Reducing ICU Mortality: To what Extent?

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Introduction

In clinical intensive care research, mortality in the intensive care unit (ICU), or hospital mortality, including time after ICU treatment, is often used as an endpoint. Indeed, mortality is a solid endpoint and reaching this endpoint is beyond doubt. It may be seen as the best and ultimate endpoint we can have in ICU research. Around 10 to 15% of all patients admitted in Dutch ICUs will die in the ICU and another 5% after ICU discharge while still in the hospital (Fig. 1). However, the absolute mortality rate is not informative enough. For purposes of evaluation, prognostic models like APACHE, SAPS, and MPM can be used to predict in-hospital mortality. The ratio of the observed mortality to the predicted mortality creates a standardized mortality ratio (SMR). The SMR is a severity of disease adjusted mortality rate.

Mortality as a Study Endpoint

The relatively high incidence of mortality in the ICU makes this endpoint valuable. Although as clinicians we try to reduce mortality, a high mortality incidence is attractive from a statistical viewpoint. For example, selective decontamination of the digestive tract (SDD) in liver transplantation does not obviously reduce mortality in single studies nor in a meta-analysis [1]. Given the in-hospital mortality rate after liver transplantation of around 10%, mortality is not a suitable endpoint for the available data in liver transplantation patients. This problem is often referred to as insufficient power. A large study population can resolve this problem but may be difficult to col-

![Fig. 1. Hospital and intensive care mortality in the Netherlands](image-url)
lect (for instance, liver transplantation patients). At present, the relatively high in-hospital mortality of 30% for septic patients or other ICU patients with multiple organ failure is attractive from an epidemiological and statistical viewpoint. An even higher mortality is reported for septic shock (Table 1). Although attractive for statisticians, clinicians would rather reduce mortality or eliminate it. Recently, several interventions have been reported that by themselves reduce mortality of ICU patients substantially. Older medications have also now been shown to reduce mortality when they are used according to new standards (steroids, insulin, SDD). In addition, a new medication is now available (activated protein C, drotrecogin alfa (activated)). An adjusted use of the mechanical ventilator can save lives compared to traditional ways of administering mechanical ventilation.

### Odds Ratios

The crude odds ratios and absolute (hospital) mortality reduction for these interventions from the original studies are shown in Table 1. At present, it is unknown what the effect of a combination of these interventions will be on mortality rates. It usually takes years for strategies to be implemented in daily practice. Therefore, the current incidence of mortality in a standard ICU cannot be seen as the lowest possible mortality rate. However, we can make estimations on theoretical grounds.

Principles of prognostic diagnostic tests using prior and posterior odds as well as chances and likelihood ratios can be used for other purposes as well. In that scenario, the test should be diagnostic/prognostic for death. The result of using multiple consecutive diagnostic tests can be predicted by multiplying likelihood ratios and odds ratios. In the estimation of mortality rates when applying four live saving strategies (1–4 or 1–3 plus 5 in Table 1) we should multiply odds ratios. The product of all odds ratios for severe sepsis patients is 0.20. This means that for a person admitted to the ICU with an *a priori* chance for dying of 40% it might be possible to reduce the mortality to 20% of the *a priori* mortality rate, resulting in an absolute mortality of 8% (40×0.20). For septic shock patients, the product of the odds ratios is 0.14, which might reduce mortality from 70 to 10%. It is difficult to believe that these tremendous mortality reductions can be obtained.