Valorisation
This thesis aimed to investigate the chain of emergency care in sepsis patients from the diagnosis sepsis to prehospital care and risk stratification at the Emergency Department (ED). This paragraph describes the consequences and innovations for daily clinical practice that (probably) arise from our findings.

Relevance

Sepsis, which is defined as a systemic inflammatory response syndrome (SIRS) to an infection, is a broad clinical entity and a deadly disease [1, 2]. The incidence of sepsis has been estimated between 15 and 19 million per year worldwide, and overall mortality is about 30% [3, 4]. A quarter of the patients presenting at the ED for the internist in Maastricht University Medical Centre are diagnosed as having sepsis according (chapter 2). Sepsis is not only an important cause of death but puts significant strain on healthcare budgets as well [5]. In the last two decades, the implementation of the Surviving Sepsis Campaign (SSC), which aims to start treatment in sepsis patients early, has proved to reduce both mortality and sepsis-related costs [6, 7, 8, 9]. This makes sense if you look at the sequence SIRS, sepsis, severe sepsis and septic shock as a process of falling dominoes. The mortality and morbidity caused by sepsis is time-dependent and increases with delay of adequate therapy [2].

Consequences and innovations in current daily practice

Only when sepsis is recognized, an early start of treatment according to the SSC is possible. The sepsis definition is an important tool to make a first differentiation between patients with and without sepsis. A clinical decision support system based on the sepsis definition could be helpful to detect sepsis earlier at the ED, and in the ambulance. However, the diagnostic accuracy of the current sepsis definition is not perfect. Therefore, in order to diagnose sepsis early, besides designing a decision support system, it is important to raise and maintain the awareness of sepsis in emergency physicians, because we showed that they perform better in diagnosing sepsis than the sepsis definition alone.

The guidelines for treatment provided by the SSC only address the treatment of the sepsis patients after arrival at the hospital and not during the pre-hospital phase [4]. However, the ambulance is the first encounter of the sepsis patient with the health care system. Since the outcome of sepsis is time-dependent, treatment of sepsis patients in the ambulance could reduce morbidity, mortality and thus, sepsis-related costs. In this thesis, we found that almost half of the sepsis patients who were assessed at the ED by the internist had been transported by the ambulance. These patients were older, more severely ill, were more often admitted to medium/intensive care units and had a higher mortality. This means that these patients would probably benefit most from early treatment of sepsis. The problem is that a substantial part of these patients sepsis are not documented to have sepsis. The mortality of these non-documented patients was twice as high than of the documented patients (25.7 vs. 12.9%). Fortunately, the recognition of sepsis can be impro-
ved, as we found that almost 50% of the missed patients could have been recognized if all vital signs had been assessed and knowledge of sepsis was improved.

Once recognized, early treatment in the ambulance with oxygen and intravenous fluids has indeed improved outcome [11, 12]. In addition to treatment with oxygen and fluids, antibiotic treatment may also be started in the ambulance. This could prove beneficial, if the results of early antibiotic treatment in the hospital can be extrapolated to the pre-hospital phase, which is never investigated before. Therefore, following the results of our studies, the first prospective randomized study, which assesses the impact of early antibiotic treatment in the ambulance on mortality and the number of (expensive) ICU admissions was recently launched in the Netherlands [13].

After arrival at the ED, the emergency physician has to identify the patients with the highest mortality risk. The mortality risk of the patients influences the resources, and thereby the costs, needed to treat the patient. The estimation of the mortality risk leads to standardized care in sepsis patients, but also to individualized and effective/efficient care (adjusted to the severity of disease and pre-existing morbidity and mortality risk). However, in the past decades, a large number of severity of sepsis scores have been developed and it is not clear which is best. We compared many scores and found that the abbMEDS is the best severity score in sepsis patients at the ED with regard to discriminatory value, feasibility and calibration. In addition, until now, the predictive value of the severity scores has not been investigated in the group of elderly patients, who form a major part of the patients with sepsis. Due to ageing of the population and their high concomitant comorbidity, there is an increase of elderly patients visiting the ED. We showed that the discriminatory value, feasibility and calibration of the abbMEDS is maintained in elderly patients.

Ideally, a sepsis-specific ED score would be part of a clinical decision support system that not only discriminates well between those who will live and those who will die, but also guides antibiotic treatment (e.g. small or broad-spectrum) and disposition (i.e. whether a patient should be admitted to the hospital and if so, to what level of care). Such guidance will lead to a more efficacious care, as was found in patients with community-acquired pneumonia (CAP). The CURB-65 score stratifies patients with CAP into three risk categories that predict 28-day mortality well and guide antibiotic treatment and disposition [14]. The implementation of CURB-65 resulted in more standardized care and reduced the use of broad-spectrum antibiotics, while patient safety was maintained [15, 16].

We found that the abbMEDS categorized patients with sepsis well with respect to two important clinical decisions, namely empirical antibiotic treatment and disposition. This is the first study towards the ability of the abbMEDS to guide clinical decisions. In order to develop the abbMEDS from a risk stratification to a decision support tool, future studies are needed to calibrate the score in a prospective multicentre trial. Next, we have to confirm that the score can indeed appropriately and safely be used to provide this support on clinical decisions. Hopefully, the implementation of clinical decision support by abbMEDS will improve survival, reduce use of broad-spectrum antibiotics and reduce healthcare costs in sepsis patients.
References


