Editorial Commentary

How to improve the care of decompensated cirrhosis: the intervention model for chronic disease management

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To improve the treatment of decompensated cirrhosis (DC) is still a major clinical issue for physicians, mainly because DC patients have a high death rate, a poor quality of life, and a high readmission rate of almost 53% at 90 days (1-3). The Australian Liver Failure (ALFIE) trial, recently published by Wigg *et al.* (4) is a landmark effort to address whether the chronic disease management (CDM)-style interventions can affect the prognosis (5). The results of this trial are illuminating and have implications for future models of care in chronic liver disease, even if it did not achieve its primary aim of lowering liver-related emergency admissions (LREA) (6). The ALFIE trial was a two-year, multicenter randomized controlled trial (RCT) that enrolled 147 patients with DC from five Australian tertiary centers. Participants were randomized to receive either a CDM-style intervention or usual care. Previous success with therapies that have been demonstrated to lower admissions and mortality in other chronic conditions, such as heart failure, served as the basis for this concept (7). The CDM intervention in the ALFIE trial was multi-component and nurse-led, incorporating individualized care plans, early outpatient review, scheduled and unscheduled nurse contact, home visits, and tools to support patient self-management (e.g., blister packs and education booklets). This trial targeted a high-risk population—patients recently hospitalized for complications of DC, including ascites, hepatic encephalopathy (HE), variceal bleeding, or spontaneous bacterial peritonitis—with a median Model for End-stage Liver Disease (MELD) score of 19. Approximately 70% had alcohol-related liver disease, and most were recruited during an inpatient stay, reflecting real-world practice. The ALFIE trial found no significant difference in overall LREA rates between the intervention and control groups (incident rate ratio 0.89, P=0.666), nor was there a survival benefit (hazard ratio 1.14, P=0.646). At face value, these results may appear disappointing.

However, a closer look shows several positive points. Most notably, the incidence of HE-related LREA was significantly reduced in the intervention arm (hazard ratio 1.87, P=0.007). Given the potentially preventable nature of HE and its high cost and morbidity, this finding is of clinical importance. It suggests that timely support, adherence-promoting tools, and early recognition may meaningfully impact this complication. Additionally, there was a clear shift in the pattern of hospitalizations: the intervention group had significantly more elective admissions, especially for procedures such as paracentesis. This change, while not captured in the primary endpoint, indicates more organized and preemptive care, with fewer chaotic emergency presentations—a hallmark of improved health system function. The ALFIE trial showed improvements in several process and patient-reported outcomes, in addition

to hospitalization metrics. The intervention group showed a significant improvement in quality-of-care markers such as hepatocellular carcinoma surveillance, vitamin D level monitoring, and bone density testing. These reflect better adherence to best practice guidelines and enhanced delivery of comprehensive liver care. Patient-reported outcomes also trended positively. The intervention group reported improved self-management skills, fewer barriers to medication adherence, and higher quality of life [as measured by EuroQoL 5-Dimension (EQ-5D) visual analog scale (8), P=0.044] at three months—the peak period of intervention intensity. These improvements are clinically meaningful, particularly in a disease where patients often feel overwhelmed and disengaged from care.

Several considerations should be discussed in relation to the ALIFIE trial's failure to demonstrate a benefit in total LREA or mortality. First, the delivery of the intervention was constrained. Nurses were employed only part-time, lacked prior experience with cirrhosis management, and faced frequent turnover during the trial. This likely diluted the intervention's intensity and continuity, both of which are critical in managing complex chronic illness. Second, access to key supportive services—such as addiction treatment and mental health care—was limited across participating sites. With alcohol-related liver disease as the dominant etiology accounting for approximately 70%, this represents a structural gap. The CDM models are unlikely to succeed in DC unless they integrate behavioral health and substance use treatment components. Third, the control group in this trial received high-quality standard care, including frequent outpatient follow-up and access to dieticians and pharmacists. The marginal benefit of the intervention may thus have been blunted by an already high baseline standard of care—likely higher than what is available in many community or non-tertiary settings. Finally, the ALIFE trial coincided with the coronavirus disease 2019 (COVID-19) pandemic, which disrupted healthcare delivery globally. Although the authors attempted to mitigate these effects, they may have impacted both arms unequally, particularly the components of care that relied on in-person visits and continuity.

Therefore, we should consider several factors when designing future clinical trials with comparable goals. In the first place, since the 'dose' of the intervention matters with suboptimal implementation undermining effectiveness, investing in full-time, well-trained liver nurses and reducing staff turnover will be critical. Especially for alcohol-associated cirrhosis, the comprehensive CDM must include dedicated pathways for alcohol use disorder treatment, psychiatric support, and social services. As a matter of fact, for such a subgroup, alcohol cessation is the best chance to potentially change the course of this debilitating illness So, both physicians and nurses should be upskilled in tackling alcohol use disorder. Second, the future interventions might focus on patients with recent HE, low quality-of-life scores, or poor outpatient engagement—groups who appear to benefit more from structured care. Simultaneously, considering that many patients were still presenting with other complications than HE, researches to develop other disease modifying therapies should be also required continuously. Third, from the statistical viewpoint, counting total LREAs may not capture the nuanced benefits of care redesign. More detailed metrics such as unplanned *vs.* elective admissions, preventable admissions, and patient experience should be incorporated. Fourth, since self-management tools and education had measurable impact, incorporation of digital tools, telemedicine, and application-based coaching should be actively considered in the design of the future clinical trials, in order to further augment engagement and adherence. Last, further studies are simultaneously needed to evaluate the cost-effectiveness of this CDM model.

In conclusion, the ALFIE trial exemplifies the complexity of translating the CDM models into hepatology. It reaffirms that DC is not merely a sequence of medical crises, but a chronic illness that requires coordinated, patient-centered, and multidisciplinary care. While the ALIFE trial's primary endpoint was negative, it demonstrated improvements in specific complications, quality of care, and patient-reported outcomes—all of which are vital in this population. Subsequent efforts must address the pragmatic obstacles to implementation and individualize interventions to patient need, health system capacity, and local resource availability. By doing this, physicians might potentially change the course of this debilitating illness and create a scalable strategy for bettering outcomes in DC.

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