Effects on depressive symptoms of a 12-week virtual care intervention for diet, physical activity and smoking with and without individualized health coaching for youth with early psychosis: A randomized-controlled trial

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Abstract

Background: Depressive symptoms are common in early psychosis and impact suicide risk, functioning and engagement in health care. Clinical research supports the use of dietary and exercise interventions as adjunctive treatment for major depressive disorder. However, little is known about the impact of health behaviour interventions on depressive symptoms in early psychosis. The objective of this project is to evaluate whether participating in a 12-week individualized health coaching intervention targeting diet, physical activity and smoking cessation results in a reduction in depressive symptoms in youth with first episode psychosis as compared to access to an internet portal for self-management of the same health behaviours.

Methods: This paper is a secondary data analysis of a feasibility study involving youth with early psychosis. Participants were randomly assigned to a health coach supervised by a virtual care team (VCT) (high intensity, HI; n=29) or a self-directed learning group with access to an internet portal for self-management (low intensity, LI; n=23) for 12 weeks. Depressive symptoms were measured using the Quick Inventory of Depressive Symptomatology (QIDS-SR) at baseline, 6, 12 and 24 weeks.

Results: At baseline, 41% of participants reported moderate to severe depressive symptoms and there was no difference in baseline depressive symptoms between participants assigned to the LI and HI groups. Participants in the HI group experienced a 20% reduction in depressive symptoms as measured by the QIDS-SR over the study period as compared to the LI group (SMD=0.97, large effect size).

Conclusion: Individualized virtual health coaching to target health behaviours in youth with early psychosis may improve depressive symptoms. This pilot data requires replication in a study with a larger sample size with adequate statistical power and the ability to control for possible confounding variables.

Résumé

Contexte: Les symptômes dépressifs sont communs pendant la psychose précoce et ont un impact sur le fonctionnement des patients et leurs engagement dans les soins de santé. La recherche clinique soutient l'utilisation des interventions nutritionnelles et des activités physiques comme traitement d'appoint pour le trouble dépressif majeur. Moins est connu sur l'impact des interventions sur les comportements de santé sur les symptômes dépressifs en contexte de psychose précoce. L'objectif est d'évaluer si la participation à une intervention de coaching de santé individualisée de 12 semaines pour cibler l'alimentation, l'activité physique et le sevrage tabagique entraîne une réduction des symptômes dépressifs chez les jeunes atteints de psychose précoce par rapport à l'accès à un portail Internet pour l'autogestion de les mêmes comportements de santé.

Méthodes: Cet article est une analyse des données secondaires d'une étude de faisabilité impliquant des jeunes atteints de psychose précoce. Les participants ont été assignés au hasard à un coach de santé supervisé par une équipe de soins virtuels (VCT) (haute intensité, HI; n = 29) ou un groupe d'apprentissage autonome (faible intensité, LI; n = 23) pendant 12 semaines. Les symptômes dépressifs ont été mesurés à l'aide du Quick Inventory of Depressive Symptomatology (QIDS-SR) au départ, 6, 12 et 24 semaines.

Résultats: Il n'y avait aucune différence dans les symptômes dépressifs de base entre les groupes et 41% des participants ont signalé des symptômes dépressifs modérés à sévères au départ.Les participants du groupe HI ont connu une réduction des symptômes dépressifs mesurés par le

QIDS-SR au cours de la période d'étude par rapport au groupe LI (différence ajustée = 4,9, p = 0,006).

Conclusion: Un coaching de santé virtuel personnalisé pour cibler les comportements de santé chez les jeunes atteints de psychose précoce peut améliorer les symptômes dépressifs. Ces données pilotes doivent être répliquées dans une étude avec une taille d'échantillon plus grande avec une puissance statistique adéquate et la possibilité de contrôler d'éventuelles variables de confusion.

Acknowledgments

I would like to thank first and foremost my thesis supervisors, Dr. Jai Shah and Dr. Peter Selby. Along with my advisory committee members, Dr. Norbert Schmitz and Dr. Srividya Iyer, they challenged me to think critically, provided depth and perspective and guided me in the process of completing this thesis project. This work would not have been possible without the collaboration of the TECC-Y team in Toronto who welcomed me to continue to remain an active member of the study team remotely following my unexpected move to Montreal in the pre-COVID era. Lastly, I want to thank our study participants who devoted their time and efforts to completing study interventions and assessments to the benefit of future patients.

Contributions to Original Knowledge

This thesis project reports on the impact of participating in a 12-week individualized virtual health coaching intervention (high intensity, HI) as compared to online materials and self-management (low intensity, LI), each targeting health behaviours (diet, physical activity, smoking), on depressive symptoms in youth with early psychosis. We found that participants in the HI group experienced a reduction in depressive symptoms over the study period as compared to participants in the LI group. Being a small pilot study with many exploratory outcomes, our study was not designed to determine effect sizes. Nonetheless, our findings represent a significant contribution given the minimal body of scientific literature regarding the mental health impact of health behaviour interventions in schizophrenia (and even smaller literature base in those with first episode psychosis).

We are also the first to report on the effect of a virtual intervention to target health behaviours on depressive symptoms in youth with early psychosis. The study intervention and all study procedures were delivered virtually using a custom designed e-platform and via telephone. Our virtual intervention is therefore novel, timely and actionable – employing health coaches who are supervised by an interdisciplinary team of specialists in a weekly virtual rounds format. Compared to traditional health service delivery models, the TECC-Y intervention may be more resource efficient, may increase access to care in locations limited by geography and may assist patients in becoming more active participants in their care in a health care system that can be fragmented and difficult to navigate.

Contribution of authors

As first author of this thesis, I (**Laura LaChance**) made a significant contribution to the conceptualization, design, data analysis, interpretation of results and writing of this thesis.

This thesis project is a secondary analysis of data gathered from a recently completed study entitled: "Technology-Enabled Collaborative Care for Youth (TECC-Y) with Early Psychosis". Dr. LaChance is a co-investigator on the original study (1). I will outline my contributions to the parent study below.

I first became involved with the TECC-Y study in the fall of 2017. At the time, I was working as a psychiatrist and clinician scientist at the Slaight Centre for Youth in Transition (First episode psychosis clinic and research centre) at the Centre for Addiction and Mental Health in Toronto. When I joined the team, the basic study design had been established and funding had been obtained (via the Medical Psychiatry Alliance) but there were many details left to sort out. Initial steps included finalizing the protocol and obtaining ethics approval. During these early days, I suggested the measures for diet quality and physical activity that were ultimately used in the study. I also played a key role in adapting NAVIGATE healthy living modules for our low intensity group as well as providing content and feedback during the development of our custom e-platform. I participated in writing of the protocol and REB applications. Much of this work occurred through weekly "small group" meetings attended by the principal investigator, research assistants and 2-3 core research collaborators. The entire multi-site team included over 20 research collaborators. My role also included acting as the liaison between the study team and Slaight clinical and research centre which was the major recruitment site for our study. Other

contributions included conducting interviews to select our health coaches and recruiting members of the virtual care team. Weekly research team meetings continued through to the end of participant recruitment and I continued to contribute as a member of the virtual care team until study completion. Thus, I became intimately familiar with what is required to run a clinical trial and learned many skills that I will be able to apply to future research projects. When the team decided to introduce a qualitative component to our study, I participated in developing the qualitative interview guide. Lastly, I have contributed to writing the final TECC-Y paper which will be submitted for publication this year as well as the protocol paper.

I left CAMH in fall of 2018 and moved to Montreal. I continued my work with the TECC-Y team during a maternity leave and once I started my MSc at McGill, decided that I could conduct a secondary data analysis as my thesis project. Thus I continued my work with TECC-Y in this new frame. It is worth mentioning that from the outset, my main interest in TECC-Y has been to evaluate any changes in mental health outcomes associated with participating in the TECC-Y intervention. This is in line with my longstanding research interest in understanding the impact of nutrition interventions on mental health and how to incorporate such interventions into mental health service delivery models. I brought this unique area of expertise to the TECC-Y team.

Dr. Peter Selby is the principal investigator of the TECC-Y study and provided overall supervision and revision of this thesis. He initially conceptualized the TECC-Y study and obtained funding.

Dr. Jai Shah provided overall supervision and revision of this thesis.

Dr. Scott Veldhuizen conducted the statistical analysis and mixed effects models for this thesis.

Rosa Dragonetti is the main research assistant on the TECC-Y project (parent study). She participated in obtaining funding, writing the study protocol, obtaining REB approval and hiring the other research assistants (below). With such a large study team, Rosa took on a major role verifying compliance with procedures, delegating tasks and keeping the various team members organized.

Huma Taj, Danielle Dawson, Iqra Ashfaq, and Lenka Vojtila served dual roles as the parent study health coaches and research assistants.

Chapter 1 - Thesis introduction

Literature Review

Early psychosis represents a diagnostically heterogenous group with approximately 55% of patients with a schizophrenia spectrum disorder (SSD) and one third with affective psychosis (psychotic depression or bipolar disorder) (2). Specialized early intervention teams have been developed for individuals with first episode psychosis in an effort to reduce barriers to care, improve treatment delays, alter illness trajectory and improve outcomes (3). First episode psychosis services include both medical and psychosocial interventions in the context of a multidisciplinary team (4).

Individuals with psychosis are at risk of premature mortality and face a shortened life expectancy of 8-20 years compared with the general population (5). Furthermore, the most common cause of mortality in this group is associated with cardiovascular disease despite significant progress in improving this metric in the general population in Canada (5). Initiating treatment with an antipsychotic medication contributes to metabolic dysregulation observed in individuals with SSD (6). However, glucose dysregulation is already present in drug-naïve individuals and unaffected first-degree relatives, suggesting that metabolic dysregulation may be inherent to the illness itself (7, 8). Comorbid cardiometabolic disease also contributes significantly to the cost of treating SSD (9), proving further rationale to support the development of interventions for the prevention of cardiovascular disease in this high-risk group.

In considering the various factors that contribute to increased cardiovascular disease morbidity and mortality in individuals with schizophrenia, a closer look at health-related behaviours is required. For instance, high levels of sedentary behaviour, smoking and poor diet quality often cluster in this population. A recent systematic review and meta-regression analysis reported that individuals with SSD engaged in higher levels of sedentary behaviour compared to controls and that participants tended to underestimate the extent of their sedentary behaviour when compared with objective measures (10). Myles et al. reported that the estimated prevalence of tobacco use in individuals with early psychosis was 58.9% (95% CI, 54.3%–63.4%) based on a meta-analysis of 10 studies, which is significantly higher than the general population (11). Individuals with schizophrenia were also more likely to consume a lower quality diet that was higher in energy and sodium (12, 13).

Engaging in health-promoting behaviours such as healthy diet, regular physical activity and smoking cessation has long been recommended as part of cardiovascular disease risk reduction and treatment in the general population. In comparison, the uptake of such evidence-based interventions as part of treatment as usual for individuals with schizophrenia is low even though they are recommended by the European Psychiatric Association and a recent delphi expert consensus study (14-16).

What is more, an emerging area of literature suggests that participating in interventions to improve health-risk behaviours may have to potential to impact not just physical health but *mental health* outcomes in SSD. A Cochrane review reported that exercise interventions can have positive effects on both physical and mental health outcomes in schizophrenia (17). A

recent systematic review of dietary intervention trials that reported on a mental health outcome in individuals with schizophrenia found that 19 of 25 studies reported improvement in one or more mental health domains (18). Quitting smoking does not appear to worsen symptoms of schizophrenia and may even improve symptoms of major depressive disorder (19).

The few clinical trials to evaluate interventions to improve health behaviours in first episode psychosis have yielded mixed results and even fewer have reported on mental health outcomes. For example, Lovell et al. reported that a healthy lifestyle intervention to target diet and physical activity in youth with FEP showed no effect on BMI or depressive symptoms compared to TAU. This intervention consisted of 7 individual sessions with a recovery worker over 6 months with one booster session at 9-10 months, access to physical activity programming, cooking groups, and online psychoeducational materials (20).

In contrast, a 12-week multi-component intervention part of the Keeping the Body in Mind (KBIM) program was evaluated as part of a cluster randomized controlled trial(21). The study intervention included peer support, individual sessions with both a dietician and exercise physiologist, as well as access to cooking classes and a supervised gym environment. Participants included youth with FEP from two similar community-based early psychosis services where one service was randomized to the KBIM program and the other standard care. The KBIM program was effective in improving diet quality, increasing physical activity and preventing antipsychotic-induced weight gain in youth with FEP compared to standard care. Depressive symptoms were not measured but there was a statistically significant improvement in Global Assessment of Functioning in participants randomized to the intervention group

compared to standard care at 12-weeks (21, 22). The KBIM Xtend program was a single-arm study that recruited two-thirds of participants who completed the active arm of the original study. Follow-up was extended to two years, with ongoing access to peer support, cooking groups and supervised gym but with reduced frequency of individual follow-up. Diet quality was improved mostly driven by increased fruit and vegetable intake and variety, decreased glycemic load and discretionary (ultra-processed) food intake and sodium. At two years, 75% of participants did not experience clinically significant weight gain and mean weight gain was 1.8 kg compared to baseline weight (23). Participants also described improved self-esteem, increased hopefulness, improved mood and improved motivation (24).

A pilot feasibility study evaluated the M^3 ("Meals, Mindfulness and Moving Forward") program, including participants with FEP and a chosen support person, in comparison to community-based TAU for youth with FEP. This 6-week lifestyle intervention included the following elements: "Mindfulness meditation, cooking classes, field trips to supermarket and a low-cost fast-food restaurant for hands on learning, nutrition education, exercise (walking, home-exercises, taiko drumming, and ju jitsu), and moderated group discussion". At 12-weeks, participants in the intervention group demonstrated a reduction in positive symptoms and a trend toward reduced BMI (25).

Finally, a large (n=341) multi-site RCT evaluated the effect of a 40-week intervention on weight in individuals with SSD including a subset with FEP. The intervention included both individual and group components and provided education on physical activity, nutrition and weight management. Mental health outcomes were included as secondary outcomes. At 12 months,

there were no statistically significant differences between participants in the intervention group compared to the control group in weight reduction, physical activity, dietary intake, BPRS or depression (26).

A number of gaps in the current literature exist. First, no study has evaluated the effect of a health behaviour intervention on depressive symptoms in youth with FEP as a primary outcome. Moreover, all existing study interventions were delivered in-person; it remains to seen whether a virtual care model is effective both to engage youth with FEP and to change behaviour. If a virtual care model is demonstrated to be effective, this may serve to increase feasibility and access, and decrease resource intensiveness of health behaviour interventions in this population. No study has evaluated the effect of a virtual intervention to target health behaviours on depressive symptoms in youth with early psychosis.

Rationale & objectives

The peak age of onset for schizophrenia is between age 15 and 30 (27), a phase of life where many are completing their schooling, beginning their careers and individuating from their families of origin. The functional and psychological consequences of an episode of psychosis during this vulnerable and transitional time can be profound, and depressive symptoms are common before, during and after a first episode of psychosis (28). Antidepressants may be effective but as is the case with major depressive disorder (MDD) in the general population, this condition is often inadequately treated (29). Adjunctive treatment with dietary or physical activity interventions are supported by clinical research in individuals with MDD including in

FEP (30, 31). Quitting smoking has also been associated with a reduction in depressive symptoms (32). However, the effect of health behaviour interventions on depressive symptoms in youth with early psychosis is not clearly understood.

This thesis project therefore seeks to evaluate whether participating in a 12-week individualized health coaching intervention to target diet, physical activity and smoking cessation results in a reduction in depressive symptoms in youth with early psychosis as compared to access to an internet portal for self-management of the same health behaviours. It is hypothesized that individualized health coaching to target diet, physical activity and smoking will result in a greater decrease in depressive symptoms over the study period as compared to access to an online platform to guide self-management.

Chapter 2 - Body of the Thesis

Methods

Study Design

The current project is a secondary analysis of data collected as part of the TECC-Y study (1), which will be referred to as the parent study. The current thesis aims to evaluate whether participants of the parent study's high-intensity group experienced a change in depressive symptoms over time as compared with participants in the low-intensity group. The primary outcome of the parent study was participant engagement thus the parent study was not statistically powered to detect a change in depressive symptoms.

The parent study was a feasibility randomized controlled trial of a collaborative virtual care intervention developed to improve health behaviours in youth with first episode psychosis. Its aims were as follows: To evaluate participant engagement in TECC-Y, to compare the feasibility (recruitment and retention) of the HI and LI groups, to assess the feasibility of collaboration between different health disciplines in different institutions as part of the TECC-Y virtual care team and health coaches. It was hypothesized that participating in TECC-Y would increase participant engagement in addressing and ultimately improving health behaviours (diet, physical activity, smoking) and that TECC-Y would improve satisfaction of health care providers. Appropriate ethical approvals were obtained and the trial was prospectively registered with clinicaltrials.gov (Registry ID: NCT03610087). A full description of the parent study is available elsewhere (1).

Participants and setting

The parent study took place entirely via an online platform (www.mpateccy.net) or by telephone, including study visits, assessments and virtual care team meetings. There was no reimbursement for participants in the study. Relationships with participants' local care providers were uninterrupted. Inclusion criteria were the following: (a) age 16 to 29 years, (b) resident of Ontario, Canada, (c) clinical diagnosis of psychosis in the past 5 years, (d) currently stable on psychiatric medication (no changes to medication for 4 weeks), (e) access to telephone and/or internet, (f) able to provide informed consent and (g) able to understand and read English. Youth who became psychiatrically unstable during the study period were placed on hold and their capacity to re-join in the study was assessed by their treating team.

Participants were recruited from one of 3 participating hospital sites in Ontario: CAMH, SickKids and Trillium Health Partners. CAMH is a specialized mental health academic hospital and SickKids is a pediatric academic hospital; both are located in Toronto. Trillium Health Partners is a general community hospital situated in Mississauga, a city of 700,000 people located in the Greater Toronto Area. Following informed consent and randomization, participants were provided with a unique access code for the virtual platform. Research assessments were completed via the online platform at their own pace at baseline, 6, 12 and 24 weeks after the baseline visit. Recruitment commenced on 1 August 2018 and was completed on 31 December 2019. Follow-up ended on 31 March 2020.

Study intervention

The parent study intervention will be described here; please refer to Figure 1 for a visual representation. Participants were randomly assigned (1:1) to the intervention (high-intensity; HI) or comparison (low-intensity; LI) group. High-intensity participants completed a 12-week intervention that included virtual meetings with a health coach for up to 60 minutes per week. Health coaches assist patients in developing the skills and confidence they need to make changes in their self-identified health goals. The study health coaches worked individually with HI participants to improve health behaviours in 3 domains: physical activity, diet, and smoking. In addition, health coaches facilitated communication between participants' health care providers and recommended referrals to local resources. HI participants also received access to an interactive custom-designed e-platform with infographic modules and webinars designed by the research team.

The TECC-Y intervention was designed to promote health behaviour change by increasing access to high quality individualized care that would otherwise be difficult to access due to geographic, financial, or logistical barriers. On a weekly basis, health coaches met by phone with the virtual care team, which consisted of a psychiatrist, addictions specialist, physical activity specialist, nutrition specialist, and person with lived experience of mental illness. Cases were discussed in an interdisciplinary rounds format and virtual care team members provided supervision and recommendations to the health coaches on a weekly basis. The following elements of psychiatric care were employed by the health coaches in working with study participants: motivational interviewing, behavioural activation, cognitive adaptation training, goal setting, and therapeutic alliance. Participants randomized to the LI intervention received

access to the e-platform only, which included modules to guide self-management and a discussion board moderated by the health coaches. The modules were based on the healthy living modules from the NAVIGATE program (33) and adapted to a self-learning format with an appropriate level of complexity for individuals with severe mental illness. LI participants did not have access to individual sessions with the health coaches. All assessments were completed using the e-platform in both groups over the study period.

Throughout the HI intervention, health coaches encouraged participants to explore the impact of their substance use (including cigarettes) on their mental and physical health, set goals related to substance use, explore barriers to change, and reduce or abstain from substance use. The adoption of a harm reduction or abstinence-based approach was guided by participant goals. Motivation to change health behaviours was measured at baseline, 6 weeks, 12 weeks and 24 weeks using a readiness ruler (visual analog scale) to rate participants' perceived importance and confidence in making changes to their diet, physical activity and smoking. The VCT provided guidance to health coaches on the implementation of other motivational interviewing techniques based on weekly rounds discussions between the health coaches and VCT. When nicotine replacement or other medical or external supports were indicated, health coaches provided referral or facilitated connections with local community resources. The study intervention did not include direct prescription of nicotine replacement treatment. We did not measure the possible impact of nicotine replacement treatment on antipsychotic medication dosing or account for possible anti-depressant effects of nicotine replacement treatment. The dietary intervention was centred on improving nutrient density as opposed to restricting calories. Participants were educated about the Mediterranean dietary pattern and specific nutritional recommendations were

developed for each participant based on their goals, preferences and limitations. Efforts were made to provide participants with feasible strategies to implement dietary recommendations such as recipes, shopping lists or education regarding basic cooking skills.

In general, health coaches supported participants to increase daily physical activity by encouraging more physical activity into daily life (i.e. walking or biking for transit, taking the stairs) in addition to structured exercise time (i.e. running, strength training, yoga). Individualized practical strategies were provided including referral to community resources where participants could access facilities for physical activity (i.e. recreation centres, parks, low-cost fitness) and specific exercise programs when indicated. Efforts were made throughout the study period to engage participants in a client-centred manner by focusing on goals that were important to them while gently challenging them to explore areas core to the study intervention. Participants were repeatedly encouraged to reflect on the impact of their health behaviours on their physical and mental health.

Outcome Measures

A variety of measures were utilized to collect data in the parent study at baseline, 12 and 24 weeks. They will be outlined here followed by a more detailed description of the measures of interest to the current thesis. Participant engagement was measured using a visual analog scale. For example, “On a scale of 1 to 10, by participating in this program, I believe I will be able to make positive changes to how I eat / my level of physical activity / my smoking”. Engagement was also measured through data analytics of e-platform use and number of contacts with the health coach. Validated scales were used to measure the following: Medication Adherence

Rating Scale (MARS), Alcohol Smoking and Substance Involvement Screening Test (ASSIST), Heaviness of Smoking Index (HSI), Alcohol Use Disorders Identification Test (AUDIT), Quality of Life Scale (QLS) semi-structured interview. A Readiness Ruler (RR) was used to measure participants' confidence and importance of making changes in health behaviours using a visual analog scale from 1-10. These Demographic information and information about psychiatric medications was also collected at baseline.

Depressive symptoms were measured using the Quick Inventory of Depressive Symptomatology (QIDS-SR). This is a self-report 16-item questionnaire with a score ranging from 0-27. A score of 6-10 is considered to be consistent with mild depression, 11-15 with moderate depression and 16-27 with severe depression. This questionnaire has been validated for use in youth (34). The QIDS-SR has also been demonstrated to reliably measure depressive symptoms in individuals with schizophrenia in accordance with the aforementioned cut-offs and was found to agree moderately with the CDSS, the gold standard for measuring depressive symptoms in schizophrenia (35).

Physical activity was measured using the Simple Physical Activity Questionnaire (SIMPAQ) (36). This is a 5-item clinical tool designed to assess levels of physical activity in populations at high risk of sedentary behaviour. It has been validated for use in 23 countries (37). For an estimate of total self-reported moderate-vigorous physical activity (MVPA) time, time spent walking (box 3) and exercising (box 4) were combined to provide total MVPA (hours per week).

Diet quality was measured via adherence with the Mediterranean dietary pattern with the Mediterranean Diet Adherence Screener (MEDAS) (38). This dietary pattern was chosen since the Mediterranean diet is widely accepted as a dietary strategy to promote cardiometabolic health (39). The 14-item MEDAS questionnaire has been validated in several countries across Europe as well as a UK population at high risk of cardiovascular disease (40, 41), but not for use in youth or mental health populations. No tool to assess Mediterranean diet adherence specifically for youth was available at the time of study design, but we were not the first group to utilize the MEDAS in a young adult population. A recent population-based study of diet quality and correlates among n=3031 Lithuanian youth aged 18-36 found that higher score on the MEDAS was associated with female gender, higher levels of education and higher levels of physical activity (42). Specifically, the MEDAS asks about two eating habits: A preference for olive oil and white vs. red meat. The following 12 items capture the frequency of consumption of various food categories: Olive oil, animal fat, vegetables and fruits, fish, nuts, commercially available pastries / cakes / cookies, sugar sweetened beverages and meals cooked with garlic, onion, or tomato. The questionnaire also asks about moderate red wine consumption. A score of 0 is assigned to an item where the users' consumption does not meet criteria for a pre-defined level of "healthy consumption" and 1 is assigned if the user meets criteria for "healthy consumption" of the item.

Given the questionnaire has not been validated for youth or mental health populations and that our study involved participants who are at risk for either cognitive impairment or negative symptoms, a few modifications to the MEDAS were initiated. The language was simplified and we provided examples of portion sizes using the "Zimbabwe hand jive" method (43). The item

pertaining to moderate alcohol consumption was also removed to avoid any misinterpretation that the study team was recommending alcohol use to our participants. This meant that the scale was scored out of 13 instead of 14 points. Please refer to Table 1 for the adapted version of the MEDAS questionnaire. A score less than 7 is considered low adherence with a Mediterranean diet, medium adherence was defined as 8-9 points and high adherence by greater than 10 points. Given strong evidence supporting the Mediterranean diet in prevention and treatment of major depressive disorder and cardiovascular disease, high adherence with a Mediterranean dietary pattern was used as a proxy for high diet quality in the TECC-Y study.

Statistical Analysis

Descriptive statistics by group were calculated including reporting on baseline QIDS-SR score by group and overall. For intervention effects on depressive symptoms (QIDS-SR), mixed effects models were applied with random intercepts and identify link functions. Time was measured as the number of days elapsed between the study baseline and each administration of the outcome instrument for each individual. Time effects were treated as linear and group differences were tested over time with group*time interaction terms. Because randomization produced a moderate group imbalance on employment status, we also conducted a sensitivity analysis by repeating models for health behaviour outcomes with the addition of employment status and an employment status*time interaction. We included all participants who provided data sufficient for analysis, regardless of the treatment received, consistent with intention to treat analysis. All statistical analysis was completed using Stata 16 (StataCorp. 2019. Stata Statistical Software: Release 16. College Station, TX: StataCorp LLC).

Results

In the parent study, n=510 participants were assessed for eligibility, with n=70 randomized to either the LI or HI group. The TECC-Y CONSORT diagram is displayed in Figure 2 and specifies reasons participants were excluded from or ineligible for the study. The current thesis analyzed data from the same participants as the parent TECC-Y study.

Baseline sample characteristics are shown in Table 2. The analysis included n=23 participants in the LI group and n=29 in the HI group. The mean age of participants was 23.4 (SD=3.1) and in both groups, nearly half of participants identified as non-white. Most participants had a self-reported diagnosis of unspecified schizophrenia spectrum and other psychotic disorder followed by bipolar disorder, schizophrenia, schizoaffective disorder and psychotic depression. Groups were generally similar at baseline, except that considerably more participants in the LI group reported their working status as 'unemployed'. There were no group differences in baseline data for diet quality, smoking, and physical activity.

The mean QIDS-SR at baseline was 9.3 (SD=5.4), which is consistent with mild depression overall. There was no significant difference in mean QIDS-SR score across groups at baseline (2 tailed unpaired t test, p=0.85). Combining both groups at baseline, 10% met criteria for severe depression, 31% met criteria for moderate depression, 29% met criteria for mild depression and 30% did not demonstrate clinically significant depressive symptoms based on QIDS-SR scores.

Change over 24 weeks differed significantly between groups for the QIDS-SR: -0.94 (95% CI = -1.56 to -0.32) with a statistically significant reduction in depressive symptoms over time in the

HI group as compared to the LI group. Specifically, QIDS-SR scores decreased by 0.94 points per month (30 days) in the HI group as compared to the LI group, resulting in a relative reduction in QIDS-SR scores of 5.26 points (SMD = 0.97, large effect size) over 24 weeks in the HI group as compared to the LI group. Table 3 reports change over 24 weeks by group for depressive symptoms, diet quality and physical activity.

Chapter 3 - Discussion

Summary of main findings

In conclusion, we report that participating in a 12-week individualized virtual heath coaching intervention to target diet, physical activity and smoking resulted in a statistically significant decrease in depressive symptoms for youth with first episode psychosis as compared to a control group who received access to online materials about diet, physical activity and smoking to guide self-management. Statistically, this finding has a large effect size; from a clinical perspective, a change in 5.26 points on the QIDS-SR over 24 weeks is significant, representing a 20% reduction in depressive symptoms. This pilot data represents the first evidence that a virtual care intervention to target health behaviours can improve depressive symptoms in youth with FEP. Depressive symptoms are common in this population, inadequately treated, and have important implications for suicide risk, functioning and engagement in care (44). Interventions targeting health behaviours in youth with FEP may in turn result in an improvement in physical health by modifying risk factors for metabolic and cardiovascular disease.

Context of the current literature

Previous studies have measured the prevalence of major depressive episodes in youth who have experienced a first episode of psychosis: depression is a common comorbidity. A cohort study of n=122 adults with FEP reported that 30% of participants met criteria for a major depressive episode according to the Calgary Depression Scale for Schizophrenia (CDSS) either during or after the onset of psychosis (45). In a follow-up study, 35% of the original sample were

depressed one year later (46). In our own study, 70% of participants demonstrated clinically significant depressive symptoms at baseline with 41% classified in the moderate to severe range.

Clinical trials have demonstrated the efficacy of dietary interventions as adjunctive treatments for depressive symptoms in the context of major depressive disorder (MDD). The first randomized controlled trial of a whole-diet (dietary pattern) intervention as an adjunctive treatment for MDD was published in 2017. In that study, authors recruited adults with at least moderate severity MDD and a relatively poor diet quality. Participants in the intervention group experienced a statistically significant reduction in depressive symptoms over the study period as compared to the control group with a number needed to treat of 4.1 for remission from depression (47). This intervention also proved cost effective (48). In a subsequent study, youth with elevated levels of depressive symptoms (moderate to severe symptoms on DASS-21 depression subscale) and poor diet quality were randomized to a 3-week dietary intervention or habitual diet group. Participants in the intervention group experienced a statistically significant reduction in depressive symptoms (measured by CES-D) as compared to the habitual diet group consistent with a moderate effect size (cohen's d = 0.65) (49). Until now, however, no studies have examined the effects of dietary intervention on depressive symptoms in a first episode psychosis population.

According to a Cochrane review, exercise is moderately effective as a treatment for MDD (30). Exercise is recommended as a first line monotherapy for mild to moderate depression in the most recent CANMAT guidelines, the Canadian treatment guidelines for MDD (50). Meta-analytic data has revealed that exercise can improve a range of clinical symptoms in schizophrenia

including depressive symptoms (51). Fewer studies have examined the impact of exercise interventions on depressive symptoms in first episode psychosis. According to one randomized-controlled trial, participating in a 12-week yoga or aerobic exercise intervention resulted in a decrease in depressive symptoms (CDSS) with moderate effect size as compared to waitlist control in women with early psychosis (52).

Smoking cessation has been shown to improve both depressive and anxiety symptoms, and not to exacerbate symptoms of schizophrenia (19, 32). No studies have evaluated the effect of smoking cessation on depressive symptoms in youth with FEP.

Various mechanisms have been suggested to explain the positive effects of dietary and exercise interventions on depressive symptoms. In youth with first episode psychosis, it has been observed that exercise interventions can reduce systemic inflammation (IL-6 levels) (53) and markers of oxidative stress (54), two biological mechanisms that have been implicated in the etiology of depression as well as early psychosis. Dietary interventions may exert their positive effect on depressive symptoms in early psychosis by a variety of mechanisms including impacts on the gut microbiome and gut-brain axis, reducing systemic inflammation and oxidative stress and by addressing vitamin and mineral insufficiency (55). One cannot ignore the possible psychological therapeutic benefit for depression of engaging with a health care provider to discuss health behaviours such as diet and exercise regardless of actual behaviour change.

According to a systematic review and meta-analysis of barriers and facilitators to exercise in individuals with severe mental illness (SMI), the most common barriers were low mood and

stress (61% of patients) and lack of support (50%). Conversely, the most common motivators to participate in exercise were improving mood (81%) and reducing stress (78%) (56). An emphasis on these more proximal consequences of health behaviour change (as compared to preventing cardiovascular disease in the long term) may serve to enhance compliance and motivation to participate in interventions to target health behaviour change. This may particularly relevant in the setting of negative or cognitive symptoms in the context of early psychosis.

Strengths and limitations

A notable strength of this thesis is the novelty and relevance of its findings. We are the first to report that a virtual health coaching intervention to target health behaviours can improve depressive symptoms in FEP as compared to access to materials to guide self-management of health behaviours. This is relevant given the frequency and significance of inadequately treated depressive symptoms in FEP. Our findings must also be considered in the context of mitigating metabolic dysregulation during treatment with antipsychotic medications. Although not the focus of the current thesis, it is widely accepted that helping patients with FEP to quit smoking, improve diet quality and increase physical activity can have positive impacts on their risk of metabolic and cardiovascular disease. Furthermore, the virtual delivery of the TECC-Y health coaching intervention is timely given the recent uptick in acceptability and implementation of virtual mental health care due to the COVID-19 pandemic.

The current thesis is not without limitations. Given that the parent study was designed as a feasibility trial to evaluate participant engagement, it was not powered to detect clinically

meaningful effects on health behaviours or other clinical outcomes. The original target sample size was n=120 participants though recruitment and obtaining REB approvals and data sharing agreements from three institutions proved challenging and n=70 participants were randomized. Of the n=52 participants with adequate data available for analysis, only 5 participants reported severe depressive symptoms at baseline and 30% did not demonstrate clinically significant depressive symptoms at baseline. Thus, only n=34 participants reported clinically significant depressive symptoms at baseline. As such, scale attenuation (floor effect) may have limited the effectiveness of the study intervention. Group allocation was unblinded to both participants and evaluators following group assignment, which could have led to expectation bias from the perspective of participants. The self-report nature of outcome measures likely mitigated any possible expectation bias from the perspective of evaluators. Lastly, the number and intensity of study visits was not balanced between the groups. It is possible that the observed effect is attributable in part to the increased social support received by participants in the virtual health coaching group (i.e. not specific to the intervention itself), as compared to participants assigned to self-management (57). In order to be included in the study, participants were required to be clinically stable with no changes in antipsychotic medication for 4 weeks prior to study entry. That being said, it is possible that medication changes during the study period could have impacted depressive symptoms.

Future directions

This pilot data supports the completion of larger, adequately powered studies to first evaluate whether a virtual health coaching intervention is effective to change health behaviours in this

population and whether these changes translate to improvements in physical and mental health outcomes. A larger sample size would increase statistical power to control for potential confounders such as financial status. In a subsequent clinical trial, other mental health outcomes could be considered such as PANSS or BPRS and a minimum level of depressive symptoms could be required at baseline as an inclusion criteria. Lastly, the control intervention would need to be reconsidered to ensure that the frequency and length of visits with the research team are balanced across both groups.

Tables and figures

Table 1: Adapted 13-item Questionnaire of Mediterranean diet adherence

Questions	Criteria for 1 point
1. Is olive oil the main cooking fat used?	Yes
2. How many tablespoons of olive oil are used each day? Include cooking, salads, and meals eaten away from home.	≥4 tbsp
3. How many servings of vegetables do you eat per day? - 1 serving = 1 fist of leafy vegetables or ½ fist of canned, fresh, or frozen vegetables	≥2 (≥1 portion raw or as a salad)
4. How many servings of fruit do you eat per day? - 1 serving = 1 whole fruit (1 fist) or ½ fist of canned, fresh, or frozen fruit	≥3
5. How many servings of red meat, hamburger, or sausages do you eat per day? - 1 serving = palm of hand	<1
6. How many servings of butter, margarine, or cream do you eat per day? - 1 serving = 1 thumb	<1
7. How many sugar sweetened beverages do you drink per day? - 1 serving = 1 small can (330 ml)	<1

Questions	Criteria for 1 point
8. How many servings of beans and legumes do you eat per week? - 1 serving = 1 fist (cooked)	≥3
9. How many servings of fish/seafood do you eat per week? - 1 serving = palm of hand	≥3
10. How many times per week do you eat packaged or store bought cakes, pastries, cookies etc…	<3
11. How many servings of nuts do you eat per week? - 1 serving = 1 cupped hand or 2 thumbs of nut butter	≥3
12. Is chicken, turkey or rabbit usually eaten instead of veal, pork, hamburger or sausage?	Yes
13. How many times per week do you eat pasta, rice, or vegetable dishes seasoned with garlic, onions, leeks, or tomato sauce?	≥2

Table 2. Sociodemographic Variables at Baseline by Study Group (N (%))

	Study Group	
	Low Intensity (n=23)	**High Intensity (n=29)**
Age (mean (SD)) (missing = 6)	24.3 (SD=2.9)	22.7 (SD=3.2)
Gender (missing = 2)		
Female	13 (57%)	11 (41%)
Male	10 (43%)	15 (56%)
Other	0 (0%)	1 (4%)
Born in Canada (missing = 2)	11 (48%)	18 (67%)
Cultural identity = White or European (missing = 2)	11 (48%)	13 (48%)
Highest Level of Education (missing = 2)		
< Secondary	2 (9%)	2 (7%)
Secondary	8 (36%)	9 (33%)
Any post-secondary	13 (57%)	16 (59%)
Marital Status (missing = 3)		
Single or separated	18 (82%)	26 (96%)
Cohabiting	4 (18%)	1 (4%)
Worked in Past Year (missing = 4)	10 (45%)	16 (62%)
Employment status (missing=2)		
Student, Retired, Housewife/husband	4 (17%)	5 (19%)
Disability	0 (0%)	1 (4%)
Employed (including self-employed)	7 (31%)	14 (52%)
Volunteer work, unpaid	2 (9%)	0 (0%)
Unemployed	12 (52%)	7 (26%)
Financial Situation (missing = 2)		
Can't make ends meet	6 (26%)	2 (7%)
Have just enough to get along	11 (48%)	11 (41%)
Are comfortable	1 (4%)	5 (19%)
Supported by a caregiver	5 (22%)	9 (33%)
Body Mass Index Category (missing = 19)		
Normal (18.5 to 25)	3 (30%)	10 (43%)
Overweight (25 to <30)	4 (40%)	8 (35%)
Obese (≥30)	3 (30%)	5 (22%)
Primary Psychotic Disorder (missing = 6)		
Schizophrenia	3 (14%)	3 (13%)
Schizoaffective Disorder	2 (9%)	3 (13%)
Bipolar I Disorder	6 (27%)	6 (25%)
Depression with Psychosis	1 (5%)	2 (8%)
Unspecified Schizophrenia Spectrum or Other Psychotic Disorder	10 (45%)	10 (41%)
Comorbid Mental Health Diagnosis (Self-Report) (missing = 5)		
Depression	4 (17%)	5 (21%)
Anxiety (apart from PTSD)	5 (22%)	3 (13%)
Trauma-related (PTSD or DD)	2 (9%)	2 (8%)

Figure 1. TECC-Y model for High-Intensity (Intervention Group) Participants

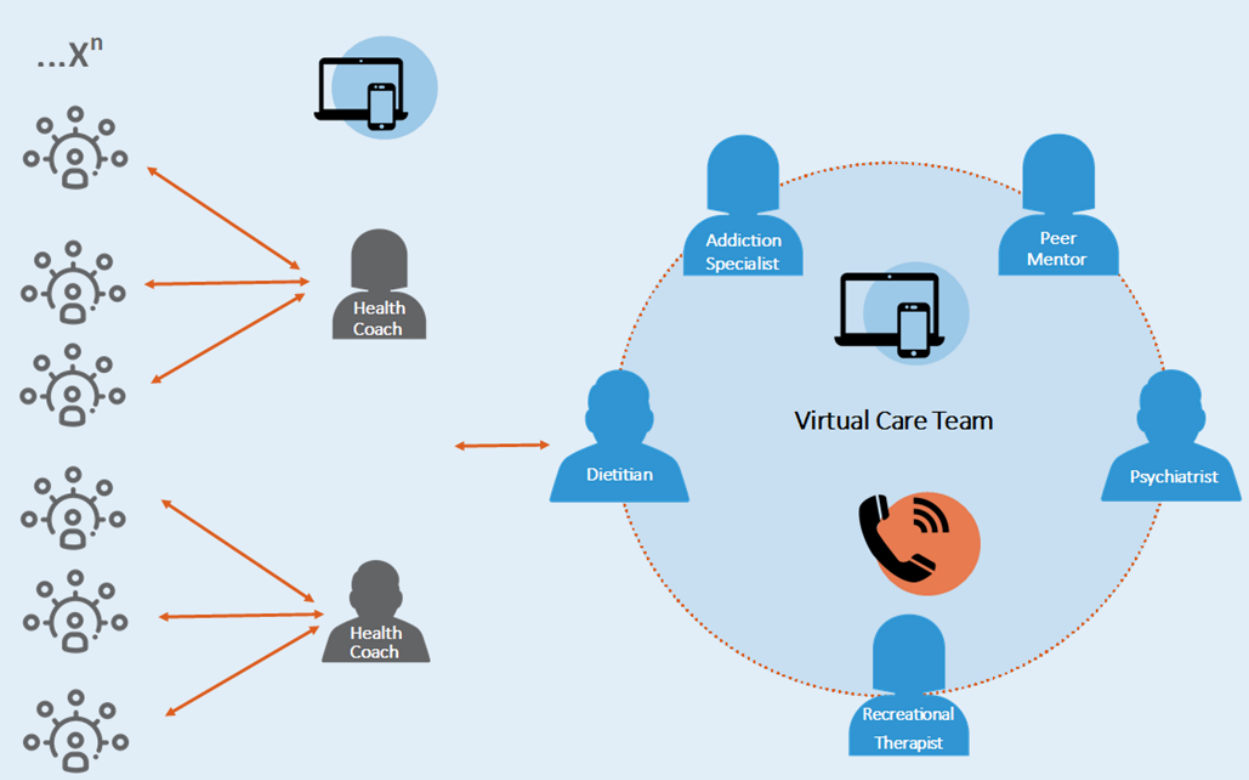

Figure 2: TECC-Y Consort Diagram

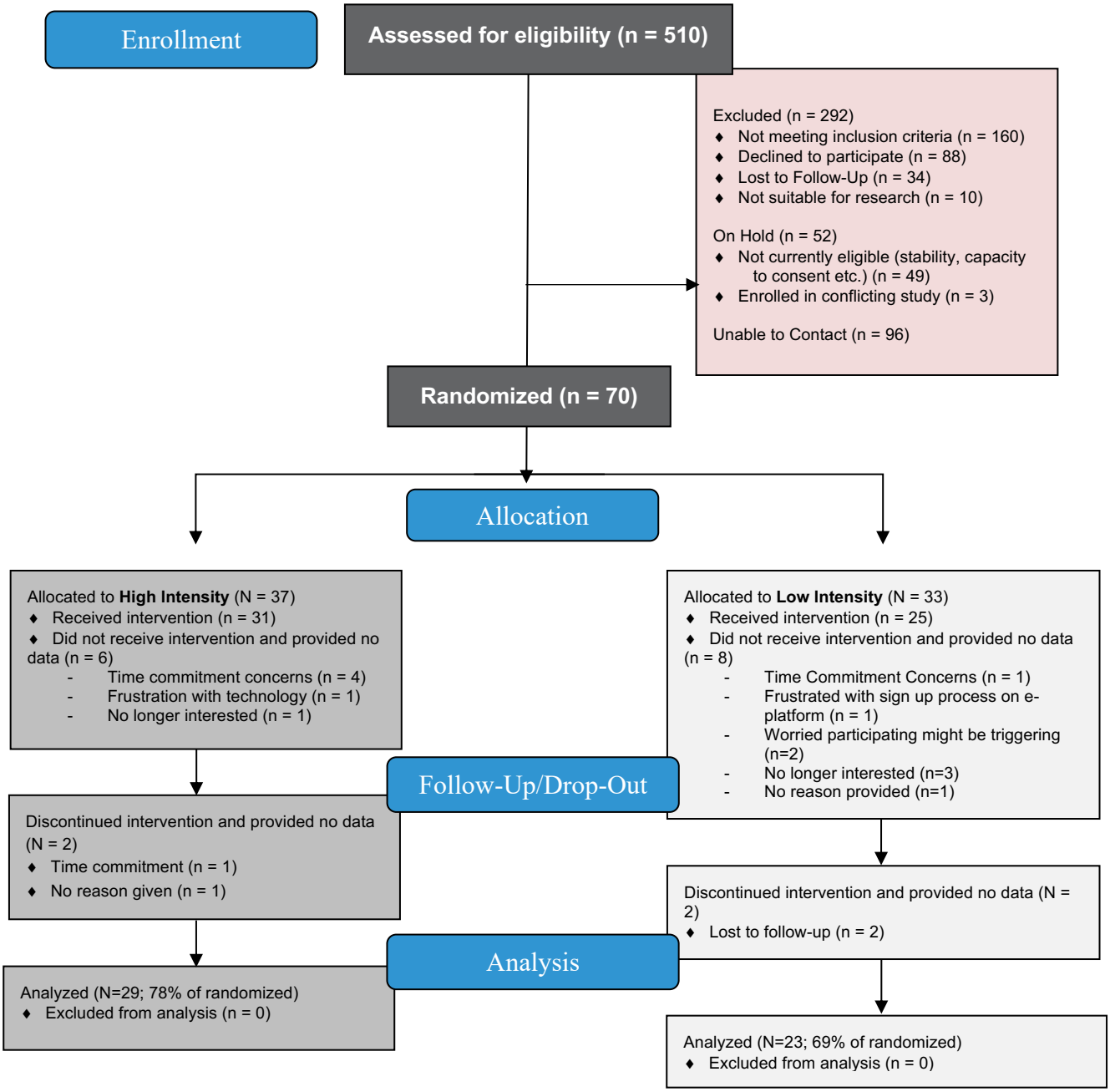

Table 3: Model fixed effect coefficients for all depressive symptoms, diet quality and physical activity

	n	Group=HI	p	Time (30d)	p	Group*time	p	Intercept	p
MEDAS	49	1.12 (0.06, 2.18)	0.04	0.1 (-0.07, 0.28)	0.23	-0.03 (-0.27, 0.2)	0.78	2.96 (1.63, 4.3)	<0.001
QIDS	49	-0.46 (-3.19, 2.28)	0.74	0.29 (-0.16, 0.74)	0.2	-0.94 (-1.56, -0.32)	0.003	8.17 (4.75, 11.59)	<0.001
SIMPAQ: Average MVPA	26	0.11 (-1.3, 1.52)	0.88	0.14 (-0.2, 0.49)	0.42	-0.07 (-0.52, 0.39)	0.78	0.58 (-0.96, 2.13)	0.46

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