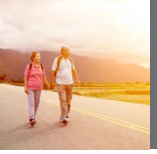
The Economist INTELLIGENCE UNIT

The Cost of Silence

Cardiovascular disease in Asia

An Economist Intelligence Unit report

Commissioned by AMGEN



Executive summary

Cardiovascular diseases (CVDs), disorders of the heart and blood vessels, are the leading global cause of death annually. They levy a substantial financial toll on individuals, their households and the public finances. These include the costs of hospital treatment, long-term disease management and recurring incidence of heart attacks and stroke. They also include the costs of functional impairment and knock-on costs as families may lose breadwinners or have to withdraw other family members from the workforce to care for a CVD patient. Governments also lose tax revenue due to early retirement and mortality, and can be forced to reallocate public finances from other budgets to maintain an accessible healthcare system in the face of rising costs.

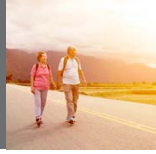
Of the total direct and indirect costs of ischaemic heart disease (IHD)[1] and stroke in the eight countries in this study—China, Australia, Hong Kong, Japan, Singapore, South Korea, Taiwan and Thailand—an estimated US$53bn is attributable to four modifiable risk factors: smoking, hypertension, obesity and high cholesterol.[2]

Despite their negative impact, these risk factors are too often ignored, particularly the two "silent" or less visible risk factors of hypertension and high cholesterol, which may not have overt symptoms. Even for those who have had a CVD event—in the form of a heart attack or stroke—only around a third of men and women meet the target lifestyle and medication changes set by their physicians. This is despite the fact that these sufferers are among the highest at-risk groups for further coronary and cerebral events, and have a death rate six times higher than those who do not have coronary heart disease.[3]

As such, there is a need for more awareness of the ways in which people should actively work to reduce their CVD risk. There is also a need for more primary and secondary preventative support from health agencies, policymakers and non-governmental groups.

To inform the decisions and strategies of these stakeholders, The Economist Intelligence Unit and EIU Healthcare, its healthcare subsidiary, have conducted a study of the prevalence and costs of the top four modifiable risk factors that contribute to CVDs across the Asian markets of China, Australia, Hong Kong, Japan, Singapore, South Korea, Taiwan and Thailand.

1 Ischaemic heart disease refers to the narrowing of the arteries that feed oxygen to the heart. It is also known as coronary heart disease, which is a group of heart diseases that includes stable angina, unstable angina, heart attack, and sudden cardiac death
2 EIU Healthcare
3 WHO, Prevention of recurrences of myocardial infarction and stroke study, 2005



Key takeaways

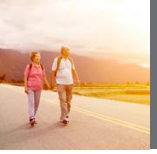
- **The rising incidence of CVD poses a substantial challenge to Asia-Pacific markets.** The rising incidence and expected treatment costs of CVDs challenge the sustainability of many healthcare financing models in the region. Early retirement and functional disability from rising CVD incidence also erode the tax base and put pressure on social service budgets. This can lead to fiscal constraints that have a regressive impact on citizens. Reducing risk factor incidence, which could reduce and even prevent CVDs, is a more preferable strategy.

- **The four main modifiable cardiovascular risk factors pose a communications challenge for governments and health agencies.** Because the effects of the four risk factors on cardiovascular health—smoking, hypertension, obesity and high cholesterol—can accumulate over many years, individuals have little to no knowledge that they have increased their risk for CVD until symptoms occur. This makes preventing these risk factors all the more challenging.

- **Hypertension is the risk factor that contributes the highest cost.** Hypertension is exerting the greatest population-attributable cost across the eight markets with an estimated total of US$18bn annually, according to Economist Intelligence Unit estimates. Across the other estimated annual risk factor costs, high cholesterol contributes US$15bn, smoking US$11bn, and obesity $8bn.

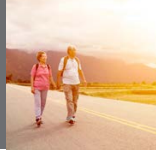
- **The costs of CVDs are not fixed.** Greater awareness and policymaker attention can substantially reduce CVD costs as many obstacles and corresponding solutions have been identified as effective. For example, the World Heart Federation provides a number of roadmaps to manage CVD risks brought on by hypertension, high cholesterol and smoking. For the two "silent" risk factors, the pathways are similar: improve patient and physician awareness of key risk factors, increase access to diagnostic testing, empower patients with knowledge, and provide professional support and affordable drug access to manage their risks.

- **Policy options for primary prevention include choice "nudges".** Policy options for primary prevention of all risk factors include "nudges" to positively influence dietary choices, such as improved food labelling or partnerships with companies to encourage food reformulation to remove unhealthy ingredients. Investment in green spaces in urban areas and subsidised access to health facilities can also encourage physical activity.



- **Effective secondary prevention can also significantly affect costs and outcomes.** The recurrence rates for people suffering from a CVD event are high. For instance, in Australia, the risk of a subsequent stroke is 43% in the ten years following the first event,[4] and the mortality rates for known sufferers of CVDs are substantially higher than those not at high risk. Across the span of a first CVD event and one's death, the cost for disease management and the treatment of secondary events can be significant. Prioritising at-risk groups can also drive positive impacts on CVD cost management.

4 D A Cadilhac et al, "Estimating the long-term costs of ischemic and hemorrhagic stroke for Australia: new evidence derived from the North East Melbourne Stroke Incidence Study (NEMESIS)", Stroke, 2009



About the research

The Cost of Silence: Cardiovascular disease in Asia is a report by The Economist Intelligence Unit and EIU Healthcare. It provides a study of the economic impact of CVD risk factors on the following Asian markets: China, Australia, Hong Kong, Japan, Singapore, South Korea, Taiwan and Thailand.

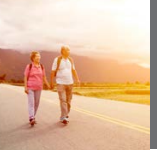
Specifically, the study captures the cost of ischaemic heart disease (IHD) and stroke. IHD, also called coronary heart disease (CHD) or coronary artery disease, is the term given to heart problems caused by narrowed heart (coronary) arteries that supply blood to the heart muscle, which can lead to stable angina, unstable angina, myocardial infarctions or heart attacks, and sudden cardiac death. Stroke is characterised by the sudden loss of blood circulation to an area of the brain due to blockage of brain vessels, or a haemorrhage or blood clot.

This study further combines an evidence review of existing research on CVDs and primary research in the form of expert interviews.

For more information on the methodology of the cost calculations and evidence review, please see the appendix.

We would like to thank the following experts who took part in the research process.

- Bill Stavreski, general manager, heart health and research, Heart Foundation Australia
- Kwan Yu Heng, honorary research scientist, Khoo Teck Puat Hospital, Singapore
- Dr Shin Young-soo, regional director for the Western Pacific (China, South Korea, Japan, Hong Kong), World Health Organisation (WHO)
- Min Zhao, researcher, University Medical Center Utrecht, Netherlands
- Tomonori Hasegawa, professor and chair, Department of Social Medicine, Toho University Graduate School of Medicine, Japan
- Dr Martin Cowie, professor of cardiology, Imperial College London, UK
- Dr Renu Garg, medical officer, non-communicable diseases, WHO Thailand
- Nikki Earle, Heart Foundation research fellow, University of Auckland, New Zealand

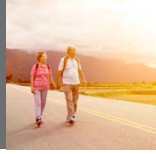


- Dr Susan Wells, public health physician, section of epidemiology and biostatistics, School of Population Health, University of Auckland, New Zealand

- Dr Shizuya Yamashita, president, Japan Atherosclerosis Society

The Economist Intelligence Unit would also like to thank the anonymous citizens and patients from South Korea, Australia and Singapore who participated in the research underpinning the case studies in this report.

This report was written by The Economist Intelligence Unit. Adam Green was the author and Rashmi Dalai edited the report with assistance from HuiQi Yow and Scott Aloysius.



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Chapter 1: Confronting the rise of CVD in Asia

The prevalence of CVD

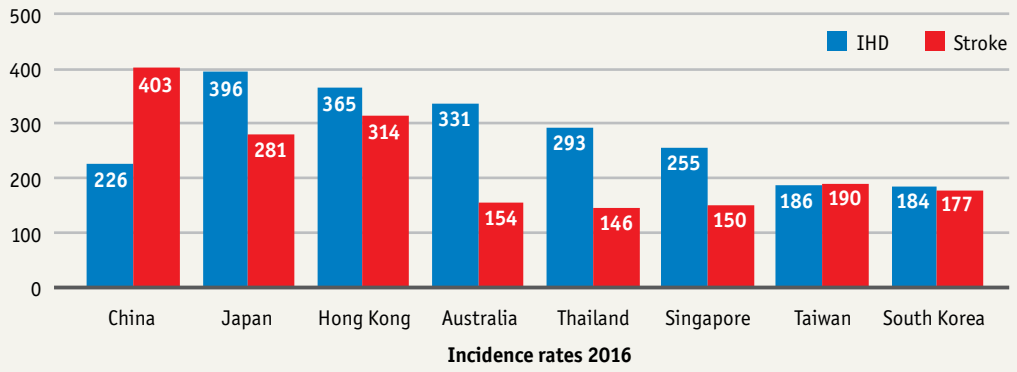
Approximately 423m adults globally live with CVDs[5], and 18m people die from them annually. This makes CVDs responsible for an estimated 31% of all annual deaths worldwide[6] and the leading cause of death. Four out of five CVD deaths are due to heart attacks and stroke.

The incidence rate of CVDs in Asia-Pacific is on the rise, driven primarily by stroke and IHD.[7] On a market-by-market basis, the highest stroke incidence in the region is in China, at 403 cases per 100,000, followed by Hong Kong and Japan, according to the latest WHO data from 2016. IHD incidence is highest in Japan and Hong Kong, with approximately 396 cases and 365 cases per 100,000 respectively in 2016, and the lowest in South Korea with 184.

Recurrence rates of CVD events are also significant. For example, in Australia, the risk of a subsequent stroke is 43% in the ten years following the first event, and 30% of patients with established CHD experience more than one recurrent event.[8,9]

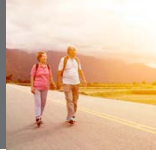
Stroke mortality is worse in Asia-Pacific compared with the West, with the exception of Japan, where mortality is low compared

Figure 1: Heart pain
Incidence rates of IHD and stroke per 100,000 population



Source: Global Burden of Disease Study, EIU Healthcare estimates

5 Dr Gregory Roth et al, "Global, regional and national burden of cardiovascular diseases for 10 causes, 1990 to 2015", Journal of the American College of Cardiology, 2017
6 WHO, Cardiovascular diseases (CVD), 2017
7 WHO, Global health estimates 2016: Deaths by cause, age, sex, by country and by region, 2000-2016, 2018
8 D A Cadilhac et al, "Estimating the long-term costs of ischemic and hemorrhagic stroke for Australia: new evidence derived from the North East Melbourne Stroke Incidence Study (NEMESIS)", Stroke, 2009
9 T G Briffa et al, "Population trends of recurrent coronary heart disease event rates remain high", Circulation: Cardiovascular Quality and Outcomes, 2011



with South, East and South-east Asian averages.[10] Similarly, while mortality from stroke has been on the decline in China on the whole, mortality rates are considerably higher in rural areas compared with urban areas. The incidence of CVD overall has also risen since the early 1990s, driven by factors including increased body mass and reduced exercise.[11] This suggests healthcare quality is improving in the cities faster than elsewhere overall, although not necessarily for all income groups.[12,13]

Counting the costs

Increased CVD incidence can be financially catastrophic in low- and middle-income contexts as CVDs can have serious consequences for patients' functional abilities. Research indicates that a quarter of CVD patients report being disabled to the extent that they are unable to participate in their core daily activities such as mobility, self-care and communication—a figure likely much higher for those who suffer a full-blown heart attack or stroke.[14]

The fiscal implications for governments are also serious. Public finances are hit by the loss of citizens from the economy due to early retirement or physical impairment, with knock-on effects for economic productivity and tax revenue. An Australia-based estimate in 2009 found that early retirement due to CVDs has a national aggregate impact of US$781m in lost income, US$160m in lost income taxation, US$60m in government benefit payments and US$531m in lost GDP.[15]

Understanding the high degree of these costs across Asia can help raise the need for a greater focus on minimising, preventing and ameliorating the effects of CVDs. To this end, the study below provides cost estimates based on published medical literature of the direct and indirect costs of CVD in eight Asia-Pacific markets: Japan, Australia, Thailand, Singapore, China, Taiwan, South Korea and Hong Kong.

The costs are defined in this study as follows:

- Direct costs: hospitalisation, drugs, rehabilitation and outpatient care.

- Indirect costs: productivity losses, informal care, and costs due to early mortality and early retirement.

To calculate the direct and indirect costs of each risk factor related to CVDs, we used population attributable fractions (PAFs), which are a common way to estimate the proportion of all cases in the whole study population (exposed and unexposed) that may be attributed to the exposure. PAFs provide a method of understanding the proportional reduction in population disease or mortality that would occur if exposure to a risk factor were reduced. The PAF methodology is also a common way of understanding how much money might be saved from treating a disease should common risk factors for that disease be reduced.

10 Narayanaswamy Venketasubramanian et al, "Stroke Epidemiology in South, East, and South-East Asia: A Review", Journal of Stroke, 2017
11 Li Y et al, "Potential Impact of Time Trend of Life-Style Factors on Cardiovascular Disease Burden in China", Journal of the American College of Cardiology, 2016
12 Wei-Wei Chen et al, "China cardiovascular diseases report 2015: a summary", Journal of Geriatric Cardiology, 2017
13 Wenzhi Wang, "Trend of declining stroke mortality in China: reasons and analysis", Stroke and Vascular Neurology, 2017
14 Schofield D, "The personal and national costs of CVD: impacts on income, taxes, government support payments and GDP due to lost labour force participation", International Journal of Cardiology, 2013
15 Schofield D, "The personal and national costs of CVD: impacts on income, taxes, government support payments and GDP due to lost labour force participation", International Journal of Cardiology, 2013

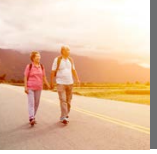


Figure 2: The population attributable fractions for each risk factor

PAFS FOR CVD RISK FACTORS (MEN)	CHINA	AUSTRALIA	TAIWAN	SOUTH KOREA	THAILAND	JAPAN	HONG KONG	SINGAPORE
Obesity	2%	4%	2%	2%	2%	2%	2%	2%
Smoking	14%	6%	11%	15%	12%	10%	14%	8%
High cholesterol	5%	14%	5%	7%	9%	9%	5%	9%
Hypertension	13%	8%	12%	8%	14%	13%	15%	11%

PAFS FOR CVD RISK FACTORS (WOMEN)	CHINA	AUSTRALIA	TAIWAN	SOUTH KOREA	THAILAND	JAPAN	HONG KONG	SINGAPORE
Obesity	8%	8%	8%	7%	10%	6%	10%	8%
Smoking	1%	5%	1%	1%	1%	3%	1%	2%
High cholesterol	7%	11%	7%	9%	12%	12%	7%	13%
Hypertension	12%	5%	10%	6%	15%	9%	10%	8%

Source: EIU Healthcare, WHO prevalence rates for adults over 25

The cost data presented represent the total cost of CVD in a particular country due to the specified risk factor. For example, if high cholesterol was to be eliminated in the eight selected countries, approximately US$15bn in associated annual costs of IHD and stroke that are due to this risk factor could be saved.

Other relevant costs not included in the estimates due to data constraints include the foregone fiscal costs and taxes CVD patients withdraw from the economy. Data and forecasts for these and other country-level details can be found in the report's methodology appendix.

Indirect costs versus direct costs

On the whole, the indirect costs of CVD outweigh the direct costs, reflecting the longer-term disability impact of stroke; 57% of the total costs incurred across the selected Asia-Pacific markets are the so-called indirect impacts versus 43% that are attributed to direct costs.

Understanding direct costs

The direct costs analysed in this study refer to: *hospitalisation, drugs, rehabilitation* and *outpatient care*.

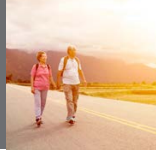
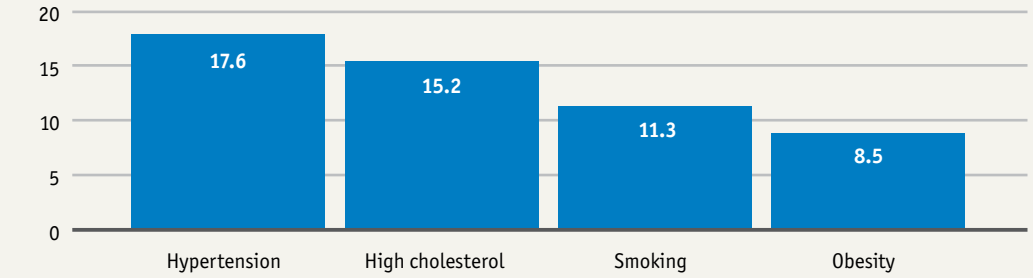
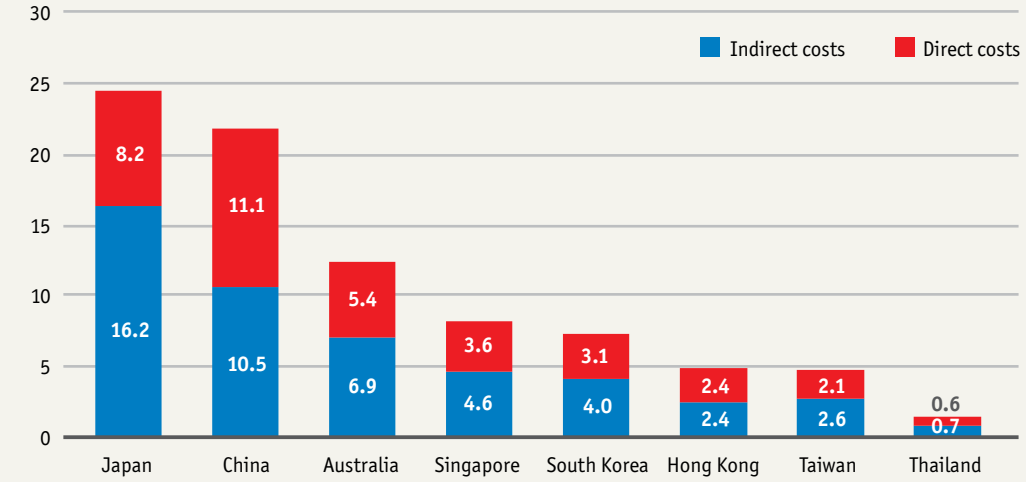


Figure 3: Capturing costs
Attributable costs by risk factor for selected Asia-Pacific markets (US$ bn)



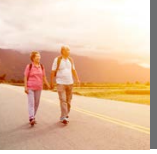
Source: EIU Healthcare; includes Japan, Australia, Thailand, Singapore, China, Taiwan, South Korea and Hong Kong

Figure 4: Being direct
Annual indirect and direct costs of CVDs in selected Asia-Pacific markets (US$bn)



Source: EIU Healthcare; includes Japan, Australia, Thailand, Singapore, China, Taiwan, South Korea and Hong Kong

Hospital interventions at the point of a CVD event depend on its cause: a blood clot, arterial narrowing or a bleed that can be ascertained by tests and scans. Options will include thrombolysis to dissolve the clot, a stent in the case of narrowed arteries or cauterisation of the artery in the case of an intracranial haemorrhage. This can be followed by several days of further care and rehabilitation in the hospital setting.



According to one study, heart failure patients in Asia spent between 5 and 12.5 days in hospital, with 3% to 15% readmitted within 30 days. They incur costs varying from US$813 in Indonesia to nearly US$9,000 in South Korea.[16] In Taiwan, medical costs during the first year after an acute stroke—comprising hospitalisation, readmission and ambulatory care at 44%, 29% and 27% of total costs respectively—were reported as US$5,553.[17]

Staff wages are a major determinant of those hospital costs. "A majority of the cost of health delivery is the cost of employment," says Martin Cowie, professor of cardiology at Imperial College London and co-author of the above-cited study. Such costs range from the surgical specialists who perform procedures, such as coronary artery bypass grafts, as well as the administrative and management staff.

These direct costs can repeat multiple times for CVD patients as, without proper disease and risk factor management, recurrence can be likely. One study on the prevention of stroke recurrence in South, East and South-east Asia found first-year stroke recurrence rates ranging from 2.2% to 25.4%.[18]

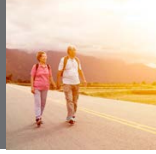
Understanding indirect costs

The indirect costs of CVDs refer to the many consequences that such diseases have on the longer-term functioning of the patient. In the case of a stroke, they are a much higher share of costs, largely due to the functional impairment strokes can cause in movement, speech and bodily control. One study shows that non-fatal strokes cause a 1.5-fold greater loss of disability-adjusted life years compared with non-fatal myocardial infarction.[19]

This study collates indirect costs as made up of productivity losses, informal care, and costs due to early mortality and early retirement. However, further research efforts could expand the range of costs that are indirect, such as lost taxes to government resulting from people's more limited engagement in the labour force. In the context of an ageing region, which already faces a fiscal challenge as the non-working share of the population grows relative to the working share, such costs will be of increasing significance. In 2016 approximately 12.4% of Asia's population was 60 years of age or older. This proportion is projected to increase to more than a quarter, or 1.3bn, by 2050.[20]

The burden of indirect costs (and direct costs if personally incurred) are particularly high for those with lower incomes. When a formerly productive adult family member can no longer work, this can lead to the selling of assets, the departure of a family member from the labour force, or under-investment in areas like children's education. One China-based study found that catastrophic health expenditure (CHE) could be higher than 50% for low-income rural families.[21] A region-wide assessment of out-of-pocket costs of hospitalisation for acute coronary syndromes, the largest ever prospective observational study

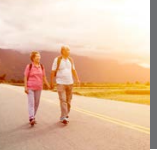
16 Eugenio B. Reyes, "Heart failure across Asia: Same healthcare burden but differences in organization of care", International Journal of Cardiology, 2016
17 Converted from NT$170,376 at August 21st 2018 exchange rate. Hsuei-Chen Lee et al, "Readmission, mortality, and first-year medical costs after stroke", Journal of the Chinese Medical Association, 2013
18 Chin YY et al, "Prevalence, risk factors and secondary prevention of stroke recurrence in eight countries from south, east and southeast asia: a scoping review", Med J Malaysia, 2018
19 Meng Lee et al, "Trends in Incident and Recurrent Rates of First-Ever Ischemic Stroke in Taiwan between 2000 and 2011", Journal of Stroke, 2016
20 UN ESCAP, Ageing in Asia and The Pacific: Overview, 2017
21 Dengfeng Wu et al, "Improvement of the reduction in catastrophic health expenditure in China's public health insurance", PLOS One, 2018



of the household economic burden associated with chronic disease, found that CHE for those without insurance was approximately 79% (China), 67% (Thailand), 32% (Hong Kong) and 20% (Singapore).[22]

"Due to late detection [of CVDs], people die younger, often in their most productive years," says Dr Shin Young-soo, WHO regional director for the Western Pacific. "The poorest people are affected most, and there is sufficient evidence at the household level to prove that CVDs and other non-communicable diseases NCDs contribute even more to poverty, owing to high out-of-pocket expenditures. This has ramifications in other sectors of society that then feed into the lack of effective and equitable healthcare services that are responsive to society's needs".

22 Stephen Jan et al, "Catastrophic health expenditure on acute coronary events in Asia: a prospective study", Iranian Journal of Public Health, 2016



Chapter 2: The four modifiable risk factors

There are four primary modifiable risk factors for CVDs. Each of these contributes to the primary cause of CVDs, atherosclerosis, in which fatty plaque deposits, or atheroma, accumulate on the delicate lining of the arteries. Eventually these deposits narrow the lumen of the arteries, obstructing blood flow. Alternatively, atheroma may break into fragments and form clots or thrombi. Both of these herald serious consequences for the body's organs, depending on the location of the blockage. For example, a coronary artery obstruction leads to death of part of the heart muscle, otherwise known as a myocardial infarction.

The four primary CVD risk factors examined in this report are:[23]

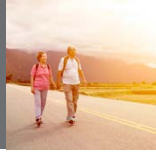
- **Hypertension:** the percentage of the population aged 25 or older having systolic blood pressure ≥ 140 mmHg and/or diastolic blood pressure ≥ 90 mmHg.
- **High cholesterol:** the percentage of people having a total cholesterol level of ≥5.0mmol/L.
- **Smoking:** the percentage of the population aged 15 or older who smoke any tobacco products.
- **Obesity:** the percentage of the population aged 20 or older having a body mass index (BMI) ≥ 25 kg/m2.

Diabetes is also a risk factor for CVD but was not included in this analysis. See the cost calculation methodology for more information.

Hypertension

Blood pressure in the arteries acts to propel blood through the vascular system, and is reflective of the contraction and relaxation of the left ventricle of the heart. It both affects and is affected by the condition of the arteries, and is also influenced by the strength of cardiac output and the level of resistance in the peripheral blood vessels.

High blood pressure causes damage to blood vessels, leading to rupture, leakage or the development of clots. The clinical manifestation of this will depend on which target organ is affected. Stroke, for example, results from damage to cerebral arteries and may take the form of a clot (an ischaemic stroke) or a bleed (a haemorrhagic stroke).



High cholesterol

Cholesterol is used by the body to synthesise certain hormones, bile acids, and vitamin D. Although some cholesterol is manufactured by the liver, the majority is derived from diet. Low-density lipoprotein (LDL) is the main carrier of cholesterol in the blood responsible for delivering cholesterol to tissues.

When blood vessels are damaged, such as due to sustained high blood pressure, LDL migrates into the arterial connective tissue; this further leads to blockage of an artery.[23] A high LDL-C/HDL-C ratio indicates an elevation in the level of LDLs in the blood. This makes cholesterol levels an indication of a greater risk of developing plaques in the arteries. LDL cholesterol is thus a causal and cumulative risk factor for heart attacks and stroke. WHO prevalence data indicate that high cholesterol has a slightly higher prevalence in women than in men.[24]

Smoking

The aetiology of smoking's link with CVDs is complex. Smoking is thought to affect blood circulation in several ways. First, absorption of nicotine and carbon monoxide in tobacco smoke leads to release of adrenaline and noradrenaline, which cause blood vessels to narrow temporarily. In a chronic smoker, the normal restoration of blood vessel tone is lost over time, and eventually a state of permanent change to the blood vessels ensues.[25] This damages the delicate arterial lining, making tissues more susceptible to plaque deposits.

Second, chemicals in cigarette smoke cause an inflammatory response in the lining of the arteries, in which white blood cells known as macrophages take up position in the artery linings. This creates a favourable condition for the development of fatty atheroma deposits.

Obesity

Obesity causes overstimulation of the sympathetic nervous system, which results in increased blood pressure. It is also associated with insulin resistance, particularly for people who have proportionally high levels of abdominal and visceral fat. Furthermore, people who are overweight are likely to have increased activity of the angiotensin-aldosterone system due to the additional demands on the kidneys.

While obesity and high blood pressure are inextricably linked, obesity is also thought to be an independent risk factor[26] because it places additional pressure on the heart, alters lipid metabolism and increases levels of fibrinogen that can contribute to blood clots.

Risk factor interaction

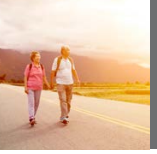
Although each of these risk factors exerts an individual, clinically discernible effect, clusters of risk factors tend to act synergistically to raise

23 Davignon J and Ganz P., "Role of endothelial dysfunction in atherosclerosis", Circulation, 2004

24 World Health Organization. Global Health Observatory data repository [Internet]. Geneva: World Health Organisation; [updated 2016; cited 31st July, 2018]. Available from: http://apps.who.int/gho/data/node.main.A867?lang=en.

25 Janet T Powell, "Vascular damage from smoking: disease mechanisms at the arterial wall", Vascular Medicine, 1998

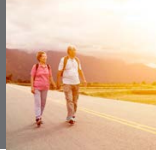
26 Helen B. Hubert MPH et al, "Obesity as an Independent Risk Factor for Cardiovascular Disease: A 26-year Follow-up of Participants in the Framingham Heart Study", 1983



the individual risk of CVDs. For example, people with diabetes are more likely to also carry excess body weight and suffer from hypertension. A person with obesity is more likely than someone in the general population to also have high levels of dietary fat, hypertension and diabetes. Smoking is implicated in a range of cardiovascular pathologies due to its effect of chronic systemic inflammation, oxidative stress and the subsequent physiological response that includes production of atherosclerotic plaques.[27]

This clustering effect means that risk management must target a variety of factors and health promotion interventions must also take a holistic view.

27 John A Ambrose MD and Rajat S Barua MD, "The pathophysiology of cigarette smoking and cardiovascular disease: An update", Journal of the American College of Cardiology, 2004



Silent risk factors: the public health challenge

Of the four modifiable cardiovascular disease (CVD) risk factors, two—hypertension and high cholesterol—are "silent". A person may not know they are at risk until resulting CVD symptoms are at an advanced stage like breathlessness and chest pain, or there is an event such as a heart attack or stroke. Even after such an event, adherence to treatment regimens and lifestyle changes may be hard to maintain if people cease to feel symptoms or discomfort.

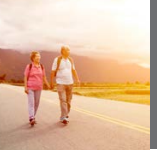
This is particularly concerning given that high blood pressure is often a top risk factor. For example, high blood pressure is the most dangerous CVD risk factor in Japan, says Shizuya Yamashita, president of the Japan Atherosclerosis Society. These are followed by smoking, dyslipidemia and diabetes, which he accords equal weight.

Bill Stavreski, general manager of heart and research at Heart Foundation Australia, adds that people may underestimate their risk of CVD after taking treatments. "People believe that if their cholesterol levels and their blood pressure levels have lowered then they're so-called fixed and that they don't need to continue. That's probably due to the fact that you cannot see or feel blood pressure and cholesterol, they are not as pronounced or promoted as lifestyle factors like diet, weight and exercise."

People may also discontinue treatment if they are exposed to alarmist media messages about health risks associated with drugs. In 2013 a documentary in Australia on the programme Catalyst, argued that there were dangers associated with statins, which led to an estimated 10% to 15% reduction in statin usage. The show has since been repudiated and withdrawn. While many eventually resumed their statin regimen, around 5% did not. Mr Stavreski criticises the documentary for its "bad science".

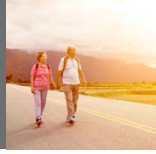
In the wider region, the distribution of risk factors across gender lines could be better understood. A global study by Min Zhao, researcher at the University Medical Center Utrecht in the Netherlands, found that women were less likely to achieve their targets for total cholesterol and LDL cholesterol.[28] "Lack of knowledge among female patients about their disease or the necessity of adequate guideline-recommended treatment could contribute to these sex differences in risk factor management," says Ms Zhao of the findings.

28 Min Zhao et al, "Sex differences in risk factor management of coronary heart disease across three regions", Heart, 2017



Furthermore, experts warn that there is much diversity in public awareness over silent CVD risks in Asia. "Health literacy [levels] are hugely variable across Asia-Pacific" argues Dr Cowie. "In Thailand, many of the population has no idea what high blood pressure is and its relation to salt in diet. You move to Singapore and Hong Kong, and general health literacy, particularly in the young, is good and comparable to Europe and North America."

While awareness-raising is an obvious public intervention, some countries have also pursued harder regulations to deal with consumer products that aggravate silent risk factors such as bans on trans fats (expected in Thailand from early 2019), health warnings on foods with high saturated fats, and collaboration with stakeholders, like street vendors, to reduce use of certain cooking oils.



Chapter 3: Risk factor trends across Asia-Pacific

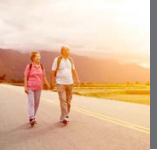
Asia-Pacific is a heterogeneous region, from the high-income markets of South Korea and Australia to emerging markets like Thailand. Diets, lifestyle habits and levels of health literacy vary widely, as do genetic predispositions and socioeconomic dynamics.

Smoking is one notable and significant risk factor across men in all studied markets (except for Australia where public campaigns against smoking have shown success). For example, Renu Garg, medical officer of the WHO Thailand, says that although Thailand's high smoking levels have declined slightly, recent surveys suggest a rise of around 3% to 5% among school-aged females.

Diet quality is also at risk. It has become "cheaper and more convenient to purchase food from stores, most of which is imported such as flour, sugar and canned meat," says Dr Shin.[29] "Due to social and economic barriers to access to more nutritious food, people do not have much of a choice when it comes to their diets. While there are countries with taxes in place on unhealthy food and sugar-sweetened beverages, not all countries have legislation or policies in place to support healthy diet or physical activity."

Ethnicity is also relevant to CVD risk factors and outcomes in the region, notably Australia and New Zealand. "Cardiovascular health outcomes differ across ethnic groups, particularly for indigenous populations where outcomes tend to be less favourable," says Nikki Earle, a research fellow at the University of Auckland. "There are many reasons for this, including modifiable risk factors such as smoking, obesity, diet and physical activity, non-modifiable risk factors such as genetics, and socioeconomic factors. It's important to understand these differences in order to design appropriate prevention programmes for high-risk populations and reduce these inequalities."

29 The WHO Western Pacific region includes China, South Korea, Japan, Hong Kong and Australia.



Chapter 4: CVD Personas

The Unaware: Preeda

Preeda, 39, works as a shop assistant in the bustling MBK shopping mall, an eight-storey complex in Bangkok. Due to long working hours and her lengthy commute to and from her home on the outskirts of Bangkok in Nong Chok, she usually buys street food in the local area for lunch; as it is cheap, fresh and easily available. Unbeknownst to her, this food is very high in sodium and palm oil. The latter is a source of saturated fat and the former a heart disease risk contributor due to its impact on blood pressure. She also often eats instant noodles for her dinner, as it is an easy-to-prepare meal for her two young children and husband, but it is also very high in salt content. Between meals, Preeda and her family frequently eat foods high in trans-fats such as crispy snacks, cookies and dry fast foods.

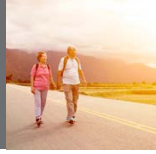
Preeda's two children follow their mother's lead in their diets and food preferences and are gaining weight. After decades in which Thailand faced under-nutrition, overweight children are seen as a sign of wellbeing and progress, so Preeda is not concerned about their long-term health prospects. Her husband, like many Thai men, smokes heavily inside and outside their apartment. With limited ventilation, this also affects Preeda and the children through passive inhalation.

Thailand's universal basic health coverage programme gives everybody access to a once-yearly NCD screening in which blood pressure, blood sugar, height and weight are recorded along with lifestyle habits like smoking. However, Preeda has not taken up her consultations as she does not think of herself as at risk and has no symptoms. She also sees stroke and heart disease as risks mainly for those in their fifties and older, and mostly affecting men.

Once her children are more independent, Preeda plans to spend more time exercising and taking more time to cook healthier food. For now she doesn't feel she has time to worry much about her health with her long working hours and commute.

The moderately aware: Craig

Craig is 59 and lives in Sydney, where he works long hours for an accounting firm. While he was an avid cricket player in his youth, a slipped disc injury made exercise very painful. He has been self-conscious of his increasing weight, and is in the "overweight" territory, with a body mass index of around 26. However, most of his friends and peers are either moderately or severely overweight so he thinks of it as an aesthetic issue, natural to middle age.



A few months ago, Craig began noticing he was occasionally short of breath while walking. Initially he ignored it, but one morning the feeling did not pass as it usually did. He saw his GP, who sent him straight to the hospital, where he was diagnosed with unstable angina.

He was shocked to learn of his condition. Since then, he has cut back on alcohol. He eats less sugar, chocolate and fatty foods and participates in a rehab programme with a personal trainer. He also takes more notice of heart health stories in the news and media, including research findings about dietary risks. But he is often left confused about contradictory findings such as optimal levels of alcohol consumption.

He had a stent inserted and takes statins and beta-blockers to lower his cholesterol and blood pressure, although he does not always stick with his medications as he does not like taking pills. He also sees his GP regularly for medication reviews and attends a nurse-led clinic to monitor his blood pressure and cholesterol levels. While his cholesterol is still high, at 6.1mmol/l, it is significantly lower than before he started on regular statins. His target total plasma cholesterol level is 5 mmol/l.

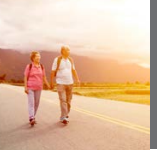
While the episode has been a scare, Craig is fortunate the condition was caught before he suffered a full-blown heart attack. He now feels in control of his destiny. The combination of medical interventions and lifestyle changes has, he hopes, put him on a safer path so that he can look forward to a healthier retirement and spending more time with his wife, children and grandchildren.

The acutely aware: Kwon

Kwon, who ran a food shop, regularly smoked, experienced intense stress and ate an unhealthy diet high in fatty foods. Eight years ago, he began feeling an occasional heaviness in his shoulders, especially when working in the morning food market. At first, his wife would relieve the pain by massaging the area but it intensified over time. Eventually, while smoking a cigarette, he experienced a twisting feeling that was akin to a squid cooking on a grill. A few days later, the feeling returned while drinking with friends.

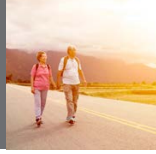
He went to the hospital and was given medication for gastritis, which made him feel bloated and unwell. A few days later, he experienced chest pains and sweating for eight hours. He took a taxi to Seoul National University Hospital. By the time he arrived, he was experiencing a full-blown heart attack. He underwent emergency surgery and the introduction of stents. Doctors said his arteries were clogged and he may have had only an hour to live. A few years later, he returned to the hospital after experiencing dizziness and had a third stent inserted. He now takes a series of medications.

His lifestyle has changed as a result of the distressing episode. He now stays away from greasy foods and has increased his vegetables



and fish consumption. He tries to exercise more regularly and does Danjeon breathing exercises to relax his body. He also takes four types of medicines for myocardial infarction, including aspirin, and has used medication for hyperlipidemia for seven years.

His wife helps, encouraging him not to take cream with his coffee and cooking healthier food. His stress levels have gone down as he has retired from work. He has also stopped smoking. However, Kwon regrets not being able to join his friends in eating his favourite foods or enjoying a cigarette. He also still cannot run or walk fast.



Conclusion: Solutions for an ageing continent

The Asia-Pacific's CVD burden sits within the broader context of a rise in NCDs, due partly to ageing populations and partly to economic transition. It is a threat to the health and financial security of citizens and a burden on the public finances. Efforts to increase access to healthcare over recent decades will be undermined if cost-cutting measures are required to balance the books.

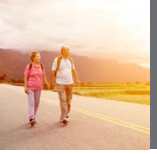
Positively, many risk factors for CVDs are modifiable through primary and secondary preventions, across behaviour, lifestyle and medical domains. Looking forward, a powerful CVD action plan is one that targets multiple points along the "continuum" from primary prevention to cost-effective treatment methods and secondary prevention. Innovation in service delivery and greater leveraging of data, digital technology and wearable devices can also help optimise CVD detection and management in cost-effective ways.

Primary prevention

The modifiable CVD risk factors are well understood by the medical community, but imploring the general population to adopt healthier diets, quit smoking and increase exercise is not enough. The asymptomatic nature of CVD risks means people consistently fail to heed health warnings.

There is a toolbox of evidence-based policies, and many ideas in circulation, which governments can consider to positively guide choices. Dietary labelling to flag unhealthy fats and sugars, collaborations with street vendors to reduce the use of CVD-linked ingredients, and partnerships with food manufacturers in areas like health certification and food reformulation, are worthwhile options. "Sin taxes" on products high in sugar and unhealthy fats are another, although these can be regressive in practice as poor people spend proportionally more on food and drink than the wealthy. Food zoning, which restricts unhealthy facilities like vending machines around offices or schools as well as packing rules to make health warnings prominent on products like cigarettes, are also considered by some as effective tools.

Choice-influencing interventions require multi-agency collaboration since such policies span many departmental portfolios including commerce, trade and even intellectual property. Dr Garg says that CVDs require a whole-of-government approach. "We have to create environments where people can adopt healthier lifestyles. Actions to reduce CVD risks are also lying



with other sectors—the ministry of commerce, finance, agriculture, they all have to act."

Treatment

How the healthcare system treats CVDs that are emergent or already acute is the second domain for action. Investing in screening facilities, across wide geographies and accessible for all, can identify at-risk individuals before their condition becomes acute, leading to lifestyle interventions that could prevent or delay a stroke or heart attack. "Early detection is key in treating CVDs, and yet people don't always have access to primary healthcare services where they can be diagnosed and treated," says Dr Shin.

Once a CVD is full-blown, moving some care to outside of hospital settings can help manage costs and keep facilities available for the many other emergency needs. One option is facilities that check intermediate-level symptoms such as mild chest pains, which may not require emergency care. These rapid access cardiology (RAC) services are hospital co-located, cardiologist-led outpatient clinics that provide prompt assessment of patients. One recent Australia-based review found that outpatient RAC was an accepted, effective and safe pathway for management of low-intermediate risk chest pain.[30]

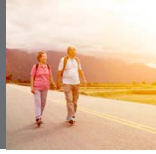
Costs can also be controlled by service design innovations. Harmonised treatment protocols can increase the quality of care, reduce errors and improve efficiency. One global initiative, the *Optimise Heart Program*, takes the form of a heart failure "toolbox" that contains best practice clinical protocols using pre- and post-discharge checklists. These capture key aspects of heart failure like heart rate, blood pressure, kidney function and medicine use.

"Many hospitals don't have protocols about how to manage heart failure when patients are admitted, and 5-10% of people will die when admitted," says Dr Cowie, who developed the initiative. "Physicians know in theory how a person with heart failure should be managed and what drugs and education are required, but often that is challenging to deliver on a day-in-day-out basis, particularly in busy settings with limited resources. We took best practice protocols, just two sides of A4, from different hospitals, and used them as a template for others around the world." Reviews of the programme show benefits including optimised drug prescribing, raised awareness and low costs.[31] Hospitals from South Korea, Taiwan, Thailand and Singapore are already participating in the initiative.

Secondary prevention

Experiencing a heart attack or stroke is strongly predictive of a recurrent event, especially if the patient's lifestyle does not change or the underlying problem is not managed by appropriate medication. Behavioural and medical interventions after

30 Klimis et al, "Rapid Access Cardiology (RAC) Services Within a Large Tertiary Referral Centre—First Year in Review", *Heart, Lung and Circulation*, 2018
31 Cowie et al, "The Optimize Heart Failure Care Program: Initial Lessons from global implementation", *International Journal of Cardiology*, 2017

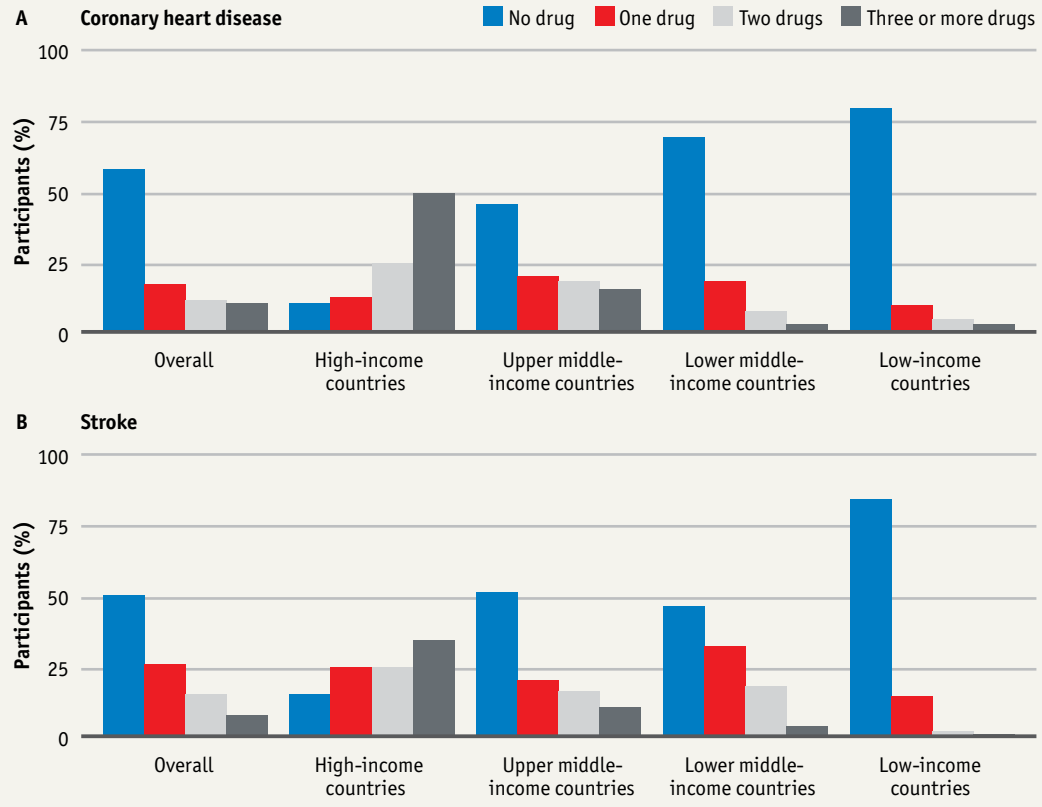


a heart attack or stroke are thus critical in protecting patients' long-term health and reducing the chance of recurrence.

The World Heart Federation's *Roadmap for Secondary Prevention of Cardiovascular Disease* outlines the necessary elements of a strong secondary prevention strategy, which entails a combination of priority medications (aspirin, ACE inhibitors, statins and beta-blockers) and lifestyle interventions (cardiac rehabilitation, smoking cessation, physical activity, a healthy diet and stress management).[32]

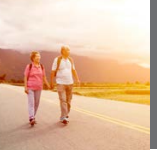
Lifestyle interventions include educational resources that inform people of the diet and physical activity regimen they should follow. These can also leverage basic technologies, according to the World Heart Federation roadmap, such as text messaging support to those trying to quit smoking.

Figure 5: Number of drugs taken by patients with known CVDs



Source: World Heart Federation Roadmap for Secondary Prevention

32 Perel et al, "Reducing Premature Cardiovascular Morbidity and Mortality in People with Atherosclerotic Vascular Disease", *Global heart,* 2015



However, too often, patients fail to adhere to lifestyle regimens whether due to lack of information, low motivation or inadequate access to facilities. Community-based cardiac rehabilitation is one option, which can take place in settings like community halls, public gyms, private gyms and outdoor spaces under the supervision of cardiac rehabilitation specialists. Singapore is one country actively exploring such approaches; the Singapore Heart Foundation (SHF) runs gym-based exercise classes led that are supervised by a physiotherapist and supported by therapist assistants and administrative staff. SHF also has an in-house nutritionist to advise service users of dietary care. "More ownership is given to the patient to manage his or her health by setting goals together with the cardiac rehabilitation specialist. They are also taught to monitor their blood pressure, heart rate and hypocount if diabetic," says Kwan Yu Heng, honorary research assistant at Khoo Teck Puat Hospital in Singapore.

Wearable technology is increasingly part of disease management. This includes tools such as digital "plasters" for stroke victims that can send wireless medical data to therapists to monitor responses to therapies and functional recovery.[33]

Finally, medication proven to reduce recurrent events include antiplatelet agents, renin-angiotensin-aldosterone system antagonists, beta-blockers and lipid-lowering therapies. Evidence shows a wide discrepancy across high-, middle- and low-income countries in terms of the number of medications prescribed to those with CVD. High-income country patients tend to be prescribed multiple medications and low-income countries tend to be prescribed none.

Taken together, a combination of evidence-based behavioural and lifestyle interventions, comprehensive screening programmes, flexible and tailored treatment mechanisms outside of hospital settings, and wearable technologies can help healthcare systems in Asia-Pacific tackle the rise of CVDs in a financially sustainable manner.

33 Phallab Ghosh, "Wearable tech aids stroke patients", BBC, 2018

Appendix

Country Chapters

Singapore

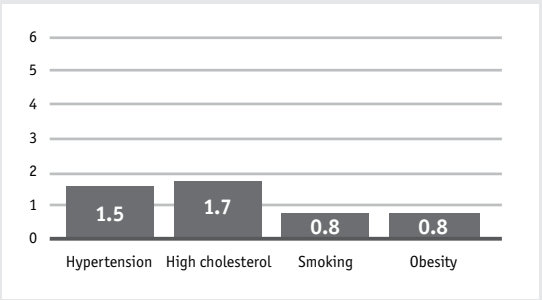
- **Approximately one in three deaths in Singapore is due to CVDs:** CVDs, or disorders of the heart and blood vessels, account for 30% of deaths in Singapore each year. IHD account for 18.5% and cerebrovascular disease (including stroke) account for 6.3% of total deaths.[34]
- **CVDs levy US$8.1bn in direct and indirect costs on individuals, their households and the public finances.**
- **Modifiable risk factors account for an estimated US$4.9bn or 60% of the total indirect and direct costs in Singapore.**
- **A reduction of hypertension and high cholesterol in both genders would significantly reduce the costs of CVD in Singapore.**

Figure 6: PAFs for CVD risk factors

SINGAPORE	MALE	FEMALE
Obesity	2.4%	7.7%
Smoking	8.1%	1.5%
High cholesterol	8.9%	12.5%
Hypertension	10.5%	8.2%

Source: EIU Healthcare

Figure 7: Annual cost of top four modifiable risk factors in Singapore (US$bn)



Source: EIU Healthcare

34 Singapore Heart Foundation, *About the Heart and heart Disease*, 2017

Hong Kong

- **IHD is the third leading cause of death in Hong Kong:** Approximately 3,500 people each year also die from stroke, making it the fourth leading cause of death behind heart disease and a major cause of adult disability.[35]

- **Mortality rates have been in slow decline but incidence rates are not.** Since 1990[36] a fall in acute myocardial infarction deaths—a major form of IHD—has underpinned the decline in mortality rates for IHD. However, rates of IHD are on the rise due to the growing proportion of older people, diminished physical activity and susceptibility to obesity from diet. In 2016 11 people died from IHD per day with a male/female ratio of 1.5:1.[37]

- **CVDs levy US$4.8bn in direct and indirect costs on individuals, their households and the public finances.**

- **Modifiable risk factors account for an estimated US$3.1bn or approximately 65% of the total costs of CVD in Hong Kong.**

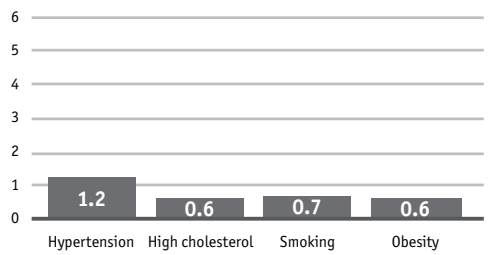
- **A reduction in high cholesterol and hypertension in both genders, and of smoking in men would significantly reduce the costs of CVD.**

Figure 8: PAFs for CVD risk factors

HONG KONG	MALE	FEMALE
Obesity	2.3%	9.7%
Smoking	14.2%	0.6%
High cholesterol	5.1%	7.4%
Hypertension	15.1%	10.3%

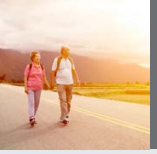
Source: EIU Healthcare

Figure 9: Annual cost of top four modifiable risk factors in Hong Kong (US$bn)



Source: EIU Healthcare

35 Hong Kong Stroke Fund, *About us,* 2018
36 Hong Kong Department of Health, *Coronary Heart Diseases,* 2018
37 Hong Kong Department of Health, *Coronary Heart Diseases,* 2018



Thailand

- **IHD is the number one cause of mortality in Thailand, according to WHO estimates.** Stroke is ranked third and CVDs overall are the cause of 29% of deaths.[38] Thailand's burden of stroke is predicted to increase primarily due to the rising incidence of hypertension, the prevalence of which rose from 22% to 24.7% between 2002 and 2014.[39]

- **Monitoring of blood pressure is improving in Thailand but not all citizens diagnosed seek treatment.** The proportion of people with undiagnosed high blood pressure fell from 71.4% in 2004 to 44.7% in 2014. While not all citizens diagnosed seek treatment, WHO data indicates that treatment rose from 8.6% to 29.7% over the same period.[40]

- **CVDs levy US$1.3bn in direct and indirect costs on individuals, their households and the public finances.**

- **These modifiable risk factors account for an estimated US$1.0bn or approximately 77% of the total costs of CVD in Thailand.**

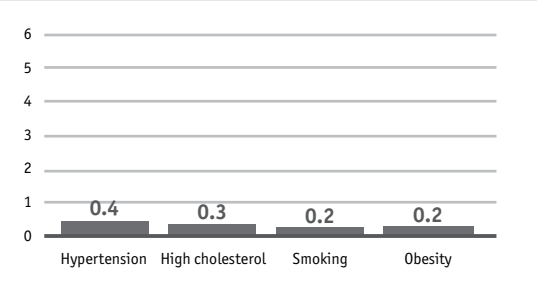
- **A reduction in high cholesterol and hypertension in both genders, and of smoking in men would significantly reduce the costs of CVD.**

Figure 10: PAFs for CVD risk factors

THAILAND	MALE	FEMALE
Obesity	1.9%	10.0%
Smoking	12.2%	0.7%
High cholesterol	8.8%	11.9%
Hypertension	14.3%	14.7%

Source: EIU Healthcare

Figure 11: Annual cost of top four modifiable risk factors in Thailand (US$bn)



Source: EIU Healthcare

38 WHO, *Country Cooperation Strategy Thailand*, 2017
39 Dr Renu Garg, 2013
40 Dr Renu Garg, 2013

Japan

- **While stroke's mortality rate has decreased over recent decades,**[41] it remains one of the leading causes of death and disability.[42] With Japan's population among the most aged of all Asian economies, the number of stroke patients is expected to rise in absolute terms.

- **A rise in the prevalence of hypercholesterolemia and diabetes is predicted.** This is widely linked with changing diets and increasingly sedentary lifestyles and suggests a gradual increase in incidence of IHD over a longer time frame.[43]

- **CVDs levy US$24.3bn in direct and indirect costs on individuals, their households and the public finances.**

- **According to EIU estimates, these modifiable risk factors account for US$15.9bn or approximately 65% of the total costs of CVD in Japan.**

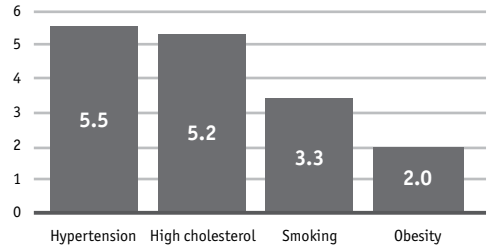
- **A reduction in hypertension and high cholesterol in both genders, and of smoking in men would significantly reduce the costs of CVD.**

Figure 12: PAFs for CVD risk factors

JAPAN	MALE	FEMALE
Obesity	2.1%	6.1%
Smoking	10.3%	3.3%
High cholesterol	9.3%	11.9%
Hypertension	13.3%	9.1%

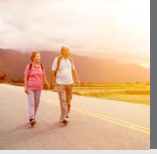
Source: EIU Healthcare

Figure 13: Annual cost of top four modifiable risk factors in Japan (US$bn)



Source: EIU Healthcare

41 Ueshima H. "Explanation for the Japanese paradox: Prevention of increase in coronary heart disease and reduction in stroke", *Atheroscler Thromb,* 2007
42 Takashima et al, "Incidence, Management and Short-Term Outcome of Stroke in a General Population of 1.4 Million Japanese", *Circulation Journal,* 2017
43 Kita T. "Coronary heart disease risk in Japan—an East/West divide?", *European Heart Journal,* 2004



South Korea

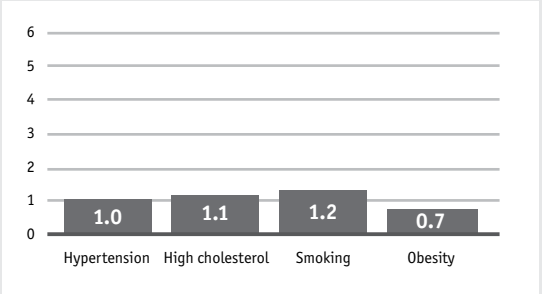
- In South Korea, stroke is the dominant CVD, the leading cause of death from a single-organ disease, with limited reduction in risk factors over recent decades.[44,45]
- While the country's IHD prevalence is 184 per 100,000, the lowest of the countries examined in this report, rapidly ageing demographics suggest a worrying future. The country now has more people over the age of 60 than people in their twenties[47] and age is correlated with increased likelihood of CVDs.[47]
- CVDs levy US$7.2bn in direct and indirect costs on individuals, their households and the public finances.
- According to EIU estimates, these modifiable risk factors account for US$4.0bn or approximately 56% of the total costs of CVD in South Korea.
- A reduction in hypertension and high cholesterol in both genders, and of smoking in men would significantly reduce the costs of CVD.

Figure 14: PAFs for CVD risk factors

SOUTH KOREA	MALE	FEMALE
Obesity	2.2%	7.4%
Smoking	14.9%	1.3%
High cholesterol	6.7%	9.1%
Hypertension	8.1%	5.9%

Source: EIU Healthcare

Figure 15: Annual cost of top four modifiable risk factors in South Korea (US$bn)



Source: EIU Healthcare

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China

- **Modernising diets and contributing to over 2.5 million new stroke cases annually.**[48] Prevalence is acute in central and north east regions[49] with incidence rising as high as 486 per 100,000 person-years.[50] Stroke is also a leading cause of family poverty in rural China.[51]

- **IHD has been the single fastest riser among causes of premature death in China, from seventh in 1990 to second, behind stroke, by 2010.**[52] Risk factors, including age and obesity, have combined with environmental issues such as ambient particulate air pollution to drive IHD-related hospital admissions, particularly in urban centres. At a rate of 98.3/100,000[53] mortality rates are moderate by global standards, but high by OECD levels.

- **CVDs levy US$21.7bn in direct and indirect costs on individuals, their households and the public finances.**

- **According to EIU estimates, these modifiable risk factors account for US$13.6bn or approximately 63% of the total costs of CVD in China.**

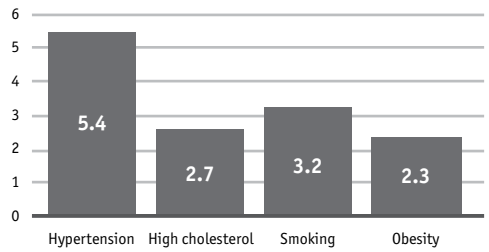
- **A reduction in hypertension and high cholesterol in both genders, and of smoking in men would significantly reduce the costs of CVD.**

Figure 16: PAFs for CVD risk factors

CHINA	MALE	FEMALE
Obesity	2.3%	8.4%
Smoking	14.2%	0.6%
High cholesterol	5.1%	7.4%
Hypertension	12.7%	12.1%

Source: EIU Healthcare

Figure 17: Annual cost of top four modifiable risk factors in China (US$bn)



Source: EIU Healthcare

48 Chen Z, "The mortality and death cause of national sample areas" *Beijing: Peking Union Medical University Press*, 2008
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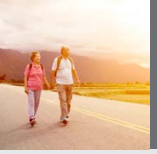


Taiwan

- **Stroke was the leading cause of death in Taiwan in 2014.** Its proportionate mortality was reported as 7.2%, with the annual-age standardised mortality rate from 2001 to 2012 almost halving to 30.8 per 100,000.[54] Low levels of physical activity, associated with risks of high blood pressure and cholesterol, and a higher sodium intake due to a contemporary diet, are all broader trends and a cause for concern.[55]

- **CVDs levy US$4.7bn in direct and indirect costs on individuals, their households and the public finances.**

- **These modifiable risk factors account for US$2.7bn or approximately 57% of the total costs of CVD in Taiwan.**

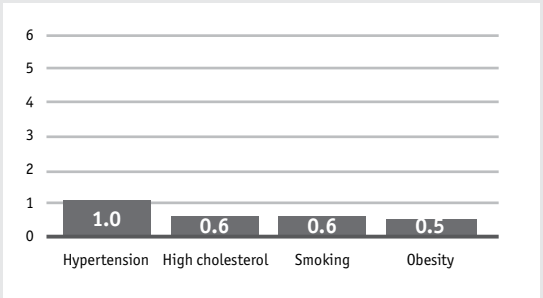
- **A reduction in hypertension and high cholesterol in both genders, and of smoking in men would significantly reduce the costs of CVD.**

Figure 18: PAFs for CVD risk factors

TAIWAN	MALE	FEMALE
Obesity	2.3%	8.4%
Smoking	11.3%	1.5%
High cholesterol	5.1%	7.4%
Hypertension	11.6%	9.7%

Source: EIU Healthcare

Figure 19: Annual cost of top four modifiable risk factors in Taiwan (US$bn)



Source: EIU Healthcare

54 Fang-I Hsieh and Hung-Yi Chiou, Stroke: Morbidity, Risk Factors, and Care in Taiwan, *Stroke*, 2014
55 Pacific Bridge Medical, Heart Disease *Growing Quickly in Taiwan*, 2017

Australia

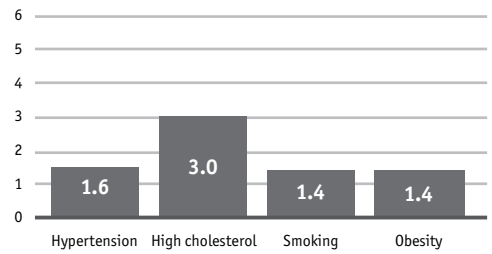
- **CVD remains the number one cause of death in the country and the leading cause of premature death.** Men in Australia have double the rate of IHD incidence compared with women, while the incidence rate of stroke is more evenly split between genders. In 2016 IHD was the leading cause of death for men, at 13%.[56]
- **These diseases impose US$12.3bn in direct and indirect costs on individuals, their households and the public finances.**
- **According to EIU estimates, these modifiable risk factors account for US$7.5bn or 61% of the total costs of CVD in Australia.**
- **A reduction in high cholesterol and hypertension in both genders would significantly reduce the costs of CVD.**

Figure 20: PAFs for CVD risk factors

AUSTRALIA	MALE	FEMALE
Obesity	4.0%	7.6%
Smoking	6.0%	5.4%
High cholesterol	13.6%	11.0%
Hypertension	8.0%	5.4%

Source: EIU Healthcare

Figure 21: Annual cost of top four modifiable risk factors in Australia (US$bn)



Source: EIU Healthcare

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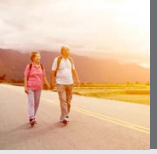


Cost calculation methodology

1. Introduction

We have developed a study which uses cost estimates from the literature and population attributable fractions (PAFs) in order to investigate the economic impact of cardiovascular disease (CVD) in the following key Asian countries:

- China
- Australia
- Taiwan
- South Korea
- Thailand
- Japan
- Hong Kong
- Singapore

The aim of this study was to provide policymakers with a cross-country comparison of the prevalence of CVD in each country, and estimate the financial impact of key risk factors associated with CVD. The financial element of this study assessed both the direct and indirect costs of CVD. The key risk factors we considered in this report were:

- Smoking
- Hypertension
- Obesity
- High cholesterol

2. Methods

To estimate the economic impact of CVD, we took the following key approaches:

1 Conducted a comprehensive search of the literature to explore existing work aiming to estimate the financial burden of IHD and stroke, or CVD as a whole, in the countries of interest. We extracted relevant data from the literature which identified where the major costs, both direct and indirect, fall

2 Reported the prevalence of ischemic heart disease (IHD) and stroke in each country of interest which together, represent people with CVD

3 Reported the prevalence of each CVD risk factor in each country and compared countries in terms of where the main burden lies

4 Investigated the proportion of the overall (direct and indirect) cost of CVD, attributable to each risk factor, using population attributable fractions.

2.1 Literature review

The costs of treating CVD can be sizeable for the public health system. These costs include a combination of treatment and related rehabilitation costs, lost economic output

and the loss of many years of productive life due to cardiovascular-linked mortality. In order to establish the extent of these costs, we extracted information from the literature reporting annual direct and indirect costs of IHD and stroke, to calculate the cost of CVD as a whole.An information specialist performed this comprehensive literature review, using the following sources to search for the literature:

- Embase.com (which covers Embase and Medline)
- PubMed
- Google Scholar
- Google

Figure 1 outlines the variables included for estimating the cost of CVD. Where it was possible, we noted how these annual costs were accrued to determine how comparable each cost estimate was across countries. As cost estimates were reported across a range of years and a range of currencies, we converted all costs to United States Dollars (USD) and adjusted for inflation using consumer price indices to make all costs current to the year 2016.

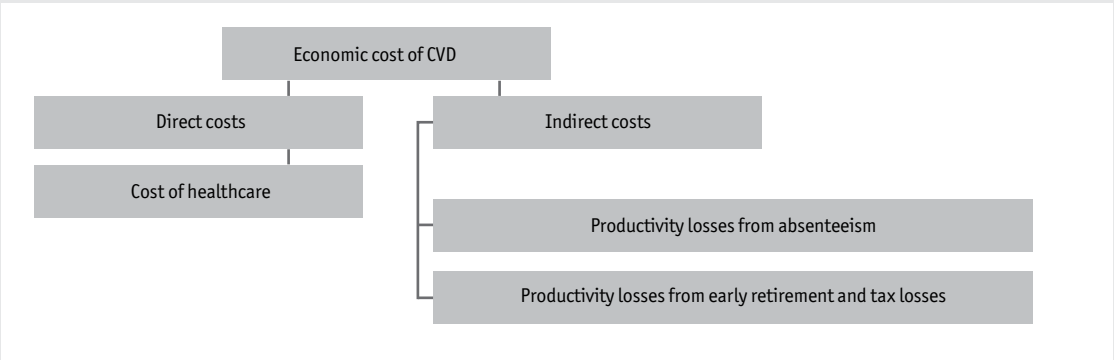
- Direct costs refer to healthcare costs associated with diagnosis and medical treatment for people with CVD. We were interested in the proportion of the direct costs of CVD attributable to four different risk factors known to be medically associated with CVD

- Indirect costs assess the broader losses of productivity to an economy due to a person with CVD being less productive at work, dropping from the workforce due to early death, early retirement ages and tax losses.

2.2 Prevalence of CVD

We extracted prevalence data from the Global Burden of Disease study,[1] which has data for all the countries of interest in this study apart from Hong Kong. We therefore interpolated the prevalence estimates for Hong Kong. Figure 23 reports the prevalence of IHD and Stroke.

Figure 22: The economic cost of CVD



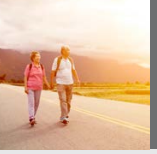


Figure 23: Prevalence of IHD and Stroke in countries of interest

MEASURE	COUNTRY	IHD	STROKE
Prevalence	China	22,903,967	28,601,199
Prevalence	Japan	4,529,173	2,541,936
Prevalence	Singapore	94,875	46,521
Prevalence	South Korea	820,160	763,992
Prevalence	Thailand	1,726,807	578,552
Prevalence	Australia	610,011	247,948
Prevalence	Taiwan	376,350	374,060
Prevalence	Hong Kong	135,133	168,747

2.3 Prevalence of each risk factor

In order to understand geographically where the major impact for each risk factor falls, we also reported the prevalence of risk factors in each country, by gender and where possible, adjusted the prevalence estimates for both Asian populations, and Australia and New Zealand. This information also helped validate our cost estimates, as we assumed that those countries which have the highest risk factors also had the highest associated costs for that risk factor. The prevalence data for each risk factor was extracted from the World Health Organization (WHO)[2] and the NCD Risk Factor Collaboration.[3] The risk factors were reported as percentages, and are defined as:

- Smoking: the percentage of the population aged 15 or older who smoke any tobacco products
- Raised blood pressure: the percentage of the population aged 25 or older having systolic blood pressure ≥ 140 mmHg and/or diastolic blood pressure ≥ 90 mmHg
- Overweight: the percentage of the population aged 20 or older having a body mass index (BMI) ≥ 25kg/m2
- High cholesterol: the percentage of people having cholesterol ≥ 190 mg/dl (5.0mmol/l))

Diabetes is also a risk factor for CVD considered in this analysis, however, there were a few reasons it was not possible to include it. Firstly, diabetes is closely related to obesity, which can lead to collinearity when aiming to analyse the effect of both obesity and diabetes on the same outcome. This is because a high body mass index is the main risk factor for diabetes, but other risk factors such as diet, hypertension, family history, alcohol consumption, low physical activity, smoking and cholesterol are also significantly associated with diabetes.[4] This

means that all of the risk factors are correlated to the risk of diabetes, thus including this in the analyses might over or underestimate the risk.[4] We excluded diabetes from our analyses to prevent this happening.

The prevalence estimates for each risk factor for both Asian and Caucasian populations had to come from a random sample of the general population, with clearly indicated survey methods and risk factor definitions. The WHO[2] and the NCD risk factor collaboration[3] are official sources of data, are constantly updated and provide data on prevalence for all the study countries therefore were suitable data sources. Figure 24 describes the prevalence of each risk factor in each country for males and females.

Figure 24: Prevalence of each risk factor in each country (%)[2, 3]

PREVALENCE OF RISK FACTORS (MEN)	CHINA	AUSTRALIA	TAIWAN	SOUTH KOREA	THAILAND	JAPAN	HONG KONG	SINGAPORE
Overweight (BMI≥25.0 kg/m2)	35%	71%	35%	34%	29%	33%	35%	36%
Smoking	49%	18%	39%	51%	42%	35%	49%	28%
High cholesterol (raised total cholesterol (≥5.0 mmol/L)	32%	55%	32%	42%	55%	58%	32%	56%
Hypertension (SBP ≥ 140 mm Hg) or diastolic blood pressure ≥ 90 mm Hg	21%	18%	20%	14%	24%	22%	26%	18%
PREVALENCE OF RISK FACTORS (WOMEN)								
Overweight (BMI≥25.0 kg/m2)	30%	58%	30%	26%	36%	22%	35%	27%
Smoking	2%	14%	5%	4%	2%	11%	2%	5%
High cholesterol (raised total cholesterol (≥5.0 mmol/L)	35%	55%	35%	43%	56%	56%	35%	59%
Hypertension (SBP ≥ 140 mm Hg) or diastolic blood pressure ≥ 90 mm Hg	17%	12%	13%	8%	20%	13%	14%	11%

Prevalence estimates include people aged 25 and above and are age-standardised. Cholesterol data was last updated in 2008, smoking data in 2013, Blood pressure data in 2015 and overweight data in 2017

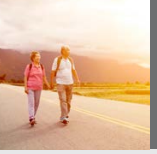
Figure 24 suggests:

In men:

- High cholesterol has the highest prevalence, followed by smoking
- Australia has the highest prevalence for being overweight

In women:

- High cholesterol has the highest prevalence, followed by being overweight
- Smoking prevalence is low across most countries compared to the smoking prevalence in men



High cholesterol is the most prevalent risk factor for both men and women.

2.4 Population attributable fractions (PAFs)

We used population attributable fractions (PAFs) to calculate the costs of each risk factor related to CVD. PAFs are a common way to estimate the proportion of all cases in the whole study population (exposed and unexposed) that may be attributed to an exposure. They provide a method for understanding the proportional reduction in population disease or mortality that would occur if exposure to a risk factor were effectively removed from a population (e.g. if everyone stopped smoking)[6]. We chose this methodology because it is an accepted way of estimating the health outcomes associated with specific risk factors, and it offers us an opportunity to estimate how much money might be saved from treating a disease, should common risk factors for that disease be reduced.[7, 8]

The costs associated with each risk factor due to occurrence of CVD are estimated based on the following equation:

$$\mathbf{PAF} = Pd=(RR-1)/RR$$

Where:

Pd = proportion of the population exposed to each risk factor (for which we used the data outlined in section 2.3).

HR = adjusted hazard ratio of mortality associated with each risk factor

Direct costs of a risk factor = (Hab x PAFab)

Where:
a (by risk factor)
b (by sex)
Hab costs for public and private (GP and specialists) consultation to treat 'a' disease in 'b' sex
PAFab = population attributable fraction of risk factor on 'a' disease in 'b' sex.

In order to estimate the PAFs for each of the study countries, we used hazard ratios for each risk factor from the literature,[8] using a study which investigated risk factors for CVD in Asian and Caucasian populations. The advantages of this study are its large sample size (314,024 participants), and incorporation of studies from diverse populations across the Asia-pacific region.[8] To ensure the PAF calculations were valid, the categories which define the prevalence of each risk factor, had to be consistent with the hazard ratios reported from the literature.[8] We made sure the categories of each risk factor from the WHO matched the defining units of the hazard ratios.

To summarise the inputs for the PAF calculations, we use the hazard ratios from Peters et al[8] for all risk factors and prevalence data from the WHO and

NCD risk factor collaboration.[2,3] A further strength of Peters et al[8] is that it reports separate hazard ratios for both Asian and Caucasian populations which allowed us to make adjustments for the varying ethnicities of the populations across countries. This means that the hazard ratio differs for each risk factor between the Asian countries (China, Taiwan, South Korea, Thailand, Japan, Hong Kong and Singapore) and the Caucasian countries in this study (Australia).[8] Figure 25 reports the hazard ratios for each risk factor in both Asian populations and Australia and New Zealand. Figure 26 reports the resultant PAF for each risk factor in each country.

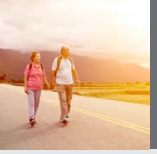
Figure 25: Hazard ratios for Asian and Australian populations as reported by Peters et al[4]

	PETERS ET AL[4]			
	ASIAN		AUSTRALIA AND NEW ZEALAND	
RISK FACTOR	WOMEN *HR*	MEN *HR*	WOMEN *HR*	MEN *HR*
Total cholesterol	1.27	1.19	1.25	1.33
Body Mass Index	1.39	1.07	1.15	1.06
Smoking	1.42	1.41	1.6	1.51
Hypertension	3.61	2.44	1.79	1.79

Figure 26: Population attributable fractions adjusted for Asian and Australian populations, and corresponding risk factor categories

COUNTRY	CHINA	AUSTRALIA	TAIWAN	SOUTH KOREA	THAILAND	JAPAN	HONG KONG	SINGAPORE
	PAFS FOR CVD RISK FACTORS (MEN)							
Overweight (BMI≥25.0 kg/m2)	2%	4%	2%	2%	2%	2%	2%	2%
Smoking	14%	6%	11%	15%	12%	10%	14%	8%
High cholesterol (≥5.0 mmol/L)	5%	14%	5%	7%	9%	9%	5%	9%
Hypertension (SBP ≥ 140 mm Hg) or diastolic blood pressure ≥ 90 mm Hg	13%	8%	12%	8%	14%	13%	15%	11%
	PAFS FOR CVD RISK FACTORS (WOMEN)							
Overweight (BMI≥25.0 kg/m2)	8%	8%	8%	7%	10%	6%	10%	8%
Smoking	1%	5%	1%	1%	1%	3%	1%	2%
High cholesterol (raised total cholesterol (≥5.0 mmol/L)	7%	11%	7%	9%	12%	12%	7%	13%
Hypertension (SBP ≥ 140 mm Hg) or diastolic blood pressure ≥ 90 mm Hg	12%	5%	10%	6%	15%	9%	10%	8%

Population attributable fractions adjusted using hazard ratios for the Asian and Australian populations from Peters et al[4] (figure 25).



2.6 Interpolation

In some instances we could not find cost data for all the countries of interest, so we used a method called interpolation to create best estimates based on available data from other countries. Interpolation is a method which is used for making economic estimates where no (or limited) published data exists, based on a baseline country with the most complete data.[9] The Global Burden of Disease[1] had no prevalence data for IHD or stroke in Hong Kong, therefore we interpolated prevalence data from China using reasonable adjustments according to the difference in population size. We found no consistent source of cost data for Taiwan, Thailand and Singapore, and therefore we interpolated the costs from South Korea. South Korea was chosen as the baseline for our interpolation calculations as the healthcare spend per head is equivalent to the average healthcare spend per head across all the countries of interest. We then used the ratio of the healthcare spend per head of each country as a scale factor for those countries where costs were missing.

Although we found many studies that looked at the economic impact of CVD in terms of indirect costs, generally these costs only considered lost wages and salaries. We wished to include in our analysis the impact on the reduction in the aggregate costs to the state from lost taxation revenue. Where available, we extracted literature that estimated tax losses in each country, and where there were no data on tax losses, we interpolated missing data based on further reasonable assumptions from the other countries. These assumptions included the prevalence of IHD and Stroke, and the average income tax revenue in each country.

3. Results

From a total of 274 potentially relevant articles, we found 98 studies that included relevant cost data relating to the economic impact of CHD/IHD and/or stroke. We prioritised studies with a large sample size, calculating direct and indirect costs based on data from national surveys or the whole population, leaving 26 studies for inclusion in our analysis. Of these studies:

- Nine reported CHD or IHD
- 14 reported stroke
- 13 reported other related CVD conditions

Seven studies were included in the final costs, a summary of which are included in the appendix. We found data on the direct costs broadly related to inpatient and outpatient visits, medications, and transportation costs. Some of these costs are accrued from the private sector and some from the public sector. Although it would be of interest to compare healthcare spending and the impact of IHD and stroke on national income based on the organisation of public and private healthcare, this becomes challenging because of the fluctuations in reporting between studies. There are differences among countries with regard to the healthcare/welfare system, which may partly explain

large variations of healthcare spending across countries and world regions. Therefore, this makes pooling of existing data on healthcare funding (public/private) unfeasible using the data we found in the literature.

3.1 Direct and indirect costs per country

The direct and indirect costs are reported separately for IHD and stroke in Figure 27. Figure 28 reports the direct, indirect and total costs for each country.

Figure 27: Annual direct and indirect costs of CVD by country

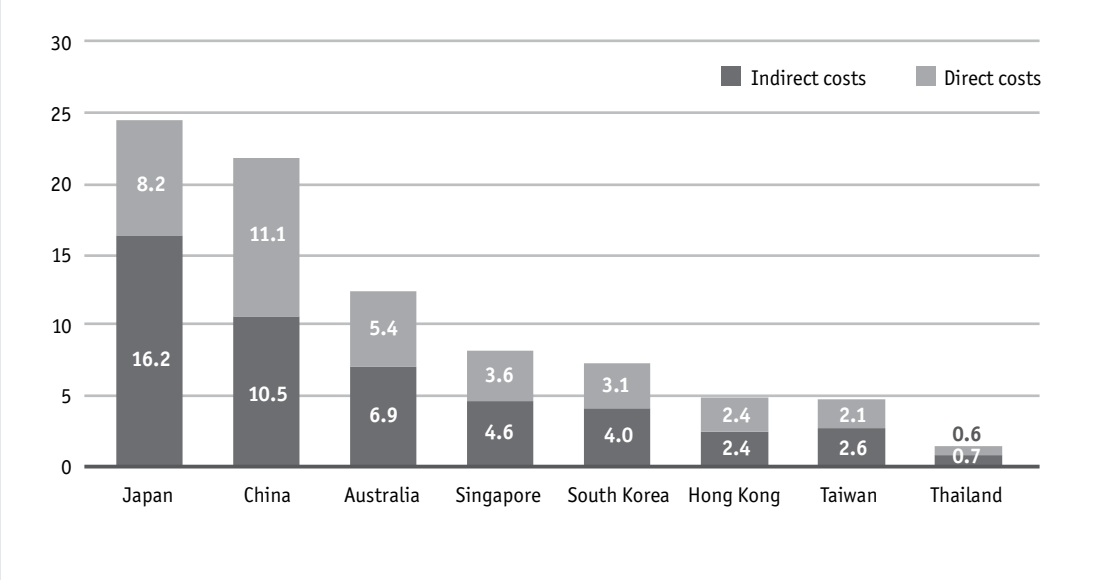


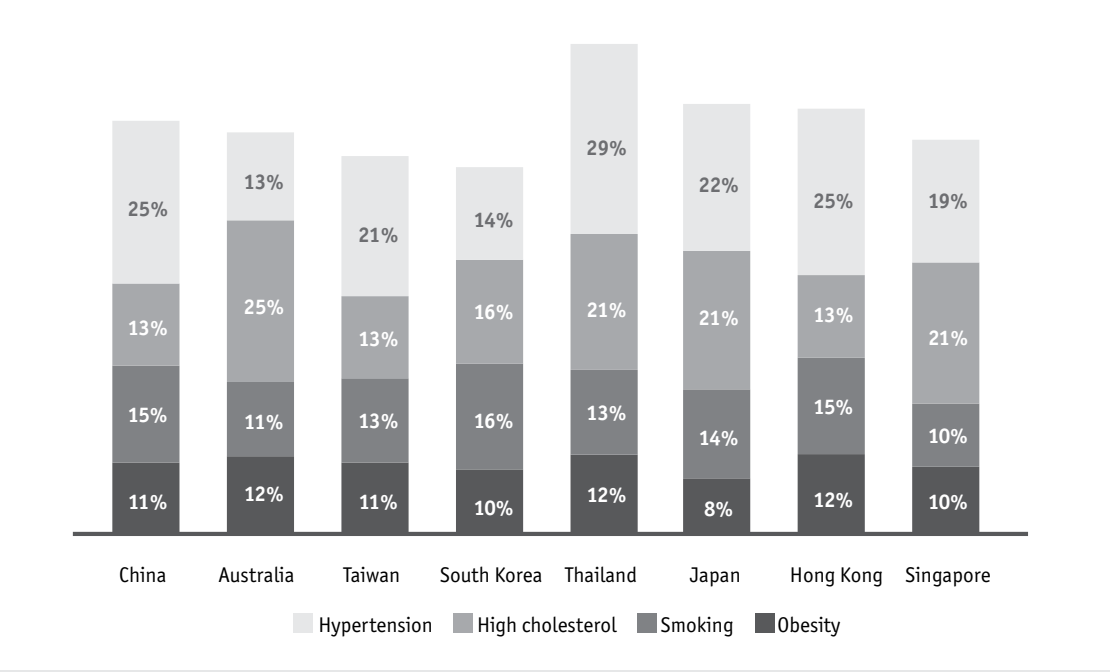
Figure 28: Annual costs of IHD, stroke, and total CVD, by country (2016 USD)

COUNTRY	CHINA	AUSTRALIA	TAIWAN	SOUTH KOREA	THAILAND	JAPAN	HONG KONG	SINGAPORE
COST (USD) TOTAL, PER YEAR (IHD)								
Direct	4,630,969,609	4,469,518,274	1,251,963,411	1,901,525,095	351,475,158	5,736,525,729	2,228,975,369	2,163,129,390
Indirect	5,069,611,138	2,804,835,725	785,666,706	1,193,297,620	220,567,412	10,626,317,655	1,398,788,272	1,357,466,782
Total	9,700,580,747	7,274,353,999	2,037,630,117	3,094,822,715	572,042,570	16,362,843,384	3,627,763,641	3,520,596,172
Total CVD	**21,657,537,647**	**12,253,353,999**	**4,707,637,815**	**7,150,122,254**	**1,321,618,292**	**24,344,401,579**	**4,835,430,303**	**8,133,807,767**
COST (USD) TOTAL, PER YEAR (STROKE)								
Direct	6,504,992,867	881,000,000	809,093,242	1,228,878,648	227,144,158	2,418,653,998	171,341,408	1,397,942,908
Indirect	5,451,964,032	4,098,000,000	1,860,914,457	2,826,420,891	522,431,564	5,562,904,196	1,036,325,254	3,215,268,688
Total	11,956,956,900	4,979,000,000	2,670,007,698	4,055,299,539	749,575,722	7,981,558,195	1,207,666,662	4,613,211,596
Total CVD	**21,657,537,647**	**12,253,353,999**	**4,707,637,815**	**7,150,122,254**	**1,321,618,292**	**24,344,401,579**	**4,835,430,303**	**8,133,807,767**

3.2 Proportion of total spend attributable to each risk factor

Figure 29 describes the % spend on each risk factor by disease.

Figure 29: % annual spend on each risk factor using Peters et al[8]



4. Limitations

It is important to remember when interpreting the figures used in this study they are all based on cost data available in the literature, and are not original calculations. There were also further limitations with the cost estimates from the literature we used. Direct and indirect costs differed quite significantly in some cases between studies reporting data for the same country. Therefore we chose the cost estimate we judged to have been calculated using the most robust methods, and based on larger sample sizes.

PAFs, while providing a practical method for defining the reduction in costs that would be achieved if the risk factor was entirely removed in the population, it is important to remember that complete removal of an exposure, is often unrealistic. Take smoking, for example: even with legal restrictions and cessation or clean-up programmes, many people will continue to expose themselves or be exposed.[10] Also, because many diseases are caused by multiple risk factors, and individual factors may interact in their impact on overall risk of disease, PAFs for individual risk

factors often overlap and add up to more than 100%, which can make PAFs difficult to interpret, despite being quite a common result.[5]

Although the WHO provides a consistent source of risk factor data across countries, the WHO states itself, that the risk factors in some countries is based on poor data, or data with many gaps. There was also a slight discrepancy data inputs for the PAF for cholesterol. This is because the WHO reports total cholesterol as 5.0mmol/l, and the study we used to extract hazard ratios of the risk factor[8] reports total cholesterol as 5.2 mmol/l. However, we considered the difference in measurement between 5.0 and 5.2mmol/l to be arbitrary, as previous literature reports an expected measurement error of ±10% in all total cholesterol readings.[11] Therefore the discrepancy between prevalence and hazard ratio cholesterol categories used for the PAF calculations we considered to have little effect on the results. The results of this study should be interpreted with caution, but they are also best estimates based on available literature and health statistics.

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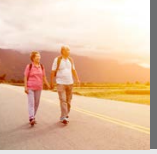

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Cost results summary

Australia

IHD

- **Indirect cost:** Zheng H, Ehrlich F, Amin J. Productivity loss resulting from coronary heart disease in Australia. Applied Health Economics and Health Policy. 2010;8(3):179-89.

  - **Sample size:** N/A (population)

  - **Indirect cost measures:** Productivity Loss (Friction Method)

China

IHD and Stroke

- **Direct cost, indirect cost:** Zhang J, Chaaban J. The economic cost of physical inactivity in China. Preventive Medicine. 2013;56(1):75-8.

  - **Sample size:** N/A (population)

  - **Direct cost measures:** hospital care expenditure, drug expenditures, physician care expenditures, and additional direct health expenditures (other professionals, public health, health research, prepayment administration, etc.)

  - **Indirect cost measures:** the value of economic output lost because of illness, injury-related work disability, or premature death before retirement

Japan

IHD

- **Direct cost, indirect cost:** Gochi T, Matsumoto K, Amin R, et al. Cost of illness of ischemic heart disease in Japan: A time trend and future projections. Environmental Health and Preventive Medicine. 2018;23(1).

  - **Sample size:** N/A (population)

  - **Direct cost measures:** medical cost directly related to the disease and includes costs associated with treatment, hospitalization, laboratory investigations, and drugs (both for hospitalization outpatient)

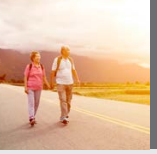
  - **Indirect cost measures:** morbidity (opportunity cost lost resulting from hospitalization and visit to hospitals) + mortality (the loss of human capital (human capital method))

South Korea

CHD

- **Direct cost, indirect cost:** Chang HS, Kim HJ, Nam CM, et al. The socioeconomic burden of coronary heart disease in Korea. Journal of Preventive Medicine and Public Health. 2012;45(5):291-300.

  - **Sample Size:** n =959,037



- **Direct cost measures:** medical costs and transportation costs

- **Indirect cost measures:** lost opportunity due to morbidity and premature death and informal care costs

- **Note:** Data from national health insurance claims

Stroke

- **Direct cost, indirect cost:** Lim SJ, Kim HJ, Nam CM, et al. Socioeconomic costs of stroke in Korea: Estimated from the Korea national health insurance claims database. Journal of Preventive Medicine and Public Health. 2009;42(4):251-60.

  - **Sample Size:** n= 882,143 (national health insurance claims)

  - **Direct cost measures: Not reported**

  - **Indirect cost measures: Not reported**

  - **Note:** N includes strokes >30y, may exclude younger patients

Thailand

Stroke

- **Direct Cost:** Kaur P, Kwatra G, Kaur R, et al. Cost of stroke in low and middle income countries: A systematic review. International Journal of Stroke. 2014;9(6):678-82.

  - **Sample Size:** N/A (population)

  - **Direct cost measures:** Direct medical cost of a stroke episode

Singapore

Stroke

- **Direct costs:** Ng CS, Toh MPHS, Ng J, et al. Direct medical costs of stroke in Singapore. International Journal of Stroke. 2015;10(A100):75-82.

  - **Sample size:** 700 patients with stroke from 2006-2012 randomly selected from database.

  - **Direct cost measures:** Direct medical costs associated with stroke

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