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The Qualitative Interview Study of Persistent and Non-Persistent Substance Use in the MTA: Sample Characteristics, Frequency of Use, and Reasons for Use 05-07-17

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Declaration of Interests

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Abstract

Objective: To evaluate perceptions of participants in the Qualitative Interview Study (an add-on to the Multimodal Treatment Study of ADHD) about frequent use and reasons for substance use (SU).

Method: Longitudinal assessments identified 39 ADHD cases and 19 peers with Persistent SU, and 86 ADHD cases and 39 peers without Persistent SU. In adulthood, an open-ended interview was administered, and SU excerpts were indexed and classified to create sub-topics (Frequent use and Reasons for use and non-use of alcohol, marijuana, and other drugs).

Results: For marijuana, the Persistent compared to Non-Persistent SU group had a significantly higher percentage of participants describing frequent use and giving reasons for use, and the ADHD compared to the peer group had a significantly higher percentage giving "stability" as a reason for use.

Conclusion: Motivations for persistent marijuana use may differ for adults with and without a history of ADHD in childhood.

Keywords

Substance use; qualitative research; marijuana; MTA study; ADHD

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INTRODUCTION

The Multimodal Treatment Study of Children with Attention-Deficit/Hyperactivity Disorder (ADHD), known as the MTA, was initiated in 1994 as a randomized clinical trial (RCT) designed to evaluate effects of intensive treatments provided by state-of-the-art protocols with and without stimulant medication. After baseline diagnosis of 579 children (7 to 9 years old) with ADHD-Combined Type, cases were randomly assigned to treatment-by-protocol for medication management (Med), Behavior Modification (Beh), or their combination (Comb) provided by MTA staff for 14-months, or assigned to treatment-as-usual obtained from non-MTA clinicians for a Community-Comparison (CC) treatment. On the primary outcome measure of the study (ADHD symptom severity) the groups with medication provided by protocol (Med and Comb) showed greater benefits than the other two groups (Beh and CC). Ten months after the end of treatment-by-protocol in the 14-month RCT, the MTA transitioned into an observational long-term follow-up (LTF) study. At this point (2 years after baseline), 289 randomly selected classmates were added as a local normative comparison group (LNCG). During the LTF, both groups were assessed 3, 6, 8, 10, 12, 14, and 16 years after baseline. The LTF was intended to track the developmental course of ADHD from childhood to adulthood, to monitor extended use of stimulant medication provided by non-randomized, self-selected treatment in community settings, to perform exploratory analyses and generate hypotheses about possible long-term effects of stimulant medication, and to evaluate outcomes in early adulthood. The initial findings the LTF (Jensen et al, 2007) showed that the relative benefits of medication in the RCT (e.g., greater reduction in symptom severity) dissipated during childhood (by the 3-year assessment), and subsequent findings (Molina et al, 2009) indicated relative benefits of medication did not reappear in adolescence (at the 6- or 8-year assessment). A recent report (Swanson et al, 2017) indicated the no significant residual benefits of extended self-selected treatment-as-usual with stimulant medication on symptom severity in adulthood (at the 12-, 14-, or 16-year assessment).

In addition to ADHD symptom severity, outcomes related to substance use (SU) have been reported. The SU outcome measure was based on the Substance Use Questionnaire (SUQ) that was administered in childhood (Molina et al., 2007), adolescence (Molina et al., 2013; Molina et al., 2009), and adulthood (Hechtman et al., 2016; Molina et al., in preparation). The SUQ provided a quantitative measure of SU (self-reported frequency of use), which revealed important ADHD-LNCG differences at each developmental stage, including earlier emergence and greater continuation of SU in the ADHD group compared to the LNCG. However, these analyses did not detect significant effects of medication on SU outcomes based on comparisons of the randomized treatments of the RCT or the self-selected patterns of extended treatment in the LTF.

The Qualitative Interview Study (QIS) was developed for further exploration of SU in the MTA. Innovative assessment methods were used based on the Ecocultural Family Interview (EFI) approach (Weisner, 2014) adapted for the MTA (the M-EFI). The M-EFI was an open-ended, conversational interview with the participants in adulthood. It provided unconstrained narrative accounts reflecting perceptions, attitudes, and opinions about 11 topics (including SU): General Functioning, ADHD, SU, Work, Future, Family, Peers, School, Turning

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Points, Self-knowledge, and Conclusion. Excerpts about these topics (from one to several sentences in the narratives) were identified by investigators (see Weisner et al, in press) to provide data for qualitative and quantitative analysis (see Lasky et al., 2016; Jensen et al., in press; Mitchell et al, in press). Also, an innovative design was used to focus on a subset of the full MTA sample, with enrichment by strategic selection of cases with early emergence of SU in adolescence and continued manifestation of SU in adulthood (i.e., Persistent SU). The cases with a history of Persistent SU were expected to comprise a small proportion of the longitudinal MTA sample, but this subgroup has been described as theoretically important (Chassin et al, 2004) and associated with increased major health risks (Swift et al, 2000; Zeisser et al, 2012). Thus, the QIS was an exploratory study of SU and ADHD, using an innovative assessment of outcome (with the M-EFI) and an innovative design (with enrichment for cases with a history of Persistent SU). These aspects of the QIS were intended to broaden previous evaluations and to explore additional associations of SU with ADHD.

This paper has four purposes. The first two are methodological and use data from the standard MTA assessment battery: (a) to provide details about the origin of the QIS sample and the selection of ADHD and LNCG cases with histories of Persistent SU and Non-Persistent SU and (b) to compare the strategically selected QIS subgroups on demographic factors, treatment histories, and frequency of use of different substances in adulthood. The other two purposes are empirical and use qualitative data from the M-EFI: (c) to compare the Diagnostic groups (ADHD and LNCG) and the Persistence groups (Persistent SU and Non-Persistent SU) on self-assessment of Frequent use expressed in the unconstrained narratives and (d) to describe and evaluate the Reasons for use (and for non-use) of different substances mentioned spontaneously during the M-EFI.

METHODS

General Outline of the Formation of the QIS Sample

There were several steps in the formation of the QIS sample. First, the study was conducted when the MTA cases were in adulthood, which restricted recruitment to the cases retained up to this point. Second, only four of the original sites (Duke University, UC Irvine, UC Berkeley, and Montreal Children's Hospital) collected data for the QIS add-on study, which excluded participants from the other 3 sites (Columbia University, University of Pittsburgh, and Long Island Jewish Hospital). Third, strategic recruitment utilized the SUQ data from the MTA assessments conducted at 8 assessment points of the LTF (from 2 to 16 years after baseline) to define SU history integrated across multiple assessment points and across multiple substances. Developmentally sensitive thresholds were used to define SU appropriately for the range of ages of the participants at assessment points over the course of the LTF (see Table 1). This provided a target for strategic selection of cases with histories of Persistent SIU, defined as any SU by early adolescence (at the 2- or 3-year assessment points), monthly SU during adolescence (at the 6- or 8-year assessments), and weekly SU in adulthood (at the 12-, 14-, or 16-year assessments). Because a small percentage of the MTA cases were expected to meet these rigorous criteria, all ADHD and LNCG participants who met (or approached) these criteria for Persistent SU were recruited to enrich the QIS sample.

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The remaining MTA participants were assumed to have a history of no SU or SU restricted to some but not all developmental stages. Random selection from these ADHD and LNCG cases was used to establish the Non-Persistent SU subgroups with about twice the number of cases as those strategically selected for the Persistent SU subgroups.

Weisner et al (in press) described some general demographic characteristics of the QIS sample (sex, race/ethnicity, and site), and found no significant differences between the ADHD group (n=125) and LNCG (n=58). To provide additional context for interpretation of the findings from the QIS study, further evaluation is provided for additional demographic variables shown in epidemiologic studies to be associated with SU (Household Education Level, Socio-Economic Advantages, and Welfare Status), as well as a refinement of the evaluation of Sex and Race/Ethnicity provided by Weisner et al (in press). In addition to comparisons based the full MTA sample for Diagnosis in childhood (ADHD vs LNCG), comparisons were made of the successive subsets of cases from the full MTA sample based on retention into adulthood, site participation in data collection, and selection by strategic and random processes. This produced 4 subgroups (ADHD Persistent, ADHD Non-Persistent, LNCG Persistent, and LNCG Non-Persistent), which were compared on the 5 key demographic variables to assess possible confounding in the QIS sample.

Origins of the Sample Available for the QIS

As shown in Table 2-A, at recruitment of the full MTA sample, the ADHD group (n=579) and the LNCG (n=289) did not differ in percentage of male and female participants, as expected due to group-matching at baseline. The recruitment of the LNCG participants from the same schools as the ADHD cases was intended to match the groups on other demographic factors, but random selection (after obtaining consent from over 50% of the classmates) of a small subset of the volunteers resulted in some differences: the LNCG compared to the ADHD group had a slightly but significantly lower percentage of households with public assistance (12.5% vs 18.0%) and higher percentage of households with socio-economic advantages (44.6% vs 37.6%). Both of these differences are consistent with the hypothesis that the ADHD group had increased risk for SU relative to the LNCG. However, other hypotheses could be proposed, such as that classmate volunteers for the LNCG had decreased risk for SU compared to the non-volunteers in the schools where random selection was used to form the LNCG.

As shown in Table 2-B, retention of the MTA sample was high, with 476 ADHD and 267 LNCG cases having at least one observation in adulthood (at 12, 14, or 16 years after baseline). Significant differences associated with retention were observed, which were similar to those reported by Howard et al. (2016) for comparisons of cases with complete and incomplete observations for the full ADHD group and full LNCG. The retained compared to non-retained subgroup had a higher percentage of female participants and higher percentage of households with high parental education and socioeconomic advantages, and a lower percentage of participants from households with public assistance and from racial/ethnic minorities. These differences suggest retention was associated with protection against SU.

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As shown in Table 2-C, 325 ADHD and 159 LNCG cases were retained in adulthood from the 4 QIS sites. Compared to the 3 non-QIS sites, these retained cases had a higher percentages of households with high parental education and socioeconomic advantages, and a lower percentage of households with public assistance and non-white racial/ethnic status. These differences suggest site participation was associated with protection against SU. In summary, ADHD diagnosis was associated with increased sociodemographic risk for SU, while participant retention in the MTA and site participation in QIS-data collection were associated with decreased sociodemographic risk.

Demographics of the Selected QIS Subgroups

As shown in Table 3-A, statistical comparisons of the ADHD group (n=325) and LNCG (n=159) revealed that in the retained cases available for the QIS study, Diagnosis of ADHD in childhood continued to be associated with household characteristics conveying risk for SU (lower socio-economic advantages and higher public assistance). As shown in Table 3-B, the strategic selection of cases with Persistent SU identified (as expected) a small proportion of the sample (n=39 or 12.0% of the ADHD cases and n=19 or 11.9% of the LNCG cases). By the QIS definition, the remaining cases had Non-Persistent SU, constituting a large proportion of the sample (n=286 or 88.0% of the ADHD and n=140 or 88.1% of the LNCG cases). Random selection was employed to identify and recruit a subset of these Non-Persistent SU cases for the QIS subgroups (n=86 or 26.5% of the remaining ADHD cases and n=39 or 24.5% of the remaining LNCG cases). Thus, in the available sample, the ratio of Non-Persistent to Persistent SU cases was about 7.50 to 1, but by recruiting all of the cases with Persistent SU and only a subset of the cases with Non-Persistent SU, the ratio was reduced to 2.55 to 1. The resulted in about a 3-fold enrichment of Persistent SU in the QIS sample.

To evaluate the main effect of Diagnosis, the ADHD group (n=125) and the LNCG (n= 58) were compared on the 5 key demographic variables. In these cases selected for the QIS sample, the demographic differences manifested in the larger available groups (see Table 3A) remained significant: the ADHD group had a significantly lower percentage of cases from households with socio-economic advantages and higher percentage with public assistance). To evaluate the main effect of Persistence, the Persistent SU (n=58) and the Non-Persistent SU (n=125) groups were compared on the 5 key demographic variables, and none of the differences were significant. Furthermore, additional exploratory comparisons were made for the 4 QIS subgroups shown in Table 3B reflecting the interaction of the Diagnosis and Persistence factors. The subgroup size for the combinations of selected cases resulting in some cell sizes that were too small for the chi square test (i.e., for the subgroups with Persistent SU and Welfare, there were 0 cases in the ADHD group and 1 case in the LNCG). For the comparisons based on adequate cell sizes, none of the differences was significant. Therefore, the composition of subgroups based on Persistence of substance use into adulthood was not considered biased by the 5 key baseline variables, and these demographic variables were not used as covariates in subsequent analyses.

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Medication Use in the 4 Subgroups of the QIS Sample.

Analyses were performed to evaluate whether history of medication use in the RCT or LTF phases of the MTA (Table 4) was associated with the formation of the ADHD group of the QIS sample. Within the Non-Persistent SU ADHD subgroup, group-matching was imposed for recruitment from the 4 randomly assigned treatment groups of the RCT (Med, Beh, Comb, and CC). As shown in Table 4-A, this was successful: participants from each of the 4 assigned treatment groups comprised 25% of this subgroup (as intended). Also, even though group-matching was not used for recruitment of the Persistent SU ADHD subgroup, about 25% of the participants were from each of the 4 randomly assigned treatment groups. Thus, randomly assigned use of medication in the RCT phase of the MTA was not confounded with the formation of the Persistent and Non-Persistent SU ADHD subgroups of the QIS.

In the LTF phase of the MTA, self-selected patterns of extended medication use emerged (see Table 4-B), which are evaluated here to determine if they were associated with the formation of the QIS sample. Naturalistic subgroups based on 3 patterns of extended use of medication (Negligible, Inconsistent, and Consistent) were described in detail by Swanson et al (2017), and will be summarized here. Treatment-as-usual in the community from childhood through adolescence was monitored by the Services for Children and Adolescent, Parent Interview (SCAPI; Jensen et al., 2004), administered at each assessment point up to 10 years after baseline (or until age 18). A consensus cutoff was used to identify whether at least the minimum of acceptable treatment occurred during each interval (≥ 10 mg/day for more than 50% of the days). Sequences of intervals above and below this cutoff (> minimal or < minimal) from baseline to the 10-year assessment point (or until age 18) were used to define patterns of extended use of medication. The two extreme sequences defined the Negligible (all intervals < minimal) and Consistent (all intervals ≥ minimal) patterns of treatment, and all other sequences were merged to define the Inconsistent (≥ minimal in some but not all intervals) pattern of treatment. Also, at each assessment, the SCAPI documented the daily doses taken and number of days treated during the interval since the previous assessment. For each interval, the cumulative methylphenidate equivalent (ME) dose was estimated by multiplication (daily doses x days treated). Across the 6 intervals from baseline to the 10-year assessments, the cumulative ME doses were summed to estimate the total ME dose from childhood through adolescence.

The Persistent SU and Non-Persistent SU subgroups within the ADHD group were compared to determine if they differed in percentages of cases with the three self-selected patterns of extended medication use. As shown in Table 4-B, the percentages were not statistically different for the Persistent SU subgroup (Negligible = 23%, Inconsistent = 69%, and Consistent = 8%) compared to the Non-Persistent SU subgroup (Negligible = 19%, Inconsistent = 75%, and Consistent = 6%). Also, the average total cumulative ME dose did not differ significantly for the Persistent SU (57,885 mg) and Non-Persistent SU (54,961 mg) ADHD subgroups. In summary, neither assigned treatment groups in the RCT phase nor self-selected naturalistic subgroups based on extended use of medication in the LTF phase were significantly associated with the Persistent and Non-Persistent SU ADHD subgroups of the QIS, so adjustments for these medication variables were not made in subsequent analyses reported here.

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The MTA Ecocultural Family Interview (M-EFI)

Primary Indexing by Topic—Weisner et al (in press) provides details about data collection using the M-EFI and the initial analysis of content of the unconstrained narratives provided by the QIS participants. This qualitative interview inquired about participants' perceptions regarding multiple domains of functioning, treatment, and intersection with SU history. Based on a combination of inductive and deductive approaches, 11 general (main) topics were specified. In a guided conversation with prompts provided by the interviewer, participants were encouraged to "tell their own story" about each topic. If any of the 11 topics was not addressed spontaneously (or if inadequate information was provided), the interviewer provided a prompt to elicit additional information on the topic (e.g., ("I noticed on the questionnaire you did at the last assessment, that you said you have been using marijuana --- tell me more about that"). The interviews were transcribed and entered into Dedoose (www.Dedoose.com), a qualitative/mixed method data analysis program (Lieber & Weisner, 2010). Using Dedoose to process the open-ended narratives, excerpts of the interview (from one to several sentences in length) were coded (indexed) by specifying the applicable topic. As described by Weisner et al (in press), for the n=183 participants in the QIS, 3,566 SU excerpts were identified in the M-EFI narratives, with an average of 19.48 SU excerpts per participant. The Type of substance (nicotine, alcohol, marijuana, or other illicit drug) was identified in the SU excerpts. (The excerpts related to nicotine are not evaluated here). An evaluation of reliability of assignment of excerpts to topics was performed, and adequate reliability across multiple investigators was documented (Kappa coefficients >.70).

Secondary Indexing by Sub-topic—Weisner et al (in press) also described 9 sub-topics of the general SU topic (i.e., emotional functioning and initiation/maintenance of SU; impact of negative experiences on SU; opportunities for SU; ADHD drugs and SU; impact of family on SU; perception of SU as a negative experience; impact of seeing others "go down wrong path" on SU; extent of positive impact of SU; impact of SU on ADHD symptoms). These SU sub-topics were not prompted during the M-EFI (as were the 11 main topics when inadequately addressed), but they were indexed along with the main topics when the M-EFI data were being processed using Dedoose.

In a previous report on the QIS sample and the M-EFI, Lasky et al (2016) focused on excerpts one of the 11 main topics (Work) listed above. They described methods to identify and to evaluate and additional salient sub-topic related to "context of work" (i.e., how Work environment affected the manifestation of ADHD). Even though prompts were not provided for this extra sub-topic, the relevant spontaneous commentary in the M-EFI narratives was notable, with many excerpts describing a connection between environmental context of work and manifestation of ADHD symptoms (e.g., decreased ADHD symptoms in stimulating environments and increased in boring environments). The reliability of two investigators assessing this subtopic analysis was high (88% agreement).

Here, a similar method was used to focus on a different main topic (i.e., SU), and to identify and evaluate two additional sub-topics (i.e., Frequent use and Reasons for use and non-use). To generate the data for the analyses presented here, categorical levels for these sub-topics

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were established by using the method described in detail by Lasky et al (2016). The excerpts for 10 example participants were examined by two investigators, who then recommended a cutoff (more than once a week) as a categorical definition of Frequent use for others to apply. Also, they recommended two broad categories of Reasons (for use and non-use), with five options for sub-categories within each of broad categories for indexing this sub-topic (see Table 5).

Quantitative and Qualitative Measures and Methods for Analyses

Quantitative Measure of Frequency of Use from the SUQ—The SUQ provide a quantitative measure of frequency of substance use at each of the 8 assessment points (from 2- to 16-years after baseline), separately for the 3 types of substances (Alcohol, Marijuana, and Other Drugs). The SUQ had different (age-appropriate) questions about frequency of use across assessment points (e.g., per month or per year), and the variations were harmonized (e.g., uses per month were multiplied by 12 to convert to uses per year) to provide a consistent estimate across assessment points. The SAS PROC MIXED software was used to analyze the quantitative outcome measures from the SUQ (uses per year for 3 different types of substances). For each analysis, one within-subject factor (Assessment Point: 2 to 16 years after baseline) and two between-subject factors [Diagnosis (ADHD vs. LNCG) in childhood and Persistence (Persistent vs. Non-Persistent) of substance use] were specified and used. The least square means (LSMs) for frequencies of use at each of the assessment points were generated by the SAS PROC MIXED output. For the 4 subgroups (ADHD Persistent, ADHD Non-Persistent, LNCG Persistent, and LNCG Non-Persistent), the LSM estimates represent the marginal means over a balanced population and thus adjusted for other factors in the statistical model associated with groups with unequal number of cases or missing observations on some cases. The LCM estimates at the 16-year assessment point provide context from the qualitative measure of frequencies of use from the SUQ (“Which substances were being used?” and “How often were they being used?”) for comparison to the qualitative data (self-perception of Frequent use) from the M-EFI.

Qualitative Measures of Frequent Use and Reasons for Use—All but one of M-EFI interviews (n = 124) of the recruited ADHD cases and all of those from the recruited LNCG cases (n = 58) were available for indexing of these sub-topics. The SU excerpts were read by 4 research assistants (each assigned 40 to 50 participants). For the SU excerpts for each participant, any spontaneous mention of frequency of use was marked for each type of substance (Alcohol, Marijuana, and Other Drugs).

Frequent use was determined by reviewing all of the SU excerpts describing frequency of current use (in adulthood, when the interview was administered). Based on the established cutoff (more than once a week), each participant was classified as Frequent user (or not) for each type of substance. Chi-Square analyses were used to evaluate the percentage of cases with Frequent use (or not) and whether the percentage differed for the two levels of the Diagnosis (ADHD and LNCG) factor, for the two levels of Persistence (Persistent SU and Non-Persistent SU) factor, and for the interaction of these two factors (i.e., within each level of Diagnosis, whether the percentage of cases differed for the Persistent SU and Non-Persistent SU subgroups).

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Reasons for Use and Non-Use were also reviewed. In the SU excerpts, descriptions of why each substance was used (or not used) were identified using the two broad categories of Reasons (for use or non-use) and classified using the multiple options within each broad category (see Table 4). Participants were classified based on at least one (or no) spontaneous mention of a reason for each possibility. Chi-Square analyses were used to evaluate (for each of the 3 types of substance and for each of the 5 reasons for use and 5 reasons for non-use) whether the percentage of cases was different for the two levels of the Diagnosis (ADHD and LNCG) factor, for the two levels of Persistence (Persistent SU and Non-Persistent SU) factor, and for the interaction of these two factors (i.e., within each level of Diagnosis, whether the percentage of cases differed for the Persistent SU and Non-Persistent SU subgroups).

RESULTS

Frequency of SU in the QIS Sample in Adulthood from the SUQ and the M-EFI

In the SAS PROC MIXED analyses of the quantitative data on frequency of use from the SUQ (see Figure 1), the main effect of Diagnosis (ADHD vs LNCG) in childhood was not significant for any 3 types of substance, but the main effect of Persistence (Persistent SU vs Non-Persistent SU) of substance use into adulthood was significant for all 3 types of substances. Also, the two-way interaction of Persistence x Assessment Point was significant for Alcohol ($F(7,808) = 4.26$, $p < 0.0001$), Marijuana ($F(7,915) = 12.10$, $p < 0.0001$), and Other Drugs ($F(7,790) = 2.64$, $p < 0.01$). As shown in Figure 1, for the Persistent SU subgroups the average yearly frequencies of SU increased substantially during adolescence, reached peaks in early adulthood (except for a low level of use of Other Drugs in the LNCG), and then declined slightly. The most frequently self-reported substance was Marijuana (with a peak at about 450 uses/year), which was about 3 times higher than for Alcohol (with a peak about 160 uses/year) and about 7 times higher than for Other Drugs (with a peak about 60 uses/year). In contrast, as expected by strategic selection, the Non-Persistent SU subgroups showed slower increases and reached lower levels at the 16-year assessment point in adulthood, and did not show early peaks.

The LSMs from the SAS Proc Mixed analyses were used as the estimates of yearly frequencies of use at the 16-year assessment point (near the time when the M-EFI was administered). LSMs were obtained for each of the 3 types of substances and are shown in Table 6-A. Analyses of these end-points revealed a pattern of significant and non-significant for the Diagnosis and Persistence factors that was similar to the pattern for analyses of outcome based on the average across all 8 assessment points (see above). The Diagnosis (ADHD vs LNCG) factor was not significant: the LSMs did not differ significantly for the ADHD group and the LNCG for any of the 3 types of substance. The Persistence (Persistent SU vs Non-Persistent SU) factor was significant: the LSMs were significantly higher for the Persistent SU group than the Non-Persistent SU group for Marijuana, 371.7 vs 120.1 uses/year, $t(828) = 6.73$, $p < 0.0001$, and Other Drugs, 38.4 vs 7.7 uses/year, $t(1384) = 3.38$, $p < 0.0007$, but not for Alcohol, 116.0 vs 90.0 uses/year, $t(1229) = 1.69$, $p = 0.0904$. Additional comparisons of the 4 subgroups defined by the interaction of the Diagnosis and Persistence revealed that within the ADHD group, the LSMs were significantly higher for the Persistent

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SU subgroup than the Non-Persistent SU subgroup for all 3 types of substance [Alcohol (135.6 vs 98.6, $t[1245] = 2.07$, $p < 0.0386$), Marijuana (385.5 vs 151.2, $t[858] = 5.41$, $p < 0.0001$), and Other Drugs (43.1 vs 1.1, $t[1386] = 3.96$, $p < 0.001$)], but within the LNCG, the difference was significant only for Marijuana (357.9 vs 89.5, $t[812] = 4.42$, $p < 0.0001$).

Chi-square analyses of the qualitative data (percentage of cases with Frequent SU from the M-EFI -- see Table 6-B) revealed a pattern of significant and non-significant effects that were remarkably similar to the pattern from the analyses of quantitative data from the SUQ at the 16-year assessment point described above (uses/year -- see Table 6-A). As in the analyses of the main effects for the quantitative measure (see above), the analysis of the qualitative measure indicated that the Diagnosis (ADHD vs LNCG) factor was not significant for any of the 3 types of substance, but the Persistence (Persistent vs Non-Persistent) factor was significant for Marijuana, due to higher percentages of participants describing frequent use in the Persistent than the Non-Persistent group (42.1% vs 16.8%), and the difference was in the same direction and almost significant for Other Drugs (7.0% vs 1.6%). Also, as in the analysis of the quantitative measure, in the analysis of the qualitative measures the interaction of the Diagnosis and Persistence factors indicated that within the ADHD group, the Persistent and Non-Persistent subgroups differed significantly in the percentage of frequent users for all 3 types of substances, but within the LNCG none of these differences was significant.

There was one exception to the similarities of finding from the quantitative and qualitative measures: the ordering of Type of substance was different. Over all participants in the QIS, on the quantitative measure from the SUQ the highest rate of use was for Marijuana (246 uses/year), which was more than twice as high as for Alcohol (103 uses/year), but on the qualitative measure from the M-EFI, the highest percentage for Frequent use was for Alcohol (30.8%) rather than for Marijuana (24.7%). In addition, the qualitative data revealed that the ordering of Type (Alcohol > Marijuana) was due to the Non-Persistent SU subgroup: despite lower percentages than for the Persistent SU subgroup, the percentage for Alcohol (28.0%) was higher than for Marijuana (16.8%), while for the Persistent SU group the percentages were the same for Alcohol (42.1%) and Marijuana (42.1%). This surprising relationship was present both in the ADHD Non-Persistent SU subgroup (30.2% for Alcohol vs 18.6% for Marijuana) and in the LNCG Non-Persistent subgroup (23.1% vs 12.8%).

Reasons for Use and Non-Use from the M-EFI

Chi-square analyses of Reasons for “use” and “non-use” (percentage of participants spontaneously giving each reason) are shown in Table 7. Due to the complexity created by including all three types of substances (Alcohol, Marijuana, and Other Drugs), this table is presented in two parts: Part I shows the main effects for the Diagnosis and Persistence factors, and Part II shows their interaction. As in previous analyses, there were few significant differences associated with the Diagnosis factor (see Table 7, Part I): the ADHD-LNCG difference was not significant for any of the analyses of the Reasons for “use” or “non-use”, with one notable exception -- a significantly higher percentage of cases in the ADHD group than in the LNCG gave “stability” as a Reason for “use” (47.7% vs 29.2%, $p < 0.03$). However, the Persistence factor was significant (see Table 7, Part I) for 4 of the 5

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Reasons for “use” for Marijuana and for Other Drugs (but none for Alcohol), due to higher percentages in the Persistent than Non-Persistent group. There was no consistent pattern of significant differences between these two groups for the 5 Reasons for “non-use”, with one reason for Alcohol non-use (Education) given by significantly higher percentage of cases in the Non-Persistent group and one reason for Marijuana non-use (Guilt) given by a significantly higher percentage of the Persistent SU group.

The interaction of the Diagnosis and Persistence factors (see Table 7, Part II) showed many significant differences between the Persistent SU and Non-Persistent SU subgroups within the ADHD group (i.e., for 4 of 5 reasons for use), but few significant differences within the LNCG (i.e., only one reason for Marijuana use and two for Other Drugs use). This pattern of significance and non-significance was similar to the pattern in the analyses of Reasons for “use” for the qualitative measure of Frequent use (see Table 6-B).

In addition to the evaluation of the Diagnosis and Persistence factors, the ordering of Type of substance was evaluated for this qualitative outcome measure (Reasons for “use” and “non-use”). Across all participants, Alcohol was the substance with Reasons spontaneously mentioned by the greatest percentage of the participants (n = 175/182 or 96.2% of the cases), followed by Marijuana (n = 157/182 or 86.3% of the cases) and Other Drugs (n = 126/182 or 69.2% of the cases). Within each Type of substance, “recreation” was given as a reason for use by the highest percentage of participants for Alcohol (78.9%), Marijuana (66.7%), and for Other Drugs (49.2%), and “avoidance of consequences” was given as a reason for non-use by the highest percentage of participants for Alcohol (44.6%), Marijuana (44.0%), and Other Drugs (54.0%).

DISCUSSION

The QIS was an add-on study of a subset of the well-characterized MTA sample of young adults with and without a diagnosis of childhood-onset ADHD. It was designed to explore additional relationships between persistent SU and ADHD that emerged in the prospective LTF phase of the MTA and to generate new hypotheses about SU in adults with a history of ADHD. The main findings related to the four purposes of the study (stated in the introduction) will be summarized here.

First, the origins of the QIS sample were described. Subgroups were based on the two factors under investigation -- Diagnosis (ADHD vs LNCG) in childhood and Persistence (Persistent SU and Non-Persistent SU) of substance use into adulthood. The unbalanced groups were explained. Even though ADHD represents a small minority of the population (5–10%), by deliberate oversampling the MTA sample recruited only half as many LNCG cases (n=289) as ADHD (n = 579). Thus, based on the design of the MTA, the available cases for the Diagnostic groups were unbalanced, with more ADHD cases than LNCG cases. They remained unbalanced in the QIS sample after the selection of 124 ADHD cases and 58 LNCG cases. Also, as expected, a small minority of the cases had Persistent SU (about 12%). Since these cases were expected to be highly informative about the relationship between ADHD and SU, all were included in the QIS. Despite this relative enrichment by including all of the Persistent SU cases and random selection of only a minority of the

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available Non-Persistent SU cases, the selected groups remained unbalanced, with 58 in Persistent SU group and 125 in the Non-Persistent SU group.

Second, the exploratory analyses of demographic variables known to be associated with SU in the population were described. Since the QIS sample was not intended to be representative of the population, processes that operated to form the subgroups were evaluated to determine if these important demographic factors were confounded with the Diagnosis and Persistence factors. significant differences between the ADHD group and the LNCG were identified for two baseline variables (socioeconomic advantages and household public assistance), but no significant differences were documented between the QIS subgroups with Persistent SU and Non-Persistent SU. Thus, the observed difference between the Persistent and Non-Persistent SU groups on the SUQ and M-EFI outcome measures are not likely to be due to these demographic factors. Also, treatment history within the ADHD group was evaluated to determine if use of stimulant medication differed between the subgroups with Persistent SU and Non-Persistent SU. Potential medication effects were evaluated (and ruled out) by extensive analyses of the distribution of cases from the 4 groups defined by the assigned treatment conditions of the RCT phase and the distribution of cases from 3 naturalistic subgroups formed by self-selected patterns of extended treatment during the LTF. Although additional analyses are in progress in the full MTA sample regarding associations over time, the current findings are consistent with previous reports (Molina et al., 2009, 2013) that did not provide statistical support for associations between substance use and either assigned or self-selected treatment with stimulant medication.

Third, the analyses of two measures of frequency of substance use revealed remarkably similar findings related to the Diagnosis (ADHD vs LNCG) and Persistence (Persistent SU and Non-Persistent SU) factors. The quantitative SUQ measure (average uses per year) and the qualitative M-EFI measure (percentage with self-professed Frequent use) were distinctly different outcome measures of frequency of SU, and the methods of analyses (SAS Proc Mixed analysis of a continuous outcome variable vs Chi Square analysis of a categorical outcome variable) were distinctly different also. Despite these methodological differences, the patterns of significant and non-significant effects of Diagnosis and Persistence were very similar: for both measures of frequency, very few significant differences between the ADHD group and the LNCG were observed, but many of the differences between the Persistent SU and Non-Persistent SU groups were significant. However, the qualitative and quantitative measures of frequency did show differences in the evaluation of Type of substances. For example, the self-reported use of Marijuana on the SUQ was extremely high in the Persistent SU subgroups (371.7 uses/year, or more than once a day) compared to Alcohol (120.1 uses/year, or about twice a week). This should be interpreted in the context of a strong secular trend of increasing marijuana use over the time when the MTA was conducted (1993 to 2013), which more than doubled from 1989 to 2008 (Zeisser et al, 2012). Also, in the unconstrained narratives of the M-EFI, the ADHD cases with Persistent SU apparently did not deny or under-estimate substance use compared to the LNCG cases: the percentages of participants with frequent use were significantly higher in the ADHD group than the LNCG for all 3 types of substances (Alcohol, 50.0% vs 26.3%, $p < 0.035$; Marijuana, 47.45 vs 31.6%, $p < 0.001$; Other Drugs, 10.5% vs 0%, $p < 0.001$), and within the Non-Persistent group, the percentages were higher (although the difference was not significant) for the

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ADHD group than the LNCG for Marijuana (31.6% vs 12.8, p = 0.087) and Alcohol (18.6% vs 12.8%, p = 0.787). This generates the hypothesis that under-reporting (as observed for self-reports of symptoms of ADHD) was not manifested in self-reporting of SU.

Fourth, the exploratory analysis of Reasons for “use” (and “non-use”) of substances suggests some insights regarding possible motivations for the use of Marijuana. After strategic selection for Persistent SU, ADHD group and the LNCG did not differ significantly in frequency of use on either the SUQ (385.5 vs 357.9 uses per year) or on the M-EFI (27.4% vs 19.8% of cases with self-perception of frequent use). However, the diagnostic groups did differ significantly on why substances were used: higher percentage of the ADHD group than the LNCG gave “stability” as a Reason for use. These findings build on recent studies indicating individuals with ADHD may have some unique perceptions about (or physiologic responses to) marijuana (Harty, Pedersen, Gnagy, Pelham, & Molina, 2015; Mitchell, Sweitzer, Tunno, Kollins, & McClernon, 2016). Also, they are consistent with the findings of the companion paper by Mitchell et al. (in press), who addressed the topic of emotionality and marijuana in the excerpts from the M-EFI and reported that a higher percentage of ADHD than LNCG cases with Persistent SU perceived beneficial effects of marijuana use (improved negative mood; improved ADHD symptoms). Taken as a whole in the QIS, in the unconstrained narratives of the M-EFI, many of the ADHD cases expressed the belief that marijuana provides emotional “stability” and improves symptoms of ADHD (Weisner et al, under review; Mitchell et al, in press). This may reflect perceived self-medication of symptoms of ADHD and/or dysregulated mood.

Limitations of the Qualitative Interview Study

The QIS has several limitations. First, many analyses were presented here. For example, the analyses of 10 Reasons (5 for “use” and 5 for “non-use”) for the 3 types of substances (Alcohol, Marijuana, and Other Drugs) resulted in 30 analyses, with comparisons of main effects based on the two factors of interest (Diagnosis and Persistence) shown in Table 7 (Part I), as well as for their interaction (shown in Table 7 (Part II). The significance level was not adjusted for multiple tests, which was justified by considering these analyses exploratory (i.e., to generate hypotheses rather than to test hypotheses). Therefore, the significant and non-significant main effects and interactions effects in these exploratory analyses must be interpreted cautiously. The patterns of effects may provide the most relevant findings. It is worth noting that very similar patterns of significant and non-significant effects emerged across multiple analyses, with many significant differences for comparisons of the Persistent SU and Non-Persistent SU group, but few for comparisons of the ADHD group and the LNCG.

Second, even though there was relative enrichment of the QIS sample for Persistent SU, the Non-Persistent SU group was larger by a factor of two. Therefore, within the group with Persistent SU, the comparison of ADHD and LNCG cases would be based on smaller subgroups than contrasts of the Non-Persistent subgroups. Also “by design”, the ADHD group and the LNCG were unbalanced, and within the LNCG, the comparison of subgroups with Persistent and Non-Persistent SU cases would be based on smaller subgroups than contrasts of the ADHD subgroups. In the exploratory analyses of QIS, the unbalanced group

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sizes for the levels of Diagnosis (ADHD vs LNCG) and Persistence (Persistent SU and Non-Persistent SU), as well as the relatively small number of cases in some of the subgroups, complicates and limits the statistical power of the comparisons described here. For example, even though the magnitude of the difference between the Persistent and Non-Persistent subgroups similar for the LNCG (44.2% – 20.0% = 24.2%) and the ADHD group (60.5% – 40.9% = 19.6%), the difference did not reach statistical significance for the LNCG ($p = 0.07$). Due to these issues related to sample sizes, caution is required for interpretation of lack of statistical significance for comparisons of subgroups within the groups (i.e., LNCG and Persistent SU) with the smaller number of cases.

Third, the participants of the QIS were drawn from only 4 of the 7 original MTA sites. Some of the demographic characteristics differed for the participating and non-participating sites, with reduced risk for SU in the participating sites. If the other 3 sites had been included, effects on SU may have been different in geographical locations where risk for SU was higher than in the locations of the QIS sites.

Fourth, the subgroups evaluated here represented the total QIS sample (125 ADHD cases and 58 LNCG cases) described by Weisner et al (in press). However, different criteria could be applied to select subsets of the total QIS sample, as in evaluation of “turning points” by Jensen et al (in press), who selected equal subgroups of n = 20 SU Persisters, n = 20 SU Desisters, and n = 20 Abstainers for comparison, or as in the evaluation of “emotional functioning” by Mitchell et al (in press), who selected n = 67 SU Persisters and n = 25 SU Desisters for comparison. In Appendix A, the characteristics of these different subsets of the sample across the four papers of the Special Issues on the QIS are described and compared. The findings reported here may be different if the same analyses were performed for other subsets of the sample.

Fifth, Persistent SU was not evaluated in the cases that did not complete the MTA assessments in adulthood. Therefore, differential retention (or drop-out) of the cases with Persistent SU compared to those with Non-Persistent SU could not be determined for the QIS study. If the classification of SU was known for the cases that were not retained, a different pattern of significant and non-significant effects may have been documented in the analyses of the Diagnosis and Persistence factors.

Sixth, the evaluation of demographic factors known to be associated with SU did not show the expected differences between the groups with Persistent SU and Non-Persistent SU. The lack of significance could be due to low statistical power related to the size of the QIS sample. Alternatively, this may be due to multiple effects related to the origin and selection of the QIS sample that may have interacted to counteract other demographic effects. The exploratory analyses reported here suggest the hypothesis that the innovative design of the QIS and the strategic recruitment of the participants of the study may have masked some traditional associations with demographic variables.

Conclusions

This article builds upon the background provided by Weisner et al. (in press), providing further background and context for the other reports in this Special Issue about emotional

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functioning (Mitchell et al., in press) and turning points (Jensen et al., in press) in the lives of individuals with ADHD and SU. The details about the strategic selection of the QIS sample from the larger MTA sample and demographics of the subsample selected for the QIS provides context for the further emphasis on subsamples that differed across the four contributions to the Special Issue (as outlined in Appendix A). This article (along with the others) demonstrates the utility of a qualitative approach to SU assessment to identify perceptions about frequent use and reasons for use of substances. Along with the other three papers in this Special Issue of the journal, this paper explores how some characteristic of Persistent SU may be different in individuals with a childhood history of ADHD in various stages of SU development (i.e., initiation, escalation, maintenance, and cessation).

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Appendix:: Summary of the MTA Qualitative Interview Study (QIS): Sample Size and Descriptions for Reports in this Special Issue

Weisner et al (in press) Sample (n = 183)[1]	**Swanson et al (in press) Sample (n = 183)**[2]	**Jensen et al. (in press) Sample (n = 183)**[3]	**Mitchell et al. (in press) Sample (n = 92)**[4]
ADHD (n = 125)	Persistent SU (n = 58)	Qualitative SU Classification (n = 183)	SU Persisters[5] (n = 67)
LNCG (n= 58)	39 ADHD	SU Persisters[5] (n = 67)	50 ADHD
	19 LNCG	50 ADHD	17 LNCG
	Non-Persistent SU (n = 125)	17 LNCG	SU Desisters[5] (n = 25)
	86 ADHD	SU Desisters[5] (n = 58)	20 ADHD
	39 LNCG	39 ADHD	5 LNCG
		19 LNCG	
		Abstainers (n = 32)	
		18 ADHD	
		14 LNCG	
		SU Late Starters (n = 16)	
		9 ADHD	
		7 LNCG	
		SU Resumers (n = 10)	

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Weisner et al (in press) Sample (n = 183)[1]	Swanson et al (in press) Sample (n = 183)[2]	Jensen et al. (in press) Sample (n = 183)[3]	Mitchell et al. (in press) Sample (n = 92)[4]
		9 ADHD	
		1 LNCG	
		Primary Analysis (n = 60)	
		SU Persisters[5] (n = 20)	
		10 ADHD	
		10 LNCG	
		SU Desisters[5] (n = 20)	
		10 ADHD	
		10 LNCG	
		Abstainers (n = 20)	
		10 ADHD	
		10 LNCG	

Notes. SU = Substance Use.

[1] Weisner et al (in press) described the general methods for the Qualitative Interview Study (QIS), including the recruitment of participants from the ADHD group and from the LNCG and the 17 topics covered by the QIS. The ADHD group and the LNCG were compared on demographic variables (age, sex, race/ethnicity) and site of participants (Berkeley, Duke, Irvine, and Montreal), and no difference was significant. The two groups were also compared on the average ratings (on a 0–8 scales, with 0 = unimportant to 8= very important) applied to the excerpts of the QIS on the 9 main topics coded for SU, and only 1 of the 7 (seeing others go “down wrong path”) showed a significant difference (ADHD = 4.99 vs LNCG = 3.85, $t(72) = 2.68$, $p < 0.006$).

[2] Swanson et al (in press) described the origins of the QIS sample based on initial recruitment of ADHD (n = 576) and LNCG (n = 289) cases, retention into adulthood of the ADHD (n= 476) and LNCG (n = 267), and participation of the 4 sites of ADHD (n = 325) and LNCG (n = 159) cases. The 4 subgroups defined by Diagnosis in childhood and Persistence of substance use were compared on 5 demographic variables related to substance use (sex, and household education, social-economic, public assistance, and race/ethnicity status) with no clear evidence of confounding, and were compared on perceived frequency and reasons given in the interview for use and non-use of substances.

[3] Jensen et al. (in press) described additional qualitative classification procedures that yielded a total of 67 SU persisters (50 ADHD, 17 LNCG), 58 SU desisters (39 ADHD, 19 LNCG; this sample was narrowed to 33 of the 58 on the basis of heavier use [two previous assessments documenting ongoing SU] and a subsequent ≥ four years of ongoing abstinence), 32 Abstainers (18 ADHD, 14 LNCG), 16 SU Late Starters (9 ADHD, 7 LNCG), and 10 SU Resumes (9 ADHD, 1 LNCG). From these qualitative classification procedures, 10 ADHD and 10 LNCG participants were randomly selected from the SU Persister group, the SU Desister group, and the Abstainer group (male to female ratio of 4:1) to yield a final sample of 60 participants. ADHD subjects reported fewer social advantages to avoid SU than non-ADHD subjects. SU Desisters and SU Persisters reported more social advantages of using drugs than abstainers. SU Persisters reported both more negative and positive psychological/physiological effects of SU. ADHD subjects reported fewer positive role models in their lives. Non-ADHD patients reported more positive turning points than ADHD subjects, regardless of SU status.

[4] Mitchell et al (2016) included participants who were classified using qualitative procedures SU Persisters (50 ADHD, 17 LNCG) among the 58 SU Desisters described in Jensen et al., the 25 participants who reported lighter rates of SU were reported on (lighter SU was in comparison to the other 33 within the SU Desister group). SU Persisters perceived SU positively affects emotional states and positive emotional effects outweigh negative effects. No ADHD group effects emerged. Qualitative analysis identified perceptions that cannabis enhanced positive mood for ADHD and LNCG SU Persisters, and improved negative mood and ADHD for ADHD SU Persisters.

[5] Jensen et al. and Mitchell et al. used SU Persisters and SU Desisters to describe their samples derived from qualitative classification (in addition to quantitatively-based SUQ classification), which is different from the use of Persistent SU and Non-Persistent SU described in this paper that relied solely on quantitative classification based on the SUQ. Given the different approaches to classification, these different forms of terminology were adopted.

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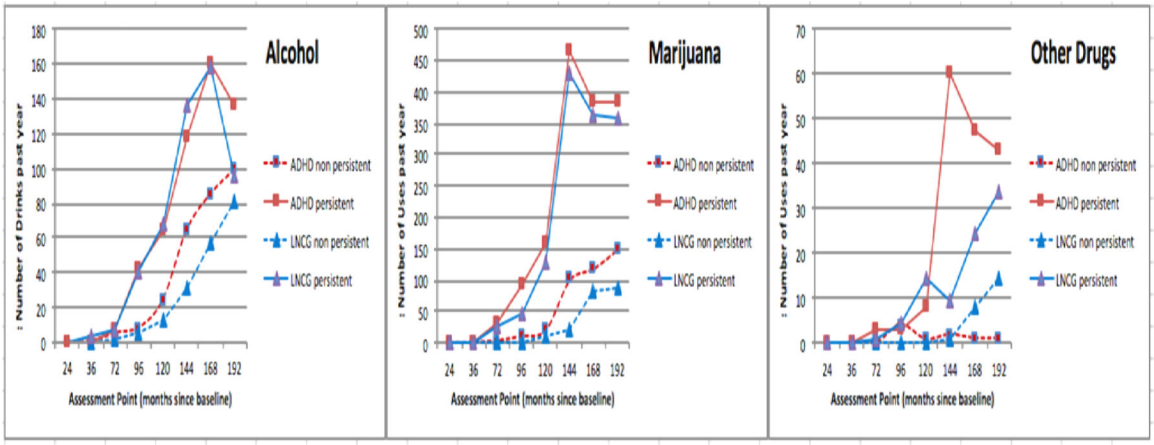

Figure 1:
Trajectories of Substance Use in the Subgroups from the Substance Use Questionnaire

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Table 1.

Criteria for defining persistent SU: developmental thresholds for coding a positive substance use report

	Alcohol	**Marijuana**	**Prescription Medications (e.g., stimulants, narcotics]**	**Other Illicit Drugs (e.g., inhalants, cocaine)**
Early Adolescence (24/36 months, mean ages 10.4 & 11.7 years)	Ever had a drink of alcohol, > just a sip (at 24/36 m or by age 15)	Ever tried marijuana	Ever used > prescribed or without a prescription	Ever used
Mid to Late Adolescence (6 & 8 year follow-ups, mean ages 14.9 & 16.8 years)	Once a month or > past 6 months for any drinks, or >2, binges, or drunkenness.	Once/month or > in the past 6 months.	Used > prescribed or without a prescription, once/mo. or > in past 6 months	Once/month or > in the past 6 months.
Transition Year (10 year follow-ups, mean age 18.7 years)	Once/month > in past 6 months, for any or 3+ drinks, binging, or drunkenness.	Once/month or > in the past 6 months.	Used > prescribed or without a prescription, once/mo. or > in the past 6 months	Once/month or > in the past 6 months.
Early Adulthood (12–16 year follow-ups, mean ages 21.1, 23.2, 25.3 years)	Binge drinking (women > 3, man > 4 drinks weekly or > in the past year	Weekly or more often in the past year	Used > prescribed or without a prescription, weekly or > in the past year	Weekly or > in the past year

Note. Mean ages are reported for the ADHD group but are similar for the LNCG. The 10-year assessment straddles late adolescence and early adulthood. A report of SU at either or both of the 2- and 3-year assessments was counted as one positive report. Two of the five positive reports were required to occur in adolescence (between the 2-year and 8-year follow-up assessments). Three were required to occur in adulthood (between the 10-year and 16-year follow-up assessment), with one of the three at the 14-year or 16-year follow-up assessment near the qualitative interview. For recruitment, the strict criteria were relaxed for borderline cases (n=7 for ADHD and n=8 for LNCG) to increase the number of participants in the Persistent SU subgroups.

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Table 2:

Effects of Initial Recruitment, Retention in Adulthood, and Participation of Sites

A: RECRUITED					**ADHD**						**LNCG**	
					N=579			**p<**			**N=289**	
% Female					19.7%			0.913			19.4%	
% High EDU					45.9%			0.073			53.0%	
%High SEA					37.6%			0.019			44.6%	
% Welfare					18.0%			0.022			12.5%	
% Minority					39.2%			0.534			37.0%	
B: RETAINED				YES		NO				YES		NO
				N=476	p<	N=103				N=267	p<	N=22
% Female				21.9%	0.005	9.8%				19.9%	0.603	16.7%
% High EDU				49.6%	0.001	28.4%				55.7%	0.120	39.6%
%High SEA				40.1%	0.011	25.7%				48.1%	0.027	27.1%
% Welfare				17.4%	0.095	24.5%				10.5%	0.017	22.9%
% Minority				37.4%	0.055	47.6%				33.6%	0.007	54.2%
C: QIS SITE			YES		NO				YES		NO	
			N=325	p<	N=151				N=159	p<	N=82	
% Female			21.2%	0.632	23.2%				22.0%	0.257	15.9%	
% High EDU			52.7%	0.001	43.7%				66.2%	0.001	35.4%	
%High SEA			42.2%	0.145	35.8%				58.6%	0.001	28.1%	
% Welfare			12.3%	0.001	28.5%				07.6%	0.049	15.9%	
% Minority			33.5%	0.011	45.7%				26.4%	0.001	47.6%	

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Table 3:

Strategic Selection of Persistent SU Cases and Random Selection of Non-Persistent SU Cases

A: AVAILABLE					**ADHD**				**LNCG**			
					N=325		**p<**		**N=159**			
% Female					21.2%		.122		22.0%			
% High EDU					52.7%		.844		66.2%			
%High SEA					42.2%		.005		58.6%			
% Welfare					12.3%		.0005		07.6%			
% Minority					33.5%		.112		26.4%			
B: PERSISTENT				YES		NO		YES		NO		
AVAILABLE				N=39		N=286		N=19		N=140		
SELECTED				N=39		N=86		N=19		N=39		
% OF AVAILABLE				12.0%		26.5%		11.9%		24.5%		
% IN SUBGROUPS				PER.	p<			PER.	p<	N-PER.		
% Female				15.4%	0.154	27.1%		22.2%	0.883	20.6%		
% High EDU				56.4%	0.649	57.7%		66.6%	0.205	76.9%		
%High SEA				46.1%	0.852	47.1%		55.6%	0.291	71.8%		
% Welfare				0.0%	a	11.8%		05.6%	b	05.1%		
% Minority				23.1%	0.463	29.4%		05.6%	0.150	20.6%		

(cell sizes of a=0 and b=1 are too small for the chi square test)

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Table 4:

Medication for Assigned RCT Groups[a] and Self-Selected Naturalistic Subgroups[b]

	Persistent SU (n=39)	**Non-Persistent SU (n=86)**
A. Assigned Treatments in the 14-month RCT		
Medication	8 (21%)	19 (22%)
Combined	10 (26%)	22 (26%)
Behavioral	10 (26%)	21 (24%)
Community	11 (28%)	24 (28%)
B. Self-Selected Treatment in the LTF		
Negligible	9 (23%)	16 (19%)
Inconsistent	27 (69%)	65 (75%)
Consistent	3 (8%)	5 (6%)
CME Dose	57,885 mg	54,961 mg

[a] indicates chi-square (2) = 0.0481, p = 0.9972

[b] indicates chi-square (2) = 0.5633, p = 0.7545

[c] indicates F(1,124) = 0.45, p = 0.5052

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Table 5:

Unprompted Reasons for Use and Non-Use of Substances Given in the M-EFI

(a) Reasons for use/continuing use
1. Stability: Engaging in SU to achieve a more stable functioning in life (including self-medication, relief of anxiety, stress, etc.). For example, “It calms me down.”
2. Adverse Peer Influence: Someone directly encouraged SU or when an admired person(s) was using. For example, “Otherwise I never felt like I fit in.”
3. Recreational: SU is attributed to curiosity or to experiment. For example, “Just to go out and have fun.”
4. Improve Quality of Life: Includes the idea everyday life is more enjoyable after engaging in SU. For example, “You know I like being in a different world.”
5. Addiction: Includes SU because of feeling compelled to use or to avoid effects of withdrawal. For example, “I guess you could say I was reliant on it.”
(b) Reasons for non-use/stopping use
1. Instability: Not being able to fulfill daily responsibilities or perform work duties due to SU due to lack of stability. For example, “I would miss or be late to class.”
2. Favorable Peer Influence: Examples by others. For example, “… hanging out with girls from that sorority who were not doing that, so I was fine with not using.”
3. Educational realization: Information (e.g., seminar, etc.) resulting in never starting or stopping SU. For example, “I learned that using can make anxiety worse.”
4. Guilt or self-awareness: Blaming or being self-conscious about SU. For example, “I was just so ashamed of it” or “I just got this feeling like I need to stop.”
5. Avoidance of Consequences: Adverse financial, legal, or health effects. For example, “I stopped for fear of getting caught” or “It was affecting my health.”

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Table 6:

Quantitative (Frequency of Use) and Qualitative (Percentage with Frequent Use) Outcome Measures

A. Least Square Means for Uses per Year from the SDQ at the 16-year Assessment Point												
		A. ALL CASES		**B. DIAGNOS**				**C. PERSISTENCE**				
				ADHD		**LNCG**		**Non-Persistent**		**Persistent**		
		n = 183		**n=124**		**n=58**		**n=125**		**n=57**		
ALCOHOL		103		117.1		88.8	0.0652	90		116	0.0904	
MARIJUANA		246		268.3		223.5	0.2303	120.1		371.7	0.0001	
OTHER DRUGS		23		22.1		24	0.8325	7.7		38.4	0.0007	
				D. DIAGNOSIS X PERSISTENCE								
				ADHD Non-Persistent		**ADHD Persistent**		**LNCG Non-Persistent**		**LNCG Persistent**		
				n=86		n=38		n=39		n=19	0.5485	
ALCOHOL				98.6		135.6	0.035	81.4		96.3	0.0001	
MARIJUANA				151.2		385.5	0.0001	89.5		357.9	0.3346	
OTHER DRUGS				1.09		43.1	0.0001	14.3		33.8		

B. Percentages of Participants with Frequent Substance Use (i.e., ≥ once/week) from M-EFI														
	A. ALL CASES			**B. DIAGNOM**					**C. PERSISTENCE**					
				ADHD		**LNCG**			**Non-Persistent**		**Persistent**			
	n=182			**n=124**		**n=58**			**n=125**		**n=57**			
ALCOHOL	56	30.8%		45	36.3%	14	24.1%	0.10	35	28.0%	24	42.1%	0.06	
MARIJUANA	45	24.7%		334	27.4%	11	19.0%	0.22	21	16.8%	24	42.1%	0.00	
OTHER DRUGS	6	3.3%		4	3.2%	2	3.4%	0.94	2	1.6%	4	7.0%	0.06	
				D. DIAGNOSIS X PERSISTENCE										
				ADHD Non-Persistent		**ADHD Persistent**			**LNCG Non-Persistent**		**LNCG Persistent**			
				n=86		n=38			n=39		n=19			
ALCOHOL				26	30.2%	19	50.0%	0.035	9	23.1%	5	0.787	0.787	
MARIJUANA				16	18.6%	18	47.4%	0.001	5	12.8%	6	0.087	0.087	
OTHER DRUGS				0	0.0%	4	10.5%	0.002	2	5.1%	0	0.317	0.317	

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Table 7:

Qualitative Outcome Measure of Reasons for Use and Non-Use (Percentage of Cases)

PART I: Main Effects for Diagnosis and Persistence Factors for Three Types of Substances														
	A. ALL CASES			**B. DIAGNOSIS**						**C. PERSISTENCE**				
ALCHOL				**ADHD**		**LNCG**				**Non-Persistent**		**Persistent**		
	(n=175)			**(n=118)**		**(n=57)**				**(n=122)**		**(n=53)**		
	n			**n**		**n**		**p**		**n**		**n**		**p**
Stability	56	32.0%		37	31.4%	19	33.3%	0.79			28.7%	21	39.6%	0.15
Negative Peer Influence	90	57.4%		59	50.0%	31	54.4%	0.59		60	49.2%	30	56.6%	0.37
Recreational	138	78.9%		91	77.1%	47	82.5%	0.42		92	75.4%	46	86.8%	0.09
Improve Quality of Life	4	2.3%		3	2.5%	1	1.8%	0.74		3	2.5%	1	1.9%	0.82
Addiction	16	9.1%		13	11.1%	3	5.3%	0.22		10	8.2%	6	11.3%	0.51
Instability	14	8.0%		12	10.2%	2	3.5%	0.13		11	9.0%	3	5.7%	0.45
Positive Peer Influence	12	6.9%		8	6.8%	4	7.0%	0.95		7	5.7%	5	9.4%	0.37
Education/Realization	40	22.9%		26	22.0%	14	24.6%	0.71		33	27.1%	7	13.2%	0.05
Guilt/Self Awareness	35	20.0%		26	22.0%	9	15.8%	0.33		25	20.5%	10	18.9%	0.81
Avoid Consequences	78	44.6%		53	44.9%	8	14.0%	0.90		54	44.3%	24	45.3%	0.90
MARIJUANA				ADHD		LNCG				Non-Persistent		Persistent		
	(n=157)			(n =109)		(n=48)				(n =101)		(n=56)		
	n			**n**		**n**		p		**n**		**n**		p
Stability	66	42.0%		52	47.7%	14	29.2%	0.03		35	34.7%	31	55.4%	0.01
Negative Peer Influence	71	45.2%		50	45.9%	21	43.8%	0.81		38	37.6%	33	58.9%	0.01
Recreational	104	66.2%		74	67.9%	30	62.5%	0.51		62	61.4%	42	75.0%	0.08
Improve Quality of Life	26	16.6%		19	17.4%	7	14.6%	0.66		11	10.9%	15	26.8%	0.01
Addiction	17	10.8%		13	11.9%	4	8.3%	0.50		6	5.9%	11	19.6%	0.01
Instability	21	13.4%		16	14.7%	5	10.4%	0.47		13	12.9%	8	14.3%	0.80
Positive Peer Influence	13	8.3%		9	8.3%	4	8.3%	0.99		7	6.9%	6	10.7%	0.41
Education/Realization	16	10.2%		14	12.8%	2	4.2%	0.10		13	12.9%	3	5.4%	0.14
Guilt/Self Awareness	38	24.2%		19	17.4%	9	18.8%	0.29		19	18.8%	19	33.9%	0.03
Avoid Consequences	69	44.0%		45	41.3%	24	50.0%	0.31		41	40.6%	28	50.0%	0.26
OTHER DRUGS				ADHD		LNCG				Non-Persistent		Persistent		
	(n=126)			(n=89)		(n=37)				(n=77)		(n=49)		
	n			**n**		**n**				**n**		**n**		p
Stability	20	15.9%		15	17.9%	5	13.5%	0.64		7	9.1%	13	26.5%	0.01
Negative Peer Influence	34	27.0%		25	28.1%	9	24.3%	0.66		15	19.5%	19	38.8%	0.02
Recreational	62	49.2%		47	52.8%	15	40.5%	0.21		30	39.0%	32	65.3%	0.00
Improve Quality of Life	16	12.7%		13	14.6%	3	8.1%	0.32		4	5.2%	12	24.5%	0.00
Addiction	9	7.1%		8	9.0%	1	2.7%	0.21		5	6.5%	4	8.2%	0.72

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PART I: Main Effects for Diagnosis and Persistence Factors for Three Types of Substances														
	A. ALL CASES			B. DIAGNOSIS						C. PERSISTENCE				
ALCHOL				ADHD		LNCG				Non-Persistent		Persistent		
	(n=175)			(n=118)		(n=57)				(n=122)		(n=53)		
	n			n		n		p		n		n		p
Instability	16	12.7%		14	15.7%	2	5.4%	0.11		11	14.3%	5	10.2%	0.50
Positive Peer Influence	10	7.9%		6	6.7%	4	10.8%	0.44		7	9.1%	3	6.1%	0.55
Education/Realization	41	32.5%		30	33.7%	11	29.7%	0.66		28	36.4%	13	26.5%	0.25
Guilt/Self Awareness	23	18.3%		18	20.2%	5	13.5%	0.37		17	22.1%	6	12.2%	0.16
Avoid Consequences	68	54.0%		48	53.9%	20	54.1%	0.99		37	48.1%	31	63.3%	0.10

PART II: Effects for Interaction of Daignosis and Persistence Factors for 3 Types of Substances														
				D. DIAGNOSIS X PERSISTENCE										
ALCHOL				ADHD Non-Persistent		ADHD Persistent				LNCG Non-Persistent		LNCG Persistent		
				(n=83)		(n=35)				(n=39)		(n=18)		
				n		n		p		n		n		p
Stability				25	30.0%	12	34.3%	0.66		10	25.6%	9	50.0%	0.07
Negative Peer Influence				38	45.8%	21	17.8%	0.16		22	56.4%	9	50.0%	0.65
Recreational				60	72.3%	31	88.6%	0.06		32	82.1%	15	83.3%	0.91
Improve Quality of Life				3	3.6%	0	0.0%	0.26		0	0.0%	1	5.6%	0.14
Addiction				8	9.6%	5	14.3%	0.46		2	5.1%	1	5.6%	0.95
Instability				10	12.1%	2	5.7%	0.30		1	2.6%	1	5.6%	0.57
Positive Peer Influence				4	4.8%	4	11.4%	0.19		3	7.7%	1	5.6%	0.77
Education/ Realization				19	22.9%	7	20.0%	0.73		14	35.9%	0	0.0%	0.00
Guilt/Self Awareness				18	21.7%	8	22.9%	0.89		7	18.0%	2	11.1%	0.51
Avoid Consequences				37	44.6%	16	45.7%	0.91		17	43.6%	8	44.4%	0.95
MARIJUANA				ADHD Non-Persistent		ADHD Persistent				LNCG Non-Persistent		LNCG Persistent		
				(n=71)		(n=38)				(n=30)		(n=18)		
				n		n		p		n		n		p
Stability				29	40.9%	23	60.5%	0.05		6	20.0%	8	44.4%	0.07
Negative Peer Influence				26	36.6%	24	63.2%	0.01		12	40.0%	9	50.0%	0.50
Recreational				47	66.2%	27	71.1%	0.61		15	50.0%	15	83.3%	0.02
Improve Quality of Life				8	11.3%	11	29.0%	0.02		3	10.0%	4	22.2%	0.25
Addiction				5	7.0%	8	21.1%	0.03		1	3.3%	3	16.7%	0.11

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PART II: Effects for Interaction of Daignosis and Persistence Factors for 3 Types of Substances													
				D. DIAGNOSIS X PERSISTENCE									
ALCHOL				**ADHD Non-Persistent**		**ADHD Persistent**				**LNCG Non-Persistent**		**LNCG Persistent**	
				(n=83)		**(n=35)**				**(n=39)**		**(n=18)**	
				n		**n**		**p**		**n**		**n**		**p**
Instability				9	12.7%	7	18.4%	0.42		4	13.3%	1	5.6%	0.39
Positive Peer Influence				4	5.6%	5	13.2%	0.17		3	10.0%	1	5.6%	0.59
Education/ Realization				11	15.5%	3	78.9%	0.26		2	6.7%	0	0.0%	0.26
Guilt/Self Awareness				14	19.7%	15	39.5%	0.03		5	16.7%	4	22.2%	0.63
Avoid Consequences				28	39.4%	17	44.7%	0.59		13	43.3%	11	61.1%	0.23
OTHER DRUGS				ADHD Non-Persistent		ADHD Persistent				LNCG Non-Persistent		LNCG Persistent		
				(n=56)		(n=33)				(n=21)		(n=16)		
Stability				n		n		p		n		n		p
Negative Peer Influence				6	10.7%	9	27.3%	0.04		1	4.8%	4	25.0%	0.07
Recreational				11	19.6%	14	42.4%	0.02		4	19.1%	5	31.3%	0.39
Improve Quality of Life				25	44.6%	22	66.7%	0.04		5	23.8%	10	62.5%	0.02
Addiction				4	7.1%	9	27.3%	0.01		0	0.0%	3	18.8%	0.04
				5	8.9%	3	9.1%	0.98		0	0.0%	1	6.3%	0.25
Instability														
Positive Peer Influence				10	17.9%	4	12.1%	0.47		1	4.8%	1	6.3%	0.84
Education/ Realization				5	8.9%	1	3.0%	0.28		2	9.5%	2	12.5%	0.77
Guilt/Self Awareness				20	35.7%	10	30.3%	0.60		8	38.1%	3	18.8%	0.20
Avoid Consequences				12	21.4%	6	18.2%	0.71		5	23.8%	0	0.0%	0.04