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# The costs of septic syndromes in the intensive care unit and influence of hospital-acquired sepsis

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**Abstract** *Objective:* To document the costs and outcomes of the various forms of the septic syndromes [systemic inflammatory response syndrome (SIRS), sepsis, severe sepsis, septic shock), particularly those associated with infection acquired in an intensive care unit (ICU). *Design:* Prospective data collection for all septic patients admitted to a medical ICU during a 1-year period. Costs were computed from the viewpoint of the hospital. *Results:* Mean total hospital costs were €26,256, €35,185, and €27,083 for patients with sepsis, severe sepsis, and septic shock, respectively. Total costs varied slightly according to the site of infection and the severity of sepsis but were influenced mostly by its mode of acquisition: patients having sepsis associated with ICU-acquired infection incurred total costs about three times those of patients presenting with infection and sepsis on ICU admission (from €39,908 in patients with ICU acquired sepsis to €44,851 in patients with ICU-acquired septic shock). Stratifying patients by the presence of ICU-acquired infection also showed that a first episode of infection complicated by ICU-acquired sepsis incurred at least 2.5 times more costs than a single episode of sepsis. *Conclusions:* In this series the medical costs of sepsis were not markedly influenced by its severity but by its mode of acquisition. Due to wide variations in ICU costs cost-effectiveness analyses of treatments for sepsis should document the case-mix of patients and the contribution to this of nosocomial infections.

**Keywords** Sepsis · Septic shock · Cost · Nosocomial infection · Length of stay · Economic evaluation

## Introduction

The definitions of septic syndromes have caused much controversy and debate in the past decade. Many of these questions have stemmed from the frustration accumulated following the repeatedly negative results of new therapeutic interventions aiming at controlling the inflammatory response associated with infection, hence the suggestions that new definitions are needed that would allow a quicker and easier identification of septic patients for accrual into randomized trials of new therapies [1] and would help derive more consistent and comparable results from epidemiological studies and clinical trials. Since the definitions proposed by the American College of Chest Physicians/Society of Critical Care Medicine (ACCP/SCCM) Consensus Conference appeared, several studies have described the epidemiology of the septic syndromes [systemic inflammatory response syndrome (SIRS) and sepsis, severe sepsis, and septic shock) [2, 3, 4, 5, 6, 7], and a number of clinical

**Table 1** Description of the patient population admitted to the medical ICU during the 1-year study period (*SAPS II*: Simplified Acute Physiology Score II)

| | No infection (*n*=200) | Sepsis (*n*=87) | Severe sepsis (*n*=81) | Septic shock (*n*=56) |
|---|---|---|---|---|
| Male sex (%) | 62 | 56 | 67 | 71 |
| Age (years) | 56±17 | 56±14 | 55±15 | 59±17 |
| SAPS II | 41±21 | 40±22 | 47±19 | 62±26 |
| Deaths (%) | 20 | 18 | 33 | 61 |
| McCabe (%) | | | | |
| Class 1 | 69 | 61 | 57 | 59 |
| Class 2 | 20 | 25 | 32 | 34 |
| Class 3 | 11 | 14 | 11 | 7 |

trials of adjunctive therapies have been performed. To our knowledge, no study has directly addressed the question of the costs of these syndromes, although studies have examined the potential cost-effectiveness of new therapies based on modeling of costs [8, 9, 10, 11], and a recent study has described variations in length of stay (LOS) associated with sepsis of varying severity [12]

A number of research groups are investigating the development of drugs that would reduce the severity of severe sepsis and its associated mortality, and at least one adjunctive therapy has recently been made available after 15 years of disappointing attempts [13]. New therapies will be expensive and will alter the outcomes of septic patients. Thus managers of intensive care units (ICUs) and hospitals will have to estimate the additional financial costs resulting not only from the purchase of the drug but also from the new proportion of surviving patients and alterations in the consequences of sepsis on the outcome of patients.

In this study we analyzed the costs and outcomes of patients affected by each of the three forms of the septic syndromes and compare costs and hospital mortality of sepsis, severe sepsis, or septic shock, whether ICU- or non-ICU-acquired, in patients admitted to our medical intensive care unit. We discuss the potential implications of these information for the cost evaluation of new therapies.

## Methods

### Patient population

The study was conducted at the medical ICU of Henri Mondor Hospital, one of the 50 public hospitals of the Assistance Publique-Hôpitaux de Paris group. Our hospital is a 930-bed acute care and referral university hospital with a total of 108 ICU beds. The medical ICU has 26 beds, including an acute care and a step-down unit of 13 beds each.

All patients having infection or sepsis admitted to the acute-care area were prospectively followed during a 1-year period, from May 1997 to April 1998, and included in a multicenter multinational prospective study of infection and sepsis in the ICU [14]. The patients' computerized files were subsequently retrieved and searched for resources utilization. When additional information was needed, the chart was retrieved and abstracted. Definitions for the septic syndromes were those from the ACCP/SCCM Consensus Conference [1]. Patients were included if the diagnosis of one of the septic syndromes was recorded either at the time of admission or during the ICU stay. Infections were recorded when clinically or microbiologically documented. Infected patients were characterized as having sepsis on ICU admission or having acquired sepsis during the ICU stay (i.e., occurring >48 h after admission) or a combination of the two. For the purpose of analysis each patient was included in the most severe stage of sepsis occurring during the ICU stay as a consequence of infection. Patients having two episodes of sepsis of different severity (e.g., on admission and ICU acquired) were assigned to the category of the first episode with highest severity. Data recorded prospectively on all patients included demographic information, admission diagnoses and comorbidities, site and characteristics of infection, LOS (both in the ICU and total hospital stay), the severity of underlying disease according to the classification of McCabe and Jackson [15] and outcome. Outcome (survival or death) was considered at the time of hospital discharge for the index admission.

The ICU database included 424 patients, of whom 206 (49%) were admitted to the ICU via the emergency room or the emergency prehospital care service, 42 (10%) were transferred from another hospital, and 176 (41%) were transferred from other departments of the same hospital (65 from surgical departments and 111 from medical wards). There were 224 (52.8%) who had one or more episode of infection recorded at the time of admission or later during the ICU stay. There were 87 patients (21%) with sepsis, 81 (19%) with severe sepsis, and 56 (13%) with septic shock (Table 1). Their mean Simplified Acute Physiology Score II was 45±24. The crude hospital mortality was 20% in patients having no infection vs. 35% among all infected patients, and increased markedly from 18% in patients with sepsis, to 35% with severe sepsis and 61% with septic shock ( $p < 10^{-4}$).

Table 2 shows the sources of infection recorded in the 224 infected patients. Data on the source of infection was comprehensive for 222 of these 224 patients. In 97 patients (23% of the whole cohort) the sepsis was ICU-acquired, and 46 of these had no infection recorded at time of ICU admission; 127 patients (57%) were admitted with an infection and did not acquire an additional infection in the ICU. Mortality was significantly higher in patients having ICU-acquired infection, regardless of other infection recorded on admission (50% in patients with an ICU-acquired infection vs. 31% without, $p < 10^{-4}$).

### Costs analysis

Costs of ICU and ward stay for septic and nonseptic patients were estimated from the viewpoint of the hospital. We used a costing model developed and validated at our ICU which has been previously published in detail [16]. Other authors have encountered similar difficulty in estimating medical costs and have developed models for all inpatient categories, with predicting variables pertaining to both medical condition at the time of admission and resources use during the hospitalization [17, 18, 19]. Our model was built upon a prospective collection of all resources used and direct costs (of fluids, drugs, blood products, and procedures). The volume of resources used to treat patients was estimated from the three components of the Omega score (see Appendix), a scoring system for therapeutic intensity and used for cost assessment of ICU patients [17, 20] and from the LOS. In addition to the above variables, the model includes a binary variable, indicating whether surgery or an interventional radiological procedures (such as vessel embolization or coronary angioplasty) occurred during the ICU stay. The remaining part of the hospital admission (if any) was costed using the ledger from the ward to which the patient was transferred.

Overhead costs were added ex post facto using the step-down allocation process developed for all hospitals of the Assistance Publique-Hôpitaux de Paris group following the general rules of public accounting. These averaged about 30% of total ICU costs and 15% of total costs for non-ICU wards. The unit costs used to value ICU resources were updated to 2001, and costs are presented in 2001 euros (€1=0.95 $U.S.).

**Table 2** Sources of infection and infection category recorded in 224 Intensive care unit patients*

| | Infection at ICU admission | ICU acquired | Total | |
|---|---|---|---|---|
| | | | *n* | % |
| Pulmonary | 113 | 23 | 136 | 60 |
| Catheter-related | 33 | 19 | 52 | 23 |
| Bacteremia | 21 | 6 | 27 | 12 |
| Urinary tract | 38 | 14 | 52 | 23 |
| Other | 65 | 0 | 65 | 29 |

* Data are presented as number of patients; numbers add up to more than the total number of infected patients because some patients had infection at several sites

### Statistical analysis

We analyzed costs of survivors and of deceased patients separately within each category of sepsis severity and according to the time of acquisition of infection relative to ICU admission, and the costs of septic patients with or without ICU-acquired infection. We estimated mean costs and standard deviations. Continuous variables were analyzed by both parametric and nonparametric tests (unpaired *t* test and Mann-Whitney test), because there is a currently controversy on the way to deal with the skewness of cost data [21]. Significance was attributed at the 5% level and at the 1% level for complementary two-by-two comparisons. Data were analyzed using BMDP statistical software (BMDP, Los Angeles, Calif., USA).

## Results

### Cost analysis

The LOS and costs of the ICU admission in the absence of infection and for patients with infection according to the severity of the septic response are presented in Table 3. The mean total hospital LOS and costs of patients with sepsis were significantly higher than that of patients without infection, regardless of the sepsis category ( $p$ values ranged from less than $10^{-4}$ to 0.0003). Patients with severe sepsis incurred significantly higher

**Table 3** Length of stay (*LOS*) and costs (2001 euros) of admission in the intensive care unit for infected and septic patients. Total LOS indicates the total length of stay in the hospital during the index admission

| | All patients | Deceased | Survivors | Sepsis on ICU admission | ICU-acquired sepsis |
|---|---|---|---|---|---|
| Patients with sepsis[a] | | | | – | – |
| Patients with septic shock[a] | | | | | |
| Patients having no infection | | | | | |
| No. patients | 200 | 40 | 160 | – | – |
| ICU LOS (days) | 6.5 (9.4) | 4.8 (5.8) | 7 (10) | – | – |
| Total hospital LOS, days | 20 (26.7) | 12 (18.5) | 22 (28) | – | – |
| Total costs | 12,719 (14,634) | 10,654 (11,354) | 13,012 (15,266) | – | – |
| No. of patients | 87 | 16 | 71 | 50 | 36 |
| ICU LOS (days) | 14 (17.5) | 20 (22) | 13 (16) | 7 (7) | 29 (9) |
| Total LOS | 37 (34.5) | 31.5 (30) | 39 (35) | 29 (15) | 58 (29) |
| Total costs | 26,256 (25,131) | 33,320 (33,591) | 24,503 (22,804) | 17,261 (15,710) | 39,908 (29,975) |
| Patients with severe sepsis | | | | | |
| No. of patients | 81 | 28 | 53 | 41 | 40 |
| LOS ICU | 19 (21) | 17 (16.2) | 20 (22) | 9.5 (8) | 23 (19) |
| Total LOS | 43 (37) | 27 (21) | 51 (40) | 35 (33) | 52.5 (39) |
| Total costs | 35,185 (33,490) | 31,430 (28,680) | 37,366 (36,030) | 21,461 (16,809) | 42,132 (36,142) |
| No. patients | 56 | 34 | 22 | 36 | 19 |
| LOS ICU | 12.2 (16) | 10.3 (17) | 15 (14) | 6.7 (7) | 23.5 (28) |
| Total LOS | 34 (33) | 24 (25) | 50 (37) | 25.5 (22) | 48 (40) |
| Total costs | 27,083 (25,574) | 24,632 (27,114) | 31,372 (22,646) | 17,705 (11,578) | 44,851 (34,529) |

[a] Data on the type of infection was missing for one patient

**Table 4** Comparison of costs (euros) for patients with or without ICU-acquired sepsis, according to the presence of sepsis on admission. Two-way analysis of variance found no interaction between variables. The higher cost for ICU-infected patients is explained by both prolonged length of stay (*LOS*) and higher daily cost related to intensity of care

| | Sepsis on ICU admission | |
|---|---|---|
| | Absent | Present |
| No ICU-acquired sepsis | *n*=200 | *n*=127 |
| LOS in ICU, days | 6 (9) | 9 (10) |
| Total hospital LOS | 20 (27) | 34 (32) |
| Total hospital costs | 12,719 (14,634) | 18,871 (15,129) |
| ICU-acquired sepsis | *n*=46 | *n*=42 |
| LOS in ICU, days | 25 (26) | 28 (21) |
| Total hospital LOS | 49 (44) | 53 (36) |
| Total hospital costs | 41,006 (35,481) | 49,146 (35,113) |

costs than patients with sepsis ( $p$ =0.013); however, the costs of patients with septic shock were similar to that of the former group ( $p$ =0.82). Examining costs and outcome in the 224 patients with sepsis, irrespective of its severity, we found that the average costs were comparable in the 78 nonsurvivors and the 146 survivors (€28,973 vs. €30,191, $p$ =0.23).

Segregating septic patients according to whether the septic episode occurred on ICU admission or was ICU acquired, we found that average total costs of patients having infection only at admission varied between €17,261 and €21,461 (Table 3) whereas the average costs of patients having ICU-acquired sepsis, whether or not preceded by infection at admission, varied between €39,908 and €44,851 ( $p < 10^{-4}$; Table 3). These significant differences were found by both parametric and nonparametric tests. Stratifying patients by whether sepsis occurred only during ICU stay or was preceded by sepsis on admission (Table 4) shows that acquisition of sepsis was associated with 2.5–3 times higher costs. The lower costs of patients without ICU-acquired infection were associated with much shorter LOS in the ICU, whereas the presence of ICU-acquired infection was associated with an increase in mean LOS in the ICU of 19 days, similarly in patients with and without infection on admission, and an increase in mean hospital LOS of 19–29 days (Table 4). Two-way analysis of variance confirmed that costs did not differ with increasing severity from sepsis to septic shock when controlling for the mode of acquisition of infection. Subgroup analyses of costs for patients having pulmonary infection or catheter-related infection, which were the two largest subgroups among patients with severe sepsis and septic shock, showed a significant difference with an average cost per admission of €28,548 for pulmonary infection ( $n$ =76) and €42,061 for catheter-related infection ( $n$ =18; $p$ =0.05).

In analyzing cost categories we found that the proportion of total costs attributed to drugs, fluids, and consumables increased with the patient severity, while the proportion of medical and nursing staff costs decreased. Drugs, fluids, and consumables contributed 33% of total costs in nonseptic patients, 34% in patients with mild sepsis, 41% and 44% in patients with severe sepsis and septic shock, whereas medical and nursing staff costs decreased from 47% to 45%, 38% and 32%, respectively.

## Discussion

Several conclusions can be drawn from this single institution investigation into the costs associated with septic syndromes. It is well accepted that there is a clinical continuum between the different stages of the inflammatory response from SIRS to sepsis, severe sepsis, and shock [5]; however, this continuum is not apparent when examining ICU costs. The single most important factor determining the magnitude of costs is the LOS, which is markedly influenced by the high mortality of the septic syndromes and the high incidence of ICU-acquired infection in this population. The severity of the septic response did not appear substantially to influence costs. While the average costs of patients with severe sepsis appeared significantly higher than that of patients with sepsis, this difference did not persist when patients with and without ICU-acquired infection were analyzed separately. Likewise, because of their high mortality rate (61%), patients with septic shock had a mean LOS comparable to that of patients with sepsis and did not incur higher costs on average than the latter group. At each severity level patients with ICU-acquired infection required three times more resources than patients having sepsis on ICU admission and not having ICU-acquired infection. In other words, patients with ICU-acquired sepsis incurred significantly higher costs than patients without, but within these two groups patients with either sepsis, severe sepsis, or septic shock did not generate different costs.

Our sample size compares with that of most previously published cost estimates of sepsis. Schulman et al. [10] included a sample of 234 patients; Barriere et al. [8] studied 211 patients, and Pittet et al. [22] examined 86 matched pairs of patients with ICU-acquired bacteremia. Our series of 224 patients with sepsis recorded over a 1-year period can be therefore compared to those examined in these studies. Only the study by Chalfin et al. [9] examined retrospectively from the hospital database a much larger group of 1,405 patients admitted over a 4-year period; a more recent study from Teres et al. [12] examined LOS according to severity of sepsis at ICU admission in 2,434 patients in the IMPACT cohort. The characteristics of patients included in our series also reflects the usual pattern of unselected ICU patients with sepsis. In a prospective multicenter study of 11,828 patients admitted to French ICUs Brun-Buisson et al. [2]

reported a 56% mortality rate in patients with severe sepsis and 60% in patients with septic shock. The outcome of patients with septic shock in our series is identical to that found previously in this larger study, although the outcome of patients with severe sepsis appears somewhat better (35% mortality rate). However, this figure is consistent with those recorded in recent clinical trials and in the larger European epidemiological study recently reported [14] from which the present cost study derives. Our estimates of costs should therefore be applicable to current patients affected with sepsis.

There are, however, other limitations to the generalizability of our findings. Our study is derived from the medical ICU of a university hospital, and its results may not be applicable to other types of ICU (e.g., surgical or mixed) and with different organization and structure. In addition, the data on resource utilization was obtained from one center and conversion into monetary costs results from a method developed in this same center, and our results would need external validation in other ICU populations. However, the LOS that we found in patients with various severity of sepsis on admission, the major driver of costs, is comparable to that recently reported by Teres et al. [12] who found LOS in the ICU ranging from 8 to 9 days in this population; in that study, however, the potential influence of subsequent ICU-acquired infection on resources use was not addressed.

Other authors have reported hospital costs of caring for patients with Gram-negative sepsis or bacteremia [9, 10, 8, 22, 23]. These authors either used hospital charges or estimated per diem costs times the average LOS. Barriere [8] differentiated sepsis from septic shock and found a $4,000 difference between severe sepsis and shock (a less than 10% increase, however) when multiplying the per diem cost by the LOS. We found a larger relative difference of 25% in total costs of severe sepsis than in septic shock and only a 22% relative increase in costs between survivors of septic shock compared to sepsis. Figures found by authors from the United States tend to be all in the same range of $40,000–50,000 and correspond to an estimated total LOS of 20 days with a per diem cost of $2,200–2,700. In a recent study Angus et al. [24] analyzed a large sample of hospital admissions from seven states in the United States and derived costs of severe sepsis from hospital charges. These authors reported that mean hospital costs for ICU patients with severe sepsis varied from $24,600 in nonteaching hospitals to $42,100 in teaching hospitals. This study, however, did not examine other categories of sepsis, or the influence of mode of acquisition of infection on costs. A Dutch study [11] found lower costs, directly resulting from a twice lower per diem cost of about $1,000; these costs are closer to our results for patients with severe sepsis. Differences between results obtained in the United States and ours could be explained by either the differences in unit costs and resources use between European countries and the United States or to the categorization we used. A recent study analyzing the costs of patients with severe sepsis treated with activated protein C reported somewhat lower ICU costs of about $20,000 [25].

It is apparent from our data that when considering the cost of ICU or hospital admission of patients with sepsis that one should take into account the occurrence of ICU-acquired infection. Comparisons of costs in patients with and without ICU-acquired infection consistently show, in all categories of severity of sepsis severity, a marked impact of this event on both LOS and costs (Tables 3, 4), whereas the severity of sepsis itself marginally influences costs. The costs that we estimated for patients having severe sepsis and septic shock associated with ICU-acquired infections are close to those we previously reported for patients having methicillin-resistant *Staphylococcus aureus* infection (€30,000–34,000) in the same ICU [26]. The fact that hospital-acquired infections markedly increase LOS and thereby costs has been previously demonstrated, and the latter aspect is confirmed by our findings within the context of sepsis.

We cannot conclude, however, that all costs reported here are indeed attributable to sepsis since we did not adjust for potential confounders. Our figures are likely overestimated for ICU-acquired sepsis because the LOS directly attributable to the ICU-acquired septic episode was not assessed. Conversely, the costs reported Table 4 for patients having only sepsis on admission may not represent accurately the costs of the average such patient, and actually underestimate these since the occurrence of ICU-acquired infection is not independent of a first episode of infection, which is a risk factor for the former, and it is difficult in a given patient to segregate the costs attributable to sepsis itself and its consequences. Either a case-control method or an "appropriateness evaluation protocol" (AEP), ascribing resources used to sepsis should be performed to estimate costs attributable to sepsis. However, the matching criteria on which controls for patients presenting with sepsis on admission should be selected is unclear. On the other hand, the AEP method involves subjective judgement and is very time consuming. Therefore a more conservative and prudent approach is to consider the mean costs as shown in Table 3. Despite these limitations the costs of a single episode of sepsis may be estimated from the results that we obtained when stratifying patients according to the presence of ICU-acquired infection, and such estimates could be used in costing evaluation. For example, Table 4 shows that the costs of a first episode of sepsis on ICU admission costs about €19,000, and that a second ICU-acquired episode of sepsis is associated with added costs of about €30,000.

When considering costs of patients with ICU-acquired sepsis, the confounding effect of time should be investigated. Patients who stay longer in the ICU are at increased risk for infection and are "at risk" for higher costs since LOS is a major determinant of costs. The data recorded in our study did not allow a longitudinal cost analysis to be performed, but the effect of time could be clarified in institutions where daily costs of care are recorded.

Our results have some implications for the economic evaluation of new therapies for sepsis. Because of the difference in ICU resources use it is important for predictive cost models to segregate patients with ICU-acquired infections from other patients. If such an analysis were not carried out, the expected cost outcome of reducing the severity of sepsis would be to increase costs, irrespective of the costs of the therapy itself because patients experience fewer severe symptoms but remain within the same infection category. In reality, however, costs may be expected not to change (except for the added cost of the new therapy) or to vary in different directions, according to the potential impact of the therapy on LOS and possibly on the rate of occurrence of ICU-acquired infection.

The recommendations from the Consensus Conference on sepsis undoubtedly resulted in a more consistent reporting of patients categories and made such cost comparisons easier. Accordingly, most recent clinical trials have used criteria for severe sepsis or shock in their inclusion criteria. Nevertheless, from the viewpoint of costing analysis there is a need for more in-depth analysis of risk factors and characteristics of sepsis or its more severe forms in patients with SIRS in order to perform proper cost-effectiveness analyses. In addition, the differences in costs incurred by patients having ICU and non-ICU acquired infection across the sepsis categories

**Table 5** The Omega intensive care monitoring and therapy scoring system

| Procedure | Score |
|---|---|
| Category 1: procedures scored only once during the ICU stay, irrespective of their iteration | |
| Endotracheal intubation[a] | 6 |
| Tracheostomy[a] | 6 |
| Total parenteral feeding (>35 kcal/day for at least 10 days) | 6 |
| Central venous line[a] | 3 |
| Pulmonary artery line[a] | 6 |
| Arterial line[a] | 3 |
| Intraortic balloon pump | 10 |
| Cardioversion | 3 |
| Vasoactive drugs (with >hourly arterial pressure monitoring) | 6 |
| Percutaneous pace-maker[a] | 3 |
| Thoracic or pericardial drainage[a] | 6 |
| Training for home respiratory assistance | 6 |
| Neurological monitoring (with >hourly examination for at least 24 h) | 1 |
| Cerebrospinal fluid-ventricular drainage | 1 |
| Intracranial pressure monitoring | 3 |
| Sedation for >24 h[a] | 6 |
| Suprapubic vesical bladder drainage[a] | 1 |
| Ureteral catheter[a] | 3 |
| Gastric lavage | 1 |
| Peritoneal lavage | 3 |
| Enteral feeding (>35 kcal/day for >10 days) | 3 |
| Esophageal varices tamponade[a] | 10 |
| Fibrinolysis | 10 |
| Transfusion of blood and/or blood products >35 ml/kg | 10 |
| Complex orthopedic traction | 6 |
| Category 2: procedures recorded each time they are performed | |
| Hemodialysis | 10 |
| Plasma exchange therapy | 10 |
| Transport to or from the operating room | 6 |
| Transport out-of-ICU | 3 |
| Ultrasonic echography (cardiac, abdominal)[b] | 3 |
| Endoscopy (any site)[b] | 3 |
| Category 3: procedures scored daily | |
| Hemofiltration | 10 |
| Peritoneal dialysis | 10 |
| Mechanical ventilation | 10 |
| Mask ventilation (continuous positive airway pressure or assisted ventilation) | 10 |
| Strict Isolation room | 10 |
| Complex surgical dressings | 6 |
| Continuous electrocardiography or respiratory monitoring | 4 |

[a] Scored if procedure performed or monitored in the ICU
[b] Scored only if performed at the bedside in the ICU

were so important in our study that it would need to be confirmed by other groups. Theses differences would have an impact on the external validity of cost-effectiveness analyses. For example, the expected benefits of obtaining reversal from severe sepsis to sepsis vary greatly depending on the respective proportions of ICU- and non-ICU-acquired infection among infected patients. The implications for economic evaluation of new therapeutic agents should not be underestimated, particularly as new adjunctive therapies are now available [13].

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## The Omega score

Table 5 presents the basis for calculating the Omega score. This score, which is similar to the Therapeutic Interventions Scoring System, was developed by the French Multicenter Group of ICU Research and is currently used in cost evaluation of French medical ICUs The Omega score includes 47 different procedures classified into three categories: procedures recorded only once during the ICU stay, irrespective of their iteration (Omega 1), procedures recorded every time they are performed (Omega 2), and procedures recorded daily in the ICU (Omega 3). The total Omega score is calculated on the last ICU day.

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