

## Appendix–Detailed Methods

### Prevalence of Cardiovascular Disease and Risk Factors

Hyperlipidemia, defined in this study as high total cholesterol (200 mg/dL and above), is a significant risk factor for CVD. In 2013, 27.1% of Turkish males and 31.7% of females aged 15 and older reported high cholesterol, and the prevalence peaked between 45 and 64 years for males and between 55 and 74 years old for females. Further, 7% of males and 8.2% of females were found to have high LDL-cholesterol (160 mg/dL and above) (1).

Hypertension, also known as high blood pressure, is also an important risk factor for CVD. In a 2015 study, it was reported that the prevalence of hypertension was 31.8% overall (27.5% for males and 36.1% for females), and the prevalence was higher for individuals 65 years and older (2)

Type 2 diabetes mellitus, similar to hypertension, is an important risk factor for CVD. The prevalence of type 2 diabetes in the Turkish population was estimated at 13.7% in 2010 (3).

Tobacco smoking is an important risk factor for several chronic conditions, including CVD. In 2012, it was estimated that the overall rate of tobacco smoking in Turkey was 27.1%, and the prevalence was higher for males (41.5%) than for females (13.1%) (4).

Overweight and obesity have increasingly become a concern as a major risk factor for CVD. In 2013, the prevalence rate of overweight Turkish males was estimated at 37.4%, and of females at 28.8%. The prevalence of obesity was estimated at 15.3% for males and 29.2% for females, and the rates increased after age 35 (1).

Physical inactivity has also increasingly become an important risk factor for CVD. In 2011, it was estimated that 28.1% of Turkish males and 37.5% of females were physically inactive (5).

Inadequate fruit and vegetable consumption is frequently used as an indicator for a healthy diet. Fruits and vegetables are a significant source of essential nutrients, vitamins, and fiber. Their consumption is a well-known protective factor for a number of conditions including CVD. It was estimated that 88.5% of Turkish males and 85.6% of females consume fruits and vegetables less than the weekly recommended amount of 5 days per week or more (5).

### Relative Risk of Cardiovascular Disease

Hyperlipidemia: The added risk of developing IHD due to hyperlipidemia was drawn from work by Mainous et al. (6). The authors found that having a history of hyperlipidemia (and more specifically high LDL-cholesterol) increases the risk of developing coronary heart disease by 54% for men (RR=1.54, 95% confidence interval (CI) 1.26–1.88), and 58% for women (RR=1.58, 95% CI 1.22–2.06). Although hyperlipidemia is an undisputed risk factor for IHD, the association between cholesterol and stroke has been a controversial topic in the past (7, 8). In this study, the added risk of developing ischemic stroke from hyper-

**Appendix Table 1. Prevalence of conditions and risk factors by sex and age groups, Turkey**

Risk factors	Male	Female
Hyperlipidemia	15-24: 6.3%	15-24: 5.8%
	25-34: 20.2%	25-34: 17.7%
	35-44: 33.2%	35-44: 31.5%
	45-54: 40.3%	45-54: 48%
	55-64: 38.5%	55-64: 54.7%
	65-74: 32.7%	65-74: 52.5%
Hypertension	75≥: 28.2%	75≥: 46.1%
	18-64: 27.5%	18-64: 36.1%
Tobacco use	65+: 43.3%	65+: 43.3%
	41.5%	13.1%
Overweight	15-24: 17.7%	15-24: 14.3%
	25-34: 38.9%	25-34: 31.2%
	35-44: 46.3%	35-44: 34.8%
	45-54: 47.4%	45-54: 33.2%
	55-64: 43.2%	55-64: 31.2%
	65-74: 42.5%	65-74: 33%
Obesity	75≥: 43.4%	75≥: 36.9%
	15-24: 4.4%	15-24: 5.6%
	25-34: 10.7%	25-34: 15.9%
	35-44: 20.1%	35-44: 33.9%
	45-54: 24.7%	45-54: 48.5%
Type 2 Diabetes	55-64: 26%	55-64: 56.9%
	65-74: 20.4%	65-74: 49.8%
	75≥: 12.3%	75≥: 34.6%
	20-24: 2%	20-24: 2%
	25-34: 4%	25-34: 4%
	35-44: 10%	35-44: 10%
Physical inactivity	45-54: 21%	45-54: 21%
	55-64: 31%	55-64: 31%
	65-74: 35%	65-74: 35%
	75≥: 34%	75≥: 34%
	28.1%	37.5%
	Low fruit and vegetable consumption	15-24: 89.4%
25-34: 90.2%		25-34: 88.9%
35-44: 87.2%		35-44: 87.5%
45-54: 84.6%		45-54: 84.7%
55-64: 79.3%		55-64: 81.6%
65-74: 82.3%		65-74: 85.9%
	75≥: 85.7%	75≥: 88%

**Appendix Table 2. Relative risk estimates by condition and risk factor/pre-condition**

	Hyperlipidemia	Tobacco Smoking	Hypertension	Type 2 Diabetes	Low Fruit and Vegetable Consumption	Overweight and Obesity	Physical Inactivity
Cerebrovascular Disease	Ischemic Stroke: 1.60 (M&F)	1.43 (M); 1.72 (F)	3.0 (M&F);	1.40 (M&F)	1.17 (M); 1.05 (F)	Obesity: 1.25 (M); 1.26 (M&F) Overweight: 1.05 (M&F)	1.25 (M); 1.22 (F)
Ischemic Heart Disease	1.54 (M); 1.58 (F)	1.60 (M); 3.22 (F)	1.44 (M); 2.43 (F)	1.60 (M&F)	1.10 (M); 1.24 (F)	Obesity: 1.10 (M); 1.72 (M); 3.10 (F) Overweight: 1.29 (M); 1.80 (F)	1.10 (M); 1.25 (F)

M: male; F: female

lipidemia was drawn from a case-control study by Tirschwell et al., and estimated at 60% (RR=1.60, 95% CI 1.30–2.0) (9).

**Hypertension:** In the 2006 guidelines on primary prevention of stroke from the American Heart Association/American Stroke Association, hypertension (defined as having a systolic blood pressure  $\geq 140$  mm Hg or diastolic  $\geq 90$  mm Hg) was reported to increase the risk of ischemic or hemorrhagic stroke by 200% (10). In the study referenced earlier by Mainous et al. (6), hypertension increased the risk of IHD by 44% for men and 143% for women.

**Type 2 diabetes mellitus:** In a study published by Stratton et al. (11), the risk of stroke was 40% higher for individuals with the highest glycemia level (HbA1c  $\geq 9\%$ ) compared to for individuals with lower glycemia (HbA1c  $< 9\%$ ). The highest level of glycemia also increased the risk of IHD by 60%.

**Tobacco smoking:** In a meta-analysis on the relationship between cigaret smoking and CeVD, Shinton and Beevers found that being a regular smoker (defined as those currently smoking  $\geq 1$  cigaret(s) per day) increased the risk of any stroke type by 43% in men and 72% in women (12). The impact of current tobacco smoking on the risk of developing IHD was quantified in a publication by Mainous et al. (6), which leveraged the Atherosclerosis Risk in Communities study involving 14,343 participants. Being a current smoker increased the risk of IHD by 60% in men and 222% in women.

**Overweight and obesity:** In a meta-analysis of 25 studies involving over 2 million participants, Strazullo et al. (13) estimated the added risk of developing CeVD from obesity at 26% and at 5% from being overweight. In a different meta-analysis of 89 studies, obesity increased the risk of IHD by 72% for men and 210% for women, while being overweight increased it by 29% and 80%, respectively (14).

**Physical inactivity:** In a meta-analysis involving 21 prospective studies and more than 650,000 adults, low levels of physi-

cal activity was found to increase the risk of developing CeVD by 25% for men and 22% for women, compared to moderate or high levels of activity (15). In another meta-analysis of 33 studies, individuals in the lowest physical activity category had 10% (men) and 25% (women) increased risk of IHD compared to individuals in the highest physical activity category (16).

**Inadequate fruit and vegetable consumption:** Their consumption is a well-known protective factor for a number of conditions, including CVD. In two separate meta-analyzes, He et al. (17, 18) quantified the association between low fruit and vegetable consumption, defined as less than three servings per day, compared with a consumption of three to five servings per day. The increased risk of CeVD from a low consumption of fruits and vegetables was estimated at 17% for men and 5% for women, while the increased risk of IHD was 10% for men and 24% for women.

### Mortality Rates

**Appendix Table 3. Case fatality rate estimates, by condition, Turkey, 2013**

Sex	Age Group	Ischemic Heart Disease	Cerebrovascular Disease
Male	25-34	0.37%	4.46%
	35-54	0.99%	1.40%
	55-74	2.54%	2.65%
	75 $\geq$	42.10%	25.02%
Female	25-34	0.11%	3.98%
	35-54	0.27%	0.96%
	55-74	1.11%	1.66%
	75 $\geq$	9.77%	15.26%

### Estimating the Base Risk

**Appendix Table 4. Base risk estimates by age and sex, Turkey, 2015**

	Age Group	Male	Female
IHD	25-34	0.42%	0.31%
	35-54	2.14%	1.08%
	55-74	6.34%	2.92%
	75≥	1.81%	3.31%
CeVD	25-34	0.02%	0.01%
	35-54	0.40%	0.39%
	55-74	2.07%	2.30%
	75≥	1.62%	2.72%

### Indirect Costs

**Appendix Table 5. Selected Economic Indicators in Turkey, 2013**

	Participation Rate (%)	Unemployment Rate (%)	Average Weekly Earnings
Turkey	58.1	9.9	\$152 (TRY\$176)

Under the human capital methodology, indirect costs are societal productivity losses, which account for the injured individual's inability to perform his or her major activities. The value of time lost from work due to absenteeism, hospitalization, disability, and premature mortality is measured by foregone earnings calculated as average earnings, adjusted by the participation rate and unemployment rate, over the relevant period within the working life of an individual from age 15 to 65 years inclusive (see Table 5).

The mortality data for the burden of cardiovascular disease is collected from WHO's Mortality Database. Measures of the participation rate, the unemployment rate, and income/earnings are accessed from Euromonitor's Country Profiles (19) and the World Bank's World Development Indicators (20). An example of indirect costs is if a worker perishes from CVD at age 50, the foregone earnings from dying prematurely are calculated as the present value of average income that was to be earned from ages 51 to 65 (using 65 as the age of retirement). The present value of future earnings is discounted at an effective rate of 3% per year, and a real wage growth rate of 1% per year was assumed for this study.

A similar method is used to calculate the indirect costs of hospitalizations, but instead of foregone earnings being calculated over a patient's lifetime, it is calculated over the length of stay in hospital. This average length of stay in hospital in Turkey is set at 7 days for both CeVD and IHD, derived from the literature (21). As a result, the indirect costs due to hospitalizations are

foregone earnings adjusted by the participation rate and unemployment rate, over the length of stay in hospital.

Early retirement costs are generated from the literature. According to the National Institute for Public Health and the Environment (RIVM) in the Netherlands, approximately 23% of those 50 years of age and above, with perceived poor health due to chronic conditions like cardiovascular disease or a mental illness, retire early. In fact, cardiovascular disease is a strong predictor for early retirement for workers in the EU (22). This ratio is applied to the incidence of both hospitalized and non-hospitalized cases of CeVD and IHD to approximate the number people that retire early in Turkey due to the symptoms of CVD. For this briefing, the average age of early retirement is set at 58 years; therefore, indirect costs are calculated as the foregone earnings between the ages of 58 and 65 years for 23% of all new cases of CVD.

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