such as age and gender did not predict cumulative dosing, interdepartmental differences suggest heterogeneous prescribing practices. As outpatient continuation data are unavailable, total therapy duration cannot be assessed. These findings highlight current prescribing trends and provide a foundation for developing unified phenibut prescribing guidelines and considering alternative therapies at CCUH to ensure that pediatric patients receive appropriate and standardised treatment in everyday clinical practice.

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NOCTURNAL ENURESIS INDUCED BY CLOZAPINE: MECHANISMS AND MANAGEMENT STRATEGIES

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Introduction: Clozapine remains the gold-standard antipsychotic for treatment-resistant schizophrenia. However, a considerable amount of patients treated with clozapine experience nocturnal enuresis (NE). This is a stigmatising adverse effect that affects quality of life and threatens treatment adherence, still under-recognised and rarely elicited unless directly asked by the clinician.

Aim: Highlight the importance of NE associated with clozapine and explore potential pathophysiological mechanisms and management strategies.

Methods: Narrative review of literature through a search conducted on Pubmed and Google Scholar databases using the keywords "clozapine" and "nocturnal enuresis". Articles were screened for relevance to the study aim.

Results: Several studies report different rates of prevalence of clozapine-induced NE, ranging from 10% to 42% and show that this drug confers a significantly higher risk of NE than most other antipsychotics. NE is not entirely understood and is certainly a multifactorial adverse effect. Key mechanisms include peripheral α-adrenergic blockade that reduces internal sphincter tone; a paradoxical effect through potent anticholinergic action causing detrusor hypocontractility with urinary retention and consequent overflow incontinence during the night; 5-HT2A and 5-HT2C antagonism that may be involved in urinary sphincter relaxation; dopamine antagonism that can provoke an increased tonus on a hyperactive bladder, which associated with a noradrenergic deficit could alter micturition reflexes; sedative properties that blunt arousal to bladder fullness; seizure-threshold lowering effects that may cause nocturnal seizures with incontinence; and clozapine-induced polyuria due to nephrogenic diabetes insipidus or diabetes mellitus. Animal studies also showed that clozapine can change urodynamics resulting in activity reduction of the external urethral sphincter. Regarding treatment, evidence is limited to observational studies and case reports. After first-line options such as non-pharmacological measures, targeted pharmacotherapy should be considered. These include α-agonists (ephedrine/pseudoephedrine) which may increase sphincter tone, anticholinergics (oxybutynin, trihexyphenidyl) that reduce bladder activity, desmopressin that mimics antidiuretic hormone and reduces nocturnal urine production, and low-dose aripiprazole, which can be effective through its partial D2 agonism, countering D2 blockade and improving arousal. There have been single reports of success with amitriptyline, valproic acid and verapamil. All these options carry their own adverse effects and should be considered with caution and careful monitoring depending on each mechanism.

Conclusions: Clozapine-induced NE is common, even if under-reported, and complex in regards to pathophysiology. Routine enquiry of this adverse effect is crucial, considering the stigma that surrounds it and the effect on quality of life. By raising awareness to this phenomenon, early recognition and patient support may improve compliance with overall treatment. Available evidence suggests, firstly, non-pharmacological intervention, after which one should consider pharmacological options, while monitoring for adverse effects. There are several options, which reflect the various different mechanisms involved. Further controlled studies are needed to clarify mechanisms and optimize interventions. Prospective, controlled studies are essential to refine risk prediction and compare interventions that can offer quality of life to patients.

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IS PHARMACIST-LED MEDICATION REVIEW EFFECTIVE IN REDUCING PAIN INTENSITY AND IMPROVING QUALITY OF LIFE IN CHRONIC PAIN PRIMARY CARE PATIENTS?

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Introduction: Chronic pain patients in primary care often present with diverse pain conditions and underlying causes. The multidimensional nature of chronic pain constitutes a significant challenge to its management and assessment [1]. Medication review (MR), using the Dader method, involves a systematic evaluation of a patient's pharmacotherapy to optimize treatment. An advantage of this method is the adaptability to all healthcare settings [2,3]. This study aims to assess the impact of pharmacist-led MR on pain intensity (PI) and quality of life (QoL) in primary care patients with chronic pain.

Methods: A parallel-group, single-blinded, randomized trial was conducted in two primary care units in Porto, Portugal. The primary outcome was PI measured on 11-point numerical rating scale (NRS) and the secondary outcome was QoL improvement measured by the total pain interference score of the Brief Pain Inventory (BPI). Eligibility included ages between 18 and 70 years with non-cancer chronic pain (persistent or recurrent pain, >3 months) regardless of etiology and presenting with an average weekly pain PI score of ≥ 4, on the NRS scale. Random assignment to either the MR group (n=10) or the Usual Care (UC) group (n=10) for a 16-week study period was conducted. Each participant underwent one face-to-face interview per month, totaling four interviews during the study. The MR group received pharmacotherapy optimization using the Dader method, while the UC group received general advice and over the counter (OTC) medication recommendations, similar to a typical community pharmacy visit. An intention-to-treat (ITT) analysis was conducted using the general linear model of repeated measures, Analysis of Covariance (ANCOVA), with interviews as the within-subjects factor and interventions as the between-subjects factor. Baseline scores and body mass index (BMI) were used in the ANCOVA model as covariates. A p-value <0.05 was considered significant for a one-tailed test.

Results: At baseline the mean pain scores were 6.18±2.25 and 5.82±2.32 in the MR group and the UC group respectively. At week 16, MR group showed a mean pain reduction of 2.07±3.31 while the UC group showed an increase of 0.52±1.90. The adjusted between-group mean difference was -2.77 (95% CI, -4.93 to -0.62; $p = 0.008$). Regarding QoL, the BPI total pain interference score at baseline was 35.67±17.85 and 31±19.13 in the MR group and the UC group respectively. By week 16, the MR group displayed a reduction in total pain interference of 23.33±16.57 while the UC group displayed an increase of 36.33±23.92. The adjusted between-group mean difference was -17.79 (95%CI, -34.46 to 1.14; $p = 0.019$).

Conclusions: In this study, we showed that pharmacist-led MR could impact PI and QoL in chronic pain patients in primary care. A significant improvement in PI, as well as in QoL, was observed among patients receiving pharmacist-led MR. These preliminary results suggest that pharmacists play an important role in the management of chronic pain and can improve clinical outcomes in this setting.

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NEUROBIOLOGICAL PROFILES OF VULNERABILITY AND FUNCTIONAL OUTCOMES IN EARLY-STAGE PSYCHIATRIC DISORDERS: A MULTI-LEVEL MACHINE LEARNING ANALYSIS

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Introduction: Early-stage psychiatric disorders are highly heterogeneous and often associated with long-term functional disability. Despite advances in clinical staging, current risk stratification models insufficiently reflect the complex biological and psychosocial processes driving individual vulnerability. There is a critical need for data-driven approaches that integrate information across domains to identify transdiagnostic profiles of risk and resilience that are generalisable, interpretable, and clinically meaningful. Our study aimed to identify multimodal latent vulnerability signatures in early-stage psychiatric disorders and to evaluate their clinical relevance for stratifying risk of poor functional outcomes over time.
Methods: This study leveraged data from the longitudinal PRONIA cohort (N = 1,059), a multisite European study recruiting participants across ten centres in Finland, Germany, Italy, Switzerland, and the UK. Participants included help-seeking individuals meeting criteria for clinical high risk for psychosis (CHR), recent-onset depression (ROD), or recent-onset psychosis (ROP), as well as healthy controls. Multimodal baseline assessments included structural neuroimaging, polygenic risk scores, neurocognitive tests, clinical and diagnostic interviews, and self-reported childhood adversity. Follow-up assessments of functioning were conducted at 9 and 18 months. We applied multiblock sparse partial least squares (MB-SPLS), a multivariate data integration method that identifies latent structures of shared variation across modalities, within a leave-one-site-out cross-validation (LOSOCV) framework to ensure generalizability across sites. The derived latent variables (LVs) were examined for stability, interpretability, and biological plausibility. Functional outcome trajectories were modeled using longitudinal clustering of four functional domains (GAF symptoms, GAF disability, GF:Social, GF:Role), and machine learning models were trained using nested cross-validation to evaluate the predictive utility of the MB-SPLS-derived LVs. Clinical utility was further assessed via comparison with human rater predictions and decision curve analysis.
Results: We identified one robust and generalisable LV that loaded on neurodevelopmentally relevant features, including widespread cortical alterations, elevated polygenic risk scores for schizophrenia, bipolar disorder, and neuroticism, greater exposure to childhood trauma - particularly emotional abuse - and reduced cognitive performance, current functioning, and earlier social and scholastic premorbid adjustment. This multivariate profile was expressed across diagnostic groups but was most prominent in individuals with psychosis spectrum disorders (ICD-10 F2). The signature was significantly associated with poorer longitudinal functioning trajectories. Predictive modelling based on the latent scores revealed that genetic and neuroanatomical risk dimensions contributed most to distinguishing individuals with deteriorating functioning from those showing improvement - despite both groups being impaired at baseline. Compared to human predictions, the model demonstrated superior clinical utility, particularly in clinically challenging subgroups such as CHR. Decision curve analysis indicated superior net benefit of the multimodal model especially at higher threshold probabilities.
Conclusions and Relevance: The identified vulnerability signature reflects a transdiagnostic, dimensional neurodevelopmental risk profile, aligning with prior evidence on neurodevelopmental mechanisms in early-stage psychiatric disorders. This insight can inform stratified care: costly and resource-intensive assessments (e.g., MRI scans) may be most valuable in diagnostically ambiguous or clinically at-risk individuals, such as CHR cases. While MB-SPLS was not trained to predict functional outcomes, the derived LV proved clinically informative - bridging mechanistic understanding and actionable prognosis in precision psychiatry.
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PRELIMINARY FINDINGS ON LATENT CLASSES OF BURNOUT AND SENSORY SENSITIVITY PREDICTING MINFULNESS AND PSYCHOLOGICAL WELL-BEING IN NURSES

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Introduction: Burnout remains a pervasive occupational health concern among nurses, who frequently face high emotional demands, shift-related fatigue, and prolonged exposure to human suffering [1].At the same time, individual differences in sensory processing sensitivity (SPS)—a temperament trait reflecting heightened responsiveness to sensory and emotional stimuli [2]—may amplify vulnerability to occupational stress. Although burnout and SPS have been studied separately, few investigations have explored how their co-occurrence may form distinct psychological profiles that influence downstream outcomes such as mindfulness and psychological well-being [3]. Mindfulness, defined as present-focused, nonjudgmental awareness, and flourishing, often operationalized as psychological well-being, are known buffers against stress and emotional exhaustion [4,5]. This study aimed to identify latent profiles based on levels of burnout and SPS among nurses and examine how these profiles differ in terms of mindfulness and psychological well-being.
Methods: The study sample consisted of 405 nurses who completed validated self-report measures including the Maslach Burnout Inventory (MBI), the Highly Sensitive Person Scale (HSP), the Mindful Attention Awareness Scale (MAAS), and Flourishing Scale (FL). Latent Class Analysis (LCA) was conducted using two continuous indicators: burnout (BO) and total sensory sensitivity (HSP). Model fit was assessed via Akaike Information Criterion (AIC), Bayesian Information Criterion (BIC), entropy, and Bootstrap Likelihood Ratio Tests (BLRT). After identifying the optimal number of latent classes, ANCOVA tests were used to compare classes on all subscales of study measurements.
Results: We conducted a latent class analysis (LCA) on responses from 405 nurses using the Maslach Burnout Inventory and the Highly Sensitive Person Scale. The 3-class model demonstrated optimal fit and clarity (BIC = 64071.41; Entropy = 0.985), yielding Class 1 (24.9%), Class 2 (23.4%), and Class 3 (51.6%). ANCOVA models (controlling for age and gender) revealed significant class differences across all outcomes: MAAS, FL, burnout dimensions and sensory sensitivity subscales (all $p < .001$). Pairwise comparisons showed that Class 1 (low burnout/