**Specific Aims**

Precision medicine is an approach where individual differences in genetics, demographics, and patient histories are used to select the best intervention for an individual and identify the optimal time to deliver this intervention. Currently, precision medicine has primarily focused on the above-mentioned static, temporally stable, factors. However, these aspects fail to capture the dynamic nature of many health and risk factors (i.e., factors that may change over time). In fact, the federal government’s Precision Medicine Initiative explicitly highlights this temporal element when describing precision medicine’s potential for “delivering the right treatments, *at the right time*, every time to the right person.”1

In precision mental healthcare (i.e., the application of the precision medicine approach to mental health), timing is critical. Most mental health disorders are characterized by fluctuations in affective and behavioral states that covary with the severity of the underlying disorder and impact its treatment. The ability to detect these changes offers the opportunity to selectively deliver different interventions to patients that match their needs in that moment. For example, during periods of stability, patients in recovery from alcohol use disorder (AUD) might benefit from interventions that help them modify their social network and daily activities to include more time with family and friends who support their recovery. In contrast, during times of peak stress (e.g., following an argument with a significant other or a bad day at work) and associated alcohol craving, they might need focused interventions that prevent an imminent lapse back to alcohol use.

In fact, the appropriateness and/or effectiveness of many AUD interventions and patient-initiated supportive lifestyle changes differ based on the current stability of the patient’s recovery2,3. Futhermore, relapse prevention during recovery is of tantamount importance to prevent further harm from AUD4–6. Given this, a “sensing system” that can predict day-by-day changes in the probability of an alcohol lapse could allow both for temporally tailored interventions generally and for “just-in-time interventions” at key moments to prevent lapses back to alcohol use.

This sensing system will require in situ monitoring to capture day-to-day (and even moment-by-moment) experiences of the patient to quantify both healthy and unhealthy changes in their affect, behaviors, activities, and social networks. Until recently, this would have been impossible. Clinicians typically only interact with patients during office visits, and individuals often lack the objective insight needed for self-monitoring. However, with new advances in technology, we can now accomplish this through *personal sensing*, a measurement approach for collecting data from an individual’s smartphone (e.g., cellular communication, self-report surveys, GPS signal) and other sensors.

Personal sensing measures fall along an active-passive continuum depending on the level of involvement and/or burden for the individual to obtain the measure. Daily or more frequent self-report surveys (e.g., ecological momentary assessments) delivered to the patient’s smartphone anchor the active end of the continuum because their use requires substantial participant involvement. In contrast, background monitoring of cellular communications, geo-position, or activity using sensor or log data automatically collected by the smartphone anchor the passive end of the continuum. Where a measure falls on the active-passive continuum serves as a proxy for the burden imposed on the individual. Minimizing burden is necessary for a sensing system to be realistically sustainable. With AUD, patients often need lifetime monitoring and so in this situation burden is an especially relevant concern.

In this first-year project, I propose to evaluate the potential to use cellular communication logs (SMS and voice call logs) to build a temporally dynamic sensing system for the probability of future (next day) alcohol use lapse among participants who are in recovery from AUD and pursuing abstinence from alcohol. A patient’s social network has both protective and harmful effects on recovery outcomes. Cellular communication logs may provide a potentially powerful passive measure of interactions within this social network.

I will also evaluate the incremental contribution to the sensitivity of this sensing system provided by measures of contextual information regarding the people with whom the participant is communicating (e.g., pleasantness of interactions with the contact, whether the contact is supportive of their recovery, drinking history with contact). This context information will require somewhat more active measurement, but this possible burden may be justified by increased sensitivity to predict alcohol lapses. Furthermore, analysis of this contextual information will allow us to pursue explanatory questions regarding mechanisms of lapse risk (e.g., protective and harmful features of social interactions) in addition to the primarily predictive aims of this first-year project.

Therefore, to accomplish the goals of this project I propose the following specific aims:

**Aim 1: Train and evaluate the best performing machine learning model to predict alcohol lapse from cellular communication data.** I will build, train, and evaluate models with several statistical learning algorithms including penalized parametric linear classification algorithms (LASSO, ridge regression, glmnet), non-linear classification algorithms (neural networks), non-parametric classification algorithms (k nearest neighbor), and ensemble methods (random forest). These statistical algorithms will be combined with various combinations of features derived from participants cellular communications and the context for these communications. Bootstrap resampling will be used to select the top performing model. Expected model performance for new participants (i.e., participants not used to train models) will be evaluated on an independent held-out test sample using the model’s area under the receiver operating characteristic curve (AUC; i.e., plot of sensitivity vs. specificity across classification thresholds).

**Aim 2: Employ a model comparison approach to compare models that use all available features (both passive signals from communications logs and actively measured context) with models that are restricted to only passive signals.** I will identify the top performing model using all available features and the top performing model without context variables and perform a model comparison. Through this relative comparison, I will quantify any performance benefit from adding the active component of context. This will be useful for future cost-benefit analyses that weigh the incremental benefit in performance relative to burden.

**Aim 3: Evaluate the importance of feature sets within the top performing model to inform potential in situ treatments.** The most predictive features will be identified based on feature important indices. I will also combine model comparison and feature ablation methods to remove subsets of context features in order to test their predictive utility. These evaluations will provide insight into the protective and harmful aspects of social interaction on lapse risk. Such insights may guide future intervention efforts.

**Significance**

**Lapse Risk**

AUD is a chronic relapsing disease7,8. People can relapse days, weeks, months, or even years after achieving abstinence9–12. Lapses, an initial setback or slip, are often an early warning sign of relapse, a full return to previous drinking behavior5. Studies show that lapses predict future lapses, with more frequent lapses resulting in increased chances of relapse7. Likewise, longer durations of abstinence is associated with decreased chances of lapse, suggesting the stability of a patient’s recovery itself as an important predictor of abstinence7. In fact, the most important predictor of relapse is whether the individual has already had a lapse during treatment6. One explanation for the high correlation between an initial lapse and relapse is the abstinence violation effect, which states that people who internalize feelings of loss of control, guilt, and hopelessness after violating a self-imposed rule (i.e., abstinence) have a greater risk of relapse compared to those who view the lapse as external and controllable4,6. Thus, identifying when an initial lapse will occur is an important goal in preventing lapses, repeated lapses, and relapse.

To apply precision medicine to alcohol lapse intervention via a sensing system, we must be able to identify *who* is at risk of lapse and predict *when* a lapse will occur for these high-risk individuals. Much work has been done on the former through the identification of distal risk factors - stable states or traits that contribute to AUD, but do not change much over time7,9. These factors can include one’s genetic makeup, a co-occurring psychopathology, or AUD severity but are more relevant for predisposing one for AUD and less involved in the cyclical nature of lapses13. My research seeks to predict when someone will lapse through the use of proximal factors potentially predictive of lapse risk. Proximal factors are fluid and change over time7,9. They include cognitive (e.g., negative affect, craving), situational (e.g., lack of social support, risky situations), and behavioral (e.g., decreased social interactions, coping strategies) factors. Fluctuations in proximal factors often precipitate a lapse5,14,15. However, due to the dynamic nature of these predictors, a therapist who sees their patient monthly will likely be unable to monitor for these lapse risks. Yet, it is clear that recognizing these dynamic indicators of lapse risk is necessary if we want to intervene before the lapse occurs.

Given this temporal component of lapse risk, the proposed study seeks to build a temporally dynamic sensing system that can predict when lapses will occur at a day-to-day level of precision using low burden personal sensing measures. If successful, this model can be used to guide precision medicine intervention efforts by identifying *when* an AUD intervention should be deployed. This sensing system will also have the potential to create categories of factors predictive of risk severity and recovery stability. These categories can then be used for applications such as matching patients to specific levels of intervention intensity and tailoring “just-in-time interventions”.

**Social Interactions**

Many proximal lapse predictors are inherently social16. For example, decreased interactions may signify isolation common with depressive symptoms, reaching out to people in one’s social network could signify a positive coping strategy, or changes in patterns between a single person in one’s social network could indicate conflict. Accordingly, these factors are intrinsically linked to social interactions16–18.

On its own, the nature of people’s social interactions with others appears to be a salient factor relevant to lapse risk. Positive social interaction has been associated with positive alcohol treatment outcomes19–22. It is thought that the social component of self-help groups like Alcoholics Anonymous (i.e., increasing pro-abstinence relationship ties) play a major contributing role in their efficacy20,23–25. The buffering hypothesis of social support suggests that social relationships may buffer individuals against the negative effects of stress by providing a source of resources to promote adaptive responses to stress26,27. With stress being an often-cited precipitant of alcohol lapse, it is likely these buffering effects extrapolate to lapse risk28.

There is also much literature on the importance of social network influences on drinking behavior16,29. A social network made up of heavy drinkers or abstainers can ultimately influence one’s recovery towards maintaining abstinence or lapsing29–31. Individuals in recovery who maintain interactions with people who do not support their recovery is associated with decreased likelihood of maintaining abstinence. Social interactions with negative peer influences (e.g., heavy drinkers) may have more of an effect on treatment outcome than positive peer influences (e.g., abstainers)29. This relationship between social support and lapses is robust and extends to substances other than alcohol32.

**Cellular Communication Data**

Many social interactions occur or are planned over the phone. Thus, cellular communication logs offer insight into patterns of social interaction. We know that social relationships are dynamic33–36. So, with time-stamped logs we can potentially build a sensing system that tracks how these interactions fluctuate over time. For example, we can see changes in their top contacts (i.e., who they are interacting with the most). We can also examine changes in patterns of activities, such as the ratio of incoming to outgoing SMS messages or whether an individual is consistently ignoring phone calls from a contact they normally interact often with.

However, these measures may become much more powerful when we add context to these behaviors. In addition to the passive measure of communication logs, we obtained contextual information about each of the participants’ contacts via self-report (e.g., pleasantness of interactions with the contact, whether the contact is supportive of their recovery, drinking history with contact). This contact information adds an additional dimension for characterizing the nature of the social interactions. For example, context in concert with communication logs can tell us that someone is ignoring phone calls from a former drinking buddy or that their top contacts have recently shifted to include only people supportive of their recovery. Therefore, to the degree to which we can extract out information about their interactions with others through the cellular communications, these data could prove to be a potentially powerful measure of lapse risk.

One promising aspect of communication logs for lapse prediction is the ease and affordability of integrating them into a sensing system as part of a long-term recovery plan. Cellphone usage is widespread and reaches all demographics. As of 2019, 96% of U.S. adults have a cellphone; and, for adults making less than $30,000 a year, 95% have a cellphone. Studies on patients in recovery programs for substance use report similar findings with 87-94% owning a cellphone37,38. Additionally, unlike some other passive personal sensing measures (e.g., GPS, accelerometer), communication logs do not require data plans with internet access or built-in sensors that less expensive cellphones (i.e., non-smartphone) may not have for consistent data collection.

**Personal Sensing Research**

Still, the potential of cellular communication logs for lapse prediction remains an open question. There are some preliminary data that establish that personal sensing measures can be used to predict affect and behavior39–44. A 2020 study was able to predict early warning signs of a psychotic relapse in patients with schizophrenia based on behavioral anomalies detected from multiple passive personal sensing measures, including cellular communication metadata40. Other studies have used combinations of personal sensing measures to predict bipolar symptoms41,42, drug cravings43, and depression44.

These studies, however, rely on multiple measures of highly sensitive data. A single personal sensing measure that can perform at high levels of accuracy is superior to models that require additional measures and perform at similar or even higher levels. Preliminary evidence suggests people generally feel that providing their call and SMS logs are less intrusive than providing their GPS location or SMS content45. Additionally, the more data collected on an individual, the less anonymous it becomes placing individuals at higher risk in the event of a data breach.

Very little research has specifically used cellular communication data40,46–48. One good exception is a 2020 study that used mobile phone usage metadata, which includes all metadata and not just limited to call and SMS logs (e.g., time spent web browsing, time spent on social media apps)48. They were able to predict whether participants would screen positive for depression on the Beck’s Depression Inventory (BDI-II) with 77% accuracy when using the metadata alone and at 81% accuracy when age and gender were included in the model48. They also found that participants with fewer social ties, as defined by a lower number of contacts and phone calls, were more likely to be depressed48. This study is promising in that it shows the potential power of communication logs, but it is not related to substance use.

In the substance abuse literature, communication logs are often overlooked for other personal sensing measures like GPS and EMA43,49,50. One study currently in press was able to identify periods of time where individuals were at risk for a lapse in smoking50. However, their models relied on predictors obtained through a five-time daily EMA survey50. This is not uncommon with research on lapse prediction. Many studies have capitalized on self-report insight into mood and cravings from EMA or diary check-ins to predict lapses with high accuracy6,14. Unfortunately, measures that require active participation from the individual are more burdensome and sustained participation is not likely. Individuals with AUD may require lifelong monitoring and measures too high in burden are simply not realistic options for many people.

Ultimately, the studies that have used communication logs, either combined it with other personal sensing measures, had too small of sample sizes (*N* < 40) or were not related to substance use40,46–48. Additionally, none of these studies have capitalized on added contextual information for the logs. As a result, we are unable to determine how much of the model’s success was a result of the communication logs, how much better the model would have performed with added context information, or the direct relationship to alcohol lapse.

**Machine Learning and Precision Medicine**

Machine learning methods are appropriate for addressing these current gaps in the literature. Specifically, they can be used for both prediction and explanation.51

Personal sensing measures can produce hundreds to thousands of observations for a single person. Machine learning methods are well suited for such large datasets in that they require larger sample sizes to be able to test the models on different data than what it was trained with.

Additionally, a key tenant of precision medicine is its focus on risk factors specific to the individual instead of generalizing across an entire population. To capture these unique differences from one individual to another, hundreds of predictors are required. To avoid issues of overfitting (i.e., fitting the model to noise in the sample and preventing it from generalizing to new data) due to high numbers of predictors, statistical learning algorithms such as LASSO and ridge regression can be used to penalize the model coefficients (i.e., through regularization). Thus, further emphasizing the necessity of machine learning in precision medicine research.

Overall, the heavy reliance of precision medicine on distal, static factors has proven fruitful for determining *who* is predisposed to AUD and vulnerable overall for relapse. Unfortunately, this does not say anything about *when* someone will lapse. To implement interventions “just-in-time” and prior to a full relapse, proximal factors must be considered. With the advancements of personal sensing measures and machine learning methods in the field of addiction, precision medicine approaches can now capitalize on dynamic predictors of lapse risk.

**Current Study**

My proposed first-year project targets three gaps in the literature by determining the predictive power of communication logs and social context for alcohol lapse prediction (**Aim 1)**, isolating the unique contribution of entirely passive communication logs compared to the more active measure of social context (self-report contact information; **Aim 2**), and characterizing the relationship of social interactions and alcohol lapse (**Aim 3**). Therefore, I will be pursuing two prediction goals and one explanation goal.

***Prediction.*** Our primary aim is to predict when someone is going to lapse before the lapse occurs using two personal sensing measures of social interaction –communication logs and self-report contact information (**Aim 1**). Communication logs are truly passive and therefore impose no burden on the individual. Obtaining contact information via self-report does require active responding, but this will likely be for only a small amount of time and for a subset of people that the individual communicates with frequently. Thus, by adding contact information to our model, we can potentially increase power by contextualizing the social interactions with only a modest and temporary increase in burden.

Furthermore, we will perform a model comparison to quantify the added predictive power of a model containing the contact information compared to the passive-only model to determine the relative performance benefit (**Aim 2**). To our knowledge, no research directly compares the performance benefit of active and passive measures against passive only measures. This research will set the stage for future cost/benefit analysis into the incremental performance benefit relative to burden.

***Explanation.*** With the added contact information, we can answer theoretical questions and develop new theory-driven hypotheses about the underlying social mechanisms of lapse risk (e.g., Does communicating with other people in recovery increase chances of lapse?) from the top-performing feature sets (**Aim 3**). These findings can be used to guide both traditional and precision medicine approaches to intervention (e.g., What aspect of an individual’s recovery should a clinician focus on strengthening? Which area is most critical for lapse avoidance?).

**Approach**

**Overview**

This project will perform the initial analyses on a subset of data collected from 2017 – 2019 as part of a larger grant funded through the National Institute of Alcohol Abuse and Alcoholism (R01 AA024391). The following approach represents only the aspects of the project relevant to my first-year project, however, it is important to note that additional measures were used over the course of the study to obtain data from participants that are not directly relevant to this study.

**Participants**

We recruited individuals in the initial stages of recovery for AUD in the Madison area to participate in a three-month study. Avenues of recruitment included referrals from clinics, self-help groups, Facebook, radio, and television. Interested individuals were told that our research was focused on learning how mobile health technology can be used to provide individual support to anyone recovering from alcohol addiction and were given a short phone screen to determine initial eligibility (i.e., At least 18 years old, ability to read and write in English, and an eligible smartphone with existing cellphone plan).

Two hundred sixteen participants passed the initial phone screen and came in for a more in-depth screening session. Of the 216 interested participants, 199 enrolled in the study (i.e., they consented and were eligible to participate). Exclusion criteria that led to ineligibility consisted of not meeting the criteria for moderate or severe AUD (as defined by the DSM-5), not having goals of long-term abstinence, not having abstained from alcohol for at least one week, already having over two months of abstinence, or having severe symptoms of psychosis or paranoia. Of the 199 enrolled in the study, 154 provided at least one month of data and make up the sample to be used in the proposed analyses.

**Procedure**

Participants enrolled in a three-month study. This study involved five in-person visits and daily EMA surveys to document alcohol lapses (Figure 1). During the screening session we determined eligibility, obtained informed consent, and documented basic demographic information. Participants that consented and were eligible came back for a second visit to enroll in the study. During enrollment, participants were briefed on how to delete communication logs they did not want to share with us and completed a practice EMA survey. Participants also reported contacts they frequently communicated with and answered a series of questions documenting contextual information about their interactions with each contact (see *Social Context* section). Participants returned for three follow-up visits, each one month apart. At each follow-up communication logs were downloaded and contact information was updated as needed. At the third follow-up visit, participants were also debriefed and thanked for their participation.

*Figure 1*. Flowchart of in-person study visits. From enrollment to follow-up 3, participants completed 4x’s daily ecological momentary assessment (EMA) surveys to document alcohol lapses. Each follow-up visit took place one month after the prior visit.

a Demographics and static variables collected

b Cellular communication logs downloaded

**Measures**

*Cellular Communication Logs*

SMS and call logs were obtained at each study visit (month 1, month 2, and month 3) by backing up the phone directly to the study server (Table 1). At each visit participants were given the opportunity to review their logs and delete anything they felt uncomfortable sharing.

**Table 1.** Information obtained through cellular communication logs

|  |  |
| --- | --- |
| Log Type | Measure |
| SMS | Phone number of the other party |
|  | Date message was received |
|  | Date message was sent |
|  | Message type (incoming, outgoing, draft) |
|  | Contact saved in phone |
|  | Read status (read, unread) |
| Call | Phone number of the other party |
|  | Date of call |
|  | Call type (incoming, outgoing, missed, voicemail, rejected, blocked) |
|  | Facetime (iPhone only) |
|  | Call duration (in seconds) |
|  | Contact saved in phone |
|  | Caller ID (allowed, restricted, unknown, payphone) |

*Social Context*

At the time of enrollment, study staff worked with participants to document contacts that participants frequently communicated with. During this time, additional contextual information about each contact was obtained (Table 2). At each follow-up visit, any additional contacts that participants interacted with at least twice over the past month were also recorded.

**Table 2.** Contact information as measures of social context

|  |
| --- |
| Measures of Social Context |
| Type of relationship (e.g., friend, spouse, parent, co-worker, sibling) |
| Have you ever drank alcohol with this contact in the past (i.e., almost never, occasionally, almost always)? |
| What is the drinking status of this contact (i.e., drinker, non-drinker, don’t know)? |
| Would this contact drink alcohol in your presence (i.e., yes, no)? |
| Is this contact in recovery from alcohol or other substances (i.e., yes, no, don’t know)? |
| Indicate the level of support this contact provides (i.e., supportive, unsupportive, mixed, neutral) |
| Which best describes your interactions with this contact (i.e., pleasant, unpleasant, mixed, neutral)? |

*Static Variables*

At screening, participants completed a one-time survey that recorded baseline measures of demographics and other easily assessed static variables and constructs shown to be relevant to lapse (Table 3). While such static variables alone are not sufficient to predict when a lapse will occur, they can contribute to identifying who is generally more likely to lapse. Additionally, these static variables can moderate our time-varying social variables and in the context of such interactions become time-varying predictors themselves.

**Table 3.** Static variables and demographic measures recorded during the screening session

|  |  |
| --- | --- |
| Variable | Measure |
| Demographics | Age |
|  | Sex |
|  | Race |
|  | Ethnicity |
|  | Education |
|  | Employment |
|  | Income |
|  | Marital Status |
| Alcohol | Alcohol Use History |
|  | DSM-5 Checklist for AUD |
|  | Young Adult Alcohol Problems Test |
|  | WHO-The Alcohol, Smoking and Substance Involvement Screening Test |
| Mental Health | Symptom Checklist-90-Revised |
|  | Intolerance of Uncertainty Scale |
|  | Anxiety Sensitivity Index |
|  | Distress Tolerance Questionnaire |
| Family | McMaster Family Assessment Device |
| Personality | Multidimensional Personality Questionnaire Brief Form |

*Lapses*

Alcohol lapses serve as our outcome variable to provide labels for training our model and testing the efficacy of its performance. Lapses were measured via a short four-time-daily EMA survey. From the EMA we gathered responses to three lapse-related questions (Table 4). Additionally, we asked about their desire to remain abstinent as a way to assess continued study eligibility.

**Table 4.** Ecological momentary assessment (EMA) outcome measures of lapse

|  |
| --- |
| EMA Measures of Lapse |
| Have you drank any alcohol you have not yet reported? |
| Please indicate the date/hour of the first drink that you have not yet reported |
| Please indicate the date/hour of the last drink that you have not yet reported |
| Is your goal still to remain abstinent in the future? |

*AUD Diagnosis*

Participants were excluded if they did not meet the criteria for an AUD diagnosis (i.e., at least four DSM-5 symptoms present over the past year). We obtained this information via self-report (see Table 3 - DSM-5 Checklist for AUD) in which participants reported yes or no to whether they agreed with 11 statements representing different DSM-5 AUD symptoms (e.g., “I often used alcohol in large amounts over longer periods of time than I intended”, “My alcohol use resulted in my not fulfilling major obligations at work, school, or home”). These statements are based off the Structured Clinical Interview for the DSM-5 module E. Responses to this checklist will also be used to score AUD severity and added to the sensing system as a potential predictor of lapse.

**Candidate Statistical Learning Algorithms**

Candidate algorithms for our lapse risk prediction model include penalized parametric linear (LASSO, ridge, glmnet) and non-linear (neural networks) classification algorithms, non-parametric classification algorithms (k nearest neighbor), and ensemble methods (random forest).

**Feature Engineering**

Feature engineering is the process of transforming raw data to create a representation of the data that increases a model’s predictive power.52 These transformations can include imputation of missing data, removing irrelevant predictors, handling issues of multicollinearity, normalizing a skewed distribution, accounting for interactions between predictors, and creating interpretable predictors based on prior knowledge.53

One example of feature engineering can be seen with handling the time-stamped communication logs. Entering the raw communication log dates and times into the model may yield some predictive power, but when transformed to dummy-coded features, such as weekends, happy hour, holidays, one can clearly see a more direct relationship to lapse risk. These features can be aggregated to represent daily, weekly, or monthly totals and averages and then analyzed to recognize changes over time (e.g., more activity during happy hour this week).

My first-year project will utilize feature engineering methods through interactions of static and time-varying social variables (i.e., average duration of calls as a function of sex) and through counts, sums, and proportions of social variables at various temporal windows (e.g., number of weekly interactions with supportive contacts, total contacts in recovery, ratio of incoming to outgoing messages).

**Model Training and Performance Evaluation**

Candidate statistical learning algorithms will be trained on a subset of the data (training sample) using combinations of features derived from participants cellular communications and social context information. Bootstrap resampling will be used to select the top performing model. Expected model performance for new participants (i.e., participants not used to train models) will be evaluated on an independent held-out test sample using the model’s area under the receiver operating characteristic curve (AUC; i.e., plot of sensitivity vs. specificity across classification thresholds).

Additionally, we will conduct a model comparison between our top performing model using all available features, and the top performing model restricted to only the passive communication logs. The incremental benefit in performance will be inferentially evaluated by comparing AUC values.

**Contribution to Theory**

Proximal lapse risk predictors are not conclusive in the literature. We will identify the most predictive time-varying features and interactions of static and time-varying features based on feature important indices.

Furthermore, I will remove subsets of social context features through feature ablation and test the predictive utility of the features with model comparisons. These evaluations will provide explanatory value in understanding the relationship between certain social features and alcohol lapse.

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