around medoids with the number of clusters ranging from 2 to 10. Our protocol runs following four checkpoints; (i) validity [ClValid package], (ii) re-evaluation of validity results and unbiased determination of the winning algorithm [NbClust package], (iii) stability test [ClusterStability package] and (iv) generalizability [predict.strength package] testing for the most optimal clustering solution. Thereafter, we investigated whether the identified FThD subgrouping solution was associated with neurocognitive performance, social and occupational functioning by using Welch's two-sample t-test or Mann-Whitney-U test based on the distribution of data, and explored the interrelation of these domains with network analysis by using qgraph package with the spearman correlation matrix among variables. All analyses and univariate statistical comparisons were conducted with R version 3.5.2. We used the False Discovery Rate (FDR)37 to correct all P-values for the multiple comparisons.

Results: The k-means algorithm-based on two-cluster solution (FThD high vs. low) surviving these validity, stability and generalizability tests was chosen for further association tests and network analysis with core disease phenotypes. Patients in FThD high subgroup had lower scores in global (pfdr = 0.0001), social (pfdr < 0.0001) and role (pfdr < 0.0001) functioning, in semantic (pfdr < 0.0001) and phonological verbal fluency (pfdr = 0.0004), verbal short-term memory (pfdr = 0.0018) and abstract thinking (pfdr = 0.0099). Cluster assignment was not informed by the global disease severity (pfdr = 0.7786) but was associated with more pronounced negative symptoms (pfdr = 0.0001) in the FThD high subgroup.

Discussion: Our findings highlight how the combination of unsupervised machine learning algorithms with network analysis techniques may provide novel insight about the mappings between psychopathology, neurocognition and functioning. Furthermore, they point how FThD may represent a target variable for individualized psycho-, socio-, logotherapeutic interventions aimed at improving neurocognition abilities and functioning. Prospective studies should further test this promising perspective.

O6.5. JUMPING TO CONCLUSIONS ABOUT DECISION NOISE? A COMPUTATIONAL ANALYSIS OF THE RELATIONSHIP BETWEEN BELIEF UPDATING AND PSYCHOTIC SYMPTOMS IN A LARGE UK BIRTH COHORT

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Background: A number of studies show that people with psychotic disorders have abnormal belief-updating processes. In a commonly-used decision-making task, the beads task, participants infer which of two jars, each with a different ratio of coloured beads, a presented bead is drawn from, with an option to request further beads before reaching a decision. Previous studies suggest that people with psychotic symptoms request fewer beads (draws to decision; DTD) indicative of a 'Jumping to conclusion' (JTC) bias. In a modified version of this task, participants estimate the probability that beads have been drawn from one of the two jars on a sliding scale over a sequence of beads and are also told that the jar the beads are drawn from may switch. In this task, people with psychotic symptoms revise their estimations disproportionately in response to a change in colour of beads in a sequence (overadjustment bias).

It is not clear what specific belief-updating processes drive these biases, how they arise, or if their association with psychotic symptoms is independent of confounding. We examined whether abnormal belief-updating processes are associated with psychotic experiences in a large, population-based sample, and whether they mediate the association between trauma and psychotic symptoms.

Methods: We used data from the Avon Longitudinal Study of Parents and Children birth cohort (n=2,879). Past-year frequent or distressing psychotic experiences (PEs) were assessed using the semi-structured PLIKS interview at age 24. Performance on the DTD and probability estimation tasks at age 24 were assessed using behavioural indices and computational modelling parameters (using 'costed Bayesian' and Hidden Markov Models respectively). Logistic regression was used to examine the association between belief-updating parameters (DTD task: cost of sampling, decision noise; Probability estimation task: adjustment rate, inference length, decision confidence, prior expectation of reversal, decision noise) and PEs. Estimates were adjusted for confounders (genetic risk for schizophrenia, socio-economic status, cognitive function). Mediation analysis tested abnormal belief-updating processes as a mediator between exposure to trauma (assessed ages 0–17 years) and age-24 PEs.

Results: In the DTD task, increased decision noise was associated with PEs (adjusted OR=1.89, 95% CI: 1.14, 3.13, p=0.014). There was little evidence of an association between the JTC bias and PEs (OR= 1.13; 95% CI: 0.45, 2.82). For the probability estimation task, there was an association between a higher prior expectation that the jars that will switch during the sequence (expectation of reversal) and PEs (adjusted OR = 2.28; 95% CI 1.39, 3.74, p=0.001). Our findings were minimally attenuated by confounding (<10%). Exposure to trauma was also associated with greater decision noise in the DTD task, but there was little evidence that this abnormal belief-updating parameter mediated the relationship between trauma and PEs (<1% mediated).

Discussion: Our results suggest that abnormal belief-updating processes (increased decision noise; greater prior expectation of reversal) are associated with PEs, and that this is not explained by general cognitive ability, shared genetic risk, or social background. Previous observations of association between the JTC bias and psychosis may be due to sub-optimal performance rather than a bias for making a decision on less evidence. The results also suggest that an increased expectation of change is associated with the early stages of psychosis symptom development. Our mediation result does not support the hypothesis that the belief-updating processes examined here lie on the causal pathway between trauma exposure and PEs.

O6.6. MULTIMODAL PROGNOSIS OF NEGATIVE SYMPTOM SEVERITY IN INDIVIDUALS WITH INCREASED RISK OF DEVELOPING PSYCHOSIS

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Background: Precise prognosis of clinical outcomes in individuals at clinical high-risk (CHR) of developing psychosis is imperative to guide treatment selection. While much effort has been put into the prediction of transition to psychosis in CHR individuals, prognostic models focusing on negative symptom progression in this population are widely missing. This is a major oversight bearing in mind that 82% of CHR individuals exhibit at least one negative symptom in the moderate to severe range at first clinical presentation, whereas 54% still meet this criteria after 12 months. Negative symptoms are strong predictors of poor functional outcome irrespective

of other symptoms such as depression or anxiety. Prognostic tools are therefore urgently required to track negative symptom progression in CHR individuals in order to guide early personalized interventions. Here, we applied machine-learning to multi-site data from five European countries with the aim of predicting negative symptoms of at least moderate severity 9-month after study inclusion.

Methods: We analyzed data from the 'Personalized Prognostic Tools for Early Psychosis Management' (PRONIA; www.pronia.eu) study, which consisted of 94 individuals at clinical high-risk of developing psychosis (CHR). Predictive models either included baseline level of negative symptoms, measured with the Structured Interview for Prodromal Syndromes, whole-brain gyrification pattern, or both to forecast negative symptoms of moderate severity or above in CHR individuals. Using data from the clinical and gyrification model, further sequential testing simulations were conducted to stratify CHR individuals into different risk groups. Lastly, we assessed the models' ability to predict functional outcomes in CHR individuals.

Results: Baseline negative symptom severity alone predicted moderate to severe negative symptoms with a balanced accuracy (BAC) of 68%, whereas predictive models trained on gyrification measures achieved a BAC of 64%. Stacking the two modalities allowed for an increased BAC of 72%. Additional sequential testing simulations suggested, that CHR patients could be stratified into a high risk group with 83% probability of experiencing at least moderate negative symptoms at follow-up and a medium/low risk group with a risk ranging from 25 to 38%, when using the two models sequentially. Furthermore, the models trained to predict negative symptom severity from baseline symptoms were less predictive of role (60% BAC) and social (62% BAC) functioning at follow-up. However, the model trained on gyrification data also predicted role (74% BAC) and social (73% BAC) functioning later on. The stacking model predicted role, and social functioning with 64% BAC and 66% BAC respectively.

Discussion: To the best of our knowledge this is the first study using state-of-the-art predictive modelling to prospectively identify CHR subjects with negative symptoms in the moderate to above moderate severity range who potentially require further therapeutic consideration. While the predictive performance will need to be validated in other samples and may be improved by expanding the models with additional predictors, we believe that this pragmatic approach will help to stratify individual risk profiles and optimize personal interventions in the future.

O7. Oral Session: Physical/ Mortality

O7.1. ASSOCIATION BETWEEN PATTERNS OF COMORBID MENTAL DISORDERS AND MORTALITY-RELATED ESTIMATES. A NATIONWIDE, REGISTER-BASED COHORT STUDY BASED ON 7.5 MILLION INDIVIDUALS LIVING IN DENMARK

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Background: Comorbidity within mental disorders is common – individuals with one type of mental disorder are at increased risk of subsequently developing other types of disorders. Previous studies are usually restricted to temporally-ordered pairs of disorders. While more complex patterns of comorbidity have been described (e.g. internalizing and externalizing disorders), there is a lack of detailed information on the nature of the different sets of comorbid mental disorders. Additionally, mental disorders are associated with premature mortality, and people with two or more types of mental disorders have a shorter life expectancy compared to those with exactly one type of mental disorder. The aims of this study were to: (a) describe the prevalence and demographic correlates of combinations of mental disorders; and (b) estimate the excess mortality for each of these combinations.

Methods: We conducted a population-based cohort study including all 7,505,576 persons living in Denmark in 1995–2016. Information on mental disorders and mortality was obtained from national registers. First, we described the most common combinations of mental disorders defined by the ICD-10 F-subchapters (substance use disorders, schizophrenia spectrum disorder, mood disorders, neurotic disorders, etc.). Then, we investigated excess mortality using mortality rate ratios (MRRs) and differences in life expectancy after disease diagnosis compared to the general population of same sex and age.

Results: At the end of the 22-year observation, 6.2% individuals were diagnosed with exactly one type of disorder, 2.7% with exactly two, 1.1% with exactly three, and 0.5% with four or more types. The most prevalent mental disorders were neurotic disorders (4.6%) and mood disorders (3.8%), even when looking particularly at persons with a specific number of disorders (exactly one type, exactly two types, etc.). We observed 616 out of 1,024 possible sets of disorders, but the 52 most common sets (with at least 1,000 individuals each) represented 92.8% of all persons with diagnosed mental disorders. Mood and/or neurotic disorders, alone or in combination with other disorders, were present in 64.8% of individuals diagnosed with mental disorders. People with all combinations of mental disorders had higher mortality rates than those without any mental disorder diagnosis, with MRRs ranging from 1.10 (95% CI 0.67 – 1.84) for the two-disorder set of developmental-behavioral disorders to 5.97 (95% CI 5.52 – 6.45) for the three-disorder set of schizophrenia-neurotic-substance use disorders. Additionally, any combination of mental disorders was associated with shorter life expectancies compared to the general population, with estimates ranging from 5.06 years [95% CI 5.01 – 5.11] for the one-disorder set of organic disorders to 17.46 years [95% CI 16.86 – 18.03] for the three-disorder set of schizophrenia-personality-substance use disorders.

Discussion: Within those with mental disorders, approximately 2 out of 5 had two more types of mental disorders. Our study provides prevalence estimates of the most common sets of mental disorders – mood disorders (e.g. depression) and neurotic disorders (e.g. anxiety) commonly co-occur, and contribute to many different sets of comorbid mental disorders. The association between mental disorders comorbidity and mortality-related estimates revealed the prominent role of substance use disorders with respect to both elevated mortality rates and reduced life expectancies. Substance use disorders are relatively common, and these disorders often feature in sets of mental disorders. In light of the substantial contribution to premature mortality, efforts related to the 'primary prevention of secondary comorbidity' warrant added scrutiny.

O7.2. MENTAL HEALTH AND SOMATIC STATUS OF YOUNG CHILDREN (0–6 YEARS) BORN TO PARENTS WITH SEVERE MENTAL ILLNESSES - A NATIONWIDE DANISH REGISTER STUDY

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