Senescence is an autonomous state of cell cycle arrest which is an important mechanism preventing malignant transformation. Recent evidence suggests that cellular senescence may also have a double-edged effect, contributing to chronic liver diseases (CLDs) and hepatocellular carcinoma (HCC). Senescent cells release a secretome, known as the senescence-associated secretory phenotype (SASP), which regulates the clearance of senescent cells through the recruitment of leukocytes from the circulation. We hypothesised that the SASP modulates leukocyte recruitment by regulating the phenotype of human hepatic sinusoidal endothelial cells (HSEC), the gatekeeper for leukocyte homing to the liver. To elucidate the underlying mechanisms, we undertook qPCR of SASP-treated HSEC and found that plasmalemma vesicle-associated protein (PLVAP) was transcriptionally regulated by SASP treatment. PLVAP is an endothelial-specific molecule recently highlighted in single-cell sequencing studies and has previously been implicated in monocyte trafficking during foetal development.

PLVAP expression was studied in human patient samples at the gene and protein level via qPCR and immunohistochemistry. To understand the effects of the SASP on PLVAP expression, HSEC were isolated from human livers by immunomagnetic selection and subject to 24-hour treatment with conditioned medium from RAS-senescent IMR90 fibroblasts (RAS-CM). PLVAP expression was then determined by qPCR and immunocytochemistry followed by high-content imaging. We observed strong PLVAP expression on endothelium in CLD and HCC patients, and confirmed that PLVAP expression *in vitro* is upregulated in primary HSEC by the senescent cell secretome.

To study the effects of RAS-CM treatment on monocyte recruitment and the contribution of PLVAP, we undertook flow adhesion assays under physiologically low shear stress with primary HSEC and monocytes isolated from peripheral blood. RAS-CM promoted monocyte adhesion and transmigration across HSEC. To investigate whether PLVAP plays a role in SASP-mediated monocyte recruitment, flow assays were performed with siRNA-treated or anti-PLVAP antibody-inhibited HSEC. We found that the proportion of adhered monocytes which underwent transendothelial migration was significantly impaired in PLVAP-inhibited HSEC. Following flow assays, cells were then fixed and analysed by confocal microscopy. We demonstrated that monocyte transmigration occurred predominantly via the paracellular route, in association with CD31 and independently of intercellular adhesion molecule 1, with PLVAP closely associating with the actin cytoskeleton. These results demonstrate that PLVAP plays an important role in SASP-driven monocyte recruitment across human HSEC. Furthermore, PLVAP expression in CLD and HCC may be driven by tissue senescence and could be a novel approach to target aberrant monocyte recruitment in liver disease.

P030

OUTCOMES OF INCOMING AND OUTGOING SECOND OPINIONS FROM A UK LIVER TRANSPLANT CENTRE – A ROADMAP FOR PAN-UK CENTRE DATA COLLECTION

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Background Second (2nd) transplant centre opinions for patients declined for liver transplantation (LT) are considered a rarely needed, but important component of the assessment process. There remains a lack of published data pertaining to the numbers of patients referred for 2nd opinions and their outcomes in the UK.

Aim To identify and track outcomes of patients referred into our LT centre (Birmingham, UK) for 2nd opinions (INCOMING) and those referred to a different centre (OUTGOING) between January 2012 - December 2020.

Methods INCOMING: all new outpatient referrals to the Birmingham LT Unit from out-of-region centres (n=1751) were reviewed and requests for 2nd opinions were collated. OUTGOING: patient records of those not listed at the Birmingham LT Unit (n=426) were reviewed to identify those referred for 2nd opinion to one of the 6 other UK LT centres. NHS identification numbers were cross-checked with NHSBT regarding LT elsewhere.

Results INCOMING: 23 2nd opinions (17 Leeds, 3 Royal Free, 1 Edinburgh, 1 Cambridge, 1 King's) were provided by Birmingham. Median age was 53 and the commonest aetiology was alcohol related liver disease (ArLD) (n=15; 65%). The risk of alcohol addiction/relapse was the main reason for initial LT refusal in 8 of these cases. Of the 2nd opinions, 13/23 (57%) patients remained unsuitable for LT after review and case discussion. The remaining 10/23 (43%) underwent a formal LT assessment, of whom 5 were deemed 'too high risk', 3 listed (1/3 subsequently transplanted) and 2 died pre-assessment.

OUTGOING: 8 Birmingham patients (aetiologies NAFLD, ArLD, LT graft loss, Budd-Chiari, PSC, venous thrombosis) were referred to other LT centres (4 King's, 2 Royal Free, 1 Cambridge, 1 Leeds) for a 2nd opinion. Of these, 3/8 (38%) were assessed and listed for LT by King's (1 transplanted, 2 waiting), 2 were assessed and declined LT, 2 were unsuitable for assessment and 1 died before being seen.

Cumulatively, only 6/31 (19%) of 2nd opinions were deemed suitable to list for LT.

Conclusions Requests for a 2nd centre LT opinion are rare. The majority (>80%) are still deemed 'too high risk' (alcohol, medical/anaesthetic risk) for LT after a 2nd LT centre opinion. There is a large discrepancy between the numbers of patients declined LT in the UK and the number of 2nd opinions sought. Further work is required to understand the reasons for this. A national UK LT assessment database would enable greater LT decision making.

P031

THE IMPLEMENTATION OF THE NATIONAL HEALTH SERVICE ENGLAND SERVICE FOR HEPATITIS C ANTIBODY TESTING IN COMMUNITY PHARMACIES: A NATIONAL SURVEY OF HEPATITIS C OPERATIONAL DELIVERY NETWORKS

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Introduction To meet and maintain World Health Organisation Hepatitis C (HCV) elimination target, it is essential that testing is scaled up and targeted at high-risk individuals. In September 2020 NHS England (NHSE) commissioned an advanced service to test people who inject drugs for HCV in

community pharmacies. This service is available to people who are injecting drugs but not on opiate substitution therapy. We surveyed operational delivery network (ODN) staff across England to understand the current implementation of the NHSE advanced service.

Method Service leads and key stakeholders within each ODN in England were identified by the Hepatitis C Trust. The survey was designed using Microsoft Forms. It was advertised through the NHSE HCV newsletter and distributed by HCV Action. Results were analysed using Microsoft Excel.

Results We received 22 responses from 20 out of 23 ODNs (87%). We analysed the results per ODN (n=20). In two ODNs there were two respondents, if the answers matched we included the answer once; if one respondent had a definitive answer and the other an unknown response, the definitive answer was used; and if there were contradictory answers, the response from this ODN was excluded.

Fourteen (70%) ODNs had met with a representative from the local pharmaceutical committee and 95% of ODNs had pharmacies that had registered interest in the advanced service, with more than ten pharmacies registering interest in the majority of ODNs (12 (63%)). Four (20%) ODNs had arranged additional training for pharmacies. Fourteen (70%) respondents were aware of their referral pathway. Two (10%) ODNs reported that the pharmacist would perform a dry blood spot test to check RNA status if a client was antibody positive. Only three (15%) ODNs reported that testing had started in their region, despite eight (40%) ODNs reporting a prior pilot of pharmacy-based HCV testing.

16/22 (73%) of respondents wanted further guidance on the implementation of the service, this included guidance with the initial set up and how to effectively communicate between clinicians and pharmacists. Qualitative feedback about the service was varied, however, a consistent theme was the need to expand the eligible population for the service.

Conclusions The NHSE HCV antibody testing service has started in a small number of community pharmacies in a minority of ODNs. Many ODNs have had prior successful pilot testing programme. There is therefore an opportunity to learn from these experiences to support the implementation of the national service.

P032 INCREASING BURDEN OF ALCOHOL-RELATED LIVER DISEASE IN THE UK ASSOCIATED WITH THE CORONAVIRUS PANDEMIC

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During the first UK national coronavirus pandemic lockdown (Mar-Jul 2020), alcohol sales increased 30% in supermarkets. Surveys reported that 20% of people increased their alcohol consumption and numbers of high-risk drinkers increased by 13%. Post-lockdown, clinicians noted high numbers of alcohol-related liver disease (ArLD)-related admissions. We hypothesised that greater alcohol consumption in high-risk drinkers

contributed to this increase. We conducted a national service evaluation to document the number and severity of unplanned ArLD hospital admissions pre- and post-lockdown.

We performed a retrospective service evaluation in 28 UK hospitals of all unplanned admissions during a one-week period in August 2019 and the same period in August 2020. The protocol was approved by the lead site's Clinical Audit Department and registered at participating sites. We applied a validated coding algorithm that more accurately identifies ArLD admissions than using only ArLD codes in the primary diagnosis.¹ Eligible cases were manually reviewed and data extracted into a pre-designed collection tool. Data collected included demographics, diagnosis, alcohol use and liver disease severity scores, which were compared between evaluation periods.

There was an 18% absolute increase in unplanned hospital admissions for patients with ArLD in the evaluation period in 2020 compared to 2019 (263 vs 223). Demographics were similar between the two periods (mean age 55; 37% female). In-hospital mortality was similar (9.0% vs 7.2%) and there were no differences between proportions of patients with complications of liver disease including variceal bleeding and alcoholic hepatitis. Patients in both evaluation periods had similar severity of liver disease with mean Child Pugh score of 8 and MELD 14. Those with alcoholic hepatitis had mean MELD 20 (SD 7.5) and discriminant function 90 (SD 70).

In the post-lockdown period, there were more active alcohol drinkers (151 vs 196; 75% vs 68%) than pre-lockdown. Mean consumption per patient was higher (154 vs 127 units alcohol/week; p=0.02). More patients reported drinking spirits post- vs pre-lockdown (31% vs 22%; p=0.06).

This national service evaluation demonstrates an increase in unplanned ArLD hospital admissions post-lockdown with patients reporting heavier alcohol use. Although there were no differences in clinical presentations or outcomes, these patients have advanced liver disease with high short-term mortality. These data suggest the pandemic has disproportionately affected high-risk drinkers and demonstrate the heavy burden of ArLD in the UK. There is an ongoing need to develop long-term strategies to improve these patients' outcomes.

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P033 DELIVERY OF LIVER SERVICES WITHIN PRIMARY CARE CAN IMPROVE TREATMENT OUTCOMES IN PERSONS EXPERIENCING HOMELESSNESS

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Background Persons experiencing homelessness (PEH) often have complex health needs compounded by difficulty accessing healthcare. Liver disease is the third commonest cause for death in PEH after accidents and suicides. Some studies have identified chronic hepatitis C (CHC) in up to 50% of this population. Alcohol disorders are also extremely common.