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The effect of executive function on adherence with a cardiac secondary prevention program and its interaction with an incentive-based intervention

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ABSTRACT

Participation in secondary prevention programs such as cardiac rehabilitation (CR) reduces morbidity, mortality, and hospitalizations while improving quality of life. Executive function (EF) is a complex set of cognitive abilities that control and regulate behavior. EF predicts many health-related behaviors, but how EF interacts with interventions to improve treatment adherence is not well understood. The objective of this study is to examine if EF predicts CR treatment adherence and how EF interacts with an intervention to improve adherence. Data were collected from 2013 to 2018 in Vermont, USA. 130 Medicaid-enrolled individuals who had experienced a qualifying cardiac event were enrolled in a controlled clinical trial and randomized 1:1 to receive financial incentives for completing secondary prevention sessions or to usual care. In this secondary analysis, effects of EF on CR adherence (defined as completing ≥30/36 sessions) were examined in 112 participants (57 usual care, 55 intervention) who completed an EF battery. Delay-discounting, a measure of impulsivity, predicted CR adherence ($p = 0.01$) and interacted with the incentive intervention, such that those who exhibited greater discounting of future rewards benefitted more from the intervention than those who discounted less ($F(1, 104) = 5.23$, $p = 0.02$). Better cognitive flexibility, measured with the trail-making-task, also predicted CR adherence ($p = 0.02$). While EF has been associated with adherence to a variety of treatment regimens, this interaction between an incentive-based intervention to promote treatment adherence and EF is novel. This work illustrates the value of considering individual differences in EF when designing and implementing interventions to promote health-related behavior change.

1. Introduction

Adherence to secondary prevention guidelines following a major cardiac event results in a decrease in cardiac mortality and cardiac events and reduced hospitalizations (Ades, 2001; Doll et al., 2015; Anderson et al., 2013). For example, after a major cardiac event such as myocardial infarction (MI) or coronary artery bypass graft surgery (CABG), completion of cardiac rehabilitation (CR), a secondary prevention program, is associated with a 31% reduction in one-year hospital readmissions, a 26–36% reduction in cardiovascular mortality, and a 26% reduction in all-cause mortality (Heran et al., 2011; Taylor et al., 2004; Lawler et al., 2011). Consequently, attendance at CR is given the highest level of recommendation (i.e. Class 1) and strength of evidence in the secondary prevention guidelines established by the American Heart Association (AHA) and the American College of Cardiology (ACC) (Anderson et al., 2013).

However, adhering to secondary prevention programs such as CR can be challenging. Only 18–34% of eligible patients in the US attend CR (Suaya et al., 2007; Fang, 2017), and not all patients who attend complete the program (Martin et al., 2012; Pack et al., 2015; Armstrong et al., 2015). Completion of these programs is particularly challenging for vulnerable populations such as patients with lower-socioeconomic status (SES), who complete significantly fewer sessions than their higher-SES counterparts (Gaalema et al., 2017a; Gaalema et al., 2017b; Daly et al., 2002). This limited success in secondary prevention is problematic as patients with lower-SES are also at higher risk for recurrent cardiac events and death compared with their more affluent or better-educated counterparts. For example, following discharge from a hospitalization for MI, patients with lower-SES have a 1-year death rate following discharge more than double that of more affluent patients

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(Alter et al., 2006; Govil et al., 2009). Given the remarkably high-risk profiles of patients with lower-SES, and their increased risk of morbidity and mortality from cardiovascular disease, understanding their unique obstacles to accessing treatment and improving attendance at CR is a necessary challenge.

One inherent patient characteristic that has been found to predict treatment adherence is executive function (EF). EF is a broad term to describe top-down cognitive processes underlying decision-making and behavior regulation. One way EF has been described is as "the ability to maintain and manage goals, and use those goals to bias ongoing processing"(Friedman and Miyake, 2017). Secondary prevention is a complex set of goals that require prioritizing, advanced planning, and resisting impulsive choices, processes that require the behavioral and cognitive capabilities that fall under the EF domain. In addition to medication adherence and changes in diet and physical activity, attending a secondary prevention program such as CR requires planning to schedule appointments, remembering to attend and dress appropriately, organizing coverage for other responsibilities, and obtaining transportation. Additionally, participation in the program entails engaging in behaviors (exercise) or inhibiting others (smoking) that, while beneficial in the long term, may be unpleasant in the short term. EF has been shown to be useful in understanding many health-related behaviors (Hall and Marteau, 2014), and has been demonstrated to predict adherence to medical regimes including appropriate medication dosing, exercise interventions, and heart failure management (Hall et al., 2008; Stilley et al., 2010; McAuley et al., 2011; Alosco et al., 2012).

EF has also been shown to correlate with SES (Hackman et al., 2010), such that lower-SES populations have more EF challenges. This correlation could help explain the disparity seen in completion of secondary prevention programs by SES (Gaalema et al., 2017a; Gaalema et al., 2017b). Given that populations with lower-SES may encounter more obstacles to accessing care (i.e. transportation, time off of work, etc.) and accessing care places higher demands on what may already be a reduced set of cognitive resources, the lower adherence to secondary prevention for these patients is not surprising. Therefore, interventions that target EF deficiencies or work to ease EF effort may be particularly effective for this population.

Given the importance of completing secondary prevention programs such as CR, designing interventions to improve program completion is critical. Understanding how interventions interact with EF processes can improve how we design and implement interventions to promote secondary prevention. Individual facets of EF are both correlated and distinct (Miyake and Friedman, 2012), suggesting that they could differentially interact with interventions. For example, interventions to support issues with planning and execution of complex behavior may not be as effective with patients whose difficulties are with self-regulation. One way to begin to tease out this relationship is to test the associations of different aspects of EF with program adherence within the context of a successful adherence intervention.

One promising intervention, often referred to as contingency management, improves treatment adherence by providing financial incentives contingent upon objective verification of successful completion of treatment visits (Gaalema et al., 2019; Higgins et al., 1994). Incentives improve adherence and completion by supplying an immediate reinforcer to bridge the temporal gap between current behavior (adherence) and longer-term health outcomes (Bickel et al., 2014; Higgins et al., 2012; Odum, 2011; Silverman et al., 2019). It has also been hypothesized that incentives may be especially useful in patients who make impulsive choices (have a bias towards responding to immediate consequence and discounting delayed consequences), as incentives could potentially harness this bias towards the immediate outcome by providing an immediate positive outcome (Higgins et al., 2012; Ades and Gaalema, 2012).

A recently completed clinical trial provides a unique opportunity to examine issues of EF and secondary prevention adherence. In this trial hospitalized patients were randomized to either usual care or to contingency management, where they received incentives for attending and completing secondary prevention rehabilitation sessions. Participants also completed a comprehensive EF battery allowing us to examine the questions of how different facets of EF predict adherence to a secondary prevention program and how they interact with an incentive-based intervention to increase program adherence.

2. Methods

Detailed descriptions of the intervention are published elsewhere (clinicaltrials.gov NCT02172820) (Gaalema et al., 2019; Gaalema et al., 2016). Briefly, 130 lower-socioeconomic status patients (defined as receiving state-supported insurance, e.g. Medicaid) who experienced a cardiac event qualifying them for enrollment in a secondary prevention program (cardiac rehabilitation) were randomized to a usual care condition or to a condition where they received financial incentives on an escalating schedule for completing CR program visits. The CR program is an outpatient program consisting of 36 individualized progressive exercise sessions coupled with symptom monitoring and educational sessions. Data presented here are from the 112 participants who completed the EF battery which was collected prior to intervention delivery. Those who attended at least 30 visits were considered to have completed the CR program. Data included in this study were collected from 2013 to 2018 and analyzed in 2018 and 2019. All study procedures were approved by the University of Vermont IRB.

2.1. Behavioral economics and intervention services assessment battery

The Behavioral Economics and Intervention Services Core (BEIS) within the Vermont Center on Behavior and Health (VCBH) supports investigators studying health-related decision-making and its neurobiological underpinnings. The BEIS' EF assessment battery includes standard measures of EF (below) as well as IQ, mood, and quality of life. Measures encompass multiple cognitive domains and testing types (non/standardized and objective/subjective), to maximize the EF profiles captured.

The vocabulary and matrix reasoning subtests of the Wechsler Abbreviated Scale of Intelligence - IV (WASI) were administered to provide an estimate of full scale IQ (Weschler, 1999). Self-perceived overall health status was measured using the visual analogue scale (anchors; "Best imaginable health state" at 100 and "Worst imaginable health state" at 0) from the Euro-Quality of Life (EQ-5D™), a standardized, self-report measure of health outcome for use in adults {euroqol.org}. Mental health was assessed using the "anxious/depressed syndrome" and the "total problems" scales from the Achenbach System of Empirically Based Assessment (ASEBA®). The Adult Self Report (ASR; for use in adults 18–59 years) (Achenbach and Rescorla, 2003), and the Older Adult Self Report (OASR; for 60 years and above) (Achenbach et al., 2004). T-scores from both scales have been normed by age and sex. Borderline and clinical levels (T-scores ≥ 65 or ≥60, respectively) can distinguish clinically-referred individuals.

Objective EF was characterized using a variety of measures. The Delay Discounting (DD) task models impulsivity by presenting a series of hypothetical choices between receiving $1000 after some delay (1 day, 1 week, 1 month, 6 months, 1 year, 5 years, and 25 years) or a smaller amount immediately (ranging from $40 to $990) (Bickel et al., 1999). The task is adaptive and adjusts the immediate value until it is worth the same as the delayed value, the "indifference point." The indifference points are then plotted as a function of the standardized delay curve (where 25 years = 1). Responses on DD hypothetical tasks have been shown to correspond closely to tasks using real rewards (Johnson and Bickel, 2002). The variable of interest is the Area Under the plotted Curve (AUC), calculated by dividing the curve into trapezoids and totaling the area of each. The area is equal to $(x2 - x1)[(y1 + y2)/2]$, where x1 and x2 are successive delays, and y1 and y2 are the indifference points associated with these delays (Myerson et al., 2001). AUC ranges from 0 to 1, with 1 representing no discounting. Two tests from the Delis-Kaplan Executive Function System (D-KEFS™) (Delis et al., 2001) were administered; the Trail Making Task (TMT) assesses cognitive flexibility and the Tower Task requires spatial planning and problem solving. Variables of interest, normed by age and presented as scaled scores, included time to completion of the number-letter switching condition on the TMT and the total achievement score on the Tower Task. The Stop Signal Task (SST) is a computer-administered test of response inhibition. Briefly subjects responded to two equally probable "go" signals (the letters "X" or "O") unless accompanied by an auditory "stop". The interval between the onset of the go and stop signals was adjusted to achieve a 50% inhibition success rate (valid if within 31–68%). Dependent variables include the "go" reaction time (GoRT), variability of GoRT (larger standard deviation of GoRT indicate deficits in attention), and stop signal reaction time (longer SSRT indicates deficits in response inhibition) (Logan et al., 1984; Logan et al., 1997).

Subjective EF was assessed using the Behavioral Rating Inventory of Executive Function, a validated and standardized measure of subjective executive function in an everyday environment (BRIEF-A) (Roth et al., 2005). The BRIEF-A consists of 75 items measuring two indices: the Behavioral Regulation Index made up by inhibit, shift, emotional control, and self-monitor scales and the Metacognition Index including initiate, working memory, plan/organize, task monitor and organization of materials scales. A Global Executive Composite score provides a summary of EF overall. Higher scores indicate more problems and thus worse EF. T scores are determined by age against a national sample. Impairment was defined as a T-score equal to or > 65. All data included in this analysis passed the three validity scales included in the measure (negativity, infrequency, and inconsistency).

All statistical analyses were done using SAS 9.4. Descriptive statistics, see Table 1 for a comprehensive list of variables examined, are reported for intake data and differences between study conditions were identified using chi square and Student's *t*-test. Repeated, mixed model ANOVAs were used to test for interactions with the intervention. Finally, a logistic model including all variables with a significant main effect ($p < 0.05$) on CR completion was fitted to the data.

3. Results

Of the 130 participants randomized 86% (112) completed the intake assessment, which included the EF battery. Attendance at intake did not differ by treatment condition (57 control, 55 intervention). Baseline demographics of the sample by treatment condition and by CR non/completer group are presented in Table 1. Consistent with what was reported in the main outcomes paper, which included all 130 participants (Gaalema et al., 2019), the incentive intervention improved adherence, nearly doubling completion of the CR program within the 112 participants who completed the EF battery (65% vs. 33%). Consistent with the main outcomes (Gaalema et al., 2019), smoking status, and assignment to the incentives intervention were significant univariate predictors of CR completion. However, unlike the main outcomes paper, age was also a significant univariate predictor, with younger patients less likely to complete the program. No other clinical or demographic characteristics examined differed significantly at baseline between those who did and did not successfully complete CR.

Patients in this study were fairly typical for lower-SES patients in this area. All were insured through Medicaid (and thus had limited income) and only 17% had achieved a college degree. Of those who were of working age (< 65), only 35% were employed. Patients also tended to be rural, only 36% lived within 10 km of the CR clinic. Of those further than 10 km from the clinic, average distance from the clinic was 34 km.

EF at intake is presented for the entire cohort and by non/completer group in Table 1. Performance by the cohort overall on standardized measures (BRIEF-A and D-KEFS) fell within the average range

Table 1
Baseline characteristics by CR completion.

	Total (n = 112)	Completer (n = 55)	Non-completer (n = 57)	p value
Incentives condition	55 (49)	36 (65)	19 (33)	0.0007
Female	41 (37)	23 (42)	18 (32)	0.2608
Age (range 29–80)	57.5 (9.5)	59.6 (9.4)	55.5 (9.2)	0.0208
Education (years)				
≤11 or GED	35 (31)	15 (27)	20 (35)	0.3723
12 (HS diploma)	30 (27)	13 (24)	17 (30)	0.4595
13–15	28 (25)	14 (25)	14 (25)	0.9128
≥16	19 (17)	13 (24)	6 (11)	0.0646
Race & ethnicity				
White	107 (96)	52 (95)	55 (96)	0.6185
Black	2 (2)	1 (2)	1 (2)	0.9748
Asian	2 (2)	2 (4)	0	0.1463
American Indian/ Native Alaskan	1 (1)	0	1 (2)	0.3237
Hispanic/Latina	0	0	0	–
BMI (kg/m^2)	32.5 (7.4)	32.2 (7.9)	32.9 (6.9)	0.5985
Overall health status	62.7 (21.4)	64.8 (21.0)	60.6 (21.8)	0.3025
Current smoker	41 (37)	13 (24)	28 (49)	0.0051
FS-IQ	100 (17.7)	101.6 (19.3)	98.54 (16.0)	0.3733
Surgical	26 (23)	16 (30)	10 (18)	0.1479
ASEBA (T-scores, n = 111)				
Anxious/depressed	59.7 (9.1)	59.8 (9.1)	59.6 (9.1)	0.9091
Total problems	57.1 (11.3)	56.0 (11.8)	58.1 (10.8)	0.3119
Delay Discounting (AUC)	0.405 (0.304)	0.480 (0.321)	0.331 (0.269)	0.0101
D-KEFS (scaled scores)				
Trail Making Task	9.8 (3.1)	10.4 (2.8)	9.0 (3.3)	0.0192
Tower Task	10.1 (3.0)	9.9 (2.9)	10.4 (3.1)	0.4022
Stop Signal Task (ms)				
GoRT	661 (123)	658 (119)	665 (129)	0.8008
StDev of GoRT	174 (61)	174 (59)	173 (63)	0.9339
SSRT	208 (77)	220 (90)	195 (58)	0.1013
BRIEF (T-scores)				
Behavioral Regulation Index	56.1 (11.7)	55.1 (12.0)	57.0 (11.4)	0.4045
No. impaired	22 (20)	9 (18)	13 (24)	0.4474
MetaCognition Index	55.4 (11.9)	55.8 (12.9)	55.0 (10.9)	0.7535
No. impaired	24 (23)	13 (25)	11 (20)	0.4998
Global Executive Composite	56.0 (11.7)	55.7 (12.5)	56.2 (11.0)	0.8101
No. impaired	25 (22)	11 (22)	14 (25)	0.6377

M (SD) or no. (%). p values calculated by chi square or two-tailed, Student's *t*-test. Significant variables are bolded. Abbreviations: HS, high school; BMI, body mass index; FS-IQ, full scale intelligence quotient; ASEBA, Achenbach System of Empirically Based Assessment; D-KEFS, Delis-Kaplan Executive Function System; TMT, Trail Making Task; GoRT, Go Reaction Time; SSRT, stop signal reaction time; DD, Delay Discounting; AUC, area under the curve. Data were collected 2013-2018, Burlington, VT, USA.

compared to normative, national samples matched by age (T-scores within 43–57 and scaled scores of 8–12). However, 22% of participants reported experiencing a high enough number of problems with EF in the last month to be considered "impaired" on the BRIEF-A (T-Score ≥ 65). The number of participants reporting impaired EF did not differ between non/completer groups, nor did scores on individual scales (data not shown), indices, or summary composite (Table 1).

On objective EF measures, participants less likely to discount future rewards (less impulsive) on the DD task, and those with greater cognitive flexibility, as measured with the TMT, were more likely to complete CR (Table 1, Fig. 1). The steepest discounters (first quartile, AUC ≤ 0.113) attended an average of 7 fewer sessions than shallower discounting participants (third quartile, AUC ≥ 0.619) (19 ± 15 vs 26 ± 14 sessions, respectively). Those performing in the top quartile on TMT (scaled scores of ≥12) attended approximately 10 more sessions than those in the lowest quartile (scaled scores of ≤ 8) on average (26 vs 16 sessions, respectively). SST and Tower Task were not

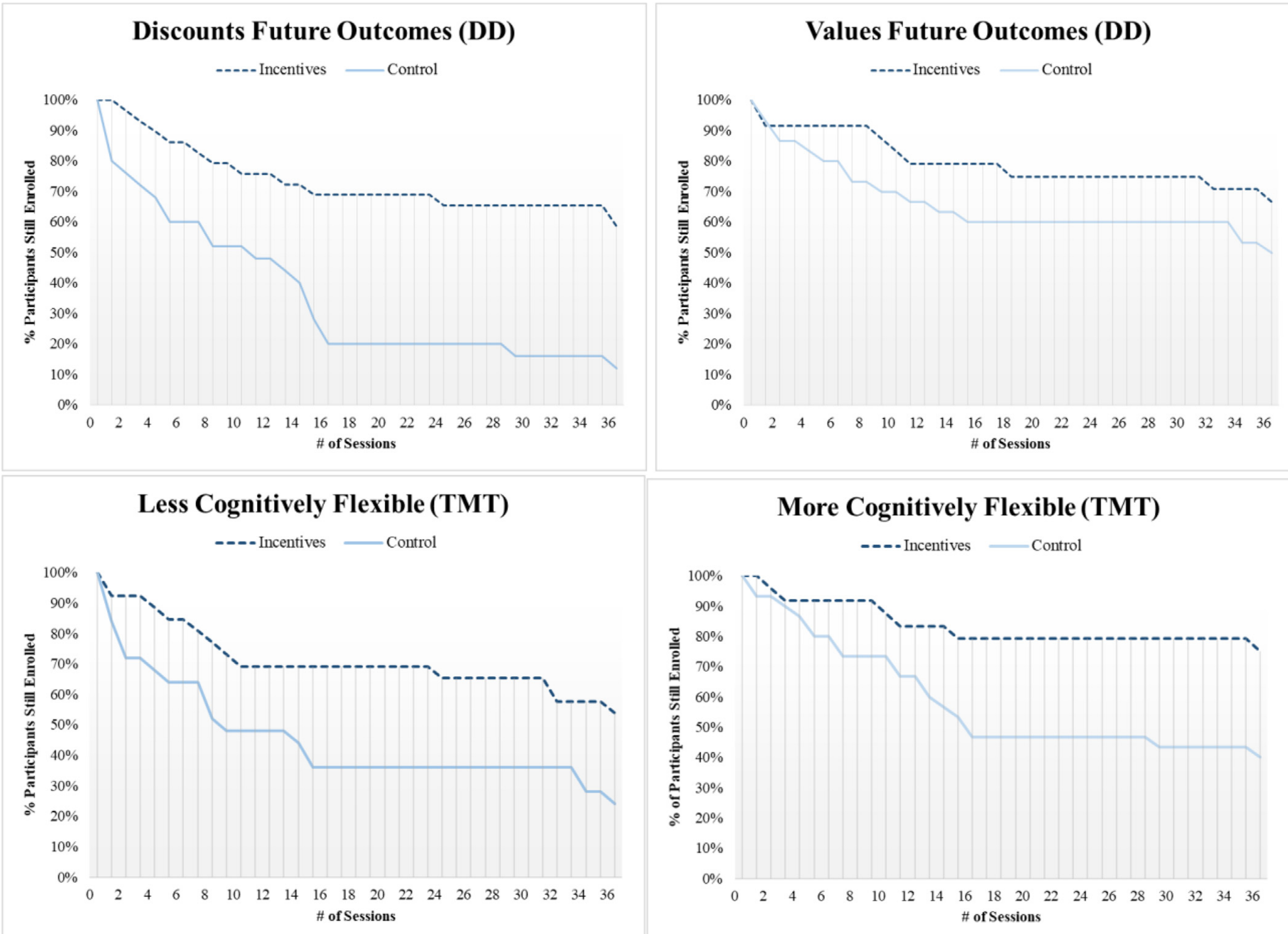

Fig. 1. Illustrative figure to demonstrate the interaction effect of delay discounting and treatment condition and the main effects of Trail Making Task and Delay Discounting on number of CR sessions completed.

A median split was used to dichotomize participants by low and high performance on EF tasks based on A) Delay Discounting scores or B) Trail Making Task scaled scores and then grouped by treatment condition. Graphs show the percent of each group that were still attending at each point through the 36 possible sessions. Data were collected 2013-2018, Burlington, VT, USA.

significant predictors of CR completion. Age, another predictor of CR completion, varied widely in this sample and has been shown to impact DD and SST performance. Analyses were repeated for DD and SST controlling for age and it did not change these relationships.

Next, repeated, mixed model ANOVAs were used to determine whether baseline EF variables interacted with the intervention to predict successful completion of CR. There was a significant interaction of intervention and DD task performance on CR completion (AUC ($F(1, 105) = 5.65$, $p = 0.019$)), with non-completers being more impulsive than completers in the usual care but not the financial incentives conditions (Fig. 1). Said differently, financial incentives appeared to negate the effect of impulsivity on treatment dropout. Interactions were not detected with any other EF variable.

The conventional means of calculating AUC has been criticized as overweighting the contribution of some indifference points over others, specifically those at longer delays, thus having the potential to magnify differences at long delays (Borges et al., 2016). One suggested alternative is to use AUC_{logd} as a way of maintaining the scaling of the delays while correcting some of the imbalance. AUC_{logd} was calculated using methods defined by Borges et al. (2016). We then repeated the mixed model ANOVAs and found the same, significant interaction of intervention with CR completion on AUC_{logd} of DD ($F(1, 105) = 6.8$, $p = 0.0104$).

Finally, a logistic regression predicting CR completion was conducted including all variables identified to have a significant main effect on the outcome (SAS proc. logistic; treatment condition, current smoking status, age, DD, TMT, and the group × DD interaction). In this model ($\chi^2(6) = 40.0$, $p < 0.0001$), treatment condition, DD, TMT, smoking, and the interaction between treatment condition and DD were significant ($p < 0.05$) predictors of CR completion (Table 2). The predictive strength of the EF variables remained even after including the demographic predictors and the intervention in the model.

Table 2
Logistic regression predicting CR completion.

	B	SE	Wald	df	*p* value	Exp(B)
Incentivized condition	−1.7500	0.4931	12.5961	1	0.0004	0.174
Age	0.0319	0.0298	1.1471	1	0.2842	1.032
Current smoker	0.5858	0.2835	4.2676	1	0.0388	1.796
DD	2.1113	0.8681	5.9146	1	0.0150	8.259
TMT	0.1836	0.0833	4.8569	1	0.0275	1.201
Incentive × DD	2.0975	0.8937	5.5077	1	0.0189	8.146

Abbreviations: TMT, Trail Making Task; DD, Delay Discounting. Data were collected 2013-2018, Burlington, VT, USA.

4. Discussion

Given the underutilization of so many proven secondary prevention strategies, the question of how to improve program adherence is of utmost importance. Focus must also be brought to vulnerable populations, such as those with lower-SES, who bear a disproportionate share of the risk while also facing more barriers to accessing and adhering to secondary prevention. Consistent with prior literature, EF, specifically delay discounting and cognitive flexibility, was found in this study to predict adherence to a secondary prevention program. Importantly, however, the financial incentive intervention interacted with delay discounting in promoting adherence, suggesting that it was the more impulsive patient who especially benefitted from the incentives intervention. Given that impulsivity and other EF deficits are over-represented in lower-SES populations it is important to delineate associations between EF, secondary prevention adherence, and interventions that are capable of promoting program adherence in at-risk populations.

Greater impulsivity in the form of discounting the value of delayed rewards, assessed here using a delay-discounting of hypothetical monetary rewards task, is considered to represent a trans-disease process that is associated with socioeconomic disadvantage and early-in-life adversity conditions and underpins vulnerability to addictions, obesity, and a range of other conditions for which behavior or lifestyle is a proximal cause (Bickel et al., 2014; Achenbach et al., 2004; Bickel et al., 2019; Duffy et al., 2018; Green et al., 1996; Reimers et al., 2009). Financial incentives have been shown to substantially improve treatment adherence in these populations (Higgins et al., 1994; Higgins et al., 2012; Davis et al., 2016). Demonstrating that incentives seem especially effective in those who discount the future steeply brings us closer to being able to target interventions to those who would most benefit (Loree et al., 2015).

Given that incentives appear to be a promising intervention to overcoming excessive temporal discounting, it would be useful to identify interventions that could help address or compensate for challenges in other facets of EF. Cognitive flexibility (TMT) was another predictor of secondary prevention adherence. One way to help overcome deficits in this area to improve secondary prevention could be to take a compensatory approach, seeking to create environmental supports that improve secondary prevention by reducing cognitive burdens (Maples and Velligan, 2008). Case management is an example of a compensatory approach. A case manager can assess the challenges to a patient in adhering to secondary prevention, helping with scheduling, arranging transportation, providing reminders, and otherwise serving as an external support to help overcome the challenges of engaging in post-cardiac event care. Indeed, telephone-delivered case management has been shown to improve mental health-related quality of life and physical functioning among depressed post-CABG patients (Rollman et al., 2009) and case management interventions have been shown to lead to increased health resource utilization (Gardner et al., 2005). It would be interesting to explore how such an intervention would interact with aspects of EF, such as cognitive flexibility.

There are limitations of the current study that should be noted. This was a relatively small and racially homogenous population which might limit generalizability. Strengths of this study include the extensive EF battery conducted in the context of an intensive program adherence intervention, providing important novel data about the interaction between EF and an intervention to promote CR/secondary prevention in an understudied, at-risk population. Future work should examine the impact of a cardiac event on EF, how EF might recover over time, and if completing secondary prevention impacts EF recovery.

5. Conclusions

Performance on tasks measuring EF, specifically delay discounting and cognitive flexibility, predicted completion of a secondary prevention program. Additionally, an incentive intervention interacted with delay discounting, wherein the intervention was most beneficial among those who discount future outcomes more steeply, a condition associated with socioeconomic disadvantage. Given the challenges of lower-SES patients to complete secondary prevention and the over-representation of EF challenges in this population, the findings from this study can be useful in helping to design effective interventions to improve secondary prevention adherence.

Declaration of competing interest

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