

# Will screening individuals at high risk of cardiovascular events deliver large benefits?

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**YES** Provisional modelling by the Department of Health suggests that up to 9500 heart attacks and strokes and 2000 deaths could be prevented each year by its plan to screen for and manage vascular risk in people aged between 40 and 74.<sup>1</sup> Checks would comprise a brief history, examination, and blood test and could take place in general practices or pharmacies. The programme will be implemented in 2009-10 at an annual cost of about £250m (€315m; \$465m).<sup>1</sup> This strategy assumes that the high risk approach to preventing cardiovascular disease is effective and cost effective, which we believe to be true.

A large World Health Organization review comparing high risk and population-wide interventions to prevent cardiovascular disease globally showed that treating high risk patients with aspirin, off-patient statins, and blood pressure lowering drugs was not only cost effective but would avert more disability adjusted life years (DALYs) worldwide than population based interventions to reduce salt intake, obesity, and cholesterol concentrations.<sup>1, 2</sup> Furthermore the high risk approach was much more effective and cost effective than approaches targeting high risk factors (such as treatment of hypertension). Rose was right to point out the disadvantages of high risk factor approaches, but he didn't assess the high predicted cardiovascular risk approaches.<sup>3</sup> The key questions to be resolved are how best to define high risk and the optimal mix of high risk personal strategies with other population strategies.<sup>4, 5</sup>

## Potential impact

Myriam Hunink's 1997 disease modelling study suggested that over two thirds of the fall in deaths from coronary heart disease in the US between 1980 and 1990 occurred among the 6% of 35-84 year old Americans with prior coronary disease.<sup>6</sup> Her hypothesis is even more relevant today with the increasing num-

bers of people with coronary disease<sup>7</sup> and the widespread availability of affordable, effective drugs. Between one third and one half of all major coronary disease events in 35-74 year olds now occur in the 5-6% of the population with a previous cardiovascular disease event,<sup>8, 9</sup> and triple therapy with aspirin, statins, and blood pressure lowering drugs can reduce event rates by two thirds or more.<sup>10, 11</sup> If only half these very high risk patients were adherent, this combination of drugs alone would be responsible for a 10% fall in national coronary disease event rates in less than 10 years.

To achieve a similar national reduction in coronary disease events, a primary prevention strategy would need to lower the average coronary risk in the rest of the population by about 20%—a huge challenge, now that much of the low hanging fruit receptive to population-wide strategies has been picked.<sup>12</sup>

## Targeting very high risk patients

The most cost effective strategy for preventing cardiovascular events therefore starts by targeting patients who have had a cardiovascular disease event. They are at the highest risk (10 year risk is usually >40%), there are relatively few of them, they are easy to identify, and they are likely to be more motivated than

patients without symptoms. However, the NHS intends to provide drug based management for everyone aged between 40 and 74 years with a 20% cardiovascular risk over 10 years.<sup>1</sup> If, for example, the QRISK2 cardiovascular disease risk prediction equation<sup>13</sup> was used to identify patients meeting the NHS treatment thresholds, then about 10% of Britons aged 35-75 years would be recommended for drug treatment, in addition to the 5-6% with a history of cardiovascular disease.

However, about twice the number of asymptomatic patients would need to be treated to prevent half the number of events achieved by treating those with prior cardiovascular disease.

Currently, most patients with established cardiovascular disease are not taking triple therapy. The treatment gap is closing very slowly, but the number of low risk people treated far exceeds the number of high risk

people treated.<sup>14</sup> So priority must be given to ensuring general practitioners are able to manage patients with prior cardiovascular disease before widening the net too far.

New equations to predict risk of cardiovascular disease are better calibrated to UK populations,<sup>13, 15</sup> and their accuracy is improving with the addition of measures of social deprivation and ethnicity, providing an opportunity to target primary prevention more accurately while simultaneously reducing social inequities. However, as risk thresholds for treatment are lowered, large numbers of patients will be eligible for drugs. To cope with the increased workload and cost, simplified primary prevention treatment regimens are required. The recent NICE lipid guidelines are a good start, recommending 40 mg of simvastatin for all asymptomatic high risk patients, without any dose tailoring or systematic follow-up.<sup>16</sup> Similar recommendations are required for blood pressure lowering drugs, and the end game may turn out to be a single daily combination pill.

## Getting the right balance

Too often debate about prevention of cardiovascular disease is polarised between opposing evangelists for the high risk and population-wide approaches. An agnostic approach based on effectiveness and cost effectiveness is preferable. Cost effective high risk strategies must be complemented by cost effective population-wide interventions.

**Competing interests:** RJ and AR are investigators on several randomised controlled trials investigating the effectiveness of polypills for managing risk of cardiovascular disease.

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The Department of Health is planning to identify and treat all adults over 40 at high risk of a cardiovascular event. **Rod Jackson and colleagues** argue that a well targeted programme will save many lives, but **Simon Capewell** thinks whole population approaches would be more cost effective

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**NO** Evidence supporting the high risk approach for preventing cardiovascular disease is disappointing. The strategy has low effectiveness and is associated with high cost, residual risk, medicalisation, and increasing inequalities. Whole population approaches are cheaper and more effective.

#### Low effectiveness

The large OXCHECK trial (of a nurse led health check plus health education and follow-up tailored to the level of cardiovascular risk) had only modest effects on cardiovascular events.<sup>1</sup> Indeed, more recent literature raises further concerns.<sup>2,3</sup> Healthcare professionals' advice to stop smoking or take more exercise also has frustratingly modest effects.<sup>4</sup>

All screening programmes are imperfect. Even with generous resources, the call, recall, and follow-up systems require major commitments. Drop outs are substantial. Screening failures will be more common in the more deprived groups, who experience higher rates of disease, thus increasing inequalities.<sup>5,6</sup>

All cardiovascular risk scoring systems are inaccurate and potentially confusing. Even the best risk charts have predictive accuracy of only 60-70% for an individual patient.

**Over 80% of British men aged 65-74 would be categorised as high risk, needing treatment**



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Furthermore, a bewildering variety of charts exist. Many general practitioners do not understand, interpret, or use the charts well.<sup>2,7</sup>

Treatment failure will also reduce systematic population benefit. Even in motivated patients, about 5% will be intolerant of statins and 10% intolerant of antihypertensive drugs.<sup>8,9</sup> Furthermore, long term adherence with hypertension therapy or statins is consistently less than 50%.<sup>10</sup>

#### Residual risk

Drugs do not eliminate the underlying pathology. They merely put a sticking plaster over the problem. The patient remains physiologically hypertensive and vulnerable to hypercholesterolaemia. Thus, stopping treatment will rapidly lead to recurrence of the pathological state with raised cardiovascular risk.

Even with continuing therapy, the risk of subsequent cardiovascular events is reduced by only about 15% with successful control of blood pressure<sup>11</sup> and by about 25% with cholesterol reduction.<sup>12</sup> The efficacy of statins in primary prevention may be even lower, particularly in women.<sup>13</sup> There is also uncertainty about how these benefits might add up. Even optimistically assuming a hypothetical combined risk reduction of 40% (that is, 15%+25%), over half the cardiovascular risk will remain. This conflicts with many patients' expectations. It is also brave to assume that efficacy in randomised control trials translates into equal effectiveness in the messy realities of clinical practice.<sup>14</sup>

#### Cost

The high risk approach would commit the majority of middle aged adults to lifelong drug treatment with huge costs. Over a quarter of UK adults have cholesterol concentrations above 5.2 mmol/l and over half have blood pressure above 140/80 mm Hg. Indeed, over 80% of British men aged 65-74 would be categorised as high risk, needing treatment.<sup>15</sup> This partly reflects a progressive reduction in treatment thresholds. Thus, more individuals become eligible for treatment, but the number needed to treat

inflates while side effect rates persist and costs spiral.

There are also non-financial costs. The high risk approach medicalises healthy people, turning them into lifelong patients. The implicit message for patients is that "the doctor can fix it." This takes responsibility away from the individual and may encourage further risk taking behaviour. For instance, continuing consumption of junk foods high in salt and saturated fats.

Furthermore, quality of life often decreases after starting treatment for hypertension or hyperlipidaemia.<sup>16,17</sup> A high risk label also has serious implications for personal health insurance. Thus, given the choice, most people would rather opt for behavioural change than lifelong medication.<sup>17</sup>

The focus on individuals also favours affluent and educated people, thus increasing social inequalities. Disadvantage can occur at every stage in the process, from the person's health beliefs and health behaviour, through presentation, negotiation, participation, and adherence with treatment.<sup>18,19</sup>

#### Cost effectiveness

The high risk approach distracts attention from cheap policy interventions that reduce risk factors across entire populations. Small reductions in population cholesterol concentrations, blood pressure, or smoking can translate into substantial reductions in cardiovascular events and deaths.<sup>20,21</sup> Some two decades ago, Geoffrey Rose suggested that: "A large number of people exposed to a small risk may generate many more cases than a small number exposed to a high risk."<sup>22</sup> Empirical evidence to support the Rose hypothesis has progressively emerged from Swedish patients with hypertension, British middle aged men, Dutch and Irish adults, and a pan-European dataset.<sup>21,23-25</sup>

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