Lifestyle programs as prevention of weight gain in patients with a first-episode psychosis: a review.

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INTRODUCTION

Severe mental illness (SMI) like psychotic disorders, bipolar disorders, and severe depression have a high impact on public health worldwide. Patients affected by SMI are confronted by an average life expectancy diminished by 9 to 14.5 years when compared to the general population. (1–3) This discrepancy can partially be attributed to an elevated risk of suicides an accidents among this group: 17.5% of deaths among people with mental disorders are due to unnatural causes. However, the primary reason for this reduced life expectancy is due to a higher prevalence of chronic diseases including vascular diseases, diabetes, respiratory illness and obesity. (4) Cardiovascular disease contributes to 70% of causes of mortality among patients diagnosed with SMI. (5)

Patients with SMI are confronted not only by higher mortality, but also by a higher morbidity due to chronic diseases. Comorbidities start at an earlier age and are more often combined compared to the general population. (6)-(7) Worldwide, the cardiovascular disease (CVD) prevalence in patients with SMI is 9.9% with an OR of 1.53 (8). The prevalence of type 2 diabetes mellitus in people with SMI is 11.3%, whereas in the general population, it is 2.9%. (9) Also, 50-60% of people with SMI have abdominal obesity. This is 1.43 times higher than in the healthy population. (10) The relative risk of metabolic syndrome (the combination of abdominal obesity, high blood pressure, low HDL cholesterol, elevated triglycerides and hyperglycemia) is 1.58 in people with SMI. (10)

Some contributing factors are found worldwide: unhealthy lifestyle factors, known side effects of psychiatric medications, limited access to healthcare and disparities in healthcare delivery. (11) As unhealthy lifestyle factors we see that for example people in the UK with SMI are more likely to smoke (46% vs. 27.7%), to abuse alcohol (13.5% vs. 3.7%) and to abuse drugs (12.8% vs. 2.1%) which all contribute to cardiovascular risk. (7)

Antipsychotics, antidepressants, and mood stabilizers are associated with elevated risks of several health conditions. These medications have been linked to increased risks of obesity, dyslipidemia, diabetes mellitus, thyroid disorders, and cardiovascular diseases (12). For example, antipsychotic medications have been shown to lead to significant weight gain. In the short term (≤ 12 weeks), AP use resulted in an average weight gain of 3.22 kilograms and an increase of 1.4 points in BMI compared to a placebo. In the long term (> 12 weeks), the weight gain had even an average of 5.30 kilograms and an increase of 1.86 points in BMI. (13)

Individuals with mental disorders experience significant healthcare disparities worldwide, particularly in the diagnosis and treatment of common conditions like arterial hypertension or diabetes. Barriers for seeking help for physical problems include waiting room anxiety, lower motivation, lower socioeconomic status and a lack of insurance. However, there is also a stigma among medical caregivers towards individuals with mental disorders, often resulting in patients' complaints not being taken seriously and insufficient explanations provided when they do seek healthcare (14). For example, registration rates for blood pressure are lower in populations with co-existing mental disorders, and when they have the diagnosis of hypertension, they receive medication treatment less frequently. (15)

An important part of prevention and treatment of chronic conditions like arterial hypertension, diabetes and obesity in the general population are healthy lifestyle interventions. Research into the positive effects of lifestyle interventions for patients with mental disorders remains relatively scarce, with many existing studies lacking information about cost-effectiveness (16). However, interests in this

field are increasing since the United Nations General Assembly adopted the Convention on the Rights of persons with Disabilities in 2006, defining the protection of people with disabilities worldwide, also specifying explicitly people with SMI. (17) In 2019, the Lancet Psychiatry Commission published a manifest to promote further research, but also to remind national health institutions to give greater consideration to this vulnerable population. (11)

The findings about barriers for seeking help suggest that patients with SMI may benefit from a more assertive approach, such as a guided lifestyle program or an early implementation of medication like metformin (or in the future, GLP-1-analogues). Our current research focuses on various interventions, including dietary changes and tailored exercise programs in patients witch a first-time psychosis who are thus for the first time exposed to antipsychotic medications (antipsychotic-naïve patients). Evaluation will primarily revolve around easily measurable primary endpoints like weight and waist circumference. The aim of this study was to search the literature for effective lifestyle programs for people with first-time psychosis to avoid weight gain or even lose weight.

METHOD

Design

This is a systematic literature review on the current evidence on lifestyle programs for people with first-time psychosis. We used the PRISMA 2020 checklist as a guidance throughout the process and for reporting the data.

Search strategy

For an oversight, see figure 1. We conducted a search in the leading medical databases Medline and EMBASE library targeting papers published in the last ten years. For an effective search strategy, we developed a search string using MeSH (Medical Subject Headings) terms and synonyms related to "psychosis" AND "lifestyle interventions" (see Annex 1). In our first attempts, we also included the MeSH term "Weight", but this approach generated too few results.

Eligibility criteria

The explicit inclusion and exclusion criteria for the review are reported here. We included studies reported in Dutch or English, as the researchers speak Dutch as native language. We included studies published in the last ten years targeting all individuals with a first-time episode of psychosis, as we would have liked to see the effects on cardiometabolic risk of an early intervention in health behaviour at the start of antipsychotic treatment. We included all types of quantitative and qualitative studies concerning effects of lifestyle interventions like physical therapy and diet modification on the parameters that are relevant for cardiometabolic risk (e.g. weight, waist circumference, amount of physical activity). We excluded studies based on solely telephone or online interventions. We also excluded studies based on exercise or diet intervention solely as a treatment of the psychological disease itself and not as a cardiovascular prevention method.

Study selection

We used Zotero as the primary reference manager. First, we deleted all duplicate references. All titles and abstracts were screened to identify the potentially relevant papers. This was followed by a full-text screening for further selection refinement. When the relevance is unclear, a second researcher was consulted to discuss and decide upon final inclusion or exclusion in the review. After the final

selection, two study papers published the same data in another format. One of these papers was excluded as well.

Data extraction and synthesis

We extracted the following data from the included articles: the authors, country and year of publication, the design, the lifestyle intervention used, the study design and setting, the inclusion criteria, the sample, and the results. We marked where significant effects were reported.

Quality appraisal

We used the CASP quality appraisal tools for the different kinds of studies included. For every study, we filled in an appropriate questionnaire on paper according to study type published by CASP. Afterwards, we summarized these annotations in the result section below.

RESULTS

Study selection

After a thorough selection as described in the Methods section, we found 9 articles in total that were published in the last ten years and met our selection criteria.

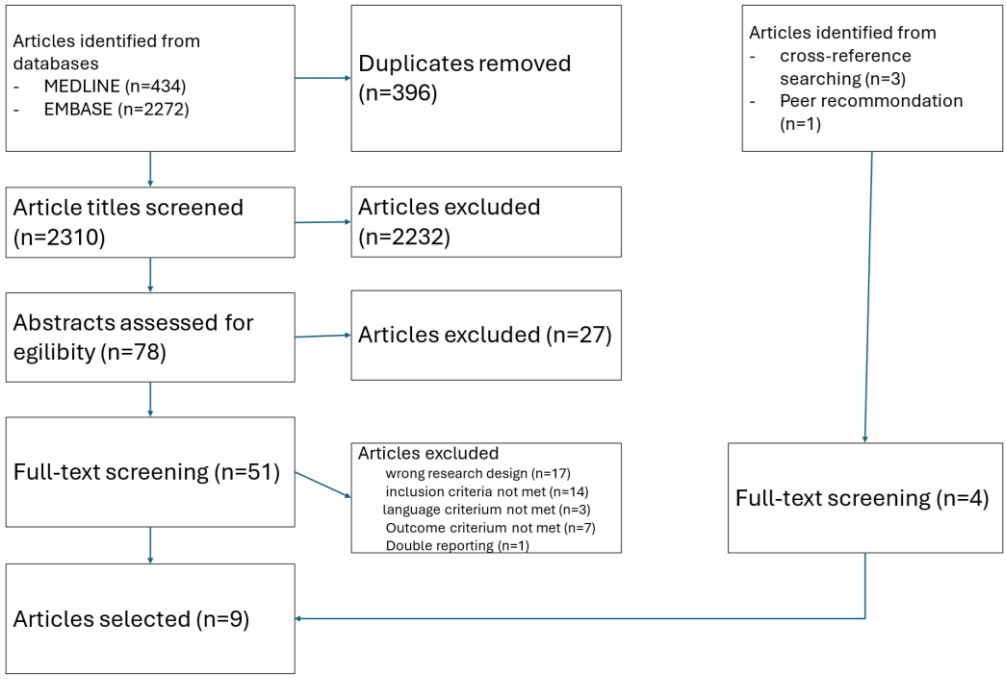

Figure 1: search strategy chart

Data extraction

For a summarizing table of the extracted data, see Annex 2.

Quality appraisal

Designs

After a thorough selection of studies, there is only one blinded randomized controlled trial involved (n=1). Other trials included are non-randomized controlled intervention trials (n=2), non-randomized one-arm intervention trials (n=4) and two-arm intervention trials (n=1). This means that only 3 studies could compare with a control group. All publications are reported in the English language.

Population

The heterogeneity between the population involved is a first issue, with different studies using different definitions of first-time episode of psychosis (e.g. time since onset) and the duration of antipsychotic medication intake. Some studies only involved patients below 35 years.One study only involved males and no females. All the studies excluded patients with chronic comorbidities like diabetes, cardiovascular disease or autoimmune disorders.

In most studies, the number of participants was rather low, mostly because of the costs of the interventions and the difficulties with engaging psychiatric patients. Dropout rates where relatively high, with patients retracting their consent or not showing up at the sessions and thus leading to *survival bias*. This is in line with other studies conducted with psychiatric patients. One study did not account for the drop-outs and performed no intention-to-treat analysis.(18)

Selection bias is certainly an issue in all the studies. Patients were often recruited through posters on the campus, which could lead to selection bias as the recruited patients probably are already more motivated to undergo lifestyle interventions and engage in physical activities. Most studies also included patients of only one campus/center, so there is a higher change that patients all live in the same neighbourhoods or receive the same psychological treatment from the same caregivers. Control groups where often recruited at other campuses, leading to confounding by cluster. However, this approach is logical, since the interventions often required training of the caregivers involved and required changes of the logistics on campus.

Interventions

In two studies, patient could choose to not let themselves be measured at the end of the period, probably leading to another bias where only the more proud patients weighted themselves. Hawthorne effect, where people tend to make more efforts when they know they are being measured, is probably an issue in all of the studies conducted.

Data Results

Patient characteristics

All studies enrolled outpatients following a mental health care program. All patients are diagnosed with a first time-psychosis, mostly within broader psychotic disorders such as schizophrenia, schizoaffective disorders, bipolar disorders or severe depression with psychotic features. Four studies only recruited patients below the age of 35 years. Two studies recruited participants within one to twelve months post-diagnosis (19,20), while four other studies recruited participants up to two to five years after diagnosis. (21–26) In one study, time of diagnosis was unclear. (18)

Intervention characteristics

Four of the studies implemented solely an exercise plan, one study implemented an individualized dietary plan, three studies implemented a combination of diet and exercise and one study organized solely learning and planning sessions to empower patients.

Duration of the exercise sessions varied between 10-12 weeks. All of the studies used the recommendations for physical activity of the world Health Organisation (WHO) as a basis for building a program. Some studies focused more on cardiovascular exercise, while others focused on both cardiovascular exercise and weight training. The SHAPE trial even included a variety of activities, with apart from fitness training also Thai Chi, yoga, Pilates and small team games like badminton to maximize motivation in different kinds of settings.

Dietary interventions varied between 12-26 weeks. All of the studies implementing a dietary plan focused on more than calory restriction alone. Education was also focused on food quality, shopping lists and cooking techniques. The Mediterranean Diet study provided a standard weekly diet plan adjusted to the sex of the participants, while the three KBIM studies offered a more individualized plan overviewed by dieticians.

Measuring setpoints varied between 12-26 weeks. The duration of follow-up was less than 6 months in most studies. Only three studies reported effects on the longer term of one year up to two years.

Loss to follow-up of more than 20% was present in six studies. Reasons given for dropping out varied widely (e.g. lack of motivation, re-admission to inpatient setting, too unwell or tired, not wanting weight registration…), but physical adverse effects of the given intervention was rarely the case.

Weight and waist circumference outcomes

Almost all the studies reported limited or non-significant change in body weight or BMI after the conducted lifestyle intervention. Only three studies, including the initial Keeping the Body in Mind (KBM) and the STEPWISE trial, compared with a control group receiving no lifestyle intervention treatment. The initial KBM study could compare the lack of significant weight gain with a control group who did have a significant weight gain, whereas in the STEPWISE trial there was no significant difference between the intervention group and the control group. (19,21) In the 2016 KBM study, patients were recruiter earlier after disease onset (< 1 month).

Waist circumference did significantly reduce in four out of five studies where waist circumference was measured. However, in one of those three studies waist circumference did not differ anymore from baseline several months after the completion of the intervention.

Costs

All studies took actions to maximize participation, such as free gym membership cards or reimbursing transport. All supervised and non-supervised sessions were conducted for free. However, only two studies reported the costs incurred for their intervention. The SHAPE trial estimated costs at £260-£400 per person per annum. The STEPWISE trial estimated societal costs for participants at £11,332 whereas for the control group, the estimated costs were £10,305.

DISCUSSION

Summary of results

Overall, the interventions with supervised exercise or dietary consultations showed limited or non-significant changes in body weight, with few studies comparing against control groups receiving no intervention. There was no study that could show weight loss. If we would compare with previous studies, we would have expected an average weight gain of 3.22 kilograms after twelve weeks of AP use in a control group and 5.30 kg on the longer term. (13) Interestingly, earlier intervention initiation (< 1 month post-diagnosis) seemed to yield better weight-related outcomes, but there was only one study focused on this group. Waist circumference reduction was observed in several studies, suggesting potential benefits for central adiposity management, albeit sustainability varied among studies. On the other hand, a non-supervised intervention with solely information and planning sessions led to no difference in weight gain between the intervention and control group.

Few studies reported about the costs of the interventions. However, there is a heterogeneity between studies in terms of participation efforts made. In all of the studies, caregivers underwent extra training. Most studies made caregivers call participants during the intervention to maximise engagement. One study even provided in taxies to make sure that participants could attend the group exercise sessions, highlighting the difficulties to motivate the vulnerable group of SMI patients.

Strengts and limitations

In most studies, intervention groups were rather small, making the comparison of subgroups (e.g. age, gender, type of AP) difficult. Statistical analysis was therefore impossible to conduct in our systematic review.

Intervention groups were often recruited in the same mental health centres in the same neighbourhoods with the same caregivers and facilities, having had exact the same training, making it difficult to compare the results of our review with the general population.

Duration of intervention was relatively short. In the general population, we would also expect only a weight loss of 1-2 kg after 10-12 weeks of exercise alone. (27)

Loss to follow-up was significant in most studies, indicating challenges in maintaining patient engagement despite the researchers effort. Reasons for dropout were diverse, with physical adverse effects of interventions itself being rare. Lack of motivation or worsening of the SMI were the most given reasons for drop-out. It is possible that only the most motivated and sportive patients with SMI keep up with the programs. Another possibility is that the patients with the least side-effects or lesser burden of disease could persevere, raising the question that this group might have had less weight gain anyway.

Implications

Data is suggesting that an intense program with supervised sport sessions, but also individual diet consultations, can lead to avoiding weight gain in the first few years of AP use in patients with SMI. The role of group sessions (peers) seems important in this population. Solely educating people with SMI but not offering supervised sessions or group sessions with peers does not seem to lead to the desired results. The KBIM trials, implementing both diet and exercise seemed to have the most durable results on maintaining weight or even loss of weight.

Early intervention seems to have the best results, despite the limited research in early intervention. This seems logical, as weight loss seems to be very difficult regarding these data and the biggest AP-related weight gain is expected in the first three months. (13) When diagnosing someone with SMI and when prescribing antipsychotics, it should be an automatism to propose a healthy lifestyle program shortly after the reduction of psychotic symptoms.

The effort to keep patients motivated and engaged during the process seems to be even more difficult in people with SMI than in the general population. Even when offered a very broad range of activities and possibilities, like in the SHAPE trial, people with SMI seem to find it hard to find autonomous motivation to keep exercising. This has implications for the costs that must be made directly (e.g. providing sessions for free, involve peers, providing transportation) as indirectly (training caregivers not only in educating people with SMI in exercise and diet, but also to keep them motivated by positive verbal persuasion, feedback etc). Despite this, we belief that prevention is not only more effective but also more cost-effective than therapy for CVD, just like in the general population. And even if weight gain can not be totally avoided, implementation of exercise and a healthy diet in everyday life is already a protecting factor for cardiovascular and other noncommunicable diseases. (28)

So when giving specific advice to health centres wanting to implement a healthy lifestyle program, we would advice to train caregivers like dieticians and physiotherapists in positive communication with people with SMI. A program should focus on both exercise and healthy eating with the WHO recommendations as target. Implementation of this program needs to be early after disease onset to avoid the first and biggest weight gain (13), as is seems to be harder to lose weight than to avoid weight gain. Sufficient resources should be allocated, so that supervised sessions and group sessions for both exercise and healthy eating can be offered.

Further research

Since randomized controlled trials (RCTs) are considered the golden standard for clinical research, it's essential to have more RCTs with larger sample sizes to strengthen the evidence. Longer follow-up periods are needed to assess the long-term effects of interventions accurately. Additionally, efforts should be made to minimize selection bias. Strategies to improve participant engagement and retention should be implemented and validated to avoid high dropout rates.

THANK WORD

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ANNEX

Annex 1: search string

Psychosis	"psychotic disorders"[MeSH Terms] OR "psychotic"[All Fields] OR "psychotic disorders"[All Fields] OR "psychosis"[All Fields] OR “psychotic episode”[tiab] OR “psychotic state”[tiab] OR “psychotic illness” [tiab] OR “psychotic symptoms” [tiab] OR “psychotic disturbance” [tiab] OR “psychotic behavior” [tiab] OR “psychotic reaction” [tiab] OR “schizophrenic episode” [tiab] OR “acute schizophrenia” [tiab] OR “first-time psychosis” [tiab] OR “acute exacerbation of schizophrenia”[tiab]
Lifestyle interventions	“lifestyle risk reduction”[MeSH] OR “Health Behaviour”[MeSH] OR “Diet Therapy”[MeSH] OR “Exercise therapy”[MeSH] OR “Behavioral modification”[tiab] OR “lifestyle modification”[tiab] OR “Healthy Lifestyle Program”[tiab] OR “Behavioral Therapy”[tiab] OR “nutritional therapy” [tiab] OR “Dietary Intervention”[tiab] OR “Dietary counselling”[tiab] OR “nutrition counselling”[tiab] OR “Physical Therapy”[tiab] OR “Physical exercise program” [tiab] OR “Movement Therapy” [tiab] OR “Kinetic therapy”[tiab]

Annex 2: overview of studies

Table 1: Study Charasteristics

Ref.	Country	eerste auteur	design	population	n	Intervention	outcome measurement	main result
Keeping the body in mind	Australia	Curtis 2016	non-randomized controlled intervention trial	outpatients with first-time psychosis within the first month since commencement of antipsychotic medication	26 (16 completed)	12-week intervention with motivational interviewing, weekly dietetic consultations and a personalized excercise program	weight, waist circumference after 12 weeks	intervention group: mean weight gain of 1.8 kg (95% CI -0.3, 2.5) control group: mean weight gain of 7.8 kg (95% CI 4.8, 10.7)
Keeping the body in mind	Australia	Curtis 2018	non-randomized one-arm intervention trial	outpatients with first-time psychosis within the first month since commencement of antipsychotic medication	12	12-week exercise intervention of previous study followed by a 2-year step-down program	weight, waist circumference after 2 years	non-significant weight gain of 1.3 kg (95 CI: -4.0 to 6.6), p=0.6. Non-significant waist circumference increase by 0.1 (−4.9 to 5.1) cm (p=0.9)
Keeping the body in mind	Australia	Curtis 2024	retrospective study	youth agd 15-27 years with first-episode psychosis within the first two years since commencement of antipsychotic medication	182 (134 completed)	individualized training and dietary program supervised by a KBIM team (nurse consultant, dietician, physiologist, peer worker)	Weight, waist circumference after 12 weeks	mean weight gain of 1.5 kg (p=0.002), no significant increase in waist circumference (p=0.23)
IBEEP	UK	Firth 2018	non-randomized controlled intervention trial	Outpatients aged 14-35 with first-time psychosis within the first 5 years of diagnosis using an Early Interventin in pyschosis (EIP) service	31 (25 completed)	10-week program of ≥90 min of moderate-to-vigorous activity each week	BMI, waist circumference after 10 weeks	BMI unchanged (-0.34, p=0.265). Waist circumference decreased by 2 cm (p=0.008)
IBEEP 2	UK	Firth 2016	non-randomized one-arm intervention trial	outpatients aged 14-35 with first-time psychosis within the first 5 years of diagnosis using an Early Intervention Psychosis (EIP) service	20 (17 completed)	10-week program of ≥90 min of moderate-to-vigorous activity each week with afterwards verbal encouragement to continue exercising	waist circumference after 6 months	Waist circumference decreased at 10 weeks (-2.4cm, P =0.008), but at 6 months no difference from baseline

Ref.	Country	eerste auteur	design	population	n	Intervention	outcome measurement	main result
SHAPE	UK	Smith 2020	non-randomized one-arm intervention trial	Outpatients with first-time psyschosis within the first three years after onset	113 (26 completed)	combined exercise and health behaviour intervention over a 12-week period in a weekly supervised group setting	weight, waist circumference, health risk behaviours after 12 months	No significant changes in body weight
	Greece	Ntalkitsi 2022	two-arm intervention trial	Outpatients with a first-time psychosis taking an antipsychotic associated with a higher weight gain risk (AP2) compared with patients taking an antipsychotic with a lower weight gain risk (AP1)	21	implementation of the Mediterranean diet trough a diet plan	weight, cholesterol, eating habits after 6 months	No significant changes in body weight in both groups, however significant improvement in eating habits in both groups
STEPWISE	UK	Holt 2018	randomised controlled trial	outpatient adults with a first-episode psychosis within the first three years afer onset prescribed an antipsychotic for more than one month	412 (241 completed)	four intensive 2.5h group learning and planning sessions followed by 2-weekly telephone contacts and 3 booster group sessions	weight, waist circumference after 12 months	no significant weight loss or gain between the intervention and control group
	Canada	Abdel-Baki 2013	non-randomized one-arm intervention trial	overweight outpatient males of 18-35 years within a first-episode psychosis center and a sedentary lifestyle with stable symptoms	25 (16 completed)	30-minte sessions of aerobic interval training (how many a week?)	weight, waist circumference after 14 weeks	significant waist circumference reduction of 4.3 cm, non-significant weight loss

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