Diabetes is a major risk factor for ischaemic heart disease; the relative risk increases at least twofold among diabetic men and even more so for women.1 Diabetes is associated with more extensive coronary artery disease and an increased risk of cardiac death.2 Even in the absence of frank diabetes, glucose intolerance has been associated with a heightened risk of coronary artery disease independent of age, blood pressure, and other risk factors.3 Moreover, patients with diabetes are more likely to sustain an acute myocardial infarction,4 and in these patients diabetes is a major independent predictor of morbidity and mortality.5

Symptomatic patients
Because the prevalence of coronary artery disease is higher in diabetic than non-diabetic populations, the probability of disease in the diabetic patient with typical angina is also high. In most cases, this allows a confident clinical diagnosis to be made without the need for non-invasive testing. In many diabetic patients, however, angina is atypical, presenting the physician with a more difficult diagnostic task.

It is clear that when chest pain is atypical the probability of coronary disease will be lower, but will remain appreciably higher in diabetic than non-diabetic patients with similar symptoms. For this reason the physician should retain a low threshold for the non-invasive investigation of diabetic patients, particularly when symptoms are atypical. In this situation, where the pretest probability of disease is intermediate, the potential value of stress testing is greatest; a positive test increases probability towards the level found in a patient with typical symptoms, while a negative test lowers it to the point where further cardiac investigation may be considered unnecessary.

Whether the potential value of stress testing in diabetic patients with atypical symptoms can be realised must depend on the diagnostic accuracy of the test being equivalent in diabetic and non-diabetic populations. There are no data that permit an unequivocal answer to this question although it could be argued that on theoretical grounds the diagnostic accuracy of these tests might be lower in diabetes as the diffuse nature of the coronary disease tends to mask regional perfusion defects during imaging studies. These concerns, however, though not tested in clinical trials, are not supported by clinical experience, which provides no reason to suppose that the diagnostic yield of non-invasive investigation is not equivalent in diabetic and non-diabetic patients.

A separate question is whether, having diagnosed coronary artery disease, treatment produces equivalent benefit in symptomatic diabetic and non-diabetic patients? Again, the diffuse disease affecting many patients with diabetes has the potential to intensify ischaemia and cause severe symptoms. While there is no evidence that diabetes reduces responsiveness to medical treatment, it makes revascularisation by angioplasty or bypass surgery more difficult and hazardous.6,7 Nevertheless, in most of those whose angina fails to respond to medical treatment, the risks of revascularisation are outweighed by the benefits.8

Asymptomatic patients
Early reports from the Framingham investigators of an increased incidence of painless myocardial infarction in diabetics9 have since been complemented by reports of an increased incidence of silent ischaemia, which we and other investigators have attributed to autonomic neuropathy.10,11 Although this predisposition to silent ischaemia has not been a universal finding (particularly in studies that have not tried to identify neuropathic subgroups12,13), the extent to which it might occur has important implications for the diagnostic process, as cardiac investigation is usually driven by chest pain. Although we have recommended that in the diabetic patient with atypical symptoms thresholds for non-invasive testing should be lower than for non-diabetic patients, we would not recommend that all diabetic patients should be screened regardless of symptoms. Silent ischaemia may be more common in patients with diabetes, but it is reasonable to assume that in the asymptomatic diabetic population generally, the probability of coronary artery disease will be low, ensuring a correspondingly low diagnostic yield from non-invasive testing. This may not apply to all subgroups; Nesto et al investigated 30 diabetic patients with peripheral vascular disease but no clinical suspicion of coronary artery disease and found that 57% had thallium defects compatible with reversible ischaemia or previous infarction.14 These abnormalities were most frequent in patients with multiple additional risk factors, a group with a cardiovascular event rate of up to 30% in the next five years.15 Bayes’s theorem would predict a high diagnostic yield from non-invasive investigation in this group,16 and some diabetologists are now proposing a programme of selective screening in diabetic patients without suspected coronary artery disease, targeted at the subgroup with multiple additional risk factors. This proposal, however, is almost certainly misguided because Wolfson and Jungner’s classic criteria for successful screening17 are not fulfilled. In particular, it is not clear how a stress test would influence management of these asymptomatic patients in whom the cornerstone of medical management will be strict risk factor modification, regardless of the result. Most physicians would argue similarly for aspirin in view of the high cardiovascular event rate. As for cardiac catheterisation, this would merely confirm the diagnosis in patients with an abnormal stress test, but would rarely if ever provide clear grounds for revascularisation as there is no evidence base to support a policy of angioplasty or surgery for asymptomatic patients with diabetes. Indeed, it is possible to speculate that because the risks of revascularisation are relatively high in diabetes, they would exceed any potential benefit in patients without cardiac symptoms.
Conclusions
Physicians should have a low threshold for non-invasive investigation of diabetic patients with symptoms suggestive of coronary artery disease, particularly if the presentation is atypical when the results will be of greatest diagnostic value. Screening of asymptomatic diabetic patients cannot be recommended, regardless of risk factor profiles, because it would make no useful contribution to management. Recent medical history is littered with examples of unhelpful, often detrimental, screening programmes and we should avoid adding to this undistinguished list.

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Investigation of coronary artery disease in diabetes: is screening of asymptomatic patients necessary?

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