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1. Validation and Clinical Utility of the Psychosis Metabolic Risk Calculator (PsyMetRiC) in Early Psychosis

Introduction

Psychotic disorders are associated with high somatic morbidity, primarily due to increased cardiometabolic risk, including type 2 diabetes (T2D), obesity, and cardiovascular disease (CVD). These conditions significantly reduce quality of life, increase treatment costs, and contribute to premature mortality. Metabolic syndrome (MetS), characterized by dysregulated glucose-insulin homeostasis, adiposity, hypertension, and dyslipidemia, serves as an early marker of cardiometabolic risk and strongly predicts progression to T2D, CVD, and severe outcomes such as myocardial infarction and cerebrovascular events.[1] Cardiometabolic risk prediction algorithms, including the Finnish Diabetes Risk Score (FINDRISC), are widely used in clinical practice. However, these tools were developed for middle-to-older adults and fail to account for the early emergence of cardiometabolic disturbances in individuals with psychotic disorders, leading to significant underprediction of risk. To address this gap, the Psychosis Metabolic Risk Calculator (PsyMetRiC) was developed in the UK to estimate the 6-year MetS risk in first-episode psychosis (FEP) patients aged 18–35 years. PsyMetRiC has potential clinical utility in guiding personalized interventions to mitigate CVD risk in this high-risk population. Accurate detection of cardiometabolic risk in early psychosis is essential to reducing morbidity and mortality.[2] This study externally validated and recalibrated PsyMetRiC in a Finnish early psychosis cohort and compared its clinical utility to FINDRISC, a general population risk prediction tool.

Methods

This validation study comprised 18–35-year-old patients with first-episode psychosis and ultra-high-risk patients with psychosis who did not have metabolic syndrome from the Helsinki Early Psychosis and Turku Early Psychosis Study cohorts. Two versions of PsyMetRiC were tested: the full model,

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which included BMI, sex, ethnicity, smoking status, prescription of a metabolically active antipsychotic drug, high-density lipoprotein, and triglyceride concentrations; the partial model, which excluded biochemical predictors; and the simplified FINDRISC, which included BMI, sex, systolic blood pressure, and fasting glucose. Both PsyMetRiC and FINDRISC's clinical utility and predictive performance were evaluated using decision curve, discrimination, and calibration studies. PsyMetRiC (PsyMetRiC-Fi) was recalibrated for a specific site.

Results

In this study, 278 individuals with early psychosis (58.6% male, mean age 24.8 years, mean BMI 23.5, 37.8% smokers) were included. PsyMetRiC demonstrated superior discrimination (C = 0.72, 95% CI 0.59–0.82) compared to its partial model (C = 0.70, 95% CI 0.59–0.80) and FINDRISC (C = 0.63, 95% CI 0.54–0.71). Calibration plots indicated minor miscalibration in PsyMetRiC, which improved post-recalibration, while FINDRISC showed greater miscalibration. Decision curve analysis confirmed PsyMetRiC's clinical utility, with recalibrated models enhancing risk management. At a 15% risk threshold, recalibrated PsyMetRiC full and partial models provided net benefits of 0.13, potentially preventing 52% and 50% more MetS cases, respectively, compared to 4% with FINDRISC (Figure 1). In the clinical-high-risk for psychosis patients (CHR) group, PsyMetRiC full and partial models had C-statistics of 0.71 (95% CI 0.58–0.85) and 0.66 (95% CI 0.51–0.80), respectively.

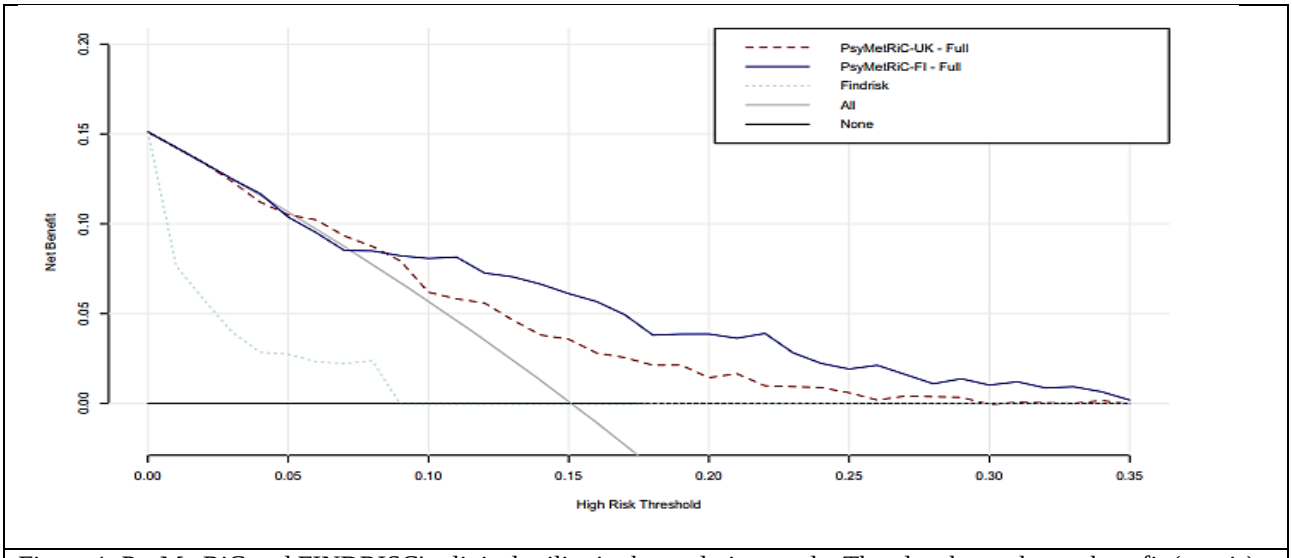

Figure 1. PsyMetRiC and FINDRISC's clinical utility in the analytic sample. The plot shows the net benefit (y-axis) of the original PsyMetRiC and recalibrated PsyMetRiC-Fi full and FINDRISC over a range of risk thresholds (x-axis) against intervening in all (gray line) or none (black line).

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Discussion

This study shows that PsyMetRiC-Fi is more suitable for use in the Finnish early psychosis population than comparable general population-based tools and its value in this group was comparable to earlier external validations carried out globally. FINDRISC's calibration analysis showed that this early psychosis sample consistently underpredicted risk.[2] Perry BI et al. developed an age-appropriate algorithm to forecast the likelihood that young individuals with psychosis will acquire incident metabolic syndrome, which is a risk factor for cardiometabolic morbidity and mortality. PsyMetRiC has the potential to be a useful tool for clinicians providing early intervention services. It may help them make individualized, well-informed decisions about lifestyle modifications and antipsychotic medication selection.[3]

Conclusion

Patients with early psychosis can benefit from using PsyMetRiC to estimate their cardiometabolic risk. It provides more accurate risk prediction and has higher discriminatory accuracy than other systems.

PsyMetRiC-Fi promises to be a potential tool for routine use in the future by medical professionals who treat adolescents who have psychosis or are at risk of developing psychosis.

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2. Association of Different Aspects of Social Relationships on Dementia Risk: A Prospective Cohort Study

Introduction

Dementia is a growing global public health issue, projected to affect 153 million people by 2050.[1] The efforts to reduce future cases focus on developing curative treatments and identifying modifiable risk factors for primary prevention. Studies suggest that addressing factors such as hypertension, obesity, hearing loss, physical inactivity, poor diet, and low social engagement may delay or prevent dementia. Also, it was shown that social activities, larger social networks, high-quality relationships, and low loneliness are associated with reduced dementia risk. However, the definitions of these social constructs are often unclear and overlapping, and few studies have examined the underlying pathways connecting social relationships to dementia risk. Additionally, socio-emotional factors like depressive symptoms may mediate this association, though this remains untested.[2] This study aimed to (1) identify distinct facets of social relationships through factor analysis, (2) explore their links to dementia risk, and (3) assess the role of depressive symptoms as a mediator.

Methods

This observational study included 7,536 participants. Thirty-six questionnaire items on social relationships, collected during Wave 2 of the English Longitudinal Study of Ageing, underwent exploratory and confirmatory factor analysis. Data were gathered biennially, covering health status, socioeconomic position, social well-being, lifestyle, and cognition. Identified factors were analyzed as predictors using Cox proportional hazard models to assess dementia risk through Wave 9, with adjustments for demographic and cardiovascular risk factors. Mediation by depressive symptoms was examined using structural equation modeling with effect decomposition.

Results

In this study, factor analysis identified six distinct social factors. Over a median follow-up period of 11.8 years (IQR: 5.9–13.9 years), 501 participants developed dementia. Multivariable Cox regression assessed the relationship between social relationship factors and incident dementia. Higher scores for frequency and quality of contact with children (HR = 0.88; $p = 0.021$) and frequent social activity engagement (HR = 0.84; $p < 0.001$) were associated with a reduced dementia risk. Conversely, higher

scores for loneliness (HR = 1.13; p = 0.011) and negative social support experiences (HR = 1.10; p = 0.047) were linked to an increased dementia risk (Table 1). Mediation analysis revealed a significant partial mediation effect of depressive symptoms across all four factors. Additional analyses found minimal evidence for reverse causation.

Factors associated with Dementia	HR	p value
Frequency and quality of contact with children	0.88	0.021
More frequent social activity engagement	0.84	<0.001
Loneliness	1.13	0.011
Negative experiences of social support	1.10	0.047

Table 1. Higher factors scores associated with Dementia

Discussion

This study found that frequent and high-quality social interactions, social leisure activities, and lower levels of loneliness and negative social experiences were associated with a reduced dementia risk, independent of demographic and cardiovascular factors.[2] Similarly, Wang et al.'s meta-analysis linked that high social engagement and frequent social contact are significantly linked to a lower risk of dementia, whereas loneliness is associated with an increased risk. Additionally, the presence of a large social network was identified as a protective factor. Strengthening social connections may serve as a viable strategy for dementia prevention.[3]

Conclusion

This study concludes that the frequency and quality of social interactions, social activity engagement, and perceived loneliness are associated with dementia risk. These factors may serve as targets for dementia prevention programs, potentially mitigating risk through the reduction of depressive symptoms.

Strong social relationships and active engagement reduce dementia risk, making them key targets for prevention strategies.

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3. Interconnections among Depression, Anxiety, and Sleep Disturbances in Obstructive Sleep Apnea

Introduction

Obstructive sleep apnea syndrome (OSAS) is a common respiratory disorder affecting 5–10% of the population, characterized by breathing pauses during sleep, leading to sleep fragmentation and excessive daytime somnolence. OSAS has been linked to various metabolic comorbidities, impaired quality of life, and an increased risk of automobile accidents.[1] Psychological distress, including depression and anxiety, is prevalent in OSAS patients, and addressing these comorbidities, rather than just disordered breathing may significantly improve patient outcomes. Studies on the relationship between depression, anxiety, and sleep disturbances have predominantly used syndromic assessments. However, network analysis offers a novel approach to explore the interrelationships among these symptoms. For example, network studies have identified critical symptoms, such as "Subjective Sleep Quality" and "Uncontrollable Worry," that play pivotal roles in the symptom network. While network analysis has been applied in other populations, its use in OSAS remains limited.[2] This study used network analysis to investigate the complex interrelationships between depressive, anxiety, and sleep disturbance symptoms in OSAS patients.

Methods

In this analysis, a total of 621 patients with OSA completed the questionnaires. The Hospital Anxiety and Depression Scale (HADS) was used to assess symptoms of depression and anxiety, and the Pittsburgh Sleep Quality Index (PSQI) was used to assess symptoms of sleep disturbance. The symptom network's centrality was measured using the indices 'anticipated influence' and 'bridge anticipated influence'. The network structure of symptoms related to depression, anxiety, and sleep disturbance was estimated using the Least Absolute Shrinkage and Selection Operator (LASSO) technique and the Extended Bayesian Information Criterion (EBIC). A Network Comparison Test (NCT) was used to assess the differences between the mild to moderate OSA and severe OSA

networks. The NCT uses various invariance metrics and is a two-tailed permutation technique for comparing two networks.

Results

In this study, 313 of them were diagnosed with severe OSA, while 308 were classified with mild to moderate OSA. There were 79.7% men, and the average age was 45.34±13.65 years (mean±SD). The average scores for HADs and sleep disruption were 12.22±7.89 (mean±SD) and 9.69±4.58, respectively. Network research showed that D6 ("Feeling slowed down") had the highest bridge expected influence values in the networks, while A6 ("Experiencing sudden feelings of panic") had the highest predicted influence value. According to the NCT results, individuals with mild to moderate OSA and those with severe OSA had substantially different edge weights (M=0.263, p=0.008). Patients with mild to moderate OSA and those with severe OSA did not significantly differ in global strength (S=0.185, p=0.773), but they did differ significantly in edge weights (M=0.263, p=0.008) (Figure 1). Also, strong similarities between the two networks were indicated by the similarity coefficient (S=0.185).

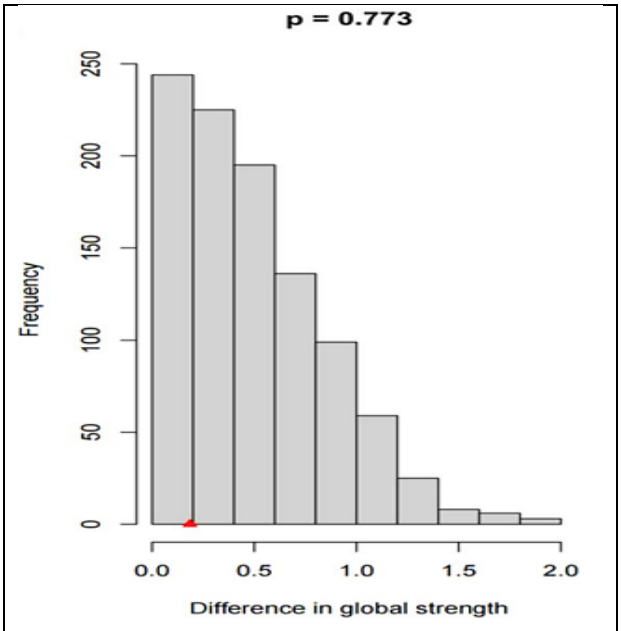

Figure 1. Results of the network comparison tests. Global strength differential of the network.

Discussion

This study identified strong connections between anxiety symptoms, with the most direct link observed between A2 ("Having a frightened feeling as if something awful is about to happen") and A6 ("Getting sudden feelings of panic"). A second key connection was found between sleep duration and sleep efficiency (SDu and SE), followed by a third link between A3 ("Worrying thoughts") and A6 ("Sudden feelings of panic").[2] These findings align with a similar network analysis by Zhang L et al. which also highlighted the strong connection between A2 and A6 in rheumatoid arthritis patients. This replication suggests that the relationship between these two symptoms may be a general feature of anxiety symptom networks, not limited to OSA.[3]

Conclusion

This study highlights the complex relationships among depression, anxiety, and sleep disturbances in patients with obstructive sleep apnea (OSA). These findings enhance the understanding of the psychological comorbidities associated with OSA and inform the development of targeted, personalized treatment strategies.

Symptoms with the highest expected influence and bridge roles (e.g., A6 and D6) should be prioritized as key targets for intervention and treatment in obstructive sleep apnea (OSA) patients.

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4. A case of Anxiety in Hypothyroidism: Cause or Coexistence?

Introduction

Hypothyroidism is a common endocrine disorder influenced by factors such as age, sex, genetics, race, environmental elements like iodine and selenium intake, and varying diagnostic criteria.[1] It is categorized into three types: primary hypothyroidism, where the thyroid gland fails to produce adequate T3 and T4 hormones; secondary hypothyroidism, caused by insufficient secretion of thyroid-stimulating hormone (TSH) from the pituitary gland; and tertiary hypothyroidism, where hypothalamic dysfunction leads to reduced production of thyrotropin-releasing hormone (TRH). Anxiety disorders, characterized by excessive fear and worry, share symptoms with thyroid dysfunction, including restlessness, palpitations, fatigue, and irritability, complicating diagnosis.

Hypothyroidism, though distinct, can also mimic anxiety symptoms, leading to misdiagnosis and delayed treatment. Since thyroid dysfunction is diagnosed through blood tests, many cases remain undetected or mistaken for primary anxiety disorders.[2] This case report highlights a misdiagnosis where hypothyroidism presented with anxiety-like symptoms, underscoring the critical need to rule out endocrine disorders before assigning a psychiatric diagnosis.

Case presentation

A 32-year-old female presented with generalized muscle tension, persistent fatigue, and lethargy. She reported difficulty initiating sleep, frequent restlessness, and chronic tension, often accompanied by headaches and a sense of unease. Additionally, she experienced cognitive dysfunction described as "brain fog", mood fluctuations, impaired concentration, excessive worry, irritability, and emotional exhaustion. Initially, the patient consulted an external private physician, where her vital signs were within normal limits. She was prescribed sertraline (50 mg daily) for presumed anxiety and advised to reduce stress. However, no psychiatric or additional medical evaluations were conducted at that time. Two months later, due to persistent symptoms and lack of improvement with sertraline, she sought a second opinion at the hospital. She reported ongoing fatigue, cognitive impairment, and sleep disturbances, expressing concerns that sertraline had exacerbated her symptoms, causing drowsiness, nausea, and restlessness. A comprehensive physical and neurological examination revealed no abnormalities except facial puffiness, particularly around the eyes, slight facial erythema, cold extremities, and generalized cold intolerance. Thyroid examination demonstrated a gland of normal size with no palpable abnormalities or bruit.

A psychiatric assessment using the Generalized Anxiety Disorder-7 (GAD-7) screening tool yielded a score of 7, indicating mild anxiety requiring symptom monitoring and routine follow-up (Table 1). Thyroid function tests revealed elevated thyroid-stimulating hormone (TSH) and reduced thyroxine (T4) levels, confirming a diagnosis of hypothyroidism. The patient was subsequently referred to endocrinology for further evaluation and treatment.

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How often has the patient been bothered by the following symptoms over the past 2 weeks	Not at all (0 points)	Several days (1 point)	More than half the days (2 points)	Nearly every day (3 points)
Feeling nervous, anxious, or on edge	-	X	-	-
Not being able to stop or control worrying	-	X	-	-
Worrying too much about different things	-	X	-	-
Trouble relaxing	-	X	-	-
Being so restless that it's hard to sit still	X	-	-	-
Becoming easily annoyed or irritable	-	-	X	-
Feeling afraid as if something awful might happen	-	X	-	-

TABLE 1: Generalized Anxiety Disorder-7 screening chart

Total score = 7 (mild anxiety)

GAD-7 total score for the seven items ranges from 0 to 21

0-4: minimal anxiety; 5-9: mild anxiety; 10-14: moderate anxiety; 15-21 severe anxiety

Management included initiation of levothyroxine (100 mcg daily) to be taken on an empty stomach 20 minutes before breakfast. Sertraline was tapered to 25 mg over two weeks and then discontinued. At a two-month follow-up, the patient reported marked clinical improvement. Cognitive clarity was noticeable by the second week of therapy, with near-complete resolution of anxiety-like symptoms by the fourth week. Energy levels significantly improved, and she experienced restful sleep without interruptions. She described a transformative improvement in her daily functioning, including enhanced concentration and task completion, overcoming long-standing procrastination. By the third month of levothyroxine therapy, thyroid function tests showed normalization of TSH and T4 levels, albeit at the upper limit of the reference range. Consequently, the levothyroxine dose was reduced to 50 mcg. By the fourth month, her thyroid levels were well within the normal range, prompting a further reduction to 25 mcg. Monthly thyroid function monitoring was implemented to maintain hormonal balance while preventing overtreatment.

Discussion

Endocrine disorders can present with anxiety-like symptoms, mimicking disorders like GAD and leading to misdiagnosis. Timely thyroid assessment is crucial, especially in atypical or treatment-resistant cases. A thorough medical evaluation, including physical examination and laboratory tests, should complement psychological assessment in patients with anxiety symptoms.[3] GABA, a key

inhibitory neurotransmitter, is disrupted in hypothyroidism, affecting mood and cognition. Liu et al. found reduced GABA+ levels in the mPFC of hypothyroid patients, which normalized after six months of levothyroxine (L-T4) treatment. This suggests GABA dysregulation contributes to hypothyroid-related cognitive impairment, with L-T4 offering potential therapeutic benefits.[4]

Conclusion

This case demonstrates the crucial association between endocrine and mental illnesses, underlining the importance of a complete and multidisciplinary diagnostic approach when patients exhibit anxiety-like symptoms. Although hypothyroidism is essentially an endocrine illness, it can have psychological signs that are similar to anxiety disorders, potentially leading to misdiagnosis and delayed treatment.

Thyroid function tests are essential in assessing anxiety-like symptoms, as thyroid disorders can mimic psychiatric conditions.

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