Prognostic modeling to evaluate the in-hospital and long-term mortality of intensive care patients
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Chapter 1

General introduction
1.1 Introduction

Over the last three decades interest in quality of health care has increased by health care professionals and policy makers due to the perceived need of continuous quality improvement and transparency to the public. To get insight in the quality of health care, quality indicators such as in-hospital mortality rates are frequently used. When comparing hospitals by mortality rates the high and low performing hospitals can be identified (1,2), suggesting that hospitals with lower mortality perform better than hospitals with higher mortality. However, differences in patient case-mix (e.g. diagnoses, age, and sex) influence mortality rates of hospitals. High mortality risk, for example, could be an indication for more complex and severely ill admitted patients to the hospital. Consequently, fair and meaningful comparison of the performance of hospitals based on mortality rates requires adequate case-mix adjustment of the raw mortality data. This means that patient characteristics that influence mortality should be considered. To this end, several initiatives have been undertaken to collect the relevant raw data about the patient in medical quality registries. In these quality registries data collection should be standardized to provide reliable case-mix adjustment and to enable quality monitoring, quality improvement, and comparison of different hospitals. Case-mix adjustment is commonly done by using prognostic models. To date, several prognostic models have been developed for the total hospital population and also for specific patient groups such as the Intensive Care Unit (ICU) population or the cardiac surgery population.

The prognostic models that are frequently used in the domain of ICU predict in-hospital mortality risk while adjusting for case-mix. The long-term mortality is often ignored, as it is harder to obtain the relevant data after patients leave the hospital. However, there are several reasons to consider the long-term mortality next to the in-hospital mortality. One of the reasons is that the in-hospital mortality can differ between hospitals due to differences in hospital discharge policies, the number of patients transferred to another hospital, and/or the number of patients admitted from another hospital. Ignoring these factors may when considering in-hospital mortality lead to biased results. More important is that for patients the long-term mortality is more relevant than the in-hospital mortality.

This thesis addresses the validation and comparison of different prognostic models currently used in health care with a main focus on the models used for the ICU population. This first chapter introduces the domain of intensive care and describes the quality assessment in the intensive care by using prognostic models. Next, we underline the importance of assessing the long-term mortality of ICU patients. This chapter concludes with an outline of the thesis.
1.2 Intensive Care

Intensive care is defined as “a service for patients with potentially recoverable conditions who can benefit from more detailed observation and more invasive treatment than can safely be provided in general wards or high dependency areas”. This definition originates from the second half of the 20th century and since then the intensive care has been much expanded. Nowadays, care in the ICU is very complex and delivered in a highly technical and labor-intensive environment. Along with these developments also the cost of intensive care has increased substantially, resulting in a high proportion of the health care budget spent for the ICU (3). In 2011 there were 91 Dutch ICUs which were categorized by the Netherlands Society for Intensive Care (NVIC) in three levels: 46 level 1 ICUs, 22 level 2 ICUs, and 23 level 3 ICUs. Level 1 ICUs are the smaller less equipped ICUs which should contact a higher level ICU in the region to discussed the possible need for transfer after a treatment period of 3 days. Level 3 ICUs are the larger and most equipped ICUs. As almost all ICUs offer all types of care, the average volume per type of treatment per hospital is relatively low. This low volume per type of treatment is increasingly leading to discussion about centralization of the Dutch ICUs. It has been postulated that redistribution of the Dutch ICUs can lead to lower costs while improving quality and thereby reducing mortality (4). Currently, around 23% of the total Dutch hospital mortality is attributable to the death of ICU patients. The average mortality among all hospitalized patients is approximately 1.5%, while the average mortality among ICU patients is approximately 20%.

1.3 National Intensive Care Evaluation foundation

The National Intensive Care Evaluation (NICE) foundation (5) was established in 1996 by a group of intensivists to facilitate quality monitoring and quality improvement initiatives in Dutch ICUs. At the start of the registry, information was collected on severity of illness at ICU admission and outcome only. Over the years the registration has been extended with information on daily organ functioning, complications, quality indicators (e.g. nurse-to-patient ratio, glucose regulation, and duration of mechanical ventilation), and will be further extended with nursing workload information. The NICE registry performs analyses on the registered data, provides feedback reports, and offers the participants an online tool for monitoring quality indicators. The feedback reports and online tool can be used to compare the quality of care between ICUs but also for monitoring the quality of care of an ICU over time. This approach allows the identification of critical points in the care process and facilitates meaningful discussions about ICU treatment and organization improvements. Subsequently this can lead to actual improvement of quality of care at the ICU.
Currently, 85 ICUs are participating in the NICE registry, which amounts to about 90% of all Dutch ICUs. The participating ICUs are mixed medical-surgical units located in university hospital, teaching hospital or non-teaching hospital and are widespread over the Netherlands. The registry contains information of more than 600,000 ICU admissions providing an important basis for quality assessment and scientific research. As the ICU population is a heterogeneous group of patients with different reasons for ICU admission, varying severity of illness and different ages it is meaningless to directly compare the outcome (mortality) of different ICUs. This thesis is focused on using the registry data for case-mix adjustment to allow for comparison of ICUs.

1.4 Prognostic models used for case-mix adjustment

Prognostic models use different variables to adjust for case-mix differences, some use administrative data and others use clinical data for adjustment. Also the clinical data that are used differ between the models. The hospital standardized mortality (HSMR) model (9,10) is developed for all hospitalized patients and uses routinely collected administrative data to correct for case-mix differences. The Acute Physiology And Chronic Health Evaluation (APACHE) II and IV, and the Simplified Acute Physiology Score (SAPS) II models are developed specifically for ICU patients and use clinical data for case-mix correction (6-8). Although these last three models use clinical data, they differ in the specific clinical data that are used. As example, the APACHE II and APACHE IV models use, in contrast to the SAPS II model, the reason for ICU admission as covariate. All mentioned models have in common that they are logistic regression models providing an estimate of the in-hospital mortality risk, which is a probability, based on the characteristics of the patients (e.g. severity of illness, demographics etc.). There are diverse applications of the prognostic models in practice (11). Prognostic models can be used to identify high risk patients and as tool to correct for the severity of illness when comparing different treatment groups (i.e. high predicted mortality risks indicate high severity of illness). For instance when comparing the outcome of patients with and patient without a certain treatment the results have to be adjusted for the difference in severity of illness between the two groups. A common application of prognostic models is the use for benchmarking purposes, i.e. the process of comparing a quality indicator across different hospitals and/or with a reference value. One of the most frequently used quality indicators for benchmarking hospitals is the standardized mortality ratio (SMR). The SMR is the ratio of the observed in-hospital mortality and the expected in-hospital mortality as estimated by the prognostic models. The SMR is used by physicians and managers as the case-mix adjusted outcome to measure the quality of care, to compare their outcomes to the national average or to perform longitudinal analyses. The SMR can be calculated for the total population but also for specific subgroups for example patients with a specific reason
for ICU admission or patients admitted on a certain day of the week or in a certain hour of a day. The use of prognostic models to assess the quality of care has been the subject of discussion in many studies (2,12,13). Research has shown that different prognostic models result in different impressions about the quality of care within the same hospital (14,15). These differences might be caused by the fact that each model emphasizes different aspects of the case-mix or that the models are developed in different years for different patient populations. To correct for the latter factor it has been suggested to customize (i.e. also called recalibrate) the prognostic models before using them on a new setting (e.g. different patient population, other country, different year of admission etc.) (16,17).

1.5 Long-term mortality of ICU patients

The prognostic models commonly used for case-mix adjustment all predict the in-hospital mortality. However, it has been postulated that benchmarking of ICUs ideally should be done based on long-term mortality instead of the frequently used in-hospital mortality. In the Netherlands the observed mortality in the ICU population 3 months after hospital discharge is 5.4%. This additional mortality after hospital discharge can be partly explained by the additional mortality caused by the preceding ICU admission or by the preexisting comorbidities of the ICU patients. As the mortality in the first three months after hospital discharge is substantial, it is worthwhile to analyze the influence of assessing the SMR based on the in-hospital mortality or based on the long-term mortality. Besides the substantial mortality in the first three months after hospital discharge there are several more reasons to consider the long-term mortality instead of the in-hospital mortality. First, the in-hospital mortality can be influenced by the difference in hospital discharge policies (e.g. a hospital that discharges many patients to a hospice or that transfers many patients will have a high hospital survival, even if it has properly corrected for differences in case-mix) (18). Second, insight in the factors that influence long-term mortality could be used by clinicians and can help to identify interventions that might improve long-term mortality (19). Third, the true goal of ICUs is long-term survival with an acceptable quality of life (20). Finally, the high resource consumption and costs of ICUs above that of general hospital care (21) may be considered excessive if long-term survival is poor. One important disadvantage of using the long-term mortality of hospitalized patients is that the needed data is harder to obtain than in-hospital mortality. In the Dutch ICUs there is no systematic approach to assess and register the long-term information. Besides, when the long-term mortality of ICU patients is described in the literature, it is difficult to compare these outcomes between the studies due to differences in follow-up starting point (ICU admission, ICU discharge, or hospital discharge) and follow-up end-point. Linkage of hospital data with death registers provides a feasible method for obtaining long-term mortality after hospitalization. This linkage allows assessment of long-term
mortality and the development and validation of case-mix adjusted prognostic models of ICU long-term mortality.

1.6 Objectives of this thesis

Although studies have been published examining the performance of prognostic models and the outcome of ICU patients, still many questions remain. For instance which prognostic model has the highest performance? What happens after hospital discharge of ICU patients? The three main research questions and corresponding objectives answered in this thesis were:

1. How do prognostic models perform in the Dutch ICU population?
   a. Assess and compare the performance of commonly used prognostic models in health care especially in the field of intensive care.

2. Is there an association between ICU admission time and the case-mix adjusted mortality?
   a. Determine the association between ICU admission time and mortality by calculating the relative risk while adjusting for severity of illness.

3. What is the long-term mortality of ICU patients and does the choice of follow-up end point (i.e. in-hospital mortality or long-term mortality) affect the quality indicator SMR?
   a. Examine and describe the long-term mortality of ICU patients.
   b. Assess the performance of the APACHE IV model when applied for long-term mortality predictions of ICU patients.
   c. Assess the effect of using the in-hospital mortality versus the long-term mortality on the SMR.
1.7 Outline of this thesis

In Chapter 2 we compared the performance and robustness of a model based on administrative data (the customized HSMR model, originally developed for all hospitalized patients) and a model based on clinical data (the customized SAPS II model, originally developed for ICU patients) in the Dutch ICU population. Furthermore, the effect of severity of illness on the calculated SMRs based on these two models is examined. The postulation in this study was that prognostic models based on administrative data can provide valid adjusted in-hospital mortality rates in specific patient populations. In Chapter 3 we performed an external validation of the APACHE IV model, developed in 2006, in the Dutch ICUs. Before newly developed models can be incorporated by quality registries, the models should be validated and compared to older existing models to assure adequate quality of the used prognostic models for case-mix adjustment. In Chapter 3 we assessed the performance of the APACHE IV model and compared this performance to that of the SAPS II and APACHE II models. All of these three models are based on clinical data and were specifically developed for the ICU patients.

Prognostic models are frequently used to calculate the case-mix adjusted SMR for benchmarking purposes. In Chapter 4 we compared the SMR of ICU patients admitted during office hours and of ICU patients admitted during off hours to determine whether the case-mix adjusted in-hospital mortality is associated with ICU admission time. The prognostic models mentioned above all predict the in-hospital mortality, disregarding the long-term mortality. In Chapter 5 we conducted a literature review on the long-term outcome of ICU patients. In addition, we describe the mortality after hospital discharge in Dutch patients surviving ICU admission in Chapter 6. In Chapter 7 we validated the performance of the APACHE IV model when applied for the prediction of the long-term mortality of ICU patients. Furthermore, we analyzed the effect of using the in-hospital mortality versus the long-term mortality on the SMR.

Finally, in Chapter 8 we provided an overall discussion of our major results and their implications and addressed the merits and limitations of the different studies.
Chapter 1

References