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Article Review

Health-related quality of life in sepsis survivors

Qualidade de vida relacionada à saúde em sobreviventes à sepse

Calidad de vida relacionada con la salud en sobrevivientes de sepsis

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Objective: to identify the evidence available on the changes in health-related quality of life of patients who survived an episode of sepsis. **Methods**: the LILACS, MEDLINE CINAHL Cochrane Library, Web of Science and Scopus databases were used. **Results**: of the 1729 publications identified, 16 were included in the study. Patients who survived an episode of sepsis presented reduction in the quality of life when compared to the general population or to other groups of patients who had an episode of severe illness, even after long periods following discharge from hospital, independently of the scale used, of the patients' clinical characteristics, and their country of origin. The changes in the quality of life are mainly related to the physical and mental aspects. **Conclusion**: knowledge of the changes in quality of life of patients who survived an episode of sepsis demonstrates the need for long-term monitoring of these patients.
Descriptors: Quality of Life; Sepsis; Mortality.

Objetivo: identificar as evidências disponíveis sobre as alterações da qualidade de vida relacionada à saúde de pacientes que sobreviveram a um episódio de sepse. **Métodos**: foram utilizadas as bases de dados LILACS, MEDLINE, CINAHL e Biblioteca Cochrane, Web of Science e Scopus. **Resultaos**: das 1729 publicações identificadas, 16 foram incluídas no estudo. Pacientes que sobreviveram a um evento de sepse apresentaram diminuição da qualidade de vida quando comparados à população geral ou a outros grupos de pacientes que tiveram um episódio de doença grave, mesmo depois de longos períodos pós-alta hospitalar, independente da escala utilizada, das características clínicas dos pacientes e do país de origem. As alterações da qualidade de vida estão relacionadas principalmente aos aspectos físicos e mentais. **Conclusão**: o conhecimento das alterações na qualidade de vida dos pacientes que sobreviveram a um episódio de sepse demonstra a necessidade de acompanhamento em longo prazo desses pacientes.
Descritores: Qualidade de Vida; Sepse; Mortalidade.

Objetivo: identificar evidencias disponibles sobre cambios en la calidad de vida relacionada con la salud de pacientes sobrevivientes a un episodio de sepsis. **Métodos**: se utilizaron las bases de datos LILACS, MEDLINE, CINAHL y Cochrane Library, *Web of Science y Scopus*. **Resultados**: de las 1.729 publicaciones identificadas, 16 fueron incluidas en el estudio. Pacientes que sobrevivieron a un evento de sepsis presentaron disminución en la calidad de vida en comparación con la población en general o de otros grupos de pacientes que tuvieron episodio de enfermedad grave, incluso después de períodos posteriores al alta hospitalaria, independientemente de la escala utilizada, características clínicas de pacientes y país de origen. Cambios en la calidad de vida están principalmente relacionados con aspectos físicos y mentales. **Conclusión**: el conocimiento de cambios en la calidad de vida de pacientes sobrevivientes a un episodio de sepsis señala necesidad de seguimiento a largo plazo de estos pacientes.
Descriptores: Calidad de Vida; Sepsis; Mortalidad.

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Introduction

Sepsis is a worldwide health problem, and is the main cause of death in Intensive Care Units. It presents with different levels of severity, depending on the characteristics of the patient and on the time which has passed since its initial manifestations. Severe sepsis corresponds to sepsis associated with organ dysfunction, while septic shock is characterized by persistent hypotension which does not improve following volemic replacement, the administration of vasoactive agents being necessary in order to maintain arterial pressure[1]. In the United States, more than 1 million hospitalizations took place due to sepsis in 2007, with a mortality rate of 29%[2]. The Brazilian Sepsis Epidemiological Study (BASES) showed that the mortality rates of patients with systemic inflammatory response syndrome, sepsis, severe sepsis and septic shock are of 24.2%, 33.9%, 46.9% and 52.2%, respectively[3].

Although the results of the outcome of the clinical situation in the short term, such as hospital mortality, are of extreme importance, they do not enable one to evaluate how the critical illness and the intensive care affect health and well-being subsequent to discharge from hospital. Among sepsis survivors, the mortality rate remains high in the first year following discharge from hospital, it being the case that the increased risk of death can persist for approximately five years subsequent to hospitalization[4-6]. During sepsis, the infection initiates an inflammatory process which compromises the organism's defenses, resulting in the alteration of the peripheral metabolism, the coagulation process, and hemodynamic stability, leading to multiple organ failure and death. The patients who survived sepsis may continue to suffer from compromising of the organic functions, which results in symptoms such as dyspnea, fatigue and depression, leading to physical, social and emotional harm which results in a reduction of these patients' health-related quality of life[7].

Considerations regarding health-related quality of life are important in the context of critical care, as the clinical interventions can maintain life, but the resulting state of health may be evaluated as worse than death[8]. Hence, this knowledge is necessary for supporting the health professionals', patients' and family members' evaluation of clinical and economic benefits of new interventions, as well as the patient's perspectives.

In the light of the variety of specific characteristics which interfere with and are related to the septic patient, there is a need to seek, in the literature, these patients' main changes in health-related quality of life subsequent to discharge from hospital. This study's results could contribute such that the nursing team, as well as the multidisciplinary team, may acquire reliable elements which make it possible to support proposals for interventions directed towards improvement of septic patients' health-related quality of life. The present study's objective, therefore, was to identify the evidence available in the literature regarding the aspects of health-related quality of life of patients who survived an episode of sepsis.

Method

In order to develop this integrative review, six stages were undertaken: identification of the theme of the review, search for the studies in the literature, categorization of the studies, evaluation of the studies, interpretation and critical evaluation of the results, and presentation of the integrative review[9].

For the selection of the articles, the LILACS, MEDLINE, CINAHL, Cochrane Library, Web of Science and Scopus databases were consulted, using the controlled descriptors: sepsis, septic shock and quality of life; and the non-controlled descriptor: severe sepsis. In addition, a manual search of articles was undertaken based on the list of references of the publications found. The search was undertaken in March 2014. This study's guiding question was: what is the evidence available relating to aspects of health-

related quality of life of patients who survived an episode of sepsis?

The inclusion criteria adopted were: original articles which addressed health-related quality of life or perceived state of health of patients who survived an episode of sepsis, severe sepsis, or septic shock, published in journals in the English, Spanish, French or Portuguese languages, and without delimitation of the publication period. The exclusion criteria were: studies undertaken with individuals aged below 18 years old or which evaluated the effect of an episode of sepsis in childhood regarding health-related quality of life in adulthood, publications which assessed the effects of specific treatments for sepsis in comparison with the standard treatment, regarding health-related quality of life, and publications which were not categorized in the classification of the level of evidence used[10].

A total of 1,729 articles were identified, of which 42 were preselected through reading of the titles and abstracts. Twenty-six articles were excluded, for the following reasons: 20 did not address the theme of the review, three were in languages other than those established in the method, one was not available for consultation in physical or electronic databases, one was an editorial, and one was an abstract. As a result, 16 articles were included in this review.

In order to extract data from the articles, an instrument elaborated by the authors was used, based in the literature[11]. The publications selected were classified according to the methodological outline and level of evidence, and the summary of the data is presented descriptively.

Results

A total of 16 articles was analyzed in full, with nine being found in the Web of Science, MEDLINE and Scopus databases[4,12-19], one article found in the Web of Science, MEDLINE, Scopus, LILACS and CINAHL databases[6], one article was found in the Web of Science, Scopus, LILACS and CINAHL databases[20], one article was found in the Web of Science, MEDLINE and CINAHL databases[21], one article was found in the Web of Science and MEDLINE databases[5], one article was found only in the Scopus database[22] and one was located through a manual search in publications of the area studied[23].

The publications found were published between 1995 and 2013. Of the 16 publications, 10 were European (62.5%)[4,13-15,17,19,21-24], three were North-American (18.7%)[5,12,16], two were Latin American (12.5%)[6,20] and one was undertaken in Asia (6.3%)[18]. In relation to language of publication, 14 articles were published in English[4,5,12-19,21-24] and two, in Portuguese[6,20].

All the publications presented observational designs, characterizing them as transversal[4-6,12,13,15,16,18-23] and longitudinal studies[14,17], with level of evidence IV. The number of participants who had survived sepsis in the studies varied from ten[4] to 156[15]. The time of evaluation of health-related quality of life following discharge from hospital was also different between the studies, varying from two[21] to 117[6] months following discharge from hospital.

In relation to the instruments used for evaluating health-related quality of life, the SF-36 – Medical Outcomes Survey - 36 items (SF-36) was used in eight studies[5,6,12,14,17,19,23,24], and the EuroQol EQ-5D was used in six studies[4,13,15,19,20,24], while other instruments were used in only one study, such as the World Health Organization Performance Score[22], St George`s Respiratory Questionnaire[5], Patrick's Perceived Quality of Life Scale[12], The Adult Neuropsychological History Form and The Symptom Survey[16] and the Medical Outcomes Survey - 12 items (SF-12)[24]. The summary of the articles included in this integrative review is presented in Figure 1.

Author/Year	Results and Conclusions
McLauchlan et al[22]	Fifteen months after discharge from hospital, 59% of the patients (n=24 of 59) were able to undertake self-care and were independent. Older adults return to their previous state of health more slowly and incompletely. Sepsis survivors have a health-related quality of life which justifies the expenditure on the treatment.
Davidson et al[5]	Patients with sepsis and acute respiratory dysfunction syndrome (n=27) had health-related quality of life which was significantly inferior to the patients with trauma and acute respiratory dysfunction syndrome (n=46). The low scores for health-related quality of life were observed in the domain of functional capacity (57.0±25.0 *vs.* 65.0±25.0) of the SF-36 and pulmonary symptoms of the St George`s Respiratory Questionnaire (41.0±20.0 *vs.* 53.0±24.0), 25 months subsequent to discharge from hospital. Survivors of sepsis and acute respiratory dysfunction syndrome present reduction of health-related quality of life in comparison with controls, mainly in the domain of functional capacity and pulmonary symptoms.
Heyland et al[12]	The survivors of sepsis (n=30) had lower scores in relation to the general population in the domains of functional capacity (48.3±32.7 *vs.* 72.3±23.3), physical aspects (45.0±43.2 *vs.* 68±34.0), general state of health (55.9±20.4 *vs*. 64.5±20.3), vitality (46.7±23.8 vs. 58.8±21.0) and social aspects (65.8±32.0 *vs.* 80.6±22.7). The health-related quality of life of sepsis survivors, 16 months after discharge from hospital, was significantly lower than that of the general population.
Granja et al[13]	A higher percentage of sepsis survivors reported fewer problems than controls only in the dimension of anxiety/depression (56% vs. 39%). Evaluation of health-related quality of life, using the EuroQol-5D, six months after discharge from the intensive care unit, indicated that, among survivors of severe sepsis and septic shock, health-related quality of life is similar to that of survivors of critical illnesses admitted without sepsis.
Jagodič et al[4]	Almost 60% of the patients from the sepsis group (n=10) reported problems in the usual activities, 56% mentioned pain and 56% had mobility problems. In contrast, most patients (74%) reported almost not having problems with self-care. Depression and anxiety were more frequently detected in the trauma group (n=29), but the difference in relation to the sepsis group was not significant (p= 0.1). There was no difference in health-related quality of life in the five dimensions of the EuroQol-5D among the groups.
Hofhuis et al[14]	In the patients who had survived sepsis (n=95), health-related quality of life declined significantly during their stay in the intensive care unit, and improved in the six months following discharge from hospital for the domains of social aspects (53.0±26.5 *vs*. 80.3±23.8), vitality (30.2±16.2 *vs*. 59.8±21.5), emotional aspects (56.7±45.0 *vs.* 72.0±42.0) and mental health (57.1±11.4 *vs*. 69.8±15.4). In relation to the pre-admission values, six months subsequent to discharge, the score had improved for the domains of physical aspects (39.2±44.4 *vs.* 56.4±47.4), functional capacity (59.4±33.4 vs. 69.0±32.9) and general state of health (46.9±24.1 *vs*. 58.1±30.5). The domain of mental health underwent a decline upon discharge (57.1±11.4), but after six months had returned to the values of the general Dutch population (69.8±15.4 *vs*. 76.9±17.9). The scores of the SF-36 were lower than that of the general population in six of the eight dimensions, with the exception of social aspects (80.3±23.8 *vs.* 82.0±24.6) and pain (83.1±25.2 *vs.* 70.5±24.6). In spite of the patients presenting improvement in health-related quality of life following discharge from hospital, this is incomplete in comparison with the pre-admission state and with the general Dutch population.

Figure 1a – Summary of the studies included in the integrative review, by design, main results and conclusion

Author/Year	Results and Conclusions
Poulsen et al[23]	The patients who survived sepsis (n=70) obtained lower scores in the summary of the physical components (36.0, (29.0-43.0)) in comparison with the controls (n=494) from the general population adjusted for age and sex (51.0 (42.0-55.0)). A similar result was observed in patients without comorbidity before inpatient treatment in the intensive care unit (34.0 (27.0-39.0)). According to 81% of the patients, the loss of muscle mass was mainly responsible for the physical harm, and the number of people who needed home care doubled.
Karlsson et al[15]	The survivors of severe sepsis (n=156), when compared with the reference values adjusted for age and sex, presented worse results on the EuroQol summary index (70.0 (54.0-89.0) *vs.* 86.0 (81.0-88.0)) and on the EuroQol *Visual Analog Scale* (58.0 (35.0-75.0) *vs.* 70.0 (68.0-77.0)). The mean calculated QALY following severe sepsis was 10.9 (9.7-12.1), and the costs calculated for QALY were 2,139 Euros for the survivors and non-survivors. The health-related quality of life was lower after severe sepsis than prior to the critical illness as evaluated by the EuroQol-5D.
Lazosky et al[16]	According to the Sickness Impact Profile Individual form, greater difficulty with work was reported in the sepsis group (n=8) (24.5±31.1) than in the control group (n=15) (2.2±8.47). When the retired individuals were excluded from the analysis, the individuals in the sepsis group presented high global scores in the Sickness Impact Profile Individual form than the control group (13.6±3.5 vs. 4.4±3.6). In relation to the control group, the individuals who survive the situation of sepsis present compromise of the health-related quality of life up to four years subsequent to discharge from hospital.
Westphal et al[6]	There was significant compromise of health-related quality of life in the group which survived sepsis (n=36) in relation to the control group (n=36) in the domains: functional capacity (62.0 *vs*. 93.0), vitality (51.0 *vs.* 60.0), mental health (63.0 vs. 75.0), pain (57.0 *vs.* 76.0), general health status (55.0 vs. 56.0), physical aspects (67.0 *vs.* 85.0) and social aspects (76.0 *vs.* 89.0). Severe sepsis or septic shock can result in significant compromise of health-related quality of life.
Nesseler et al[17]	The scores of the SF-36 were lower in the sepsis group prior to hospitalization than in the French population in the domains of functional capacity (47±37 vs. 84±21), physical aspects (37±45 vs. 81±32), pain (43±36 vs. 73±24), general state of health (56±10 vs. 69±19), vitality (36±25 vs. 60±18), social aspects (64±34 vs. 82±21), emotional aspects (48±47 vs. 82±32) and mental health (55±23 vs. 69±1). Six months subsequent to discharge from hospital, the patients who had survived sepsis (n=46) still presented health-related quality of life inferior to that of the general French population in the domains of functional capacity (58±29 vs. 84±21), physical aspects (37±42 vs. 81±32), pain (55±29 vs. 73±24), general state of health (56±10 vs. 69±19), vitality (43±21 vs. 60±18), social aspects (62±32 vs. 82±21), emotional aspects (47±42 vs. 82±32) and mental health (59±21 vs. 69±1). Although the values of some domains of the SF-36 had improved six months after the beginning of the situation of septic shock, health-related quality of life remained lower than in the general French population.
Rosendahl et al[21]	In comparison with the German population, patients (n=55) and wives (n=55) reported worse quality of life related to mental health (pacient = 41.2± 13.4; wife = 42.7±11.78) (d= −1.43, 95%CI −2.18 to −0.68 for patients; d= −1.16, 95%CI −1.79 to −0.53 for wives). The patients presented greater scores for exhaustion (d= −1.7, 95%CI −2.74 to −0.69) and reported significantly impaired quality of life related to physical health (d= −1.60, 95%CI −2.36 to −0.85) in comparison with the general German population. The quality of life related to mental health was significantly related between the ill persons and spouses (p= 0.002). Patients and spouses act as emotionally interdependent systems, with physical and mental health related.
Contrin et al[20]	Patients who survived sepsis (n=50) and were aged over sixty years old mentioned significantly more problems related to mobility (64.7% vs. 40%), selfcare (66.7% vs. 25%), the usual activities (60.0% vs. 14.3%), pain and discomfort (69.5% vs. 40.9%) and anxiety and depression (71.4% vs. 28.6%).
Zhang et al[18]	No difference was observed between the sepsis survivors (n=42) and the critically-ill patient (n=33) in the eight domains of the SF-36. Compared with the community, the sepsis survivor presented worse values in the domains of functional capacity (79.1±21.2 vs. 88.4±13.69), physical aspects (64.4±43.2 vs. 72.5±40.4), vitality (71.1±18.9 vs. 78.7±15.1), social aspects (83.6±24.5 vs. 91.3±14.5), emotional aspects (78.6±39.5 vs. 91.5±23.7) and mental health (77.4±20.3 vs. 85.2±13.5). Compared with the general Chinese population, the sepsis survivor had a reduction in the domain of physical aspects (64.4±43.2 vs. 80.5±21.9). The patients with sepsis had health-related quality of life which was comparable, in the long term, with the critically-ill controls, but lower than that of those living in the community.
Cuthbertson et al[19]	In patients who survived sepsis (n=67) the physical component of the SF-36 obtained significantly worse scores than that of the control population in three and a half (41.8±11.8 vs. 50.0±10.0) and five years (44.8±12.7 vs. 50.0±10.0) following discharge from hospital. There was no difference in the mental component in five years. Patients who had severe sepsis presented significantly lower health-related quality of life in comparison with the general population, but scores of the mental component of the SF-36 were only slightly below that of the general population up to five years after the severe sepsis.
Orwelius et al[24]	The patients who survived sepsis (n=91) did not present difference in the health-related quality of life six months after discharge from the intensive care unit, in comparison with patients admitted to ICU without sepsis (n=222). The health-related quality of life of patients receiving inpatient treatment with sepsis was not significantly different from those hospitalized without sepsis, six months subsequent to discharge from hospital.

Figure 1b – Summary of the studies included in the integrative review, by design, main results and conclusion

Discussion

This review regarding health-related quality of life of individuals who survived an event of sepsis observed that patients who developed sepsis presented reduction in health-related quality of life, even after long periods subsequent to discharge from hospital, regardless of the scale used, the study population, and the country of origin.

In order to understand the impact of the septic event on health-related quality of health, various studies have used a control group and compared the health-related quality of life of the sepsis survivor with that of the general population[6,12,14,15,17,19,23]. Patients with sepsis presented inferior health-related quality of life in comparison with the general population of North America[12], Holland[14], Finland[15], Denmark[23], France[17], Ireland[19] and Brazil[6]. However, comparing the patients who survived an episode of sepsis with the general population can result in biases, as an episode of serious illness and hospitalization in an intensive care unit can leave sequelae, be these physical or mental.

This issue may be partially resolved when one compares health-related quality of life of the patient who survived sepsis with that of another group of critically-ill patients. When the health-related quality of life of patients who survived sepsis was compared with that of patients who had an episode of severe heart disease, it was observed that the patients with sepsis presented more sensory, physical and behavioral symptoms than the cardiac patients[16].

Similar results were obtained when health-related quality of life of sepsis survivors was compared with that of patients who suffered trauma and were hospitalized in the intensive care unit[5]. In this study, the sepsis survivors presented lower scores in the domains of general state of health and vitality of the SF-36 instrument. These results indicated that the reduction in health-related quality of life, following hospitalization in the intensive care unit for sepsis, cannot be attributed only to the treatment in the intensive care, but is related to the sequelae of the sepsis. One Brazilian study demonstrated that patients who survived an episode of sepsis mentioned significantly more problems related to mobility, self-care, usual activities, pain and discomfort and anxiety and depression than patients who had been hospitalized in the intensive care unit, but without sepsis[20].

In various of the studies analyzed, the sepsis survivors presented reduction in the physical domain of health-related quality of life[6,12,14,16,23]. The loss of physical function in the critically-ill patient may be related to various factors, such as prolonged immobilization[25-26], generalized inflammation[27], insufficient nutrition and the administration of corticoids[28]. The patients who develop sepsis are exposed to all the potential causes and may, therefore, experience a profound impairment of their physical function subsequent to discharge from hospital.

Besides the physical changes, changes related to the emotional component are also observed[5,6,14-16,23]. The cognitive, emotional and sensory changes found in the sepsis survivors may be related to encephalopathy observed in these patients. One study from the 1980s, which evaluated the brains of twelve patients who died as a result of sepsis, demonstrated a series of abnormalities, including micro-abscesses, particularly in the cerebral cortex, petechiae, and microscopic ischemic lesions[29]. Sepsis can entail irreversible damage to the brain due to neuronal death resulting from regional ischemias, the excess production of free radicals, glutamate excitotoxicity and cellular apoptosis[30].

One important aspect to be observed is that, in spite of the marked decline in health-related quality of life subsequent to the situation of sepsis, there is a gradual improvement in the months which follow discharge from the intensive care unit. The sequential evaluation of health-related quality of life with the SF-36 instrument demonstrated reduction in the domains of functional capacity, physical aspects, general state of health, vitality and social aspects[14].

In spite of the progressive improvement, up to 31 months subsequent to discharge from hospital, it was possible to observe significant impairment in the physical and mental components when compared to the population which had not had sepsis[6].

In addition to the consequences of sepsis relating to the patient's health-related quality of life, sepsis and its sequelae can affect the health-related quality of life of people who directly coexist with the patient. One study which evaluated the health-related quality of life of the sepsis survivor and his partner identified that patients and spouses showed hidden or clinically relevant symptoms of anxiety and depression, and that approximately two thirds of both reported symptoms of posttraumatic stress[21].

One of the limitations of the studies which evaluated the health-related quality of life of patients who survived an episode of sepsis is the losses between the number of patients who were discharged from hospital and those who survived up until the time of the interview[6,23]. As a result, some works had a small number of participants, which may have led to an underestimate of the real effect of the sepsis on the survivor's health-related quality of life[4,16]. In addition to this, in some studies, many potential participants did not respond to the questionnaires because they did not have the physical or psychological conditions; had these individuals been included in the analysis, the data would probably have been even more alarming[5,6,12,23].

An aspect which is important to consider in patients with sepsis is the syndrome's costs. In Brazil, the mean cost of hospitalizing a patient with septic shock is US$9,632.00, with mean hospitalization of 9 days[31]. Furthermore, on average, the life of a patient who survives sepsis is reduced by 2.6 years and half of the individuals who survive an episode of sepsis are unable to return to work, which generates extra burdens for the family members and for the State[23].

In general, the years lived, adjusted by health-related quality of life, are considered an important measure regarding the efficacy of the healthcare, although the number of studies remains very limited[32]. A study undertaken in 2009 provided a new perspective on the measurements of health-related quality of life in survivors of severe sepsis, using the EQ-5D score[15]. The authors' main conclusion was that health-related quality of life was lower, but reasonable for the patients who survived sepsis.

Although the majority of the studies demonstrate reduction in the health-related quality of life of the patients who survived sepsis, four studies obtained different results[4,13,22,24]. In one study which compared health-related quality of life of patients who survived an episode of sepsis with critically-ill patients without sepsis, no difference was observed between the sepsis group and the control group, apart from the dimension of anxiety/depression, in which the sepsis group obtained better performance[13]. In this study, more losses occurred in the sepsis group compared with the control group, which may have induced biases. A similar result was obtained in a study in which health-related quality of life of patients hospitalized in the intensive care unit with sepsis was compared with that of patients hospitalized as a result of trauma but without sepsis[4]. One of the weak points of this study was the large number of losses in the two groups, which resulted in few participants evaluated, 24 months subsequent to discharge from hospital.

The careful evaluation of health-related quality of life is essential in the assistance to the health professionals, to the patient, and to his family, as new interventions are evaluated which allow the team which attends the septic patient to plan the actions with greater thoroughness, for the greater effectiveness of the actions, principally, after discharge from hospital. One important aspect to be highlighted regarding the health-related quality of life of the patient who has survived sepsis is that the nursing care can have a positive effect on the psychological well-being of the patients and their family members.

Conclusion

This review demonstrated that the patients who survived an episode of sepsis present a significant reduction in their health-related quality of life, which tends to improve with the passing of time. Knowledge of the changes in the health-related quality of life of patients who survive an episode of sepsis demonstrates the need to monitor these patients over the long-term.

Collaborations

Silveira LM and Stabile AM contributed to the design, search for and analysis of the articles, the editing of the manuscript, and the approval of the version to be sent for publication. Dessotte CAM, Dantas RAS and Matioli MR contributed with the editing of the manuscript and the final revision.

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