

were not individually statistically significant, but were clearly consistent with the findings of the meta-analysis. Importantly, there was no question of harm. Thus there is no need to change current practice for statins in patients with diabetes. In the near future, trials such as the Study of Effectiveness of Additional Reductions in Cholesterol and Homocysteine (SEARCH) and Study of Heart and Renal Protection (SHARP) will be completed and shed further light on this issue.

While statins are expected to reduce the incidence of fatal and non-fatal myocardial infarctions, they are not a panacea, and patients on statins are liable to other causes of morbidity and mortality. In any case, treatment decisions should be based not on the reduction in relative risk but on the reduction in absolute risk or its reciprocal, the number needed to treat.<sup>9</sup> If a patient has a high absolute cardiovascular risk, even a modest reduction in relative risk gives meaningful clinical benefits. Additionally, one should consider life expectancy, concomitant diseases, and quality of life.<sup>10</sup> Apart from drug treatment, one must not forget the importance of lifestyle changes, such as cessation of smoking, healthy diet, and regular exercise.

Bernard M Y Cheung

Department of Clinical Pharmacology, Division of Medical Sciences, University of Birmingham, Birmingham B15 2TH, UK  
b.cheung@bham.ac.uk

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## Sedation in the intensive-care unit: good and bad?

During mechanical ventilation, sedation and analgesia are given to reduce discomfort and pain, and to minimise oxygen consumption, all of which are extremely important for critically ill patients. Risks exist for both undersedation and oversedation. Oversedation is probably very frequent in today's intensive-care units,<sup>1</sup> and a trial by Kress and colleagues of spontaneous awakening (ie, daily interruption of continuous intravenous sedation in mechanically ventilated patients) has been shown to substantially reduce the time on ventilation.<sup>1</sup> The benefit for patients is twofold. First, sedative drugs accumulate in the body far beyond the treatment period. Second, a lack of awakening led clinicians to expose patients to unnecessary neurological imaging.<sup>1</sup>

In today's *Lancet*, Timothy Girard and co-workers<sup>2</sup> present a multicentre randomised trial in which they assessed a wake up and breathe protocol in 336 mechanically ventilated patients. These investigators wanted

to extend the Kress protocol and to combine daily spontaneous awakening trials with subsequent spontaneous breathing trials involving ventilator weaning in a two step approach. The Girard protocol resulted in more days breathing without assistance (3.1 additional days in the 28-day study, 95% CI 0.7–5.6), earlier discharge from both intensive-care units and hospitals, and better 1-year survival than patients in the control group, who received patient-targeted sedation plus a daily spontaneous breathing trial. At first sight, these results seem to reinforce the idea that accumulation of sedation can be avoided or minimised with benefit for patients. But sedation is also an important component of care for critically ill patients, and before we adopt Girard's approach, critical appraisal of their study and of the care delivered in the control group is needed.

One surprising aspect of Girard and colleagues' control group was that there was no requirement for sedatives

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to be stopped in the control group before a spontaneous breathing trial (sedatives were stopped before a trial in 31% of control patients). The authors argue that waiting for interruption of sedation would have delayed the start of ventilator weaning in the controls. This difference could have introduced bias against control patients for three reasons. First, daily screening for criteria to do a spontaneous breathing trial, including interruption of sedation, is often a prompt to stop sedation. In the Girard study, because sedation interruption was not a prerequisite for testing spontaneous breathing, one wonders whether this incentive to lift sedation was lacking in the controls. Second, a notable feature of Girard's study was the early time at which weaning started (ie, awakening followed by spontaneous breathing in the experimental group, or spontaneous breathing without awakening in the control group): enrolment could begin as soon as 12 h after intubation, positive end-expiratory pressure could be up to 8 cm H<sub>2</sub>O, moderate doses of vasopressors could be used, and infusion of sedatives could be continuing. This early initiation differs from previous approaches and may have had different consequences in each group. Indeed, many more spontaneous breathing trials failed in the control group than in the experimental group (456 vs 284). I expected to see a similar number of failures in both arms, together with a delay in the control arm because of a lack of awakening. Instead, there was no time difference in passing spontaneous breathing trials between the two arms, but many more failures in the control arm. This difference probably resulted from spontaneous breathing

trials being done in semi-awake patients under sedation in the control group by virtue of the protocol. Failing a spontaneous breathing trial might be stressful, and the consequences for patients are unknown; however, the few data available on patients' recollection suggest that failure is a painful experience.<sup>3</sup> Reducing the effort of breathing by sedation and mechanical ventilation has an important role in the treatment of shock, for example. Early disconnection from the ventilator could be deleterious and unfavourable to control patients. Third, by generating more negative tests due to sedation, the design may have induced another bias: although clinicians were supposed to be unaware of failed trials, they could have been more likely to delay ventilator weaning because they knew that patients were not ready.

Girard and colleagues describe the wake up and breathe approach as well tolerated. We have little information on what patients experienced, what degree of pain occurred (analgesics were withdrawn during 85% of awakenings), or on patients' discomfort (although 42 awakening trials failed because of pain, anxiety, or agitation), stress after intensive care, or recollection. More patients in the experimental group than in the control group self-extubated. A better assessment of patients' perception of the approach is therefore needed; the authors tell us that they plan to report neuropsychological outcomes separately. Although the long-term mortality benefit in favour of the experimental group seems attractive, the reason for this mortality difference, which involves a different death rate after discharge from the intensive-care unit, is not straightforward. Do more days in intensive care on mechanical ventilation, or spent with continuous infusion of sedatives, explain the 1-year mortality difference through a higher susceptibility to complications? Or could negative effects of multiple failures of spontaneous breathing trials in patients in the control group contribute to this mortality difference?

The amount of time needed for research personnel to use the wake up and breathe approach is unknown and might limit opportunities for safe implementation in routine care. Daily interruption of sedatives is far from being universally accepted. What are the real difficulties of applying this approach out of the context of a trial? The actual staff available (doctors, nurses, therapists, etc) is probably a more important factor for efficient ventilator weaning than having a protocol per se.<sup>4,5</sup> To be applicable and relevant, a ventilator-weaning approach has to be

simple, feasible, and safe. The data presented by Girard and co-workers might seem appealing even with the potential shortcomings of difficult to conduct trials such as this one. But uncertainties about the control group in this study, and about the resources needed for implementation, mean that more information is needed to show that the approach is feasible and safe in everyday practice. Additionally, I am concerned that indiscriminate use of the technique could be harmful in cases in which sedation is helpful to the patient.

#### Laurent Brochard

Medical Intensive Care Unit, AP-HP, Centre Hospitalier Albert Chenevier-Henri Mondor, Créteil, France; and INSERM U841, 94000 Créteil, France  
laurent.brochard@hmn.aphp.fr

I am named as one of the inventors of a system for ventilation and weaning which is being commercialised by Dragër Medical. Dragër fund part of my research on this system.

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## Does improved detection of ill babies improve mortality?

Faced with the suffering of so many babies and their families in areas with scarce health-care facilities, clinicians in countries with poorly distributed resources desperately seek tools to help reduce the gap between recommended care and reality. When it comes to child health, this scarcity of services is well known: many ill babies are not brought to clinics, and healthy babies sometimes take up the valuable time of expert personnel. What can be done to address this problem?

By setting the Millennium Development Goals (MDGs), world leaders have agreed to make living conditions better for all inhabitants of the planet; unfortunately they have not concomitantly trimmed other expenditures to increase health budgets, but they have suggested investment policies.<sup>1</sup> Under MDG 4, child mortality in children less than 5 years of age is meant to drop by two-thirds between 1990 and 2015. Assuming a linear decrease, in 2008 we should be halfway to this goal: a landmark far from being reached.<sup>2</sup>

In today's *Lancet*, The Young Infants Clinical Signs Study Group, a group of clinicians in six countries,<sup>3</sup> report a score that optimises the screening of babies up to age 59 days in an effort to avoid overburdening of local hospitals. The study group were also concerned with the achievement of MDG 4. Can we anticipate the results of using the score? Will it help improve the care of ill babies? And will it contribute to the achievement of MDG 4?

The study group's screening technique was designed to withhold further care from infants with a low enough

risk of serious illness not to be referred to a hospital. The accuracy of the method (85% sensitivity, 75% specificity) is good enough to optimise hospital resources, because it would reduce the number of healthy babies referred. As a consequence, concerned clinicians will be reassured, although there is a cost of 13% false negatives—ie, babies labelled as being at low risk who will develop a disorder that needs hospital care.

In recognition of the limited services in many countries, the rationale behind the use of risk scores is that further care should be reserved for patients needing it (ie, those at high risk). Until a decade ago, WHO and the Pan American Health Organisation (PAHO) fostered the risk approach in allocating patients to different levels of care<sup>4</sup> in the hope that better use of available resources would improve overall health. Scarce resources could be devoted to difficult cases, leaving primary care for patients with low risk of complications.

But the risk approach is difficult to implement: patients at high risk are, in practice, denied access to appropriate treatment.<sup>5</sup> Additionally, patients at low risk do have complications. For example, in Tanzania,<sup>6</sup> despite use of the risk approach to refer women with high-risk pregnancies, only 21% of such women living more than 5 km from a hospital gave birth in it, and 5% of pregnancies labelled low-risk were followed by complicated deliveries. In general terms or for optimisation of resource use, administrators may accept a 5% figure, but 50 patients per 1000 with no access to

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