# Estimating the Contribution of Selected Risk Factors in Attributable Burden to Stroke in Iran

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## Abstract

**Background:** Knowledge of the magnitude of avoidable burden by risk factors is needed for health policy, priority setting, and preventing stroke. The aim of this study was to estimate the contribution of selected risk factors including hypertension, overweight, obesity, tobacco use, and physical inactivity to the attributable burden of stroke in Iran.

**Methods:** The World Health Organization Comparative Risk Assessment (CRA) methodology was employed to calculate the Potential Impact Fraction (PIF) and percentage of avoidable burden of stroke, which attributed to its risk factors among Iranian adults in 2009. Prevalence of risk factors was obtained from the 5th STEPS survey of chronic disease risk factors which conducted in 2009. PIF was estimated on both theoretical minimum and feasible minimum risk. A simulation procedure incorporating sources of uncertainty was used to estimate the uncertainties for the attributable burden.

**Results:** About 15.7% (95% uncertainty intervals: 5.8- 23.5) of attributable Disability Adjusted Life Years (DALYs) to stroke in adult males and 15.8% (95% uncertainty intervals: 5.8- 23.5) in adult females are avoidable after changing the current prevalence (16.0% and 16.1% for males and females, respectively) of hypertension to 10% in both sexes.

**Conclusion:** This work highlighted the important role of hypertension and overweight. Accordingly, policy makers are advised to consider these risk factors once implementing interventional program in Iran.

**Keywords:** Stroke, Potential impact fraction, Risk factor, Burden, Iran

## Introduction

Cerebrovascular diseases is the second leading causes of death above the age of 60 years (1) and caused 46.6 million Disability Adjusted Life Years (DALYs) in 2004 (2). Three million women and 2.5 million men die from stroke every year (1). Cardiovascular diseases including stroke are the main cause of death in Iran. In addition, prevalence of hypertension, overweight, obesity, tobacco use and physical inactivity among Iranian adult males in 2009 were 16.07, 39.04, 10.10, 20.39 and 28.28%, respectively and the corresponding value for women were 16.12, 48.99, 20.46, 1.02 and 49.91%, respectively(3).

High blood pressure (BP) is known as a main reason for stroke, ischemic heart disease (IHD) and attributable burden to such diseases (4). Researches established that overweight is associated with increased risk of many diseases (5). World Health Organization (WHO) estimates that in adults aged above 30 years, increases in BMI

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above 21 kg/m² are associated with an estimated 23% of ischemic stroke and 21% of IHD, 39% of hypertensive disease(6).

Knowledge of the magnitude of attributable burden to stroke by its risk factors, especially based on updated data on prevalence and national- specific measures of effect is needed for health policy, priority setting, and preventing stroke. The contribution of a risk factor to morbidity or mortality can be estimated by comparing the burden due to the observed exposure distribution in a population with that from another distribution (rather than a single reference level such as non-exposed) as described by the generalized "potential impact fraction" (PIF)(7).

PIF or the generalized impact fraction introduced by Walter in 1980 and defined as the fractional reduction of a disease resulting from changing the current level of a risk factor to other modified levels(8).

A counterfactual analysis requires that the current distributions of an exposure be compared to some alternative distribution of the exposure. The choice of the counterfactual exposure distributions depends on various criteria. Murray and his colleague (9) are introduced four types of these exposure distributions, which include theoretical minimum risk, plausible minimum risk, feasible minimum risk, and cost-effective minimum risk. Theoretical minimum risk level can be considered as zero level of an exposure or risk factor. Plausible minimum refers to an imaginable level of exposures and feasible one is an exposure distribution, which has been observed or achieved in some population. Finally, cost-effective minimum considers the cost of exposure reduction (through the set of cost-effective interventions) as an additional criterion for choosing the alternative exposure scenario (9). Consider to lack of the knowledge of the magnitude of attributable burden to stroke by its risk factors, especially based on updated data, our study aimed to estimate the contribution of selected risk factors including hypertension, overweight, obesity, tobacco use, and physical inactivity to the attributable burden of stroke in Iran.

## Material and Methods

### *Estimates of avoidable burden*

Estimates of attributable burden were made Using WHO comparative risk assessment (WHO-CRA) methodology. WHO-CRA is a methodology that evaluates not only the disease burdens attributable to the existing risk factors, but also the effects of interventions on these risk factors, and the potential avoidable future burden (7). Population impact fraction was calculated to estimating avoidable burden. PIF were defined as follows:

$$PIF = \frac{\int_{x=0}^{m} RR(x)P(x)dx - \int_{x=0}^{m} RR(x)P'(x)dx}{\int_{x=0}^{m} RR(x)P(x)dx}$$

Where RR(x) is the relative risk at exposure level x, P(x) is the population distribution of exposure, P'(x) is the counterfactual distribution of exposure, and m the maximum exposure level (8).

### *Prevalence of exposure to the risk factors in the population*

Prevalence of risk factors was obtained from the 5th STEPS survey of chronic disease risk factors. This STEPS survey of chronic disease risk factors in Iran was carried out in 2009 as the 5th round concluding socio demographic and behavioral information, physical measurements such as height, weight and blood pressure (10). PIF was estimated on both theoretical minimum and feasible minimum risk. In present study, lowest minimum risk for all dichotomous risk factors were considered as zero in the 1st scenario. The second scenario, feasible minimum risk, for hypertension, overweight, obesity, tobacco use and physical inactivity in adult males were considered as 10%, 30%, 5%, 10% and 15%, respectively. The corresponding prevalence for women was determined as 10%, 40%, 12%, 0% and 25%, respectively.

Hypertension, overweight and obesity were defined as systolic blood pressure equals or greater

than 140 mmHg, diastolic blood pressure equals or greater than 90 mmHg, or use of anti-hypertensive drugs, body mass index equals or greater than 25 kg/m², and body mass index equals or greater than 30 kg/m², respectively.

### Relative risk of disease occurrence given exposure

Data on measures of effect were obtained from the published literature, which developed WHO-CRA methodology (6). Corresponding RR, which measured association between stroke and its risk factors, was shown in Table 1.

**Table 1:** Risk factors, their exposure variables, theoretical and feasible -minimum-risk exposure distributions, disease outcomes for risk factors prevalence and magnitude of risk factors

| Risk Factor | Exposure Variable | Outcome | Measure of Association (Magnitude)* | | Risk Factor Prevalence** % | Theoretical Minimum Risk (Scenario 1) | Feasible Minimum Risk (Scenario 2) | PIF (Scenario 1) % | PIF (Scenario 2) % |
|---|---|---|---|---|---|---|---|---|---|
| Over-weight | BMI≥ 25 | Stroke | Male | 1.35 | 39.04 [38.36,39.72] | 0 | 30 | 12.0 | 2.8 |
| | | | Female | 1.25 | 48.99 [48.34,49.63] | 0 | 40 | 10.9 | 2 |
| Obesity | BMI≥ 30 | Stroke | Male | 1.5 | 10.10 [9.697,10.51] | 0 | 5 | 4.8 | 2.4 |
| | | | Female | 1.6 | 20.46 [19.96,20.98] | 0 | 12 | 10.9 | 4.5 |
| Hyperten-sion | SBP ≥ 140 and/or DBP ≥ 90 mmHg and/ or use of anti- hypertensive drugs | Stroke | Male | 5.43 | 16.07 [15.55,16.61] | 0 | 10 | 41.6 | 15.7 |
| | | | Female | 5.43 | 16.12 [15.72,16.52] | 0 | 10 | 41.7 | 15.8 |
| Tobacco Use | Percentage who currently smoke tobacco daily | Stroke | Male | 1.17 | 20.39 [19.84,20.95] | 0 | 10 | 3.4 | 1.71 |
| | | | Female | 1.17 | 1.02 [0.87,1.19] | 0 | *** | 0.2 | NA |
| Physical Inactivity | Percentage with low levels of activity (defined as <600 MET-minutes/week) | Stroke | Male | 1.1 | 28.28 [27.41,29.17] | 0 | 15 | 2.8 | 1.3 |
| | | | Female | 1.1 | 49.91 [48.92,50.9] | 0 | 25 | 4.8 | 2.4 |

*Reference 6
** Reference 2
*** Because of the low prevalence of smoking in women (1.02), feasible minimum risk level was not defined.

### Sensitivity analyses

Uncertainty for the PIFs was estimated by Monte Carlo simulation procedure which incorporating sources of uncertainty around point estimate of risk factors. We used the @RISK software version 5.5 for Excel (11) which allows multiple recalculations of a spreadsheet, each time choosing a value from the normal probability distributions, which defined for all risk factors. For each of the input variables (Prevalence of the Risk factors), 95% uncertainty ranges were calculated bounded by the 2.5th and 97.5th percentiles of the 1000 iteration values generated. At the next step, 95% uncertainty intervals for PIFs were calculated using estimated uncertainty ranges for the each risk factor by the above mentioned simulation procedure.

# Results

The PIFs for hypertension, overweight, obesity, tobacco use, and physical inactivity are shown for males and females in Table 1 for stroke. Table 2 shows the 95% uncertainty intervals for all of the risk factors related PIFs at both lowest and feasible minimum risk level. About 15.7 percent of attributable DALYs to stroke (95% uncertainty intervals: 5.8- 23.5) in adult males and 15.8% (95% uncertainty intervals: 5.8- 23.5) in adult females are avoidable from changing the current prevalence of hypertension to 10% in both sexes.
 The PIFs for other risk factors at lowest minimum risk are shown in table 1. Moreover, modify-ing the current distribution of the overweight, obesity and physical inactivity to feasible minimum risk lead to avoided 2.8(95% uncertainty intervals: 0- 6), 2.4(95% uncertainty intervals: 0.5- 4.2) and 1.3 percent (95% uncertainty intervals: 0.5- 2)  of DALYs which attributed to stroke in males and 2(95% uncertainty intervals: 0.5 5.4), 4.5(95% uncertainty intervals:1.7- 7.3), and 2.4%(95% uncertainty intervals: 1- 3.8) in females, respectively. Tobacco use and overweight related PIFs were higher in men. While hypertension, obesity, and physical inactivity related PIFs were higher in adult women.

**Table 2:** Uncertainty intervals for PIFs based on estimated uncertainty ranges around point estimate of risk factors by Monte Carlo simulation procedure

| Risk Factor | Relative Risk | | Prevalence% (95% Uncertainty ranges) | PIFs % (95% Uncertainty Interval)* | |
| --- | --- | --- | --- | --- | --- |
| | | | | At the theoretical Minimum Risk level | At the feasible Minimum Risk level |
| **Overweight** | Males | 1.35 | 39.04 (28- 50) | 12.0 (8.9- 14.9) | 2.8 (0- 6) |
| | Females | 1.25 | 48.99 (35- 65) | 10.9 (8- 14) | 2 (0- 5.4) |
| **Obesity** | Males | 1.5 | 10.10 (6-14) | 4.8 (2.9- 6.5) | 2.4 (0.5- 4.2) |
| | Females | 1.6 | 20.46 (15- 26) | 10.9 (8.3- 13.5) | 4.5 (1.7- 7.3) |
| **Hypertension** | Males | 5.43 | 16.07 (12- 20) | 41.6 (34- 47) | 15.7 (5.8- 23.5) |
| | Females | 5.43 | 16.12 (12- 20) | 41.7 (34- 47) | 15.8 (5.8- 23.5) |
| **Tobacco Use** | Males | 1.17 | 20.39 (15- 26) | 3.4 (2.5- 4.2) | 1.71 (0.8- 2.6) |
| | Females | 1.17 | 1.02 (0.7- 1.03) | 0.2 (0.1- 0.2) | - |
| **Physical Inactivity** | Males | 1.1 | 28.28 (20- 36) | 2.8 (2- 3.5) | 1.3 (0.5- 2) |
| | Females | 1.1 | 49.91 (35- 65 ) | 4.8 (3.4- 6.1) | 2.4 (1- 3.8) |

* Incorporating sources of uncertainty for the prevalence of corresponded risk factor

## Discussion

As we mentioned above, modifying the current distribution of the hypertension, overweight to lowest minimum risk level i.e. zero lead to avoided 41.6 and 12.0% of DALYs which attributed to stroke in males. The corresponding values for females were 41.7 and 10.9%, respectively. These findings indicate the important role of hypertension and overweight, which comply with the results of Norman and his colleagues (4) that found 51% of stroke in males and 48% in females were attributable to SBP $\geq$ 115 mmHg. It is evident that the greater contribution of hypertension is mainly the result of its strong association with stroke. In the Western Pacific and South-east Asian regions for the WHO, the PAFs for hemorrhagic stroke mortality and ischemic stroke mortality in males (females) are about 66% (49%) and 44% (45%), respectively(12). In another study (13) about 54% of stroke was attributed to high blood pressure.

In addition, the greater contribution of overweight is probably the result of its prevalent in Iranian adults. The results of a study, which was conducted in Korea (14), showed that smoking, high blood pressure, high BMI and physical inactivity related PIFs at feasible minimum risk for males were 0.524, 0.612, 0.000, and 0.591, respectively. The corresponding values for females were 0.335, 0.455, 0.000, and 0.544. The findings of a study in Iran (15) which conducted to determine the attributable burden of risk factors in non-contagious diseases in Markazi Province reported that PIFs for overweight and obesity in males for stroke were 0.729% and 2.53%, respectively. In addition, PIFs for overweight and obesity in females were 6.21% and 7.85%, respectively. In this study, all PIFs were calculated at lowest minimum risk and the data source, which has been used for deriving the prevalence of risk factors, was different from our study.

Calculating 95% uncertainty interval for PIFs which incorporated uncertainty ranges around the prevalence of risk factors indicates that sources of uncertainty does not averted the estimated attributable burden at the lowest minimum risk level. However, we found that at the feasible minimum risk level, PIFs especially hypertension related PIF are affected by uncertainty around the point estimate of its prevalence.

Deriving the current distribution of risk factors from an updated source i.e. 5th STEPS survey of chronic disease risk factors, in our study is the strength and milestone. On the other hand, corresponding measures of effect in present study as a main limitation were obtained from non-country specific source (6). So that we proposed future studies estimates PIFs and attributable burden using an updated and country- specific source. Finally, we concluded that for better planning, decision-making and convincing health authorities, as well as reporting avoidable DALYs rather than the percentage of avoidable burden, PIF should be applied to update and revise burden of stroke.

## Ethical considerations

Ethical issues (Including plagiarism, Informed Consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc) have been completely observed by the authors.

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