deteriorating during TACE [2], comparison of LT with liver resection and with forms of HCC treatment such as radiofrequency ablation, TACE using drug eluting beads, ^{90}Yttrium therapy, etc. We agree that liver resection may offer a similar survival benefit as LT. That is particularly true for Asian countries, less for the Western world [3]. This differential indication was, however, not the point of our publication. Likewise, the problem if lab-MELD, matchMELD, regular or rescue allocation impact prognosis was not intended to be addressed, as it deserves studies using a much greater cohort of patients and can, therefore, not be answered by a single centre analysis. Even if described in the publication we would stress the following aspects mentioned by the authors of the letter: TNM classification usually indicates pTNM and has, therefore, to be deduced from the surgical specimen (Table 2, [1]) not being available during the initial assessment. Considerations about the indication for LT in patients with T1 or T2 tumours are justified in scientific context but must be questioned in clinical practise due to the impreciseness of imaging (29 of 70 = 41%; [4]). Of course, all patients were included in the overall survival analysis and time from first TACE to LT – the only period which is of interest in the study context – is demonstrated in Table 1, [1]. After all, we cannot recognize the "bias" challenged in the Letter as the authors ignore the issue of our publication.

In one point we agree explicitly with the authors of the submitted letter: A change of the allocation rules based on our publication would be premature and the "...finding(s) should be verified in a larger prospective study..." as stated in the last sentence of the publication.

Conflict of interest

The author declared that he does not have anything to disclose regarding funding or conflict of interest with respect to this manuscript.

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Coordinated care in cirrhosis; the need for further randomized controlled trials

To the Editor:

We read with interest the recent study on care coordination for cirrhotic patients by Morando *et al.*, with an accompanying editorial [1,2]. Firstly, we would like to congratulate the Padova group for focusing their research interest on this important topic and patient population.

We must, however, correct the statement of the editorialists that this study represents the "first prospective trial in the cirrhosis population" [2]. We highlight the publication of our own randomized controlled trial of coordinated cirrhosis care, which preceded the publication of the Padova study in the literature [3].

Referencing of our earlier study may have been helpful for the readership because, unlike the Padova study, it was a fully randomized controlled trial (RCT) with outcomes that were very different. We did not detect any improvement in either hospitalization measures or mortality in the 12 months following an intervention with a care co-ordination model.

A major limitation of the Padova study is its lack of a blinded and completely randomized group allocation procedure, which was instead based on retrospective matching of known confounders. As a consequence, it remains possible that the beneficial effects seen were not related to the new care model, but instead to more competent physicians in the intervention team or to unknown confounders that were not balanced between the groups. Unfortunately details of the allocation procedures provided are insufficient to determine the levels of stratification used for each confounder and whether all patients commenced their treatment programs within a similar timeframe following discharge.

There was also a lack of process measures performed during the trial, which would help support claims that the model was effective. For example, there were no data confirming that preventative medications prescribed were actually taken by patients, or that patient attendance at scheduled appointments was improved. Authors propose increased contacts with specialist physicians as explanation for improved outcomes in the coordinated care group. However, no analysis was performed to support the claims for associations between outcomes and greater specialist visit numbers being associated with reduced risk of mortality.

In relation to mortality, the authors chose not to discuss the distribution of events throughout the study. A careful examination of the Kaplan Meier curves does however reveal some important details. Firstly, there was an increased risk of death for standard care patients during the first 3 months of the trial relative to

expected deaths for patients at this level of MELD/Child Pugh score. There was also an increased risk of mortality in the intervention group compared to the standard care group in the second half of the trial. Additionally, the much lower risk for the coordinated care group in the first 3 months followed by a higher risk indicates that benefits of the program were mostly achieved early on and were therefore probably not strongly related to the total number of visits/time spent with clinicians. Likewise, the unexpectedly high death rate in the standard care group suggests either that the standard care program provided was below the average standard care program, that the patients in this group were sicker in respects to factors other than their MELD score, or perhaps that the group allocation procedure lead standard care patients to a more delayed treatment following discharge.

With respect to the data on readmissions, knowledge of the unadjusted effects of the program, in addition to the adjusted effects, would have been useful to determine if confounding was present. The adjusted nature of the analysis, rather than a simple unadjusted comparison, perhaps reflects the observational nature of the study since an RCT automatically eliminates confounding from both known and unknown risk factors and does not therefore require statistical adjustment. We were also intrigued that although the analysis suggests an important effect of the intervention, a surprising additional result was that several known risk factors for readmission, including age and MELD, were not independent predictors beyond the group allocation. This suggests that the group allocation effect on readmission was strongly associated with these variables. We highlight the possibility that good coordinated care for sick patients may generate an increase in emergency readmissions in the short term, via improved access to care. This was an interesting finding in our study [3] and has also been noted by other investigators [4].

For new care models to be adopted in cirrhosis the evidence base must be of the highest order, as it has been the case for other diseases such as heart failure [5]. In the absence of high quality evidence, the significant upfront costs associated with re-organizing care along new models, are unlikely to be funded by current health care systems. Although we believe instinctively these models will work, these two important studies do not yet provide proof of principle for coordinated care models in cirrhosis. Further well-designed, randomized investigations in this field are still required.

Conflict of interest

The authors declared that they do not have anything to disclose regarding funding or conflict of interest with respect to this manuscript.

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Reply to: "Coordinated care models in cirrhosis; the need for further randomized controlled trials"

We are making a step forward

To the Editor:
We would like to thank A.J. Wigg *et al.* for their interest in our study about a new model of care coordination by consultant hepatologists in outpatients with cirrhosis and ascites [1]. We regret that the Editorialists have not considered their publication but, such is life! Moreover, it should be recognized that the appearance of the two manuscripts on PubMed were very close each to one other. In their letter [2] A.J. Wigg *et al.* highlighted once again that our study was not randomized and suggested that the differences in outcomes of the two groups of our work were not linked to the process of management as outpatients, but to confounding factors that were not well balanced between the two groups. The circumstance that our study was not randomized has been already stressed by ourselves and by the editorialists. We also set out to explain the reasons why we decided to perform this type of study. As far as the enrollment and the matching process are concerned, as we stated in the paper, patients were enrolled consecutively on discharge from hospitalization due to acute decompensation of cirrhosis, and subjected to matching for a large number of