March 22nd, 2023

Dear editors,

Thank you for provisionally accepting our paper entitled, "Randomized Intervention and Outpatient Follow-Up Lowers 30-day Readmissions for Patients with Hepatic Encephalopathy, Decompensated Cirrhosis" to your esteemed journal. We addressed all the advice recommended by the reviewers. Please find below our responses to the reviewers comments.

- 1. Reviewer 1
 - a. Language correction and formatting completed throughout the manuscript. All of these changes can be seen in the track change version of the manuscript below. The clean manuscript follows.
 - b. The following citations were added as per the suggestion in the discussion section of manuscript:
 - i. Bajaj etal 2019
 - ii. Tapper et al 2017
 - iii. Chirapongsathorn et al 2016
 - iv. Kanwal et al 2016
 - v. Frenette et al 2022
- 2. Reviewer 2
 - a. Reviewer has pointed to removing the unnecessary information about the COVID-19 from the manuscript. We removed the unnecessary information and only left pertinent information to show how it limited our ability to recruit patients for our trial.
 - b. Grammatical errors including punctuation in Table 3 and 6 have also been fixed.

Of note, our authors signature page is below.

We hope that with addition of information and guidance provided by reviewers, our manuscript quality has further improved. Please let us know if there are any questions.

Sincerely on behalf of all co-authors,

Antoinette Pusateri, MD



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4 SIGNATURES OF ALL AUTHORS

This declaration must be signed by all authors. The manuscript will be rejected immediately if we find the declaration was not signed by authors themselves. The signature list for all authors is as follows:

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1 <u>TITLE PAGE</u>

- 2 Study Title: Randomized Intervention and Outpatient Follow-Up Lowers 30-day Readmissions
- 3 for Patients with Hepatic Encephalopathy, Decompensated Cirrhosis
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33	Antoinette Pusateri and Khalid Mumtaz- study design, team administration, training team	
34	members for recruiting, recruiting patients for study, interpreting data, drafting manuscript; both	
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38	recruiting patients for study, drafting manuscript; approved the final submitted version of	
39	manuscript_	
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43	Haikady N. Nagaraja- analyzed data, edited manuscript, and approved the final submitted	
44	version of this manuscript.	Deleted: manuscript
45		
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54	patients with decompensated cirrhosis (CCTS ID#: 6018)".
55	
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64	Potential competing interests:
65	There no competing interests declared by the authors.
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72 ABSTRACT

73 Background

- 74 We previously reported national 30-day readmission rates of 27% in patients with
- 75 decompensated cirrhosis (DC).

76

77 Aims

78 We studied prospective interventions to reduce early readmissions in DC at our tertiary center.

79

80 Methods

- 81 Adults with DC admitted July 2019 to December 2020 were enrolled and randomized into the
- 82 intervention (INT) or standard of care (SOC) arms. Weekly phone calls for a month were
- 83 completed. In the INT arm, case managers ensured outpatient follow-up, paracentesis, and
- 84 medication compliance. Thirty-day readmission rates and reasons were compared.

85

86 Results

- 87 Calculated sample size was not achieved due to COVID-19; 240 patients were randomized into
- 88 INT and SOC arms. 30-day readmission rate was 33.75%, 35.83% in the INT versus 31.67% in
- the SOC arm (p=0.59). The top reason for 30-day readmission was hepatic encephalopathy (HE,
- 90 32.10%). There was a lower rate of 30-day readmissions for HE in the INT (21%) versus SOC
- 91 arm (45%, p=0.03). There were fewer 30-day readmissions in patients who attended early
- 92 outpatient follow-up (n=17, 23.61% v. n=55, 76.39%, p=0.04).
- 93
- 94 Conclusions

95	Our 30-day readmission rate was higher than the national rate but reduced by interventions in
96	patients with DC with HE and early outpatient follow-up. Development of interventions to
97	reduce early readmission in patients with DC is needed.
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99	Keywords: decompensated cirrhosis; hospital readmissions; interventions
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118	INTRODUCTION	
119	Cirrhosis affects approximately 5 million annually ¹ and has been reported to be the 8 th leading	
120	cause of death with more than 40,000 deaths annually in the United States $\frac{2}{3\pi}$ A study on the	Deleted:
121	burden of gastrointestinal, liver, and pancreatic diseases in the United States revealed that liver	Deleted: .
122	diseases had the highest mortality at $3.1\%^3$ Jn addition to high mortality, cirrhosis is also	Deleted:
123	associated with high morbidity. The sequelae of decompensated cirrhosis (DC) are often	Deleted: .
124	managed during hospital admissions and include volume overload in the form of ascites, edema	
125	or hepatic hydrothorax, portal hypertension leading to bleeding esophageal or gastric varices, as	
126	well as hepatic encephalopathy (HE), hyponatremia, acute kidney injury (AKI), and spontaneous	
127	bacterial peritonitis (SBP) ⁴	Deleted:
128		Deleted: .
129	Several studies have demonstrated hospital readmissions in DC place a large financial burden on	Deleted: how DC disease progression reflected in
130	the United State healthcare system. The 30-day readmission rate has been reported to be 20%-	
131	$37\%_{\pi}^{5-14}$ We have recently published on early readmission rates up to 27% in patients with DC	Deleted:
132	and developed the Mumtaz readmission risk score based on United States data. ¹⁵ We also	Deleted: . Deleted: .
133	reported that nearly one-third of patients with HE were readmitted within 30 days, and early	
134	readmission adversely impacted healthcare utilization and calendar-year mortality $\frac{16}{4}$	Deleted:
135		Deleted: .
136	Interventions to reduce readmissions have been shown to be safe and effective. For instance,	Deleted: In previous studies,
137	Morales et al. developed HEPACONTROL program including a hepatologist follow-up exam	Deleted: i
138	within 7 days after discharge. This program resulted in a reduction in 30-day readmissions, 60-	
139	day mortality, emergency department visits and associated costs ¹⁷ / _* Similarly, another group	Deleted:
140	demonstrated that follow-up with a "care management check-up" as opposed to "standard	Deleted: .

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157	outpatient care" reduced 30-day readmission, 12-month mortality and saved 1500 euros per		
158	patient month of life $\frac{18}{4}$	Deleted:	
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160	There is a paucity of prospective studies on interventions to reduce early readmission rates in	Deleted: the	
161	patients with DC. Therefore, we prospectively studied 30-day readmission rates in patients with		
162	DC and compared various interventions (INT) with standard of care (SOC) to reduce early	Deleted: the	
163	readmission rates. We hypothesized that DC patients in the INT arm would have decreased 30-		
164	day readmission versus the SOC arm.		
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184 <u>METHODS</u>

- 185 This study was conducted at the Ohio State University Wexner Medical Center (OSUWMC),
- 186 Columbus, Ohio from July 2019 to December 2020. Our study was approved by OSUWMC
- 187 Institutional Review Board. All aspects of the studying involving human participants including
- 188 informed consent for enrollment were in accordance with the ethical standards of our
- 189 Institutional Review Board and with the 1964 Helsinki Declaration and its later amendments or
- 190 comparable ethical standards.
- 191

192 Screening

- 193 All patients admitted with DC to the hepatology (inpatient or consult) service were screened for 194 enrollment. Patients meeting inclusion criteria were approached for study consent. Of note, due 195 to the global COVID-19 pandemic, beginning March 2020, only COVID negative patients were 196 approached for informed consent. Elective readmissions for inpatient procedures including 197 endoscopy, trans-arterial chemoembolization (TACE), transjugular intrahepatic portosystemic shunt (TIPS), paracentesis or readmissions unrelated to DC such as motor vehicle accidents were 198 199 excluded. 200 201 **Randomization and Data Collection**
- 202 Study data were collected and managed using REDCap hosted at The Ohio State University
- 203 Wexner Medical Center.^{19,20} Informed consent was obtained from all individual participants
- 204 included in the study. Consented patients were randomly assigned to either the INT arm or the
- 205 SOC arm in a 1:1 ratio using the RedCap randomization tool. The following data were collected
- 206 on all patients via RedCap software including demographics (age, sex, insurance type, income

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209	based on the zip code), hospitalization data (date of index admission defined as initial admission
210	during which patient consented for study, reason for admission, length of stay (LOS) defined as
211	difference in days between index admission date and index admission discharge date, discharge
212	disposition, associated cost of care of admission as obtained through medical record billing tab),
213	etiology of cirrhosis (alcoholic and non-alcoholic including viral, non-alcoholic fatty liver
214	disease, autoimmune, primary biliary cirrhosis, primary sclerosing cholangitis or cryptogenic),
215	complications of cirrhosis {HE, AKI, ascites, variceal bleeding, SBP, hepatorenal syndrome
216	(HRS), coagulopathy, portal hypertension, hepato-pulmonary syndrome (HPS), hepatocellular
217	carcinoma (HCC)}, and procedures performed during admission {esophago-gastro-
218	duodenoscopy (EGD), colonoscopy or flexible sigmoidoscopy, paracentesis, transjugular
219	intrahepatic portosystemic shunt (TIPS) and hemodialysis (HD) on admission and discharge}.
220	We also collected data including Elixhauser comorbidity index, discharge medications, and
221	laboratory data (complete blood counts, serum creatinine, liver function tests including total
222	bilirubin, INR, and sodium). Child Turcotte Pugh (CTP) and Sodium-model for end stage liver
223	disease (MELD-Na) score were calculated from the data. The nurse case manager (CM) also
224	recorded labs & medications at readmission & discharge and associated cost of readmission.
225	Status of early readmission, liver transplantation, and mortality at one year were also collected.
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227	Follow-up

227 Follow-up

The CM phoned each patient enrolled in either arm weekly for 30 days after index discharge to find out if the patient has been readmitted to OSUWMC or another hospital. In the INT arm, during the call CM also ensured i) early (defined as within 30 days from index admission discharge) outpatient hepatology follow-up ii) compliance of medication, iii) arrangement of

232	outpatient paracentesis if needed, and reviewed outpatient hepatology clinic follow-up records.
233	SOC arm as per our center's protocol had to be taken care of by the primary inpatient team. This
234	included arranging early outpatient clinic follow-up, providing list of medications, and advice for
235	outpatient paracentesis if needed at the time of discharge. Due to the nature of intervention, the
236	study could not be blinded.

238 Definition of outcomes

239 Early readmission was defined as admission within 30 days of index admission discharge.

240 Reasons for readmission were gathered by CM by reviewing the electronic medical record

241 (EMR) of all enrolled patients readmitted at OSUWMC or outside hospital within 30 days of

242 index admission. Predictors of early readmission were also compared in the two arms.

243

244 Sample Size

Based on the sample size calculation, target of recruitment for the study was 848 patients, 245 246 admitted to the hospital with DC under the hepatology (inpatient and consult) services. Patients 247 were randomly assigned in a 1:1 ratio into INT or SOC arms. Based on our previous study using 248 the NRD administrative database, we expected a 30-day readmission rate of 27% among patients 249 meeting inclusion criteria, which yield 114/424 patients with 30-day readmission events, thus 250 meeting the target sample size. Based on this calculation, a total sample size of 848 (424 per group) provided 80% power to detect a 30% decrease in 30-day readmission rate (from 27% to 251 19%) with a type I error rate of 0.05. However, planned sample size could not be achieved due to 252 253 the COVID-19 pandemic related restriction started in our center in March 2020. Therefore, we

254	end up with available sample size of a total of 240 patients. The modified CONSORT Flow
255	diagram for enrollment in our study trial is illustrated in Figure 1.
256	
257	Statistical analysis:
258	Means of continuous response variables between two groups were compared using robust t-test
259	(Welch test). Proportions were compared using Chi-square or Fisher's exact test as applicable.
260	Logarithmic transformation was used for comparing the length of stay (LOS) and admission cost
261	across groups. Level of significance was kept at 0.05 for each comparison. JMP Version 15 (SAS
262	Institute, NC) was used for all the analyses.
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RESULTS 277 278 **Initial Screening Data** 279 From July 1, 2019, to December 1, 2020, 1392 patients were screened. Due to the COVID-19 280 pandemic, recruitment was held from March 2020 to July 2020 and subsequently resumed until 281 December 2020. Out of the patients screened, only 499 (35.85%) were eligible for inclusion; 282 however, 240 patients consented and randomized: 120 each into the INT and SOC arm (Figure 283 1). 284 285 Patient demographics and clinical characteristics 286 The mean age of patients was 56.34±11.19 years, majority were males (135, 56.25%), belonged to White race (n=202, 84.17%) and non-Hispanic or Latino ethnicity (n=227, 94.58%). Almost 287 two-thirds of the patients had public insurance (n=76, 31.67% on Medicare and n=70, 29.17% on 288 289 Medicaid); 73 (30.42%) had private insurance. At admission, the mean MELD-Na score and 290 mean Child Pugh Score were 21.89±8.03 and 9.36±1.96, respectively. Major etiology of cirrhosis was alcohol (n=121, 50.42%) followed by non-alcoholic fatty liver disease (n=79, 291 292 32.92%) and viral hepatitis (n=43, 17.92%). Furthermore, 116 (48.33%) patients were actively under evaluation for liver transplantation. 293 294 295 **Characteristics of index admissions** 296 The index admission mean LOS was 8.13±5.83 days (median 6, range 1-43 days). The mean cost of index admission was \$60,595±\$47,174 (n=225, median \$42,932, range \$1,630-251,991). The 297

- 298 top five reasons for index admission included volume overload (n=111, 46.25%), acute kidney
- injury (n=65, 27.08%), hepatic encephalopathy (n=45, 18.75%), variceal bleed (n=42, 17.50%),

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301	lower GI bleed (n=19, 7.92%) and hyponatremia (n=16, 6.67%). The top five interventions
302	performed were EGD (n=136, 56.67%), paracentesis (n=115, 47.92%), colonoscopy/flexible
303	sigmoidoscopy (n=24, 10 %), hemodialysis (n=15, 6.25%) and TIPS (n=10, 4.17%). Most
304	patients were discharged from index admission to home (n=159, 66.25%) followed by home with
305	health care (n=42, 17.50%) and skilled nursing facility (n=32, 13.33 %, Table 1).
306	
207	Characteristics and reasons for early readmissions

307 Characteristics and reasons for early readmissions

- 308 Overall, 81 (33.75%) patients were readmitted within 30 days of discharge. The major reasons
- 309 for first readmission included hepatic encephalopathy (n=26, 32.10%) followed by volume
- 310 overload (n=22, 27.16%), acute kidney injury (n=16, 19.75%), variceal bleed (n=12, 14.82%)
- and hyponatremia (n=10, 12.35%). 14 patients were readmitted twice, 3 admitted thrice and one
- admitted 5 times within 30 days. The mean time to first readmission was 12.65±7.55 days
- 313 (median 12 days, range 1-30 days). The mean length of stay of first readmission was 8.11 ± 8.98
- 314 days. The mean cost of stay of first readmission was $55,548.29 \pm 65,164.91$ (Table 2). Those
- readmitted had a higher MELD score on index admission (23.54±7.80 v. 21.05±8.03, p=0.02)
- and index discharge (21.67±7.95 v. 19.39±6.89, p=0.03) than those not readmitted. Similarly,
- those readmitted had a higher index admission creatinine $(1.80\pm1.53 \text{ v} 1.39\pm1.16, \text{ p}=0.03)$,
- 318 index discharge creatinine (1.61±1.34 v, 1.20±0.97, p=0.02), and higher index admission INR
- 319 $(1.80\pm0.64 \text{ v}, 1.63\pm0.50, p=0.05)$ than those not readmitted.
- 320

321 Comparison of demographics and clinical characteristics in two intervention arms

- 322 Demographics including age, race, ethnicity, income, and insurance were comparable in two
- 323 groups, as well as etiology of cirrhosis, MELD-Na score, CTP score, status of evaluation for

324	liver transplant. There were majority females in the INT arm (60/120, 50% v. 45/120, 32.50%)
325	and males in SOC arm (75/120, 62.50% v. 60/120, 50%, p=0.03, Table 3). Index admission
326	characteristics, disposition and index admission were also comparative in two arms (Table 4 and
327	Table 5)

329 Comparison of reasons of 1st readmission and outcomes in the INT v SOC arm

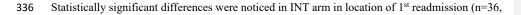
330 There was no difference in the readmission rates for patients in the INT (n=4, 35.83%) versus

331 SOC arm (n=38, 31.67%, p=0.59, Table 6). Other outcomes including number of readmissions

332 within 30 days (p=0.65), index admission cost (p=0.49), index admission LOS (p=0.63), 1st

readmission LOS (p=0.58), all readmissions' LOS (p=0.82) and waiting time for 1st readmission
(p=0.06) were comparable in two arms.

335



337 83.72% at OSU as compared to n=23, 60.5% outside hospital, p=0.03), and lesser 1st readmission

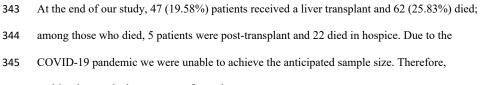
with HE in the INT arm (n=9, 20.9%) vs SOC (n=17, 44.7%, p=0.03). Finally, contingency

analysis of readmission data showed fewer readmissions in patients who attended outpatient

 $\label{eq:states} 340 \qquad follow-up \ within \ 30 \ days \ of \ discharge \ from \ index \ admission \ (n=17, \ 23.61\% \ v. \ n=55, \ 76.39\%,$

341 p=0.04).

342



346 multivariate analysis was not performed.

347	DISCUSSION
348	This prospective randomized study investigated early readmission rates and healthcare utilization
349	in patients with DC. Our readmission rate of 33.75% is higher than the United States national
350	average (27%). While our nurse CM interventions did not reduce told readmissions, we found
351	that HE was the top reason for readmission and <u>such</u> interventions were helpful in reducing early
352	readmissions in patients with HE, This is an important lesson learned given increased burden of
353	HE on hospitalizations, falls, mortality, impaired QOL and caregiver burden, ²¹ In the validation
354	of readmission using "LIRER score", Freitas et al, showed that HE was not only a predictor of
355	30 days readmission independent of MELD score, index, first-year, two-years & overall
356	mortality, but also HE at admission had significantly higher mean LIRER scores $\frac{22}{7}$ Furthermore
357	HE patients on Medicare and geographically from the South or Midwest have higher in-hospital
358	mortality ²³ Considerable research has been done to address HE readmissions. Bajaj et al found
359	that efforts to reduce medication-precipitated HE, prevent aspiration pneumonia and optimize
360	HE medications on hospital discharge should be areas of focus to decrease HE readmissions. ²⁴
361	Tapper et al. demonstrated that development of a checklist for HE protocols integrated into the
362	electronic medical record and order entry system reduced odds of 30-day readmission for
363	patients with HE (from 39.2% to 27.6%) ²⁵ Thus, our results are congruent with existing
364	evidence that interventions should be invested in post-discharge education and communication
365	for all patients with cirrhosis, especially with HE.
366	
367	One of the components of intervention in our study was to arrange appointment of patients in the
368	clinic within a week with their hepatologist, Patients with DC who attended their follow up

appointment within 30 days of discharge from index admission had fewer readmissions. This

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We performed a prospective randomized study to understand the fundamentals of early readmission in patients with DC. Our study enrollment was seriously impacted due to COVID-19 global pandemic in the second year of enrollment. Therefore, calculated sample size was not achieved and could not validate our hypothesis. We believe that due to sample size issues, we faced the challenges of type II errors and have false negative findings. Despite inability to enroll patients according to sample size issues, we learned many lessons from this study with pragmatic interventions.

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400	suggests that overall, in our cohort, outpatient linkage with a hepatologist should be a priority to		
401	reduce readmission rates ²⁶ Morales et al in their retrospective HEPACONTROL program looked	(Deleted:
402	at the impact of follow-up of cirrhotics within 7 days after discharge with a hepatologist. They	(Deleted: .
403	reported reduced 30-day readmission, 60-day mortality and rate of emergency department visits		
404	and associated costs in those who followed up within 7 days, ¹⁷ Morando et al demonstrated that	(Deleted:
405	follow up with a "care management check-up" group as opposed to "standard outpatient care"		Deleted: . Moreover,
406	reduced 30-day readmission, reduced 12-month mortality, and saved almost 1500 euros per		
407	patient month of life $\frac{18}{3}$ While Kanwal et al found early outpatient follow-up after discharge was	(Deleted:
408	associated with a small increase in readmissions, they found an lower overall mortality in their		
409	patients with cirrhosis admitted to Veterans Affairs hospitals. ⁹ Thus our results are also	(Deleted: [Kanwal, 2016 #449]. Our
410	consistent with the current evidence that patients with DC likely benefit from early post-	(Deleted: congruent
411	hospitalization follow up with specialty providers 27.28		Deleted: with
411	nospitalization follow up with specialty providers.	(Deleted: .
412			
413	One of the major limitations of our study was inability to enroll patients according to the	(Deleted: the
414	proposed sample size due to the COVID-19 pandemic. Our study was underpowered to perform	_(Deleted: Due to COVID-19 pandemic, o
717			
415	multiple regression analysis to detect differences in readmission rates in INT versus SOC arm.		
416	From March 2020 to July 2020 our recruitment process was put on hold due to hospital	(Deleted: The impact of the pandemic on translational and clinical research has been well described ²⁵⁻²⁷ . Turner-
417	regulations to reduce patient and staff exposure. Despite this major limitation, we were able to		McGrievy et al described how the pandemic has impacted multiple phases of prospective research including
418	enroll 80.17% (279 consented out of 348 approached) of patients in our study.		recruitment, assessment, intervention, and retention. Regarding recruitment, authors pointed to lack of trust in the scientific community, ethical issues while interacting with patients for non-essential research during the COVID-19
419		l	pandemic ²⁵ .
420	This study was also performed in the setting of a large academic medical center and a high-		

421 volume liver transplant center. While our methods and results may be applicable to the clinical

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442	practice of other such centers, the same impact may not be appreciated by smaller, community	
443	hospitals that are not liver transplant centers.	
444		
445	Future work in patients with DC should continue to focus on prospective intervention strategies	Deleted: similar
446	to reduce early readmissions and educate patients and providers. To achieve desired sample size,	
447	we would suggest collaborations with various centers to identify and recruit patients with DC	
448	into a multicenter prospective cohort. Given our finding that there were fewer readmissions in	
449	patients with follow-up within 30 days, studies should evaluate the use of telehealth visits for	Deleted: T
450	follows up, especially in the COVID19 era ₂ as outlined by Stotts et al ²⁹	Deleted:
451		(Deleted: .
452	In conclusion, this prospective randomized study investigated the impact of various pragmatic	
453	interventions to reduce early readmission and healthcare utilization in patients with DC. Qur	Deleted: Due to the COVID19 pandemic, o
454	study was underpowered to detect statistically significant differences in readmission rates in INT	
455	versus SOC arm. We reported that readmission rate of our medical center was 33.75% and HE	
456	was the top reason for readmission. We found a reduction in early readmission in patients with	
457	HE in the INT arm and those who attended their follow up appointment within 30 days of	
458	discharge from index admission. We demonstrated that simple interventions in patients with DC	
459	are pragmatic and there is need for more prospective multicenter trials in this area of research.	
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559 <u>TABLES</u>

Table 1 Characteristic features of index admission by readmission status

	Total	Not readmitted (n=159)	Readmitted (n=81)	p-value
Index Admission Characteristics		,		
Reasons for Admission ¹ (n, %)				
Acute Kidney Injury	65, 27.08%	41, 25.79%	24, 29.63%	0.54
Hyponatremia	16, 6.67%	11, 6.92%	5, 6.17%	1.00
Hepatic Encephalopathy	45, 18.75%	26, 16.35%	19, 23.46%	0.22
Volume Overload	111, 46.25%	81, 50.94%	30, 37.04%	0.06
Variceal bleed	42, 17.50%	31, 19.50%	11, 13.58%	0.29
Lower GI bleed	19, 7.92%	11, 6.92%	8, 9.88%	0.45
Spontaneous Bacterial Peritonitis (SBP)	21, 8.75%	14, 8.81%	7, 8.64%	1.00
Complications of Cirrhosis During Admission ¹ (n, %)				
Presence of acute kidney injury (AKI)	80, 33.33%	50, 31.45%	30, 37.04%	0.39
Hepatic Encephalopathy (HE)	49, 20.42%	31, 19.50%	18, 22.22%	0.62
Ascites	139, 57.92%	95, 59.75%	44, 54.32%	0.49
Variceal bleeding	37, 15.42%	26, 16.35%	11, 13.58%	0.71
Spontaneous Bacterial Peritonitis (SBP)	16, 6.67%	12, 7.55%	4, 4.94%	0.59
Hepatorenal syndrome (HRS)	14, 5.83%	8, 5.03%	6, 7.41%	0.56
Coagulopathy	56, 23.33%	36, 22.64%	20, 24.69%	0.75
Portal hypertension	46, 19.17%	34, 21.38%	12, 14.81%	0.30
Hepato-pulmonary syndrome (HPS)	15, 6.25%	8, 5.03%	7, 8.64%	0.27
Hepatocellular carcinoma (HCC)	11, 4.58%	6, 3.77%	5, 6.17%	0.51
Procedures Performed During Admission ¹ (n, %)				
Esophago-gastro-duodenoscopy (EGD)	136, 56.67%	92, 57.86%	44, 54.32%	0.68
Paracentesis	115, 47.92%	73, 45.91%	42, 51.85%	0.41
Emergent Transjugular intrahepatic portosystemic shunt (TIPS)	10, 4.17%	9, 5.66%	1, 1.23%	0.17
Hemodialysis (HD)	15, 6.25%	7, 4.40%	8, 9.88%	0.16
Colonoscopy/flex sig	24, 10.00%	18, 11.32%	6, 7.41%	0.37
Disposition ¹ (n, %)	<i>.</i>			
Home	159, 66.25%	107, 67.30%	52, 64.20%	0.66
Home with Home Health Newly Arranged	39, 16.25%	24, 15.09%	15, 18.52%	
Home with Home Health Previously Arranged	3, 1.25%	2, 1.26%	1, 1.23%	
SNF newly Arranged	21, 8.75%	16, 10.06%	5, 6.17%	
SNF Previously Arranged	11, 4.58%	5, 3.14%	6, 7.41%	
Left Against Medical Advice	2, 0.83%	1, 0.63%	1, 1.23%	
Transfer (long term acute care hospital)	3, 1.25%	2, 1.26%	1, 1.23%	
Homeless	2, 0.83%	2, 1.26%	0, 0.00%	

¹indicates patient can have more than one of variable listed

Table 2 Characteristics and Reasons for Readmission

Readmission status	N	%
No	159	66.25
Yes	81	33.75
Number of Readmissions within 30 days		
0	159	66.25
1	63	26.25
2	14	5.83
3	3	1.25
5	1	0.42
Location of 1st Readmission		
OSU	59	72.84
Outside Hospital	22	27.16
Reason for 1st Readmission ¹		
Hepatic Encephalopathy	26	32.10
Volume Overload	22	27.16
Acute Kidney Injury	16	19.75
Variceal bleed	12	14.82
Hyponatremia	10	12.35
Lower GI bleed	4	4.94
Spontaneous Bacterial Peritonitis (SBP)	3	3.70
LOS of first Readmission (n=81, mean±SD), median =5, range =1 to 69	8.11±8.98	
LOS of All Readmissions (n=105, mean±SD), median =4, range =0 to 124	9.03±14.42	
Cost of first readmission (n=45, mean±SD), median=\$31,848.95, range \$765-325,656.38	\$55,548.29±65,164.91	
Waiting time for first Readmission (n=81, mean \pm SD), median=12, range = 1-30]	12.65±7.55	

al characteristics by	y randomization a	rm	
Intervention	Standard of Care	p-value	
(n=120)	(n=120)		
56 54+11 21	56 14+11 21	0.78	-
50.54±11.21	50.14±11.21	0.78	-
22 26 670/	28 22 220/	0.70	-
	,	0.79	
	,		-
13, 10.83%	12, 10.00%		-
			-
		0.03	-
60, 50.00%	45, 32.50%		-
			-
/	,	0.22	
15, 12.50%	23, 19.17%		
		0.81	
3, 2.50%	1, 0.83%		
4, 3.33%	5, 4.17%		
\$68,045±\$21,370	\$68,455±\$21,651	0.88	
			1
33, 27, 50%	30, 25,00%	0.78	
		0.10	
			-
			-
	,		-
			-
9, 7.5070	14, 11.0770		-
4 2 220/	2 2 50%	0.54	-
		0.34	-
			-
			-
	/		-
			-
1.99±1.61	1.84 ± 1.48	0.45	
21.32±8.19	22.47±7.85	0.27	
20.07±7.74	20.25±6.93	0.84	Deleted: SD)
9.31±2.02	9.41±1.89	0.69	~ ~ ~
8.44±1.86	8.73±1.89	0.24	Deleted: n
			Deleted:]
61, 50.83%	60, 50.00%	1.00	Deleted:) ¹
42, 35.00%	37, 30.83%	0.58	· · · · · · · · · · · · · · · · · · ·
21, 17.50%	22. 18.33%	1.00	Deleted: (
1, 4.76%	3, 13.64%	0.80	
19, 90.48%	18, 81.82%		
			1
1, 4,76%	1.4.55%		
1, 4.76%	1, 4.55%	1.00	-
6, 5.00%	7, 5.83%	1.00	
6, 5.00% 1, 0.83%	7, 5.83% 1, 0.83%	1.00	
6, 5.00% 1, 0.83% 2, 1.67%	7, 5.83% 1, 0.83% 2, 1.67%	1.00 1.00	
6, 5.00% 1, 0.83% 2, 1.67% 0, 0.0%	7, 5.83% 1, 0.83% 2, 1.67% 3, 2.5%	1.00 1.00 0.25	
6, 5.00% 1, 0.83% 2, 1.67%	7, 5.83% 1, 0.83% 2, 1.67%	1.00 1.00	
6, 5.00% 1, 0.83% 2, 1.67% 0, 0.0% 3, 2.5%	7, 5.83% 1, 0.83% 2, 1.67% 3, 2.5% 0, 0.0%	1.00 1.00 0.25 0.25	
6, 5.00% 1, 0.83% 2, 1.67% 0, 0.0%	7, 5.83% 1, 0.83% 2, 1.67% 3, 2.5%	1.00 1.00 0.25	
	Intervention (n=120) 56.54±11.21 32, 26.67% 75, 62.50% 13, 10.83% 60, 50.00% 60, 50.00% 105, 87.50% 113, 94.17% 3, 2.50% 4, 3.33% \$68,045±\$21,370 33, 27.50% 24, 20.00% 26, 21.67% 5, 4.17% 23, 19.17% 9, 7.50% 4, 3.33% 7, 5.83% 38, 31.67% 32, 26.67% 39, 32.50% 1.99±1.61 21.32±8.19 20.07±7.74 9.31±2.02 8.44±1.86 61, 50.83% 42, 35.00% 21, 17.50% 11, 4.76% 19, 90.48%	Intervention (n=120)Standard of Care (n=120) 56.54 ± 11.21 56.14 ± 11.21 $32, 26.67\%$ $28, 23.33\%$ $75, 62.50\%$ $80, 66.67\%$ $13, 10.83\%$ $12, 10.00\%$ $60, 50.00\%$ $75, 62.50\%$ $60, 50.00\%$ $75, 62.50\%$ $60, 50.00\%$ $75, 62.50\%$ $60, 50.00\%$ $45, 32.50\%$ $105, 87.50\%$ $97, 80.83\%$ $15, 12.50\%$ $23, 19.17\%$ $113, 94.17\%$ $114, 95.00\%$ $3, 2.50\%$ $1, 0.83\%$ $4, 3.33\%$ $5, 4.17\%$ $33, 27.50\%$ $30, 25.00\%$ $24, 20.00\%$ $24, 20.00\%$ $24, 20.00\%$ $24, 20.00\%$ $24, 20.00\%$ $24, 20.00\%$ $23, 19.17\%$ $30, 25.00\%$ $7, 5.83\%$ $3, 2.50\%$ $7, 5.83\%$ $7, 5.83\%$ $7, 5.83\%$ $7, 5.83\%$ $7, 5.83\%$ $31, 25.83\%$ 1.99 ± 1.61 1.84 ± 1.48 21.32 ± 8.19 22.47 ± 7.85 20.07 ± 7.74 20.25 ± 6.93 9.31 ± 2.02 9.41 ± 1.89 8.44 ± 1.86 8.73 ± 1.89 $61, 50.83\%$ $60, 50.00\%$ $42, 35.00\%$ $37, 30.83\%$ $21, 17.50\%$ $22. 18.33\%$ $11, 4.76\%$ $8, 18.82\%$	$\begin{array}{c c c c c c c c c c c c c c c c c c c $

581 Table 3 Comparison of patient demographics and clinical characteristics by randomization arm

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¹indicates patient can have more than one of variable listed

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Table 4 Characteristic features during index admission in two randomization arms

Index Admission Characteristics	Intervention (n=120)	Standard of Care (n=120)	p-value
Reasons for Admission ¹ (n, %)	· /		
Acute Kidney Injury	30, 25.00%	35, 29.17%	0.56
Hyponatremia	10, 8.33%	6, 5.00%	0.44
Hepatic Encephalopathy	22, 18.33%	23, 19.17%	1.00
Volume Overload	59, 49,17%	52, 43.33%	0.44
Variceal bleed	21, 17.50%	21, 17.50%	1.00
Lower GI bleed	8, 6.67%	11, 9.17%	0.63
Spontaneous Bacterial Peritonitis (SBP)	9, 7.50%	12, 10.00%	0.65
Complications of Cirrhosis During Admission ¹ (n, %)			
Presence of acute kidney injury (AKI)	39, 32.50%	41, 34.17%	0.89
Hepatic Encephalopathy (HE)	25, 20.83%	24, 20.00%	1.00
Ascites	70, 58.33%	69, 57.50%	1.00
Variceal bleeding	21, 17.50%	16, 13.33%	0.48
Spontaneous Bacterial Peritonitis (SBP)	10, 8.33%	6, 5.00%	0.44
Hepatorenal syndrome (HRS)	7, 5.83%	7, 5.83%	1.00
Coagulopathy	32, 26.67%	24, 20.00%	0.29
Portal hypertension	19, 15.83%	27, 22.50%	0.25
Hepato-pulmonary syndrome (HPS)	10, 8.33%	5, 4.17%	0.29
Hepatocellular carcinoma (HCC)	6, 5.00%	5, 4.17%	1.00
Procedures Performed During			
Admission ¹ (n, %)			
Esophago-gastro-duodenoscopy (EGD)	68, 56.67%	68, 56.67%	1.00
Paracentesis	60, 50.00%	55, 45.83%	0.61
Transjugular intrahepatic portosystemic shunt (TIPS)	7, 5.83%	3, 2.50%	0.33
Hemodialysis (HD)	5, 4.17%	10, 8.33%	0.29
Colonoscopy/flex sig	13, 10.83%	11, 9.17%	0.83
Disposition (n, %)			
Home	83, 69.17%	76, 63.33%	0.44
Home with Home Health Newly Arranged	17, 14.17%	22, 18.33%	
Home with Home Health Previously Arranged	2, 1.67%	1, 0.83%	
SNF newly Arranged	7, 5.83%	14, 11.67%	
SNF Previously Arranged	6, 5.00%	5, 4.17%	
Left Against Medical Advice	1, 0.83%	1, 0.83%	
Transfer (Long term acute care hospital)	3, 2.50%	0, 0.00%	
Homeless	1, 0.83%	1, 0.83%	

¹indicates patient can have more than one of variable listed

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Standard of Care Intervention (n=120) (n=120) p-value Index Admission Labs Sodium (mmol/L, mean±SD) 132.59±5.58 132.28±6.28 0.68 Serum Creatinine (mg/dL, mean±SD) 1.42±1.11 1.64±1.47 0.19 5.90±9.10 6.19±7.80 Total Bilirubin (mg/dL, mean±SD) 0.79 Albumin (g/dL, mean±SD) 2.83±0.59 2.85±0.55 0.72 INR (mean±SD) 1.68 ± 0.52 1.70 ± 0.59 0.80 Hemoglobin (g/dL, mean±SD) 10.22±2.34 10.02 ± 2.04 0.48 Ascites (n, %) 35, 29.17% 35, 29.17% 0.44 Absent 26, 21.67% Slight 34, 28.33% Moderate 59, 49.17% 51, 42.50% Encephalopathy (n, %) 91, 75.83% 96, 80.00% 0.78 None Grade 1-2 22, 18.33% 18, 15.00% 6, 5.00% Grade 3-4 7, 5.83% Dialysis At Least Twice in Last Week (n, %) No 117, 97.50% 115, 95.83% 0.72 Yes 3, 2.50% 5, 4.17% Index Admission Discharge Labs 134.72±4.14 134.95±3.57 Sodium (mmol/L, mean±SD) 0.64 Serum Creatinine (mg/dL, mean±SD) 1.31±1.06 1.37±1.18 0.69 Total Bilirubin (mg/dL, mean±SD, n=237) 5.50±8.80 5.39±6.96 0.92 Albumin (g/dL, mean±SD, n=237) 2.98 ± 0.64 2.94±0.61 0.65 1.69±0.45 INR (mean±SD, n=238) 1.71±0.49 0.65 Hemoglobin (g/dL, mean±SD) $9.21{\pm}1.68$ $9.30{\pm}1.69$ 0.68 Ascites (n, %) 42, 35.00% 39, 32.50% 0.35 Absent Slight 56, 46.67% 66, 55.00% 22, 18.33% Moderate 15, 12.50% Encephalopathy (n, %) None 117, 97.50% 112.93.33% 0.10 2, 1.67% 8, 6.67% Grade 1-2 Grade 3-4 1, 0.83% 0,0.00%

114, 95.00%

6, 5.00%

110, 91.67%

10, 8.33%

0.44

Table 5 Clinical and laboratory features during index admission and discharge in two randomization arms

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No Yes

Dialysis At Least Twice in Last Week (n, %)

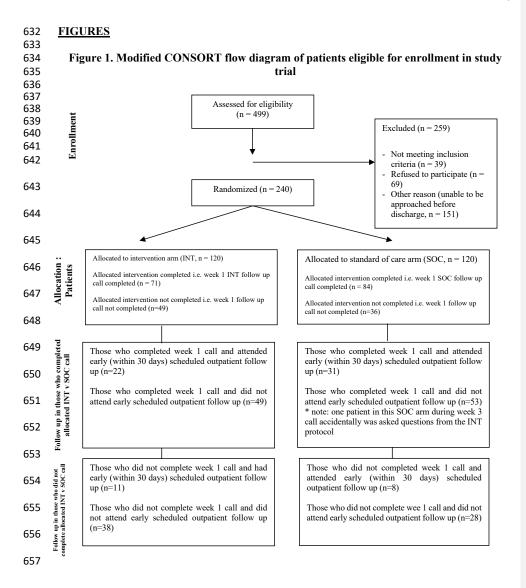
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		Standard of Care		
	Intervention (n=120)	(n=120)	p-value	
Readmission (n, %)				
No	77, 64.17%	82, 68.33%	0.59	
Yes	43, 35.83%	38, 31.67%		
Number of Readmissions within 30				
days (n, %)				
0	77, 64.17%	82, 68.33%	0.65	
1	31, 25.83%	32, 26.67%		
2	9, 7.50%	5, 4.17%		
3	2, 1.67%	1, 0.83%		
5	1, 0.83%	0, 0.00%		
Location of 1 st Readmission (n, %)				
Our institution	36, 83.72%	23, 60.53%	0.03	
Outside Hospital	7, 16.28%	15, 39.47%		
Reason for 1 st Readmission ¹ (n, %)				
Acute Kidney Injury (AKI)	10, 23.26%	6, 15.79%	0.58	
Hyponatremia	4, 9.30%	6, 15.79%	0.50	
Hepatic Encephalopathy (HE)	9, 20.93%	17, 44.74%	0.03	
Volume Overload	13, 30.23%	9,23.68%	0.62	
Variceal bleed	6, 13.95%	6, 15.79%	1.00	
Lower GI bleed	1, 2.33%	3, 7.89%	0.34	
Spontaneous Bacterial				
Peritonitis (SBP)	2, 4.65%	1, 2.63%	1.00	
Other	20, 46.51%	22, 57.89%	0.37	
Index Admission Cost (mean±SD <u>.</u> n=116+109]	61,581±47,825	59,547±46,669	0.46	Deleted:) [
Index Admission LOS (mean±SD)	8.17±5.56	8.08±6.11	0.63	
First Readmission LOS (n=43+38 ₂ mean±SD)	7.58±7.57	8.71±10.41	0.58	
All Readmissions LOS (n=60+45,	1.50-1.51	0./1±10.71	0.50	Deleted:) (
mean±SD)	9.28±16.88	8.69±10.44	0.82	Deleted:) (
Waiting time for first Readmission (n=43+38, mean±SD)	11.16±7.10	14.34±7.77	0.06	Deleted:) (

610 Table 6 Outcomes and reasons of readmission characteristics by randomization arms

¹indicates patient can have more than one of variable listed



1 <u>TITLE PAGE</u>

2	Study Title: Randomized Intervention and Outpatient Follow-Up Lowers 30-day Readmissions
3	for Patients with Hepatic Encephalopathy, Decompensated Cirrhosis

4

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35 approved the final submitted version of this manuscript.

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- 45
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70 <u>ABSTRACT</u>

71 Background

72 We previously reported national 30-day readmission rates of 27% in patients with

73 decompensated cirrhosis (DC).

74

75 Aims

We studied prospective interventions to reduce early readmissions in DC at our tertiary center.

78 Methods

Adults with DC admitted July 2019 to December 2020 were enrolled and randomized into the

80 intervention (INT) or standard of care (SOC) arms. Weekly phone calls for a month were

81 completed. In the INT arm, case managers ensured outpatient follow-up, paracentesis, and

82 medication compliance. Thirty-day readmission rates and reasons were compared.

83

84 **Results**

85 Calculated sample size was not achieved due to COVID-19; 240 patients were randomized into

86 INT and SOC arms. 30-day readmission rate was 33.75%, 35.83% in the INT versus 31.67% in

the SOC arm (p=0.59). The top reason for 30-day readmission was hepatic encephalopathy (HE,

88 32.10%). There was a lower rate of 30-day readmissions for HE in the INT (21%) versus SOC

- arm (45%, p=0.03). There were fewer 30-day readmissions in patients who attended early
- 90 outpatient follow-up (n=17, 23.61% v. n=55, 76.39%, p=0.04).

91

92 Conclusions

93	Our 30-day readmission rate was higher than the national rate but reduced by interventions in
94	patients with DC with HE and early outpatient follow-up. Development of interventions to
95	reduce early readmission in patients with DC is needed.
96	
97	Keywords: decompensated cirrhosis; hospital readmissions; interventions
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116 **INTRODUCTION**

Cirrhosis affects approximately 5 million annually¹ and has been reported to be the 8th leading 117 cause of death with more than 40,000 deaths annually in the United States.² A study on the 118 119 burden of gastrointestinal, liver, and pancreatic diseases in the United States revealed that liver diseases had the highest mortality at 3.1%.³ In addition to high mortality, cirrhosis is also 120 121 associated with high morbidity. The sequelae of decompensated cirrhosis (DC) are often 122 managed during hospital admissions and include volume overload in the form of ascites, edema 123 or hepatic hydrothorax, portal hypertension leading to bleeding esophageal or gastric varices, as 124 well as hepatic encephalopathy (HE), hyponatremia, acute kidney injury (AKI), and spontaneous 125 bacterial peritonitis (SBP).⁴

126

Several studies have demonstrated hospital readmissions in DC place a large financial burden on the United State healthcare system. The 30-day readmission rate has been reported to be 20%-37%.⁵⁻¹⁴ We have recently published on early readmission rates up to 27% in patients with DC and developed the Mumtaz readmission risk score based on United States data.¹⁵ We also reported that nearly one-third of patients with HE were readmitted within 30 days, and early readmission adversely impacted healthcare utilization and calendar-year mortality.¹⁶

133

Interventions to reduce readmissions have been shown to be safe and effective. For instance, Morales et al. developed HEPACONTROL program including a hepatologist follow-up exam within 7 days after discharge. This program resulted in a reduction in 30-day readmissions, 60day mortality, emergency department visits and associated costs.¹⁷ Similarly, another group demonstrated that follow-up with a "care management check-up" as opposed to "standard

139	outpatient care" reduced 30-day readmission, 12-month mortality and saved 1500 euros per
140	patient month of life. ¹⁸
141	
142	There is a paucity of prospective studies on interventions to reduce early readmission rates in
143	patients with DC. Therefore, we prospectively studied 30-day readmission rates in patients with
144	DC and compared various interventions (INT) with standard of care (SOC) to reduce early
145	readmission rates. We hypothesized that DC patients in the INT arm would have decreased 30-
146	day readmission versus the SOC arm.
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162 <u>METHODS</u>

163 This study was conducted at the Ohio State University Wexner Medical Center (OSUWMC),

164 Columbus, Ohio from July 2019 to December 2020. Our study was approved by OSUWMC

165 Institutional Review Board. All aspects of the studying involving human participants including

166 informed consent for enrollment were in accordance with the ethical standards of our

167 Institutional Review Board and with the 1964 Helsinki Declaration and its later amendments or168 comparable ethical standards.

169

170 Screening

All patients admitted with DC to the hepatology (inpatient or consult) service were screened for enrollment. Patients meeting inclusion criteria were approached for study consent. Of note, due to the global COVID-19 pandemic, beginning March 2020, only COVID negative patients were approached for informed consent. Elective readmissions for inpatient procedures including endoscopy, trans-arterial chemoembolization (TACE), transjugular intrahepatic portosystemic shunt (TIPS), paracentesis or readmissions unrelated to DC such as motor vehicle accidents were excluded.

178

179 Randomization and Data Collection

Study data were collected and managed using REDCap hosted at The Ohio State University
Wexner Medical Center.^{19,20} Informed consent was obtained from all individual participants
included in the study. Consented patients were randomly assigned to either the INT arm or the
SOC arm in a 1:1 ratio using the RedCap randomization tool. The following data were collected
on all patients via RedCap software including demographics (age, sex, insurance type, income

185 based on the zip code), hospitalization data (date of index admission defined as initial admission during which patient consented for study, reason for admission, length of stay (LOS) defined as 186 187 difference in days between index admission date and index admission discharge date, discharge 188 disposition, associated cost of care of admission as obtained through medical record billing tab), 189 etiology of cirrhosis (alcoholic and non-alcoholic including viral, non-alcoholic fatty liver 190 disease, autoimmune, primary biliary cirrhosis, primary sclerosing cholangitis or cryptogenic), 191 complications of cirrhosis {HE, AKI, ascites, variceal bleeding, SBP, hepatorenal syndrome 192 (HRS), coagulopathy, portal hypertension, hepato-pulmonary syndrome (HPS), hepatocellular 193 carcinoma (HCC)}, and procedures performed during admission {esophago-gastro-194 duodenoscopy (EGD), colonoscopy or flexible sigmoidoscopy, paracentesis, transjugular 195 intrahepatic portosystemic shunt (TIPS) and hemodialysis (HD) on admission and discharge}. 196 We also collected data including Elixhauser comorbidity index, discharge medications, and 197 laboratory data (complete blood counts, serum creatinine, liver function tests including total 198 bilirubin, INR, and sodium). Child Turcotte Pugh (CTP) and Sodium-model for end stage liver 199 disease (MELD-Na) score were calculated from the data. The nurse case manager (CM) also 200 recorded labs & medications at readmission & discharge and associated cost of readmission. 201 Status of early readmission, liver transplantation, and mortality at one year were also collected. 202

203 Follow-up

The CM phoned each patient enrolled in either arm weekly for 30 days after index discharge to find out if the patient has been readmitted to OSUWMC or another hospital. In the INT arm, during the call CM also ensured i) early (defined as within 30 days from index admission discharge) outpatient hepatology follow-up ii) compliance of medication, iii) arrangement of outpatient paracentesis if needed, and reviewed outpatient hepatology clinic follow-up records.
SOC arm as per our center's protocol had to be taken care of by the primary inpatient team. This
included arranging early outpatient clinic follow-up, providing list of medications, and advice for
outpatient paracentesis if needed at the time of discharge. Due to the nature of intervention, the
study could not be blinded.

213

214 Definition of outcomes

Early readmission was defined as admission within 30 days of index admission discharge.

216 Reasons for readmission were gathered by CM by reviewing the electronic medical record

217 (EMR) of all enrolled patients readmitted at OSUWMC or outside hospital within 30 days of

218 index admission. Predictors of early readmission were also compared in the two arms.

219

220 Sample Size

221 Based on the sample size calculation, target of recruitment for the study was 848 patients, 222 admitted to the hospital with DC under the hepatology (inpatient and consult) services. Patients 223 were randomly assigned in a 1:1 ratio into INT or SOC arms. Based on our previous study using 224 the NRD administrative database, we expected a 30-day readmission rate of 27% among patients 225 meeting inclusion criteria, which yield 114/424 patients with 30-day readmission events, thus 226 meeting the target sample size. Based on this calculation, a total sample size of 848 (424 per 227 group) provided 80% power to detect a 30% decrease in 30-day readmission rate (from 27% to 19%) with a type I error rate of 0.05. However, planned sample size could not be achieved due to 228 229 the COVID-19 pandemic related restriction started in our center in March 2020. Therefore, we

230	end up with available sample size of a total of 240 patients. The modified CONSORT Flow
231	diagram for enrollment in our study trial is illustrated in Figure 1.
232	
233	Statistical analysis:
234	Means of continuous response variables between two groups were compared using robust t-test
235	(Welch test). Proportions were compared using Chi-square or Fisher's exact test as applicable.
236	Logarithmic transformation was used for comparing the length of stay (LOS) and admission cost
237	across groups. Level of significance was kept at 0.05 for each comparison. JMP Version 15 (SAS
238	Institute, NC) was used for all the analyses.
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253 <u>RESULTS</u>

254 Initial Screening Data

- From July 1, 2019, to December 1, 2020, 1392 patients were screened. Due to the COVID-19
- 256 pandemic, recruitment was held from March 2020 to July 2020 and subsequently resumed until
- 257 December 2020. Out of the patients screened, only 499 (35.85%) were eligible for inclusion;
- however, 240 patients consented and randomized: 120 each into the INT and SOC arm (Figure1).
- 260

261 Patient demographics and clinical characteristics

- 262 The mean age of patients was 56.34±11.19 years, majority were males (135, 56.25%), belonged
- to White race (n=202, 84.17%) and non-Hispanic or Latino ethnicity (n=227, 94.58%). Almost
- two-thirds of the patients had public insurance (n=76, 31.67% on Medicare and n=70, 29.17% on
- Medicaid); 73 (30.42%) had private insurance. At admission, the mean MELD-Na score and
- 266 mean Child Pugh Score were 21.89±8.03 and 9.36±1.96, respectively. Major etiology of
- cirrhosis was alcohol (n=121, 50.42%) followed by non-alcoholic fatty liver disease (n=79,
- 32.92%) and viral hepatitis (n=43, 17.92%). Furthermore, 116 (48.33%) patients were actively
- 269 under evaluation for liver transplantation.
- 270

271 Characteristics of index admissions

272 The index admission mean LOS was 8.13±5.83 days (median 6, range 1-43 days). The mean cost

- 273 of index admission was \$60,595±\$47,174 (n=225, median \$42,932, range \$1,630-251,991). The
- top five reasons for index admission included volume overload (n=111, 46.25%), acute kidney
- 275 injury (n=65, 27.08%), hepatic encephalopathy (n=45, 18.75%), variceal bleed (n=42, 17.50%),

lower GI bleed (n=19, 7.92%) and hyponatremia (n=16, 6.67%). The top five interventions
performed were EGD (n=136, 56.67%), paracentesis (n=115, 47.92%), colonoscopy/flexible
sigmoidoscopy (n=24, 10%), hemodialysis (n=15, 6.25%) and TIPS (n=10, 4.17%). Most
patients were discharged from index admission to home (n=159, 66.25%) followed by home with
health care (n=42, 17.50%) and skilled nursing facility (n=32, 13.33%, Table 1).

281

282 Characteristics and reasons for early readmissions

283 Overall, 81 (33.75%) patients were readmitted within 30 days of discharge. The major reasons

for first readmission included hepatic encephalopathy (n=26, 32.10%) followed by volume

285 overload (n=22, 27.16%), acute kidney injury (n=16, 19.75%), variceal bleed (n=12, 14.82%)

and hyponatremia (n=10, 12.35%). 14 patients were readmitted twice, 3 admitted thrice and one

admitted 5 times within 30 days. The mean time to first readmission was 12.65±7.55 days

288 (median 12 days, range 1-30 days). The mean length of stay of first readmission was 8.11±8.98

days. The mean cost of stay of first readmission was $55,548.29 \pm 65,164.91$ (Table 2). Those

readmitted had a higher MELD score on index admission (23.54±7.80 v. 21.05±8.03, p=0.02)

and index discharge (21.67±7.95 v. 19.39±6.89, p=0.03) than those not readmitted. Similarly,

those readmitted had a higher index admission creatinine $(1.80\pm1.53 \text{ v} 1.39\pm1.16, \text{ p}=0.03)$,

index discharge creatinine (1.61±1.34 v, 1.20±0.97, p=0.02), and higher index admission INR
(1.80±0.64 v. 1.63±0.50, p=0.05) than those not readmitted.

295

296 Comparison of demographics and clinical characteristics in two intervention arms

297 Demographics including age, race, ethnicity, income, and insurance were comparable in two

298 groups, as well as etiology of cirrhosis, MELD-Na score, CTP score, status of evaluation for

liver transplant. There were majority females in the INT arm (60/120, 50% v. 45/120, 32.50%)
and males in SOC arm (75/120, 62.50% v. 60/120, 50%, p=0.03, Table 3). Index admission
characteristics, disposition and index admission were also comparative in two arms (Table 4 and
Table 5)

303

304 Comparison of reasons of 1st readmission and outcomes in the INT v SOC arm

305 There was no difference in the readmission rates for patients in the INT (n=4, 35.83%) versus

306 SOC arm (n=38, 31.67%, p=0.59, Table 6). Other outcomes including number of readmissions

307 within 30 days (p=0.65), index admission cost (p=0.49), index admission LOS (p=0.63), 1st

readmission LOS (p=0.58), all readmissions' LOS (p=0.82) and waiting time for 1st readmission

- (p=0.06) were comparable in two arms.
- 310

311 Statistically significant differences were noticed in INT arm in location of 1^{st} readmission (n=36,

312 83.72% at OSU as compared to n=23, 60.5% outside hospital, p=0.03), and lesser 1st readmission

with HE in the INT arm (n=9, 20.9%) vs SOC (n=17, 44.7%, p=0.03). Finally, contingency

analysis of readmission data showed fewer readmissions in patients who attended outpatient

follow-up within 30 days of discharge from index admission (n=17, 23.61% v. n=55, 76.39%,

316 p=0.04).

317

At the end of our study, 47 (19.58%) patients received a liver transplant and 62 (25.83%) died; among those who died, 5 patients were post-transplant and 22 died in hospice. Due to the COVID-19 pandemic we were unable to achieve the anticipated sample size. Therefore,

321 multivariate analysis was not performed.

322 DISCUSSION

This prospective randomized study investigated early readmission rates and healthcare utilization 323 324 in patients with DC. Our readmission rate of 33.75% is higher than the United States national 325 average (27%). While our nurse CM interventions did not reduce told readmissions, we found 326 that HE was the top reason for readmission and such interventions were helpful in reducing early 327 readmissions in patients with HE. This is an important lesson learned given increased burden of HE on hospitalizations, falls, mortality, impaired OOL and caregiver burden.²¹ In the validation 328 329 of readmission using "LIRER score", Freitas et al, showed that HE was not only a predictor of 330 30 days readmission independent of MELD score, index, first-year, two-years & overall mortality, but also HE at admission had significantly higher mean LIRER scores.²² Furthermore 331 332 HE patients on Medicare and geographically from the South or Midwest have higher in-hospital mortality.²³ Considerable research has been done to address HE readmissions. Bajaj et al found 333 334 that efforts to reduce medication-precipitated HE, prevent aspiration pneumonia and optimize HE medications on hospital discharge should be areas of focus to decrease HE readmissions.²⁴ 335 336 Tapper et al. demonstrated that development of a checklist for HE protocols integrated into the electronic medical record and order entry system reduced odds of 30-day readmission for 337 patients with HE (from 39.2% to 27.6%).²⁵ Thus, our results are congruent with existing 338 evidence that interventions should be invested in post-discharge education and communication 339 340 for all patients with cirrhosis, especially with HE.

341

One of the components of intervention in our study was to arrange appointment of patients in the clinic within a week with their hepatologist. Patients with DC who attended their follow up appointment within 30 days of discharge from index admission had fewer readmissions. This 345 suggests that overall, in our cohort, outpatient linkage with a hepatologist should be a priority to reduce readmission rates.²⁶ Morales et al in their retrospective HEPACONTROL program looked 346 347 at the impact of follow-up of cirrhotics within 7 days after discharge with a hepatologist. They 348 reported reduced 30-day readmission, 60-day mortality and rate of emergency department visits and associated costs in those who followed up within 7 days.¹⁷ Morando et al demonstrated that 349 follow up with a "care management check-up" group as opposed to "standard outpatient care" 350 reduced 30-day readmission, reduced 12-month mortality, and saved almost 1500 euros per 351 352 patient month of life.¹⁸ While Kanwal et al found early outpatient follow-up after discharge was 353 associated with a small increase in readmissions, they found an lower overall mortality in their patients with cirrhosis admitted to Veterans Affairs hospitals.⁹ Thus our results are also 354 355 consistent with the current evidence that patients with DC likely benefit from early posthospitalization follow up with specialty providers.^{27,28} 356

357

One of the major limitations of our study was inability to enroll patients according to the proposed sample size due to the COVID-19 pandemic. Our study was underpowered to perform multiple regression analysis to detect differences in readmission rates in INT versus SOC arm. From March 2020 to July 2020 our recruitment process was put on hold due to hospital regulations to reduce patient and staff exposure. Despite this major limitation, we were able to enroll 80.17% (279 consented out of 348 approached) of patients in our study.

364

365 This study was also performed in the setting of a large academic medical center and a high-366 volume liver transplant center. While our methods and results may be applicable to the clinical

367 practice of other such centers, the same impact may not be appreciated by smaller, community368 hospitals that are not liver transplant centers.

370 Future work in patients with DC should continue to focus on prospective intervention strategies 371 to reduce early readmissions and educate patients and providers. To achieve desired sample size, 372 we would suggest collaborations with various centers to identify and recruit patients with DC into a multicenter prospective cohort. Given our finding that there were fewer readmissions in 373 374 patients with follow-up within 30 days, studies should evaluate the use of telehealth visits for follows up, especially in the COVID19 era, as outlined by Stotts et al.²⁹ 375 376 377 In conclusion, this prospective randomized study investigated the impact of various pragmatic 378 interventions to reduce early readmission and healthcare utilization in patients with DC. Our 379 study was underpowered to detect statistically significant differences in readmission rates in INT 380 versus SOC arm. We reported that readmission rate of our medical center was 33.75% and HE 381 was the top reason for readmission. We found a reduction in early readmission in patients with 382 HE in the INT arm and those who attended their follow up appointment within 30 days of 383 discharge from index admission. We demonstrated that simple interventions in patients with DC 384 are pragmatic and there is need for more prospective multicenter trials in this area of research. 385 386 387 388 389

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479 <u>TABLES</u>

Table 1 Characteristic features of index admission by readmission status

	Total	Not readmitted (n=159)	Readmitted (n=81)	p-value
Index Admission Characteristics		, , , , , , , , , , , , , , , , , , ,		
Reasons for Admission ¹ (n, %)				
Acute Kidney Injury	65, 27.08%	41, 25.79%	24, 29.63%	0.54
Hyponatremia	16, 6.67%	11, 6.92%	5, 6.17%	1.00
Hepatic Encephalopathy	45, 18.75%	26, 16.35%	19, 23.46%	0.22
Volume Overload	111, 46.25%	81, 50.94%	30, 37.04%	0.06
Variceal bleed	42, 17.50%	31, 19.50%	11, 13.58%	0.29
Lower GI bleed	19, 7.92%	11, 6.92%	8, 9.88%	0.45
Spontaneous Bacterial Peritonitis	21, 8.75%	14, 8.81%	7, 8.64%	1.00
(SBP)	21, 0.7570	11, 0.0170	7, 0.0170	1.00
Complications of Cirrhosis During				
Admission ¹ (n, %)				
Presence of acute kidney injury	80, 33.33%	50, 31.45%	30, 37.04%	0.39
(AKI)	30,22.3370		20,2,101/0	0.09
Hepatic Encephalopathy (HE)	49, 20.42%	31, 19.50%	18, 22.22%	0.62
Ascites	139, 57.92%	95, 59.75%	44, 54.32%	0.62
Variceal bleeding	37, 15.42%	26, 16.35%	11, 13.58%	0.71
Spontaneous Bacterial Peritonitis	16, 6.67%	12, 7.55%	4, 4.94%	0.59
(SBP)	10, 0.0770	12, 7.5570	-, -, -, -, 0	0.57
Hepatorenal syndrome (HRS)	14, 5.83%	8, 5.03%	6, 7.41%	0.56
Coagulopathy	56, 23.33%	36, 22.64%	20, 24.69%	0.75
Portal hypertension	46, 19.17%	34, 21.38%	12, 14.81%	0.30
Hepato-pulmonary syndrome (HPS)	15, 6.25%	8, 5.03%	7, 8.64%	0.27
Hepatocellular carcinoma (HCC)	11, 4.58%	6, 3.77%	5, 6.17%	0.51
Procedures Performed During	11, 4.5070	0, 5.7770	5,0.1770	0.51
Admission ¹ (n, %)				
Esophago-gastro-duodenoscopy	136, 56.67%	92, 57.86%	44, 54.32%	0.68
(EGD)	150, 50.0770	72, 37.0070		0.00
Paracentesis	115, 47.92%	73, 45.91%	42, 51.85%	0.41
Emergent Transjugular intrahepatic	10, 4.17%	9, 5.66%	1, 1.23%	0.17
portosystemic shunt (TIPS)	10, 11/70	,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,	1, 1.2370	0.17
Hemodialysis (HD)	15, 6.25%	7, 4.40%	8, 9.88%	0.16
Colonoscopy/flex sig	24, 10.00%	18, 11.32%	6, 7.41%	0.10
Disposition ¹ (n, %)	27, 10.0070	10, 11.3270	0, /. 11 / 0	0.57
Home	159, 66.25%	107, 67.30%	52, 64.20%	0.66
Home with Home Health Newly	39, 16.25%	24, 15.09%	15, 18.52%	0.00
Arranged	59, 10.2570	27, 13.07/0	15, 10.5270	
Home with Home Health	3, 1.25%	2, 1.26%	1, 1.23%	
Previously Arranged	5, 1.2570	2, 1.2070	1, 1.2370	
SNF newly Arranged	21, 8.75%	16, 10.06%	5, 6.17%	
SNF Previously Arranged	11, 4.58%	5, 3.14%	6, 7.41%	
Left Against Medical Advice	2, 0.83%	1, 0.63%	1, 1.23%	
	2, 0.85%	2, 1.26%	1, 1.23%	
Transfer (long term acute care hospital)	3, 1.2370	2, 1.2070	1, 1.2370	
	2 0 820/	2 1 260/	0.000/	
Homeless	2,0.83%	2, 1.26%	0, 0.00%	

¹indicates patient can have more than one of variable listed

I able 2 Charactel	istics and iteasons i	or incaum
Readmission status	Ν	%
No	159	66.25
Yes	81	33.75
Number of Readmissions within 30 days		
0	159	66.25
1	63	26.25
2	14	5.83
3	3	1.25
5	1	0.42
Location of 1st Readmission		
OSU	59	72.84
Outside Hospital	22	27.16
Reason for 1st Readmission ¹		
Hepatic Encephalopathy	26	32.10
Volume Overload	22	27.16
Acute Kidney Injury	16	19.75
Variceal bleed	12	14.82
Hyponatremia	10	12.35
Lower GI bleed	4	4.94
Spontaneous Bacterial Peritonitis (SBP)	3	3.70
LOS of first Readmission (n=81, mean±SD), median =5, range =1 to 69	8.11±8.98	
LOS of All Readmissions (n=105, mean±SD), median =4, range =0 to 124	9.03±14.42	
Cost of first readmission (n=45, mean±SD), median=\$31,848.95, range \$765-325,656.38	\$55,548.29±65,164.91	
Waiting time for first Readmission (n=81, mean ±SD), median=12, range = 1-30]	12.65±7.55	

Table 2 Characteristics and Reasons for Readmission

501

Table 3 Comparison of patient demographics and clinical characteristics by randomization arm

Table 3 Comparison of patient demographics and clinic			
	Intervention (n=120)	Standard of Care $(n-120)$	p-value
Patient Demographics	(n=120)	(n=120)	
Age (mean±SD)	56.54±11.21	56.14±11.21	0.78
Age Group (n, %)	50.54±11.21	J0.14±11.21	0.78
65+	32, 26.67%	28, 23.33%	0.79
40-64	75, 62.50%	80, 66.67%	0.79
18-39	13, 10.83%	12, 10.00%	
Gender (n, %)	15, 10.85%	12, 10.00%	
Male	60, 50.00%	75, 62.50%	0.03
Female	60, 50.00%	45, 32.50%	0.03
Race (n, %)	00, 30.00%	43, 52.30%	
White	105, 87.50%	97, 80.83%	0.22
	15, 12.50%	23, 19.17%	0.22
Other	15, 12.50%	23, 19.17%	
Ethnicity (n, %)	112 04 170/	114.05.000/	0.01
Not Hispanic or Latino	113, 94.17%	114, 95.00%	0.81
Hispanic or Latino	3, 2.50%	1, 0.83%	
Unknown / Not Reported	4, 3.33%	5, 4.17%	0.00
Zip Code Income (mean±SD)	\$68,045±\$21,370	\$68,455±\$21,651	0.88
Employment Status (n, %)			
Unemployed	33, 27.50%	30, 25.00%	0.78
Disabled	24, 20.00%	24, 20.00%	
Retired	26, 21.67%	30, 20.00%	
Employed, Part Time	5, 4.17%	3, 2.50%	
Employed, Full Time	23, 19.17%	28, 23.33%	
Other / Unknown	9, 7.50%	14, 11.67%	
Insurance Type (n, %)			
Self-pay	4, 3.33%	3, 2.50%	0.54
No Charge / Other / Unknown	7, 5.83%	7, 5.83%	
Private Insurance	38, 31.67%	35, 29.17%	
Medicare	32, 26.67%	44, 36.67%	
Medicaid	39, 32.50%	31, 25.83%	
Number of admissions at OSU for DC in last 1 year (mean±SD)	1.99±1.61	$1.84{\pm}1.48$	0.45
MELD Score Admit (mean±SD)	21.32±8.19	22.47±7.85	0.27
MELD Score Discharge (mean±SD, n = 117+118)	20.07±7.74	20.25±6.93	0.84
CP Score Admit (mean±SD)	9.31±2.02	9.41±1.89	0.69
CP Score Discharge (mean±SD)	8.44±1.86	8.73±1.89	0.24
Etiology of Cirrhosis (Index Admission ¹ , n, %)			
Alcoholic	61, 50.83%	60, 50.00%	1.00
Non-alcoholic fatty liver	42, 35.00%	37, 30.83%	0.58
Viral	21, 17.50%	22. 18.33%	1.00
Hep B	1, 4.76%	3, 13.64%	0.80
Hep C	19, 90.48%	18, 81.82%	
Hep B and C	1, 4.76%	1, 4.55%	
	6, 5.00%	7, 5.83%	1.00
Cryptogenic		1, 0.83%	1.00
Cryptogenic Autoimmune	1. 0.83%		
Autoimmune	1, 0.83%		1.00
Autoimmune Primary sclerosing cholangitis	2, 1.67%	2, 1.67%	1.00
Autoimmune Primary sclerosing cholangitis Hemochromatosis	2, 1.67% 0, 0.0%	2, 1.67% 3, 2.5%	0.25
Autoimmune Primary sclerosing cholangitis Hemochromatosis Alpha 1 Anti-Trypsin Deficiency	2, 1.67%	2, 1.67%	
Autoimmune Primary sclerosing cholangitis Hemochromatosis Alpha 1 Anti-Trypsin Deficiency Under Evaluation for Liver Transplant (n, %)	2, 1.67% 0, 0.0% 3, 2.5%	2, 1.67% 3, 2.5% 0, 0.0%	0.25 0.25
Autoimmune Primary sclerosing cholangitis Hemochromatosis	2, 1.67% 0, 0.0%	2, 1.67% 3, 2.5%	0.25

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¹indicates patient can have more than one of variable listed

Index Admission Characteristics	Intervention (n=120)	Standard of Care (n=120)	p-value
Reasons for Admission ¹ (n, %)	(11-120)	(II-120)	
Acute Kidney Injury	30, 25.00%	35, 29.17%	0.56
Hyponatremia	10, 8.33%	6, 5.00%	0.36
Hepatic Encephalopathy	22, 18.33%	23, 19.17%	1.00
Volume Overload	59, 49.17%	52, 43.33%	0.44
Variceal bleed	21, 17.50%		1.00
Lower GI bleed	8, 6.67%	21, 17.50%	0.63
	9, 7.50%	<u>11, 9.17%</u> 12, 10.00%	0.65
Spontaneous Bacterial Peritonitis (SBP)	9, 7.30%	12, 10.00%	0.03
Complications of Cirrhosis During			
Admission ¹ (n, %)	39, 32.50%	41 24 170/	0.89
Presence of acute kidney injury (AKI)		41, 34.17%	1.00
Hepatic Encephalopathy (HE)	25, 20.83%	24, 20.00%	1.00
Ascites	70, 58.33%	69, 57.50%	
Variceal bleeding	21, 17.50%	16, 13.33%	0.48
Spontaneous Bacterial Peritonitis (SBP)	10, 8.33%	6, 5.00%	0.44
Hepatorenal syndrome (HRS)	7, 5.83%	7, 5.83%	1.00
Coagulopathy	32, 26.67%	24, 20.00%	0.29
Portal hypertension	19, 15.83%	27, 22.50%	0.25
Hepato-pulmonary syndrome (HPS)	10, 8.33%	5, 4.17%	0.29
Hepatocellular carcinoma (HCC)	6, 5.00%	5, 4.17%	1.00
Procedures Performed During Admission ¹ (n, %)			
Esophago-gastro-duodenoscopy (EGD)	68, 56.67%	68, 56.67%	1.00
Paracentesis	60, 50.00%	55, 45.83%	0.61
Transjugular intrahepatic portosystemic shunt (TIPS)	7, 5.83%	3, 2.50%	0.33
Hemodialysis (HD)	5, 4.17%	10, 8.33%	0.29
Colonoscopy/flex sig	13, 10.83%	11, 9.17%	0.83
Disposition (n, %)	-)		
Home	83, 69.17%	76, 63.33%	0.44
Home with Home Health Newly Arranged	17, 14.17%	22, 18.33%	
Home with Home Health Previously Arranged	2, 1.67%	1, 0.83%	
SNF newly Arranged	7, 5.83%	14, 11.67%	
SNF Previously Arranged	6, 5.00%	5, 4.17%	
Left Against Medical Advice	1, 0.83%	1, 0.83%	
Transfer (Long term acute care hospital)	3, 2.50%	0, 0.00%	
Homeless	1, 0.83%	1, 0.83%	

Table 4 Characteristic features during index admission in two randomization arms

Table 5 Clinical and laboratory features during index admission and discharge in tworandomization arms

1 un	Standard of Care				
	Intervention (n=120)	(n=120)	p-value		
Index Admission Labs		(1 120)	p-value		
Sodium (mmol/L, mean±SD)	132.59±5.58	132.28±6.28	0.68		
Serum Creatinine (mg/dL, mean±SD)	1.42±1.11	1.64±1.47	0.19		
Total Bilirubin (mg/dL, mean±SD)	5.90±9.10	6.19±7.80	0.79		
Albumin (g/dL, mean±SD)	2.83±0.59	2.85±0.55	0.72		
INR (mean±SD)	1.68±0.52	1.70±0.59	0.80		
Hemoglobin (g/dL, mean±SD)	10.22±2.34	10.02±2.04	0.48		
Ascites (n, %)					
Absent	35, 29.17%	35, 29.17%	0.44		
Slight	26, 21.67%	34, 28.33%			
Moderate	59, 49.17%	51, 42.50%			
Encephalopathy (n, %)					
None	91, 75.83%	96, 80.00%	0.78		
Grade 1-2	22, 18.33%	18, 15.00%			
Grade 3-4	7, 5.83%	6, 5.00%			
Dialysis At Least Twice in Last Week (n, %)					
No	117, 97.50%	115, 95.83%	0.72		
Yes	3, 2.50%	5, 4.17%			
Index Admission Discharge Labs					
Sodium (mmol/L, mean±SD)	134.72±4.14	134.95±3.57	0.64		
Serum Creatinine (mg/dL, mean±SD)	1.31±1.06	1.37±1.18	0.69		
Total Bilirubin (mg/dL, mean±SD, n=237)	5.50±8.80	5.39±6.96	0.92		
Albumin (g/dL, mean±SD, n=237)	2.98±0.64	2.94±0.61	0.65		
INR (mean±SD, n=238)	1.71±0.49	1.69±0.45	0.65		
Hemoglobin (g/dL, mean±SD)	9.30±1.69	9.21±1.68	0.68		
Ascites (n, %)					
Absent	42, 35.00%	39, 32.50%	0.35		
Slight	56, 46.67%	66, 55.00%			
Moderate	22, 18.33%	15, 12.50%			
Encephalopathy (n, %)					
None	117, 97.50%	112.93.33%	0.10		
Grade 1-2	2, 1.67%	8, 6.67%			
Grade 3-4	1, 0.83%	0, 0.00%			
Dialysis At Least Twice in Last Week (n, %)					
No	114, 95.00%	110, 91.67%	0.44		
Yes	6, 5.00%	10, 8.33%			

	Intervention (n=120)	Standard of Care (n=120)	p-value
Readmission (n, %)			1
No	77, 64.17%	82, 68.33%	0.59
Yes	43, 35.83%	38, 31.67%	
Number of Readmissions within 30	, ,		
days (n, %)			
0	77, 64.17%	82, 68.33%	0.65
1	31, 25.83%	32, 26.67%	
2	9, 7.50%	5, 4.17%	
3	2, 1.67%	1, 0.83%	
5	1, 0.83%	0,0.00%	
Location of 1 st Readmission (n, %)			
Our institution	36, 83.72%	23, 60.53%	0.03
Outside Hospital	7, 16.28%	15, 39.47%	
Reason for 1 st Readmission ¹ (n, %)			
Acute Kidney Injury (AKI)	10, 23.26%	6, 15.79%	0.58
Hyponatremia	4, 9.30%	6, 15.79%	0.50
Hepatic Encephalopathy (HE)	9, 20.93%	17, 44.74%	0.03
Volume Overload	13, 30.23%	9, 23.68%	0.62
Variceal bleed	6, 13.95%	6, 15.79%	1.00
Lower GI bleed	1, 2.33%	3, 7.89%	0.34
Spontaneous Bacterial Peritonitis (SBP)	2, 4.65%	1, 2.63%	1.00
Other	20, 46.51%	22, 57.89%	0.37
Index Admission Cost (mean±SD, n=116+109]	61,581±47,825	59,547±46,669	0.46
Index Admission LOS (mean±SD)	8.17±5.56	8.08±6.11	0.63
First Readmission LOS (n=43+38, mean±SD)	7.58±7.57	8.71±10.41	0.58
All Readmissions LOS (n=60+45, mean±SD)	9.28±16.88	8.69±10.44	0.82
Waiting time for first Readmission (n=43+38, mean±SD) indicates patient can have more than one of	11.16±7.10	14.34±7.77	0.06

Table 6 Outcomes and reasons of readmission characteristics by randomization arms

¹indicates patient can have more than one of variable listed

