SPECIAL ARTICLE

The effects of implementation of the Surviving Sepsis Campaign in the Netherlands

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ABSTRACT

To reduce unintentional and avoidable adverse events in patients in hospitals in the Netherlands, a patient safety agency (VMS) programme was launched in 2008. Among the VMS topics, the programme 'optimal therapy in severe sepsis', according to the international Surviving Sepsis Campaign (SSC), aims to improve early diagnosis and treatment of sepsis to reduce sepsis mortality by 15% before the end of 2012.

We analysed compliance data submitted to the international SSC database from the Netherlands and compared these data with published international SSC results.

Data of 863 patients, representing 6% of the international data (n=14,209), were used for analysis. In the Netherlands, the resuscitation bundle compliance improved significantly from 7% at baseline to 27% after two years (p=0.002). Internationally, the resuscitation bundle compliance increased significantly from 11 to 31% (p<0.001). In contrast with the international results (18% baseline, 36% after two years), the compliance with the management bundle did not improve (24% baseline, 25% after two years). At baseline, hospital mortality was significantly higher compared with internationally (52 *vs* 37%; p=0.03) and decreased significantly from 52% at baseline to 35% after two years (p=0.049). In the Netherlands, the decrease in mortality was significantly more pronounced after implementation of the SSC (p<0.001).

In the Netherlands, following implementation of the SCC guidelines, compliance with the resuscitation bundle increased significantly, while compliance with the management bundle remained unaffected. This was associated with a significant improvement in hospital survival. In view of the VMS programme and goals, further implementation of the SSC is warranted.

KEYWORDS

Compliance, implementation, management bundle, resuscitation bundle, Surviving Sepsis Campaign

INTRODUCTION

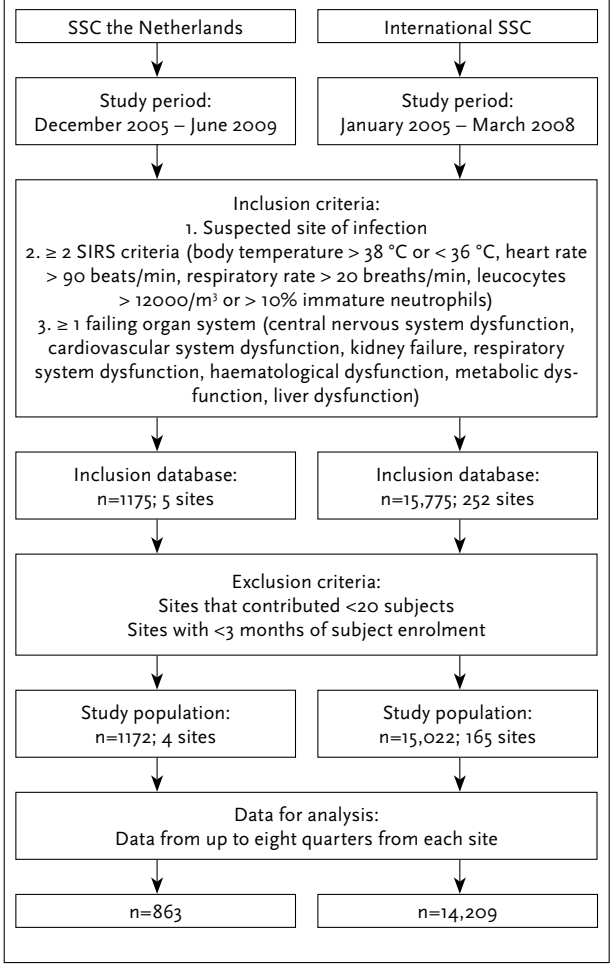
In the Netherlands, it is estimated that 15,500 patients with severe sepsis and 6000 patients suffering from septic shock are annually admitted to an intensive care unit (ICU).[1] With a mortality rate of 30 to 50% severe sepsis/septic shock is the most important cause of death in non-cardiac ICU patients.[2] To provide better guidelines to improve early diagnosis and treatment of severe sepsis and to reduce its mortality, the Surviving Sepsis Campaign (SSC) was launched in 2002.[3,4] The most important SSC guideline recommendations are summarised into two bundles: the resuscitation bundle (six elements to start immediately and to be completed within six hours) and the management bundle (four elements to be completed within 24 hours), published in 2004.[3,5] Since then, the sepsis bundles have been adopted in ICUs,[6-8] emergency departments,[9-11] and nursing wards.[12-18]

In the Netherlands, a national committee and SSC website was established facilitating the possibilities to report bundle compliance and patient outcome to the international database. In addition, the Dutch Association of Hospitals (NVZ), Dutch Federation of University Medical Centres (NFU), Order of Medical Specialists (Order), National Expert Centre for Nursing (LEVV), and the Association for Nurses in the Netherlands (V&VN) initiated the National Patient Safety Agency (VMS: www.vmszorg.nl). VMS aims to reduce the unintentional and avoidable damage in patients in Dutch hospitals by 50% by December 2012. Among other VMS topics, the early diagnosis and treatment of patients with severe sepsis are specific guideline items. The goal of the VMS is to increase compliance with the resuscitation bundle and management bundle elements to an average of 80% and to reduce both the in-hospital mortality and the mortality within 30 days after the diagnosis of severe sepsis by 15% compared with mortality data from 2007.

Recently, the results of the international guideline-based performance programme were published.[12] Patient data and bundle performance data of 14,209 patients from 165 sites worldwide demonstrated that compliance with the SSC bundles was associated with continuous quality improvement in sepsis care and a sustained decrease in mortality.

The aim of our present study was to analyse the data submitted by hospitals in the Netherlands and to compare these results with the international SSC results.

Figure 1. *Study population: SSC database the Netherlands and the international SSC database*



MATERIALS AND METHODS

Study design and population

Patient data and bundle compliance data were collected from December 2005 to June 2009. Inclusion criteria were adult patients (>18 years) admitted to emergency departments, clinical wards, and ICUs with a suspected or proven infection, ≥2 systematic inflammatory response syndrome (SIRS) criteria, and ≥1 failing organ system.[11,18] Participating sites that included ≤20 patients and sites with <3 months of patient enrolment were excluded for this study (*figure 1*).

The global SSC improvement initiative was reviewed and approved by the Cooper University Hospital Institution Review Board. As patient data were obtained anonymously and no patient-related interventions were carried out, no additional approval from an Ethics Committee was necessary.

Data collection and variables

The database used for this study was part of the international SSC database.[12] The relevant patient characteristics included department of admission (from emergency department, from other unit or ICU with other diagnosis), site of infection, diagnosis, and hospital mortality (*table 1*). In accordance to country-specific privacy laws, patient age and gender were not collected in the international SSC database and were therefore also not available for our study.

Performance data of the six resuscitation bundle elements and performance data of the four management bundle elements were collected (*table 2*). The bundle element 'drotrecogin alfa policy' implies that each hospital has formulated its own drotrecogin alfa policy. If the policy is to treat patients with drotrecogin alfa, a patient that did not receive the drug is classified as not compliant. If the policy is not to administer drotrecogin alfa, and the drug is not given, this is viewed as compliant to the local policy. If no formal policy is present, the patients that fulfil the criteria but did not receive the drug are scored as not compliant.

All data were organised by quarter, with the first three months that a site entered patient data into the database

Table 1. *Patient characteristics: the Netherlands versus international*[12]

	Subjects, % the Netherlands (n = 1172)	Subjects, % International (n = 15,022)	P-value*
Admission			
From emergency department	28.2	52.4	<0.001
From other unit	57.8	34.8	<0.001
ICU with other diagnosis	14.1	12.8	-
Diagnosis			
Severe sepsis	24.1	28.5	0.001
Septic shock	75.9	71.5	0.001
Site of infection			
Pneumonia	47.2	44.4	-
Urinary tract infection	9.3	20.8	<0.001
Abdominal	36.5	21.1	<0.001
Meningitis	1.8	1.6	-
Skin	3.6	5.9	0.001
Bone	1.0	1.2	-
Wound	5.0	3.8	0.04
Catheter	3.7	4.1	-
Endocarditis	1.7	1.1	-
Device	1.0	1.1	-
Other infection	5.9	12.7	<0.001

*** Significant differences between patient characteristics from the Netherlands and the international patient characteristics (<0.05)**
ICU; intensive care unit

defined as the first quarter, regardless of when those months occurred. Data from up to eight quarters from each site were used to analyse bundle compliances (*figure 1*). Furthermore, data from the initial quarter (first quarter of data submission from each institution during the two-year data analysis period) and the final quarter (the last quarter of data submission from each institution during the two-year data analysis period) were used to compare changes in compliance with the bundle elements between the initial quarter and the final quarter and to compare the data from the Netherlands with the international data.

Outcome measures

The primary outcome measure was change in compliance with the entire resuscitation bundle and management bundle, and change in the completion of the ten individual bundle elements. We included hospital mortality rate as secondary outcome measure.

Statistical analysis

Data are presented as percentages, odds ratios (ORs) with 95% confidence intervals (95% CI). To analyse the differences in compliance rates between the quarters, both overall and for each of the ten separate elements, we used the Chi-square test. In a similar way, we analysed the differences in compliance rates between the Netherlands and the international results. Due to the relatively small number of patients from the Netherlands, the Fisher's exact test was used to analyse the differences between bundle compliance in the initial quarter compared with the final quarter. To determine the effect of the SSC on the compliance rate of the bundles over the study period we used linear regression analysis. To analyse the impact of compliance with the individual bundle elements, a multivariate logistic regression analysis was performed. A two-tailed p value below 0.05 was considered statistically significant. Data were analysed using SPSS 16.01 (SPSS, Chicago, IL) and Graph Pad V 5.0 (Graph pad Prism software).

Table 2. *Compliance with the resuscitation and management bundle elements in the Netherlands: percentages per quarter (n = 863)*

	Q 1[a] n=62	Q 2[a] n=97	Q 3[a] n=128	Q 4[a] n=117	Q 5[a] n=139	Q 6[a] n=127	Q 7[a] n=93	Q 8[a] n=100
Resuscitation bundle (n)								
1. Measure lactate (863)	71	77	69	76	75	79	86	79
2. Blood cultures before antibiotics (863)	60	52	58	66	58	63	56	70
3. Broad-spectrum antibiotics (863)	50	59	48	47	51	56	50	54
4. Fluids and vasopressors (785)	86	90	80	77	83	81	90	79
5. CVP >8 mmHg (633)	45	55	55	39	50	54	58	58
6. ScvO2 >70% (629)	8	24	25	24	45	37	38	49
Completion of all resuscitation bundle elements (863)	7	12	13	15	18	21	19	27
Management bundle (n)								
1. Steroid policy (628)	63	82	75	77	73	81	86	91
2. Drotrecogin alfa policy followed (863)	73	62	54	50	46	60	57	72
3. Glucose control (863)	50	50	53	53	61	56	59	47
4. Plateau pressure control (634)	88	80	77	78	75	77	83	84
Completion of all management bundle elements (863)	24	17	20	16	17	26	22	25

[a]**Represents each quarter of data submission from each institution during the two-year data analysis period, regardless of total number of each institutions participation.**

RESULTS

Nationwide, 1172 patients from four different general hospitals were included in the SSC database (*figure 1*). Internationally, 15,022 patients from 165 different sites were included. In contrast to the international data, where patients were most likely admitted to the ICU through the emergency department, most patients came to the ICU from the general nursing ward in the Netherlands. Furthermore, significantly more septic shock patients were included (p=0.001) and the sites of infection were not comparable with the international data (*table 1*).

Since analysis of the bundle compliance was limited to the first two years of patient inclusion at each site, the compliance data of 863 patients, representing 6% of the international analysed data, were used for further analysis. For the international bundle compliance analysis, data of 14,209 patients were available (*figure 1*).

CHANGE IN BUNDLE COMPLIANCE

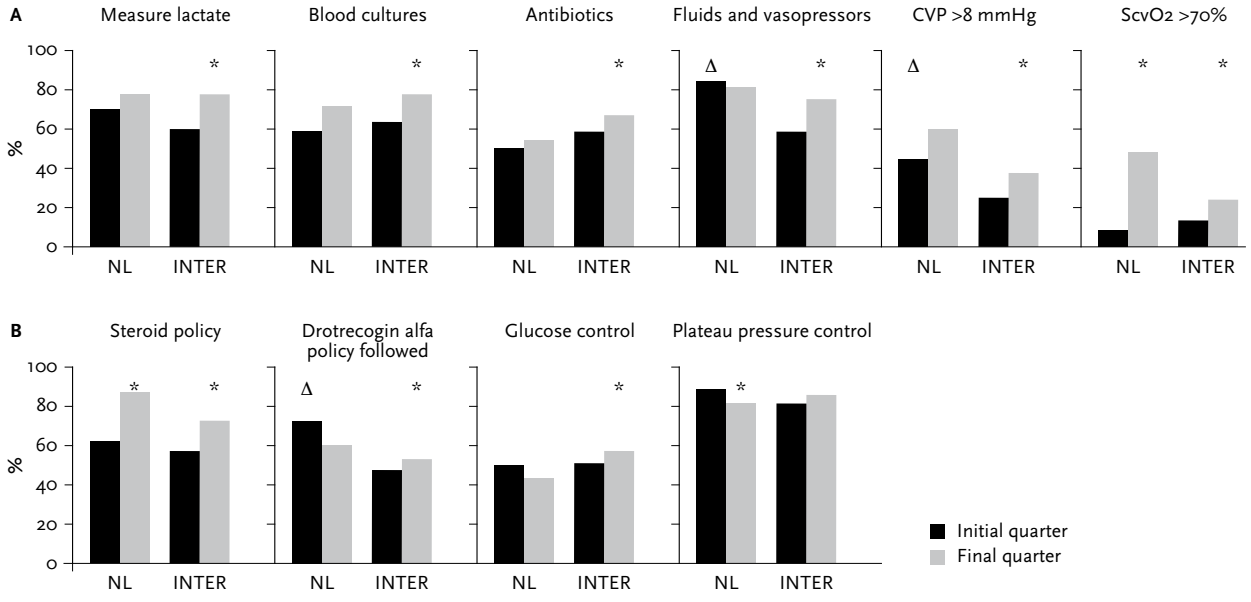
The compliance with the complete bundles and the individual bundle elements by quarter during two years in the Netherlands are represented in *table 2*. During the first quarter, the compliance rate with the resuscitation bundle and management bundle was 7% and 24% respectively, compared with 11% and 18% internationally.[12]

Although in the initial quarter no significant differences in the overall bundle compliance rate between the Netherlands and the international bundle compliance rate were found (resuscitation bundle p=0.27; management bundle p=0.25), the compliance with three individual bundle elements ('administration of fluids and vasopressors', 'achieving a CVP >8 mmHg', and 'drotrecogin alfa policy followed') was significantly higher (p<0.001) in the first quarter in the Netherlands (*figure 2*).

In the Netherlands, the compliance rate with the complete resuscitation bundle improved significantly to 27% (*p*=0.002) by the end of two years, and statistically significant improvement was achieved by the fifth quarter (*figure 3A*). Internationally, the compliance with the resuscitation bundle increased to 31% by the end of two years, achieving statistical significance (p<0.0001) by the second quarter (*figure 3A*). For the management bundle no statistically significant differences in compliance rates between baseline and the end of two years were found in the Netherlands (*figure 3B*), while internationally, the compliance with the management bundle significantly increased from 18 to 36% by the end of two years.[12]

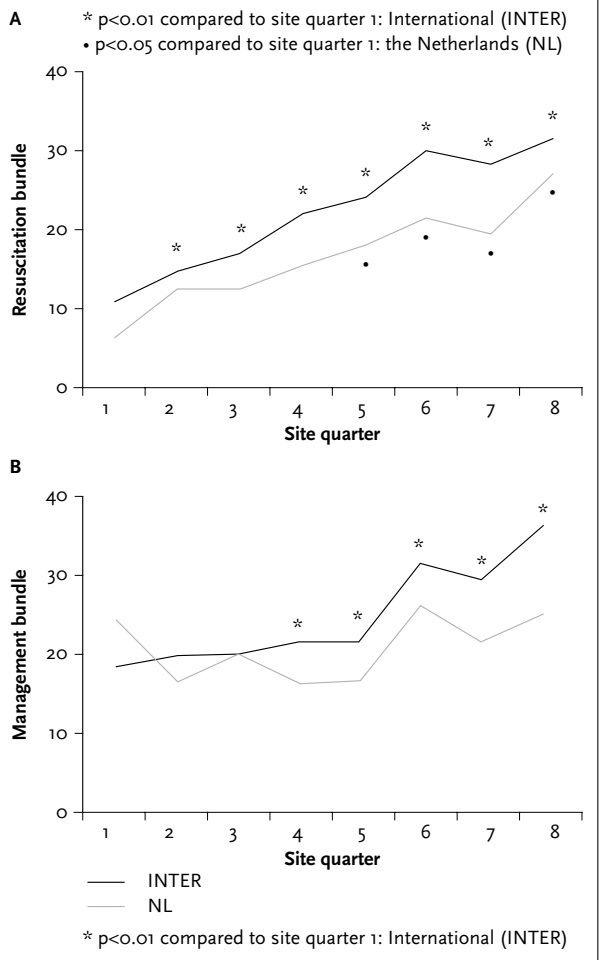
Changes in compliance with the individual bundle elements between the initial quarter and the final quarter are presented in *figure 2*. In the final quarter, a significant improvement in the completion of the individual resuscitation bundle element '$ScvO_2$ >70%'

Figure 2. *Change in compliance with the individual bundle elements in the initial quarter and the final quarter: results from the Netherlands versus the international results*[12]



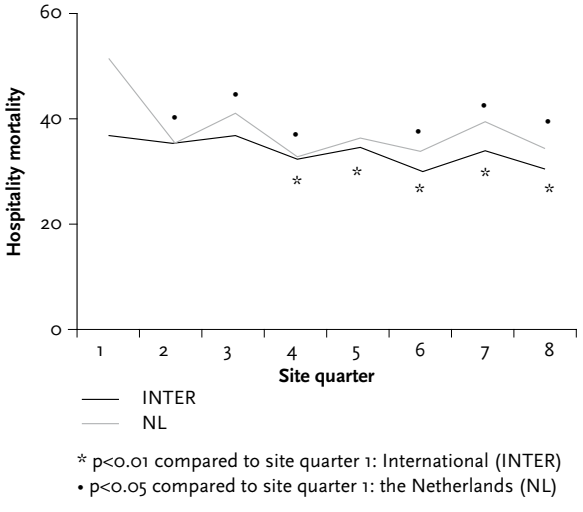
Δ Significant differences between initial quarter the Netherlands (NL) and initial quarter international (INTER).
*** Significant differences between initial quarter and final quarter.**
A, Compliance with the resuscitation bundle elements; B, Compliance with the management bundle elements.

Figure 3. *Change in bundle compliance per quarter over two years of data collection.*



A, Compliance with the complete resuscitation bundle; B, Compliance with the complete management bundle.
Results from the Netherlands (n=863) versus the international results (n=14,209)[12]

Figure 4. *Change in hospital mortality per quarter over two years of data collection.*



Results from the Netherlands (n=863) versus the international results (n=14,209)[12]

(8 to 48%; *figure 2A*), and the management bundle element 'steroid policy' (63 to 88%; *figure 2B*) was attained in the Netherlands. Internationally, the completion of all six resuscitation bundle elements and three out of four management bundle elements improved significantly.[12]

HOSPITAL MORTALITY

Data from the Netherlands showed that the hospital mortality at baseline was 52% and significantly decreased by the end of two years to 35% (p<0.05). Internationally, the baseline hospital mortality was 37% and significantly decreased to 31% (*figure 4*).[12] The hospital mortality at baseline was significantly higher in the Netherlands compared with the international hospital mortality (52 *vs* 37%; p=0.03) and the decrease in hospital mortality in the Netherlands was significantly more pronounced than the achieved decrease in hospital mortality in the international database: 17 *vs* 6% (p<0.001).

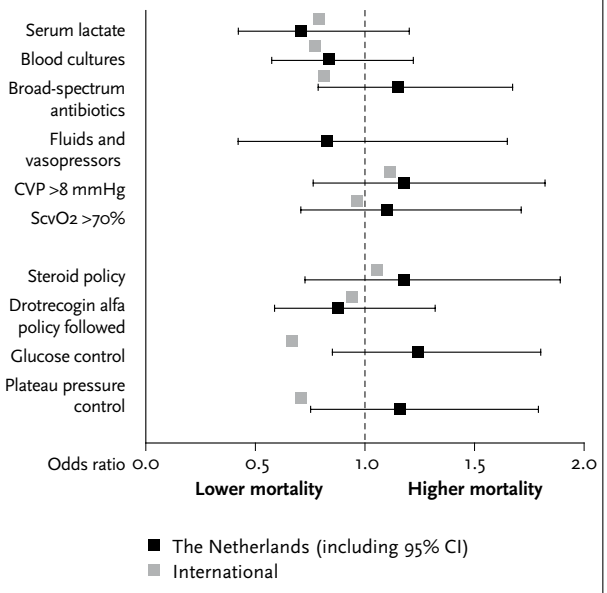
The impact of the individual bundle elements on the unadjusted hospital mortality is represented in *figure 5*. In the Netherlands, the performance of four out of ten bundle elements contributed to a lower hospital mortality, whereas seven out of nine bundle elements contributed to a lower mortality internationally (the impact of the tenth bundle element 'fluids and vasopressors' on hospital mortality was not known). The beneficial impact of 'glucose control' and 'plateau pressure control' found internationally, was not confirmed in the data from the Netherlands as the 95% CIs do not include the international data point.

Independent of changes in time, of all patients who were treated in the Netherlands in compliance with the resuscitation bundle, mortality was borderline significantly lower (31 *vs* 39%, p=0.057) compared with the patients who were not.

DISCUSSION

The main finding of our study is that in the included hospitals in the Netherlands the compliance with the resuscitation bundle significantly improved by implementation of the SSC while, in contrast with the international results, the compliance with the management bundle did not improve. The hospital mortality decreased significantly after implementation of the SSC and compared with the international data, the

Figure 5. *Impact of the individual bundle elements on the unadjusted hospital mortality.*



Results from the Netherlands (n=863) versus the international results (n=14,209)[12]

hospital mortality in the Netherlands was significantly higher at baseline and decreased significantly more after implementation of the SSC.

Although the results of the implementation of the SSC bundles have been reported in several studies,[7,8,15,17] we feel it is of importance to report the compliance rates and outcome results of patients in the Netherlands. Our data demonstrate and confirm that focus on the SSC guidelines can improve the care of patients with sepsis in the Netherlands, and that indeed this is associated with a better survival for sepsis patients. Importantly, our study does not describe the effect of implementation of the SSC bundles in all hospitals and data were only collected until June 2009. Since then, it seems likely that the SSC bundles are implemented in more Dutch hospitals and the bundle compliance further improved because of the performance of several local and national implementation programmes related to the VMS safety programme.

While the compliance with the resuscitation bundle improved significantly, compliance with the management bundle did not. The management bundle consists of therapies with proven efficacy in patients in the ICU.[3] The lack of improvement in therapies given in the ICU is a striking finding, especially since mainly intensivists are involved in the implementation efforts of the SSC guidelines. Therefore, the implementation of these therapies needs further attention.

Overall, and possibly against general belief, the complete adherence to the bundles was poor at baseline. Despite the implementation of the SSC bundles, the completion of all resuscitation bundle elements as well as all management bundle elements occurred only in approximately a quarter of all patients with severe sepsis and septic shock following implementation. Nevertheless, these results are comparable with international results.[6,7,12,20] In Spain, the implementation of the SSC bundles in 59 medical-surgical ICUs was associated with improved guideline compliance and lower hospital mortality. Compliance with the resuscitation bundle was only 13% at postintervention and 7% during long-term follow-up. Compliance with the management bundle was 20% at postintervention and 27% during long-term follow-up.[20] In other studies compliance varies from 4%[6] to 52%.[21] So far, the cost-effectiveness of the implementation of the SSC bundles in the Netherlands is not known. In Spain, a significant reduction in mortality resulted in an increase in costs per patient of only € 1736, mainly attributable to the increased length of stay.[22]

Several limitations of this study need to be addressed. At baseline, mortality was higher in patients in the Netherlands compared with the international database. Because of the significant differences in case mix (including a higher proportion of patients with septic shock, admitted from the ward, and differences in the site of infection) the relevance of this baseline difference in mortality is not clear. Since we had no access to individual patient data in the international database, adjustments could not be made. In addition, the methods used in other studies are not comparable with the methods used in our study and therefore it is not possible to benchmark the results from the Netherlands with the results from a country with a similar high baseline mortality.
Nevertheless, the increase in bundle compliance associated with an improvement in mortality is paramount and in accordance with earlier studies.[7,8,12-14,20-25] The fact that most patients in the Netherlands came from the ward, while most international patients were admitted to the ICU by the emergency department, may be relevant for the initiation of the resuscitation bundle, as sepsis patients are more likely to be treated within the time frames of the SSC bundles than ward patients. For example emergency department nurses can play a vital role in recognising and managing patients with severe sepsis.[11]

Although the literature provides a large number of different strategies to implement innovations such as the SSC bundles, e.g., educational meetings, reminders, and feedback, not one of these implementation strategies seems to be superior to the other and most show mixed results.[9-11,15,26,27] Due to the relatively small number of included patients and different implementation strategies

per hospital, we were unable to evaluate the effects of the applied implementation techniques on bundle compliance. Furthermore, the expanded attention to severe sepsis and septic shock, changes in hospital practice, changes on the level of the organisation, or not SSC related implementation techniques may (also) have contributed to the changes in bundle compliance. Therefore, it is not possible to conclude which factors were (to what degree) responsible for the achieved improvement.

In conclusion, implementation of the SSC bundles and the compliance registration improved insight into the current quality of care for patients with severe sepsis and septic shock. Comparable with other regions of the world, there is room for improvement in the treatment of these patients in the Netherlands. Both national and international improvements in SSC compliance were associated with sustained, continuous quality improvement in sepsis care and better outcome of septic patients, although in an observational study a cause-effect relationship cannot be established. Especially the lack of improvement of the compliance with the management bundle needs further attention. To achieve a higher SSC bundle compliance and better patient outcome in the Netherlands, sepsis education, repeated evaluation of the SSC bundle compliance, and participation in the VMS safety programme is necessary.

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REFERENCES

1. van Gestel GA, Bakker J, Veraart CP, van Hout BA. Prevalence and incidence of severe sepsis in Dutch intensive care units. Crit Care. 2004;8:R153-R162.
2. Angus DC, Linde-Zwirble WT, Lidicker J, Clermont G, Carcillo J, Pinsky MR. Epidemiology of severe sepsis in the United States: analysis of incidence, outcome, and associated costs of care. Crit Care Med. 2001;29:1303-10.
3. Dellinger RP, Carlet JM, Masur H, et al. Surviving Sepsis Campaign guidelines for management of severe sepsis and septic shock. Crit Care Med. 2004;32:858-73.
4. Slade E, Tamber PS, Vincent J-L. The Surviving Sepsis Campaign: raising awareness to reduce mortality. Crit Care. 2003;7:1-2.
5. Dellinger RP, Levy MM, Carlet JM, et al. Surviving Sepsis Campaign: international guidelines for management of severe sepsis and septic shock: 2008. Crit Care Med. 2008;36:296-327.
6. Lefrant JY, Muller L, Raillard A, et al. Reduction of the severe sepsis or septic shock associated mortality by reinforcement of the recommendations bundle: A multicenter study. Ann Fr Anesth Reanim. 2010;29:621-8.
7. Castellanos-Ortega A, Suberviola B, Garcia-Astudillo LA, et al. Impact of the Surviving Sepsis Campaign protocols on hospital length of stay and mortality in septic shock patients: results of a three-year follow-up quasi-experimental study. Crit Care Med. 2010;38:1036-43.
8. Zambon M, Ceola M, Meida-de-Castro R, Gullo A, Vincent JL. Implementation of the Surviving Sepsis Campaign guidelines for severe sepsis and septic shock: we could go faster. J Crit Care. 2008;23:455-60.
9. Baldwin LN, Smith SA, Fender V, Gisby S, Fraser J. An audit of compliance with the sepsis resuscitation care bundle in patients admitted to A&E with severe sepsis or septic shock. Int Emerg Nurs. 2008;16:250-6.
10. De Miguel-Yanes JM, Andueza-Lillo JA, Gonzalez-Ramallo VJ, Pastor L, Munoz J. Failure to implement evidence-based clinical guidelines for sepsis at the ED. Am J Emerg Med. 2006;24:553-9.
11. Tromp M, Hulscher M, Bleeker-Rovers CP, et al. The role of nurses in the recognition and treatment of patients with sepsis in the emergency department: A prospective before-and-after intervention study. Int J Nurs Stud. 2010;47:1464-73.
12. Levy MM, Dellinger RP, Townsend SR, et al. The Surviving Sepsis Campaign: results of an international guideline-based performance improvement program targeting severe sepsis. Crit Care Med. 2010;38:367-74.
13. Nguyen HB, Corbett SW, Steele R, et al. Implementation of a bundle of quality indicators for the early management of severe sepsis and septic shock is associated with decreased mortality. Crit Care Med. 2007;35:1105-12.
14. Shorr AF, Micek ST, Jackson WL, Jr., Kollef MH. Economic implications of an evidence-based sepsis protocol: can we improve outcomes and lower costs? Crit Care Med. 2007;35:1257-62.
15. Micek ST, Roubinian N, Heuring T, et al. Before-after study of a standardized hospital order set for the management of septic shock. Crit Care Med. 2006;34:2707-13.
16. Gerber K. Surviving sepsis: a trust-wide approach. A multi-disciplinary team approach to implementing evidence-based guidelines. Nurs Crit Care. 2010 May;15(3):141-51.
17. Carter C. Implementing the severe sepsis care bundles outside the ICU by outreach. Nurs Crit Care. 2007;12:225-30.
18. Teles JM, Silva E, Westphal G, Filho RC, Machado FR. Surviving sepsis campaign in Brazil. Shock. 2008;30 Suppl 1:47-52.
19. Levy MM, Fink MP, Marshall JC, et al. 2001 SCCM/ESICM/ACCP/ATS/SIS International Sepsis Definitions Conference. Crit Care Med. 2003;31:1250-6.
20. Ferrer R, Artigas A, Levy MM, et al. Improvement in process of care and outcome after a multicenter severe sepsis educational program in Spain. JAMA. 2008;299:2294-303.
21. Gao F, Melody T, Daniels DF, Giles S, Fox S. The impact of compliance with 6-hour and 24-hour sepsis bundles on hospital mortality in patients with severe sepsis: a prospective observational study. Crit Care. 2005;9:R764-R770.
22. Suarez D, Ferrer R, Artigas A, et al. Cost-effectiveness of the Surviving Sepsis Campaign protocol for severe sepsis: a prospective nation-wide study in Spain. Intensive Care Med. 2011;37:444-52.
23. El Solh AA, Akinnusi ME, Alsawalha LN, Pineda LA. Outcome of septic shock in older adults after implementation of the sepsis 'bundle'. J Am Geriatr Soc. 2008;56:272-8.
24. Patel GP, Elpern EH, Balk RA. A campaign worth joining: improving outcome in severe sepsis and septic shock using the Surviving Sepsis Campaign guidelines. South Med J. 2007;100:557-8.
25. Patel GW, Roderman N, Gehring H, Saad J, Bartek W. Assessing the effect of the Surviving Sepsis Campaign treatment guidelines on clinical outcomes in a community hospital. Ann Pharmacother. 2010;44:1733-8.
26. Ziglam HM, Morales D, Webb K, Nathwani D. Knowledge about sepsis among training-grade doctors. J Antimicrob Chemother. 2006;57:963-5.
27. Tromp M, Bleeker-Rovers CP, van Achterberg T, Kullberg BJ, Hulscher M, Pickkers P. Internal medicine residents' knowledge about sepsis: effects of a teaching intervention. Neth J Med. 2009;67:312-5.