Practice and perception—A nationwide survey of therapy habits in sepsis*

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Objective: To simultaneously determine perceived vs. practiced adherence to recommended interventions for the treatment of severe sepsis or septic shock.

Design: One-day cross-sectional survey.

Setting: Representative sample of German intensive care units stratified by hospital size.

Patients: Adult patients with severe sepsis or septic shock.

Interventions: None.

Measurements and Main Results: Practice recommendations were selected by German Sepsis Competence Network (SepNet) investigators. External intensivists visited intensive care units randomly chosen and asked the responsible intensive care unit director how often these recommendations were used. Responses "always" and "frequently" were combined to depict perceived adherence. Thereafter patient files were audited. Three hundred sixty-six patients on 214 intensive care units fulfilled the criteria and received full support. One hundred fifty-two patients had acute lung injury or acute respiratory distress syndrome. Low-tidal volume ventilation ≤6 mL/kg/predicted body weight was documented in 2.6% of these patients. A total of 17.1% patients had tidal volume between 6 and 8 mL/kg predicted body weight and 80.3% >8 mL/kg predicted body weight. Mean tidal volume was 10.0 ± 2.4 mL/kg predicted body weight. Perceived adherence to low-tidal volume ventilation was 79.9%. Euglycemia (4.4–6.1 mmol/L) was documented in 6.2% of 355 patients. A total of 33.8% of patients had blood glucose levels ≤8.3 mmol/L and 66.2% were hyperglycemic (blood glucose >8.3 mmol/L). Among 207 patients receiving insulin therapy, 1.9% were euglycemic, 20.8% had blood glucose levels ≤8.3 mmol/L, and 1.0% were hypoglycemic. Overall, mean maximal glucose level was 10.0 ± 3.6 mmol/L. Perceived adherence to strict glycemic control was 65.9%. Although perceived adherence to recommendations was higher in academic and larger hospitals, actual practice was not significantly influenced by hospital size or university affiliation.

Conclusions: This representative survey shows that current therapy of severe sepsis in German intensive care units complies poorly with practice recommendations. Intensive care unit directors perceive adherence to be higher than it actually is. Implementation strategies involving all intensive care unit staff are needed to overcome this gap between current evidence-based knowledge, practice, and perception. (Crit Care Med 2008; 36: 2719–2725)

KEY WORDS: sepsis; clinical practice; medical audit; questionnaires; survey

M ortality rates of severe sepsis and septic shock are still in the range of 20% to 60% (1–4). Several landmark studies have recently demonstrated that therapeutic strategies may reduce mortality substantially. Tight glycemic control in intensive care unit (ICU) patients as a preventive approach resulted in both decreased frequency of sepsis and reduced overall mortality (5). Lung-protective ventilation reduced absolute mortality in patients with acute respiratory distress syndrome (ARDS) by 9% (6). Early goal-directed therapy based on an algorithm including central venous O_2 saturation measurements (4), low-dose hydrocortisone in septic shock (2), and activated protein C (aPC) in appropriate patients (3) achieved further mortality reduction. On the other hand, large studies revealed that antithrombin (AT) therapy is ineffective (7) as is low-dose dopamine for presumed renal protection (8). These recommendations have been incorporated into guidelines for the treatment of severe sepsis, published by the American Society of Critical Care Medicine and other international groups (9, 10).

The gap between best practice and actual therapy habits may be associated with increased mortality and morbidity

(11). Only few studies have evaluated implementation of single interventions in critical care (12, 13). To date, little is known about current sepsis therapy and the uptake into clinical practice of recent major study results and recommended guidelines. Therefore, we evaluated adherence to seven recommendations in a large, nationwide, and representative sample of German ICUs.

It might be expected that larger, tertiary care institutions, when compared with smaller community hospitals, would adhere more closely to the latest study results; this has rarely been investigated. Therefore, we were careful to include a proportional selection of ICUs in hospitals from five different strata based on size.

Reports suggest that a considerable discrepancy may exist between self-assessment of guideline adherence and actual performance (14–16). Therefore, we interviewed ICU directors in a representative sample of German ICU simultaneously about their frequency of adherence to recommended best practice. This perception of adherence was compared with actual data obtained by audit of patients' medical files.

METHODS

The study was carried out by the German Sepsis Competence Network (SepNet) with 18 regional study centers, a medical coordination center (University of Jena), and a data management and biometry center (University of Leipzig). Data were collected on a cross-sectional, 1-day basis in a representative random sample of German hospitals.

Representative Hospital Sampling. A representative sample, which was stratified by size, was selected from a total of 1,380 hospitals (with a total of 488,727 beds) and 2,075 ICUs (with a total of 19,084 beds). Hospitals were divided into strata with <200, 201–400, 401–600, and >600 beds, respectively (S1–S4). Stratum 5 (S5) comprised university hospitals. A detailed description of the sampling method is given elsewhere (17).

Patients. All patients occupying an ICU bed between 6:00 AM of the study day and 6.00 AM of the following day were screened for the presence of infection, systemic inflammatory response syndrome, and organ dysfunction based on modified consensus criteria (17). Patients whose therapy was withdrawn or withheld were excluded from further analysis.

Recommended Interventions. Based on recently published recommendations by an international panel of intensivists (10) and recent major study results, the group of SepNet investigators selected seven interventions with respect to clinical relevance (Table 1). Two of

these, low-tidal volume (Vt) ventilation in patients with acute lung injury (ALI)/ARDS and glycemic control, are applicable throughout the course of the disease. Therefore, we grouped the results of the audit into time and severity-independent and time and severity-dependent recommendations.

Data Collection and Analysis. Audits were performed by external intensivists from 18 SepNet regional study centers (see Appendix) after prior central training. The auditors first gathered data on adherence to seven best practice interventions through a semistructured interview of the ICU medical director, i.e., the senior intensivist on site who is permanently in charge of local practice in the German system of closed ICUs. In the absence of the ICU director, the deputy was approached. The ICU directors could answer with "always," "frequently," "sometimes," "rarely," or "never" to each practice recommendation. Thereafter, charts of patients who fulfilled the inclusion criteria were reviewed together with the resident physician who in some cases was identical to the medical ICU director.

Patient data were anonymized in the case report forms. Electronic data entry, data management, quality control, and analysis were performed centrally. Data collected from patient documentation included maximal blood glucose levels; maximal documented Vt; administration and dosage of aPC, hydrocortisone, dopamine, and AT, all noted within 24 hrs preceding the audit.

ALI and ARDS as well as predicted body weight (PBW) were defined as described elsewhere (6). Maximum Vt (Vt max) per PBW was calculated over the preceding 24 hrs.

The study was approved by the responsible institutional ethics committees and by the federal data protection commissioner.

Statistical Analysis. We analyzed whether documented practice (i.e., maximal glucose values and Vt max in mL/kg PBW) and perceived adherence (i.e., interview responses) were significantly different across strata (i.e., hospital size). All data were categorical and are reported as absolute or relative frequencies where appropriate. Fisher's exact test was applied for all group comparisons. p values below 0.05 were considered significant. SPSS 11.0.1 (SPSS Inc., Chicago, IL) was used for data analysis.

RESULTS

Patients

Four hundred fifty-four ICUs from a random sample of 310 hospitals were visited, representing 22% of the total number of national ICUs. A total of 3,877 patients were screened for severe sepsis and septic shock. Four hundred fifteen patients met the criteria, representing an estimated total of 1,545 ICU patients with

Table 1. Recommended interventions (treatment goal)

Time and severity independent
  Low-tidal volume ventilation[a]
    (≤6 mL per kg predicted body weight)
  Glycemic control[b] (blood glucose
    4.4–6.1 mmol/L)
Time and severity dependent
  Activated protein C[c]
  Low-dose hydrocortisone
    (200–300 mg/24 hr)[d]
  Non-use of low-dose dopamine to protect
    renal function (≤ 5 μg/kg/min)[e]
  Non-use of antithrombin[f]

[a]Acute lung injury as defined by Pa_{O_2}/F_{IO_2} >200 and <300 mm Hg or acute respiratory distress syndrome as defined by Pa_{O_2}/F_{IO_2} <200 mm Hg; plus bilateral infiltrates on chest x-ray and pulmonary capillary wedge pressure <18 mm Hg and/or no signs of left ventricular failure (6).
[b]Intensive insulin therapy to maintain euglycemia (4.4–6.1 mmol/L) (5).
[c]Usage of activated protein C (3).
[d]Administration of low-dose hydrocortisone (200–300 mg/24 hr) in patients with septic shock (2).
[e]From Ref. (8).
[f]From Ref. (7).

severe sepsis or septic shock on a given day in Germany. In 49 patients, therapy was withdrawn or withheld. The remaining 366 patients in 214 ICUs received full support. One hundred ninety had severe sepsis and 166 had septic shock; in a further ten patients, the presence of septic shock could not be ruled out because of incomplete documentation. Therefore, these patients were not included when patients with severe sepsis and septic shock were analyzed separately.

Intensive Care Units

One hundred eighty-seven ICUs (41.2%) were mixed surgical/medical, 85 (18.7%) were surgical, and 65 (14.3%) were medical; the median number of beds per ICU was 10 (interquartile range, 7–12). Primary specialties of ICU directors were 55.3% anesthesiology, 26.9% internal medicine, 5.7% surgery, and 11.2% others (17). ICUs were distributed among hospital strata as follows: 106 (23.3%) in S1 (≤200 beds), 151 (33.3%) in S2 (200–400 beds), 68 (15.0%) in S3 (401–600 beds), 82 (18.1%) in S4 (>600 beds), and 47 (10.4%) in university hospitals (S5).

Time and Severity-Independent Recommendations

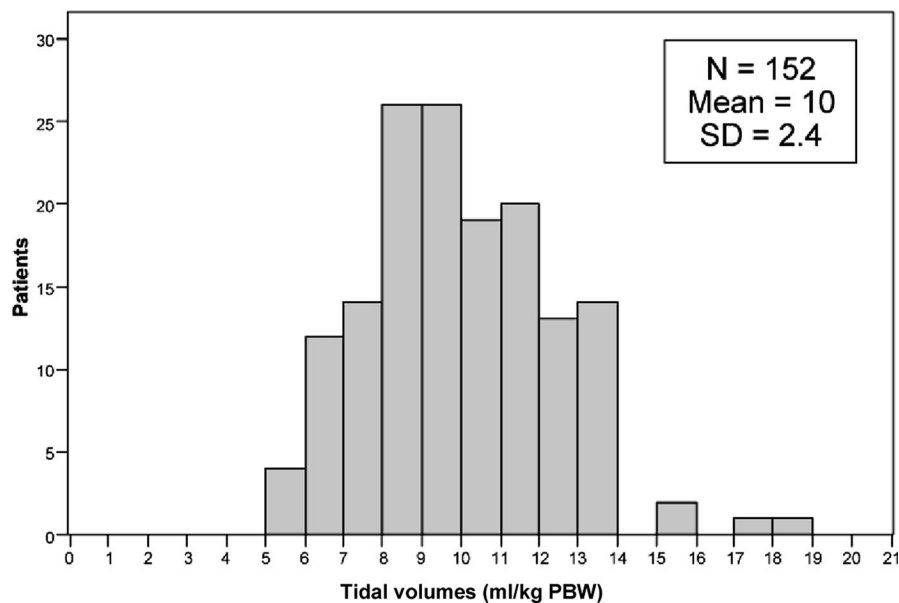*Low-Tidal Volume Ventilation.* One hundred ninety-eight patients with se-

Figure 1. Range of tidal volumes in patients with severe sepsis/septic shock and acute lung injury/acute respiratory distress syndrome. Maximal tidal volumes (mL/kg predicted body weight [*PBW*]) in 152 patients with severe sepsis and septic shock.
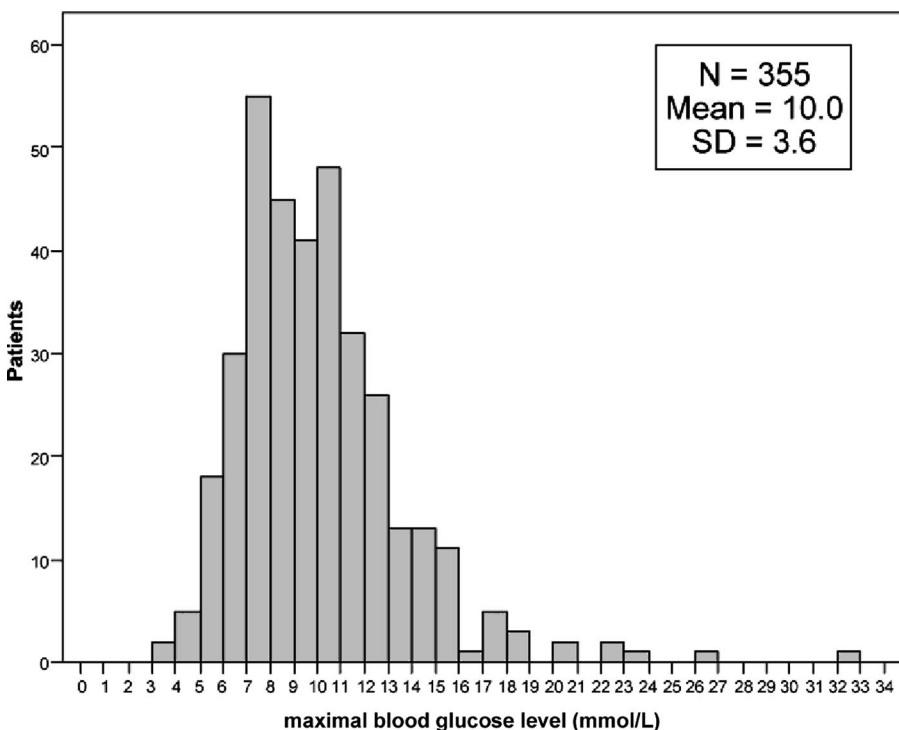

Figure 2. Range of maximal blood glucose levels in patients with severe sepsis/septic shock. Maximal blood glucose levels in 355 patients with severe sepsis and septic shock.

vere sepsis/septic shock were intubated and mechanically ventilated and fulfilled ALI/ARDS criteria. In 46 patients (23.2%), calculation of Vt in mL/kg PBW was not possible due to incomplete documentation. The remaining 152 patients were ventilated with the following Vt: four patients (2.6%) ≤6 mL/kg PBW, 26 patients (17.1%) between 6 and 8 mL/kg PBW, and 122 patients (80.3%) >8 mL/kg PBW. Mean Vt in all 152 patients was 10 ± 2.4 mL/kg PBW (Fig. 1).

Glycemic Control. Three hundred fifty-five patients with severe sepsis/septic shock had documentation of glucose values. Twenty-two of these (6.2%) were euglycemic (4.4–6.1 mmol/L), four (1.1%) had hypoglycemia (< 4.4 mmol/L). One

hundred twenty patients (33.8%) had values ≤8.3 mmol/L, and 235 (66.2%) had values >8.3 mmol/L.

Two hundred seven of 355 patients were receiving insulin therapy, four of these (1.9%) were euglycemic, and two (1.0%) were hypoglycemic. Forty-three patients (20.8%) had values ≤8.3 mmol/L and 164 (79.2%) had values >8.3 mmol/L. Mean maximal blood glucose in all 355 patients was 10.0 ± 3.6 mmol/L (Fig. 2).

Perceived Adherence and Comparison with Documented Practice. Neither documented practice (data not shown) nor perceived adherence to low-Vt ventilation ($p = 0.185$) or glycemic control ($p = 0.1361$) were significantly different across strata. Answers always and frequently were added to denote perceived adherence. A total of 79.9% of ICU directors perceived to adhere to low-Vt ventilation, whereas only 2.6% of patients received Vt ≤ 6 mL/kg PBW. A total of 65.9% of ICU directors perceived to adhere to glycemic control, whereas only 6.2% of patients were euglycemic.

Time and Severity-Dependent Recommendations

Activated protein C was administered to three (0.8%) of 354 patients. Low-dose hydrocortisone (200–300 mg/24 hr) was administered in 48 (30.4%) of 158 patients with septic shock and in 41 (23.3%) of 176 patients with severe sepsis. Three hundred sixteen (94.0%) of 336 patients did not receive AT, 304 (91.8%) of 331 patients did not receive low-dose dopamine. Hospital size or university affiliation had no significant effect on practiced therapy (data not shown).

Perceived Adherence. The answers of ICU directors to how often these measures were practiced in their ICUs are given in Table 2.

Based on their responses, perceived adherence was significantly different across strata with overestimation of aPC use ($p < 0.0001$) and under-estimation of low-dose dopamine use ($p < 0.0002$) and AT use ($p = 0.0421$) in larger and academic hospitals.

DISCUSSION

This study is the first to provide representative data on how glycemic control and low Vt ventilation for ALI/ARDS are used in patients with severe sepsis and septic shock in Germany.

Table 2. Perceived adherence to recommended interventions by hospital size

	All (N = 214)	S1 (n = 30)	S2 (n = 67)	S3 (n = 31)	S4 (n = 53)	S5 (n = 33)
Low-tidal volume ventilation						
Yes (%)	79.9	63.3	76.2	80.7	83.1	97.0
Not answered (%)	2.8	3.3	1.5	0.0	7.5	0.0
Glycemic control						
Yes (%)	65.9	63.3	59.7	71.0	66.1	75.8
Not answered (%)	0.5	0.0	0.0	0.0	1.9	0.0
Low-dose hydrocortisone						
Yes (%)	67.7	63.3	58.2	64.6	71.7	87.9
Not answered (%)	0.5	0.0	0.0	0.0	1.9	0.0
Activated protein C						
Yes (%)	1.4	0.0	0.0	6.5	1.9	0.0
Not answered (%)	1.4	0.0	1.5	0.0	1.9	3.0
Low-dose dopamine						
No (%)	79.0	46.7	73.2	80.6	92.5	97.0
Not answered (%)	0.5	0.0	0.0	0.0	1.9	0.0
Antithrombin						
No (%)	42.5	36.7	39.3	61.3	28.3	57.6
Not answered (%)	0.9	0.0	1.5	0.0	1.9	0.0

Auditors had a written guideline to help them conduct their interviews. They were obliged to adhere to the wording, however, were free to explain if uncertainties remained. The questions were worded as follows: "How often do you use the following measures" followed by the respective recommendation.

Response rates ranged from 97.2% to 99.5% depending on the intervention. Responses "always" and "frequently" were added to denote "yes." In case of non-use recommendations (antithrombin and low-dose dopamine), responses "never" and "rarely" were added to denote "no."

S1–S4, hospital size <200, 201–400, 401–600, and >600 beds, respectively; S5, university hospital.

Moreover, this study surveyed ICU directors' attitudes about whether recent therapy recommendations were put into practice in their ICU. The results show that while most patients did not receive recommended therapies, a majority of ICU directors responsible for these patients reported that they adhered to these recommendations.

We found that 80% of septic patients with ALI/ARDS were ventilated with Vt above 8 mL/kg PBW. These findings are in accordance with other surveys that indicate poor compliance with a strategy found to reduce mortality rates by almost 10%. Retrospective analyses of patient populations with ALI and ARDS showed mean Vt in a similar range between 10.3 ± 2.0 mL/kg PBW to 10.6 ± 2.4 mL/kg PBW (18, 19). A prospective monocenter survey using computerized prompts showed that only 39% of patients were ventilated with a Vt ≤ 7.5 mL/kg PBW 2 days after meeting ALI criteria (20). In a Finnish prospective multicentered survey in 138 ventilated patients with severe sepsis, mean Vt was 7.9 ± 22 mL/kg PBW. Only 15% of women were ventilated with Vt < 8 mL/kg PBW and none with less than 6 mL/kg PBW; 42.0% of men were venti-lated with Vt < 8 mL/kg PBW and 8.2% with less than 6 mL/kg (21).

It is a matter of concern that in our study 23.2% of patients' charts lacked documentation of Vt in mL/kg. In the Finnish survey, Vt could be calculated in 138 of 247 ventilated patients (21). Other investigators have noted incomplete documentation of Vt but to a lesser degree (14). However, documentation and adequate data feedback are important for all measures of quality improvement (14, 22).

Two thirds of patients with severe sepsis or septic shock and 80% of those receiving insulin therapy were hyperglycemic. Only 6% were actually in the euglycemic range within the preceding 24 hrs. This compares with 41.5% of 470 septic patients from a recent prospective multicentered study from Finland, however, without a detailed description of the methods (21). On the other hand, hypoglycemia in our study was rare and probably due to the large proportion of patients who showed a lesser degree of glycemic control. We found that mean glucose levels were 10 mmol/L. This is higher than 8.5 mmol/L found by Krinsley (23) in a group of 800 patients on a medical–surgical ICU before implementa-tion of an intensive glucose management protocol and substantially higher than the recommended threshold by the Surviving Sepsis Campaign (≤ 8.1 mmol/L) (24). Again, perception of practice did not match documented practice: 36% of ICU directors claimed that tight glycemic control was always used on their ICU. However, 13% decidedly stated not to use it at all (never).

Hydrocortisone use, despite high perceived acceptance (68% of ICU directors) and low treatment costs, was found in just 30% of septic shock patients, the only ones for whom it is recommended. Given the potential side effects of steroids in critically ill patients (25), it is of concern that we observed 23% of severe sepsis patients without shock who also received hydrocortisone treatment, although we cannot rule out that some of these patients had been in septic shock before and were being weaned off hydrocortisone.

There may be several reasons for noncompliance with best evidence. A considerable behavioral inertia seems to prevail despite the fact that study results and recommendations have been available in widely read journals from 1999 to 2001 (2–10, 24). This delay in knowledge translation from the time of publication of new evidence to implementation in clinical practice has been noted in other fields (11) as well as in intensive care (26). Our findings seem to rule out simple lack of awareness because interview data show that ICU directors know about and claim to practice these interventions. Various other barriers to change include doubts about the generalizability of study results (27), failure of communication especially in team work (28), differing attitudes of workers in the team (13, 29), threat to physician autonomy (30), and costs for new therapies (31). Concern for patient comfort and safety, as well as confusion regarding the diagnosis, may also affect implementation (32, 33). Each of these barriers may play a role in the interventions we studied.

Many of the recommendations of the Surviving Sepsis Campaign remain controversial. Although each of the interventions has been examined in at least one randomized controlled trial, these trials are not necessarily definitive or applicable to all patients. Therefore, residual controversy may explain some of our results. The use of steroids in septic shock remains controversial, with the recently published CORTICUS data suggesting no

benefit (34). The recommendations for glycemic control in severe sepsis are derived from a study in primarily nonseptic postsurgical patients (5) and the degree of evidence of this single-center study is considered to be low (35). A recent follow-up study in a medical ICU population, (36) as well as a recent multicentered study in patients with severe sepsis (37), did not show the same positive results as the primary study. Such concerns were also raised after the pivotal trial that resulted in the approval of aPC (38).

A striking finding is the gap between perception and clinical practice we observed. In Germany, the ICU director on the closed ICU is responsible for therapy and local practice habits. The reasons for the observed discrepancies are unclear. On one hand, this may represent a variation of the Hawthorne effect, in which the context of an investigation induces participants to improve their performance or, in this case, their perceived performance (39). On the other hand, whenever self-perception and actual practice were compared, they showed poor correlation and self-assessment ranked consistently better than performance (14–16, 29, 40). The evident mismatch between actual delivered care and physician perception of care in this setting raises concern about results obtained from observational surveys.

We observed great discrepancies between perceived and actual interventions for tight glucose control and low Vt ventilation. These require close cooperation of the entire ICU team. Poor agreement among ICU staff regarding responsibilities is a barrier to guideline implementation (13, 29). Under- or overperformance may result if attitudes and goals of care are not shared by the whole team (33, 41) whereas improvement of team communication can decrease the length of stay in the ICU (28).

To our knowledge, this is the first practice survey of ICUs spanning the full range of hospital size. Although the frequency of patients with severe sepsis increased with hospital size (17), practiced as well as perceived adherence to time and severity-independent measures were not associated with hospital size or university affiliation.

The single-point prevalence design has severe limitations regarding the conclusions from interventions which are time and severity-dependent, like hydrocortisone or AT, or require specific eligibility criteria like aPC. We also can not rule out that patients may have received dopamine as vasopressor and were in the process of being weaned off on the day of audit. Likewise, the use of only the lowest or highest values such as the highest blood glucose value over a 24-hr period is admittedly a limited assessment of adherence to the practice of a recommended intervention. Furthermore, the audit of patient physiologic responses, which may remain out of range despite reasonable attempts to address the abnormality, is sometimes insufficient to describe the actual practice of physicians as opposed to using treatment or process measures. These findings reflect practice habits in German ICUs and may not apply to ICUs elsewhere. The strengths of the study include the high degree of representativeness covering hospitals of all sizes and a very large sample size, an interview response rate of over 98%, and external audit by trained intensivist physicians to ensure high-quality data acquisition. The patient sample represented an estimated total of 75,000 patients with severe sepsis for the year 2003 in Germany. We excluded patients for whom therapy was limited or withdrawn and thus can rule out that therapy did not comply with practice guidelines for this reason.

CONCLUSION

In this representative survey of practiced and perceived adherence to practice recommendations for the treatment of severe sepsis on German ICUs, we found that overall compliance was poor but coupled with a strong perception to the contrary in all ICUs regardless of hospital size and university affiliation. It is noteworthy that the majority of patients did not have documented low-Vt ventilation or euglycemia.

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APPENDIX

18 SepNet Regional Study Centers

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