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Safer discharge from intensive care to hospital wards

Randomisation is necessary to disentangle intrinsic patient risk from effects of care

Papers p 1274

Intensive care in the United Kingdom is certainly underprovided relative to many developed countries. The United States spends over 1% of its gross national product on providing intensive care, while Britain spends around 0.05%—possibly twentyfold less.¹ But intensive care remains largely outside the evidence based paradigm—apparently for ethical reasons. Judging the appropriateness of intensive care provision still depends solely on apparent unmet need and observed associations of prognostic indicators with mortality. This week's *BMJ* sees another such study.²

It seems too easy to claim benefit in intensive care on the basis of biological plausibility and observational comparison alone. For example, a recent Cochrane overview of 30 trials on the effect of intravenous albumin for acute renal failure,³ which showed significant harm, was dismissed by some enthusiasts.⁴ The writings of respected and dispassionate authors who have held intensive care to be immune from randomisation do not help this apparent impasse.^{5,6} In the absence of any rigorous measurement of attributable effect, intensive care will continue to be provided on the basis of evidence that is unacceptable in other areas of health enhancement. With 21st century medical technology this is particularly unfortunate.

The acute physiology score (APACHE) developed by Knaus and others⁷ was designed to provide reliable, physiology based, indices of likely benefit by predicting hospital mortality from measurements made among critically ill adults in hospital. This score has been shown to be a potent measure of casemix that predicts mortality well in the British context⁸ and hence enables comparisons of intensive care performance to be disentangled somewhat from practice variations, be they discretionary or enforced by shortage. Obviously cases that are refused admission to intensive care units cannot be readily compared, since scoring is impossible unless a patient is admitted.⁹ In this week's *BMJ* another score is proposed, which again predicts hospital mortality based on physiological measurements (p 1274).²

Daly et al looked at some 13 000 intensive care patients in 20 centres and derived a score based on physiological and other measurements on the last day in intensive care to predict risk of death before hospital discharge. The objective of the work is to provide intensivists with an index predicting risk of hospital death associated with discharge, so that patients may be discharged sensibly from scarce intensive care unit beds to make room for severely ill patients. The authors also use it to identify extra capacity needed in intensive care units to avoid the discharge of high risk

patients. The main outcome of interest should not, of course, be mortality: it should also include a measure of survival duration and also be quality adjusted.

The measure was derived from a subset of data collected from one of the intensive care units and subsequently tested on a different subset from the same unit and on data from 19 other British centres.² Having derived a score that predicted hospital mortality well on the test data, the authors then used the score to estimate the fate of those discharged while deemed to be at high risk compared with those who were not. Taking patients who were above the risk threshold at some stage during a minimum of a three day stay in the intensive care unit, Daly et al compared the high risk discharged patients with those discharged while at lower risk. The latter had lower actual mortality than the former. The crux of the paper is this comparison, and it is used to predict the consequence of one or two days extra stay in intensive care for high risk patients, when their score would then assign them to the low risk group.

These prognostic indices cannot explain all the intrinsic determinants of mortality in a dynamic system on any absolute scale, whatever the amount of discrimination shown, and sadly the shortfall cannot even be guessed at. Disentangling intrinsic patient risk from effects of care will remain impossible without randomisation. Such evidence about the risk of unnecessary death can be seriously misleading if intensive care is going to have to be assessed in this way. For example providing more intensive care beds in response to refused admissions to intensive care seems to lead, because of consequent changes in the threshold for referral and admission, to a greater total number of refusals¹⁰—and thus, logically, to still more beds.

Similarly here the logic of these extrapolations seems to assume that all clinical decisions in intensive care units are made on the basis of intrinsic need, independently of extrinsic influence, in a static system of patient care. It assumes that experienced clinicians do not assess risk and possible benefit very well in individual patients—which could give rise to some of the observed differences. Assuming that the dominant determinant of actual risk of hospital death is a physiological risk score, however discriminatory, is unwise. Who knows what complex processes led to discharge in each case, and how they might change under different influences on the individual clinical decision. The effect of high dependency beds, to name but one factor, is unassessed by this work.

We need to understand more about the determinants of death in critically ill patients because many

lives are at risk and the care is expensive, but observational comparisons, incorporating sophisticated indices of risk, can only raise hypotheses. Daly et al certainly suggest a prospective test of their hypotheses—but secure validation of the score itself (against, for example, current APACHE scoring, which has been validated) would be another prerequisite. In the end, intensive care provision at the margin of possible benefit simply has to be assessed by random allocation like everything else about which there is legitimate doubt. There is currently no substitute—unless we are to end up spending 1% of gross national product on intensive care—whatever its actual effect.

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Continuous subcutaneous insulin infusion in type 1 diabetes

Is beneficial in selected patients and should be more widely available

Almost 25 years ago the *BMJ* published our account of a new technique for achieving long term strict blood glucose control in type 1 diabetes. Continuous subcutaneous insulin infusion,¹ or insulin pump therapy, mimics physiological delivery by using a portable electromechanical pump to infuse insulin at a slow, basal rate throughout 24 hours, with patient activated boosts when food is eaten. Developed by us as a research tool to investigate the impact of greatly improved glycaemic control on diabetic complications, continuous subcutaneous insulin infusion is now used in everyday treatment by at least 130 000 people worldwide, more than 80 000 in the United States alone.

Personal testimony from patients shows that many can achieve better control and lead a more flexible life with a continuous insulin infusion than with other methods. Ironically, in the United Kingdom, the country of its invention, only a few hundred people use it, though there is growing pressure from patients to increase its availability. Doctors' commendable caution about an unfamiliar technique that places new demands on patients and carers has been massively reinforced by the NHS's reluctance to pay for continuous insulin infusion: funding in the United Kingdom is among the lowest in Europe. But is this modest take-up in the United Kingdom justified or are we neglecting valid indications for its wider use?

Much of the scepticism about continuous subcutaneous insulin infusion derives from misunderstandings about its effectiveness, safety, and clinical use. For example, it is often thought that continuous subcutaneous insulin infusion has not been rigorously compared with modern multiple insulin injection treatment. At least 14 randomised controlled trials compare continuous infusion with intensified injection regimens. A meta-analysis of these studies showed that glycaemic control is slightly but significantly better

during insulin pump therapy, with a glycated haemoglobin percentage about 0.5% lower than on optimised injection regimens (Pickup J, Mattock M, unpublished).

As to safety, there were initial case reports of hypoglycaemic coma,² and the Diabetes Control and Complications Trial reported a high rate of severe hypoglycaemia during continuous subcutaneous insulin infusion (0.54 episodes per patient year).³ However, other trials have recorded lower rates (0.1,⁴ 0.22-0.39,⁵ 0.24,⁶ and 0.13⁷ episodes per patient year), and most evidence suggests that hypoglycaemia is either no more frequent or less common during continuous infusion than on either optimised or non-optimised injection therapy.⁴⁻⁸ In two recent trials severe hypoglycaemia was 84% less and nearly 50% less than on multiple insulin injection therapy.^{5,6} Some studies have found less hypoglycaemia with the non-associating monomeric lispro analogue than with regular human insulin as the pump insulin.⁹

The high rates of ketoacidosis on continuous subcutaneous insulin infusion reported in early studies¹⁰ were probably due to lack of experience; unsuitable pump insulin, with aggregation causing cannula blockage; and the use of less reliable pumps without alarms. Though the small subcutaneous depot of insulin would seem to put patients receiving a continuous infusion more at risk, with proper pump practice the frequency of ketoacidosis is the same as with injection therapy.⁴⁻⁷

Continuous subcutaneous insulin infusion can also help improve control in patients who suffer sharply raised blood glucose concentrations before breakfast (the dawn phenomenon).¹¹ Pumps can be programmed to increase basal infusion rates during the night to counter this dawn rise. There may be other strategies to cope with the dawn phenomenon, such as moving the evening injection of delayed action insulin