ABSTRACT

Introduction Alcohol use disorder (AUD) remains one of the most pervasive of all psychiatric illnesses conferring a massive health and economic burden. In addition to professional treatments to address AUD, mutual-help organisations such as Alcoholics Anonymous (AA) and newer entities like Self-Management and Recovery Training (SMART Recovery) play increasingly important roles in many societies. While much is known about the positive effects of AA, very little is known about SMART. Hence, this study seeks to estimate real-world patterns of utilisation and benefit from SMART Recovery as well as explore for whom (moderators) and how (mechanisms) SMART confers recovery benefits.

Methods and analysis Naturalistic, longitudinal, cohort study (n=368) of individuals with AUD recruited between February 2019 and February 2022, initiating a new recovery attempt who self-select into one of four groups at study entry: (1) SMART Recovery; (2) AA; (3) SMART+AA; (4) Neither SMART nor AA; (stratified by Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM 5) severity markers), with assessments conducted at intake, and 3 months, 6 months, 9 months, 12 months, 18 months and 24 months. Primary outcomes are: frequency of SMART and AA meetings attendance; per cent days abstinent and per cent days heavy drinking. Secondary outcomes include psychiatric distress; quality of life and functioning. Moderator variables include sex/gender; race/ethnicity; spirituality. Mediational variables include social networks; coping skills; self-efficacy; impulsivity. Multivariable regression with propensity score matching will test for patterns of attendance and effects of participation over time on outcomes and test for mechanisms and moderators.

Ethics and dissemination This study involves human participants and was approved by the Massachusetts General Hospital Institutional Review Board (Protocol #: 2017P002029/PHS). Results will be published in peer-reviewed journals and presented at conferences.

Registration This is a non-randomised, naturalistic, longitudinal, cohort study, and thus was not registered in advance. Results, therefore, should be considered exploratory.

INTRODUCTION

Alcohol and other drug use disorders confer a prodigious burden of disease, disability and premature mortality in most middle-income and high-income countries globally. To help alleviate this burden, most countries provide an array of professionally delivered addiction treatment services. Yet, despite these efforts, such services are often unable to meet both acute care and long-term relapse prevention needs of the millions or tens of millions affected annually. In response, most countries also possess an array of informal community-based peer recovery support services which can provide ongoing assistance for individuals suffering from these disorders. The oldest and largest of these are the 12-step mutual-help organisations (MHOs), such as Alcoholics Anonymous (AA). Rigorous
research evidence has now demonstrated that when AA is subjected to the same scientific standards as other addiction focused interventions it does as well on most outcomes measures, is better at sustaining abstinence and remission over time, and is highly cost-effective.1

A limitation of the current standard of care, however, borne out of a limitation in available empirical data, is the fact that referral oftentimes focuses solely on spiritually oriented 12-step organisations, such as AA, which is the only empirically supported MHO continuing the care referral option. Not everyone chooses AA as a pathway to recovery for various reasons, and alternative MHO options—although much newer and smaller—are growing and may contain many of the same positive therapeutic elements and dynamics possessed by AA.2,3 These therapeutic pathways include adaptive social network changes, increases in social abstinence self-efficacy, and reducing negative affect. Indeed, some preliminary evidence suggests such organisations may confer similar benefits for those who self-select into them.4

The largest and possibly most well known of these newer alternative MHOs is Self-Management and Recovery Training (SMART Recovery). There are approximately 1200 SMART groups nationwide and another 1000 internationally. SMART also has a strong online support presence including online meetings, forums and chat rooms. Unlike AA, SMART is founded on cognitive-behavioural principles and practices and is led by trained facilitators. It focuses on enhancing and maintaining motivation to abstain or (more recently) reduce use to non-problematic levels, coping with urges, problem solving and lifestyle balance.5 It also advocates for appropriate use of professional psychosocial and pharmacological treatments. A compelling aspect of SMART as an MHO is, because it is itself based on empirically derived cognitive-behavioural therapy (CBT) principles, it provides a philosophically compatible recovery resource that is aligned with cognitive-behavioural treatment principles, which make up a large majority of national and international evidence-based treatments.6 Consequently, SMART is appealing to many individuals with substance use disorder (SUD),5 yet due to the lack of empirical evidence supporting its effectiveness, clinicians remain less likely to discuss or refer patients to SMART.7,8 This has hindered its growth and prevented many the opportunity to learn about and try SMART.

Compared with the dozens of high-quality studies examining 12-step MHOs,9–12 there have been just a handful of studies on SMART. We conducted a systematic review of this research13 and found that only 12 studies exist (4 of which are unpublished dissertations) that have focused on SMART Recovery and used any kind of formal measurement. Most of these (8 out of the 12) are cross-sectional with mixed results and suffer from considerable biases as they possess substantial methodological limitations making it difficult to draw firm conclusions.13–16 For instance, these studies have rarely assessed mental health status or its severity, despite the high rates of comorbidity between alcohol use disorder (AUD) and mental health. Two recent high-quality studies examining SMART Recovery, however, have been conducted, one in a criminal justice context, the other examining its effect on heavy alcohol use in a randomised controlled trial.

The criminal justice study was a large quasi-experimental study of criminal offenders in Australia.15 It compared a group of individuals participating in SMART Recovery and/or a criminal justice intervention (called ‘Getting SMART’) designed to link offenders with SMART meetings following prison release, to a group of control participants who did not interact with any SMART materials or attended meetings, but who were matched on various other relevant characteristics through the use of propensity scores. The study found that participation in Getting SMART by itself, and Getting SMART+SMART Recovery meeting attendance, was associated with a reduced overall rate of reconviction with rates of reconviction reduced by 19% and 22%, respectively. For violent reconvictions, rates were reduced by 30% for Getting SMART participation and 42% for Getting SMART+SMART Recovery. While an important and promising set of results in their own right, unfortunately, the authors did not examine or report any alcohol/drug use outcomes.17

There has been only one small, randomised trial evaluating SMART Recovery, which randomised people to (1) ‘Overcoming Addictions’ (OA)—a SMART Recovery web application, (2) SMART Recovery meeting attendance, or (3) OA+SMART Recovery meeting attendance combined. The study found that participants from all groups benefited equally with respect to alcohol outcomes.18 This finding underlines the promise of SMART Recovery to provide recovery support. Unfortunately, however, this trial did not include a control group, who did not have any exposure to SMART materials. Given, however, that all groups participated in SMART, it is not clear if observed benefits were simply naturally occurring improvements in alcohol outcomes, or really a function of SMART participation. Another limitation is that it only enrolled subjects with heavy drinking problems and excluded participants with more severe forms of AUD, who more typically enrol in formal treatment and are thus in need of referral options for continuing care.

A more recent study examined participation among individuals with AUD recruited from various online and community venues with varying lengths of sobriety who self-selected into one of four different types of MHOs: AA, LifeRing Secular Organisation, SMART Recovery, and Women for Sobriety.1 This study found that SMART Recovery participants had as good alcohol outcomes as those attending other MHOs. Again, however, the study did not include a control group with no MHO involvement.

These results provide some preliminary information about real-world benefits related to SMART Recovery participation. There is very little, if any, information regarding how involved they become or the mechanisms of behaviour change through which SMART may
help individuals attain AUD remission and recovery (eg, via social changes, coping skills, recovery motivation, abstinence self-efficacy, reduced impulsivity). SMART has the potential to be a secular MHO alternative to 12-step MHOs for those preferring the secular and cognitive-behavioural foundation of SMART, yet in order to increase clinical confidence and referrals, more systematic research is needed. This study will be one of the first rigorous, real-world, evaluations of SMART providing objective estimates of recovery benefit (eg, abstinence, AUD remission, quality of life, psychosocial functioning), and will explore the mechanisms (eg, social network changes, self-efficacy, decreased impulsivity) and moderators (eg, sex, race/ethnicity, addiction severity, psychiatric co-morbidity) of behaviour change to determine how SMART Recovery may help its affiliates achieve and maintain remission from addiction and who seems to benefit most. To this end this study has the following specific aims: (1) Characterise and describe professional and non-professional recovery support service participation choices, migrations, and pathways using group trajectory analyses over a 2-year period for individuals (n=368) starting a new AUD recovery attempt. More specifically in this regard, we will investigate the real-world effectiveness of SMART Recovery by comparing outcomes of AUD individuals making a new recovery attempt (n=368) pursuing either a SMART Recovery pathway (online or face-to-face; n=184) or a non-SMART Recovery pathway (n=184). Because, according to SMART Recovery’s annual survey data, roughly half of SMART participants also attend AA, we will use a stratified design to enrol persons with AUD making naturally occurring continuing care choices vis-à-vis participation in MHOs in a balanced fashion and follow them prospectively across a 24-month period. Of note, self-selection of treatment/recovery pathway options has been shown to potentially enhance outcomes. This will be explored in this study as well. This stratified design will allow us to compare the outcomes of persons choosing to participate in SMART Recovery versus not (balanced by AUD severity), while accounting for simultaneous choices regarding AA or neither AA or SMART MHO participation. (2) Explore moderators and mechanisms of behaviour change. Exploration of factors that may help uncover who (ie, moderators) and why (ie, mechanisms) SMART affiliates benefit from participation will be investigated. Moderators will include sex and gender, addiction severity, psychiatric distress; and mechanisms will include social network changes, recovery motivation, cognitive-behavioural coping, abstinence self-efficacy and impulsivity.

**METHODS AND ANALYSIS**

**Study overview**

This study is a naturalistic, prospective, longitudinal cohort study of 368 individuals making a new recovery attempt from AUD with seven assessments over a 24-month follow-up period. Following the baseline assessment, research staff will conduct additional follow-up assessments at 3 months, 6 months, 9 months, 12 months, 18 months and 24 months after study enrolment. Assessments include both self-reports by participants using online surveys, and staff-administered assessments, conducted via phone and/or Zoom. Baseline visits were conducted from February 2019 to February 2022. Follow-up visits are ongoing and will continue until approximately February 2024. All study procedures are approved by the Institutional Review Board of Mass General Brigham (approval number: 2017P002029). Written consent was received from all participants following an explanation of the study, including confidentiality and freedom of choice to participate.

**Sample size determination**

The primary outcome variables are per cent days abstinent (PDA) and per cent days heavy drinking (PDHD; National Institute on Alcohol Abuse and Alcoholism (NIAAA)-defined). Secondary outcomes include quality of life and psychosocial functioning. To estimate a plausible effect size to be expected in PDA as a function of MHO utilisation, we examined the PDA outcomes in Project Matching Alcoholism Treatments to Client Heterogeneity (MATCH)19 for persons using AA versus not. Effects were surprisingly consistent across time, with patients with any AA utilisation reporting a higher average number of PDA than patients with no AA involvement (d=0.45, 0.39, 0.38, 0.42 and 0.39 at 3-month, 6-month, 9-month, 12-month and 15-month follow-ups, respectively). Thus, conservatively, we are powering this study to detect an effect size of d=0.35. Using Statistical Analysis Software (SAS) proc power we determined that n=130 per group are necessary to detect d=0.35, leading to a combined sample size of n=260 (equally balanced, due to stratification, in terms of AA utilisation and addiction severity). With a conservatively estimated retention rate of 75%, we would need to enrol n=347 to retain n=260. Given our stratified design (ie, 2 (SMART vs not) × 2 (12-step vs not) × 3 (mild vs moderate vs severe AUD) design=12 stratification cells), we proposed to enrol a final sample size of n=348 (ie, n=29 per cell). In addition, 20 further participants were enrolled to increase representation of individuals attending SMART Recovery and to account for participants who withdrew, were terminated from the study, were found ineligible or were otherwise no longer participating (eg, death unrelated to the study).

Using this design, we will be equally well powered to test the main effect of 12-step participation. In terms of conducting pairwise comparisons between the four possible combinations of using SMART Recovery and/or 12-step, this sample size would enable us to detect pairwise differences of medium effect size (d=0.50). Improvements over our conservatively estimated retention rate would increase power (eg, could detect d=0.46 with 85% retention).
Recruitment
Participants were recruited through SMART Recovery meetings, inpatient and outpatient treatment programmes, and a variety of commercial recruitment sources during the recruitment period (January 2019 to January 2022).

Flyers and postcards for the study were distributed around buildings of Massachusetts General Hospital, particularly around inpatient and outpatient SUD clinics. SMART facilitators were asked to advertise the study at SMART meetings and were provided with recruitment postcards and flyers. The study was also advertised on the SMART San Diego website. Additional recruitment methods included ResearchMatch, Partners eCare Research Core (PeRC), TrialFacts, Rally for Recruitment, the Metro Newspaper, radio advertisements, Massachusetts Boston Transport Authority (MBTA) advertisement, Facebook, Craigslist and Reddit. For radio, MBTA, Facebook and Craigslist advertisements, this study was advertised along with another ongoing R01 study of individuals making a new recovery attempt from AUD with similar eligibility criteria. Monthly meetings were also held with regional SMART Recovery MHO group facilitators to provide them with updates and inquire if there was anything we could provide to help facilitate study recruitment from online SMART resources or SMART meetings.

Interested individuals called the study-specific phone line, emailed the study-specific email address or filled out an online screening form. Individuals were then able to participate in a brief 10–15 min phone screen, during which eligibility criteria were confirmed (see online supplemental material 1 for a copy of Eligibility Screen). If the individual was eligible to participate, the baseline visit was scheduled and contact information for two locator contacts who can assist research staff in locating participants was collected.

Consent process
Participants completed the consent process with a trained study staff member and were encouraged to ask questions about any aspect of the study. Through this process, participants were informed about the nature and extent of the study duration and procedures including the types of assessments administered, the risks and benefits of participation, as well as the financial renumeration schedule and protocol, and given telephone and email contact information in order to contact study staff at any time during the course of the study (see Consent Form in online supplemental material 2 for more details).

Eligibility
Participants were required to be 18 years or older, living in the New England or San Diego metropolitan area, and willing to travel to Boston, Massachusetts, to complete study visits (for New England residents) or to complete study visits remotely (due to COVID-19 and for the San Diego participants). The geographical catchment area eligibility criteria was expanded to include people from the San Diego area in December 2020 to increase the number of SMART participants in the study. Since all visits were conducted remotely beginning in March 2020 due to the COVID-19 pandemic, participants from the New England area would also be considered eligible even if they could not travel to the Boston office for assessments in the foreseeable future.

Participants could be using other drugs but had to report alcohol as their primary substance of concern; they were also required to have a self-perceived alcohol problem, to meet current criteria for Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM 5) AUD using semistructured interview; to have consumed alcohol in the past 90 days and report currently engaged in a new recovery attempt defined as ‘a serious effort to abstain from drinking or to drink without problems in the past 90 days or planning to make one in the next 14 days’.

Additionally, participants were required to provide locator contact information for two close friends/family members in case we were unable to contact the participant directly; provide their social security number for reimbursement or be willing to not receive reimbursement; provide a urine sample and Breathalyser (for inperson visits) or remote saliva test (for remote visits) for biochemical verification; and provide a stable home address and contact information. These initial bioassay requirements were not required following the start of COVID-19 lockdowns which began in March 2020.

METHODS
All assessments were initially conducted (prior to COVID-19) with a study research coordinator inperson at our downtown Boston offices at the Massachusetts General Hospital (MGH) Recovery Research Institute. Each assessment consisted of staff-administered and self-administered surveys, which were completed via REDCap (a secure, web-based application designed to support data capture for research studies), a computerised task to assess impulsivity (Go/No-Go task), and biochemical verification tests of abstinence (Breathalyser, urine) for all participants at all time points. For inperson visits, the baseline and follow-up assessments lasted for approximately 3 hours. At the end of the first visit and every follow-up visit, the next follow-up was scheduled.

Due to the COVID-19 pandemic, all assessments were transitioned to be conducted remotely beginning in March 2020. During remote visits, the computerised task and urine and breath biochemical verifications of abstinence were not completed. A web-based version of the computerised task was tested, but the effects of internet speed on results made data unreliable. In lieu of the urine and Breathalyser tests, saliva tests were implemented for remote visits from March 2021 to May 2021 but were discontinued due to documented inconsistent results. Relative to inperson assessments, remote assessments were shorter with assessments lasting approximately 1.5 hours.
(for baseline) or 45 min (for follow-ups) on the phone and approximately 1 hour for participants completing surveys individually.

All participants (inperson and remote) agreed to provide their phone numbers and email information and that of two locator contacts so that they may be contacted for follow-up assessment reminders. Research staff contacted and confirmed the contact information of the locator contacts as needed if research staff loses touch with the participant. Participants indicated their preferred method of contact (phone call, email or text message) for receiving automated reminders throughout the project period. In keeping with a validated research follow-up protocol for maximising retention in clinical addiction research, after the baseline assessment, research staff proactively reached out to participants for reminders and to check if there were any changes to their contact information. Check-ins occurred 1 month, 14 days, 7 days and 24 hours before the next scheduled visit. These messages are automated and sent with Twilio, which is an approved REDCap module by Mass General Brigham.

Participants are compensated $45 for completing the baseline visit and $55, $60, $65, $70, $75 and $85 for completing the 3-month, 6-month, 9-month, 12-month, 18-month and 24-month follow-up visits, respectively. Payment for each time point is broken up into payments for the staff-administered surveys, self-administered surveys and travel reimbursement. During remote visits due to COVID-19, all participants were still paid the travel reimbursement to maintain the same payment structure used for inperson assessments.

Measures
Staff-administered measures assess the following: substance use history including capture of primary outcomes (PDHD; PDA from alcohol/other drugs), AUD and SUD status and severity (including remission status), tobacco use, treatment utilisation for physical health problems and alcohol/drug use problems, antiraving and antirelapse medications (alcohol and opioids), mental and emotional health diagnoses, hospitalisations, treatment history, and psychiatric medication use, social networks, 12-step/MHO attendance history, online resource utilisation, SMART involvement, 12-step MHO involvement (MM-HAS), recovery/abstinence time, recovery support services and formal treatment programme utilisation, substance use change over the past year (year end summary, YES), impulsivity (Go/No-go cognitive task), and biochemical verification of substance use (Breathalyser, urine drug screen).

Self-administered measures assess the following: demographics, criminal justice involvement, religiosity and spirituality (Religious Background and Behaviors Scale (RBBS), religious and spiritual intensity, Daily Spiritual Experiences Scale (DSES)), stress and psychiatric distress (Perceived Stress Scale - four item (PSS-4), Kessler Six (K6)), coping Commitment to Sobriety Scale (CSS), self-efficacy (Alcohol-Drug Self Efficacy Scale- Twenty Item (A-DSES-20), single item self-efficacy), alcohol/other drug craving Panic Anxiety Disorder Symptoms-5 item (PADCS-5), commitment to sobriety Commitment to Sobriety Scale - five item (CSS-5), substance use consequences Short Inventory of Problems - Second Edition Revised (SIP-2R), recovery status (questions about recovery, drinking goal), recovery capital Brief Assessment of Recovery Capital - Ten item (BARC-10), behavioural addictions, medical marijuana use, medication attitudes, impulsive behaviour Short Urgency Premediation Perseverance Sensation Seeking (SUPPS-S), quality of life and psychosocial functioning (Twelve Promises Scale (TPS), Quality of Life Enjoyment and Satisfaction Questionnaire (Q-LES-Q), Evaluation of Quality of Life - five dimension, three levels (EQ5D3L), European Union History-Quality of Life (EUROHIS-QOL), self-esteem, happiness and satisfaction with life), and physical health (Pittsburgh Sleep Quality Index (PSQI), pain Visual Analogue Scale (VAS), International Physical Activity Questionnaire (IPAQ), meals).

All measures were administered at each time point except for the YES, substance use disorder (SUD) Diagnostic Assessment Registration Table (DART), and questions about recovery, which were administered at baseline, 12 months and 24 months. Detailed descriptions of measures are available in online supplemental file 1.

COVID-19 impact
The COVID-19 pandemic significantly affected the conduct of study assessments as all assessments were transitioned to fully remote visits beginning in March 2020. As previously noted, this shift to remote assessments meant that we were unable to conduct the Go/No-go cognitive measure, Breathalyser or urine screen. Due to these changes, all substance use outcomes are self-reported. Self-administered saliva tests were used briefly as a replacement, but inconsistent results (eg, false negatives, partial results, no results) made data collected from these tests unreliable and this strategy was stopped.

Additionally, recruitment was halted as the study team transitioned to remote assessments and many previous recruitment methods were no longer viable (eg, recruitment from outpatient clinics, advertisements on Boston area trains). It was particularly challenging to recruit individuals attending SMART as meetings were halted, then moved to virtual-only. To address these challenges, we expanded the recruitment area to San Diego, where there is a large SMART Recovery MHO participation community. We also maintained contact with SMART facilitators throughout the recruitment period to encourage them to share the study with meeting attendees and solicit feedback on how to best improve recruitment of SMART participants.

To capture potential changes in recovery resource utilisation due to the COVID-19 pandemic, we added a staff-administered measure related to use of online recovery resources and social network site use. In addition, a
supplemental study focusing on the impact of COVID-19 was conducted, consisting of both quantitative measures and a qualitative interview with a subgroup (n=80) of study participants selected at random from the SMART, AA, SMART+AA, and neither cohorts (n=20 from each group).

Limitations
The study employs a cohort-based, naturalistic, non-randomised design and research staff are not blinded to participants' self-selected recovery pathways. The use of self-report measures, despite having good psychometric properties and adequate validation, can still yield social desirability and memory recall biases.

Patient and public involvement
No patient or public involvement.

Data analysis plan
Aim 1: Effectiveness
We will use multiple linear regression analyses to determine whether our primary stratification factor of interest (predictor: SMART vs no SMART) is associated with alcohol outcomes (primary dependent variables: PDA; PDHD) at 24-month (primary endpoint), and 3-month, 6-month, 9-month, 12-month and 18-month (secondary) follow-ups, while controlling for other confounding variables (eg, baseline variation in levels of the outcome variables) and by using propensity score matching methods that we have used successfully in prior work. We will conduct this analysis separately for participants in the stratified AA versus no AA groups, as so as to test specifically if the effect exists both within and outside of the context of simultaneously seeking help via AA. Similarly, we will repeat analyses within strata of AUD severity. We will also test longitudinal models to investigate the dynamic relationship of these various recovery pathways over time (eg, using hierarchical linear modelling as we have done previously26) controlling for baseline variation in the outcome variables.

Aim 2a: Mechanisms and moderators
We will use mediational modelling, using the product-coefficients approach21 to test how SMART Recovery confers benefit (or fails to do so). The independent variable will be stratification group (ie, SMART vs no SMART), and the outcome variables will be PDA (primary), PDHD, AUD remission, quality of life and measures of psychological functioning. The mediators will be our theorised mechanisms of change (eg, social network changes, recovery motivation, coping, self-efficacy, impulsivity), which we will quantify as change since baseline in these constructs as measured via REDCap administered scales prior to the outcome (eg, change in craving observed from baseline to 3 months would be used to predict 6-month ultimate outcomes). We will use multiple mediation to determine the relative impact of each mechanism, and moderated multiple mediation to identify differences in mechanisms across (moderator) subgroups (eg, men vs women, severe AUD addiction severity vs moderate/mild), similar to our prior approach in delineating mechanisms of behaviour change in AA.23–25

Aim 2b: Dose-response relationship of SMART Recovery
Using only data from participants in the stratified SMART group, we will use linear regression (primary outcome: PDA) to test if the level of SMART involvement, as measured by the SMART Involvement Scale, is related to PDA at 24-month (primary endpoint) and other follow-up points over time. We will use basic model-building practices to determine if such an effect persists after accounting for demographics, other important contextual variables, moderators and baseline levels of the theorised mechanisms of change. In follow-up analyses, we will conduct this analysis separately for participants in the stratified AA versus no AA groups, so as to test specifically if the effect exists both within and outside of the context of simultaneously seeking help via AA. Similarly, we will repeat analyses within strata of AUD severity.

Multiple testing
We will use the false recovery rate adjustment26 to control for multiple testing.

Missing data
Some data will inevitably be missing. We will explore patterns of missingness to determine if missingness is occurring at random (ie, unrelated to the value of the missing observation) or likely to be missing not at random. For each analysis, we will use a variety of recommended strategies to address the issue of missing data (eg, multiple imputation, maximum likelihood estimation).27 Consistency in findings across missing data methods will enhance our confidence in the findings. Note that study participation will be completely separate from SMART participation; thus, participants should feel comfortable remaining in the study regardless of whether they continue in SMART or not. Assuming some attrition, we plan to conduct analyses examining predictors of attrition and control for these.
of the translations (including but not limited to local regulations, clinical guidelines, terminology, drug names and drug dosages), and is not responsible for any error and/or omissions arising from translation and adaptation or otherwise.

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REFERENCES