medical Sciences, Tehran, Iran
Samaneh Akbarpour
Sleep Breathing Disorders Research Center, Tehran University of Medical Sciences, Tehran, Iran
Nazila Rezaei
nazila_r@yahoo.com

Non-Communicable Diseases Research Center, Endocrinology and Metabolism Population Sciences Institute, Tehran University of Medical Sciences, Tehran, Iran

---

Research Article

Keywords: Physical inactivity, Cardiovascular diseases, Coronary heart disease, Stroke, Prevalence, Population, Iran, attributable fraction, STEPs survey, Gender disparity

Posted Date: May 14th, 2026

DOI: https://doi.org/10.21203/rs.3.rs-9435609/v1

License: This work is licensed under a Creative Commons Attribution 4.0 International License.
Read Full License

Additional Declarations: No competing interests reported.

Version of Record: A version of this preprint was published at Journal of Diabetes & Metabolic Disorders on July 2nd, 2026. See the published version at https://doi.org/10.1007/s40200-026-01992-7.

Abstract

Background

Insufficient physical activity (IPA) is a key lifestyle-related cardiovascular risk factor based on evidence from prospective cohort studies. Iran has one of the highest cardiovascular diseases (CVD) burdens in the Middle East and North Africa (MENA) region. This study estimated prevalence-based population-attributable fractions (PAFs) of prevalent CVD, coronary heart disease (CHD), and stroke associated with insufficient non-occupational physical activity among Iranian adults aged ≥ 40 years.

Methods

We analyzed data from 16.552 adults aged ≥ 40 years participating in the nationally representative Iran STEPS 2021 survey. IPA was defined as < 600 metabolic equivalent task (MET) minutes of non-occupational moderate-to-vigorous physical activity per week. PAFs were estimated using Miettinen's formula by combining the prevalence of IPA among individuals with prevalent disease and sex-specific relative risks derived from a large prospective meta-analysis. Analyses incorporated sampling weights and are presented as percentages with 95% confidence intervals (CIs).

Results

The weighted prevalence of CVD was 11.48% (95% CI: 10.95–12.04), CHD 10.43% (95% CI: 9.91–10.96), and stroke 2.17% (95% CI: 1.94–2.43). IPA was more prevalent among females, older adults, and individuals with lower educational attainment. Under a modeled counterfactual scenario of sufficient non-occupational physical activity, the estimated PAF was 19.2% (95% CI: 15.1–23.2) for CVD, with higher fractions among women (25.2%) than men (16.6%) and among adults aged ≥ 60 years. Corresponding PAFs were 15.9% (95% CI: 11.2–20.5) for CHD and 17.1% (95% CI: 11.5–22.5) for stroke.

Conclusions

Using a prevalence-based modeling approach, a substantial proportion of prevalent cardiovascular disease among Iranian adults aged ≥ 40 years represent the proportion of prevalent disease theoretically preventable under modeled scenarios of sufficient non-occupational physical activity. These findings represent policy-oriented scenario estimates rather than causal effects and highlight population subgroups in which physical activity promotion may have greater public health relevance.

Trial Registration

Not applicable

1. Introduction

CVDs remain a leading cause of morbidity and premature mortality worldwide. According to Global Burden of Disease estimates in 2021, the global age-standardized burden of CVDs was estimated at 4,942.3 disability-adjusted life years (DALYs) and 245.1 deaths per 100,000 populations. The Middle East and North Africa (MENA) region bears the highest global prevalence of CVDs (9,978.7 per 100,000), exceeding the global average of 7,241.7 per 100,000 by 38%. This elevated burden is reflected in higher regional DALYs and mortality rates of 7,040.1 and 361.4 per 100,000, respectively. In Iran, the burden is even greater, with a prevalence of 10,337.8 per 100,000 population, highlighting a major public health challenge (1). Among CVD subtypes, CHD and ischemic stroke account for a substantial proportion of this burden and represent key targets for prevention strategies (1).

IPA, defined as engaging in less than 600 metabolic equivalent task (MET) minutes of moderate-to-vigorous physical activity per week, is a well-established modifiable risk factor for CVD, including CHD and stroke (2, 3). Globally, IPA is estimated to contribute to approximately 7.2% of all-cause mortality and 7.6% of CVD-related deaths (2). The World Health Organization (WHO) has reported that nearly 1.8 billion adults worldwide do not meet recommended physical activity levels (4). Data from Iran's 2021 STEPwise approach to non-communicable disease risk factor surveillance (STEPs) indicate that the prevalence of IPA exceeds the global average, suggesting a substantial potential public health impact in the national context (5). In the STEPS survey, physical activity is assessed using the Global Physical Activity Questionnaire (GPAQ), which captures occupational, transport-related, and leisure-time activity. However, most prospective studies linking physical activity to cardiovascular outcomes are based primarily on non-occupational physical activity, including leisure-time and transport-related domains(6, 7).

Occupational physical activity may have different health associations and is subject to distinct patterns of confounding and measurement error. Therefore, restricting the exposure definition to non-occupational physical activity improves conceptual alignment between exposure prevalence and externally derived relative risks and enhances interpretability of population-attributable fraction estimates.

In low- and middle-income countries such as Iran, the management of CVDs is challenged by high treatment costs and limited healthcare resources. These constraints underscore the importance of prevention-oriented strategies, among which promoting physical activity is considered one of the most cost-effective approaches to reducing the burden of CHD and stroke (8, 9).

Population-attributable fraction (PAF) is an epidemiological measure that combines the prevalence of a risk factor with externally derived relative risks to estimate the proportion of disease burden that could theoretically be prevented under a counterfactual scenario in which exposure is eliminated, assuming that the relative risks are causal and applicable to the target population(10). When adjusted relative risks are available, Miettinen's formula provides less biased estimates than simpler methods, such as Levin's equation, by accounting for confounding (11, 12).

Despite the high prevalence of both cardiovascular disease and IPA in Iran, no nationally representative study has quantified sex- and age-specific, prevalence-based PAFs of CHD and stroke associated with insufficient non-occupational physical activity. Addressing this gap may help inform prioritization of physical activity promotion within national non-communicable disease (NCD) prevention strategies.

Accordingly, this study aimed to estimate nationally representative, sex- and age-specific PAF of prevalent CVD, CHD, and stroke associated with insufficient non-occupational physical activity among Iranian adults aged 40 years and older, using data from the 2021 Iran STEPS survey and relative risks derived from large prospective cohort studies.

2. Materials and Methods

2.1. Study Design

This cross-sectional study used data from the 2021 Iran STEPwise approach to non-communicable disease (NCD) risk factor surveillance (STEPS) survey, conducted in accordance with WHO guidelines (13).

The STEPS program collects standardized, nationally representative data on major NCD risk factors through three sequential components: (1) behavioral risk factors, (2) physical and anthropometric measurements, and (3) biochemical assessments. The 2021 STEPS survey employed a multistage, stratified cluster sampling design to select participants aged ≥ 18 years from urban and rural areas of all 31 provinces of Iran. Detailed sampling procedures and data collection methods have been reported elsewhere (14).

A multistage, cluster-based, systematic random sampling method was used to select participants aged ≥ 18 years. For the present analysis, we restricted the sample to adults aged ≥ 40 years to align with the age range at highest risk for CVD. This threshold was chosen a priori because many cohort studies and prevention frameworks begin estimating CVD incidence and lifetime risk from age 40, when atherosclerotic events start to occur with sufficient frequency for stable and policy-relevant estimates (15, 16). Large population-based analyses of modifiable CVD risk factors have likewise limited primary analyses to adults aged ≥ 40 years (17, 18). In Iran, national NCD and STEPS-based work has focused on adults aged 40–70 years for CVD risk monitoring and intervention planning, reflecting the concentration of events in this age range (19, 20).

Of the 27,874 individuals who participated in the 2021 STEPS survey, 16.552 adults aged ≥ 40 years (mean age: 55.9 ± 0.1 years) with complete data on physical activity and cardiovascular outcomes were included in the final analytic sample. A detailed flow diagram describing participant inclusion and exclusion is provided in Supplementary Figure S1.

2.2. Definition and Measurement of Variables

2.2.1. Physical activity

Physical activity was assessed using version 2 of the WHO Global Physical Activity Questionnaire (GPAQ), which captures activity in three domains: occupational, transport-related, and recreational (leisure-time) (6, 7). The GPAQ allows calculation of weekly metabolic equivalent task (MET) minutes, with vigorous activity weighted at eight METs and moderate activity at four METs, in accordance with WHO guidelines. Total non-occupational physical activity was calculated by summing transport-related and leisure-time activity. IPA was defined as engaging in < 600 MET minutes per week of non-occupational moderate-to-vigorous physical activity, consistent with international recommendations (21). Participants were classified as having sufficient (≥ 600 MET minutes/week) or insufficient physical activity.

2.2.2. Cardiovascular outcomes

CVD status was determined using two standardized self-report items included in the STEPS questionnaire:1. “Have you ever been told by a doctor or health professional that you had a heart attack or chest pain from heart disease (angina) or if they reported a history of coronary artery bypass graft surgery, percutaneous coronary intervention (angioplasty), or stent placement?” 2. “Have you ever had a stroke?” For analysis, we used a composite CVD definition, considering a positive response to either question as CVD, and separate outcomes, examining CHD and stroke independently. Stroke cases were defined based on the dedicated stroke question.

2.2.3. Sociodemographic covariates

Sociodemographic characteristics were collected using standardized STEPS questionnaires. Variables included age group (40–59, ≥ 60 years), sex, marital status (single, married, widowed/divorced), education level, and urban or rural residence. Education was categorized as: 0 years (illiterate/no formal education), 1–6 years (elementary), 7–11 years (middle/high school), and ≥ 12 years (college or higher). These covariates were used for descriptive analyses to characterize the study population.

2.3. Statistical Analysis

2.3.1. Population attributable fraction (PAF)

Population-attributable fraction (PAF) was estimated as a prevalence-based measure combining contemporaneous exposure prevalence among individuals with prevalent disease and relative risks derived from prospective studies (10, 22, 23). Accordingly, PAF estimates in this study represent modeled, policy-oriented scenario measures rather than causal effects derived from the cross-sectional data.

Two key parameters determine the PAF: (1) the prevalence of the risk factor among cases and (2) the RR of the outcome associated with the risk factor (10). PAF was estimated using Miettinen’s formula, which

permits the use of adjusted RRs derived from large prospective meta-analyses that account for key confounders such as age, smoking, body mass index, and comorbidities.

This approach provides more robust and less biased estimates than simpler methods such as Levin's Eq. (11):

PAF=pc $\frac{RR-1}{RR}$

Here, pc is the weighted prevalence of IPA among individuals with CVD, CHD, or stroke, and RR represents the sex-specific adjusted relative risk of each outcome associated with non-occupational IPA.

The prevalence of IPA among individuals with each outcome was estimated from the STEPS survey data. Sex-specific relative risks were obtained from a large meta-analysis of 94 prospective cohort studies involving more than 30 million participants worldwide(24). This meta-analysis provided pooled estimates adjusted for major confounders, including age, smoking status, body mass index, and major comorbidities. Although residual confounding cannot be excluded, these pooled estimates represent the most robust and generalizable evidence currently available. The RRs were reported for each outcome separately for both sexes (overall) and for assumed non-occupational physical activity greater than 8.75 MET-hours/week, approximately 600 MET-minutes/week, as sufficient PA groups. The input RRs and corresponding CIs for total CVD, CHD, and stroke were 0.73 (0.69 to 0.79), 0.79 (0.74 to 0.84), and 0.80 (0.75 to 0.85), respectively.

2.3.2. Descriptive statistics and weighting

All analyses incorporated the complex sampling design of the STEPS survey, including stratification, clustering, and sampling weights, to ensure national representativeness. Sampling weights were derived from the 2016 Iranian National Census and adjusted for age, sex, and place of residence (14). Categorical variables were summarized as weighted proportions with corresponding 95% confidence intervals. Prevalence estimates were reported descriptively without formal hypothesis testing.

2.3.3. Software and graphical presentation

Statistical analyses were conducted using R software (version 4.3.3). PAFs and corresponding 95% confidence intervals were estimated using the PAF package (25). Confidence intervals were derived by propagating uncertainty in both exposure prevalence and relative risk estimates through simulation-based methods implemented in the package. The delta method was applied in the complex survey design to estimate confidence intervals (CIs) for the prevalence of IPA. Then the provided CIs for relative risks (RRs) from the cited meta-analysis was extracted. Finally, the CIs for prevalence (pc) and RRs was used and entered *in graphpaf package* to estimate prevalence-based PAF and corresponding CI based on the bootstrapping method. All figures were generated using the ggplot2 package.

2.4. Ethics approval and consent to participate

The study was approved by the Research Ethics Committee of the School of Medicine, Tehran University of Medical Sciences (IR.TUMS.MEDICINE.REC.1403.230) and conducted in accordance with the Declaration of Helsinki. All participants provided written informed consent, with assurance of confidentiality and voluntary participation. Data were deidentified to ensure privacy and were accessible only to the study's principal investigator and data manager. The data used for this study were accessed in 20 February 2025.

3. Results

3.1. Overall Prevalence of CVD, CHD, and Stroke

The analysis included 16,552 Iranian adults aged ≥40 years, with a mean age of 55.9 ± 0.10 years. The weighted prevalence of CVD was 11.5% (95% CI: 10.9–12.0), including 10.4% (95% CI: 9.9–10.9) with CHD and 2.17% (95% CI: 1.94–2.43) reporting a history of stroke (Table 1).

CVD prevalence increased across age groups, from 6.4% (95% CI: 5.9–6.9) among adults aged 40–59 years to 20.6% (95% CI: 19.5–21.8) among those aged ≥60 years. Similar age-related patterns were observed for CHD (5.6% to 19.1%) and stroke (1.2% to 3.8).

Higher prevalence was observed among males (14.1%, 95% CI: 13.2–15.0) than females (9.3%, 95% CI: 8.7–10.0). Urban residents had slightly higher CVD prevalence (11.8%) than rural residents (10.3%), largely reflecting differences in CHD prevalence (Table 1).

Across marital status categories, the highest CVD prevalence was observed among widowed or divorced individuals (16.2%, 95% CI: 14.5–18.1), followed by married participants (10.9%, 95% CI: 10.4–11.5) and single individuals (7.0%, 95% CI: 4.7–10.2). CVD prevalence was highest among participants with no formal education (16.0%, 95% CI: 14.8–17.4) and lowest among those with ≥12 years of schooling (8.7%, 95% CI: 7.8–9.7).

3.2. Prevalence of CVD, CHD, and Stroke by Physical Activity Status

The prevalence of CVD, CHD, and stroke according to physical activity status is presented in Figure 1. For all outcomes, higher prevalence was observed among participants with IPA compared with those meeting recommended activity levels.

Overall, CVD prevalence was 12.2% among participants with IPA and 10.2% among those with sufficient physical activity. Corresponding prevalence estimates were 11.0% versus 9.4% for CHD and 2.5% versus 1.5% for stroke.

Similar patterns were observed among females, in whom disease prevalence was consistently higher in participants with IPA than in those with sufficient activity (Figure 1).

Figure 2 shows the distribution of IPA among participants with and without CVD, CHD, and stroke. IPA prevalence was highest among females with stroke (84.3%), followed by males with stroke (66.3%). Overall, IPA prevalence was 67.1% among participants with CVD and 62.6% among those without CVD. The lowest prevalence of IPA was observed among males without CVD (54.8%).

In the overall study population, the weighted prevalence of IPA was 62.61% (Figure S2).

3.3. PAF Estimates by Sex and Age

Population-attributable fraction (PAF) estimates are presented in Table 2. The overall PAF for CVD associated with IPA was 19.2% (95% CI: 15.1–23.2).

Higher PAF estimates were observed among females (25.2%, 95% CI: 17.3–32.6) than males (16.6%, 95% CI: 15.6–17.5). By age group, PAF estimates were 19.7% (95% CI: 15.5–23.8) among adults aged ≥60 years and 18.3% (95% CI: 14.3–22.3) among those aged 40–59 years.

For CHD, the PAF was 15.9% (95% CI: 11.2–20.5) overall, with higher values among females (23.1%, 95% CI: 10.5–34.3) than males (7.2%, 95% CI: 1.1–13.1). For stroke, the overall PAF was 17.1% (95% CI: 11.5–22.5), with estimates of 20.6% (95% CI: 10.2–30.1) among females and 10.5% (95% CI: 6.0–15.1) among males.

Among females aged ≥60 years, PAF estimates were highest across all outcomes, including 26.0% for CVD, 24.0% for CHD, and 20.6% for stroke.

4. Discussion

Using nationally representative data from the 2021 Iran STEPS survey combined with relative risks derived from large prospective cohort studies, this study estimated the theoretical proportion of prevalent cardiovascular disease (CVD) that could be considered preventable under a scenario of sufficient non-occupational physical activity. Approximately one-fifth of prevalent CVD, CHD, and stroke among Iranian adults aged ≥40 years were attributable to IPA, with higher fractions observed among women and older adults. Given the cross-sectional design and reliance on self-reported outcomes, these estimates should be interpreted as policy-oriented scenario measures rather than evidence of causal effects.

The WHO has set a global target of reducing physical inactivity by 15% by 2030, while Iran has adopted a more ambitious national target of 20% (5, 26). In the context of the high prevalence of IPA observed in STEPS 2021 and effect sizes reported in prospective studies, our findings suggest that a substantial proportion of prevalent CVD (PAF: 19.2%), CHD (15.9%), and stroke (17.1%) could theoretically be prevented if insufficient activity were eliminated. These proportions were particularly high among women (CVD PAF: 25.2%) and older adults. However, reverse causality and outcome misclassification likely inflate these estimates and must be considered when interpreting the results (5).

The weighted prevalence of self-reported CVD, CHD, and stroke in this study was 11.5%, 10.4%, and 2.2%, respectively. Disease prevalence was higher among individuals with insufficient activity than among those meeting recommended levels, and IPA was more common among participants with prevalent disease. This pattern aligns with global evidence indicating that physical inactivity accounts for a substantial share of cardiovascular-related disability-adjusted life years (DALYs) worldwide (27). At the same time, IPA was significantly more prevalent among individuals with CVD than among those without, consistent with previous studies attributing this pattern to physical limitations, psychological factors, and sociodemographic constraints (28).

Because exposure and outcome were measured contemporaneously, these associations do not establish temporal ordering. Reverse causation is likely, as individuals with established cardiovascular disease—particularly stroke survivors—often reduce their physical activity after diagnosis. This may inflate IPA prevalence among cases and lead to overestimation of PAFs. In addition, misclassification of self-reported cardiovascular outcomes, especially angina and chest pain, may attenuate associations and distort subgroup patterns. Differential access to healthcare and diagnostic awareness by sex and education may further contribute to measurement error. Overall, these sources of bias are expected to primarily bias PAF estimates upward, particularly in older adults and individuals with established disease.

The burden of IPA-attributable CVD was particularly high among women and older adults. This pattern is consistent with global estimates but highlights Iran's disproportionate burden, which may be exacerbated by sociodemographic disparities such as lower educational attainment, widowhood, and limited access to preventive services (27). Our findings therefore underscore IPA as a critical yet modifiable contributor to cardiovascular disease in Iran.

Sociodemographic disparities were evident in both physical activity patterns and disease prevalence. Participants with lower educational attainment and those who were widowed or divorced had higher CVD prevalence and higher PAF estimates. Individuals with no formal education had nearly double the prevalence of CVD compared with those with ≥12 years of schooling, likely reflecting lower health literacy and reduced access to preventive care (29, 30). Similar patterns have been reported elsewhere, where higher education, income, and employment status are associated with greater physical activity participation (31). These findings highlight the importance of addressing educational inequalities in cardiovascular prevention strategies.

Marital status was also associated with disease prevalence. Single individuals showed the lowest prevalence, while married and widowed participants had higher rates. Previous research suggests that marital status influences cardiovascular health through pathways related to social support, economic stability, and health behaviors (32). Although findings across studies are not fully consistent, the social context of health remains an important determinant of physical activity and cardiovascular risk.

Age-related increases in disease prevalence were consistent with global patterns (1, 33), while modest urban–rural differences may reflect changing occupational structures and transportation environments.

Higher PAF estimates among women were observed across all outcomes. Comparable sex-specific patterns have been reported in other settings, particularly for stroke risk (3). For example, Salmantabar et al. reported stronger associations between IPA and cardiovascular outcomes among Iranian women than men (34). In contrast, some studies from East Asia have reported smaller sex differences in activity patterns (35). In Iran, sociocultural norms, limited access to women-friendly recreational spaces, and caregiving responsibilities may contribute to lower activity levels among women, particularly at older ages. These contextual factors are essential for interpreting subgroup estimates and designing appropriate interventions.

Globally, CVD prevalence continues to rise, and IPA remains a persistent risk factor (36). Evidence indicates that even low levels of leisure-time physical activity reduce stroke and coronary risk, with relative risk reductions of 20–40% reported in several meta-analyses (37, 38). Together, these findings reinforce the importance of promoting physical activity across the life course.

5. Policy Implications and Recommendations

Our findings suggest several priorities for public health policy and research in Iran. Given the substantial proportion of CVD theoretically attributable to IPA, national prevention strategies should prioritize physical activity promotion, particularly among women, older adults, and socioeconomically disadvantaged groups.

The WHO Global Action Plan on Physical Activity emphasizes governance, supportive environments, opportunity creation, communication, and monitoring as central pillars for increasing population activity levels (39). Evidence from Iran supports this approach. For example, a randomized trial of the WHO-PEN 5As counseling model demonstrated that structured primary care interventions can improve physical activity and other lifestyle behaviors (40).

Iran-specific approaches warrant further investigation through implementation research. Given that approximately one-quarter of female CVD cases were attributable to IPA, and that PAFs were highest among women aged ≥60 years, interventions should prioritize culturally acceptable and accessible opportunities for physical activity. Potential strategies include women-only walking groups in parks or schoolyards, subsidized access to municipal sports facilities, and home-based exercise programs delivered through television, radio, or digital platforms. Parallel efforts should target individuals with lower educational attainment through workplace wellness initiatives and community health worker–led activity programs, particularly in rural areas.

Embedding physical activity counseling within Iran’s primary healthcare network, including Health Houses and comprehensive health centers, could facilitate routine screening and intervention for IPA in alignment with WHO guidelines. These strategies are presented as feasible hypotheses requiring local evaluation rather than interventions directly tested in this study. Their successful implementation will require addressing broader systemic challenges, including resource constraints and organizational barriers within the healthcare system (41).

Finally, WHO guidelines recommend that adults engage in 150–300 minutes of moderate-to-vigorous physical activity per week and reduce sedentary behavior (36, 42). Promoting adherence to these recommendations, while addressing sociocultural and structural barriers, may substantially contribute to reducing the cardiovascular disease burden in Iran.

6. Strengths and Limitations

A major strength of this study is the use of a large, nationally representative sample from the 2021 Iran STEPS survey, encompassing both urban and rural populations across all provinces. The multistage cluster sampling design and application of sampling weights enhance the generalizability of the findings. The use of Miettinen's formula with adjusted relative risks derived from large prospective meta-analyses improves confounding control compared with simpler PAF estimation methods. Stratified analyses by age and sex allowed identification of population subgroups with higher modeled PAF estimates.

Several limitations should be acknowledged. First, the cross-sectional design precludes causal inference. Physical activity was measured contemporaneously, whereas cardiovascular outcomes reflected lifetime self-reported diagnoses. This temporal mismatch increases the likelihood of reverse causation, particularly among individuals with disabling conditions such as stroke, and may lead to upwardly biased PAF estimates.

Second, physical activity and disease outcomes were self-reported. Although the GPAQ is validated, recall and social desirability bias may affect activity estimates. Self-reported cardiovascular diagnoses, especially angina or chest pain, are prone to misclassification, which may attenuate true associations and distort subgroup patterns.

Third, residual confounding remains possible. Although pooled relative risks were adjusted for major confounders, factors such as diet, income, disability, and mental health were not uniformly accounted for across cohorts. Consequently, PAF estimates may be context-dependent and potentially overestimated.

Fourth, international meta-analytic relative risks were applied to the Iranian population. If true associations differ because of genetic, environmental, or healthcare system factors, misestimation may occur. In addition, PAFs represent a theoretical maximum under complete elimination of insufficient physical activity, which is unlikely to be achieved in practice.

Further, the study relied on a single baseline measure of physical activity and did not capture seasonal variation, detailed activity intensity, or sedentary behavior patterns, all of which may influence cardiovascular risk. At the same time, our findings are restricted to adults aged ≥40 years and may not be generalizable to younger adults, among whom absolute CVD risk and event counts are much lower and PAF estimates would be less stable and less directly relevant for current national prevention priorities. Finally, data collection occurred during 2021, when the COVID-19 pandemic may have altered physical activity behaviors and healthcare access, potentially affecting both exposure and outcome measures.

7. Conclusion

Using nationally representative data from the 2021 Iran STEPS survey and relative risks from prospective studies, this analysis estimated prevalence-based population-attributable fractions for cardiovascular disease, coronary heart disease, and stroke associated with insufficient non-occupational physical activity among Iranian adults aged ≥40 years. These modeled estimates represent theoretical scenario measures rather than causal effects.

Under these assumptions, IPA accounted for a substantial proportion of prevalent cardiovascular disease, particularly among women and older adults. Reverse causation and outcome misclassification may have biased these estimates upward. Nevertheless, the findings identify population groups in which physical activity promotion may have greater public health relevance.

Strengthening physical activity promotion within primary care, community settings, and urban planning frameworks may contribute meaningfully to cardiovascular disease prevention in Iran. Future longitudinal studies and implementation research are needed to establish causal relationships, evaluate context-specific interventions, and support evidence-informed policymaking aimed at reducing the national burden of cardiovascular disease.

Abbreviations

• **IPA**
Insufficient Physical Activity
• **CVD**
Cardiovascular Disease
• **CHD**
Coronary Heart Disease
• **DALY**
Disability–Adjusted Life Year
• **MENA**
Middle East and North Africa
• **MET**
Metabolic Equivalent of Task
• **PAF**
Population–Attributable Fraction
• **NCD**
non–communicable disease
• **RR**
Relative Risk
• **STEPS**
STEPwise Approach to Surveillance of Non–Communicable Disease Risk Factors

• **GPAQ**
Global Physical Activity Questionnaire
• **WHO**
World Health Organization
• **LMICs**
Low–and Middle–Income Countries
• **SE**
Standard Error
• **CI**
Confidence Interval
• **OR**
Odds Ratio
• **PA**
Physical Activity
• **UI**
Uncertainty Interval
• **CDC**
Centers for Disease Control and Prevention
• **WHO**
PEN–WHO Package of Essential Noncommunicable (Disease) Interventions

Declarations

Consent for publication

Not applicable.

Availability of data and materials

The data underlying this study are not publicly available due to the inclusion of sensitive and potentially identifiable patient information, in accordance with the Ethics Committee of the Endocrinology and Metabolism Research Institute (EMRI) at Tehran University of Medical Sciences. Researchers interested in accessing the dataset for legitimate academic purposes, such as replication or secondary analyses, may submit a formal request to the corresponding authors or the data access committee at the National Institute for Health Research (NIHR) via nihr@tums.ac.ir.

Funding

This study was funded by Tehran University of Medical Sciences, Tehran, Iran [Grant IDs 1402-4-221-69745]. funding bodies had no role in the study design, data collection, analysis, interpretation of results, decision to publish, or manuscript preparation.

Ethics approval and consent to participate

The study was approved by the Research Ethics Committee of the School of Medicine, Tehran University of Medical Sciences (IR.TUMS.MEDICINE.REC.1403.230) and conducted in accordance with the Declaration of Helsinki. All participants provided written informed consent, with assurance of confidentiality and voluntary participation. Data were deidentified to ensure privacy and were accessible only to the study's principal investigator and data manager. The data used for this study were accessed in 20 February 2025.

Patient and Public Involvement Statement:

Patients and members of the public were not involved in the design, conduct, reporting, or dissemination plans of this secondary data analysis. The study used anonymized data from the nationally representative WHO STEPS 2021 survey.

Competing interests

The authors declare that they have no competing interests.

Author contributions

Conceptualization: Mohammadamin Sabbagh Alvani ,Sepehr Khosravi, Ali Golestani, Nazila Rezaei.

Data curation: Keyvan Karimi

Formal analysis: Keyvan Karimi

Investigation: Mohammadamin Sabbagh Alvani ,Sepehr Khosravi, Ali Golestani

Methodology: Keyvan Karimi, Sameneh Akbarpour

Project administration: Nazila Rezaei, Moloud Payab

Resources: Mohammadamin Sabbagh Alvani, Keyvan Karimi, Ali Golestani, Sepehr Khosravi, Mohammad Reza Naderian, Nazila Rezaei

Supervision: Nazila Rezaei, Samaeneh Akbarpour

Validation: Mohammadamin Sabbagh Alvani, Samaeneh Akbarpour

Visualization: Keyvan Karimi

Writing – original draft: Mohammadamin Sabbagh Alvani, Keyvan Karimi

Writing – review & editing: Ali Golestani, Mohamad Reza Naderian, Sepehr Khosravi, , Elham Ahmadnezhad, Hanieh-Sadat Ejtahed, Afshin Ostovar, Moloud Payab, Maryam Selk-Ghaffari, Amirhossein

Takian, Rajabali Daroudi, sameneh Akbarpour, Nazila Rezaei

Acknowledgments

We sincerely thank our colleagues at the Non-Communicable Diseases Research Center, the Endocrinology and Metabolism Research Institute, and the National Institute of Health Research, Tehran University of Medical Sciences, for their invaluable support and collaboration throughout this study. We also acknowledge the assistance of OpenAI's ChatGPT for language editing, which contributed to improving the clarity and quality of the manuscript.

References

1. Lindstrom M, DeCleene N, Dorsey H, Fuster V, Johnson CO, LeGrand KE, et al. Global burden of cardiovascular diseases and risks collaboration, 1990–2021. J Am Coll Cardiol. 2022;80(25):2372–425.
2. Katzmarzyk PT, Friedenreich C, Shiroma EJ, Lee I-M. Physical inactivity and non-communicable disease burden in low-income, middle-income and high-income countries. Br J Sports Med. 2022;56(2):101–6.
3. Lee M, Lakshminarayan K, Sedaghat S, Sabayan B, Chen LY, Johansen MC, et al. Population attributable fraction of total stroke associated with modifiable risk factors in the United States. Am J Epidemiol. 2024;193(12):1712–9.
4. Organization WH. Nearly 1.8 billion adults at risk of disease from not doing enough physical activity: World Health Organization 2024 [Available from: https://www.who.int/news/item/26-06-2024-nearly-1.8-billion-adults-at-risk-of-disease-from-not-doing-enough-physical-activity
5. Nejadghaderi SA, Ahmadi N, Rashidi M-M, Ghanbari A, Noori M, Abbasi-Kangevari M, et al. Physical activity pattern in Iran: findings from STEPS 2021. Front public health. 2023;10:1036219.
6. Armstrong T, Bull F. Development of the world health organization global physical activity questionnaire (GPAQ). J Public Health. 2006;14(2):66–70.
7. Organization WH. Global physical activity questionnaire (GPAQ) analysis guide. Geneva: World Health Organization. 2012:1–22.
8. Pandian JD, Gall SL, Kate MP, Silva GS, Akinyemi RO, Ovbiagele BI, et al. Prevention of stroke: a global perspective. Lancet. 2018;392(10154):1269–78.
9. Ghozy S, Zayan AH, El-Qushayri AE, Parker KE, Varney J, Kallmes KM, et al. Physical activity level and stroke risk in US population: A matched case–control study of 102,578 individuals. Ann Clin Transl Neurol. 2022;9(3):264–75.
10. Mansournia MA, Altman DG. Population attributable fraction. BMJ. 2018;360.
11. Miettinen OS. Proportion of disease caused or prevented by a given exposure, trait or intervention. Am J Epidemiol. 1974;99(5):325–32.

12. Al Tunaiji H, Davis JC, Mansournia MA, Khan KM. Population attributable fraction of leading non-communicable cardiovascular diseases due to leisure-time physical inactivity: a systematic review. BMJ Open Sport Exerc Med. 2019;5(1).
13. Riley L, Guthold R, Cowan M, Savin S, Bhatti L, Armstrong T, et al. The World Health Organization STEPwise approach to noncommunicable disease risk-factor surveillance: methods, challenges, and opportunities. Am J Public Health. 2016;106(1):74–8.
14. Djalalinia S, Azadnajafabad S, Ghasemi E, Yoosefi M, Rezaei N, Farzi Y, et al. Protocol design for surveillance of risk factors of non–communicable diseases during the COVID-19 pandemic: an experience from Iran STEPS Survey 2021. Arch Iran Med. 2022;25(9):634.
15. Kannel WB, Vasan RS. Is age really a non-modifiable cardiovascular risk factor? Am J Cardiol. 2009;104(9):1307–10.
16. Driver JA, Djoussé L, Logroscino G, Gaziano JM, Kurth T. Incidence of cardiovascular disease and cancer in advanced age: prospective cohort study. BMJ. 2008;337.
17. Tian F, Chen L, Qian ZM, Xia H, Zhang Z, Zhang J, et al. Ranking age-specific modifiable risk factors for cardiovascular disease and mortality: evidence from a population-based longitudinal study. EClinicalMedicine. 2023;64:102230.
18. Hamer M, Kivimäki M, Gale CR, Batty GD. Lifestyle Risk Factors for Cardiovascular Disease in Relation to COVID-19 Hospitalization: A Community-Based Cohort Study of 387,109 Adults in UK. medRxiv. 2020.
19. Farzadfar F, Yousefi M, Jafari-Khounigh A, Khorrami Z, Haghdoost A, Shadmani FK. Trend and projection of non-communicable diseases risk factors in Iran from 2001 to 2030. Sci Rep. 2024;14(1):8092.
20. Ebrahimi H, Masinaei M, Aminorroaya A, Aryan Z, Mehdipour P, Rostam-Abadi Y, et al. Risk of incident cardiovascular diseases at national and subnational levels in Iran from 2000 to 2016 and projection through 2030: insights from Iran STEPS surveys. PLoS ONE. 2023;18(8):e0290006.
21. Organization WH. WHO Global recommendations on physical activity for health. Geneva: World Health Organization; 2011. 2021.
22. Greenland S. Measures of effect and measures of association. Mod Epidemiol. 2008:51–70.
23. Szklo M, Nieto FJ. Epidemiology: beyond the basics. Jones & Bartlett; 2014.
24. Garcia L, Pearce M, Abbas A, Mok A, Strain T, Ali S, et al. Non-occupational physical activity and risk of cardiovascular disease, cancer and mortality outcomes: a dose–response meta-analysis of large prospective studies. Br J Sports Med. 2023;57(15):979–89.
25. Ferguson J, O'Connell M. Estimating and displaying population attributable fractions using the R package: graphPAF. Eur J Epidemiol. 2024;39(7):715–42.
26. Organization WH. Global action plan on physical activity 2018–2030: more active people for a healthier world. World Health Organization; 2019.

27. Luo Y, Liu J, Zeng J, Pan H. Global burden of cardiovascular diseases attributed to low physical activity: An analysis of 204 countries and territories between 1990 and 2019. Am J Prev Cardiol. 2024;17:100633.
28. Bakhtiar AB, Hanafi MH, Alghwiri A, Manaf H. Factors affecting level of physical activity among stroke survivors: A scoping review. Malaysian J Med Sciences: MJMS. 2024;31(5):115.
29. Magnani JW, Ning H, Wilkins JT, Lloyd-Jones DM, Allen NB. Educational attainment and lifetime risk of cardiovascular disease. JAMA Cardiol. 2024;9(1):45–54.
30. Cathro CJ, Brenn T, Chen SLF. Education level and self-reported cardiovascular disease in Norway—the tromsø study, 1994–2016. Int J Environ Res Public Health. 2023;20(11):5958.
31. Arora S, Ayyathan SS, Burzynski E, Phillips V. Physical activity exercise behavior in individuals with a history of stroke: a retrospective study. Discover Med. 2025;2(1):20.
32. Humbert X, Rabiaza A, Fedrizzi S, Alexandre J, Menotti A, Touzé E, et al. Marital status and long-term cardiovascular risk in general population (Gubbio, Italy). Sci Rep. 2023;13(1):6723.
33. Prevention CfDCa. About heart disease 2024 [Available from: https://www.cdc.gov/heart-disease/about/?CDC_AAref_Val=https://www.cdc.gov/heartdisease/about.htm
34. Salmantabar P, Abzhandadze T, Viktorisson A, Reinholdsson M, Sunnerhagen KS. Pre-stroke physical inactivity and stroke severity in male and female patients. Front Neurol. 2022;13:831773.
35. Nakano W, Kobayashi S, Maezawa T, Ohashi Y, Kohno Y. Sex differences in physical activity in people after stroke: a cross-sectional study. Phys therapy Res. 2021;24(3):280–4.
36. Joynt Maddox KE, Elkind MS, Aparicio HJ, Commodore-Mensah Y, de Ferranti SD, Dowd WN, et al. Forecasting the burden of cardiovascular disease and stroke in the United States through 2050—prevalence of risk factors and disease: a presidential advisory from the American Heart Association. Circulation. 2024;150(4):e65–88.
37. De Santis F, Romoli M, Foschi M, Sciancalepore FD, D'Anna L, Barba L, et al. Risk of stroke with different levels of leisure-time physical activity: a systematic review and meta-analysis of prospective cohort studies. J Neurol Neurosurg Psychiatry. 2024;95(6):504–14.
38. Madsen TE, Samaei M, Pikula A, Yu AY, Carcel C, Millsaps E, et al. Sex differences in physical activity and incident stroke: a systematic review. Clin Ther. 2022;44(4):586–611.
39. Bull FC, Al-Ansari SS, Biddle S, Borodulin K, Buman MP, Cardon G, et al. World Health Organization 2020 guidelines on physical activity and sedentary behaviour. Br J Sports Med. 2020;54(24):1451–62.
40. Amini N, Rakhshanderou S, Ramezankhani A, Delavari A, Ghaffari M. WHO-PEN intervention in Iran's health system based on 5As healthy lifestyle counseling model: A randomized-clinical trial. J Educ Health Promot. 2023;12:18.
41. Mahdaviani B, Soleimani Z, Selk-Ghaffari M, Pourgharib shahi MH, Masoumi S, Kordi R. Barriers to physical activity in the Iranian population: findings from the STEPwise surveillance 2021. BMC Public Health. 2024;24(1):2610.

42. World Health Organization G. WHO guidelines approved by the guidelines review committee. Global recommendations on physical activity for health Geneva. Switzerland: World Health Organization; 2010.

Tables

Table 1

Socio-demographic factors of population in different disease subgroup; aged 40 years and older)

Variable		CVD+ % [95%CI]	CHD + % [95%CI]	Stroke+ % [95%CI]	Total % [95%CI]
Total population (N = 16,552; mean age: 55.94 ± 0.10)		**11.48 [10.95, 12.04]**	**10.43[9.91,10.96]**	**2.17 [1.94, 2.43]**	
Age group	40–59 years	6.45 [5.94, 6.99]	5.66 [5.191,6.181]	1.278 [1.06,1.54]	64.55 [63.73,65.36]
	≥ 60 years	20.64 [19.52,21.82]	19.09 [17.99,20.23]	3.80 [3.30,4.38]	35.45 [34.64,36.27]
Sex	Female	9.34 [8.7,10.03]	8.39 [7.78,9.047]	1.80 [1.526,2.136]	55.13 [54.28,55.97]
	Male	14.11 [13.25,15.02]	12.92 [12.09,13.8]	2.62 [2.28,3.06]	44.87 [44.03,45.72]
Residency	Urban	11.83 [11.21,12.48]	10.86 [10.27,11.49]	2.16 [1.90,2.46]	76.07 [75.35,76.77]
	Rural	10.37 [9.377,11.46]	9.0 3 [8.09,10.06]	2.20 [1.75,2.75]	23.93 [23.23,24.65]
Marriage	Single	7.02 [4.76,10.25]	5.22 [3.29,8.20]	2.41 [1.252,4.68]	2.87 [2.62,3.18]
	Married	10.96 [10.4,11.55]	9.96 [9.42,10.53]	2.03 [1.72,2.30]	85.15 [84.53,85.74]
	Widow /divorced	16.27 [14.54,18.15]	14.92 [13.25,16.74]	3.13 [2.37,4.11]	11.98 [11.44,12.54]
Schooling years	0	16.08 [14.81,17.44]	14.55 [13.33,15.86]	3.11 [2.55,3.796]	21.14 [20.47,21.83]
	1–6	12.32 [11.37,13.35]	11.07 [10.16,12.05]	2.59 [2.15,3.11]	31.50 [30.72,32.29]
	7–11	9.07 [7.85,10.30]	8.19 [7.09,9.43]	1.457 [1.02,2.04]	17.11 [16.47,17.77]
	≥ 12	8.75 [7.888,9.707]	8.09 [7.251,9.07]	1.50 [1.16,1.95]	30.25 [29.46,31.04]

Table 2
PAF of CVD to Insufficient non-occupational activity by sex and age group in population aged 40 years and older.

PAF % (95% CI)			
CVD	Female	Male	Total population
40–59 years	23.7 (16.1, 30.9)	16.1 (14.6, 17.6)	18.3 (14.3,22.3)
≥ 60 years	26.0 (17.9, 33.5)	16.8 (15.7, 18.0)	19.7 (15.5,23.8)
Overall	25.2 (17.3, 32.6)	16.6 (15.6, 17.5)	19.2 (15.1,23.2)
CHD			
40–59 years	21.3 (9.5, 32.1)	7.0 (1.1,12.8)	15.0 (10.5,19.5)
≥ 60 years	24.0 (10.9, 35.4)	7.3 (1.2,13.4)	16.4 (11.6,21.2)
Overall	23.1 (10.5, 34.3)	7.2 (1.1,13.1)	15.9 (11.2,20.5)
Stroke			
40–59 years	20.2 (9.9, 29.8)	10.1 (5.7,14.9)	16.8 (11.3,22.4)
≥ 60 years	20.6 (10.2, 30.2)	10.7 (6.1,15.4)	17.2 (11.5,22.7)
Overall	20.6 (10.2, 30.1)	10.5 (6.0,15.1)	17.1 (11.5,22.5)
Cardiovascular diseases (CVD), Coronary heart disease (CHD), Population-attributable fraction(PAF)			

Figures

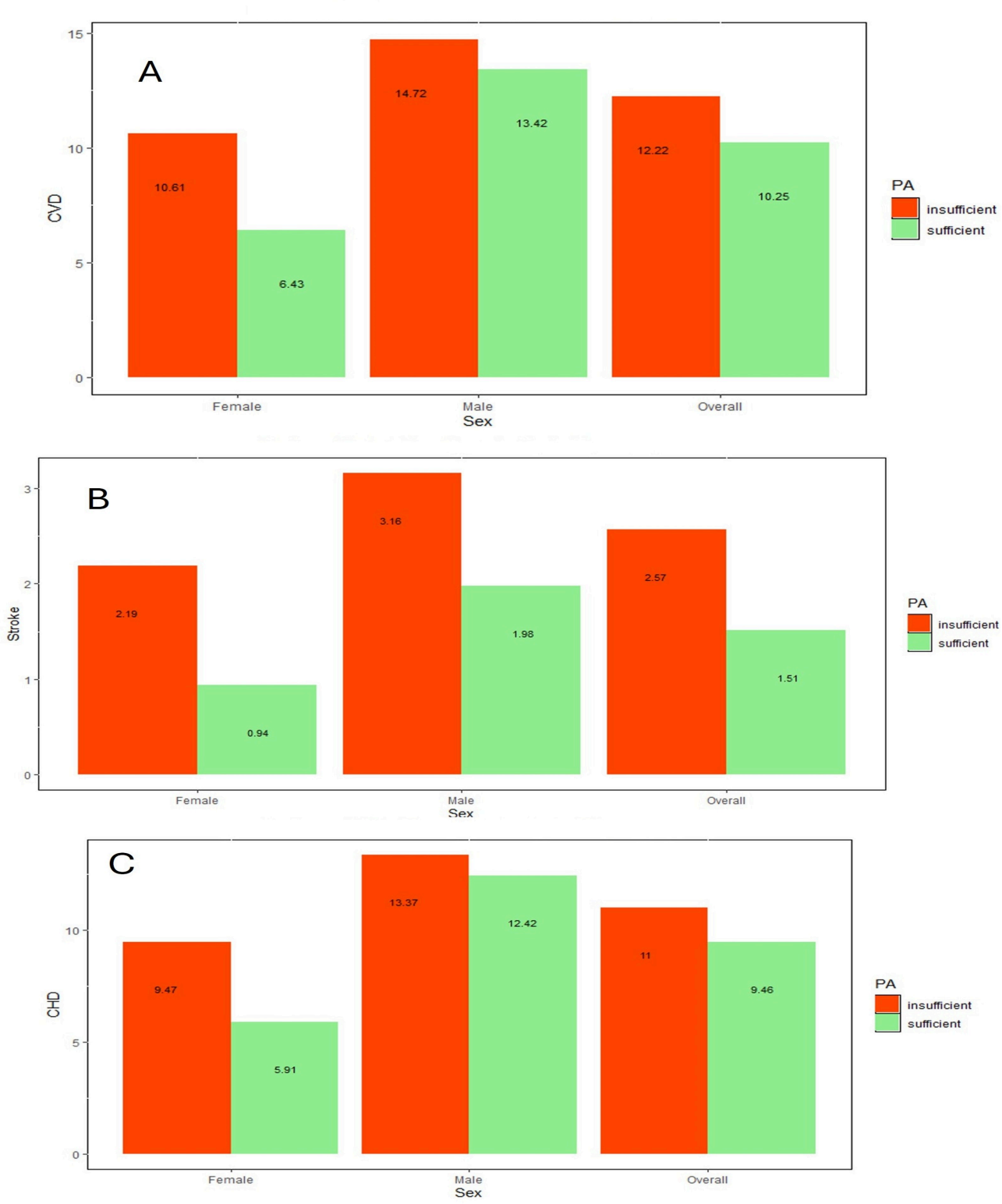


Figure 1

Weighted Prevalence (%) of cardiovascular disease (CVD) (A), Stroke (B) and coronary heart disease (CHD)(C), in the different subgroups of non-occupational physical activity among Iranian adults aged ≥40 years, Iran STEPS 2021.

Values represent cross-sectional prevalence estimates and do not imply causal associations.

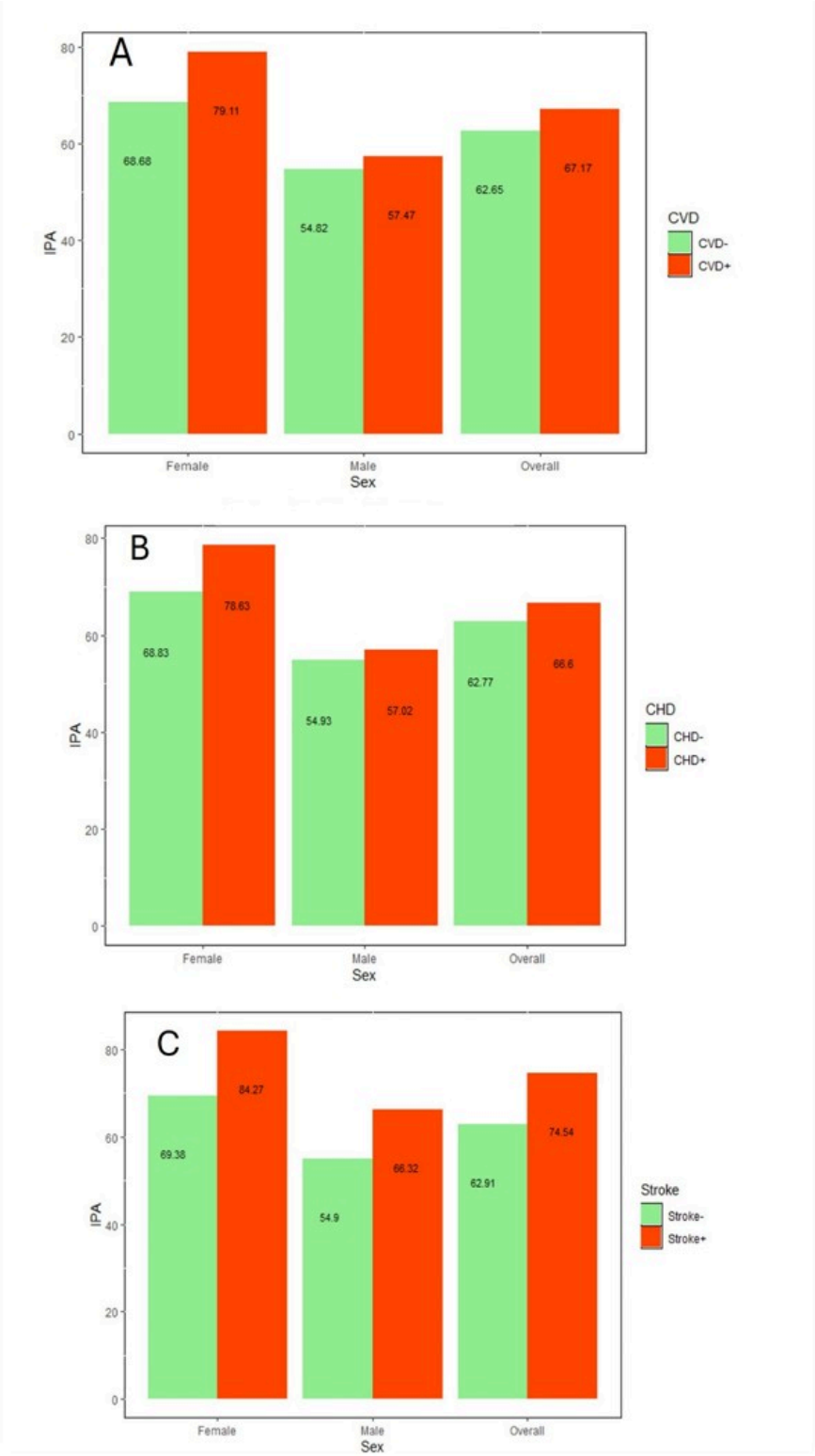


Figure 2

Weighted prevalence (%) of insufficient physical activity among participants with and without CVD (A), CHD (B), and stroke (C), stratified by sex, Iran STEPS 2021.
Physical activity levels reflect current behavior and may be influenced by post-diagnosis changes.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- FigureS1.tif
- Figures2..tif