1	A network approach to lifestyle behaviors and health outcomes in people with		
2	mental illness: the MULTI+ study III		
3	Short title: Lifestyle and health in mental illness (MULTI+ III): a network		
4	approach		
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22	Keywords		
23	Lifestyle behavior, physical health, mental health, network approach, sleep		
24			
25	Abstract		
26	Background		
27	Unhealthy lifestyle behaviors are prevalent among people with mental illness (MI), affecting		
28	their physical and mental health. Most research has focused on the isolated effects of		
29	lifestyle behaviors, leaving the interconnectedness between these behaviors and health		
30	outcomes unexplored. This study aimed to examine these relationships and identify the mos		
31	strongly connected lifestyle behavior or health outcome within a network.		
32	Methods		
33	We conducted a cross-sectional study with 423 inpatients with MI, receiving care as usual.		
34	Lifestyle behaviors, physical, and mental health outcomes were assessed through		
35	questionnaires and routine data. A Gaussian Graphical Model was estimated, and strength		
36	centrality was calculated to identify the most influential nodes.		
37	Results		
38	Mean age was 55.5 years, 42% were female and 41% were diagnosed with schizophrenia.		
39	Psychological and physical quality of life (QoL), nighttime sleep problems, and overall sleep		
40	quality were most strongly connected nodes. Sleep was strongly associated with physical		
41	QoL. Furthermore, there were negative associations between healthy food intake and		
42	cholesterol ratio, and positive associations between daily doses of antipsychotics and length		
43	of hospital stay. Node strength was stable (CS(cor = 0.7) = 0.75). No clear pattern emerged		
44	among other lifestyle behaviors and health outcomes.		

45 **Conclusions**

- This study offers insights into the interrelatedness of lifestyle behaviors and health outcomes.
- 47 Addressing sleep problems could enhance QoL and potentially influence other health
- 48 outcomes. Psychological and physical QoL were also strongly associated, emphasizing the
- importance of perceived well-being in health outcomes. Future research could explore causal
- 50 pathways to identify treatment targets to improve care.

51 Introduction

52 Unhealthy lifestyle behaviors, such as physical inactivity, unhealthy diet, a poor sleep pattern 53 and substance use, are prevalent among people with mental illness (MI)[1,2]. In recent 54 years, these behaviors have gained more attention in mental health care due to their 55 substantial role in the development of physical conditions, such as cardiovascular disease, 56 obesity and diabetes mellitus[1,3,4]. These physical conditions contribute significantly to the 57 disability and mortality of people with MI, leading to a reduced life expectancy of up to 20 58 years compared to the general population[5,6]. Despite extensive evidence and calls for 59 action[7,8], the mortality gap persists. Moreover, the proportion of physical conditions 60 appears to be increasing in people with MI, so promoting a healthier lifestyle is necessary 61 and warrants additional investment[9]. 62 Lifestyle behaviors not only impact physical health but are also linked to the onset and 63 persistence of mental disorders. Growing evidence supports the efficacy of lifestyle 64 interventions in improving both physical and mental health[2,10–14]. Furthermore, a comprehensive meta-review investigated how various lifestyle behaviors individually affect 65 66 the onset and treatment of mental disorders[2]. However, it also highlights the predominant 67 focus on the isolated effects of individual lifestyle behaviors. Since lifestyle behaviors do not occur in isolation, it is crucial to gain more understanding of their interrelations. 68 69 Research into lifestyle behaviors has primarily focused on physical activity (PA), which is 70 strongly linked to other lifestyle behaviors[2]. Regular PA has been shown to improve sleep 71 quality[15], while sleep deprivation can reduce motivation for exercise and lower overall 72 activity levels[16]. Poor sleep quality can also lead to lowered mood and reduced impulse 73 control, making it more difficult to maintain healthy behaviors[17]. Additionally, PA also plays 74 a role in cognitive functioning and executive planning, which can help better meal planning 75 and healthier food choices[18]. Conversely, sleep problems can increase dietary intake due 76 to extended wakefulness and disrupted hormonal regulation, increasing cravings for 77 unhealthy foods[19]. Furthermore, lifestyle behaviors such smoking complicate these

78 relationships. While nicotine has a stimulant effect which reduces the quality of sleep[20], 79 smoking cessation may increase appetite, which may lead to weight gain. These examples 80 illustrate the interconnected nature of lifestyle behaviors, influencing each other in ways that 81 can either support or hinder mental and physical health outcomes. It is therefore crucial that 82 we gain understanding into how these behaviors are interrelated, to address multiple lifestyle 83 behaviors simultaneously. 84 The network approach offers a powerful method for exploring these complex 85 relationships[21,22]. A psychological network consists of nodes representing observed 86 variables, connected by edges representing statistical relationships[23]. For example, the 87 Gaussian Graphical Model (GGM) estimates a network of partial correlation coefficients. 88 These coefficients represent the strength of a relation between two variables after controlling 89 for the other variables in the model[24]. Furthermore, by assessing network parameters like 90 node strength, we can gain insight into which nodes are more strongly connected than 91 others. Strongly connected nodes may signal symptoms that could potentially play an 92 important role in stabilizing the network and may be investigated as treatment targets [16]. 93 This study aims to explore the relationships among lifestyle behaviors and health outcomes, 94 and to identify the most central lifestyle behavior or health outcome in this network. In line 95 with the exploratory nature of this study, there were no specific predictions about which 96 behavior or health outcome was most central. Nevertheless, given the associations between 97 lifestyle behaviors and mental and physical health, we hypothesized that these behaviors 98 were interconnected rather than independent. Understanding these interconnections could 99 inform treatment and guide future research to address the challenges people with MI face in 100 improving their health.

101 Methods

Study design and setting

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This study is based on cross-sectional data, collected as part of a larger trial evaluating the

effectiveness and implementation of a lifestyle-focused approach for inpatients with MI (MULTI+)[20]. The overarching trial was conducted at GGz Centraal, a mental healthcare facility in the Netherlands, comprising 45 inpatient wards grouped into three clusters with approximately 800 places of residence. During the trial, all clusters initially delivered care as usual (CAU), and every six months one cluster transitioned to MULTI+ until all clusters had switched. Measurements were collected at the start of the trial, and subsequently at a sixmonth interval (after 6, 12 and 18 months) across all clusters. For the present study, we used data collected prior to each cluster's transition from CAU to MULTI+, thereby providing insights into lifestyle behavior and health outcomes of people with MI receiving CAU.

Study population

People were included if they were aged ≥16 years and had a treatment duration exceeding 10 days within one of the psychiatric wards. This time frame was pragmatically chosen to ensure that patients had sufficient exposure to treatment conditions. People were excluded if they had a limited understanding of the Dutch language or their (mental) health condition hindered informed consent.

Procedure

Data were collected during CAU, which includes pharmacological and psychological treatment, without structured lifestyle interventions. Instead, lifestyle-related activities varied between individuals or teams, depending on specific needs and available resources. Data were collected from routine screening and questionnaires. These questionnaires were administered as semi-structured interviews by trained research assistants (RA), allowing for additional clarification when needed. We collaborated with staff across 45 wards to determine the optimal conditions for conducting the semi-structured interviews, including the best time of day and location. RAs were present for several days, approaching potential participants with support from staff. RAs received training and followed a standardized interview protocol, while weekly consensus meetings were held to ensure data quality. Participants provided verbal informed consent. This procedure was employed to visually communicate the study's

objectives and methodologies, enhancing comprehension for participants. A full description of 131 132 the procedures can be found in den Bleijker et al., (2020)[25]. 133 **Outcomes** Demographic characteristics were obtained from the electronic patient file. Study measures 134 135 and psychometric properties are outlined in Table 1, with a comprehensive description 136 available in den Bleijker et al., (2020)[25]. Since lifestyle behaviors are central to our study, 137 we included multiple nodes to capture their nuances, whereas for other variables, we used 138 composite scores to reduce complexity while ensuring robust estimation. 139 Lifestyle behaviors 140 Physical activity was measured with the Simple Physical Activity Questionnaire (SIMPAQ; 141 [26]), a reliable and valid tool for assessing physical activity in people with severe MI. Sleep 142 problems were measured with the validated Scales for Outcomes in Parkinson's disease 143 Sleep (SCOPA SLEEP; [27]). We categorized smoking behavior according to the 144 categorization of the QRISK3 algorithm [28], in line with the primary outcome measure of the 145 MULTI+ trial. We used the 24-hour recall (24HR) method to measure dietary intake quality, in which foods and beverages consumed over the past 24 hours are assessed. We evaluated 146 147 this according to the National food-based dietary guidelines (FBDG). The "Wheel of Five" 148 (WoF) is part of the FBDG and includes food groups associated with a reduced risk for 149 chronic diseases [29]. Each recalled food item was classified within or outside the WoF and 150 ranked on a 1-3 scale (1=below guideline, 2=meets guideline, 3=exceeds guideline). This 151 (classification) method is not validated, but was reviewed by a dietician and consensus 152 meetings were held to improve consistency. 153 Physical health 154 We used Body Mass Index (BMI), cholesterol ratio and Mean Arterial Pressure (MAP) to 155 assess physical health. Additionally, we incorporated the Physical Quality of Life (QoL) scale 156 from the validated World Health Organization Quality of Life-BREF (WHOQoL-BREF;[30]) to 157 include a subjective perspective to our assessment of physical health.

158	Mental health
159	We used the Global Severity Index (GSI) from the Brief Symptom Inventory (BSI; [31]) to
160	measure symptom severity. The BSI is a validated and shorter questionnaire, which
161	measures symptoms of psychopathology[31]. To measure different domains of quality of life
162	(QoL), the Environmental, Psychological and Social scales of the WHOQoL-BREF were
163	included[30].
164	Medication
165	Medication use was obtained from the pharmacy's electronic system. Prescriptions are
166	converted into Daily Defined Dose (DDD) according to the Anatomical Therapeutic Chemical
167	Classification System (ATC) from the World Health Organization (WHO). The DDD is a
168	standardized unit for statistical purposes and represents the presumed average daily
169	maintenance dosage of a drug when prescribed for its main indication[32]. For this study, we
170	calculated the DDD for ATC codes N05A (antipsychotics) and N06A (antidepressants).
171	[Insert table 1]
172	Statistical analysis
173	Questionnaires were processed according to their manuals. Routine screening data were
174	checked for entry errors, which were removed. Any extreme values that were not due to
175	errors were retained to maintain a representative view of the population.
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177	Network construction
178	We estimated a Gaussian Graphical Model (GGM) incorporating all measures outlined in
179	Table 1 as continuous variables[33]. We used LASSO regularization, because the number of
180	included variables was relatively high compared to the number of observations. We opted for
181	a hyper-tuning parameter of 0, resulting in a more lenient inclusion of edges, as our study
182	aim is exploratory[34]. Since many variables were skewed, we used Spearman's rank-
183	correlation and pairwise complete observations to handle missing data[33].

184	Visualization			
185	We used the Fruchterman-Reingold algorithm for the layout of our network[35]. This			
186	algorithm positions nodes with high strength and/or more connections closer to each other,			
187	and closer to the center of the network. Thickness and saturation of edges are proportional to			
188	the strength of the conditional association. Blue edges indicate a positive conditional			
189	association, while red edges indicate a negative conditional association[36].			
190	Centrality analysis			
191	We calculated strength centrality to quantify how strongly nodes were connected to other			
192	nodes in the network. Node strength is calculated by summing the absolute weighted number			
193	and strength of all edges of a node and comparing it to those of all other nodes in the			
194	network[37].			
195	Network accuracy			
196	Before interpreting the network, we evaluated the accuracy and stability of the estimated			
197	network. We followed the bootstrap procedures as described in Epskamp et al., (2018)[24].			
198	First, we examined the stability of strength centrality using case-dropping bootstrap based on			
199	1000 samples (re-estimating the network with a different number of observations). This			
200	method quantifies the stability of the order of strength centrality with the correlation stability			
201	coefficient (CS-coefficient). A CS-coefficient of 0.7 is considered reliable. Second, we			
202	evaluated the accuracy of the edge weights. We used non-parametric bootstrapping based			
203	on 1000 samples (observations are resampled with replacement creating new datasets).			
204	Third, we performed bootstrapped difference tests between the edge-weights and the			
205	strength indices to test if these differed significantly from each another.			
206	Statistical packages			
207	The analyses have been performed in R Statistical Software[38]. For network estimation we			
208	used the estimateNetwork function in the bootnet R-package version 1.5.3[23]. Furthermore,			
209	methods for accuracy analyses are implemented in this package[24]. We used the qgraph R-			
210	package version 1.9.5 to visualize our network[39].			

Results 211 **Patient characteristics** 212 213 The study included 423 patients, of whom 42% were female and 41% had a diagnosis of 214 schizophrenia or another psychotic disorder. The mean age was 55.5 (SD=17.6, range=19-215 91), and more than half of the participants were hospitalized for more than a year. 216 Demographic characteristics are described in Table 2. Analyses were conducted with and 217 without extreme values. Because the results showed no substantial differences, the results 218 including extreme values are presented. 219 [Insert Table 2] 220 **Network analysis** 221 The network structure in Figure 1 illustrates the conditional associations among lifestyle 222 behaviors, physical health and mental health outcomes. Each node represents a symptom or 223 behavior, while each edge depicts a bidirectional partial correlation between the nodes, 224 considering all other associations in the network. The accompanying strength centrality 225 indices are presented in Figure 2. 226 [Insert Figure 1] [Insert Figure 2] 227 228 Generally, we observe a network structure in which all nodes are connected to at least one 229 other node in the network. The nodes with the highest strength centrality are psychological 230 QoL (15), physical QoL (12), nighttime sleep problems (2) and overall sleep quality (1). 231 sFigure 3 in the supplement provides an overview of the (non)significant differences between 232 strength centrality indices. 233 When investigating strength of the nodes related to lifestyle behavior, nighttime sleep 234 problems (2) was stronger than almost half of the nodes in the network. Overall sleep quality 235 (1) cannot be shown to be significantly different from many other nodes (see sFigure 3). A

strong positive connection existed between overall sleep quality and nighttime sleep problems (1-2). Furthermore, sleep was strongly associated with physical QoL, with associations between both overall sleep quality and physical QoL (1-12) and nighttime sleep problems and physical QoL (2–12). In terms of strength, psychological QoL (15) and physical QoL (12) were statistically stronger than most of the other nodes (see sFigure 3). All QoL nodes (12, 14, 15, 16) are positively associated, indicating that higher QoL in one domain is associated with higher QoL in other domains. Additionally, we observed strong negative associations between psychological QoL and both the daily dose of antidepressants (15–18) and Global Severity Index (15–13). This suggests that psychological QoL is probably lower when people take higher doses of antidepressants or when they experience more severe symptoms (and vice versa). Other strong associations in the network include the negative association between percentage of healthy food intake and cholesterol ratio (5-10) and the positive association between daily doses of antipsychotics and length of hospital stay (17-20). No clear pattern of relationships emerged among other lifestyle behaviors or physical health outcomes. **Network accuracy** Results of the accuracy analyses are available in the supplement. We quantified the stability of node strength with the CS-coefficient, which indicated that node strength stability is good and that 75% of the sample can be dropped to still maintain a correlation of 0.7 with the original strength metrics as computed on the entire sample (S(cor=0.7)=0.75; sFigure 1). Thus, the order of the variables as indexed by strength can be interpreted. sFigure 2 shows that the edges between the strongest nodes (e.g., 1–2, 12–15, 1–12 and 2–12) were present in all of the bootstrapped samples, and differed from approximately half of the other edge weights (sFigure 4). Sensitivity analyses We estimated a post-hoc network excluding antipsychotic medication use (given its impact on lifestyle behavior and health outcomes) and conducted subgroup analyses for individuals

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aged 65 and younger, and those with schizophrenia and other psychotic disorders. Visualizations show that most of the links are similar across networks. Additionally, correlation between edge-weight matrices is high (r=0.81-0.93), indicating that results remain consistent across subgroups. Results are provided in appendix 2 of the supplement. These findings support the robustness of our original findings.

268 Discussion

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This study applied a network approach to explore the complex interrelations among lifestyle behaviors and physical and mental health outcomes in people with MI. Sleep and QoL emerged as the most central nodes, based on strength centrality. Constructing this exploratory network provides valuable insights into the importance of lifestyle behaviors, health outcomes, and their interconnectedness. This complements current evidence in which such relationships were mainly analyzed in isolation. Sleep emerged as the most strongly connected lifestyle behavior, and results indicate that sleep and QoL are related (i.e. people with more sleep problems may have a lower QoL and vice versa). The well-established association between sleep disturbances and reduced QoL is particularly relevant for people with MI, who often experience sleep problems, affecting their physical and mental health[40]. Furthermore, evidence is increasing for the causal role of sleep in both the onset and treatment of various mental disorders[11]. Despite this, sleep is often perceived as a consequence of MI, rather than as a symptom to address. Sleep problems are often treated pharmacologically, which helps with sleep duration but negatively affects sleep quality and hinders daytime activity in the long term due to its sedative nature[41]. Our findings underscore the importance of addressing sleep problems, because improving sleep quality has the potential to impact other health related-outcomes in people with MI, especially QoL[42]. Qol was another central node, particularly the psychological and physical domains. These domains address intrinsic experiences of individuals, unlike the social and environmental

dimensions of QoL. The strength of these nodes emphasizes the importance of internal experiences of well-being. This aligns with research recognizing the value of such patientreported outcomes, as they provide direct insights into individuals' perceptions of their own health and quality of life[43]. Furthermore, the strong association between psychological and physical QoL aligns with the well-documented comorbidity between physical and mental health, yet physical health is often neglected in treatment[4]. While clinical guidelines emphasize monitoring and managing physical health risks of people with MI, adherence in clinical practice remains poor[44]. Our results highlight the importance of perceived psychological and physical health and its potential impact on other health-related outcomes. Contrary to prior research on the relationship between lifestyle behaviors and health outcomes, physical activity, nutrition, and smoking did not emerge as central nodes in our network. One possible explanation lies in methodological factors: the distribution of physical activity was highly skewed, potentially limiting its role in the network; smoking was categorized as a five-level variable, reducing variability; and nutrition was measured using a non-validated method, which may have introduced measurement errors. However, another relevant possibility is that sleep simply plays a more dominant role in this network than other lifestyle behaviors. Sleep is known to affect mood, cognition, and self-regulation, all of which are crucial for maintaining other healthy behaviors[45-47]. This suggests that sleep may be a key factor in improving other lifestyle behaviors, rather than these behaviors independently driving health outcomes. In the context of network analysis, this does not necessarily imply that physical activity, nutrition, or smoking are unimportant, but rather that sleep plays a more central role. Beyond the centrality of sleep and Qol, several other noteworthy associations were observed. A positive association was found between the percentage of healthy food intake and cholesterol ratio, aligning with existing research in the general population[48]. However, research on this relation remains limited in people with MI, and disrupted cholesterol levels can also be influenced by hereditary factors and psychotropic medication[49]. While our

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findings suggest a potential link between healthier dietary intake and cholesterol ratio, this estimate was unstable, and more research is needed to investigate this link. Further, the association between the use of antipsychotics and the duration of admission may be explained by the higher illness severity in people with psychotic disorders, who are more frequently and longer hospitalized compared to other psychiatric populations[50]. However, medication effects are complex, and more in-depth analyses of the underlying mechanisms of medication effects were beyond the scope of this analysis. It would be a valuable direction for future research to further explore these interdependencies, providing a more comprehensive understanding of the role of medication in an interconnected network of health behaviors.

Limitations

Several limitations affect the interpretation of our results. First, when two nodes are strongly connected, they may measure the same underlying construct (topological overlap), with the risk of misinterpretation of the network structure[51]. In our network, this concern arises in the association between psychological QoL and physical QoL, as well as between quality of sleep and nighttime sleepiness, as they originate from the same questionnaire. However, these constructs represent distinct domains within a validated questionnaire. Furthermore, results showed that the association between these domains was stable. Another limitation is missing data. The use of routine screening data helped reduce participant burden but also resulted in missing values due to low screening rates. Additionally, not all participants could complete all questionnaires due to illness severity or cognitive deficits. To account for missing values, we used the pairwise complete observations integrated in the *Bootnet package* to estimate a GGM. Finally skewed variables could have affected the stability of our results.

Clinical implications

Given the central role of sleep, addressing sleep disturbances in treatment may not only improve sleep quality, but also positively impact QoL. This can be done through Cognitive Behavioral Therapy for Insomnia, an effective first line treatment for people with MI that has

demonstrated beneficial effects[52]. Furthermore, the centrality of physical QoL underscores the need for better physical health management, especially given the heath disparities of people with MI. Likewise, the central role of psychological and physical QoL emphasizes their importance in the health status of people with MI. While this study is cross-sectional, it underscores the need to prioritize sleep and QoL in both clinical practice and research.

Conclusion and future research

This study provides a novel perspective on the interplay between lifestyle behaviors and physical and mental health outcomes in people with MI. Our findings highlight the central role of sleep and QoI in this network, suggesting that sleep disturbances are important to address in treatment. Building on these results, future research could focus on testing specific (causal) pathways through methods such as mediation analysis or network intervention analysis. For instance, by exploring whether improving sleep as a key lifestyle behavior could enhance quality of life and activate other health outcomes. These approaches would offer a deeper understanding of the mechanisms at play, which was beyond the scope of the current study. Additionally, our findings show the importance of internal experiences of QoL. Given their interconnected nature, we advocate for a holistic therapeutic approach, taking the reciprocal influence of lifestyle behavior and physical and mental health into account to improve treatment of people with MI.

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367	assisted improvements to human-generated texts for readability and style, and to ensure that
368	the texts are free of errors in grammar, spelling, punctuation and tone). The authors take full
369	accountability for the work presented.
370	Trial registration
371	ClinicalTrials.gov registration. Identifier: NCT04922749. Retrospectively registered 3rd of
372	June 2021.
373	Availability of data and materials
374	Due to the strict regulations and its sensitive nature, supporting data cannot be made openly
375	available.
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379	involvement in the study's design, data collection, analysis, interpretation, or manuscript
380	preparation.
381	Competing Interests
382	None of the authors have any competing interests
383	Supplementary Material
384	For supplementary material accompanying this paper, visit cambridge.org/EPA.
385	Abbreviations

386	MI: Mental illness
387	GGM : Gaussian Graphical Model
388	MULTI+: multidisciplinary lifestyle focused approach in the treatment of inpatients with
389	mental illness
390	SIMPAQ: Simple Physical Activity Questionnaire
391	SCOPA SLEEP: Scales for Outcomes in Parkinson's disease Sleep
392	24HR: 24-hour recall
393	FBDG: the National food-based dietary guidelines
394	WoF: Wheel of Five
395	BMI : Body Mass Index
396	MAP: Mean Arterial Pressure
397	QoL: Quality of Life
398	WHOQoL-BREF: World Health Organization Quality of Life-BREF
399	GSI: Global Severity Index
400	BSI: Brief Symptom Inventory
401	DDD: Daily Defined Dose
402	ATC: Anatomical Therapeutic Chemical Classification System
403	LASSO: Least absolute shrinkage and selection operator
404	bCI: bootstrapped Confidence Intervals
405	CS-coefficient: Correlation Stability coefficient
406	Figure and table captions

107	Table 1. Description of outcome measures. Abbreviations: SIMPAQ Simple Physical Activity
108	Questionnaire; SCOPA SLEEP Scales for Outcomes in Parkinson's disease Sleep; DP
109	Diastolic blood pressure; SP Systolic blood pressure; BSI Brief Symptom Inventory;
110	WHOQoL-BREF World Health Organization Quality of Life; DDD Daily Defined Dose; ATC
111	Anatomical Therapeutic Chemical Classification System. ¹Answering options differ between
112	questions, such as from very poor to very good, or from not at all to extremely.
113	Table 2. Patient characteristics. 1) Item frequency varies across variables due to missing
114	values resulting from low screening rates, and because not all patients could complete all
115	questionnaires due to illness severity or cognitive deficits; 2) Diagnoses in this category are:
116	Personality disorder, n=22; Neurocognitive disorder, n=11; Anxiety disorder, n=7; Trauma and
117	stressor-related disorder, n=7; Somatic symptom disorder, n=4; Other, n=5; Missing, n=5; 3)
118	The Defined Daily Doses (DDDs) of the three most frequently prescribed antipsychotics and
119	antidepressants are noted; 4) Other antipsychotics prescribed, in order of prevalence, are:
120	Haloperidol, n=38; Aripiprazole, n=32; Risperidone, n=28; Zuclopenthixol, n=20; Amisulpride,
121	n=14; Flupentixol, n =12; Pipamperone, n=9; Penfluridol, n=8. Paliperidone, n=5,
122	Chlorpromazine, n=4; Pimozide, n=4; Sulpiride, n=2; 5) Other antidepressants prescribed, in
123	order of prevalence, are: Clomipramine, n=14; Paroxetine, n=14; Venlafaxine, n=12;
124	Mirtazapine, n=11; Tranylcypromine, n=11; Fluoxetine, n=9; Sertraline, n=8; Bupropion, n=8;
125	Fluvoxamine, n=7; Amitriptyline, n=3; Imipramine, n=1; Dusolepin, n=1; Trazodone, n=1.
126	Figure 1. Graphical representation of the estimated network model including lifestyle
127	behaviors, physical health and mental health differentiated by colors. Blue edges indicate a
128	positive conditional association, red edges indicate a negative conditional association.
129	Thickness and saturation of edges is proportional to the strength of the conditional
130	association. Note: higher scores on overall sleep quality means more overall sleep problems.
131	Figure 2. Centrality plot illustrating the strength of the nodes in the network depicted in figure
132	1. Nodes are ordered from the node with the highest strength to the node with the lowest
133	strength. Node strength quantifies how strongly a node is directly connected to other nodes

434	(summing the absolute value of the edges to each node). All values are standardized, highe
435	values indicating more centrality.
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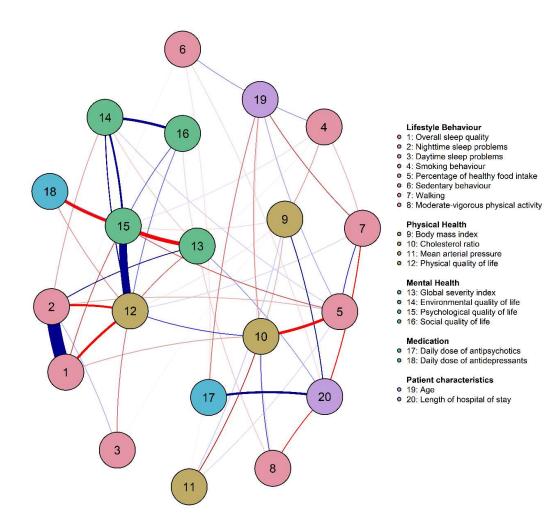
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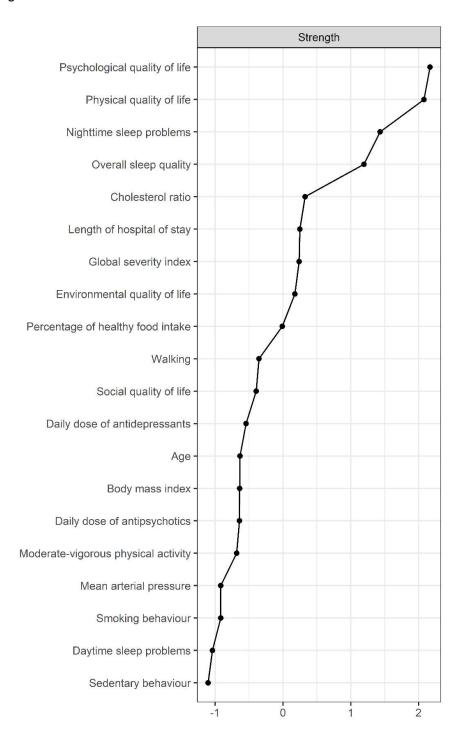
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600 Figure 1



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603 Figure 2



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Table 1 – Description of outcome measures and their psychometric properties				
Domain	Instrument and properties	Measure/domain	Calculation of item	
Lifestyle behaviors	SIMPAQ: Reliability assessments show acceptable to good consistency, with Spearman correlation coefficients ranging from ρ = .63 to ρ = .76. The validity for moderate-to-vigorous physical activity is ρ = .25 across the full sample, aligning with findings from studies in the general population. Due to insufficient evidence supporting the validity of self-reported sedentary behavior, an alternative calculation method is recommended, which we used[1].	Sedentary behavior	Subtraction of the total self-reported time spent in various forms of non-sedentary behavior (time spent in bed, walking, exercising, and engaging in incidental activities) from the total duration of 24 hours (hours/day).	
		Walking	Self-reported time spent walking (hours/week).	
		Moderate to vigorous physical activity	Self-reported time spent exercising (hours/week).	
	SCOPA SLEEP Demonstrated strong reliability for both nighttime sleep problems (α = .88) and daytime sleep problems (α = .91), as well as good construct validity in a Dutch sample of individuals with Parkinson's disease. Scores on all domains showed high correlations with established, validated instruments assessing the same constructs[2].	Overall sleep quality	1 item to evaluate overall quality of sleep, scored on a 7-point ranging from slept very well to slept very badly.	
		Daytime sleep problems	Sum score of 6 items evaluating problems with falling asleep during the day. Items are scored on a 4-point Likert scale ranging from 0 (not at all/never) to three (a lot/often).	
		Nighttime sleep problems	Sum score of 5 items evaluating insomnia. Items are scored on a 4-point Likert scale ranging from 0 (not at all/never) to three (a lot/often).	
	Routine screening Data is routinely collected by healthcare professionals as part of standard care. In line with the primary outcome measure of the overarching trial, we categorized smoking behavior according to the QRISK3 algorithm[3].	Smoking behavior	1 non-smoker 2 ex-smoker 3 light smoker (less than 10) 4 moderate smoker (10 to 19) 5 heavy smoker (20 or over)	
	A retrospective method used to quickly assess an individual's food intake. For this study, a 24-h recall was designed using the five-pass method. This method is commonly used and reduces bias[4]. The method is not validated, but consensus	Percentage of healthy food intake	The percentage of healthy food intake as a proportion of the total food intake. Food intake is evaluated to determine whether it belongs within or outside the food groups outlined in the Wheel of Five. Within each food group, rankings "1", "2" or "3" were assigned to each consumed food item (1=below guideline, 2=meets	

	meetings were held to discuss uncertainties regarding food items, and a dietician reviewed decisions.		guideline, 3=exceeds guideline). Rankings are aggregated and the percentage of healthy food intake is calculated by dividing the ranking assigned to healthy food intake by the total ranking assigned to all types of food intake.
Physical health	Routine screening Data is routinely collected by	Body Mass Index	Weight (kg) divided by the square of height (cm)
	healthcare professionals as part of standard care	Cholesterol ratio	Total cholesterol level (HDL + LDL) divided by HDL cholesterol level
		Mean Arterial Pressure	DP + 1/3(SP – DP)
	WHOQOL-BREF Shows acceptable to good internal consistency (α = .66 to α = .80), and has also been validated in people with schizophrenia, showing strong content and construct validity[5].	Physical QoL	Item scores have various options but always range from one to five, such as very poor to very good, or not at all to extremely, and are converted to domain scores (range from four to 20)[6]. Mean score of 7 items, ranging from 0 to 51
Mental health	Internal consistency ranges from α = .71 to α = .85, and the BSI is considered a reliable measure over time [7]. In a Dutch sample, it showed acceptable validity, sufficient test-retest reliability, and strong internal consistency, with α > .80 on eight of the nine scales[8].	Global Severity Index	The BSI consists of 53 items that reflect 9 symptom domains; each item is rated on a 5-point scale from 0 (not at all) to 4 (extremely). The GSI combines information about the number of symptoms and the intensity of distress. It is calculated by summing the 9 symptom dimensions, divided by the total number of items to which the individual responded[7].
	WHOQOL-BREF See psychometric properties in	Environmental QoL	Mean score of 8 items ¹
		Psychological QoL	Mean score of 6 items ¹
NAI: C	the physical health domain	Social QoL	Mean score of 3 items ¹
Medication	Information on medication use is obtained from the pharmacy's electronic system.	Dose of antipeychotics Dose of antidepressants	DDD of ATC classification N05A DDD of ATC classification N06A

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Table 2 – Patient characteristics	1		
	N ¹ 423		Min – Max
Sex, n (%) female		179 (42.3)	
Age in years, <i>m (sd)</i>	423	55.5 (17.6)	19 – 91
Diagnosis, n (%)	418		
Schizophrenia and other psychotic disorders		175 (41.4)	
Substance abuse		70 (16.5)	
Bipolar disorder		49 (11.6)	
Depressive disorder		38 (9)	
Neurodevelopmental disorder		30 (7.1)	
Other diagnoses ²		61 (14.4)	
Days of hospitalization, m (sd)	423	605 (602)	12 - 2370
• >5 years, <i>n</i> (%)		28 (6.6)	
• 1-5 years, n (%)		192 (45.4)	
• <1 year, n (%)		203 (48)	
o <1 month, <i>n (%)</i>		20 (4.7)	
Lifestyle behavior			
Sleep m (sd)			
Overall sleep quality (0-6)	412	2.3 (1.8)	0 - 6
Daytime sleep problems (0-18)	400	1.7 (2.7)	0 - 18
Nighttime sleep problems (0-15)	408	4.1 (4.3)	0 - 15
Smoking behavior: yes <i>n (%)</i>	262	162 (59.6)	
Non-smoker		58 (13.7)	
Ex-smoker		50 (11.8)	
Light smoker (< 10 cigarettes)		40 (9.5)	
Moderate smoker (10-19 cigarettes)		57 (13.5)	
Heavy smoker (>20 cigarettes)		57 (13.5)	
Percentage healthy food intake <i>m (sd)</i>	146	47.7 (15.5)	7 – 90
Physical Activity <i>m (sd)</i>			
Sedentary behavior (hours/day)	366	13.4 (2.1)	6.5 – 19.7
Walking (min/week)	389	142.4 (157.4)	0 – 840
Moderate-to-vigorous physical activity	385	49.3 (71.8)	0 - 323
(min/week), <i>m (sd)</i>			

Physical health			
Body Mass Index (BMI) m (sd)	304	26.8 (5.8)	11.5 – 44.9
Cholesterol ratio (mmol/l) m (sd)	162	4.3 (1.7)	1.4 – 10.2
Mean arterial pressure (mmHg), m (sd)	372	97.5 (10.5)	70 – 123.3
Physical Quality of Life (7-35)	299	14.1 (3.2)	5.1 – 20
Mental health			
Global Severity Index (0-4)	276	2 (0.6)	1 – 3.6
Environmental Quality of Life (8-40)	300	14.4 (2.7)	5.5 – 19.5
Psychological Quality of Life(6-30)	298	13 (3.5)	4.7 – 19.3
Social Quality of Life (3-15)	297	13.6 (3.7)	4 – 20
Medication ³	423		
 Antipsychotic medication use: yes n (%) 		295 (69.7)	
 Antipsychotic medication (DDD) 	295	.92 (1.2)	0 – 7.8
Olanzapine	95	1.25 (0.99)	0.25 – 6
Clozapine	68	0.75 (0.65)	0.04 – 3
■ Quetiapine ⁴	66	0.34 (0.4)	0.03 – 2.25
 Antidepressant medication use: yes n (%) 		142 (33.6)	
 Antidepressant medication (DDD) 		.51 (1.2)	0 – 12
■ Citalopram	23	0.05 (0.28)	0 – 2
 Nortriptyline 	20	0.03 (0.17)	0 – 1.33
■ Escitalopram ⁵	17	0.05 (0.30)	0 – 3

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