this unfairly penalises the next generation of potential ophthalmologists. Until a true unified training grade is established the number of career senior house officers in ophthalmology must be brought into line with the predicted number of specialist registrars. Only this will prevent capable juniors wasting immense effort and several crucial years.

Maintaining the current service commitment after such rationalisation requires a rethinking of the working practice of senior house officers, with skill mix and the employment of paramedical staff to reduce the non-medical workload and amalgamation of inpatient units where appropriate. An expansion in the number of visiting senior house officers and general practice trainees (with clearly defined objectives and appraisal) seems timely.

We have no wish to discourage potential ophthalmologists from a rewarding choice of career, but competition at the most junior level is fierce and some will be disappointed after several years of highly specialised training and examination. The Ophthalmic Trainees' Group is preparing a career information pamphlet, available on request to all those intending to become ophthalmologists.

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1 Hopkisson B. Word of warning to junior ophthalmologists. *BMJ* 1995;310:62. (7 January.)

More urologists are needed

EDITOR,—The classified advertisements supplement of 14 January contains advertisements for seven consultant posts in urology. Throughout Britain about 40 specialist urology posts are unfilled. This year 10 accredited trainees will become eligible to apply for consultant posts. The new deal for junior doctors demands a substantial increase in the number of consultants. In my segment of south east London (Greenwich, Bexley, and Bromley) 3·5 consultant urologists struggle to serve 750 000 people. When we recently advertised for a new consultant none of the applicants was accredited. Even if the number of training posts was doubled tomorrow those in them would take five years to be ready to practise.

Who then is to provide the service to the increasing number of patients with urological problems? At present only two courses of action exist: the creation of a substantial number of staff grade posts to fill the urgent shortfall in services and a recruitment drive on the Continent, led and financed by the government, for suitably trained people. The need is acute; action is necessary now.

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Assessing blood glucose control in diabetes mellitus

Use precise analytical methods

EDITOR,—In their study of the use of glycated haemoglobin concentrations to indicate glycaemic control Eric S Kilpatrick and colleagues used targets, related to the methods used, which were based on multiples of the SD of a reference range derived from non-diabetic subjects.[1] They found considerable differences in the classification of diabetic patients, which depended on the method, despite the methods giving similar absolute values for haemoglobin A_1 (HbA_1).[2] This, however, does not necessarily show different measurements of glycated haemoglobin to be inherently non-comparable indicators of glycaemic control. The electrophoretic method used is much more imprecise than the high performance liquid chromatography with which it was compared.[2] This is relevant because the estimate of a population reference range has components of both analytical and biological variation and will be broader for a method with high variability. Therefore, a given HbA_1 measurement will be fewer multiples of the SD from the non-diabetic reference mean when the imprecise method is used. Indeed, the authors have shown exactly this point, with the results of electrophoresis indicating apparently better glycaemic control.

This effect can be minimised by using multiples of the biological SD to define target concentrations. This can be illustrated by using the authors' quoted reference ranges and estimates of the analytical variation for the two methods of measuring HbA_1.[2] If coefficients of variation for the analytical component are assumed to be 2·0% for high performance liquid chromatography and 8·3% for the electrophoretic method, the biological coefficients can be estimated as 7·54% and 8·53% respectively.[3] These are similar, and if a mean of 8·0% is taken the biological SDs at the midpoint of the reference interval are 0·45% for high performance liquid chromatography and 0·50% for electrophoresis. If these are used to set clinical targets an HbA_1 concentration of 12·3% is 13·7 biological SD above the mean for high performance liquid chromatography and 12·0 biological SD above the mean for electrophoresis, compared with 14·0 total SD for high performance liquid chromatography but only 8·0 for electrophoresis. Therefore, targets derived from biological variation would have given a much better consensus in the classification of patients by the two methods. In practice the total SD is close to the biological SD when the analytical variation is small, as is the case with high performance liquid chromatography.[3,4]

It is important that precise analytical methods are adopted and that bias between methods is minimised. Until this is more universally achieved, however, we suggest that target concentrations should always be defined on the basis of biological variation when the analytical imprecision is large.

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1 Kilpatrick ES, Rumley AG, Dominiczak MH, Small M. Glycated haemoglobin values: problems in assessing blood glucose control in diabetes mellitus. *BMJ* 1994;309:983-6. (15 October.)
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Variant haemoglobin may affect measurements

EDITOR,—We agree that Eric S Kilpatrick and colleagues' study suggests the need for greater standardisation of methods used for estimating glycated haemoglobin concentrations.[1] The estimation of glycated haemoglobin in patients with variant haemoglobins also urgently needs standardisation. An external quality assessment of the measurement of glycated haemoglobin in such patients by laboratories in the North West Thames region showed alarming discrepancies in the results obtained (C E Andrew and P Harrison, national meeting of Association of Clinical Biochemists, 1991). For some samples the variability was so large as to alter completely the interpretation from one of very poor diabetic control to one of overcontrol likely to lead to hypoglycaemic episodes. An additional worrying finding was the varying methods used to calculate results, which partly accounted for the discrepancies. While some of the laboratories that used electrophoresis or ion exchange methods expressed haemoglobin A_1 and haemoglobin A_{1c} as a percentage of total haemoglobin—that is, haemoglobin A plus variant—others expressed their results as a percentage of the non-glycated fraction, haemoglobin A_0, or of haemoglobin A_0 plus haemoglobin A. In these circumstances comparison of results obtained with different methods from any one sample becomes meaningless.

To add to these difficulties, most ion exchange and electrophoretic methods have the problem of coelution of haemoglobin F (HbF) with glycated haemoglobin, which leads to overestimation of the latter.[2] Small increases in HbF are not uncommon in diabetic patients and are often unrecognised.[3] Hence methods that cannot resolve HbF from glycated haemoglobin adequately are unsuitable for estimating glycated haemoglobin and should be abandoned as soon as possible.

Until we have greater standardisation and guidelines about estimating glycated haemoglobin concentrations in diabetic patients with variant haemoglobins, all patients with newly diagnosed diabetes should undergo a haemoglobinopathy screen. This should include measurement of HbF at the time of initial presentation to enable correct interpretation of results.

All laboratories should be willing to provide information about the method used to measure glycated haemoglobin, the mode of calculations of results, and interference from variant haemoglobins including HbF. Clinicians would also be well advised to ascertain necessary information about the methods used from their laboratory colleagues.

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1 Kilpatrick ES, Rumley AG, Doniniczak MH, Small M. Glycated haemoglobin values: problems in assessing blood glucose control in diabetes mellitus. *BMJ* 1994;309:983-6. (15 October.)
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Like should be compared with like

EDITOR,—Eric S Kilpatrick and colleagues conclude that measurement of haemoglobin A_{1c} (HbA_{1c}) concentration is to be preferred to measurement of haemoglobin A_1 (HbA_1) concentration on the grounds that the former classified a higher proportion of diabetic patients as having poorly controlled disease.[1] But the basis of this classification—poor control being equated with a glycated haemoglobin concentration >5 SD from the reference population mean—is flawed because the coefficient of variation of the reference population mean is not the same for the methods of measurement compared. Inevitably, if (as is the case) the SD is much smaller for HbA_{1c} than for HbA_1 measured by electrophoresis but the means differ proportionately much less, any criterion of poor control based on the same number of SDs above the mean will classify a higher proportion of the HbA_{1c} values as indicating poor control than will be the case for HbA_1 values measured by electrophoresis. In numerical terms a limit of 5 SD for HbA_{1c} (mean 4·02% (SD 0·28%)) is 5·44%, representing a 35·3% increment; whereas a limit of

5 SD for HbA_1 measured by electrophoresis (mean 6·30% (SD 0·75%)) is 10·05%, representing an increment of 59·5%. It might be expected that more patients would have an increment of >35·3% by one test than had an increment of >59·3% by a second test when the two tests are so similar (that is, the main part of HbA_1 is HbA_{1c}).

If like was compared with like, however, the reported differences in the proportions of diabetic patients classified as having poorly controlled disease would largely disappear. Thus the 5 SD limit of 5·44% for HbA_{1c} represents an increment of 1·35 times the mean concentration in the non-diabetic reference population. For HbA_1 measured by electrophoresis, 1·35 times the reference population mean is 8·51% or 2·95 SD. Inspection of figure 2 in the paper allows the proportion of the population inside this limit for HbA_1 measured by electrophoresis to be estimated by addition of the numbers in the first two boxes to half the number in the third box (2-4 SD). This yields a figure of 0·25, which is indistinguishable from that for HbA_{1c}. The total relative frequency for HbA_1 measured by electrophoresis, however, seems to be not 1·0 but something less; therefore this estimate would have to be confirmed by a reworking of the original data.

We suggest that a more acceptable way of undertaking comparisons under circumstances such as these might be to work solely in terms of multiples of a measure of central location of the reference data (mean, median, or mode); such an approach has been used successfully for many years in antenatal screening, in which α fetoprotein and human chorionic gonadotrophin concentrations are measured as multiples of the median. The choice of which multiple to use as a limit is arbitrary, but if multiples of the mean values corresponding to 3 SD and 5 SD for HbA_{1c} are used the cut off points approximate to 1·20 and 1·35 times the mean respectively.

In summary, therefore, we suggest that if the data were reanalysed and like was compared with like then the reported difference in the proportion of patients categorised as having poorly controlled disease would probably disappear. If this was the case the conclusions reached would be very different. Points three to five of the paper's clinical implications would need to be withdrawn and a statement to the effect that there was little difference between the methods substituted. Use of multiples of the SD is an inappropriate method of comparing methods of measuring glycated haemoglobin when coefficients of variation in the control population are different between the methods. Thus the guidelines from the European IDDM Policy Group should also be reconsidered as this was the source of this inappropriate method of comparison.[2]

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2 European IDDM Policy Group. Consensus guidelines for the management of insulin-dependent (type I) diabetes. *Diabet Med* 1993;10:990-1005.

Authors' reply

EDITOR,—Susan Standing and Richard Taylor suggest that use of a fixed biological variation to express SD may help in the comparison of methods of measuring haemoglobin A_1 (HbA_1) that have different imprecisions. This may be simplified further as the imprecision of the assay affects only the spread of results: it does not affect either the mean glycated haemoglobin concentration in a reference population or the median value in a diabetic population. Thus it would seem more useful to avoid problems with the imprecision of assays by eschewing the use of the SD in favour of comparison of a diabetic patient's result with the mean non-diabetic value.

In a situation analogous to that used in screening for Down's syndrome and for neural tube defects, a diabetic patient's result could be expressed as a multiple of the mean value (MoM) in non-diabetic people. If this is applied to our study the median diabetic HbA_1 value measured by high performance liquid chromatography was 1·46 MoM—that is, 46% higher than the non-diabetic mean, which is similar to the value of 1·48 MoM found when electrophoresis was used. As with Standing and Taylor's suggestion, however, this method of comparison still leads to discrepancies when HbA_1 is compared with haemoglobin A_{1c} (HbA_{1c}): even when the same patients and high performance liquid chromatography instrument were used to measure both HbA_1 and HbA_{1c} the median HbA_{1c} value implied poorer glycaemic control at 1·57 MoM. As a guide, the group who were intensively treated in the diabetes control and complications trial had a median HbA_{1c} value of approximately 1·40 MoM while the value in the conventionally treated group was 1·80 MoM.[1]

Thus, while comparisons of two methods of measuring either HbA_1 or HbA_{1c} that use the MoM may be valid, comparisons of HbA_1 with HbA_{1c} remain problematic. S Bulusu reinforces the need, recognised by the British Diabetic Association, for more standardisation in measurements of glycated haemoglobin. The errors in the accuracy and imprecision of assays introduced by both haemoglobin variants and abnormal fetal haemoglobin concentrations are well known,[2,3] but most methods of analysis remain affected.

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Identifying relevant studies for systematic reviews

EDITOR,—Carl Counsell and Hazel Fraser make a useful point when they describe the different methods of identifying trials used by the Cochrane Stroke Review Group: electronic searches, review of cited papers, searches of registers of trials, and communication with individual people and organisations.[1] We have also used several methods to identify randomised controlled trials for a project that entails meta-analyses of randomised trials of treatment of multiple myeloma.[2] Of the 123 trials identified, 29 were identified from registers of trials, 28 through personal contacts, 20 from published abstracts, 18 from published papers, 15 by computer assisted searches of the literature, and 13 through mentions in a publication. This shows the wide range of sources used to compile the initial list of trials. Among the trials that were identified by personal contact with the trialists was the Italian M-80 study, which, although relevant to two prior reviews,[3,4] had not been identified previously because it was neither published nor included in a widely available register of trials.

We strongly recommend, therefore, that anyone conducting a systematic review should use as many search strategies as possible to identify, and subsequently collect data from, all relevant randomised controlled trials.[5]

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De inertia urbanorum

First law of thermodynamics applies

EDITOR,—Ronald Williams states that it follows from Newton's second law that a car that accelerates three and a half times as fast as his car uses three and a half times as much energy.[1] This is wrong: the relevant law of physics is not Newton's second but the first law of thermodynamics—"energy can be neither created nor destroyed." A car moving at 60 mph (96·5 km/h) has gained the same amount of energy from the combustion of the fuel used by its engine regardless of how long it has taken to reach that speed; hence the energy used by the engine is the same. This assumes that the efficiency of the engine is the same and disregards friction and air resistance. These factors might work either way in a practical case.

Another way of getting the same result is to realise that the more powerful car travels a shorter distance during the acceleration period and to apply the definition of work done, which is force multiplied by distance. The more powerful car engine applies a force three and a half times greater for a distance three and a half times smaller, so it does the same amount of work.

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1 Williams R. De inertia urbanorum. *BMJ* 1994;309:1741-5. (24-31 December.)

Author's reply

EDITOR,—I am ashamed to say that C J Squire is correct: the energy required for a given operation depends on the work done rather than the force used. The fact that it is many years since I read a physics textbook does not excuse my elementary mistake. Even if the fuel consumption in these two instances was identical—which is improbable, as more energy is likely to be wasted as heat and sound, if not also as friction, by the faster accelerating engine—my slower car will have travelled three and a half times as far in reaching 60 mph, which in terms of fuel is still a distinct ecological advantage.

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