Editorial

Dealing with the critical care aftermath: where to from here?

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One of the most important developments in critical care over the last 10 years has been the recognition that while overall survival is important, the quality of life post discharge is crucial (1). The rate of recurring major illness and/or mortality is increased in the year after ICU discharge and the patient may have residual physical, cognitive and psychosocial problems lasting from 5 to 15 years (2). There has been a proliferation of research directed as to the actual nature, distribution and degree of impairments and to interventional studies to prevent or ameliorate these poor outcomes both early in intensive care and in post intensive care follow up. Despite this most primary care clinicians have little knowledge of the potential and range of impairments post critical care discharge. Lack of continuity and co-ordination of care is evident in most countries and centres.

In the June 28th version of *JAMA*, Schmidt *et al*. (3) report a randomized controlled trial investigating follow up of critical are survivors including 9 intensive care units in Germany and totalling 291 subjects in total. The main inclusion criteria were adults who had suffered an episode of either severe sepsis (as per previous SCCM guidelines) or septic shock. This comprehensive program, delivered post hospital discharge, comprised a specifically trained team including nurse case managers and primary care clinicians who interviewed the intervention group and used a formulated questionnaire to detect problems in physical, psychological or cognitive areas. Both patients and primary care physicians were provided with evidence based information on the process of sepsis and the aftermath. The initial contact with the intervention group was a 60 minutes face to face interview following by at least monthly telephone contact for 6 months. Appropriate referrals were then made according to the severity and urgency of the problem. The control group received usual care from their primary care physicians without the specific training and information on sepsis and no monitoring. However this group did receive periodic contacts (regularity not specified), referrals to specialists, prescriptions of medications and therapeutic aids.

The main outcome measure was the mental health summary score from the health related quality of life instrument short form health survey—36 (SF-36) at 6 months post discharge. There were numerous secondary outcomes including the remaining summary scores of the SF-36, functional scores, screening for malnutrition, insomnia, depression, pain, posttraumatic stress, medication adherence and ability to work.

Overall the primary outcome measure i.e., the mental health summary score demonstrated no difference between groups, despite several sensitivity analyses. There were significant differences favouring the intervention group in activities of daily living (ADL), measures of disability and physical function at 6 months and the insomnia score at 12 months. There were also trends in the physical function components of the SF-36. The authors stated that as these secondary outcomes were exploratory the secondary outcomes were not adjusted for multiple tests.

A number of clinical trials to improve outcome post hospital discharge have essentially found no difference between groups in the primary outcome (4-10). The majority of these trials tackled physical function and strength and were delivered utilizing a variety of methods ranging from one on one contact (6,9) to a manual based program (8). The major recommendations from authors of these trials were that it was recognised that there were multiple problems post ICU which could

impact synergistically and that a multidisciplinary team was preferable. Additionally it was stated (4) that a heterogeneous population of ICU survivors who had very short stays were not ideal and further studies should focus on more high acuity patients.

The planning of this current study (3) appears to have identified the shortcomings from previous trials, recommendations from centres that include these clinics as usual care and current guidelines (11-13). It has been advised that that to be successful these follow up clinics need to provide individualized screening and targeted management of physical, neuropsychiatric and cognitive outcomes. The strengths in this current trial include the baseline screening based on known problems in sepsis, the individualized management according to detected problems, the comprehensive training of PCPs, the case management of patients and the exemplary methodology within the study. Additionally the population was well chosen, sepsis is a discrete population with known poor outcomes (14) and well represented in ICU. Although a length of stay was not specific in the inclusion criteria, the minimum length of stay in both groups was 4 days. The primary outcome i.e., the mental health summary score from the SF-36 has been well validated in survivors of critical care (15).

The study should not be discarded as another non-significant trial. A cluster of secondary outcomes related to function and physical function were all significantly improved in the intervention group at 6 months. It is interesting that Schmidt *et al*. comment that initially both physical function and mental health summary scores were to be the main outcome measure and in fact there is trend in significance in physical role subscale at 12 months ($P<0.07$). While it may be argued that with so many secondary outcomes a number could be significant as random chance, all significant findings were clustered in the physical function area.

It was noted by the authors that the baseline figures for the mental health summary score for both groups were well within normal population norms, so any lack of significant improvement may have been due to a ceiling effect. This also raises the question of volunteer bias (16) in such a study as this where travel and commitment were required. The physical summary scores were well below norms, as is usual in a study on sepsis survivors. However overall agreement to participate was 81% of eligible patients asked for consent which was impressive.

One comment on the methodology was that although undergoing comprehensive interview at baseline, subjects were not given formal tests as screening but rather these were completed as secondary outcome measures at completion. The initial interview therefore although comprehensive may have been subjective and not identified actual deficits unless very severe. A further reason for less significant effects may have been the exceptional usual care within the German health system, with the control group also contacted periodically and referred to specialist agencies. An economic analysis would also have been worthwhile especially if these clinics are to become standard practice.

Additionally the intervention offered in these trials, although certainly a step in the right direction is presently very symptomatic. There needs to be a better understanding of the actual pathophysiology of the impairments i.e., the effect of critical illness, the systemic inflammation, sedation, infection and how these events cause weakness, cognitive problems and psychological problems. Work is progressing on this aspect, with both recognition within critical care units of the long term effect of interventions, and the actual mechanisms involved (17-20). Impairments may additionally persist for many years and intervention may need to continue beyond the 12 months period to demonstrate efficacy.

Further work on the mechanism of impairments may also indicate the most appropriate outcome measurements as presently 250 instruments have been utilized in studies of follow up post critical care (21), making it difficult to compare results across studies.

It is encouraging to observe further trials in this important subgroup and also that clinicians' perceptions not only those involved at intensive care level but also those in the community are realising the far reaching effects of "post ICU syndrome", particularly in sepsis syndromes. Ideally the merging number of trials can be analysed to guide researchers as to specific patients who would benefit from this intervention.

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Footnote

Provenance: This is an invited Editorial commissioned by the Section Editor Zhongheng Zhang (Department of Critical Care Medicine, Jinhua Municipal Central Hospital, Jinhua Hospital of Zhejiang University, Jinhua, China).
Conflicts of Interest: A/Professor JD Paratz and A/Professor RJ Boots are presently chief investigators for a similar trial:

Paratz JD, Kenardy J, Mitchell G, *et al*. IMPOSE (IMProving Outcomes after Sepsis)-the effect of a multidisciplinary follow-up service on health-related quality of life in patients postsepsis syndromes-a double-blinded randomised controlled trial: protocol. BMJ Open 2014;4:e004966.

Comment on: Schmidt K, Worrack S, Von Korff M, *et al*. Effect of a Primary Care Management Intervention on Mental Health-Related Quality of Life Among Survivors of Sepsis: A Randomized Clinical Trial. JAMA 2016;315:2703-11.

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