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LETTER

Chronic healthcare expenditure in survivors of sepsis in the intensive care unit

Maria E. Koster-Brouwer[1,2*], Kirsten van de Groep[1,2], Wietze Pasma[2], Hugo M. Smeets[1], Arjen J. C. Slooter[2], Dylan W. de Lange[2], Diederik van Dijk[2], Tom van der Poll[3,4], Marc J. M. Bonten[1,5], Olaf L. Cremer[2] and On behalf of the MARS Consortium

Dear Editor,

Direct expenses associated with an intensive care unit (ICU) admission for sepsis average approximately €30,000 per patient [1]. However, the total healthcare costs to society are likely to be much higher as survivors of critical illness frequently suffer from long-term sequelae [2]. These may entail both physical and cognitive impairments, as well as various psychological symptoms, which together have been coined as the post-intensive care syndrome (PICS) [3]. Previous studies have reported both increased healthcare utilization and high costs directly following sepsis events [4]. Most of these reports did not account for the premorbid status of patients, nor did they assess the rates at which costs incurred immediately after the event returned to baseline levels during follow-up, thereby precluding an accurate estimation of expenditure attributable to PICS. To overcome these limitations, we have measured healthcare utilization and costs in patients following sepsis during a 2-year follow-up period, while correcting for trends in expenditure already present during the 2 years before the event, and explored the impact of age and comorbidities. We also investigated the association between expenditure and long-term health-related quality of life (HRQoL).

We analyzed 1-year survivors of sepsis enrolled in a prospective cohort study in two tertiary ICUs in the Netherlands in 2011 and 2012 [5]. Healthcare utilization and costs were derived from a Dutch insurance company database. Changes in trends and level of expenditure were assessed using interrupted time-series analysis. HRQoL was measured using self-reported information obtained using EuroQol five dimensions questionnaires (EQ-5D; EuroQol Group, Rotterdam, the Netherlands) completed and returned by a subgroup of patients 1 year after ICU admission.

Among 373 eligible patients, 16 were lost-to-follow-up, leaving 357 subjects for final analysis (Electronic Supplementary Material (ESM) Fig. S1, Table S1). Monthly healthcare expenditure averaged €1035 (standard deviation (SD) €2009) and €3533 (SD €5190) before and after the sepsis event, respectively (crude cost difference €2498, SD 4678; $p < 0.001$) (Fig. 1; ESM Table S2). The increase in expenditure resulted predominantly from greater utilization of hospital care, long-term (home) care, and mental health care (ESM Table S2). After correction for baseline trends, the observed increase in monthly healthcare expenditure following sepsis remained [adjusted cost difference €2281, 95 % confidence interval (CI) €1755–2807; $p < 0.001$] (ESM Table S3). During follow-up, regression towards baseline reimbursement levels was observed in all subgroups, except in elderly patients with comorbidities (ESM Table S4, Fig. S2). However, overall monthly expenditure 2 years after the event was still €1690 (95 % CI €601–2799) higher than predicted by baseline trends (ESM Table S3, Fig. S2). In a subgroup of 90 patients for whom follow-up was available, mean HRQoL was 0.70 (SD 0.26), with higher mean monthly expenditure after sepsis being negatively correlated with favorable outcome (Spearman's correlation coefficient −0.439; $p < 0.001$) (ESM Fig. S3). Furthermore, a greater increase in expenditure when comparing the periods before and after sepsis (rather than absolute costs) was also significantly correlated with lower HRQoL (Spearman's correlation coefficient −0.410; $p < 0.001$).

*Correspondence: m.e.brouwer-6@umcutrecht.nl
[1] Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, Room F06.149, P.O. Box 85500, 3508 GA Utrecht, The Netherlands
Full author information is available at the end of the article

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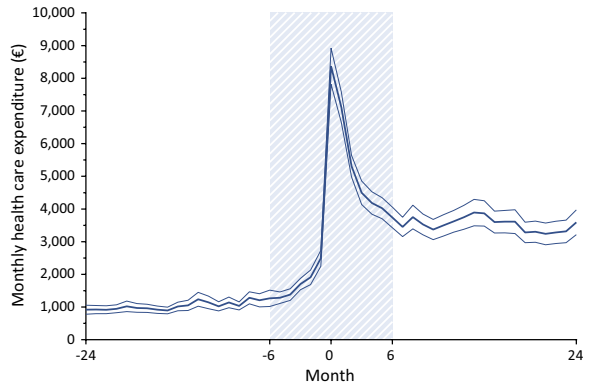

Fig. 1 Monthly healthcare expenditure in the 2 years preceding and following a sepsis episode ($n = 357$ patients). Monthly healthcare expenditure is depicted as the mean (*thick dark line*) with the standard error (*thin lines*). *Shaded area:* the 6-month periods leading up to and immediately trailing the sepsis event; costs incurred during this time interval were excluded from further analysis in order to eliminate potential carry-over effects from charges that were directly related to the sepsis event rather than to utilization of chronic health services

Although sepsis itself represents a severe but transient disease process, sepsis survivors generate substantial costs up to at least 2 years after the event which cannot be explained by pre-existing trends. Furthermore, the high utilization of healthcare resources after critical illness seems to represent a chronically diminished health status indicative of PICS.

Electronic supplementary material
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Author details
[1] Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, Room F06.149, P.O. Box 85500, 3508 GA Utrecht, The Netherlands. [2] Department of Intensive Care Medicine, University Medical Center Utrecht, Room F06.149, P.O. Box 85500, 3508 GA Utrecht, The Netherlands. [3] Center of Experimental and Molecular Medicine, Academic Medical Center, University of Amsterdam, Amsterdam, The Netherlands. [4] Division of Infectious Diseases, Academic Medical Center, University of Amsterdam, Amsterdam, The Netherlands. [5] Department of Medical Microbiology, University Medical Center Utrecht, Utrecht, The Netherlands.

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Compliance with ethical standards

Ethical approval
Ethical approval for the study was provided by the Medical Ethics Committees of participating centers, including a waiver for informed consent (IRB numbers 14-095/C, 10-056, 10-006).

Conflicts of interest
The authors declare that they have no conflicts of interest related to the subject matter.

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References

1. Koster-Brouwer ME, Klein Klouwenberg PMC, Pasma W, Bosmans JE, van der Poll T, Bonten MJM, Cremer OL (2016) Critical care management of severe sepsis and septic shock: a cost-analysis. Neth J Crit Care 24:12–18
2. Koster-Brouwer M, van de Groep K, Klein Klouwenberg P, Pasma W, van der Poll T, Bonten M, Cremer O (2015) Ongoing health care expenditure in survivors of sepsis in the intensive care unit. Intensive Care Med Exp 3[Suppl 1]:A21
3. Harvey MA, Davidson JE (2016) Postintensive care syndrome: right care, right now…and later. Crit Care Med 44:381–385
4. Weycker D, Akhras KS, Edelsberg J, Angus DC, Oster G (2003) Long-term mortality and medical care charges in patients with severe sepsis. Crit Care Med 31:2316–2323
5. Klein Klouwenberg PM, Ong DS, Bos LD, de Beer FM, van Hooijdonk RT, Huson MA, Straat M, van Vught LA, Wieske L, Horn J, Schultz MJ, van der Poll T, Bonten MJ, Cremer OL (2013) Interobserver agreement of centers for disease control and prevention criteria for classifying infections in critically ill patients. Crit Care Med 41:2373–2378