Abstract P091 Figure 1 Number of livers from UK deceased donors offered, retrieved and transplanted, 4 February 2020 to 5 April 2021

NHSE and some patient care was transferred between centres, when overwhelmed critical care necessitated temporary unit closures.

Results During 2020/21, there was a significant fall in the total number of annual liver donors (21%; 870 from 1088) and transplants (22% 749 from 950) compared to 5-year mean, prior to the pandemic. This was exclusively amongst adult recipients (23%; 672, vs 868), both elective (22%; 609 vs 778) and SU (30%; 63 vs 90), whilst paediatric activity was maintained (77 vs 81). The reduction in adult LT varied widely geographically (-3 to -43%). LT registrations fell (11%; 1063 vs 1208), again with wide geographic variation (0 to -24%).

During the 'first wave', we successfully prioritised those with highest illness severity with no reduction in 90d patient ($p=0.89$) or graft survival ($p=0.98$). There was a small (5% cf 3%) but significant ($p=0.0015$) increase in deaths/removals from the UK LT waitlist, during this time. During the 'second wave', 5 adult units temporarily closed at various times, whilst 3 'protected' LT centres were maintained at any time. Consequently, 25 waitlist registrants were transferred to protected centres with 10 undergoing LT outwith their original centre.

Discussion A sophisticated national response has maintained a safe and effective UK LT program throughout the first year of COVID. We adapted our resources, implementing phased donor restrictions and a new category for recipient prioritisation. Patients benefitted from collaborative working, enabling those in most need to be transferred and transplanted in protected centres. Consequently, we mitigated against a significant fall in LT activity. Our collaborative response serves as an exemplar for other specialist healthcare services.

P092 SOCIOECONOMIC STATUS IS NOT A BARRIER TO LIVER TRANSPLANTATION FOR PATIENTS WITH ALCOHOL RELATED LIVER DISEASE

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Introduction Alcohol related liver disease (ArLD) carries significant morbidity and mortality; approximately 75% of deaths from liver disease in the UK result from excess alcohol consumption. Liver disease prevalence shows marked

geographical variation and people with liver disease living in the most deprived quintile die on average 9 years earlier than those living in the least deprived quintile. This study reviewed records for patients referred for transplant assessment with a history of ArLD to examine for obvious demographic, social or aetiology-based discrepancies in listing decisions.

Methods Electronic records of patients with a history of ArLD referred to our unit for liver transplant assessment between January 2019 and December 2021 were retrospectively

Abstract P092 Table 1 Baseline demographics, social factors, aetiology of liver disease, period of abstinence and assessment outcome of patients referred for liver transplant assessment with a history of ArLD

	Number assessed (%)	Number listed	% of category listed
Location at time of assessment			
Inpatient	50 (40)	33	66
Outpatient	75 (60)	54	72
Sex			
Male	97 (78)	69	71
Female	28 (22)	18	64
Age (years)			
20–29	2 (2)	1	50
30–39	6 (6)	4	67
40–49	22 (22)	15	68
50–59	49 (39)	37	76
60–69	43 (34)	29	67
70–79	3 (2)	1	33
IMD Quintile			
1 (most deprived)	21 (17)	13	62
2	29 (23)	23	79
3	33 (26)	23	70
4	23 (18)	16	70
5 (least deprived)	19 (15)	12	63
Residence			
Own house	54 (43)	37	69
HA/council house/HMO/rehab	22 (18)	12	55
Rented house	16 (13)	11	69
Lives with family	10 (8)	9	90
Caravan	2 (2)	2	100
Care home	1 (1)	1	100
Unknown	20 (16)	15	75
Employment			
Active	27 (22)	18	67
Retired	21 (17)	14	67
Unemployed	77 (62)	55	71
Aetiology of liver disease			
ArLD	63 (50)	46	73
ArLD + HCC	27 (22)	16	59
ArLD + 2nd aetiology	35 (28)	25	71
Period of abstinence			
0–3 months	15 (12)	9	60
4–6 months	26 (21)	18	69
7–12 months	37 (30)	25	68
13–24 months	25 (20)	18	72
25–36 months	9 (7)	7	78
>36 months	13 (10)	10	77

reviewed. Data were collected included baseline demographics, social factors including index of multiple deprivation (IMD), aetiology of liver disease, period of abstinence and assessment outcome (table 1).

Results 125 patients with a history of ArLD were referred for transplant assessment over the 3-year period. The majority (78%) were male and most (39%) were 50–59 years. Patients living in the most deprived quintile comprised just 17% of the group. In 50% ArLD was the only aetiology listed, 27% of patients also had hepatocellular carcinoma (HCC) and 28% had a second, non-malignant, aetiology listed. Patients were divided into groups based on demographics, social factors, aetiology and period of abstinence and the outcome of the transplant assessment was recorded for each group. Table 1 illustrates the percentage of patients in each group listed for transplant. Psychological, social or substance misuse issues (including smoking) were cited as concern for listing in just 7 (5%) of cases.

Conclusion Our data demonstrates that in patients with a history of ArLD referred to this unit for transplant assessment, there is no listing bias based on socioeconomic background. However, whilst ArLD occurs more often in lower socioeconomic groups, patients from IMD quintile 1 comprised just 17% of those referred, suggesting a potential referral bias. There was no clear preference for listing patients who had a second causal aetiology for their liver disease. Very few patients were not listed based purely on social/psychological factors. This data should encourage clinicians to refer patients with a history of ArLD for transplant assessment, regardless of their socioeconomic background.

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TOLL-LIKE RECEPTOR 4 INHIBITION ACTS SYNERGISTICALLY WITH G-CSF TO PREVENT ORGAN INJURY AND INDUCE LIVER REGENERATION IN ACUTE-ON-CHRONIC LIVER FAILURE

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Background and Aims Acute-on-chronic liver failure (ACLF) is characterised by lack of regeneration. Granulocyte colony stimulating factor (G-CSF) carries pro-regenerative properties and has been shown to be of benefit in ACLF. However, the large trial of G-CSF (GRAFT study) in patients with ACLF showed no benefit and in certain groups mortality tended to be higher. This study was performed to define the mechanisms underlying the negative effect of G-CSF and determine whether its beneficial effect could be harnessed using a toll-like receptor 4 (TLR4) antagonist.

Method Two mouse models of ACLF were used: CCL4 (0.5mg/ml, 6w) to induce chronic liver injury followed by LPS i.p. (*Klebsiella*, 4mg/kg) (n=4–10) or Galactosamine (GalN) i.p. (1000mg/kg) as a second hit (n=8). 1h after, G-CSF 250µg/kg s.c. and/or TLR4-inhibitor TAK-242 10mg/kg i.p. were injected and continued every 24h. The treatment duration was 24h and 5d in the LPS model and 48h in the GalN model. Samples were stored and analysed for liver injury, inflammation, senescence and regeneration.

Results 6w CCL4 led to bridging fibrosis, TLR4 up-regulation and infiltration of G-CSFr expressing cells. LPS increased ALT levels, cell death (TUNEL+), enhanced hepatic infiltration of

neutrophils (Ly6G+), macrophages (F4/80+) and TNFα. G-CSF increased the 48h mortality from 0% to 66%, aggravated liver inflammation with macrophage and NK cell (CD45+, CD49b+, CD3-, CD19-) infiltration and IL6 expression. G-CSF +TAK-242 reduced the mortality to 0%, abrogated the liver injury (TUNEL) and liver inflammation (macrophages, neutrophils, TNFα, IL6) significantly. In the second model, GalN also induced a significant liver injury. Treatment with G-CSF +TAK-242 was significantly more effective than the individual therapies. G-CSF+TAK-242 was associated with increased liver regeneration evidenced by increased tissue expression of pSTAT3 and BCL2. CCL4+LPS induced a p53 and p16-dependent cell cycle arrest and lack of proliferation (CyclinA) in hepatocytes. G-CSF+TAK-242 mitigated senescence and significantly increased the rate of CyclinA expressing hepatocytes (figure) suggesting enhanced liver regeneration.

Conclusion The present study shows that G-CSF is deleterious in LPS-associated ACLF through further activation of inflammatory pathways and immune cell infiltration. TLR4 inhibition with TAK-242 prevented G-CSF driven tissue injury and induced liver regeneration showing evidence of synergy between the two molecules thereby providing a novel therapeutic strategy for ACLF patients.

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POTENTIAL MECHANISMS UNDERLYING THE PROTECTIVE EFFECT OF LONG-TERM ALBUMIN INFUSION IN CIRRHOSIS

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Background Long-term albumin administration has shown a reduction in mortality in hepatic decompensation, however the mechanism of this is unclear. The aims of this study were to determine (i) whether analbuminaemic (NAR) rats have greater liver injury and sensitivity to LPS (ii) whether albumin infusion is protective in NAR rats (iii) the impact of analbuminaemia and albumin infusion on the gut-liver interface and hepatic TLR4 signalling.

Methods 10 treatment groups of NAR and SD rats were studied (n=4–7); Naïve, cirrhosis (4-w after bile duct ligation (BDL)) and ACLF models (induced by lipopolysaccharide (LPS) to BDL) were studied. BDL groups: ±LPS, ±albumin infusion (1.5 g/kg i.p. for 2 weeks). Markers of liver injury: plasma ALT level and TUNEL staining; markers of gut integrity and permeability: DAB immunohistochemistry ZO-1 expression in ileum tissue; Hepatic TLR4 immunohistochemistry and related pathway genes RT2 PCR profiler were studied.

Results Liver injury: ALT levels and TUNEL positive areas were significantly higher in NAR compared with SD rats (p = 0.01 and p = 0.01), which were corrected with albumin infusion (p = 0.02, p = 0.047). Effect of LPS administration: coma-free survival was higher in SD rats than NAR rats (80% vs 40%). Effect of albumin administration: Administration of albumin to BDL rats reduced severity of liver injury and mortality after LPS administration [p = 0.001; 40% vs 100%, p = 0.04]. Markers of gut permeability: In NAR rats, the histopathological examination of the ileum and colon revealed a reduction in ZO-1 expression, which was restored with