

## Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

# Effect of a Primary Care Management Intervention on Mental Health–Related Quality of Life Among Survivors of Sepsis

## A Randomized Clinical Trial

Konrad Schmidt, MD; Susanne Worrack, MSc; Michael Von Korff, ScD; Dmitry Davydow, MD, MPH; Frank Brunkhorst, MD; Ulrike Ehlert, PhD; Christine Pausch, PhD; Juliane Mehlhorn, MD; Nico Schneider, MSc; André Scherag, MSc, PhD; Antje Freytag, PhD; Konrad Reinhart, MD; Michel Wensing, PhD; Jochen Gensichen, MD, MSc, MPH; for the SMOOTH Study Group

**IMPORTANCE** Survivors of sepsis face long-term sequelae that diminish health-related quality of life and result in increased care needs in the primary care setting, such as medication, physiotherapy, or mental health care.

**OBJECTIVE** To examine if a primary care–based intervention improves mental health–related quality of life.

**DESIGN, SETTING, AND PARTICIPANTS** Randomized clinical trial conducted between February 2011 and December 2014, enrolling 291 patients 18 years or older who survived sepsis (including septic shock), recruited from 9 intensive care units (ICUs) across Germany.

**INTERVENTIONS** Participants were randomized to usual care (n = 143) or to a 12-month intervention (n = 148). Usual care was provided by their primary care physician (PCP) and included periodic contacts, referrals to specialists, and prescription of medication, other treatment, or both. The intervention additionally included PCP and patient training, case management provided by trained nurses, and clinical decision support for PCPs by consulting physicians.

**MAIN OUTCOMES AND MEASURES** The primary outcome was change in mental health–related quality of life between ICU discharge and 6 months after ICU discharge using the Mental Component Summary (MCS) of the 36-Item Short-Form Health Survey (SF-36 [range, 0-100; higher ratings indicate lower impairment; minimal clinically important difference, 5 score points]).

**RESULTS** The mean age of the 291 patients was 61.6 years (SD, 14.4); 66.2% (n = 192) were men, and 84.4% (n = 244) required mechanical ventilation during their ICU stay (median duration of ventilation, 12 days [range, 0-134]). At 6 and 12 months after ICU discharge, 75.3% (n = 219 [112 intervention, 107 control]) and 69.4% (n = 202 [107 intervention, 95 control]), respectively, completed follow-up. Overall mortality was 13.7% at 6 months (40 deaths [21 intervention, 19 control]) and 18.2% at 12 months (53 deaths [27 intervention, 26 control]). Among patients in the intervention group, 104 (70.3%) received the intervention at high levels of integrity. There was no significant difference in change of mean MCS scores (intervention group mean at baseline, 49.1; at 6 months, 52.9; change, 3.79 score points [95% CI, 1.05 to 6.54] vs control group mean at baseline, 49.3; at 6 months, 51.0; change, 1.64 score points [95% CI, -1.22 to 4.51]; mean treatment effect, 2.15 [95% CI, -1.79 to 6.09]; *P* = .28).

**CONCLUSIONS AND RELEVANCE** Among survivors of sepsis and septic shock, the use of a primary care–focused team-based intervention, compared with usual care, did not improve mental health–related quality of life 6 months after ICU discharge. Further research is needed to determine if modified approaches to primary care management may be more effective.

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**Author Affiliations:** Author affiliations are listed at the end of this article.

**Group Information:** The SMOOTH Study Group members are listed at the end of this article.

**Corresponding Author:** Jochen Gensichen, MD, MSc, MPH, Institute of General Practice and Family Medicine, Jena University Hospital, Friedrich-Schiller-University, School of Medicine, Bachstrasse 18, D-07740 Jena, Germany ([jochen.gensichen@med.uni-jena.de](mailto:jochen.gensichen@med.uni-jena.de)).

**Section Editor:** Derek C. Angus, MD, MPH, Associate Editor, JAMA ([angusdc@upmc.edu](mailto:angusdc@upmc.edu)).

Sepsis is a major health problem worldwide.<sup>1</sup> It has been estimated that sepsis occurred in 2% of hospitalized patients in the United States in 2008, and incidence is expected to increase further in the future, with an even higher incidence in developing countries.<sup>2</sup> The risk of dying from sepsis has decreased in recent decades, owing to earlier detection and more effective treatment.<sup>3</sup> Although more patients survive sepsis and are increasingly discharged from the hospital,<sup>4</sup> they often experience functional disability, cognitive impairment, and psychiatric morbidity,<sup>5,6</sup> resulting in diminished health-related quality of life,<sup>7</sup> increased health care costs,<sup>8,9</sup> and burden on patients and their families.<sup>7,10</sup>

Many survivors of sepsis have multiple medical comorbidities that are typically managed in primary care. Yet interventions for managing sepsis sequelae in primary care have not been developed.<sup>5,11</sup> A systematic review of outpatient interventions for patients surviving critical illnesses showed heterogeneous and small effects on clinical outcomes such as depression and symptoms of posttraumatic stress disorder (PTSD).<sup>12</sup> Studies with post-intensive care unit (ICU) follow-ups of 6 months or more are rare.<sup>7</sup>

The purpose of this randomized clinical trial was to assess whether a primary care–based intervention<sup>13</sup> would improve mental health–related quality of life among survivors of sepsis compared with usual care.

## Methods

### Study Design and Population

A multicenter, unblinded, 2-group randomized clinical trial was performed. The institutional review board of the Jena University Hospital approved the study protocol (protocol available in [Supplement 1](#)). All patients and primary care physicians (PCPs) in the study provided written informed consent. Serious adverse events were reported to a data and safety monitoring board. Patients were recruited in 9 ICU study centers across Germany between February 2011 and December 2013. Follow-up assessments were completed in December 2014. Patients were eligible for inclusion if they were adult ( $\geq 18$  years) survivors of severe sepsis, (now defined as “sepsis”<sup>14</sup>) or septic shock and fluent in the German language.

Clinical diagnoses of sepsis were made by intensivists according to *International Statistical Classification of Diseases and Related Health Problems, Tenth Revision* codes (R65.1/R57.2) and American College of Chest Physicians/Society of Critical Care Medicine consensus criteria.<sup>15</sup> Baseline interviews of patients were conducted by the study team within 1 month of ICU discharge. The key exclusion criterion was cognitive impairment, as determined by the Telephone Interview of Cognitive Status (score  $\leq 27$ ).<sup>16</sup> After determining patient eligibility, the study team invited each patient’s PCP to participate in the trial.

Randomization was stratified by ICU study centers and performed using computer-generated random permuted blocks (block size range, 2–6) provided by an independent center for clinical trials at the University of Leipzig.

### Intervention

The intervention was based on the chronic care model.<sup>17</sup> Its core components included case management focusing on proactive patient symptom monitoring, clinical decision support for the PCP, and training for both patients and their PCPs in evidence-based care. Three nurses with ICU experience were trained as outpatient case managers for survivors of sepsis in an 8-hour workshop. The training included information on sepsis sequelae, communication skills, telephone monitoring, and behavioral activation of patients that included goal setting (Sepsis Case Manager Manual in [Supplement 2](#)). Each case manager worked with 38 to 65 patients, starting with a 60-minute face-to-face training on sepsis sequelae (Sepsis Help Book in [Supplement 2](#)) that took place a median of 8 days after ICU discharge (interquartile range [IQR], 2–20). This was followed by monthly telephone contact for 6 months, then once every 3 months for the final 6 months. Case managers monitored patients’ symptoms using validated screening tools (Sepsis Monitoring Checklist in [Supplement 2](#)) to assess critical illness polyneuropathy/myopathy, wasting, neurocognitive deficits, PTSD, depressive and pain symptoms, as well as patient self-management behaviors focusing on physical activity and individual self-management goals. Each case manager reported results to 1 of 3 assigned consulting physicians (medical doctors with background in primary and critical care), who supervised the case managers and provided clinical decision support to the PCPs using a structured written report that included the Sepsis Monitoring Checklist ([Supplement 2](#); eFigure 3 in [Supplement 3](#)). The reports were stratified by urgency using a traffic-light scheme: red signified “immediate intervention recommended”; yellow, “intervention should be considered”; and green, “acceptable clinical status.” Evidence-based sepsis aftercare training for the patients’ PCPs was provided in person on an individual basis by the consulting physicians (Sepsis PCP Manual in [Supplement 2](#)). Intervention delivery was considered to have high integrity if the training was delivered both to patients and to PCPs and the patient was monitored 5 or more times.

Patients in the control group received care as usual from their PCPs without additional information or monitoring. Usual sepsis aftercare included periodic contacts, referrals to specialists, and prescription of medication and therapeutic aids at quantities comparable with those for other populations with multiple chronic conditions.<sup>18</sup> In Germany, most primary care practices are privately operated by 1 or 2 PCPs, with limited access to specialist care.<sup>19</sup> There are no outpatient postsepsis/ICU follow-up clinics or national treatment guidelines for sepsis aftercare in Germany.

### Baseline Data and Outcomes

Baseline data were collected at in-person interviews with patients while they were still hospitalized. Further clinical data were obtained from their ICU records. Since the majority of patients remained hospitalized and incapacitated, baseline data collection of activities of daily living (ADL), physical function, and insomnia was not feasible.

The primary outcome was change in mental health–related quality of life between ICU discharge and 6 months after

ICU discharge, as assessed by the Mental Component Summary (MCS) score of the 36-Item Short Form Health Survey (SF-36 [range, 0-100; higher scores indicate lower levels of impairment<sup>20</sup>]). The SF-36 consists of 8 subscores and is valid and reliable in both post-ICU discharge<sup>21</sup> and German primary care populations.<sup>22</sup>

Secondary outcomes at 6 months were derived from (1) the other SF-36 scales (range, 0-100; higher scores indicate lower levels of impairment); (2) overall survival; (3) mental health outcomes, including the Major Depression Inventory (range, 0-50; higher scores indicate greater impairment<sup>23</sup>), the Posttraumatic Symptom Scale (range, 10-70; higher scores indicate greater impairment<sup>24</sup>), and the Telephone Interview of Cognitive Status (range, 0-50; higher scores indicate greater impairment<sup>16</sup>); (4) functional outcomes including ADL (range, 0-11; higher scores indicate lower levels of impairment<sup>25</sup>), the Extra Short Musculoskeletal Function Assessment regarding physical function (XSFMA-F) and disability (XSMFA-B [range for both, 0-100; higher scores indicate greater impairment<sup>26</sup>], the Graded Chronic Pain Scale including a Disability Score and Pain Intensity (range, 0-100; higher scores indicate greater impairment<sup>27</sup>), the Neuropathy Symptom Score (range, 0-10; higher scores indicate greater impairment<sup>28</sup>), the Malnutrition Universal Screening Tool (range, 0-2; higher scores indicate greater impairment<sup>29</sup>) including body mass index,<sup>30</sup> and the Regensburg Insomnia Scale (range 0-40; higher scores indicate greater impairment<sup>31</sup>).

Process-related outcomes included the Patient Assessment of Care for Chronic Conditions (range, 0-10; higher scores indicate lower levels of impairment)<sup>32,33</sup> and measures of medication adherence, the modified Morisky questionnaire (range 1-5; higher scores indicate greater impairment,<sup>34</sup> and the Short Form for Medication Use (range, 0-12; higher scores indicate greater impairment.<sup>35</sup> In addition, process-related data from PCP documentation were derived, including PCP contacts (No.), referrals to specialists (No.), level of nursing, inability to work (days), remedies and therapeutic aids (No.), and length of stay in the hospital and rehabilitation clinic (days). All 31 secondary outcomes prespecified in the statistical analysis plan (Supplement 4) are reported in eTables 2-8 in Supplement 3.

In addition, we also included as secondary outcomes all of the above measured at 12 months after ICU discharge. Outcome assessment was conducted by nonblinded assessors by telephone.

Initially, the MCS as well as the Physical Component Summary score of the SF-36 were chosen for primary outcome to provide a multicomponent score reflecting health-related quality of life (as noted in the study protocol<sup>13</sup> and the ISRCTN registration). However, based on review of the literature<sup>12</sup> highlighting the importance of mental health outcomes in post-ICU care, the primary outcome was specified to the MCS.

### Statistical Analysis

The aim of the study was to detect a difference at 6 months of 5 points or more in mean MCS scores, since this amount of change is thought to be clinically meaningful.<sup>22</sup> A common standard deviation of 10 was assumed on the basis of a typical German population with acute and chronic diseases.<sup>36</sup> At a 2-sided sig-

nificance level of  $\alpha = .05$ , a total of  $2 \times 86 = 172$  patients were required to detect the above-mentioned effect with a power of 90%. Allowing for an additional approximately 40% for drop-outs and mortality, an initial sample size of 287 was required.

The confirmatory test for the primary outcome was the Welch *t* test for independent groups, which was run in the intention-to-treat population. The confirmatory analyses did not consider intrapractice clustering because 155 (96.9%) of intervention practices and 141 (95.1%) of control practices included only 1 patient. The effect clustering and missing values were explored using, for example, linear mixed models and imputations by regression models. Details on methods and results of exploratory sensitivity analyses are provided in the eMethods in Supplement 3.

All secondary outcome analyses were exploratory and not adjusted for multiple tests. These analyses were performed using the *t* test, Fisher exact test, and the Wilcoxon-Mann-Whitney test, as appropriate. Overall survival was estimated using the Kaplan-Meier method, with study groups compared using the log-rank test. A confirmatory and exploratory 2-sided significance level of  $\alpha = .05$  was applied, and effect size estimates with 95% confidence intervals were reported.

All statistical analyses were performed using R version 3.2.3 (R Project for Statistical Computing).<sup>37</sup>

## Results

### Baseline Characteristics

A total of 361 patients were eligible, of which 291 (80.6%) agreed to participate, with 148 patients randomized to the intervention and 143 patients to the control group (Figure). Overall, baseline characteristics were well balanced (Table). The mean age of the cohort was 61.6 years (SD, 14.4); 244 patients (84.4%) received mechanical ventilation, and the median ICU length of stay was 26 days (IQR, 13-46). Mental health-related quality of life was close to that of the normal population (mean MCS score, 49.0 [SD, 12.5]), physical health-related quality of life was low (mean SF-36 [Physical Component Summary] score, 25.3 [SD, 8.8]); 68 of 281 (24.2%) had substantial depressive symptoms, 41 of 281 (14.6%) reported substantial PTSD symptoms, and 54 of 276 (19.6%) indicated severe pain (Table). Among the entire cohort, 164 of 277 (59.2%) reported neuropathic symptoms.

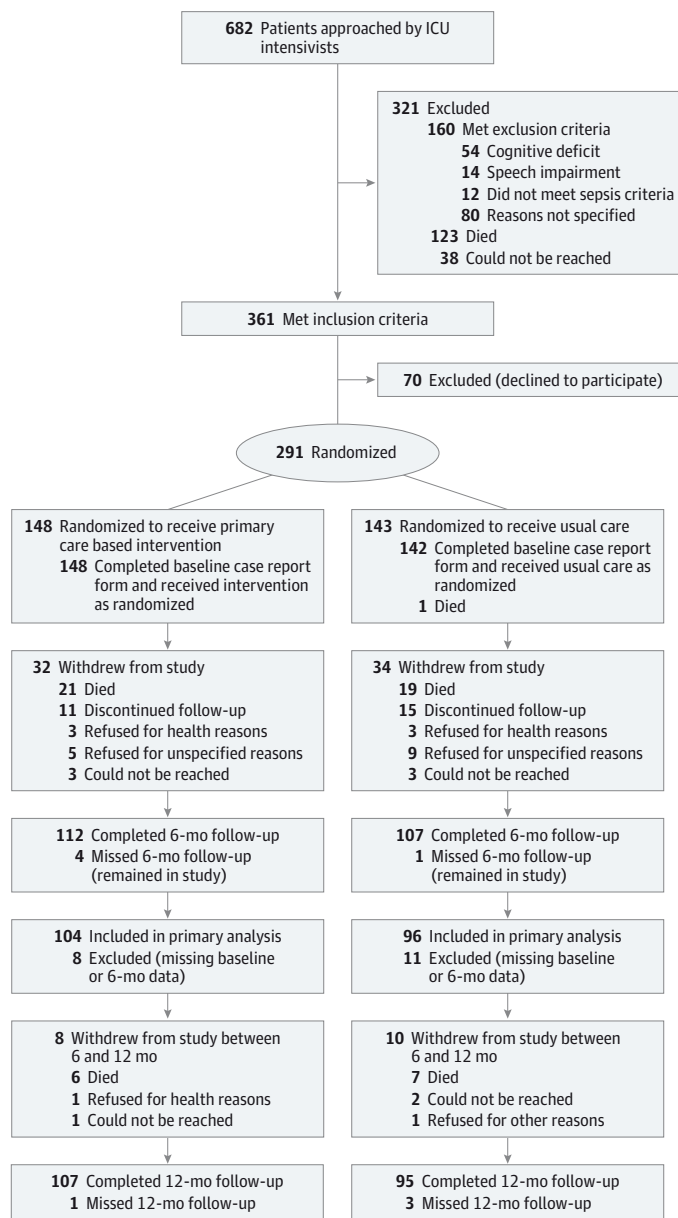
### Follow-up

All included 291 patients were cared for by 159 intervention PCPs and 148 control PCPs. Because of some patient-initiated PCP changes, the number of PCPs was slightly larger than the number of patients (eMethods in Supplement 3). Among the 307 assigned PCPs, 294 (95.8%) were willing to participate. Loss to follow-up due to withdrawal or nonresponse totaled 66 patients (22.7%) at 6 months and an additional 18 patients (6.2%) at 12 months after ICU discharge and was evenly distributed across study groups (Figure).

### Intervention Delivery

Of the 148 patients assigned to the intervention, 130 (87.8%) received patient training from case managers; 125 (84.5%) of

Figure. CONSORT Flow Diagram of Patient Recruitment and Retention During the Study



ICU indicates intensive care unit.

their PCPs received training from a consulting physician. There was a mean gap of 62.38 days (IQR, 36-99) between ICU discharge and PCP training, caused by the wide range of patient clinical courses. One hundred-four patients (70.3%) in the intervention group received the planned intervention at high levels of intervention integrity (eFigure 2 in Supplement 3). Incomplete intervention was usually attributable to death of the patient (24 [54%] of those with fewer than 5 monitoring calls). Reduction of motor function (204 [27.1%]) and pain intensity (201 [27.2%]) were the postsepsis symptoms most rated “red” (ie, “immediate intervention recommended”) in all 756 structured monitoring reports (eTable 10 in Supplement 3).

No adverse events related to the intervention were reported.

### Primary Outcome

There was no significant difference between groups in the primary outcome: The mean change MCS score was 3.79 score points (95% CI, 1.05 to 6.54) for the intervention group and 1.64 score points (95% CI, 1.22 to 4.51) for the control group, leading to a mean treatment effect of 2.15 (95% CI, -1.79 to 6.09);  $P = .28$ ; baseline mean, 49.1 for intervention vs 49.3 for control; 6-month mean, 52.9 for intervention vs 51.0 for control (all data related to  $n = 200$  patients [ $n = 104$  intervention,  $n = 96$  control]), with both MCS scores available at baseline and 6 months; due to rounding, change scores presented may not add up precisely). These results were unchanged in several sensitivity analyses (eTable 1 in Supplement 3).

Table. Baseline Characteristics

Characteristic	All (N = 290)	Intervention (n = 148)	Control (n = 142)	Not Available	
				Intervention	Control
<b>Sociodemographics</b>					
Age, mean (SD), y	61.6 (14.4)	62.1 (14.1)	61.2 (14.9)	0	0
Men, No. (%)	192 (66.2)	105 (70.9)	87 (61.3)	0	0
Married, No. (%)	148 (52.1)	84 (57.9)	64 (46.0)	3	3
Educational status <high school, No. (%)	98 (34.0)	54 (36.7)	44 (31.1)	1	1
<b>Care Measures</b>					
Recent surgical history, No. (%)				2	1
Emergency	106 (36.8)	49 (33.6)	57 (40.1)		
Elective	62 (21.5)	34 (23.3)	28 (19.7)		
No history	73 (25.3)	39 (26.7)	34 (23.9)		
Source of infection, No. (%)					5
Community acquired	102 (36.0)	54 (37.2)	48 (34.8)		
Nosocomial					
ICU or intermediate care	139 (49.1)	70 (48.3)	69 (50.0)		
General ward or nursing home	42 (14.8)	21 (14.5)	21 (15.2)		
ICU length of stay, d				16	11
Mean (SD)	34.4 (27.2)	31.5 (27.7)	35.2 (26.7)		
Median (IQR)	26 (4-27)	23 (4-26)	29 (5-28)		
Mechanical ventilation, No. (%)	244 (84.4)	121 (82.3)	123 (86.6)	1	1
If applicable, d				5	4
Mean (SD)	18.5 (19.2)	17.0 (17.5)	19.9 (20.7)		
Median (IQR)	12 (4-27)	10 (4-26)	14 (5-28)		
Renal replacement therapy, No. (%)	82 (28.5)	43 (29.3)	39 (27.7)	1	2
If applicable, d				5	5
Mean (SD)	12.3 (13.2)	11.9 (13.7)	12.8 (12.8)		
Median (IQR)	8 (4-15)	7 (4-14)	8 (5-16)		
<b>Clinical Measures</b>					
Charlson Comorbidity Index, mean (SD) <sup>a</sup>	4.0 (2.9)	4.0 (3.0)	4.0 (2.9)	1	1
ICD-10 diagnoses, No.				6	7
Median	9	9	10		
Mean (SD)	10.1 (4.7)	9.6 (4.4)	10.6 (5.1)		
BMI, mean (SD)	27.3 (6.0)	27.3 (6.0)	27.3 (5.9)	3	9
Depression				3	6
MDI, mean (SD) <sup>b</sup>	18.1 (10.0)	18.4 (9.8)	17.8 (10.1)		
Depressive symptoms, No. (%)	68 (24.2)	36 (24.8)	32 (23.5)		
PTSD				3	6
PTSS-10, mean (SD) <sup>c</sup>	23.6 (10.4)	24.0 (11.0)	23.2 (9.7)		
Score >35, No. (%)	41 (14.6)	22 (15.2)	19 (14.0)		
TICS-M, mean (SD) <sup>d</sup>	33.4 (3.6)	33.7 (3.4)	33.1 (3.9)	1	0
Neuropathic symptoms				4	9
NSS, mean (SD) <sup>e</sup>	3.6 (3.2)	3.6 (3.3)	3.7 (3.1)		
Score 3-10, No. (%)	164 (59.2)	83 (57.6)	81 (60.9)		
Pain					
Intensity: GCPS PI, mean (SD) <sup>f</sup>	43.8 (24.4)	43.7 (25.6)	43.9 (23.1)	5	9
Disability: GCPS DS, mean (SD) <sup>f</sup>	36.2 (34.6)	36.0 (34.5)	36.4 (34.8)	7	12
Severe pain: GCPS category >1, No. (%)	54 (19.6)	26 (18.2)	28 (21.0)	5	9
<b>Health-Related Quality of Life, Mean (SD)<sup>g</sup></b>					
SF-36				12	15
MCS	49.0 (12.5)	48.8 (12.5)	49.2 (12.6)		
PCS	25.3 (8.8)	25.9 (9.4)	24.7 (8.0)		

Abbreviations: BMI, body mass index; GCPS DS, Graded Chronic Pain Scale Disability Score; GCPS PI, Graded Chronic Pain Scale Pain Intensity; ICD-10, International Statistical Classification of Diseases and Related Health Problems, Tenth Revision; ICU, intensive care unit; MDI, Major Depression Inventory; NSS, Neuropathic Symptom Score; PTSD, Posttraumatic Stress Disorder; PTSS, Posttraumatic Symptom Scale; SF-36 MCS, Short Form 36 Health Survey Mental Component Score; SF-36 PCS, Short Form 36 Health Survey Physical Component Score; TICS-M, modified Telephone Interview for Cognitive Status.

<sup>a</sup> Range of possible scores, 0-37. High score indicates high impairment.

<sup>b</sup> Range of possible scores, 0-50. High score indicates high impairment.

<sup>c</sup> Range of possible scores, 10-70. High score indicates high impairment.

<sup>d</sup> Range of possible scores, 0-50; includes only values greater than 27 (inclusion criterion). High score indicates low impairment.

<sup>e</sup> Range of possible scores, 0-10. High score indicates high impairment.

<sup>f</sup> The range of possible scores is 0-100. High score indicates high impairment.

<sup>g</sup> Range of possible scores, 0-100. High score indicates low impairment.

## Secondary Outcomes

A total of 63 secondary outcomes were analyzed at both 6 and 12 months (including the 12-month MCS score).

A respective 28 (6 months) and 30 (12 months) outcomes did not show significant differences (at an uncorrected  $\alpha = .05$ ) between both groups, including physical health–related quality of life and mental health outcomes (eTable 2 and eTable 3 in Supplement 3). Overall mortality was 13.7% ( $n = 40$ ) at 6 months after ICU discharge and 18.2% ( $n = 53$ ) at 12 months after ICU discharge (eFigure 1 in Supplement 3). If any, potential intervention effects were observed in measures of functional outcomes only: at 6 months, sepsis survivors receiving the intervention had better physical functioning (mean XSFMA-F score, 38.0 [95% CI, 32.5 to 43.5] vs 46.9 [95% CI, 40.9 to 52.9];  $P = .04$ ; difference,  $-8.9$  [95% CI,  $-17.02$  to  $-0.78$ ]), less physical disability (mean XSFMA-B score, 42.5 [95% CI, 36.6 to 48.4] vs 52.4 [95% CI, 46.2 to 58.7];  $P = .03$ ; difference,  $-9.9$  [95% CI,  $-18.49$  to  $-1.31$ ]), and fewer ADL impairments (mean, 8.6 [95% CI, 8.0 to 9.1] vs 7.6 [95% CI, 7.0 to 8.2];  $P = .03$ ; difference, 1.0 [95% CI, 0.16 to 1.84]) than usual care. After adjusting for pre-specified baseline covariates, these potential effects were persistent. In addition, survivors of sepsis receiving the intervention had potentially fewer sleep impairments at 12 months after ICU discharge than controls (mean Regensburg Insomnia Scale score, 10.3 [95% CI, 9.2 to 11.4] vs 12.1 [95% CI, 10.8 to 13.4]; difference,  $-1.8$  [95% CI,  $-3.5$  to  $-0.10$ ]).

In addition, the PCP documentation data at 6 and 12 months provided no evidence for group differences in PCP care (eTable 8 in Supplement 3).

## Discussion

Among survivors of sepsis, a primary care–based intervention, compared with usual care, did not improve mental health–related quality of life.

To our knowledge, this is the first large-scale, randomized controlled clinical trial of an intervention to improve outcomes in survivors of sepsis in primary care.

This sample of survivors of sepsis had similar mean ages and rates of existing comorbidities as compared with other cohorts.<sup>38,39</sup> The prevalence of depressive and PTSD symptoms was slightly less than that among other populations of survivors of critical illness,<sup>40,41</sup> whereas neuropathic symptoms and severe pain were more frequent.<sup>42,43</sup> Physical function, as measured by the SF-36 Physical Function subscore, was substantially lower than in the German population (mean, 85.71 [SD, 22.1];  $n = 2886$ )<sup>36</sup> and also lower than in some comparable cohorts<sup>44,45</sup> and intervention studies.<sup>46,47</sup> Thus, patients may have been more sensitive to the intervention's focus on increasing motivation to be physically active.

Study patients were exposed to longer durations of mechanical ventilation and ICU length of stay than reported in other studies.<sup>4</sup> ICU length of stay and duration of mechanical ventilation were shown to generally be longer in Europe than in the United States, especially in survivors of sepsis.<sup>48,49</sup> In addition, extensive ICU length of stay may have facilitated patient identification by the intensivists.

There was no evidence for a differential treatment effect on the study's primary outcome, postsepsis MCS scores. This finding is similar to those from previous trials of care management interventions following critical illness.<sup>12,46,47,50</sup> The absence of an intervention effect on the primary and most secondary outcomes can be considered using the PICO (Population, Intervention, Controls, Outcome) frameworks.<sup>51</sup>

## Population

The studied cohort experienced heterogeneous clinical multiple conditions. This primary care–based intervention may not have been sufficiently focused to address all their diverse medical and psychological needs.<sup>52</sup> Future trials may evaluate interventions in different patient subgroups targeting specific postsepsis sequelae. Larger samples should be included to address smaller but potentially still clinically relevant effects of primary care interventions.

## Intervention

The exploratory analyses indicated no intervention effects on mental health symptoms. These results may reflect lack of intervention intensity and specificity or absence of clinically effective interventions. However, there is growing evidence that after critical illness, mental health outcomes can be improved through effective psychological interventions targeting specific syndromes.<sup>52,53</sup>

## Controls

According to process data derived from control PCPs (eTable 8 in the Supplement), usual sepsis aftercare in Germany seems to be highly intensive. PCP training and consultation may have been insufficient to yield a meaningful improvement in the level of care. Observational research may provide more insights into existing usual sepsis aftercare in diverse health care systems.

## Outcome

The wide range of postsepsis sequelae may not be adequately reflected in a rather global outcome measure, such as change in SF-36 MCS score. Furthermore, the cohort's baseline mental health–related quality of life was similar to healthy population norms in Germany, reflecting a limited potential for improvement in the MCS score. Last, the exclusion of patients with more severe cognitive dysfunction may have led to a ceiling effect compared with other trials. For future trials, more specific primary outcomes should be considered.

Up to years after the ICU discharge, many patients seem to share their needs with a reliable medical professional.<sup>54</sup> Yet the PCP is not involved systematically in post-ICU care.<sup>55,56</sup> This study may shed light on PCP relevance, addressing major concerns recently identified as “barriers to practice.”<sup>57</sup> These include checks on transition from ICU through to community reintegration, linkage, and clinical decision support to primary care, inclusion of a case manager, and educational information for patients and PCPs. Compared with the large-scale PRACTICAL trial on follow-up care in ICU clinics,<sup>47</sup> this study defines a clear

function for the PCP in sepsis aftercare. Follow-up care combining specialized ICU clinics and integrated PCPs may improve outcomes.

This study's exploratory findings suggest possible improvements of physical function and ADL impairments. Additional research is needed to confirm these results. Possible mechanisms of action for these findings may include increased patient motivation (despite the presence of pain) to partake in physical activity owing to regular case manager telephone calls with goal-setting and basic behavioral activation. Increased PCP supportiveness in the intervention group may also have motivated patients to be more proactive, possibly reflected by the increased rating in number of Patient Assessment of Care for Chronic Conditions items (eTable 9 in Supplement 3).

This study has strengths and limitations. It was possible to enroll a large number of patients in spite of the challenges of recruiting critically ill patients for research.<sup>58</sup> Intervention integrity went as planned<sup>59</sup> (eFigure 2 in Supplement 3), including the acceptance of an external medical consultant by the patient's PCP. These findings are encouraging for further interventions in the primary care setting.

Loss to follow-up was balanced between the groups and low, in contrast to sample size calculations that allowed for 40% dropout. Baseline values were missing for some secondary outcomes owing to patients' severely impaired clinical condition. A carryover effect (from treatment to control) may have occurred for 1 PCP, inducing a bias toward a null effect. Calling control patients to collect follow-up data may have led to an intervention effect, possibly leading to underestimation of the intervention effects.<sup>60</sup> In addition, nonblinded outcome assessments also may have biased the results.<sup>61</sup> The intervention is not generalizable to all survivors of sepsis in various outpatient settings.

## Conclusions

Among survivors of sepsis or septic shock, the use of a primary care–focused team-based intervention, compared with usual care, did not improve mental health–related quality of life 6 months after ICU discharge. Further research is needed to determine if modified approaches to primary care management may be more effective.

### ARTICLE INFORMATION

**Author Affiliations:** Institute of General Practice and Family Medicine, Jena University Hospital, Jena, Germany (Schmidt, Worrack, Mehlhorn, Schneider, Freytag, Wensing, Gensichen); Center of Sepsis Control and Care (CSCC), Jena University Hospital, Jena, Germany (Schmidt, Worrack, Brunkhorst, Pausch, Scherag, Reinhart, Gensichen); Group Health Research Institute, Group Health Cooperative, Seattle, Washington (Von Korff); Department of Psychiatry and Behavioral Sciences, University of Washington School of Medicine, Seattle (Davydow); Center of Clinical Studies, Department of Anesthesiology and Intensive Care Medicine, Jena University Hospital, Jena, Germany (Brunkhorst); Department of Psychology, University of Zuerich, Zuerich, Switzerland (Ehlert); Institute for Medical Informatics, Statistics and Epidemiology, University of Leipzig, Leipzig, Germany (Pausch); Department of Anaesthesiology and Intensive Care Medicine, Jena University Hospital, Jena, Germany (Reinhart); Department of General Practice and Health Services, University of Heidelberg Hospital, Heidelberg, Germany (Wensing).

**Author Contributions:** Drs Schmidt and Gensichen had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

**Study concept and design:** Schmidt, Davydow, Brunkhorst, Ehlert, Freytag, Reinhart, Wensing, Gensichen.

**Acquisition, analysis, or interpretation of data:** Schmidt, Worrack, Von Korff, Pausch, Mehlhorn, Schneider, Scherag, Reinhart, Wensing, Gensichen.

**Drafting of the manuscript:** Schmidt, Davydow, Schneider, Scherag, Wensing, Gensichen.

**Critical revision of the manuscript for important intellectual content:** Schmidt, Worrack, Von Korff, Davydow, Brunkhorst, Ehlert, Pausch, Mehlhorn, Freytag, Reinhart, Wensing, Gensichen.

**Statistical analysis:** Schmidt, Worrack, Pausch, Schneider, Scherag, Freytag, Wensing, Gensichen.

**Obtained funding:** Reinhart, Gensichen.

**Administrative, technical, or material support:** Worrack, Brunkhorst, Mehlhorn, Schneider, Freytag, Gensichen.

**Study supervision:** Schmidt, Davydow, Brunkhorst, Ehlert, Scherag, Wensing, Gensichen.

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**SMOOTH Study Group:** The authors and Anne Bindara-Klippel, Carolin Fleischmann, MD, Ursula Jakobi, MD, Susan Kerth, Heike Kuhnsh, Friederike Mueller, MD, Mercedes Schelle, Paul Thiel, MD (Institute of General Practice and Family Medicine, Jena University Hospital); Mareike Baenfer, Sabine Gehrke-Beck, MD, Christoph Heintze, MD (Charité University Medicine Berlin); Andrea Geist, Torsten Schreiber, MD (Zentralklinik Bad Berka); Christian Berhold, MD, Marcel Corea, MD, Adrian Freytag, MD, Herwig Gerlach, MD, MBA, Rainer Kuehnemund, MD, Josefa Lehmk, MD, Peter Lehmkuhl, MD, Lorenz Reil, MD, Guenter Tiedemann, MD, Susanne Toissaint, MD, Siegfried Veit, MD (Vivantes Clinics Berlin); Anton Goldmann, MD, Michael Oppert, MD, Didier Keh, MD, Sybille Rademacher, MD, Claudia Spies, MD, Lars Toepfer, MD (Charite University Medicine Berlin); Frank

Kleffisch, MD (Paulinen Hospital Berlin); Ute Rohr, MD, Hartmut Kern, MD (DRK Clinics Berlin); Armin Sablotzki, MD (St Georgs Hospital Leipzig); Frank Oehmichen, MD, Marcus Pohl, MD (Bavaria Clinic Kreischa); Andreas Meier-Hellmann, MD (Helios Clinic Erfurt); Farsin Hamzei, MD (Moritz-Clinic Bad Klosterlausnitz); Christoph Engel, MD (Institute for Medical Informatics, Statistics and Epidemiology, University of Leipzig); Michael Hartmann, MBA, MPH, Christiane Hartog, MD (Jena University Hospital); Jürgen Graf, MD (University Clinic Frankfurt); Günter Ollenschlaeger, MD, PhD (ÄZQ Berlin); Gustav Schelling, MD (University Clinic LMU Munich).

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