Project Details	
Project Code	PHS27Br Abeysekera
Title	The early detection and management of liver disease: improving outcomes in an underserved patient group.
Research Theme	Population Health Sciences
Project Type	Dry lab
Summary	Liver disease is leading cause of mortality in working age and a major cause of working life years lost. It disproportionately impacts patients with people in underserved communities. This project will collaborate with the Children of the 90s birth cohort to track the trajectories of risk factors in young adults. We will determine the prevalence of liver disease in young adults, the genetic signatures associated with liver fibrosis development and examine the life course for risk factors. This will inform targeted public health approaches to mitigate liver disease morbidity, and form the basis for future projects.
Description	Background: Liver disease in young adults. There is a dearth of literature exploring the burden of liver disease in young adults. The Avon Longitudinal Study of Parents and Children (ALSPAC) performed over 4000 transient elastography (TE) assessments for liver fibrosis, finding 1 in 5 and 1 in 40 participants aged 24 years having steatosis (fatty liver) and fibrosis, respectively. Individuals at the greatest risk of fibrosis are those with metabolic risk factors and alcohol use disorder, with a 4-fold increased odd. Recently ALSPAC completed the “Focus at 30 years” Liver clinic to delivered over 3000 transient elastography measurements to assess the fibrosis prevalence. 2770 participants have provided blood samples. Ethical approval has been granted by the ALSPAC Law and Ethics Committee. The ALSPAC liver clinic finished in 2025 to facilitate analyses from 2026. Serology analysis of 2770 samples from the 30-year clinic is due to complete in Autumn 2026. This would include liver blood tests, fasting glucose and lipid profiles. Serology will allow a student to perform a comprehensive normative and longitudinal assessment of cardiometabolic serological markers. ALSPAC also has alcohol and smoking measures of participants since their adolescence and steatosis (fatty liver) measures at 17, 24, and 30 years of age. Key research question: Determine the prevalence of liver disease in young adults aged 30 years, utilising the ALSPAC birth cohort. Explore the trajectory of risk factors that lead people to develop liver disease early. Hypothesis: Liver fibrosis prevalence, based on TE results, would increase between years 24 and 30. Analysis: The majority of ALSPAC participants with fibrosis will have steatotic liver disease (alcohol and metabolic dysfunction associated steatotic liver disease), with viral hepatitis prevalence extremely low in this population. We would supervise a student to use multivariable logistic regression models to examine differences between binary outcomes of (i) steatosis and (ii) fibrosis, based on TE results. The main covariates of interest include body mass index (BMI), waist circumference-to-height (WCHt) ratio (as surrogate of adiposity), alcohol consumption, dietary measures, smoking, socioeconomic status, sex, and ethnicity. This will provide much-needed normative data on young-

	adult liver health of value to clinical guidelines, such as guiding the timing and targeted liver risk screening in the general population. Trajectories of risk factors and determinants of early liver fibrosis development. Aim: To evaluate the influence of cardiometabolic and alcohol consumption on the risk of liver fibrosis development at 30 years of age. Outcome of interest: Primary outcome of interest is liver fibrosis. Steatosis will be a secondary outcome. Exposures if interest: Using the rich ALSPAC data resource we would explore these exposures of interest at 9, 17, 24 and 30 years: BMI, WCHt ratio (44), low-density lipoprotein, very low-density lipoprotein, triglycerides, high-density lipoprotein, fasting glucose, alanine transaminase, aspartate aminotransferase, gamma glutamyl transferase. We will also assess daily alcohol and smoking use. Potential confounders: Sex, gestational age, maternal age at delivery, maternal pre-pregnancy obesity, socioeconomic status. Analysis: We would supervise a student to study the life course of key cardiometabolic and alcohol risk factors for fibrosis longitudinally to explore patterns of change in these factors and gain a detailed insight into the manner in which they change through the developmental period of adolescence to young adulthood. These results will then inform analyses in which a student could incorporate the fibrosis and steatosis outcomes generated from the liver clinic. Appropriate models – including mixed effects regression analyses and structured life-course analyses - will be employed to firstly estimate the magnitude of the associations between these risk factors with liver outcomes at 30 years. Structured life-course modelling is a powerful technique for investigating hypotheses around sensitive periods of change in risk factors spanning the life-course when considering their impact on a subsequent outcome. A student could estimate the effects of these exposures on liver disease in young adulthood. A student could evaluate if there are sensitive periods for an impact of change in, or accumulation of, risk factors on liver fibrosis at 30 years and its progression from 17 to 30 years – a unique possibility here. The success of this project will support a future funding application for the next ALSPAC Liver clinic when participants are 40 years old. Patient and Public Involvement supporting this project: Two valuable consultation sessions with the ALSPAC Public and Advisory Panel (APPAP; 20 members) have helped shape the concepts described here. Participants said conveying that nuance in the future needs to be clear to avoid scare-mongering. We discussed how alcohol and obesity interact and that future targeted public health campaign to raise awareness would need to involve clear social media messaging and potentially health influencers. We would expect a student to discuss future messaging to participants and parents if they did identify critical time periods of risk factors to be targeted.
Can be completed part time?	No

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