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Depression in adolescents

Philip Hazell

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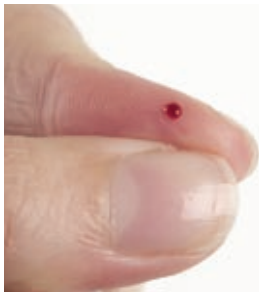
Self monitoring of blood glucose in type 2 diabetes

Clinicians should stop patients doing this if it has no benefit



RESEARCH, p 132

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Competing interests: SRH is principal investigator in an ongoing randomised controlled trial comparing blood glucose to urine testing in newly diagnosed individuals with type 2 diabetes.

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Self monitoring of blood glucose costs the NHS more than £100m (€150m; $200m) each year and the cost is rising.[1] For many people with insulin treated diabetes and their families, blood glucose self monitoring is an essential tool, enabling them to confirm hypoglycaemia or high glucose concentrations and to take corrective action. Yet large numbers of patients diligently record the results and then do nothing with them.

In this week's *BMJ* Farmer and colleagues report the results of a primary care trial in patients with well controlled type 2 diabetes who were not taking insulin. They found no evidence of an effect of blood glucose self monitoring on glycaemic control, with and without structured education, compared with usual care.[2] This study confirms that the contribution of self monitoring is not clear in type 2 diabetes, particularly for those treated with diet alone or oral agents other than sulphonylureas. Furthermore, there is wide geographical variation in the use of self testing by such patients.[3]

One view is that providing such technology to diabetic patients treated with tablets or diet is a waste of time and money, because there is little an individual can do with the results.[4] Others believe that the information provided by blood glucose testing is a powerful motivating factor,[5] encouraging self management of diabetes by allowing patients to measure directly the impact of their behaviour, such as the effect of eating on postprandial glucose or the glucose lowering effect of exercise. Some,[6 7] but not all,[8] observational studies have shown that, even in patients treated by diet alone, those who measure their blood glucose more often have better outcomes, including Hb_{A1c} concentration and mortality. Such positive associations may simply show, however, that those who are highly motivated (reflected in the frequency of blood testing) are likely to do well in the long term.

A limited number of prospective studies have randomised patients to blood glucose self monitoring or to no monitoring. A recent meta-analysis reported a modest mean improvement in Hb_{A1c} concentration of around 0.3%, but the confidence intervals were so wide that this difference was not significant.[9] Importantly, the meta-analysis comparing blood and urine testing found no difference in Hb_{A1c} concentrations. This suggests that blood glucose self monitoring has little effect on glycaemic control in patients treated with diet or metformin. Structured education on using the information obtained from self monitoring to adjust insulin dosing, however, leads to sustained improvements in glycaemic control in type 1 diabetes,[10] and this might also apply to those with type 2 diabetes.

In the diabetes glycaemic education and monitoring trial (DIGEM), Farmer and colleagues directly test the contribution of blood glucose self monitoring on glycaemic control, with and without structured education, in 450 people in primary care with diabetes treated by tablets or diet, with relatively tight glycaemic control.[2] Patients were randomised to receive usual care (and were asked not to test their blood), basic information on self management and limited blood self testing, or training in self management and encouragement to undertake more intensive blood monitoring. At one year, Hb_{A1c} concentration was unchanged in the usual care group, and marginally and equally improved in the other two groups, with no significant difference among the three.

The trial was well designed and conducted but had some limitations. Patients who were already testing their blood more than twice a week were excluded (possibly removing those who found glucose monitoring valuable and leaving individuals who had already used and rejected it). Furthermore, only around 15% of those eligible entered the study, thus limiting the generalisability of the findings. In one arm of the trial the authors embedded blood glucose self monitoring within an educational intervention designed to enhance self management, yet glycaemic control did not improve. This may be because patients with relatively tight control were included, in contrast to previous studies, or because the intensive intervention was ineffective. Indeed, fewer patients randomised to the intensive arm ended up using a glucose meter than in the less intensive arm, an unexpected outcome among patients who were trained to monitor more frequently. Finally, patients seem to prefer blood glucose monitoring to urine tests,[11] and different conclusions might have been reached if patients' views had been taken into account.

The DIGEM trial has shown that in patients with established diabetes relatively well controlled by oral drugs who monitor blood glucose infrequently, little is gained in promoting blood glucose testing even in conjunction with an education programme.[2] Whether self monitoring is useful in patients at diagnosis and whether it offers advantages over urine testing (which is much cheaper) remains uncertain. None the less, the results of this study should encourage clinicians to discuss the value of glucose testing with their patients and give them the confidence to discontinue it if it is providing no benefit.

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Depression in adolescents

Adding cognitive behaviour therapy to SSRIs is unlikely to improve outcomes

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RESEARCH, p 142

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Around 3-5% of adolescents are affected by clinical depression worldwide.[1,2,3,4] Although specific data on depression are not available, an Australian survey found 26% of adolescents with mental disorders were treated in general or paediatric practice, while only 9% received care from specialist mental health services.[3]

Episodes of depression generally last about seven to nine months. Probability of relapse is 40% within two years and 70% after five years.[5] Depression can be devastating to a young person's academic and social development and can adversely affect family relationships, especially if the problems are misunderstood.

Optimal treatment for depression in adolescents is unclear. Concern about an increased rate of suicidal behaviours with antidepressants in trials in adolescents has led to safety warnings about their use in Europe, North America, and Australasia.[6] Should adolescents with depression be prescribed antidepressants, and if so, should they be given only with psychotherapy?

In this week's *BMJ*, a randomised controlled trial (adolescent depression antidepressant and psychotherapy trial; ADAPT) by Goodyer and colleagues compares a selective serotonin reuptake inhibitor (SSRI) alone and with cognitive behaviour therapy in 208 people aged 11-17 years with depression.[7] In these adolescents, depression had not responded to a brief psychosocial intervention or was severe at the outset. The investigators tried hard to reflect "real world" conditions—the participants were heterogeneous for previous treatment exposure, self harm, suicidal thoughts, subtype of depression, and comorbidity. The primary outcome was a change in score on the Health of the Nation outcome scales for children and adolescents from baseline. They conducted assessments at six, 12, and 28 weeks, so that follow-up extended beyond that usually seen in trials of antidepressants. The trial found no significant difference in treatment effect between groups at any time point.

The trial reported a 40% treatment response in both groups at 12 weeks, which is somewhat lower than that seen in other treatment studies for depression in adolescents. This may have been due to the exclusion of adolescents who had already responded to the brief psychosocial intervention. By 28 weeks the response rate had increased to nearly 60%.

The improvement in response rate from 12 to 28 weeks is noteworthy, as most treatment trials have been shorter in duration,[8] and they may have underestimated the treatment response. The conclusion challenges the recommendation by the National Institute for Health and Clinical Excellence (NICE) and other bodies that SSRIs should be given to moderate and severely depressed adolescents only, in combination with a psychological therapy.[8,9]

ADAPT is the fourth study to assess the combination of SSRI and cognitive behaviour therapy over monotherapy for depression in adolescents. The treatment for adolescents with depression study (TADS) found that the combination of fluoxetine and cognitive behaviour therapy was better than fluoxetine or behaviour therapy alone in reducing depressive symptoms. Combined treatment and fluoxetine alone were equally effective in achieving a clinical response and superior to cognitive behaviour therapy alone.[10] The most recent trial found no advantage of sertraline plus cognitive behaviour therapy over monotherapy in rates of remission or moderation of depressive symptoms after 12 weeks of treatment, and at follow-up after nine months.[11] The third trial also found that the addition of cognitive behaviour therapy to SSRIs had no significant effect on symptoms of depression.[12]

The results of the ADAPT trial suggest a further trend away from the positive findings of TADS. Differences in the dose and duration of treatment and in the choice of primary outcome measure may have contributed to the variation in study outcomes, but the data suggest that combining cognitive behaviour therapy with an SSRI had only a modest advantage over an SSRI alone in treating depression in adolescents.

Combining cognitive behaviour therapy with an

SSRI may have other advantages, such as reducing suicidal thoughts and prolonging the benefit of treatment, but evidence for this across the four trials is equivocal. Suicidal thinking was lowest in the group receiving combined treatment in one study,[10] but two studies found no significant difference.[7 11] Suicidal thinking was not measured in the fourth study,[12] which found higher remission rates after 52 weeks for combined treatment than for SSRI monotherapy.[12] In contrast, the ADAPT study found no significant differences between groups in remission rates after 28 weeks.[7]

What does this mean for clinicians managing adolescents with depression? Contrary to the NICE guidelines,[8] evidence suggests that monotherapy with an SSRI is a reasonable treatment option for moderate to severe depression in adolescents, particularly if access to cognitive behaviour therapy may be delayed. The SSRI must be given at a high enough dose and for an adequate amount of time, as some patients take 12 weeks or longer to respond.

Of note, people randomised to monotherapy with an SSRI in the ADAPT and other trials received a high level of clinical care, with frequent clinical reviews and rigorous monitoring of the benefit of treatment and adverse events. The implication for clinical practice is that good quality pharmacological treatment involves more than simply writing the prescription.

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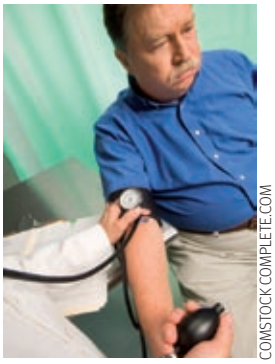
Cardiovascular risk models

Moral implications of models based on absolute risk could be better understood



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RESEARCH, p 136

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Risk scores based on the Framingham heart study reflect the higher risks of cardiovascular disease in the 1970s and 1980s and tend to overpredict current risks. They do not include family history, body mass index, use of antihypertensive drugs, or measures of social class. Omitting socioeconomic status as a predictor increases the health gap between rich and poor: the risks in poor people are underestimated and undertreated, and risks in rich people are overestimated and overtreated.

In this week's *BMJ* Hippisley-Cox and colleagues derive a new cardiovascular disease risk score (QRISK) for the United Kingdom and validate its performance against the Framingham cardiovascular disease algorithm and a newly developed Scottish score (ASSIGN).[1] They found that QRISK provided more appropriate risk estimates to help identify high risk patients on the basis of age, sex, and social deprivation. The QRISK score indicates that in the United Kingdom about 3.2 million men and women aged 35-74 are likely to be at high risk, compared with 4.7 million predicted by Framingham and 5.1 million with ASSIGN.

In rationing the use of statins for primary prevention, cardiovascular disease risk scores were developed to produce the biggest effect at minimum cost.[2] However, the distribution of risk of cardiovascular disease in healthy populations is determined largely by the age, sex, lifestyle, and socioeconomic class distribution in the population. Treatment decisions and resource allocation based on age, sex, and lifestyle have moral implications, depending on what is included in the model and what is left out. The point made by Hippisley-Cox and colleagues, that omission of socioeconomic class from risk prediction models increases health inequities between poor and rich, is correct.[1 3] But absolute risk scores also label male sex, old age, and risky lifestyles as diseases to be treated, while denying life extending drugs to women, younger people, and those living healthily. To facilitate more equitable and transparent decisions, these moral implications of cardiovascular disease risk models have to be better understood.

Firstly, all cause mortality is reduced more by moderate consumption of alcohol than by taking statins.[4] A bottle of red wine a week seems to be a health investment that increases quality adjusted life expectancy more.[5] Under a wide range of assumptions, the cost utility of red wine in primary prevention is higher than of statins—so risk models ought to target selectively reimbursed prescriptions of bottles of inexpensive red wine. On the other hand, evidence of the benefits of statins is stronger than that of nutraceuticals such as phytosterols or omega 3 fatty acids,[6 7] so why should

doctors recommend nutraceuticals, for which the effectiveness of hard clinical outcomes has not been proved, and not statins, for which we have evidence?

Secondly, absolute risk scores reduce all highly individual risk taking behaviours to a single value. In most population screening programmes for cancer, the 10 year absolute risk of death is 0.5% and numbers needed to treat are higher than 1000.[8 9] NICE (National Institute for Health and Clinical Excellence) guidelines advise that primary prevention should reduce the risk of cardiovascular disease by 20%, comparable to a 7% risk of death.[10] The number needed to treat to avoid a cardiovascular event is 20; to prevent a death it is 50. An alternative strategy is mass treatment, championed by proponents of the "polypill."[11] At all existing levels of cardiovascular disease risk over age 40, mass treatment with statins alone is always more effective than cancer screening.

Thirdly, absolute risk scores prioritise elderly people to the detriment of younger people. But ageing is part of the finite life course. These are healthy elderly people, not patients. Risk comprises the probability of an event happening and the adverse consequences of that event. The ethically and scientifically most unacceptable aspect of management by absolute risk is the ignoring of the relative importance of loss of life at different ages.[3 12] No modern society with a low risk of mortality places equal value on a death at age 45 and one at age 75.

Fourthly, absolute risk scores select those with a risky lifestyle to the detriment of those with a healthy lifestyle. Healthy smokers who refuse to quit are eligible for statins, yet smokers who quit should be denied them as quitting will lower cardiovascular disease risk. The more you choose a healthy lifestyle, the less you are supposed to wish to extend healthy life. Non-smokers, paradoxically, reap more benefits from statins than smokers. Statins reduce the probability of an event more among smokers. But if you take into account the adverse consequences of that event, statins save more life years among non-smokers, because non-smokers live much longer.[3 13]

What does this mean for clinicians faced with prioritising which patients to treat? For an individual patient, the information provided by risk models should be interpreted with caution. There is little medical or scientific justification that risk calculations with arbitrary thresholds should supersede informed choice. From a societal perspective, treating healthy people competes with other investments in health, such as reducing poverty or promoting a healthy environment. It also competes with investments in the treatment of disease, such as new cancer drugs or innovative technology, and with expensive long term care for increasing numbers of disabled elderly people. Absolute risk scores do not offer an easy escape from moral choices.

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Health for London: showing England the way?

Plans to focus hospital services and build polyclinics will have to overcome inertia and rivalries

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Last week saw the launch of *Healthcare for London: A Framework for Action*, the findings of a review led by Sir Ara Darzi, chair of surgery at Imperial College.[1] The review was commissioned by NHS London in 2006, but its contents have assumed a greater significance with the recent appointment of Sir Ara as a junior minister, charged with a wider review of the health service throughout England.[2] The terms of reference for that review make clear the government's determination "to ensure that the future of the NHS is clinically led" and that vision is pre-eminent in his London report.

The review has been based largely on the views of clinicians, concentrated into six working groups of "clinical innovators" drawn from a range of organisations, including the King's Fund, to look at clinical pathways. They looked at maternity and newborn care, services for staying healthy, acute care, planned care, long term conditions, and end of life care. Mental health was considered by a seventh group, and the overall analysis also included a public opinion poll and two "deliberative" events involving members of the public.

The resulting report makes a cogent case for change

PETER MACDIARMID/REX

in London. It describes a highly mobile, highly diverse population with stark health inequalities. Londoners are less satisfied than the rest of the English population with the health services they receive, and their needs are clearly not being met adequately. Furthermore, the review finds that the current configuration of services is not fit for purpose. It argues for more care at home and in the community, citing, for example, studies that show better outcomes for patients with chronic obstructive pulmonary disease and heart failure when they are offered targeted community services. It also points to powerful evidence that more specialisation in bigger hospitals can save lives, notably in dedicated stroke units, and calls for the urgent reconfiguration of services for stroke and trauma. In addition it calls for rapid work to improve the skills of the London Ambulance Service.

Improved services should be focused on individual needs and choices; they should be local where possible and central where necessary; they should be integrated (bridging the gap between primary and secondary care); they should encourage prevention; and they should focus on health inequalities and diversity. Perhaps inevitably, recommendations on the best location of services—including fewer, more specialist hospitals and, in the next two years, "between five and ten polyclinics" which would bring together general practices with community, diagnostic, and urgent care services—have prompted particularly widespread coverage and debate.

A great deal in this review is to be welcomed: its emphasis on outcomes, the experience of patients, and inequalities, as well as its search for a solid evidence base to drive decisions about health care services. The evidence base is, however, incomplete in some areas (how much evidence is there that polyclinics are the answer for every locality?) or absent in others (there are huge gaps in our knowledge of which interventions deliver best outcomes for such an ethnically diverse population). Nevertheless, this emphasis on evidence should help local NHS commissioners and providers construct and communicate a more robust case for change to a sceptical public.

Finally, the review says little about how the levers of system reform in the NHS can help to realise this vision. Yet it will be crucial to understand how the multiple and sometimes conflicting incentives that have already been built into the system will help or hinder the road to implementation. Payment by results (the mechanism to pay NHS providers a fixed price for each individual case treated), for example, has created powerful incentives for hospitals to pull in patients, but it may undermine collaboration between organisations[3] or create conflicts between NHS trusts and primary care trusts.[4] And the evidence so far on practice based commissioning (where general practices are given control over their commissioning budgets for secondary and community care) indicates that only modest efforts have been made to redesign primary care services to counteract the pull of hospitals.[5]

If the recommendations on the models of care are translated into diktats about the number and location of facilities, they will be seen as yet another "top down" exercise. This could cause planning blight by alienating clinicians and encouraging local commissioners to look up for instructions instead of working out their own solutions with providers.

London's health services have not been short of blueprints and plans,[6] including some from our institution[7 8] and others such as the Tomlinson report.[9] Most of their proposals foundered on the near impossibility of implementing reforms that seemed to offer much to primary care and little to hospitals. This time, there can be no doubting Sir Ara's determination to let the power of evidence overcome institutional inertia and rivalries. But if this review is to succeed where others have failed it must empower local commissioners and clinicians to use the incentives that have been built into the NHS. And if it is necessary to strengthen, amend, or realign those incentives, that too must be done.

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A UK global health strategy: the next steps

Is better health the fundamental goal, and will politicians collaborate effectively?

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A decade ago the US Institute of Medicine argued compellingly that it was no more than enlightened self interest for countries to invest in global health.[1] Such investment would help to protect their own citizens from external threats, strengthen the global economy, and contribute to international security. In the intervening period, support for placing health at the centre of foreign policy has gathered momentum. Earlier this year the Global Health and Foreign Policy Initiative was established by a group of foreign ministers convened by the Norwegian and French governments,[2] and in the United Kingdom Sir Liam Donaldson, the UK's chief medical adviser, has proposed a government-wide strategy for global health.[3]

The British proposals identify five reasons for promoting global health. These are to improve global security and health protection, enhance sustainable development, improve trade by promoting health as a commodity, maximise global public goods, and encourage a human rights approach to health. An interdepartmental steering group has been established to take this agenda forward across government and has embarked on a wide-ranging consultation to help it fill in the details.

The United Kingdom is in a strong position to provide leadership on this issue. The government has already led in areas such as international debt relief; UK overseas aid is recognised to be extremely effective; and many UK universities and government agencies are already fully engaged in the global health agenda. Yet there are also weaknesses in the UK position. Most obviously, there is the special relationship with the United States, during a period when the Bush administration has made no secret of its contempt for concerted international action to tackle many of the world's problems.[4] Another weakness, although not unique to the United Kingdom, is the inherent contradiction between promotion of health and the pursuit of other policies, such as support for British arms exporters and potential tensions between international trade and pro-poor development. Even in the health arena there are contradictions, with the Crisp report encouraging junior doctors to gain experience abroad[5] and the new system of medical training discouraging them.[6]

Sir Liam's important proposal captures the spirit of the times but, to promote real change, all those with a potential contribution to make must engage genuinely with it, wherever they are in government. For this to happen, some fundamental issues must be resolved.

Firstly, agreement is needed across government on whether the improvement of health is a fundamental goal in its own right, or whether it is simply an instrument to achieve other goals, such as promoting economic growth. This distinction becomes important when objectives conflict. Health is implicit in many of the government's stated international priorities,[7] but nowhere is there an explicit statement of the importance of improving health to match that of, for example, poverty reduction. Similarly, the millennium development goals, to which the UK government has signed up, include some important aspects of health but exclude others, such as virtually all of the burden of disease among adults.[8] As a consequence, the rapidly increasing problem of noncommunicable disease in low and middle income countries barely features on the international agenda.[9] Linked to this is the immediate need to establish clear criteria on what to include in a global health policy. Otherwise, the UK strategy will seem like a disconnected shopping list, all too easy for government ministries to ignore.

How will this national strategy be taken forward in Europe? The European Union has a common foreign and security policy, so that, with a few exceptions, member states vote as block in international forums. Achieving a European consensus on global health will not be easy, especially given some governments' preoccupation with current revisions to the European Treaties. It will be important to build alliances with like minded governments, especially those that will hold the rotating EU presidency in the near future.

The UK global health strategy must be sustained over the long term: short term fixes will not do. The creation of an interdepartmental steering group is a good first step, and the recent appointment as a minister in the Foreign Office of the committed internationalist Mark Malloch Brown bodes well. Commitment by the other political parties and, critically, by the administrations in Scotland, Wales, and Northern Ireland is also essential. The consultation process has already visited Edinburgh and Cardiff. Some mechanism is also needed to include the views of the UK's remaining overseas territories, many of which are especially vulnerable to global forces.

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