Chronic Diseases 2

Scaling up interventions for chronic disease prevention: the evidence

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Interventions to prevent morbidity and mortality from chronic diseases need to be cost effective and financially feasible in countries of low or middle income before recommendations for their scale-up can be made. We review the cost-effectiveness estimates on policy interventions (both population-based and personal) that are likely to lead to substantial reductions in chronic diseases—in particular, cardiovascular disease, diabetes, cancer, and chronic respiratory disease. We reviewed data from regions of low, middle, and high income, where available, as well as the evidence for making policy interventions where available effectiveness or cost-effectiveness data are lacking. The results confirm that the cost-effectiveness evidence for tobacco control measures, salt reduction, and the use of multidrug regimens for patients with high-risk cardiovascular disease strongly supports the feasibility of the scale-up of these interventions. Further assessment to determine the best national policies to achieve reductions in consumption of saturated and trans fat—chemically hydrogenated plant oils—could eventually lead to substantial reductions in cardiovascular disease. Finally, we review evidence for policy implementation in areas of strong causality or highly probable benefit—eg, changes in personal interventions for diabetes reduction, restructuring of health systems, and wider policy decisions.

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Introduction

To prevent death or morbidity from chronic diseases in an economically sustainable manner, an intervention should meet at least four conditions. First, the intervention must target behaviours or risk factors that have been causally associated with chronic diseases. Second, there should be knowledge that the intervention will probably lead to favourable changes in behaviours or risk factors, which should then lead to reductions in morbid or fatal events. Third, evidence should show that the intervention is cost effective in the settings in which it is implemented. Lastly, there should be evidence that the scaling up of the intervention is fiscally feasible in resource-constrained countries.

Tobacco control measures, salt reduction strategies, and multidrug strategies to treat patients with high-risk cardiovascular disease meet the first three conditions. For these interventions, causality has been proven, intervention effectiveness has been confirmed, and cost-effectiveness has been shown through modelling in resource-strained countries. The third and fourth papers in this Series[1,2] assess the evidence for the fourth condition of fiscal feasibility for the scaling up of these three interventions. However, a range of other potentially effective interventions that are proven in high-income countries but for which evidence on cost-effectiveness has not yet been gathered in countries of low or middle income are also highly plausible candidates for investigation and early adoption.

Such evidence on causation and health benefits of other interventions is usually transferable to the populations of low-income and middle-income countries. However, estimates of population attributable risk for individual risk factors, and of cost-effectiveness for specific interventions could differ substantially across these groups of countries.

A further limitation is that such evidence is mostly confined to personal interventions directed at changing the behaviours of individuals, and provides little information on non-personal policy interventions that could potentially alter individual behaviours through economic and environmental effects that operate at the societal level. The absence of such evidence is especially unfortunate, since such policy interventions could be more cost effective and affordable for resource-constrained countries than are resource-intensive interventions focused on behaviour change in individuals.

> **Key messages**
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> - Interventions to reduce chronic diseases should be both cost effective and financially feasible before scaling up in countries of low or middle income
> - Tobacco control, salt reduction, and a multidrug strategy to treat individuals with high-risk cardiovascular disease are three interventions that have strong cost-effectiveness data for scale-up in such countries
> - Further studies to assess the best national policies to reduce consumption of saturated and trans fats at a reasonable cost are needed before scaling up such interventions
> - Several other interventions do not have sufficient cost-effectiveness data for countries of low or middle income, but their effectiveness data are so compelling that their implementation, along with critical assessment, should be considered in such settings
> - There are limited data for structural interventions directed at the social determinants of chronic diseases, including health systems. This is an area that deserves immediate focused attention

In this paper we review the array of proven and potential interventions that can reduce the burdens of chronic diseases in low-income and middle-income countries, using proven causation and ability to intervene as the main criteria. Intervention effectiveness and cost-effectiveness data are reviewed where available (effectiveness data for the interventions in the third and fourth articles of this Series are reviewed within those papers[1,2]). In view of the large number of interventions, this paper is not exhaustive, but rather draws attention to several possible interventions for which there are various levels of evidence for scaling up in low-income and middle-income countries.

Intervention effectiveness

Community-based interventions

In the 1970s and 1980s a series of population-based community intervention studies were done in high-income countries to reduce risk factors for chronic disease. These studies focused on either changes in health behaviours or on risk factors such as tobacco use, bodyweight, cholesterol, and blood pressure, as well as a reduction in morbidity and mortality due to cardiovascular disease. In general, they included a combination of community-wide actions as well as those focused on individuals identified as being at high risk.

One of the earliest and most often cited community interventions is the North Karelia project,[3] which began in Finland in 1972. The community-based interventions included health education, screening, a hypertension control programme, and treatment. The first 5 years of the study saw reductions in risk factors as well as a decline in mortality due to coronary heart disease of 2·9% per year versus a 1% per year decrease in the rest of Finland.[4] During the next 10 years, reductions were greater in the rest of Finland. Over 25 years of follow-up, a large fall in coronary heart disease occurred in both the North Karelia region (73%) and the rest of Finland (63%). Although the overall difference in the reduction in deaths caused by

coronary heart disease was not significantly greater in the study area, the reduction in tobacco-related cancers in men was significant.[5] A similar study in the Stanford (CA, USA) area showed[6,7] reductions in risk factors—eg, cholesterol (2%), blood pressure (4%), and smoking rates (13%)—when compared with sites without the intervention, but there was no effect on disease endpoints.

Later, community interventions in high-income countries showed mixed results, with some showing improvements in risk factors beyond the secular decline that was occurring throughout most of the developed economies, and others showing no additional decrease. However, a meta-analysis of the randomised multiple risk factor interventions showed net significant decreases in systolic blood pressure, smoking prevalence, and cholesterol (table 1).[8–13] A decrease in total mortality of 3%, and in mortality due to coronary heart disease of 4%, were not significant. The limitation with all the randomised controlled trials includes the challenge of detecting small changes that on a population level could be significant; it is possible that a 10% reduction in mortality could have been missed.[8]

Several community intervention studies have been done in developing countries, including China,[12,13] Mauritius,[9] and South Africa[11] (table 1). The Tianjin project in China showed reductions in hypertension and obesity.[12,13] The Mauritius project, among other interventions, included a government-led programme that changed the main cooking oil from a predominantly saturated-fat palm oil to a soybean oil high in unsaturated fatty acids.[9] Overall, total cholesterol concentrations fell 14% during the 5-year study period from 1987 to 1992.[10] Changes in other risk factors were mixed, with reductions in blood pressure and smoking rates yet increases in obesity and diabetes. The Coronary Risk Factor Study in South Africa compared a control community with two communities receiving interventions at two different levels of intensity.[11] The interventions included mass media, group-sponsored

	Systolic blood pressure reduction (mm Hg)	Decrease in total cholesterol (mmol/L)	Increase in HDL cholesterol (mmol/L)	Decrease in smoking	Obesity (BMI >30)	Decrease in coronary heart disease mortality
Randomised controlled trials of multiple risk factor interventions in high-income countries						
Ebrahim & Smith[8]	4·2	0·14	..	4·2%	NS	NS
Community interventions in low-income and middle-income countries						
Hodge et al,[9] Uusitalo et al[10] (Mauritius)*	†	0·8	..	11% (m), 3% (w)	55% increase (m), 46% increase (w)	..
Rossouw et al[11] (South Africa)‡	2·3–3·6‡	NS	0·04–0·05	4·0%	NS	..
Dong,[12] Yu et al[13] (China)*	0 (m), 2 (w)	..	..	Increase	NS§	..
Zatonski et al[14,15] (Poland)	..	..	..	..	..	28%

BMI=body-mass index. NS=not significant. *No control site, so values reflect changes over time and thus not controlled for any possible secular changes. †Reductions in the prevalence of hypertension (≥160/95 mm Hg) of 19% (men) and 12% (women); mean values not reported. ‡Range of reduction among men and women in the two intervention sites compared with the control site. §Significant reduction in 45–64-year-olds but increases in younger adults.

Table 1: Effectiveness of community interventions, multiple risk factor interventions, and policy measures

educational sessions, and blood-pressure screening and follow-up with the health sector when appropriate. Both high-intensity and low-intensity interventions showed improvements in blood pressure, smoking rates, and the ratio of HDL to total cholesterol over the control community, but there was little difference between the two intervention communities.

One other significant reduction in coronary heart disease came not through a concerted community intervention but through changes in fiscal policy. In Poland, reductions in subsidies for animal products such as butter and lard led to a switch from saturated to polyunsaturated fats.[14,15] The increased consumption of polyunsaturated fats was mainly through rapeseed and soybean-based oils. There was a resultant decrease in mortality due to coronary heart disease of greater than 25% between 1991 and 2002 that could not be explained by increased fruit consumption or decreases in smoking.

Excess weight
Data from numerous cohort and metabolic studies provide consistent evidence that links excess weight and inactivity with impaired health. Excess weight increases the risks of metabolic disorders such as hypertension, dyslipidaemia, insulin resistance, and glucose intolerance. Excess weight is also strongly linked to increased risks of coronary heart disease, ischaemic stroke, type 2 diabetes mellitus, and a host of other chronic conditions.[16–18]

No large-scale randomised trials of weight reduction as an isolated intervention are available on which to estimate the benefits of weight loss in lowering the risk of coronary heart disease. However, sufficient information is available from numerous observational studies and small or short-term randomised clinical trials[19,20] to conclude that weight loss offers substantial health benefits. Modest weight loss—eg, of 5% to 10%—is associated with a significant improvement in blood pressure in individuals with and without hypertension.[20] Modest weight loss is also associated with improvements in the lipoprotein profile—ie, lower concentrations of serum triglycerides, higher concentrations of HDL cholesterol, and small reductions in total and LDL cholesterol—as well as improvements in glucose tolerance or insulin resistance[20] and with improvements in sleep apnoea.[21]

There is little consensus, however, on the single ideal dietary approach to weight reduction, although there is some consensus that those that include physical activity in addition to dietary means are more likely to be successful.[22–24] The options have included dietary advice, physical activity, behaviour modification, drug therapy, and bariatric surgery. These interventions are challenging to adhere to and can be expensive. Furthermore, few interventions have been done for a long duration or with long-term reductions in major outcomes such as cardiovascular disease among previously healthy individuals.[25] Without precise estimates of the benefit and with substantial variability in the intervention strategy, estimation of the cost–benefit ratio of weight-loss programmes or interventions has been challenging.

Physical activity
Although no large-scale, randomised trials of physical activity are available, numerous trials of moderate size and duration have been done in healthy individuals, those at high risk of cardiovascular disease, and those with existing cardiovascular disease. Despite differences in design, these trials generally show a benefit.[19,26] Data from more than 40 observational studies show clear evidence of an inverse linear dose–response relation between volume of physical activity and all-cause mortality rates in younger and older men and women. Minimal adherence to current physical activity guidelines, which yield an energy expenditure of about 4200 kJ per week, is associated with a significant 20–30% reduction in risk of all-cause mortality.[27] Shifting even late in life from a sedentary lifestyle to a more active one confers a reduction in mortality from coronary heart disease.[28]

Sodium reduction, tobacco, and high-risk management
The effects of reductions in consumption of sodium chloride on blood pressure, and that of tobacco exposure on chronic diseases, are reviewed in detail in the third paper of this Series.[1] The benefits and costs of scaling up an intervention of using a core group of medications for those with, or at high risk of, cardiovascular disease are reported in the fourth article of this Series.[2] We will thus not review the effectiveness data of the salt, tobacco, or the interventions for individuals at high risk of chronic disease here, but rather the cost-effectiveness results to place them in context with other interventions.

Cost-effectiveness of interventions
The results of the cost-effectiveness analyses presented below are listed in US$ per either quality-adjusted life-year (QALY) gained or per disability-adjusted life-year (DALY) averted, in keeping with the choice of measure used in the analyses of each article. Results are presented as cost-effectiveness ratios that refer to only direct costs of the intervention and the number of health-care dollars consumed or saved. An intervention that is deemed to be cost saving saves the health-care system resources in addition to adding QALYs or averting DALYs. Lastly, for many of the interventions the results are shown as a range of possible outcomes based on the plausible range for both the effectiveness and cost of the intervention in the literature. Where there is greater consensus on both of these parameters, a single ratio is provided for the cost-effectiveness of the intervention.

High-income countries

Table 2 summarises the results from the cost-effectiveness analyses of community interventions, obesity reduction, and physical activity.[29–33] On the basis of assumptions about cholesterol and blood-pressure reduction from population-based lifestyle education programmes and, in view of the fairly low cost of the interventions, the cost-effectiveness of such programmes seems reasonable in two cost-effectiveness analyses.[29,30] The first analysis[29] found that, between 1972 and 1977, the North Karelia hypertension programme cost about $5 per head in 1977 currency and led to a reduction of about 134 deaths (2100 life-years). About 85% of the costs were attributed to medications. Overall, the intervention resulted in a cost-effectiveness ratio of between $3600 and $4600 per QALY gained. One limitation of the analysis is that it did not include the costs of the other portions of the North Karelia programme from which these hypertensive patients were also benefiting in reducing events and mortality caused by coronary heart disease. However, the authors attempted to control for this by estimating only the reduction in coronary heart disease and stroke attributable to hypertension.

The second analysis[30] estimated the cost-effectiveness of the population-wide approaches to reducing cholesterol in the USA using estimates from North Karelia, the Stanford Three-Community Study,[34] and the Stanford Five-City Project.[6] The authors estimated that the three programmes cost between $5 and $17 per head in 1993 US$. They then used the range of 1–4% reductions in population cholesterol concentrations from these trials to model anticipated reductions in morbidity and mortality caused by coronary heart disease. Cost-effectiveness ratios of these interventions were sensitive to the cost of the intervention as well as to the expected reduction in the cholesterol concentration. In fact, the cost-effectiveness ratios ranged from being cost saving to $88000 per life-year gained, depending on the percentage reduction in cholesterol. For example, a nationwide community intervention that expects a 4% reduction in total serum cholesterol and costs $5 per person every year could save more than $2 billion over 25 years.

When all the benefits of a nationwide intervention programme, including blood-pressure reductions and smoking cessation, were included, the range was smaller and more favourable. The cost-effectiveness ratio of the intervention would range from being cost saving to costing $5900 per life-year gained using the North Karelia risk factor reductions, and from being cost saving to costing $600 per life-year saved using the reductions in the Stanford Five-City Project. When the estimate of a 2% reduction in cholesterol was used, the cost-effectiveness ratios were $3200 per life-year saved versus $38000 per life-year saved using the $5 and $17 costs per head estimates, respectively. These results are tempered somewhat by the late results of the project, which showed that by 13 years after the intervention began in the Stanford Project there was no significantly different decrease in cardiovascular events between treatment and control communities.[35]

The most extensive cost-effectiveness analysis of obesity used data from trials of diet, exercise, behaviour modification, or medications.[31] The authors compared the various interventions using a simulated cohort of obese individuals in a Monte Carlo simulation model of US women over the age of 35 years. They found that a combined strategy of diet, exercise, and behaviour modification leading to about an estimated 10% change in weight loss was the most attractive strategy at about $12600 per QALY. The results were most sensitive to the quality-of-life adjustments for obesity in terms of body image and perceived attractiveness than for obesity-related comorbidities. This base model assumed a 6% improvement in quality of life from being 10% lighter. Without adjustments for quality of life, the same strategy costs $60000 per life-year saved, mostly from a reduction in the number of events related to diabetes and coronary heart disease. No similar analysis of these interventions has been done in men. One study of morbid obesity[32] found that the cost-effectiveness of gastric bypass surgery would be $10700–35000 per QALY in men and $5400–16100 per QALY in women, with the range depending on initial weight and age.

Unfortunately, there is less cost information on physical activity interventions to determine their cost-effectiveness on a larger scale. One study, after assuming that there is a 50% reduction in coronary heart disease events from jogging, suggested that the cost-effectiveness would be around $12000 per QALY in 1988.[33] However, this estimate assumed that the intervention cost only $100 per year. Other structured community interventions have

	Cost of intervention (per head)		
	$5	$17	Other
Community intervention			
Hypertension[29]	4000	..	..
Cholesterol[30]			
4% reduction	Cost saving	1370	
2% reduction	3200	38000	
1% reduction	18100	88100	
Multiple risk factor reductions			
North Karelia estimates	Cost saving	5900	
Stanford Five City estimates	Cost saving	600	
Overweight			
Diet, exercise, and behaviour change[31]			12600
Gastric surgery (morbid obesity)[32]*			5000–35000
Physical activity[33]			
Over age 65 years			Cost saving–600
Under age 65 years			4500–142000†

Costs are in US$ for the year of study report. *Results dependent on age, sex, and starting body-mass index. †Cost saving if cost of time spent exercising not included.

Table 2: Cost-effectiveness ratios (US$/QALY gained) of interventions in high-income countries

been estimated to cost as much as $500–2000 per year per participant in 2006.[36] A review of all cost-effectiveness analyses to date on physical activity found a lack of evidence for physical activity interventions for those at low risk[37] whose only risk factor is a sedentary lifestyle. Most of the cost-effectiveness evidence favours interventions for those who have other risk factors, are older, or have comorbidities, especially heart failure.

Low-income and middle-income countries

Cost-effectiveness analyses of multiple interventions in countries of low and middle income were done as part of the Disease Control Priorities Project[38] and are reported in table 3.[38–42] The cost-effectiveness analyses on salt reduction as a result of public education are quite favourable. The intervention ranges from being cost-saving to $200 per DALY averted across the range of estimates of the cost of the intervention as well as its range of effectiveness. The tobacco interventions have similar results, with very favourable cost-effectiveness ratios for pricing measures such as taxation resulting in ratios under $100 per DALY, with the non-pricing interventions such as advertising bans and labelling of packages only being moderately higher, ranging from under $100 to just over $1000 per DALY depending on the World Bank region.[39] Juxtaposed to these population strategies, strategies involving multidrug regimens to treat patients with high-risk cardiovascular disease also seem reasonable. Multidrug interventions are estimated to be between $300 (secondary prevention) and $1000 (primary prevention for individuals with high-risk disease) per DALY averted.[41,42] All the results fall well under the gross domestic product per head for each region, making them attractive options for scale-up.

The next analyses presented include the results of a campaign to reduce saturated fat and replace it with polyunsaturated fat. In the base analysis, a 3% decrease in cholesterol and a $6 per head education cost was assumed. This resulted in a cost as low as $1800 per DALY averted in the south Asian region up to $4000 per DALY in the Middle East and north Africa region. However, if the costs for the education plan were halved, the ratio was about $900 per DALY and would be cost saving if the reduction could be achieved for under $0·50 per head, which could be possible in areas where media is much less expensive. The WHO CHOICE project estimates for the cost of the intervention were similar to the lower estimate for developing regions and produce results of about $100 per DALY averted.[40]

The authors also assessed the cost-effectiveness of replacing trans fat—chemically hydrogenated plant oils—with polyunsaturated fats. Replacing 2% of energy from trans fat with polyunsaturated fats was estimated to reduce coronary heart disease by 7–8%[43] assuming changes in LDL cholesterol only and up to a 40% reduction in coronary heart disease, assuming benefits beyond LDL cholesterol including changes in triglycerides, endothelial function, and inflammatory markers.[44] Because these changes can occur through

	Cost of intervention (per head)				
	NA	<$0·50	$1	$3	$6
Tobacco[39]*					
Price increase of 33%	2–85	..	..	..	..
Non-price interventions (media bans and education)	33–1432	..	..	..	..
Salt reduction[38,40]					
8 mm Hg reduction in systolic blood pressure	..	Cost saving	100	..	..
4 mm Hg reduction in systolic blood pressure	..	30	160	..	..
2 mm Hg reduction in systolic blood pressure	..	111	250	..	..
Fat-related interventions					
Media campaign to reduce saturated fat[38,40]†	..	Cost saving–100	..	900	2900
Replacing trans fat with polyunsaturated fat[38]					
7% reduction in coronary heart disease	..	50	..	..	1500
40% reduction in coronary heart disease	..	Cost saving	..	..	200
Multidrug regimen for high-risk cardiovascular disease[41,42]					
Primary prevention					
Absolute risk >25%	..	..	825	..	..
Absolute risk >15%	..	..	900	..	..
Secondary prevention	..	350			

Ratios are in 2001 US$. NA=not applicable. *Low to high estimates across the six World Bank regions. †Assumes 3% reduction in cholesterol.

Table 3: Cost-effectiveness ratios (US$/DALY averted) of interventions in low-income and middle-income countries

voluntary action by industry or by regulation (eg, the banning of trans fat in New York City restaurants), this initiative can be achieved without a large media campaign and high costs. According to the US Food and Drug Administration,[45] this can be achieved for less than $0·50 per head. With this cost and the conservative estimate of an 8% reduction in coronary heart disease, the intervention is highly cost effective at $25–75 per DALY averted across the developing world. Assuming the greater reduction of 40% in coronary heart disease, the intervention is cost saving.

Discussion

Policymakers in countries of lower and middle income are faced with a wide range of possible effective (and cost-effective) interventions, and they are forced to set priorities using a rational approach. They must decide in a context of uncertainty and they are faced with two issues of increasing complexity. First is how to apply evidence on policy: what are the interventions that effectively reduce the risk of chronic disease and alleviate the existing burden? Which of these are cost-effective in a low-resource setting? The second set of challenges is focused on gathering evidence for policy: what about areas where the evidence is not yet established? What about the wider determinants of chronic diseases?

There is clear evidence that many interventions are cost-effective. The Commission on Macroeconomics and

Health has proposed a standard of three times gross national income (GNI) per head per DALY averted as being cost-effective.[46] The World Bank estimates that GNI per head in 2006 was, on average, $650 for low-income countries and $3051 for middle-income countries. Tobacco interventions, salt reduction, and multidrug strategies to treat individuals with high-risk cardiovascular disease have acceptable cost-effectiveness ratios for low-income and middle-income countries on the basis of this criterion. If scale-up is feasible for many nations, then it would be reasonable to pursue these options immediately to achieve the projected goals of reducing rates of chronic disease by an additional 2% per year.

Community-based programmes seem to yield small but significant reductions in risk factors for cardiovascular disease, and could be cost-effective in countries of low or middle income, although cost-effectiveness data are lacking, even if such interventions seem reasonable in the high-income regions. The results from the earliest intervention, the North Karelia project, as is often the case, are the most impressive. Efforts since then have yielded less striking results but they remain significant from a population perspective. The results seem to have the greatest effect when public knowledge of the risk factors is limited.[47] Hence we expect that, with time, as populations become more educated, the potential reductions in mortality would fall. Thus, in countries of low or middle income where the overall knowledge of risk factors for chronic diseases remains low, we could expect reasonable reductions through education programmes. Surveys of knowledge regarding chronic diseases and their risk factors might be a reasonable initial step before scaling up educational programmes. Furthermore, the reductions from an intervention where risk factor levels are already low might not yield the same results. For example, in a country where the intake of trans fat is not very high, the potential reductions in mortality could be quite small from restricting its use.

To ensure that existing policies are applied to populations that could potentially benefit from them might seem to be enough of a challenge. Yet there is a greater challenge to face. A comprehensive approach to chronic disease will need to address the effects of wider social and economic determinants of chronic disease, such as globalisation, urbanisation, social stratification, and access to the health system itself. These are clearly related to the origin of chronic disease but there is not yet a traditionally acceptable evidence base on how to affect them. There is often no clear single intervention against the wider determinants, only a range of plausible integrated policies and actions. The international community is thus tasked to develop evidence for policy: this is the imperative to take reasonable action, to monitor and assess it, and then to propose or reject it for wider adoption as a national or international model.

Several personal interventions have been shown to be effective in both high-income and low-income settings, yet there is a lack of cost-effectiveness data. Some results are convincing enough to merit adoption on a trial basis, even in poorer countries with a rapidly advancing epidemic. A leading candidate among these is the prevention or delay of diabetes. Behaviour change has been shown to reduce the incidence of diabetes in high-risk populations in China,[48] Finland,[49] the USA,[50] and India[51] by as much 58% in 4–6 years, and further shown that a high proportion of these effects are sustained beyond the cessation of the intervention.[52] The results in India—a 28·5% reduction in risk with lifestyle modification alone—were more modest than in Finland and the USA, but they were even more promising in view of the size of the epidemic in Asia, the non-invasive screening method used, the moderate intensity (and cost) of the intervention, and the magnitude of the results based on behaviour change alone.

The changes in Mauritius and Poland suggest that fiscal policy around food consumption or other health behaviours could be equally or more effective at achieving reductions than are education programmes. However, more evidence is needed to ascertain the probable effect size in countries of low or middle income, or the cost to achieve such a reduction through policy instruments. Interventions to reduce consumption of saturated and trans fat should be the next focus beyond the core package for low-income and middle-income countries. If efforts to reduce the intake of saturated and trans fat can occur for under $1 per head, then these interventions would be either cost saving or extremely cost effective. If they are cost-neutral, or reduce costs due to reduced subsidies, then the intervention might be even more attractive.

The Commission on Social Determinants of Health, due to report in 2008, has defined a comprehensive framework for analysis and intervention on the "causes of the causes of ill-health".[53] All the factors described in the framework are directly relevant to the origin of the chronic disease pandemic and to the inequities between geographic and social groups. The structural interventions required to address these inequities will clearly be broad in nature and generally not amenable to narrow cost-effectiveness analysis. In particular, the health system is itself described as one of the intermediate social determinants of health. It can, in the words of the Commission, "directly address differences in exposure and vulnerability not only by improving equitable access to care, but also in the promotion of intersectoral action to improve health status". In integrated models such as those discussed in this Series, where chronic diseases are addressed through combined population-level interventions and clinical preventive services, both mediating roles of the health system become relevant, not just in reducing the total burden, but also in reducing the inequalities.

Available evidence does not enable us to estimate how the cost-effectiveness of interventions directed at individuals can be improved by concurrent policy interventions that create an environment in which people can more easily make and maintain choices related to

healthy behaviours. Policy interventions can also potentially alter the determinants of cost and effectiveness of interventions that affect individual behaviours. WHO's Framework Convention on Tobacco Control and the Global Strategy on Diet and Physical Activity[54] provide a guide for multisectoral actions that can reshape the environment in a way that costs of chronic disease prevention can be substantially reduced and effectiveness of several behaviour change interventions can be potentially increased. And as a priority, inefficiencies in the market for health that bar people living in poverty from accessing basic prevention and care must be addressed through direct provision of services or through health insurance.

Although the evidence for assessing policies relies on cost-effectiveness data, the evidence for implementing policies is mainly determined on the basis of definite causality and highly probable benefit. We believe both of these approaches to be part of a continuum that must guide early initiation and rigorous assessment of programmes for the prevention and control of chronic diseases in countries of low or middle income. Developing countries should quickly initiate action through these strategic pathways, even while aiming to acquire, appraise, and assimilate fresh evidence on cost-effectiveness.

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