



## Preventing coronary heart disease

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## Preventing coronary heart disease

*Does Rose's population prevention axiom still apply in the 21st century?*

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In this issue (p 659) Manuel and colleagues report how they estimated the effectiveness of three strategies to lower blood cholesterol concentrations in Canadian adults.<sup>1</sup> A "population" strategy assumed that blood cholesterol could be lowered by 2% in the whole population and deaths from coronary heart disease by 2.7%. The two other strategies were patient based, assuming that prescribing statins to subgroups of people at high risk of coronary heart disease would reduce their risk by 27%. A "single risk factor" strategy targeted patients with blood cholesterol levels greater than 6.2 mmol/l and a "baseline risk" strategy targeted those with a baseline risk of cardiovascular disease greater than 15% over five years, irrespective of their blood cholesterol levels.

Surprisingly, the population strategy, based on the axiom by British epidemiologist Geoffrey Rose that "a large number of people at small risk may give rise to more cases than a small number of people at high risk,"<sup>2</sup> was the least effective strategy. The single risk factor strategy, prescribing statins to the 1.53 million Canadians with a blood cholesterol concentration greater than 6.2 mmol/l, was calculated to prevent three times as many coronary deaths as lowering cholesterol by 2% in all 12 million Canadian adults.

By far the most effective strategy, which is estimated to prevent seven times more coronary deaths than the population strategy, was (ironically) based on another of Rose's axioms, that "all policy decisions should be based on absolute measures of risk."<sup>3</sup> This strategy uses baseline absolute risk and came from current New Zealand guidelines on managing cardiovascular risk<sup>4</sup>—the most recent of a 10 year series of guidelines strongly influenced by Rose's axiom about absolute risk.<sup>5</sup>

Although population strategies might achieve more than a 2% blood cholesterol reduction, and a 27% reduction in coronary deaths through using statins may be optimistic in routine practice, the impact of the population approach is unlikely to come close to that of the approach using baseline absolute risk. So was Rose's axiom about prevention in the population ever superior to the other approaches, or has the landscape of coronary prevention changed substantially over the past 20 years?

When Rose argued that a population strategy for preventing coronary heart disease would be more effective than targeting people with a higher single risk factor he was probably correct.<sup>6</sup> Effective drugs for lowering cholesterol were not available when he was developing his ideas, and population strategies probably had greater

potential to lower blood cholesterol by more than a few per cent. In the United States population, for example, blood cholesterol levels fell by about 5% between 1976-80 and 1988-94.<sup>7</sup> But the "low hanging fruit" of population strategies to improve nutrition, particularly the substitution of saturated fat with polyunsaturated and monounsaturated fat in processed foods, has now been picked, as reflected in the lack of further cholesterol reductions in the US in the subsequent decade. So the predicted 2% reduction in cholesterol levels from population strategies is likely to be realistic in 21st century North America.

Rose's axiom about population level interventions assumes that the risk of coronary heart disease is widely diffused in the population. Yet Manuel and colleagues estimated that about 35% of predicted deaths occurred in the 4% of Canadians with a history of symptomatic cardiovascular disease.<sup>1</sup> Rose had also shown in his own research that 41% of cases occurred among the 16% of men aged 40-59 who had pre-existing ischaemia,<sup>2</sup> but in his defense of the population approach<sup>6</sup> he chose to compare it with the approach targeting those patients with a single raised risk factor which is a poor indicator of absolute risk.

Manuel and colleagues' findings are consistent with those from a study by Hunink and colleagues of the determinants of trends in mortality from coronary heart disease in the US between 1980 and 1990.<sup>8</sup> Hunink's study showed that more than two thirds of the overall 34% decline in coronary mortality over 10 years occurred in patients with prior coronary heart disease and that reductions in risk factor for these patients accounted for a slightly greater proportion of the total decline than primary prevention (29% v 25%).

Inexplicably, in an apparently similar recent analysis of coronary heart disease mortality trends in England and Wales between 1981 and 2000, Unal and colleagues report that changes in the main risk factors through primary prevention achieved a fourfold larger reduction in deaths from coronary heart disease than through secondary prevention.<sup>9</sup> More than two thirds of all deaths from coronary heart disease postponed through primary prevention in this British study were calculated to be due to a 35% reduction in the prevalence of smoking, whereas a similar decline in smoking in the US was estimated to account for only 12% of deaths after primary prevention. On the basis of these estimates, Unal and colleagues challenge the current emphasis on secondary prevention of coronary heart disease in the United Kingdom.<sup>9</sup> However,

their analyses seem at odds with the evidence that a small proportion of the population at high absolute risk can contribute a large proportion of all deaths from coronary heart disease.

Another paper in this issue, by Tunstall-Pedoe and colleagues (p 629), seeks to explain falling blood pressure levels in the MONICA study, which included 38 populations in 21 countries over four continents.<sup>10</sup> The authors observed a similar decline at all levels of blood pressure and conclude this meant medication was unlikely to have made a significant contribution. They state this was unexpected and seem to infer that population prevention strategies are therefore superior to individual treatment strategies. However, there was almost no change in the proportion of people receiving drugs to lower blood pressure over the period of the study. Moreover, the analyses could not determine the potential population impact of blood pressure lowering treatment. Such analyses would need to have examined trends in treatment among the subgroup of patients at high absolute cardiovascular risk, who do not necessarily have high blood pressure levels. Nevertheless, the observed shift in the entire population distribution of blood pressure in so many populations is unexplained and needs further examination.

Population based prevention is the only sustainable strategy for reducing the burden of coronary heart disease.<sup>2</sup> But unless we also treat patients at high risk, we will have limited impact on morbidity and mortality from coronary heart disease in the short to medium term. Numerous effective interventions are now available for managing the risk of cardiovascular disease, and the recently proposed polypill is an exciting development.<sup>11</sup> Tools for risk assessment are also widely available to help target intensive interventions appropriately.<sup>12</sup>

This century, population strategies may have their greatest impact in low to middle income countries where relatively simple and cheap strategies, including high taxes on smoking and replacing saturated with unsaturated fats, have yet to be widely implemented. Nevertheless, individual strategies targeting patients at high risk should be introduced in parallel. If a cheap polypill delivers as expected and cuts risk by more than

half, then the impact of the developing epidemic of cardiovascular disease in low and middle income countries could be tempered while long term population strategies are put in place.<sup>13</sup> Rose's population and absolute risk axioms are both relevant to cardiovascular disease prevention in the 21st century, although their applicability is likely to vary by country and by time.

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## Nutritional supplements in cystic fibrosis

*A new study suggests they're ineffective, but concordance may have been poor*

People with cystic fibrosis and their caregivers know that the better the patient's nutritional status, the better their survival, lung function, wellbeing, and mental capabilities.<sup>1-3</sup> Poor nutrition is also associated with delayed puberty, a higher risk of pneumothorax, and a worse outcome after lung transplantation.<sup>4,5</sup>

The increased demand for energy in cystic fibrosis is well recognised.<sup>6</sup> Despite this, almost 20% of children with cystic fibrosis fall below the fifth centile for weight set by the Centers for Disease Control and Prevention,<sup>7</sup> and their height and weight z scores often decline with age. Combating nutritional failure to ensure normal growth and weight gain is therefore a key challenge for

the entire team—doctors, nurses, dietitians, psychologists, and social workers.

Nutritional management in cystic fibrosis is difficult for several medical and psychosocial reasons. One priority is the optimal medical management of malabsorption from exocrine pancreatic insufficiency and deranged enterohepatic circulation of bile. Patients continuously have to adjust the dose of exogenous pancreatic enzymes they need to take to allow assimilation of ingested food. Meanwhile, patients often need lung clearance techniques and antibiotic treatments to reduce the increased energy demand from chronic pulmonary infection and inflammation and breathing difficulties. These toddlers, children,

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