processed through Spectronaut 14 software for spectral library building, protein identification and quantification. Differentially expressed proteins were identified based on an observed fold change of ≥ 1.5 or ≤-1.5 and q-value ≤ 0.005. Pathway analysis was performed using Ingenuity Pathway Analysis (IPA) software.

**Results and Conclusions/Implications** Label-free MS analysis led to over 4,000 protein identifications, with 3,484 proteins commonly identified across all patient samples. Over 1,000 significantly differentially expressed protein candidates were identified for comparisons between NF and DCM, HOCM or ISCM. DCM-specific protein changes were strongly associated with glutamine biosynthesis, HOCM-specific protein changes were strongly associated with LXR/RXR Activation, while ISCM-specific protein changes were most associated with tryptophan degradation pathways. DCM vs NF, ISCM vs NF and HOCM vs NF had shared differentially expressed proteins that were also significantly altered at gene level (n=106). Canonical pathway analysis revealed that Choline Degradation and Lysine Degradation pathways were most strongly associated with these candidates. Expression changes for some of the top over- and under-expressed HF candidates were validated in an independent replicate dataset (PXD008934) [2]. This represents one of the largest and deepest proteomic datasets for myocardial tissue reported to date. The dataset, which complements existing transcriptomic data for these samples, has highlighted a number of significant proteins associated with different underlying aetiologies of HF. Prognosis for HF differs depending on the aetiology from which it arises. Hence, the dataset here will help in further understanding the pathogenesis of the disease, leading towards more personalised treatment.

**Conflict of Interest** N/A
compared to 40% in men(1). Despite this, even in contemporary research, female patients are poorly represented in trials. A review of 740 trials found that females accounted for only 27.3%, 26.9% and 28.6% of the coronary heart disease, acute coronary syndrome and heart failure (HF) trial cohorts, respectively(2). To gain a greater understanding of the gender disparity in HF research, we aimed to explore the variations in female representation, firstly between subtypes of HF trials, and secondly between randomised trials and clinical registries.

**Methods**
A systematic review of large randomised control trials (RCT) was carried out using Pubmed. This identified 905 results, and after removal of sub-analyses, smaller trials (<300 participants) and those not reporting participant gender, 146 were included for analysis. 17 registries were also identified.

**Results**
The 146 RCTs included a total number of 248,620 patients. For all trials, the median proportion of females was 25.8%. The lowest proportion of females was seen in trials studying ischaemic cardiomyopathy (ICM), those mandating a left ventricular ejection fraction (LVEF) <35%, and those involving an invasive procedure (table 1). The highest proportion of females was seen in RCTs assessing HF with preserved LVEF (HFpEF), as well as trials selecting older participants. When RCTs were compared to registries, the biggest difference in female representation was seen in ICM and all-comer HF trials (8%). For ICM, LVEF <35% and all-comer HF trials, significant differences were also seen between prevalence of female trial participants and population prevalence (figure 1).

**Discussion**
We identified a significant gender disparity in HF RCTs, as compared to registries and population statistics. We also identified significant variation in the female prevalence between different subtypes of heart failure, both in research and the population.

**Pathophysiology**
The combination of less obstructive coronary disease, vascular stiffness and myocardial hypertrophy, as well as a tendency to preserve LVEF after ischaemia, means women are 2-3 times less likely to present with HF with reduced LVEF, as compared to male counterparts(3-5). They therefore may not meet LVEF criteria for inclusion into RCTs.

**Investigation and Diagnosis**
Women have lower levels of cardiac biomarkers, fewer ‘classic’ electrocardiogram findings and are less likely to be referred for coronary angiography(6). If they are less frequently investigated for, and diagnosed with, these conditions, they will be less likely to enter clinical trials.

**Inclusion Bias**
Even when adjusted for prevalence, fewer females are referred for trial screening(7). Women present at a later with HF, and older patients are poorly represented in RCTs(2, 8). Previous work has identified that women perceive higher personal harm from involvement in research(9), and are 15% less willing to partake than male counterparts(10). Female HF patients are older, have a lower body mass index and poorer creatinine clearance, and therefore may not meet inclusion criteria related to medication doses, or be excluded due to comorbidities(11).

**Conclusions**
A significant gender disparity remains in HF trials; most visible in trials assessing severely reduced LVEF and ICM. As physicians we must recognise our unconscious bias to reduce differences in diagnosis and treatment of our patients. We should routinely enquire about female specific risk factors, recognise atypical presentations, and use gender-specific cardiac enzyme thresholds. Trial inclusion and exclusion criteria should be carefully reviewed. Patient and public

| ICM | 8  | 8541 | 20.0  |
| NICM | 3  | 1940 | 27.6  |
| Invasive procedure/surgery | 13 | 6852 | 22.0 |
| Device trials | 30 | 36,136 | 23.2 |
| Drug trials | 79 | 180,080 | 30.9 |
| Follow up/ communication | 18 | 19,589 | 31.8 |
| Diagnosis/risk scores | 10 | 7384 | 40.0 |
| Older participants | 5  | 4449 | 45.3 |
| **All trials** | 146 | 248620 | 25.8 |

**Abstract 115 Figure 1**
Female prevalence in RCTs, registries and the population. Stars indicate significant difference.

I115.001: **ICM:** ischaemic cardiomyopathy, **Severe LVSD:** LVEF <35%, **All HF:** Trials with no LVEF cut off, **HFpEF:** heart failure with preserved ejection fraction.
Background and Purpose: Left ventricular diastolic dysfunction (LVDD) is a key pathophysiological mechanism in heart failure with preserved ejection fraction (HFpEF) but its environmental determinants are poorly understood. Environment-wide association studies (EWAS) provide a comprehensive method to test a variety of exposures across the human environment and life-course in a high-throughput, unbiased manner. We conduct the first life-course EWAS for LVDD.

Methods: Participants were from the Medical Research Council (MRC) National Survey of Health and Development (NSHD, the British 1946 birth cohort) who had echocardiographic data recorded at age 60-64 years. LVDD (outcome) was defined by the presence of ≥2 abnormal echocardiographic parameters out of: left atrial volume index, E/e’, septal e’, lateral e’, and E/A, with normal cut-off values obtained from the American Society of Echocardiography guideline for LVDD diagnosis. 326 life course environmental factors (exposures) were investigated for their association with LVDD. Significant factors were identified using a logistic regression model adjusting for sex, body mass index and socioeconomic position (SEP), and a false discovery rate of 5%. Interactions between individual exposures were appraised using exposome correlation globes and matrices, and a principal component analysis.

Results: A total of 1616 participants were included (50.4% men, 21.4% with LVDD). We discovered 26 factors independently associated with LVDD (p ≤ 0.05) (figure 1). Significant factors from 0-18 years included childhood cognition (odds ratio [OR]: 0.83; 95% confidence interval [CI]: 0.69-0.99), quality of home conditions (OR: 0.90; 95% CI: 0.83-0.97), crowding of childhood dwelling (OR: 1.17; 95% CI: 1.05-1.30) and father’s SEP (OR: 0.74; 95% CI: 0.56-0.98). Childhood cognition displayed inter-domain positive correlations with father’s SEP and housing quality. From 19-44 years, significant factors were reading test performance (OR: 0.96; 95% CI: 0.93-0.99), oily fish consumption (OR: 0.99; 95% CI: 0.98-1) and canned fruit consumption (OR: 0.99; 95% CI: 0.98-1.00). Other significant factors were systolic blood pressure from 45-59 years (OR: 1.01; 95% CI: 1.00-1.02), and tissue plasminogen activator (OR: 1.04; 95% CI: 1.01-1.08) and urine creatinine from 60-64 years (OR: 0.96; 95% CI: 0.93-1). (Figure 2) illustrates the correlations between all exposures relevant to ages 0-18 years.

Conflict of Interest: None