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Burden of illness imposed by severe sepsis in Switzerland

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Summary

Objective: This study aims to determine the burden of illness imposed by severe sepsis in Switzerland by evaluating the direct and indirect patient-related costs for critically ill patients with severe sepsis.

Methods: In order to estimate the direct costs a retrospective analysis was undertaken using records from 61 adult patients treated in three intensive care units (ICUs) in three different University hospitals in Switzerland, in 2001. Resource use was determined by a bottom up approach and valued using centre-specific unit costs for medication, nutrition, blood products, disposables and official tariffs for laboratory and microbiology analysis, diagnostic services, and clinical procedures. By adding centre-specific personnel and basic bed (hotel) costs total direct costs in the ICU were calculated. Indirect costs resulting from unfitness for work, early retirement, and premature death were calculated using official Swiss statistics for the years 1998–2000.

Results: The mean total direct costs for a severely septic patient are CHF 41 790 (± 33 222 CHF) or CHF 3244 (± 757 CHF) per day. Non-survivors cause significantly higher costs than survivors (CHF 45 956 vs. CHF 37 759, p <0.001). The total intensive care costs in Switzerland due to severe sepsis amount to CHF 146–355 million. Indirect costs were estimated to range from CHF 347 to 844 million (predominantly due to premature death). Consequently the burden of illness of severe sepsis can be estimated to range from CHF 493 to 1199 million per year in Switzerland (1 CHF = 0.662 Euro in 2001).

Conclusion: Patients suffering from severe sepsis in Switzerland have a high mortality rate and spend a prolonged time in the ICU, leading to high direct and indirect costs. Particularly productivity losses due to premature death represent a considerable burden to the Swiss society.

Key words: intensive care; healthcare costs; burden of illness; cost of treatment; sepsis

Introduction

Increasing pressure on health care budgets worldwide emphasizes the need to address economic implications of new services and therapies. However, economic studies are still rarely found. Due to differences in healthcare systems economic questions need to be dealt with on a country-by-country basis. These differences prevent an easy application and adaptation of foreign findings to the particular country of interest. Sepsis is one of the disease areas that lately moved into medical society's focus because of its high mortality rate and the ongoing search for effective drug therapies. This general interest was recently increased by the publication of the PROWESS trial [1], which showed improved survival of severe sepsis patients treated with drotrecogin alfa (activated). The introduction of this new drug on the market certainly raises cost related questions as new promising inventions do not tend to be cheap. Additionally, sepsis is a disease generally treated in intensive care units, a fact which per se already indicates a rather high cost level. However, a fair discussion on a new therapy cannot be started without knowledge of the epidemiological and economic background. Although sepsis is a well-documented disease process regarding history, incidence and risk factors, information relating to the actual costs associated with sepsis is rare. This fact may be related to the general difficulties in undertaking cost of disease studies in intensive care units based on in-

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adequate documentation of intensive care unit (ICU) costs [2] and a lack of standardised models to determine costs [3]. However, currently there have been several publications on the cost of severe sepsis in various countries [4–7], often using a combination of methods (bottom-up, top-down approaches for direct costs and calculations based on statistical information for indirect costs). We were interested to obtain specific information regarding the cost of illness of sepsis in Switzerland. The aim of the present study was to investigate the incidence of severe sepsis in Switzerland and to determine its burden of illness based on the disease related direct and indirect costs applying the societal point of view.

Material and methods

Knowledge of the incidence of severe sepsis is mandatory in order to calculate the burden of illness. Epidemiological data was generated based on three different approaches. The first approach used literature and other sources (unpublished data, expert opinion, etc.) to get first estimates. A second approach projected mortality data given by the Federal Statistical Office of Switzerland to calculate the incidence, including not only the ICD-10 codes (International Classification of Diseases, Edition 10) of sepsis but also some organ failures most certainly due to sepsis. In a third approach severe sepsis cases were estimated based on the diagnosed disease of hospitalised patients [8]. However, patients included were not only declared sepsis cases but also patients with a disease most certainly leading to sepsis (certain percentages of these). The combination of these three approaches yielded a range of severe sepsis cases. The real number of cases most certainly lies within this incidence range.

To calculate the total costs associated with a specific medical illness or condition, health economic research generally differentiates three categories: direct costs, indirect costs, and intangible costs. Direct costs cover the actual costs of services provided, including hospitalisation costs, diagnostic tests, procedures, and medications. Indirect costs quantify the estimated loss of income as the result of illness and death. Intangible costs include the non-quantifiable costs associated with physical and emotional pain and suffering. In order to estimate the burden of illness of severe sepsis in Switzerland both direct and indirect costs have to be analysed. Resource use (i.e. the type and frequency of goods and services rendered to the patient) and the monetary value (prices and unit costs) for each type of these variables were used to estimate the direct cost of severely septic patients. Data on the resource use of severely septic patients in the ICU was collected by means of a retrospective chart analysis using patient records from three ICUs in the university hospitals of Basle, Geneva, and Zurich. The study was approved by the Ethics Committee of the hospital where required. Randomly selected records of 61 adult patients suffering from severe sepsis (defined according the ACCP/SCCM criteria [9]), with a length of stay >24 h in the year 2001 were evaluated. The chosen patient number represents about 1% of the estimated annual total number of severe sepsis cases in Switzerland. Dosage and frequency of previously defined healthcare goods and services (table 1) were assessed for each patient over the whole length of stay in the ICU and additionally some basic patient data such as age and sex, data about length of ICU stay and length of treatment, as well as data about ICU outcome (survivors or non-survivors) and infection (on ICU admission and/or acquired in ICU). All data was compiled in a database (MS Access 2000).

The assessed resources were valued with centre specific costs gathered by clinical experts and pharmacists from the hospitals involved. Hospital purchasing prices were applied to medication, consumables, nutrition, and blood products. Staff costs per day of care were calculated by dividing the summarised gross income from nurses and physicians of the specific ICU with the days of care. Hotel (basic bed) costs per day were derived from hospital administrations. Some cost data could not be provided by the three centres and was substituted with equivalent data from additional Swiss centres including the Ospedale San Giovanni in Bellinzona, Hôpital de Cadolles in Neuchâtel, and Hôpital Régional in Sion. Routine and microbiology laboratory as well as diagnostic services were calculated using official tariffs (tax points multiplied with cantonal tax point values) [10, 11]. Investment costs and depreciation of ICU equipment was not taken into account. We generally followed a conservative approach assessing the resource use data. Therefore, we deliberately omitted the resource use of the regular ward, because it was impossible to differentiate what was caused by severe sepsis or an underlying disease. All cost data was turned into costs per unit, added to the database and linked to the related resources. Specific costs for each patient were calculated by multiplying unit costs with the amount of resources

Table 1

Assessed health care goods and services.

Medication (analgesics, sedatives, steroids, antibiotics, vasoactive drugs, muscle relaxants, etc.)*
Blood and blood products (fresh frozen plasma, platelets, etc.)*
Nutritional products (enteral and parenteral nutrition, vitamin and mineral supplements)*
Volume replacement (colloids, crystalloids, etc.)*
Laboratory tests (blood analysis, urine analysis, liver function tests, coagulation, etc.)
Microbiology (blood cultures, sputum, urine, antibiotic sensitivity pattern, etc.)
Diagnostic services (X-ray, CT scan, etc.)**
Consumables (drainages, catheters, etc.)**
Staff services in ICU (physicians and nurses)
Hotel costs for ICU

* are combined in cost group medication
** are included in cost group consumables

used, and then all resource costs were summarised to total cost per patient. Finally, the mean cost and standard deviation was calculated. Costs per patient were multiplied with the estimated incidence range to obtain the total direct costs. Costs were calculated using 2001 prices. In 2001 the exchange rate to Euro was 1 CHF = 0.662.

Indirect costs were calculated using human productivity as substitute to estimate the effect of severe sepsis on society in financial terms. This human capital approach is commonly used since the human life and health cannot be expressed directly by a given monetary value [12]. Indirect costs include productivity loss (represented by lost income) due to temporary morbidity (work absenteeism), due to permanent morbidity (early retirement), and due to mortality (premature death). To give productivity a monetary value the official Swiss gross income from employment [13] was used since exact patient based income data was not available. Apart from the calculations regarding productivity loss due to mortality no gender specific calculations were possible because information was not detailed enough. The average productivity loss due to temporary morbidity was calculated by multiplying the statistical number of working days spent in hospital due to severe sepsis [8] (data about stay at home after illness was not available) with the gross income from employment per day (official Swiss gross income from employment per year divided by 220 working days = CHF 306.82 [13]) and the estimated incidence range. The productivity loss due to permanent morbidity was estimated by multiplying the number of early retirements due to sepsis with the mean working years lost and the gross income per year (CHF 67 500 [13]). The mean working years lost were calculated by deducting the average age of 51 years of patients in working age in the assessed clinical data from the official retirement age (65 years). To account for the fact that not all early retirements start on January 1 and end on December 31, one year was subtracted from the average number of life years lost per patient (half a year for the first and another six month for the last year). Since no official retirement figures were available on sepsis in Switzerland, the low Austrian value from our previous study in Austria [5] (0.16% in the year 2000, oral communication from the "Hauptverband Sozialversicherungsträger") was applied, assuming that both countries are comparable with respect to sepsis incidence, treatment and outcome. To obtain the productivity loss due to mortality the number of deaths was multiplied by the gross income per year [13] and by the average work years lost per age group and gender based on the assessed clinical data. The age and gender depending participation rate [13] was taken into account and again one year was subtracted to account for the different retirement dates as described above. Indirect costs due to mortality and permanent morbidity were discounted with 5% [14]. "Saved" old-age pensions after early death or given invalidity pensions do not enter in these direct cost calculations because they do not represent a productivity of the evaluated patient population.

The annual burden of illness imposed by severe sepsis in Switzerland was calculated by summing up the total direct and indirect costs.

Data analysis and cost calculations were done using MS Access 2000, MS Excel 2000, and SPSS 11.0. Statistical analysis of cost differences in subgroups was performed using the non-parametric bootstrapping method [15] since traditional statistical methods to analyse the difference in costs are considered inappropriate [16, 17]. This means that the observed data are treated as an empirical probability distribution which is resampled with replacement many times. Each resampling is used to provide an estimate of the cost. The repeated estimates are used to establish an empirical distribution with a sufficient sample size, from which tests of hypothesis are constructed. Bootstrapping was done within each subgroup using 1000 estimates for the analysis. Differences in length of stay were tested statistically with the Mann-Whitney U test. A p-value of ≤0.05 was accepted as a significant difference.

Results

Epidemiological estimates show that between 5800 and 14 000 sepsis cases are treated in Switzerland per year. Assuming that 60% of all sepsis cases evolve to severe sepsis [18, 19], the actual number of severe sepsis cases per year probably lies between 3500 and 8500 cases.

A total of 61 severe sepsis patients requiring 786 days of intensive care were assessed. Patient records were evaluated at three University hospitals in Switzerland including the University hospital Zurich (27 patients), Geneva (19 patients), and Basle (15 patients). The mean age of the patient

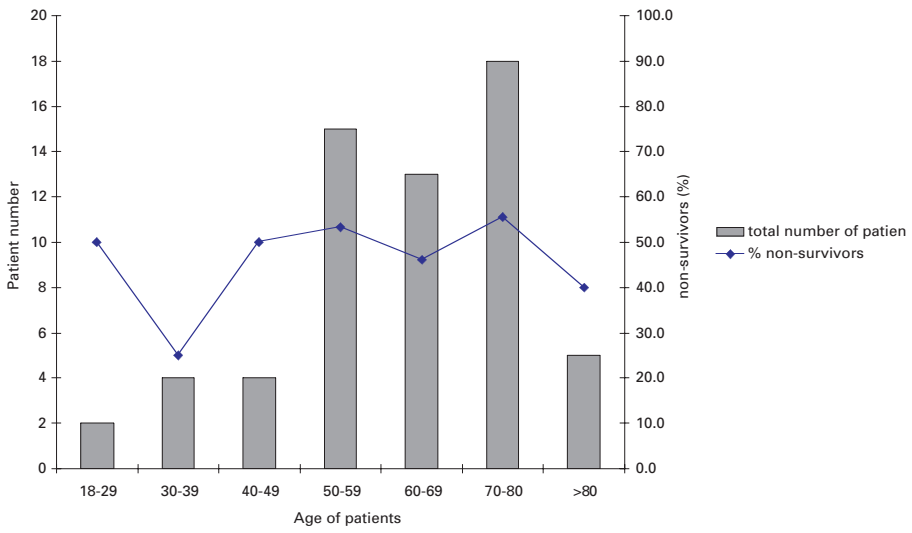

Figure 1

Age distribution of severely septic patients and percentage of non-survivors.

Figure 2

Distribution of length of stay of severely septic patients in ICU and percentage of non-survivors.

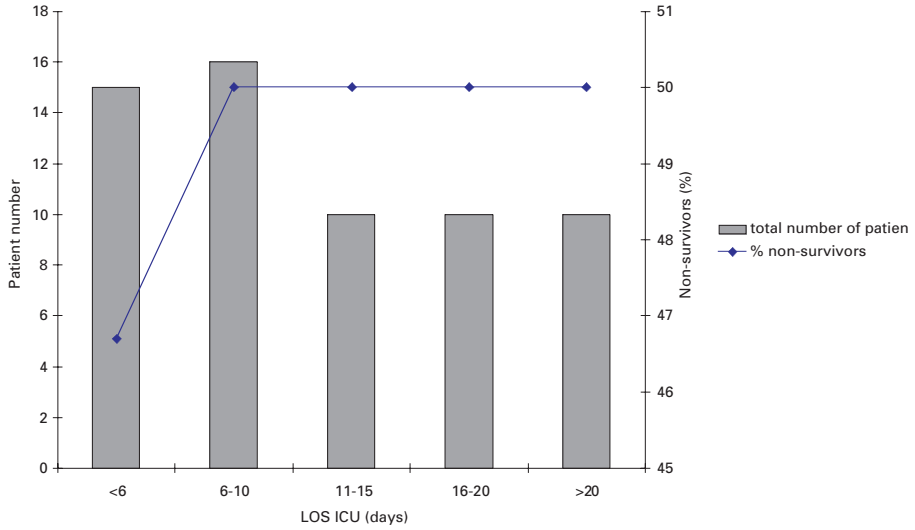

Table 2

Mean direct ICU cost per severely septic patient and per day (in CHF).

Components	per patient	per day
Medication	8020	622
Routine labs	3982	309
Microbiology	2030	158
Consumables	2726	212
Hotel costs	3803	295
Staff costs	21229	1648
Total mean direct costs	41790	3244

population was 62 years (± 15.0). The majority of patients, i.e. 57.4%, were male and 42.6% were female. An overall ICU mortality of 49.2% was observed and an overall average length of stay (LOS) in the ICU of 12.9 days (± 9.9). Survivors and non-survivors showed almost the same LOS (12.6 [± 8.7] vs. 13.2 [± 11.2] days, p = 0.897). No relation between mortality and age (figure 1) or mortality and LOS (figure 2) was found, which may be explained by the small sample size.

The mean total direct cost per severely septic patient amounted to CHF 41790 (± 33222) or CHF 3244 (± 757) per day. The cost per severely septic patient included medication, routine laboratory testing, microbiology, consumables, hotel and staff costs (table 2). Half of the costs are due to staff, 19% to drugs and related goods (fluids, blood products, nutrition etc.), and 9% are hotel costs. Non-survivors cause higher mean costs per patient than survivors (CHF 45956 (± 38464) vs. CHF 37759 (± 27260), p <0.001). Non-survivors have been found to spend almost the same number of days in the ICU as survivors. Therefore differences in costs between survivors and non-survivors can only be attributed to the higher resource use of non-survivors compared to survivors. This is also reflected by the finding that the mean cost per day is higher in non-survivors (CHF 3481 vs. CHF 3001, p <0.001), which is mainly driven by higher medication expenses (CHF 779 vs. 463, p <0.001). Based on the incidence range of 3500 to 8500 severely septic patients the total intensive care costs lay between CHF 146 and 355 million (for details see table 3).

Table 3

Total costs of severe sepsis in Switzerland per year (Mio CHF).

Costs	Low end of range (3500 patients)	High end of range (8500 patients)
Direct costs		
Medication	28.1	68.2
Routine laboratory tests	13.9	33.8
Microbiology	7.1	17.3
Consumables	9.5	23.2
Hotel costs	13.3	32.3
Staff costs	74.3	180.4
Total direct costs	146.2	355.2
Indirect costs		
Productivity loss due to work absenteeism	12.6	30.7
Productivity loss due to early retirement	4.6	10.7
Productivity loss due to premature death	329.8	802.4
Total indirect costs	347.0	843.8
Total costs of severe sepsis in Switzerland (Mio)	493.2	1199.0

Indirect costs due to severe sepsis in Switzerland were found to range from CHF 347 to 844 million. These costs are predominantly driven by the high mortality rate of severe sepsis patients, which accounts for a productivity loss ranging from CHF 330 to 802 million. Work absenteeism adds further productivity losses ranging from CHF 12.6 to 30.7 million and early retirement CHF 4.6 to 10.7 million.

Combining direct and indirect costs, severe sepsis imposes a yearly burden between CHF 493 and 1199 million to the Swiss society (table 3).

Discussion

Information about resource use and clinical data in septic patients was collected by means of a retrospective chart analysis. The used bottom up approach allowed us to estimate costs for this specific patient group more accurately than would have been possible with a top down approach. However, such data collection is time consuming and often hampered by the unavailability of certain cost data. Involving several hospitals allowed us to substitute missing cost data with data from one of the other centres, and had also a balancing effect on centre specific cost variations. As a certain percentage of underreporting of used resources in the patient files is plausible or a certain amount of resources may have been overlooked when assessing the health care goods used, we performed a sensitivity analysis to check possible cost implications when increasing the variable direct costs by 10% or 20%. Even a 20% increase in costs would not change results as they stay in the standard deviation range (± 33 222 CHF) of the originally calculated mean per patient costs. Therefore, the effect of some underreporting of resource use does not significantly influence the final results. A slight underestimation of treatment costs also results from the omission of regular ward stay which we decided on due to a lack of exact information. However, comparing the found mean ICU LOS (12.9 days) with the average hospital LOS of septic patients given in official statistics (15.8 days [8]) suggests a stay on regular ward of about 3 days per patient, which is not included in our calculations. On the other hand there might be a certain overestimation of costs since this retrospective study was carried out in university hospitals only. However, in Switzerland all ICUs are clearly defined, well equipped and adequately staffed units which provide the same level of care [20] so that resource use is comparable. Cost data were also provided by non-University hospitals, which contributed to a direct cost estimation representative for Switzerland. Generally it can be stated that a slight under- or overestimation of direct costs will have relatively little effect, as they only represent 30% of the total costs.

In a burden of illness assessment indirect costs must be included. However, estimating indirect costs is a methodological problem as they cannot be measured directly. We used the most commonly applied approach although it has limitations regarding the economic assumptions it is based on [12, 21, 22]. Indirect costs are influenced by the assumed discount rate for future costs occurring through productivity loss. We used the well accepted discount rate of 5% [14]. Applying no discount rate or a higher rate of 10% would substantially influence indirect costs (increase the indirect cost range by about 60% and lower it by about 30% respectively). Furthermore, a decreased long-term survival of patients with severe sepsis might lead to a further productivity loss. However, since literature reports are controversial regarding decreased long term survival of severely septic patients, this possibility was not taken into account.

Average ICU mortality for severe sepsis was 49.2%, which was somewhat higher than the rates found in Germany and Austria (respectively 36% and 43.2% [5, 7]). Nonetheless, the rate lies within the range of 30–50% reported in the literature [1, 23]. However, the mortality rate may have been biased by patient selection because in one centre surviving patients had to give their consent before inclusion and not all of them did. This may have led to an inclusion of non-survivors slightly above average. In addition, the observed mortality is based only on a total of 61 patients and should therefore be interpreted with caution. Apart from this, the patient population evaluated does not significantly differ in gender relation (57/43 compared with 58/42 and 66/34 in % male/female) or age (62 [± 15] vs. 58 [± 16.5] years in Germany and Austria) from severely septic patient populations studied in Germany and Austria [5, 7]. This suggests that the evaluated patient population reflects the entire severely septic patient population in Switzerland.

Comparing the Swiss cost data with those from Germany and Austria offers comparable findings [5, 7]. Non-survivors in all three countries showed higher mean costs per day than survivors, caused by higher resource use, i.e. higher medication costs. This fact results in equal or higher per patient costs for non-survivors despite similar or even shorter LOS in the ICU compared with survivors. Mean total ICU costs per patient are comparable to those found in Austria and are somewhat higher than those found in Germany.

The mean direct costs of treating a septic patient were calculated to be CHF 3244 per day. This corresponds to the total costs estimated for intensive care patients with an extraordinary nursing requirement (SGI category Ia) which is estimated to be CHF 3142 [20] (adapted for the year 2001 based on the consumer price index for hospital service [24]). Based on the assumption that intensive care

accounts for 6–10% of total hospital expenses in Switzerland [20], the total ICU costs of the year 2001 were CHF 662–1103 million [25]. Referring to the previously described range of 3500–8500 patients with severe sepsis, the cost of severe sepsis represents between 13% and 54% of the total ICU costs in Switzerland.

Based on the study results we conclude that patients suffering from severe sepsis in Switzerland have a relatively high mortality rate and spend an average of 12.9 days in the ICU. They impose an annual burden ranging from CHF 493 to 1199 million to the Swiss society.

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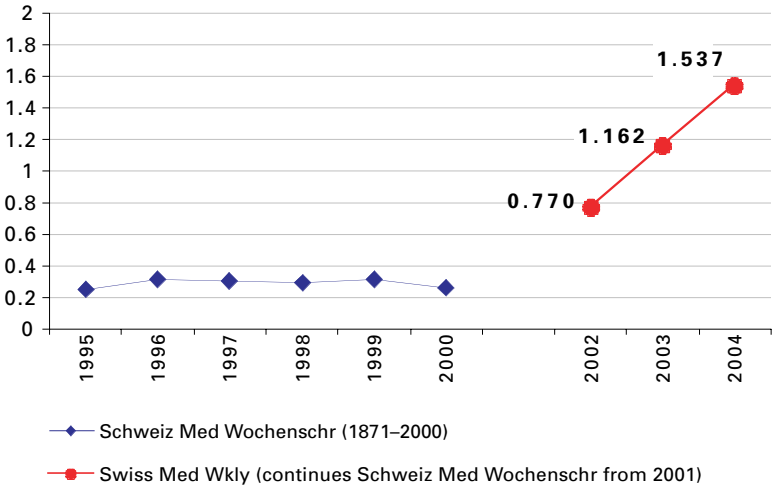

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