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Cost-Effectiveness of a Multidisciplinary Lifestyle-Enhancing Treatment for Inpatients With Severe Mental Illness: The MULTI Study V

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Economic evaluations of lifestyle interventions for people with mental illness are needed to inform policymakers and managers about implementing such interventions and corresponding reforms in routine mental healthcare. We aimed to evaluate changes in healthcare costs 18 months after the implementation of a multidisciplinary lifestyle-enhancing treatment for inpatients with severe mental illness (MULTI) versus treatment as usual (TAU). In a cohort study (n = 114; 65 MULTI, 49 TAU), we retrospectively retrieved cost data in Euros on all patient sessions, ward stay, medication use, and hospital referrals in the quarter year at the start of MULTI (Q1 2014) and after its evaluation (Q3 2015). We used linear regression analyses correcting for baseline values and differences between groups, calculated deterministic incremental cost-effectiveness ratios for previously shown changes in physical activity, metabolic health, psychosocial functioning, and additionally quality of life, and performed probabilistic sensitivity analyses including cost-effectiveness planes. Adjusted regression showed reduced total costs per patient per quarter year in favor of MULTI (B = –736.30, 95%CI: –2145.2 to 672.6). Corresponding probabilistic sensitivity analyses accounting for uncertainty surrounding the parameters showed statistically non-significant cost savings against health improvements for all health-related outcomes in MULTI compared to TAU. It is concluded that MULTI did not increase healthcare costs while improving health outcomes. This indicates that starting lifestyle interventions does not need to be hampered by costs. Potential societal and economic value may justify investment to support implementation and maintenance. Further research is needed to study this hypothesis.

Key words: schizophrenia/physical activity/diet/economic evaluation/quality-adjusted life years/implementation

Introduction

Lifestyle-related factors (e.g., a sedentary lifestyle, physical inactivity, smoking, and an unhealthy diet) play a major role in the poor physical health of people with severe mental illness (SMI) and appear to have a significant impact on their substantially shortened life expectancy compared to the general population.[1–4] Emerging evidence shows that interventions addressing lifestyle-related factors can improve cardiometabolic health, psychiatric symptoms, global and cognitive functioning, decrease the number of people smoking, and increase the quality of life.[2,5–12] However, the evidence for the long-term sustainability of lifestyle interventions for people with SMI is still limited[2,7,9,12,13] and there seems to be a gap between the increase in evidence and policies on the one hand and little change in routine care on the other.[14–18] To improve the translation of evidence into practice, there is a need for more studies evaluating both the long-term effectiveness and sustainable implementation of such interventions in real-world settings.[5,9,19] A part of evaluating the implementation is the evaluation of costs, as this can play a major role in the extent to which a new intervention will be sustainably implemented.[20] Therefore, economic evaluations of lifestyle interventions are essential in building an evidence base that is applicable in routine health care.[5] Nevertheless, there is a lack of cost analyses of lifestyle interventions in mental healthcare.[2] For example, two recent meta-reviews on physical activity interventions found no cost data in the included reviews and stressed the need for economic evaluations for the translation of evidence into practice.[5,9]

In a psychiatric hospital in the Netherlands, a multidisciplinary lifestyle-enhancing treatment for inpatients with SMI (MULTI) was implemented at three wards by a

team of psychiatrists, nurses, activity coordinators, team leaders, and a dietitian. The purpose of MULTI was to achieve overall lifestyle change, focusing on decreasing sedentary behavior, increasing physical activity, and improving dietary habits in the context of daily routine care. A pragmatic evaluation of MULTI after 18 months showed significant improvements in physical activity, cardiometabolic health and psychosocial functioning, and a decrease in psychotropic medication use, compared to treatment as usual (TAU).[21–23] Although an evaluation of implementation determinants showed that more organizational support is recommended to further improve and maintain MULTI,[24] the results are promising as MULTI was performed in the context of routine inpatient healthcare without additional resources.

This current study aims to evaluate changes in treatment costs after 18 months of MULTI, compared to TAU. Complementing previous findings, the results will enable us to better interpret the value and applicability of such an integrated approach, inform policies, and estimate whether suggested investments for maintenance are justified.

Methods

Study Design and Population

This cost analysis complements the MULTI study, a cohort study evaluating a multidisciplinary lifestyle-enhancing treatment for inpatients with SMI. MULTI was previously evaluated 18 months after its implementation at three wards in February 2014 as described elsewhere.[21–23] The three months leading up to the implementation were used to gather baseline data (Q1 2014). Data on the same parameters were collected for three months after the evaluation of MULTI (Q3 2015) to determine changes in costs of MULTI compared to TAU. Because of the observational nature of this study, whereby MULTI was already implemented pragmatically in three wards before the start of this study, no randomization took place. Therefore, we corrected for baseline differences between groups as potential confounders. The MULTI study was approved by the Medical Ethical Committee of the Isala Academy (case 14.0678). All subjects gave written informed consent under the Declaration of Helsinki.

Study Population

The cohort consisted of patients with SMI who had been hospitalized for at least one year at a psychiatric hospital of GGz Centraal (The Netherlands). Originally, patients were included in the MULTI study if they had not received any other intervention related to lifestyle within 18 months since the start of MULTI and if baseline accelerometer data were available. Patients were excluded for follow-up measurements after 18 months due to being either discharged or deceased and dropped out for further analyses if there was a lack of valid data or if they refused repeated accelerometer measurement.[21–23] Eventually, health-related outcomes were evaluated for 114 patients (65 MULTI and 49 TAU), who were included in the current cost analysis.

MULTI

The purpose of MULTI was a holistic lifestyle change with a focus on decreasing sedentary behavior, increasing physical activity, and improving dietary habits among long-term inpatients with SMI. The treatment method was based on improving the daily structure, by starting each day by getting up on time, having three joint meals per day, and participating in an active day program. The latter consisted of sports-related activities (e.g., walking, running, yoga, biking, indoor team sports), work-related activities (e.g., gardening and working in services within the hospital), psychoeducation (e.g., about side effects of medication, dietary habits), and daily living skills training (e.g., shopping, cooking). Existing activities and policies were critically reviewed and adjusted if necessary (e.g., turning the coffee meeting into a walking group, limiting the use of personal transport by patients for trips within walking distance around the hospital area). Based on heterogeneity in patients' illness severity, capabilities, and interests, the content and intensity of the day-to-day program were tailored to the particular ward and individual patients to establish sustainable change. Therefore, the actual frequency, intensity, kind of activities, and format (e.g., group or alone) could vary between patients and wards. However, it was intended that all patients were doing some of the activities in the morning and afternoon, to prevent prolonged periods lying in bed or sitting at the ward. Also, the participation of nurses in the day-to-day program was a core element.

MULTI was based on a "change from within" principle, meaning that it was developed by current staff as a different way of working and treating people, using the same staffing and resources within routine clinical care. It was supervised and disseminated per ward by the head practitioner (a psychiatrist) as an innovative treatment method aiming to improve the health status of his patients. Multidisciplinary work sessions per ward led to detailed plans to change the day-to-day programs which were shared by and between the different teams and discussed, thus leading to maximum participation and engagement needed to achieve culture change. Staff received support from the psychiatrists (psychoeducation), activity coordinators, and the dietitian. Adherence to and compliance with the treatment was discussed in the weekly multidisciplinary consultation. If a patient could not sufficiently participate in the day-to-day program (e.g., had problems getting out of bed or had low attendance during the selected activities), it was agreed to provide extra support, using motivational counseling by

their mentor (one of the nurses) or psychiatrist and by consulting an activity coordinator or dietitian if needed.

Patients who received TAU continued their treatment at their wards led by their own (non-participating) head practitioner, which mainly concerned pharmacological treatment and a less structured day program that did not include any supported lifestyle interventions or adjustments.

Cost Data

Our analysis was performed from a healthcare perspective and all costs are in 2018 Euros. Electronic medical records and meeting schedules (e.g., for daily activities) were used to identify procedures and sessions attended by the patients for both timeframes, Q1 2014 and Q3 2015, including referrals to external healthcare providers. Data on changes in medication use were obtained using raw data of a previous study evaluating these outcomes.[23]

For each session, the number of participating patients and healthcare professionals were known. The duration and time spend per healthcare professional were also available for analysis. If the digital registration did not show the specific profession of an individual healthcare professional, this was further checked (e.g., for "daily activities", which may involve different professions). Subsequently, national collective labor agreement pay tables for mental healthcare (the Dutch Association of Mental Health and Addiction Care) were used to determine the costs of the sessions, using the costing guideline of the Dutch Healthcare Institute.[25,26] Costs of admission at the inpatient units were calculated based on the care severity profile (*zorgzwaarteprofiel)* and tariffs set by the Dutch Healthcare Authority.[27] For patients who were discharged from inpatient healthcare to regional institutions for sheltered housing, costs for treatment were based on Dutch Healthcare Institute costing guideline.[26] Medication costs were determined based on prescribed daily defined doses and average prices from pharmacy pricelists based on active chemical substances laid down in the World Health Organization's Anatomical Therapeutic Chemical (ATC) Classification System.[28,29] Referral letters and physician communication were used to determine healthcare resources used by patients at other healthcare providers. Costs of these resources were determined using national tariffs set by the Dutch Healthcare Authority or by using average prices for Diagnosis Related Groups.[30,31]

To weigh the costs against health-related outcomes, we calculated deterministic incremental cost-effectiveness ratios using data of the significant changes in physical activity in total activity counts per hour (TAC/h, ActiGraph GT3X+), weight, abdominal girth, systolic blood pressure, HDL cholesterol, and psychosocial functioning (Health of the National Outcome Scale; HoNOS) in MULTI compared to TAU as found previously in adjusted regression analyses.[21,22] Additionally, we used the data on the also previously evaluated quality of life (EQ-5D-3L)[21] to calculate Quality-Adjusted Life Years (QALY) as an outcome often used in cost-effectiveness studies and by policymakers.

Statistical Analysis

All analyses were performed with IBM SPSS, version 25. Continuous variables were examined for linearity, normality, and homogeneity as assumptions for linear analysis by comparing means with medians and analyzing frequency histograms, normality plots, and plots of residuals versus predicted values. The main variable of interest in our analyses was the difference in total costs (delta costs) between Q1 2014 and Q3 2015 over the two treatment groups. Additionally, the differences in costs subgroups (i.e., ward stay, patient sessions, medication, hospital referrals) were calculated to gain more insight into specific changes. The mean difference of delta costs and corresponding 95%-confidence intervals were reported to show effect size and effect direction. As subgroup data were largely skewed, also medians and interquartile ranges were reported and uncorrected between-group differences in delta costs were tested with Mann-Whitney-U. Differences in total costs and subgroups that showed significant changes were analyzed in linear regression analyses adjusting for baseline costs (accounting for regression to the mean; i.e., patients with higher baseline costs are more likely to achieve costs reductions), and potential confounding by baseline differences in patient- and disease characteristics between MULTI and TAU. An unadjusted regression (model 1) was followed by a baseline-corrected regression (model 2), and finally a fully adjusted regression including baseline differences between groups (model 3). For each of the regressions, the coefficient (B) with a 95% confidence interval for the intervention condition was the main outcome.

Of the health outcomes where a significant difference was found in previous comparable regressions,[21,22] the pre and post measurements for MULTI and TAU were described, including the uncorrected delta difference between groups. For the evaluation of incremental cost-effectiveness ratios (i.e., dividing the delta difference in costs by the delta difference in health-related outcome between MULTI and TAU; T2 minus T1) we performed probabilistic sensitivity analyses to account for uncertainty surrounding the parameters. These analyses were run with 10 000 repetitions in which gamma and beta distributions were fitted for cost parameters and health-related outcomes, respectively. Based on these results cost-effectiveness planes were constructed.

Results

Table 1 shows the baseline characteristics of patients receiving MULTI and TAU. Costs data could be retrieved for all 114 patients. On average, patients receiving MULTI

were younger (M = –6.45 years, 95% CI: –10.27 to –2.64), had a higher baseline illness severity (M = 0.63, 95% CI: 0.17–1.08), and were more frequently diagnosed with schizophrenia or other psychotic disorders (X^2 = 21.98, P < .001) than patients receiving TAU.

Cost Analyses

To facilitate insight into changes in costs, we presented means and standard deviations for all cost groups in table 2. Medians and interquartile ranges can be found in supplementary table S1. The mean total healthcare costs per patient per quarter year at baseline (Q1 2014) were EUR 20 605 for the MULTI group and EUR 20 662 for the TAU group. The results show a decrease in these total costs between baseline and follow-up (Q3 2015) in both MULTI (M = –299, SD = 4241; Median = –315, IQR = –870 to 841) and TAU (M = –135, SD = 3271; Median = –280, IQR = –729 to 238), which was not significantly different between groups (P = .88). When looking at the underlying cost subgroups, only the change in medication costs between MULTI (M = –228, SD = 391; Median = –234, IQR = –388 to –120) and TAU (M = –170, SD = 395; Median = –116, IQR = –276 to –21) differed statistically significantly (P < .01). In both groups, there was a decrease in costs for patient sessions and hospital referrals, while there was an increase in ward stay costs. However, discharge of patients from inpatient units to sheltered housing facilities was more frequent in the MULTI group causing a relative cost-saving for ward stay in these patients. This is reflected in a smaller increase in ward stay costs in MULTI compared to TAU, and a larger increase in costs for sheltered housing facilities.

After data collection, one patient in TAU was found to have been referred to hospital to receive Coronary Artery Bypass Grafting (CABG) surgery at baseline. At an average cost of EUR 11 705, this resulted in a considerably larger skewness of the data and altered mean and median values for the TAU group. To show the impact of this outlier on the main results, we reported referral costs and total costs with and without this outlier and conducted sensitivity analyses. Removing the outlier in referral costs led to a decrease in baseline referral and total costs, and an increase in total healthcare costs for follow-up in TAU (see table 2). Without the outlier, the mean change in total costs between baseline and follow-up in TAU altered (EUR 102 vs. EUR –135), but the median change remained stable (EUR –279 vs. EUR –280) (see table 2 and supplementary table S1). The cost structure and distribution of total costs at baseline and follow-up in both MULTI and TAU without the outlier can be seen in figures 1 and 2.

We conducted adjusted linear regressions (see table 3) for changes in total costs and medication costs as the only subgroup that showed significant unadjusted differences. Both outcomes were normally distributed. After adjusting for baseline costs and baseline differences between groups, a non-significant decrease in total costs in favor of MULTI was observed. Removing the outlier did not result in substantial changes in between-group differences in the fully adjusted regression models, showing a non-significant decrease of EUR 736.28 per patient per quarter year in MULTI compared to TAU (95% CI: –2145.18 to 672.62). The fully adjusted model for medication costs showed a non-significant decrease of EUR 37.88 per patient per quarter year in favor of MULTI (95% CI: –183.05 to 107.28).

Incremental Cost-Effectiveness Ratio

Uncorrected pre and post measurements and delta differences between MULTI and TAU on quality of life and health outcomes in which significant between-group differences were found in similar adjusted regression models,[21,22] can be seen in supplementary table S2. Improvements in these health-related outcomes (i.e., physical activity, metabolic health, psychosocial functioning, and quality of life) in favor of MULTI against the reported decrease in costs are confirmed in probabilistic sensitivity analyses accounting for uncertainty surrounding the parameters (table 4). These analyses show statistically non-significant delta costs differences against health improvements for all health-related outcomes, with and without the outlier. This is reflected in the ICERs, where positive ICERs mean the increase in costs per unit deterioration in health (e.g., 1 cm increase in abdominal girth

Table 1. Baseline Characteristics of Patients (N = 114)

Outcome (scale)	MULTI (n = 65)		TAU (n = 49)	
Sex, n (%) male	43	(66.2)	27	(55.1)
Age, years, mean (SD)	**52.2**	**(8.9)**	**58.7**	**(11.6)**
Diagnosis, n (%)				
Schizophrenia spectrum and other psychotic disorders	**61**	**(93.8)**	**28**	**(57.1)**
Other disorders	**4**[a]	**(6.2)**	**21**[b]	**(42.9)**
Illness severity, CGI-S scale 1–7, mean (SD)	**5.0**	**(1.2)**	**4.3**	**(1.2)**
Years of hospitalization, mean (SD)	14.4	(10.9)	13.2	(12.7)

Significant differences between groups are shown in bold.
MULTI, MUltidisciplinary Lifestyle enhancing Treatment for Inpatients with severe mental illness; TAU, Treatment As Usual; CGI-S, Clinical Global Impression—Severity scale; EQ-5D: EuroQol five-dimension questionnaire.
[a] mood disorders (n = 2): a pervasive disorder not otherwise specified (n = 1) and an anxiety disorder (n = 1)
[b] mood disorders (n = 8): personality disorders (n = 4), alcohol-related disorders (n = 4), somatoform disorders (n = 2), delirium, dementia, and amnestic and other cognitive disorders (n = 2) and a pervasive disorder not otherwise specified (n = 1)

Table 2. Costs per Patient in Euros for Baseline (Q1 2014) and Follow-Up (Q3 2015) Including Analyzed Between-Group Differences in Delta Costs

	MULTI (n = 65)						TAU (n = 49)						Delta costs between groups[a]	
	2014		2015		Delta Costs		2014		2015		Delta Costs			
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Ward stay all patients	**19 138**	**(4668)**	**19 147**	**(3932)**	**9**	**(4105)**	**18 926**	**(4670)**	**19 509**	**(4873)**	**583**	**(2739)**	**–574**	**(642)**
Sheltered housing	0	(0)	2193	(5,513)	2193	(5513)	0	(0)	647	(3167)	647	(3167)	1547	(820)
Patient sessions	**1025**	**(645)**	**963**	**(722)**	**–62**	**(450)**	**1,025**	**(754)**	**791**	**(478)**	**–234**	**(610)**	**172**	**(104)**
Individual Sessions	300	(266)	249	(257)	–50	(219)	294	(280)	228	(267)	–66	(254)	16	(45)
Daily Activities	597	(611)	442	(591)	–155	(366)	591	(712)	338	(330)	–253	(591)	98	(96)
Group Sessions	12	(18)	20	(49)	9	(45)	16	(60)	18	(49)	2	(81)	7	(13)
Indirect time	102	(81)	244	(252)	142	(211)	75	(60)	159	(143)	84	(147)	58	(34)
Meetings	0	(2)	0	(0)	0	(2)	1	(3)	5	(28)	5	(28)	–5	(4)
Physical Therapy	14	(52)	7	(28)	–7	(44)	48	(93)	43	(116)	–5	(106)	–1	(16)
Medication	**401**	**(286)**	**173**	**(306)**	**–228**	**(391)**	**368**	**(509)**	**197**	**(449)**	**–170**	**(395)**	**–57**	**(74)***
Hospital	**41**	**(80)**	**23**	**(63)**	**–18**	**(92)**	**343**	**(1742)**	**29**	**(126)**	**–313**	**(1751)**	**296**	**(250)**
Referrals														
Without one outlier	*41*	*(80)*	*23*	*(63)*	*–18*	*(92)*	*100*	*(387)*	*30*	*(127)*	*–70*	*(412)*	*52*	*(61)*
Total Costs	**20 605**	**(4892)**	**20 306**	**(3949)**	**–299**	**(4241)**	**20 662**	**(4771)**	**20 527**	**(4966)**	**–135**	**(3271)**	**–164**	**(704)**
Without one outlier	*20 605*	*(4892)*	*20 306*	*(3949)*	*–299*	*(4241)*	*20 496*	*(4678)*	*20 598*	*(4993)*	*102*	*(2850)*	*–401*	*(668)*

[a] cost difference of MULTI compared to TAU (delta costs MULTI minus delta costs TAU).
* $P < .05$, all calculated with Mann-Whitney-U.
MULTI, MUltidisciplinary Lifestyle enhancing Treatment for Inpatients with severe mental illness; TAU, Treatment As Usual.

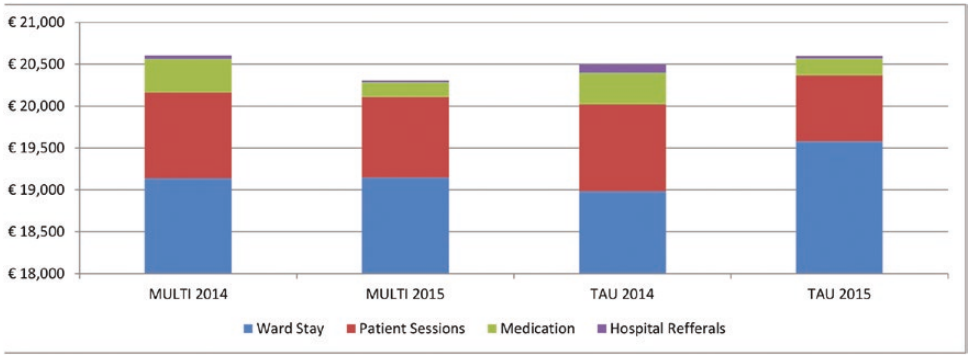

Fig. 1. Cost structure by type of costs in Euros on baseline (2014) and follow-up (2015) without the outlier. MULTI, MUltidisciplinary Lifestyle enhancing Treatment for Inpatients with severe mental illness; TAU, Treatment As Usual.

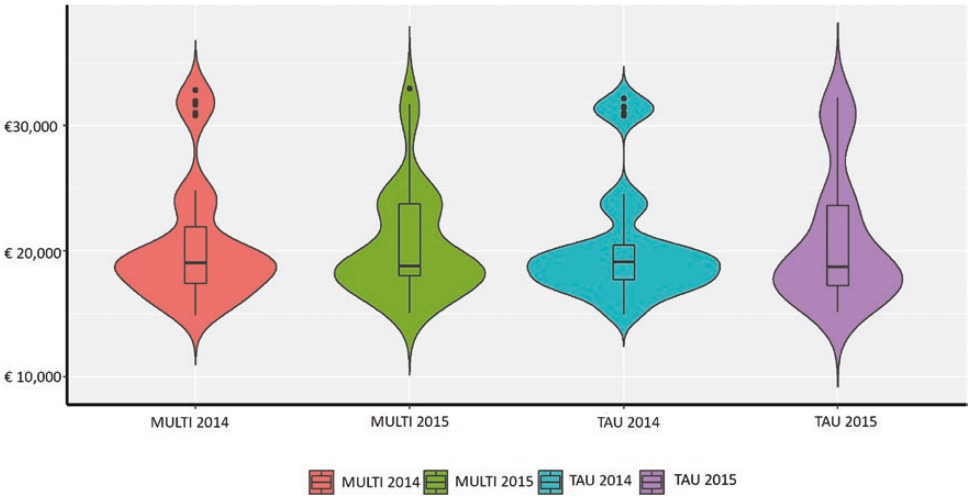

Fig. 2. Distribution of total costs in Euros on baseline (2014) and follow-up (2015) without the outlier. In addition to the boxplots (including medians and interquartile ranges), the curves show how the values in the data are distributed, with wider curves representing more data points in a region. MULTI, MUltidisciplinary Lifestyle enhancing Treatment for Inpatients with severe mental illness; TAU, Treatment As Usual.

corresponds to an increase of 90 Euros in healthcare costs per quarter year), which can also be interpreted in reverse (i.e., 1 cm decrease saved 90 Euros per quarter year).

The cost-effectiveness planes are summarized in figure 3. In all health-related outcomes except for weight, ≥80% of the repetitions delivered health improvements in MULTI compared to TAU, and in all outcomes, the majority of repetitions demonstrated that MULTI resulted in more health improvements and fewer costs compared to TAU (36% in weight to 57% in systolic blood pressure). Without the outlier, this especially changed for HDL cholesterol, while the percentage of repetitions showing both a health and cost-benefit in favor of MULTI increased in almost all other variables (41% in weight to 64% in systolic blood pressure). Individual cost-effectiveness planes for each variable can be found in the supplementary material.

Discussion

Following a previous evaluation of health-related outcomes,[21–23] this study evaluated changes in healthcare costs after 18 months of MULTI compared to TAU. We can at least state that MULTI resulted in health benefits without increasing healthcare costs. Probabilistic sensitivity analyses indicate substantial health benefits in MULTI compared to TAU, much of which was also less costly. Precise estimates of cost savings and ICERs, however, differ depending on distributions, correction for baseline differences between groups and are affected by the relatively small sample for robust cost-effectiveness analyses. Although not significant, the adjusted regression model of total costs even indicated a cost-saving of EUR 736 per patient per quarter year compared to TAU. The decrease in medication costs of EUR 38 per patient per quarter year in favor of MULTI reflects the previous finding that patients who received MULTI used less medication after 18 months compared to TAU.[23] The data show an overall reduction of costs, also in the TAU group, which may reflect the overall trend of cutback policies in Dutch mental healthcare organizations in these years. The higher costs for patient sessions in MULTI compared to TAU, especially in daily activities and in indirect time

Table 3. Linear Regression Estimating Treatment Effects of MULTI Compared to TAU on Mean Total and Medication Costs in Euros per Patient per Quarter Year

	Total sample (n = 114)		Without outlier in TAU (n = 113)	
	B	(95% CI)	B	(95% CI)
Total costs				
Crude model	–163.9	(–1609.0 to 1281.2)	–400.6	(–1801.9 to 1000.7)
Adjusted for baseline	–186.7	(–1440.5 to 1067.1)	–359.9	(–1590.7 to 871.0)
Fully adjusted[a]	–802.5	(–2227.0 to 622.0)	–736.3	(–2145.2 to 672.6)
Medication costs				
Crude model	–57.1	(–204.3 to 90.1)	–52.9	(–201.5 to 95.7)
Adjusted for baseline	–38.9	(–162.4 to 84.5)	–37.8	(–162.5 to 86.9)
Fully adjusted[a]	–37.5	(–181.8 to 106.8)	–37.9	(–183.0 to 107.3)

MULTI, MUltidisciplinary Lifestyle enhancing Treatment for Inpatients with severe mental illness; TAU, Treatment As Usual.
[a]adjusted for baseline costs and baseline differences between groups on age, diagnosis (schizophrenia and other psychotic disorders, yes/no), and illness severity.

(e.g., multidisciplinary consultation), is in line with an upsurge in activities, multidisciplinary cooperation, and psychoeducation as intended by MULTI.

The findings contribute to the scarce literature on the cost analyses of interventions promoting and supporting an active and healthy lifestyle for people with mental illness.[2,5,9] The results correspond with the reported potential of the majority of public health interventions in the general population targeting physical activity and a healthy diet to be cost-effective.[32] In a broader perspective, cost savings may be underestimated by limiting our analyses to healthcare costs, as improved health and functioning may additionally translate to lower societal costs (i.e., higher productivity, lower disability pensions, and other indirect costs). However, we know that people with SMI need extra support compared to the general population to overcome barriers associated with their health conditions, such as blunted affect, lack of initiative, apathy, cognitive deficits (e.g., memory and attention), and low health literacy rates.[33–38] This extra support most likely goes hand in hand with extra investment. Therefore, it is promising to see that following our results, there is emerging evidence for a favorable cost-benefit ratio for such interventions targeting people with (severe) mental illness.[39–43] However, in line with the need for more long-term effectiveness studies in real-world conditions to translate research into actual change in routine mental healthcare, there is a need for more studies including the evaluation of costs as part of evaluating implementation.[19] Insight into the favorable cost-benefit ratio of lifestyle interventions within conditions that reflect day-to-day healthcare for people with mental illness is an important link in informing managers and policymakers. This is essential when it comes to investment in the implementation and scale-up of such evidence-based interventions. Moreover, it is key to structurally improve the health status of people with mental illness and prevent future deterioration, which has the potential to reduce costs in the longer term.

In the context of such evidence-based lifestyle interventions, economic evaluations are especially relevant for multidisciplinary, multicomponent lifestyle interventions. An integrated approach is essential for successful lifestyle changes in people with mental illness, by focusing on multiple lifestyle behaviors (e.g., physical activity and diet), supervision by qualified experts (e.g., exercise professional or dietitian), social and educational components, motivational and supporting strategies for maintenance and tailoring to the individual.[2,10,34,44–52] A recent comprehensive overview of evidence also recommended such an approach for people with mental illness, based on the successful Diabetes Prevention Program.[2] In line with this, it is therefore already promising that especially interventions that followed a Diabetes Prevention Program showed to be costs effective.[53] MULTI is largely in line with such a design, and previous analyses also suggested that positive changes in health-related outcomes are most likely due to the integrated, multidisciplinary, and multicomponent approach as a whole rather than primarily caused by one intervention such as increasing physical activity.[21–23] The current findings confirm that much improvement in the health status of inpatients with SMI is already possible by targeting lifestyle and working (together) differently within the current context and resources. Namely, MULTI was developed by current staff as a different way of working and treating people, using the same staffing and resources within routine clinical care, without extra implementation costs. However, previously identified implementation barriers and facilitators of MULTI showed that investment in strategies addressing organizational barriers is needed to sustain this integrated approach.[24] This included more support for teams by professionals with expertise on lifestyle factors in patients with mental illness, such as dietitians, psychomotor therapists, or physical therapists within mental healthcare. In line with the evidence for successful lifestyle changes mentioned

Table 4. Results of Probabilistic Sensitivity Analyses Using 10 000 Repetitions in Which Gamma and Beta Distributions Were Fitted for Cost Parameters and Health-Related Outcomes, Respectively, Including Calculated Incremental Cost-Effectiveness Ratios (ICERs) in Euro's

	Total sample					Without outlier in TAU				
Outcome (scale)	Delta change in health-related outcome between groups[a]		Delta change in costs between groups[a]		ICER	Delta change in health-related outcome between groups[a]		Delta change in costs between groups[a]		ICER
Physical Activity[b]										
Average total activity counts per hour	4748	(–2181 to 11,863)	–171	(–2610 to 2326)	–0.04	4673	(–2506 to 11,815)	–414	(–2907 to 2,093)	–0.09
% Moderate-to-vigorous physical activity	1.07	(–0.98 to 3.10)	–163	(–2583 to 2242)	–152	1.03	(–0.97 to 3.03)	–400	(–2903 to 2097)	–388
Metabolic health[b]										
Weight (kg)	–6.21	(–91.42 to 208.46)	–153	(–2623 to 2308)	25	–7.38	(–91.70 to 207.51)	–394	(–2866 to 2090)	53
Abdominal girth (cm)[c]	–4.32	(–12.14 to 3.55)	–390	(–2939 to 2087)	90	–4.22	(–11.90 to 3.63)	–663	(–3209 to 1898)	157
Systolic blood pressure (mmHg)[d]	–6.89	(–16.28 to 2.57)	–382	(–2868 to 2177)	55	–6.94	(–16.70 to 2.63)	–649	(–3142 to 1867)	93
Cholesterol HDL (mmol/l)[e]	0.12	(–0.05 to 0.29)	–364	(–2812 to 2077)	–3,063	0.13	(–1.24 to 1.59)	–613	(–3011 to 1829)	–4832
Psychosocial functioning (HoNOS)[f,g]										
Sum score (0–44)	–2.90	(–5.59 to –0.24)	–103	(–2633 to 2370)	35	–2.80	(–5.35 to –0.20)	–362	(–2912 to 2162)	129
Impairment (0–8)	–0.78	(–1.78 to 0.23)	–116	(–2633 to 2388)	148	–0.73	(–2.49 to 0.84)	–347	(–2899 to 2230)	479
Social problems (0–12)	–1.70	(–2.87 to –0.53)	–123	(–2619 to 2374)	72	–1.67	(–2.84 to –0.51)	–374	(–2900 to 2151)	225
Quality of life (EQ-5D-3L, 0-1)[f]	0.06	(–0.08 to 0.20)	–146	(–2604 to 2341)	–2288	0.06	(–0.08 to 0.20)	–417	(–2873 to 2042)	–6564

Notes: Mean (95% CI) unless otherwise noted. MULTI: MUltidisciplinary Lifestyle-enhancing Treatment for Inpatients with severe mental illness; TAU: Treatment As Usual; HoNOS: Health of the Nation Outcome Scales; EQ-5D-3L: EuroQol five-dimension 3-level questionnaire.

[a] difference of MULTI compared to TAU (change in MULTI minus change in TAU)

[b] $N = 65$ for MULTI and $N = 43$ for TAU [22], $N = 42$ in TAU without outlier

[c] Missing change score in MULTI due to missing baseline value ($n = 1$)

[d] Missing change score in TAU due to missing baseline value ($n = 1$)

[e] Missing change score in MULTI due to missing baseline ($n = 1$) and follow-up value ($n = 1$)

[f] $N = 65$ for MULTI and $N = 47$ for TAU [21], $N = 46$ in TAU without outlier

[g] Missing change score for TAU ($n = 3$) due to patient discharge before HoNOS follow-up ($n = 3$)

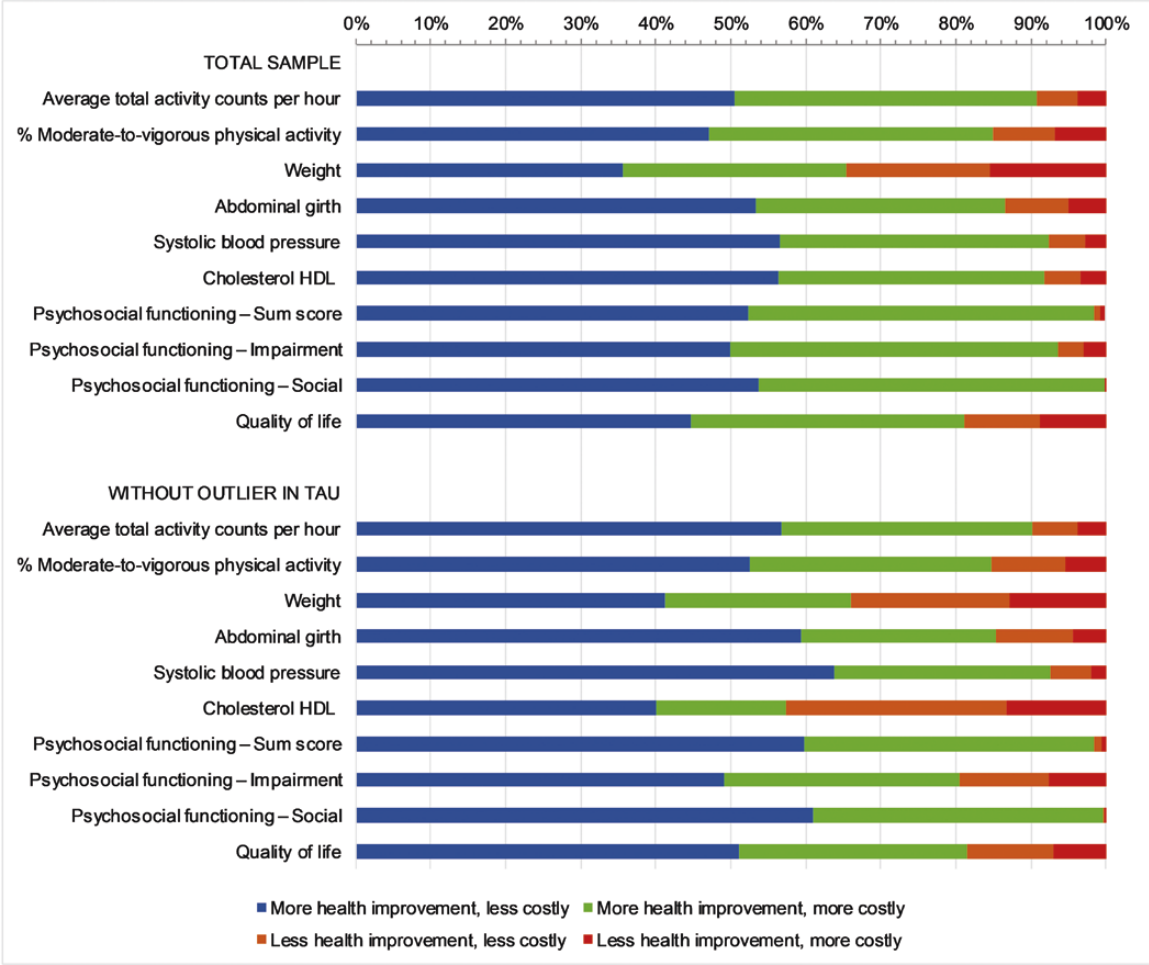

Fig. 3. Summary of the cost-effectiveness planes based on the results of probabilistic sensitivity analyses using 10 000 repetitions, in which gamma and beta distributions were fitted for cost parameters and health-related outcomes, respectively. Percentages reflect the proportions of repetitions showing more/fewer health improvements and more/fewer costs of the multidisciplinary lifestyle-enhancing treatment for inpatients with severe mental illness (MULTI) compared to treatment as usual (TAU).

above, this would in turn most likely improve patient support to overcome the barriers that they indicated that are associated with their illness. The current findings justify such an investment. For example, according to the same calculations used in our methods and context in the Netherlands, adding a full-time psychomotor therapist or dietitian for the included 65 patients will cost EUR 308 and EUR 272 per patient per quarter year, respectively. Except that this would at least partly outweigh an indicated cost-saving, especially because caseloads on a full-time basis usually serve more patients, adding this support most likely even increases the effectiveness of the MULTI. This will significantly increase support for teams and patients and can also help to upskill them. Also, from a broader economical point of view, this potential is especially relevant in inpatients. Although inpatients are a minority (22%) within the population of people with SMI in the Netherlands, for instance, they represent the majority (64%) of all healthcare costs in this group.[54] Since SMI starts at an early age[55] and somatic comorbidities are associated with more frequent rehospitalizations,[56] lifestyle interventions improving both somatic and mental health could provide lifelong benefits. Moreover, this might help to prevent some of the major health issues that are currently seen in patients with a long history of SMI. Therefore, an integrated lifestyle-enhancing treatment could have both societal and economic value in the longer term.

Limitations and Strengths

The current study has several limitations. Above all, the exact amount of cost savings should be interpreted with caution given the wide intervals of the data. For more accurate estimates it is advised to replicate cost analyses in larger samples. Nevertheless, MULTI did not cost more compared to usual care, while significant improvements in health-related outcomes were observed. Also, this was a naturalistic cohort study without an a priori set-up as a cost-effectiveness study, in which we were not able to

randomize patients (e.g., the TAU wards treated fewer patients with psychotic disorders). This design has limitations, such as the risk that groups were not similar on baseline in both characteristics and the examined outcome, in this case, cost data. By using linear regression adjusting for differences between MULTI and TAU and baseline values, we aimed for robust results. There were also no signs of contamination within TAU, reflected by a lack of increase in physical activity, for instance,[22] confirming the challenge to change lifestyle behavior in SMI without extra support. Also, the pragmatical decision to implement MULTI at those specific wards where the head practitioner acknowledged the potential of lifestyle interventions, could have introduced bias. For example, a difference in attitude with the head practitioner of the TAU wards could have impacted health outcomes in itself. Nevertheless, we think this impact was limited as policies and attitudes were similar across the organization of these six wards, and after the three wards started MULTI it was agreed to learn from these wards before broader organizational change. Another limitation is that we only gained insight into the costs three months before the start of MULTI and three months after its evaluation, which were different seasons of the year and did not include potential changes over time in between those time points. Unfortunately, due to a former transition in the electronic medical record system and a lack of data extraction alignment between the old and new system, it was not possible to retrieve valid data before 2014 (e.g., summer 2013). Also, we would not have been able to link cost data on more time points with health-related data, as the MULTI study included a pre and post measurement only. However, to the best of our knowledge, this is the first economic evaluation of a lifestyle intervention in inpatients with SMI. Future well-designed trials can help to confirm or reject current findings. Larger samples at multiple sites with more longitudinal data can provide future studies with more power to analyze costs in more detail, the course of costs over time, and further improve generalizability. Also, analyses correcting for specific differences between groups as performed in previous analyses[21,22] would most likely give more accurate estimates of changes in health-related outcomes, but this is not compatible with probabilistic analyses which were more relevant in the context of this study. Although these analyses also take uncertainty around the parameters into account, we refer to previous studies for a more comprehensive insight into changes in health-related outcomes. Lastly, the current findings are solely based on direct healthcare costs related to daily routine care received by patients. Especially for daily activities and group sessions, we may have missed data as they rely on reports by healthcare professionals regarding patients' attendance. However, it is likely that this risk applies to both groups as organizational structures are the same, which limits the potential bias in between-group comparisons. Nevertheless, although verification of these data in the relatively small team of healthcare professionals offering these activities indicated that data were valid, this could have led to both small under- and overestimations of the number of patients in these sessions. Moreover, we had no data on societal costs in addition to healthcare costs. Especially our previous finding on improved psychosocial functioning and a considerable shift of patients from inpatient units to sheltered housing facilities observed in the current data, it would be of value to look into societal costs as well (e.g., employment, less burden by disease, etc.). We hypothesize that within this context integrated lifestyle interventions such as MULTI would be even more cost-effective when we consider such costs.

This study has also several strengths. It adds to the limited literature on this topic, using data from healthcare registrations for the analyses. This resulted in reliable and valid insight into actual costs in routine mental healthcare, compared to self-reports of healthcare consumption that are often used, for instance. The current findings also provide possible evidence of changes in healthcare costs after the implementation of lifestyle interventions for environments where it is often more challenging to collect data of all costs, such as outpatient facilities. The naturalistic setting of the study improves the generalizability of the results and meets the need for observational studies to supplement randomized controlled trials to improve external validity.[57] Results of effectiveness studies and costs evaluations offer mental healthcare professionals and related policymakers the information to make evidence-based healthcare decisions.

Conclusions

In summary, the current study shows that MULTI did not cost more compared to TAU, while significant improvements in health-related outcomes were observed. Additionally, our findings indicate that MULTI can be cost-saving and justify the needed investment to optimize and sustain MULTI. We encourage cost-effectiveness studies on lifestyle interventions in routine mental healthcare as this is key to the investment in implementation and scale-up of evidence-based lifestyle interventions. Such interventions can improve the health status of people with mental illness and could have societal and economic value in the longer term. This research clearly shows that starting lifestyle interventions such as MULTI does not need to be hampered by costs, making it accessible for many mental healthcare facilities.

Supplementary Material

Supplementary data are available at *Schizophrenia Bulletin Open* online.

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Author contributions

JD: study idea, obtaining funding, study design, retrieving, processing, and analyzing data, drafting the manuscript; CvL: study design, processing and analyzing the data, drafting the manuscript; HvD: retrieving, processing and supporting analyzing data and critical review of the manuscript; GF: study design and critical review of the manuscript; IH and PvH: critical review of the manuscript. DT: study idea and critical review of the manuscript. All authors gave final approval for the version to be submitted.

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