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 $q\text{-value} \leq 0.005$. 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 v 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

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CLINICAL, PHYSICAL, COGNITIVE AND SOCIAL FRAILTY IN PATIENTS WITH CHRONIC HEART FAILURE: PREVALENCE AND ASSOCIATIONS WITH OUTCOME

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Background Recently, the American College of Cardiology (ACC) and the Heart Failure Association (HFA) of the European Society of Cardiology (ESC) proposed a four-domain approach to assess frailty in patients with heart failure (HF), to tailor treatment and potentially improve outcomes. **Aim:** To study the prevalence and prognostic value of four different types of frailty deficits: clinical, physical, cognitive and social frailty in ambulatory patients with HF.

Methods We assessed prospectively consecutive patients attending a routine follow-up visit. Patients with ≥ 5 non-HF comorbidities were classified as having a clinical deficit. Those who scored ≥ 3 using the Fried criteria were classified as having a physical deficit. Those who failed to complete a clock test accurately were classified as having a cognitive deficit. Those who lived alone or in a residential home were classified as having a social deficit.

Results 467 patients (67% male, median (25th-75th centile) age 76 (69-82) years, median (25th-75th centile) NT-proBNP 1156 (469-2463) ng/L) were enrolled. 65% of patients had clinical deficits, 52% had a physical deficit, 39% had a social

Abstract 114 Figure 1

Abstract 114 Figure 2

deficit and 18% had a cognitive deficit. 28% had 2, 19% had 3, 8% of patients had all 4 deficits; 16% had none. (Figure 1). During a median follow-up of 554 days, 82 patients died. The presence of any frailty deficit was associated with increased risk of mortality. (Figure 2) Patients with all 4 frailty deficits have a 15-fold increased risk of mortality compared to patients with no frailty deficit. A base model (including age, body mass index, NYHA class and log [NT-proBNP]) for predicting mortality at 1 year achieved a C-statistic of 0.78. Addition of all four deficits improved the performance of the base model (C-statistic = 0.82).

Conclusion Clinical, physical, cognitive and social deficits are common in patients with HF and are associated with a poor outcome. Future studies should evaluate how to optimise care for frail patients with HF using a domain management model.

Conflict of Interest none

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GENDER DISPARITY IN HEART FAILURE RESEARCH

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Background Cardiovascular disease is one of the leading causes of mortality in women, accounting for 49% of all deaths,

Abstract 115 Table 1 Summary of all HF RCTs, divided into HF aetiology and trial type.
ICM: ischaemic cardiomyopathy, LVEF: left ventricular ejection fraction, NICM: non-ischaemic cardiomyopathy

	Trials	No of patients	Female %
LVEF			
HF, LVEF <35%	56	90,033	21.9
HF, LVEF <50%	48	84,348	27.6
All HF (no LVEF cut off)	36	58,101	37.5
HF, LVEF > 50%	8	17,385	50.6
Aetiology			
ICM	8	8541	20.0
NICM	3	1940	27.6
Trial subtype			
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

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

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

ICM: ischaemic cardiomyopathy, Severe LVSD: LVEF <35%, All HF: Trials with no LVEF cut off, HFpEF: heart failure with preserved ejection fraction

opinion should be sought to explore factors influencing trial participation.

Conflict of Interest None

116 ABSTRACT WITHDRAWN

117 ABSTRACT WITHDRAWN

118 LIFE-COURSE ENVIRONMENT-WIDE ASSOCIATION STUDY (EWAS) FOR LEFT VENTRICULAR DIASTOLIC DYSFUNCTION IN THE 1946 BRITISH BIRTH COHORT

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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 ($p \leq 0.05$) (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: 0.98-1.00) 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.

Abstract 118 Figure 1 Manhattan plot displaying multivariable environment-wide associations with LVDD. Y-axis displays the $-\log_{10}(p\text{-value})$ of the logistic regression coefficient for each factor tested. X-axis indicates the exposure domains. 26 factors above the red line are significant at the $p \leq 0.05$ level. *bpproblems* = blood pressure problems, *DBP* = diastolic blood pressure, *GHQ1162* = taking longer to do things, *GHQ12.62* = doing things well, *GHQ13* = satisfied with tasks, *GHQ2162* = considering yourself a worthless person, *SBP* = systolic blood pressure, *tPA* = tissue plasminogen activator

Abstract 118 Figure 2 Exposome correlation globes for all exposures relevant to ages 0-18. Domains (key is on the right) and correlations are colour coded. Each line represents a correlation between two exposures. Correlations were analysed using Spearman's rank correlation coefficient. *Lrti* = lower respiratory tract infection