investigate the use of breath analysis as a non-invasive and simpler means of diagnosing HE, cirrhosis and harmful drinking.

Methods A bespoke breath-sampling device was used to sample one litre of breath through adsorbent tubes from patients with alcohol-related cirrhosis with (n=11) and without HE (n=23), non-alcoholic cirrhosis without HE (n=19), harmful drinkers without cirrhosis (n=7), inflammatory respiratory disease (n=18), and healthy controls (n=15). Compounds trapped on these tubes were released via thermal desorption and analysed by gas chromatography mass spectrometry for separation and detection. Multivariate discriminant analysis was used to identify volatile organic compounds to differentiate patients according to disease status and build models for disease classification.

Results Models based on the presence or absence of volatiles were tested in the patient groups. HE was correctly classified in 91.0% of patients with alcoholic cirrhosis. Patients with cirrhosis could be discriminated from those without cirrhosis with 100% accuracy in drinkers. In patients without clinical signs of HE, alcohol was correctly predicted as the underlying cause of cirrhosis in 82.6% of patients and non-alcoholic causes of cirrhosis were correctly determined in 84.2% of patients. Non-alcoholic cirrhosis, alcoholic cirrhosis, and harmful drinking could also be discriminated from healthy controls with a sensitivity of 89.5%, 97.1% and 100%, respectively.

Conclusion Breath volatiles can be used to aid the diagnosis of HE, cirrhosis, and harmful levels of drinking, therefore breath testing may offer a means to detect liver conditions non-invasively at earlier and more treatable stages.

Competing interests None declared.

PWE-288 SPONTANEOUS BACTERIAL PERITONITIS: PREVALENCE ON ADMISSION TO A TERTIARY CENTRE AND SUBSEQUENT OUTCOME

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Introduction Spontaneous bacterial peritonitis (SBP) is a sinister complication of cirrhosis associated with poor survival (approximately 38% at 1 year¹). However, a diagnosis of SBP does not represent, in its own right, an indication for liver transplantation in the UK under current listing criteria.

Methods We sought to investigate the prevalence and subsequent mortality in patients with an admission diagnosis of SBP. We retrospectively identified 366 consecutive cases admitted with ascites to our liver unit during the calendar year 2009. Of these 271 (74%) patients underwent diagnostic paracentesis at time of admission and were included for further analysis.

Results Of the 271 cases, 26 (9.6%) were diagnosed with SBP at admission on the basis of an ascitic fluid white cell count above 250 cells/mm³ (25 cases). Patients with positive cultures but no white cell response were only included if symptomatic (one case). Alcohol was the underlying aetiology in 17 cases (65.4%) and clinical presentations were as follows: routine paracentesis (14 cases), associated pleural effusion (four cases), variceal haemorrhage (three cases), abdominal pain (two cases), jaundice (two cases), encephalopathy (one case). Ascitic culture on two patients grew gram-negative bacilli, both resistant to quinolones being used for prophylaxis. One ascitic culture grew *Lactobacillus* spp. and one a mixed growth of *Enterococcus faecalis* and gram-positive cocci. Three patients (11.5%) died during the index admission. Three patients (11.5%) had successfully undergone liver transplantation and were alive 6 months after admission. Overall mortality at 6 months from an admission diagnosis of SBP was 50%.

Conclusion SBP is not uncommon in cirrhotic patients with ascites, can often present silently and is associated with high mortality. Resistance to standard quinolone prophylaxis and isolation of gram-positive bacteria are more recent phenomena in this group of patients. All cirrhotics admitted with significant ascites should undergo diagnostic paracentesis to exclude SBP and assessment for liver transplantation must be an urgent consideration in appropriate candidates. Listing criteria may need to be revised to include SBP as a standard indication.

Competing interests None declared.

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PWE-289 CRITICAL ILLNESS EARLY WARNING SCORES RETAIN ACCURACY IN PATIENTS WITH LIVER DISEASE—AN ANALYSIS OF 182 000 INPATIENT OBSERVATION SETS

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Introduction Aggregate weighted track and trigger systems (AWTTS) can identify critically ill patients at high risk of mortality. However, these scores use features of the Systemic Inflammatory Response Syndrome (SIRS) that may be altered in liver disease such as resting tachycardia and hypotension secondary to hyperdynamic circulation, blunted pyrexial response or hyperventilation due to encephalopathy. These scores have not been evaluated in patients with liver disorders. We therefore examined whether a range of AWTTS, including the VitalPac Early Warning Score (ViEWS), retain accuracy in liver disease.

Methods Clinical observations were recorded on a computerised database (VitalPac) for all admissions between July 2006 and April 2011 in a large hospital serving a population of 650 000. Adults assigned International Classification of Diseases (ICD-10) codes for liver disease, either as primary or comorbid diagnosis, were identified. ViEWS scores of 0–19¹ were allocated to all vital sign sets. Each set contained: date/time, pulse, blood pressure, respiration, temperature, neurological status using either the Alert-Verbal-Painful-Unresponsive scale or Glasgow Coma Score, pulse oximetry and use of supplemental oxygen. Datasets were analysed with respect to number of patients needed to be seen by a doctor if escalation occurred at that score and inpatient mortality within 24 h.

Results We identified 44 328 observation sets for patients with a primary liver diagnosis (PLD) code of which 519 (1.17%) were followed by death within 24 h. For those with a non-primary liver diagnosis (NPLD) 138 217 observations were made and 1157 (0.84%) resulted in death. There were no differences at any ViEWS score in the prediction of 24-h mortality and number needed to be seen for patients assigned a PLD or NPLD, compared to all adult hospital admissions (Abstract PWE-289 figure 1). The area under the receiver-operating characteristics curve (95% CI) was 0.886 for all patients and 0.888 and 0.883 for those with PLD and NPLD respectively.

Conclusion Using an electronic database of all clinical observations and diagnostic codes, we found the accuracy of predicting death within 24 h was retained in the presence of liver disease regardless of primary or secondary diagnosis. We have now expanded this work to include analysis of 34 additional AWTTS scores and distinct clinical presentations of hepatic disorders.

Competing interests T Hydes: None declared, P Schmidt Shareholder with: Director of a company with a minority shareholding in the development of Learning Clinic

software, G Smith: None declared, D Prytherch Shareholder with: Spouse holds shares in the Learning Clinic software development company, R Aspinall: None declared.

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PWE-290 ACTIVE ALCOHOL CONSUMPTION INDUCES FUNCTIONAL IMMUNE PARESIS BUT PARADOXICALLY PROMOTES ENDOTOXIN TOLERANCE IN THOSE WITH ADVANCED ALCOHOL-RELATED CIRRHOSIS

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Introduction Patients with alcohol-related cirrhosis (ARC) are particularly prone to infection which is frequently a precipitant of organ failure and death. Neutrophil dysfunction has been reported in patients with ARC. Sepsis and associated endotoxemia occur in approximately 40% of hospitalised patients. Neutrophil TLRs are able to sense pathogens and induce inflammatory responses but whether active alcohol drinking is protective or detrimental in this context remains unknown. The aim of this study was to characterise the neutrophil phenotype, TLR2/4/9 expression and plasma cytokine profile in patients with ARC who were abstinent (n=13) compared to those who were drinking (n=16), split by MELD score 15 compared to healthy controls (n=12).

Methods Neutrophils isolated from patients with ARC were studied ex vivo at baseline, and following 2-h stimulation with lipopolysaccharide (LPS) and the bacterial degradation protein fMLP. Neutrophil phenotype and TLR expression were determined using anti-CD16 (PE); -CD11b (APC-Cy7); -TLR2 (Alexa Fluor 488); -TLR4 (biotin conjugated PE-Cy7 Streptavidin) and -TLR9 (APC) by flow cytometry. Intracellular cytokine production pre- and post-stimulation will be measured by CBA.

Results The severity of cirrhosis (MELD15) or abstinent/active drinking status did not significantly impact on resting CD16, CD11b, TLR2 and 9 expression. TLR 2/9 expression on exposure to LPS and fMLP showed downregulation in those who were active alcohol-drinkers compared to the baseline. Conversely TLR4 expression was upregulated in the abstinent group with MELD >15; an effect significantly abrogated by the effect of active drinking (p=0.004). Active alcohol consumption did not however change TLR4 expression in those with MELD.

Conclusion Active alcohol consumption was shown to downregulate functional TLR2/9 expression resulting in immunoparesis with potential susceptibility to Gram-positive infection. However, active alcohol consumption was shown to abrogate the increased TLR4 responses to endotoxin stimulation seen in the abstinent ARC cohort with MELD >15. This implies that alcohol paradoxically promotes endotoxin tolerance and may act as a potential protective mechanism against Gram-negative insults in those with advanced cirrhosis.

Competing interests None declared.

PWE-291 MAPK SIGNALLING REGULATES THE DEVELOPMENT OF A CHOLANGIOCELLULAR PHENOTYPE FROM HCC IN POST-TACE LIVER TRANSPLANTS

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Introduction During normal liver wound-healing, tissue injury causes inflammation and cell death, which in turn orchestrates compensatory cell proliferation and regeneration.¹ If resolution of the injury cannot be obtained the resulting unchecked healing process can lead to cancer. Similar injury-induced repair mechanisms occur in response to chemotherapeutic treatments.¹ We recently found that the use of pre-transplantation TACE for HCC promotes the development of a mixed cholangiocellular phenotype that is associated with the expression of CD133, a marker of hepatic progenitor cells (HPC). This phenomenon is associated with higher post-transplantation tumour recurrence.² The molecular bases for the development of the cholangiocellular phenotype have not been investigated before. In this study we identified key oncogenic effectors involved with a “switch” from HCC to cholangiocellular phenotype resulting from liver injury induced by TACE treatment.

Methods Ten cases of post-TACE (doxorubicin/lipiodol) treated HCC examined after transplantation at King's College Hospital were selected for the study. HCC patients not treated by TACE before transplantation were used as control group. Formalin-fixed section from main tumour mass embedded in paraffin blocks were used to perform immunohistochemistry in order to delineate which component of the MAPK signalling pathway is associated with the hepatocholangiocellular phenotype and expression of HPC markers (CD133 and CK19).

Results Among the post-TACE liver explants, approximately 50% of the neoplastic cells resembling bile ductules (cholangiocellular differentiation) showed nuclear expression of a specific phospho-activated component of the MAPK cascade. Furthermore, half of the cells positive for activated-MAPK showed proliferative activity, as determined by Ki67 staining. Expression of activated-MAPK was not detected in the non-TACE treated group of liver transplant.

Conclusion The development of the mixed hepato-cholangiocellular phenotype in HCC patients after TACE-inflicted liver injury relates to activation of a specific MAPK signalling pathway that promotes proliferation of HPC. Attenuation of this signalling pathway could be used to prevent the “uncontrolled” proliferation and differentiation of progenitor cells before liver transplantation in HCC patients, and thus improving the tumour recurrence rate.

Competing interests None declared.

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PWE-292 NAFLD: BELOW THE RADAR EVEN ON SURFACING IN SECONDARY CARE!

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Introduction Non-alcoholic fatty liver disease (NAFLD) is becoming a common cause for secondary care referral. While simple steatosis does not lead to liver related morbidity, non-alcoholic steatohepatitis (NASH) may lead to cirrhosis and hepatocellular carcinoma. Currently, non-invasive imaging including ultrasonography (USS) may reveal fatty infiltration. Many patients attend secondary care for USS, in whom NAFLD may be identified incidentally. While the true prevalence and burden of NAFLD in the community remains unclear, patients attending for USS in whom NAFLD is identified could provide the opportunity to reduce disease burden by monitoring for any complications. The aims of this study were to assess