Supplementary Online Content

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eMethods

Evaluating Behavioral Data Quality

Data quality was evaluated prior to any hypothesis testing in study-eligible participants. We implemented a two-stage process. First, a cut-off was used based on single-subject model-fits (adjusted-r^2<0.1). Sessions below this cut-off were automatically deemed as of poor-quality. Second, at least two investigators visually inspected the raw choice data for each of the remaining sessions for each participant. A consensus decision was made regarding whether the data indicated sufficient understanding of, or attentiveness to, the task. We considered the data from a session to be of acceptable quality if the likelihood that the lottery would be chosen increased as the monetary value and winning probability of the lottery increased, and thus these data could be reliably fit with our model. Examples of good and poor-quality behavioral data are shown in eFigure 1. These criteria were applied to individual sessions; thus, a participant could remain in the study cohort but have one or more sessions censored in the analysis. A participant's entire data set was removed only if we observed poor-quality data for every session. This resulted in the censoring of 59 individual study sessions (leaving a total of 777 sessions from 836). Twenty-eight additional sessions were censored because we obtained values of the ambiguity tolerance parameter β outside the classically interpretable range (-3 to 3), leaving a total of 749 sessions for analysis. That is, 10.4% of all sessions completed were excluded either due to poor-quality behavioral data or extreme model fits (12.2% for patients, 4.8% for controls). See eFigure 2 for session-by-session information on sessions completed but excluded based on these criteria by diagnostic group.

Importantly, we note that these exclusions did not qualitatively impact our main conclusions. Performing the time-lagged mixed-effects logistic regression analysis reported in the main text in the full data set (without any data quality exclusions) with participants' raw data (model-free average proportion of lottery choices) as predictors of prospective opioid use led to the same finding as in the reduced dataset with the model-based measures as predictors. Ambiguity tolerance, measured as overall proportion of ambiguous-risk minus known-risk lottery choice, was a significant positive predictor of opioid use [*B*=2.65, *SE*=0.91, *t*(597)=2.92, *P*=0.004, standardized adjusted-*OR*=1.46] while known-risk tolerance, measured as overall proportion of known-risk lottery choice, was a non-significant predictor [*B*=-0.65, *SE*=0.83, *t*(597)=-0.78, *P*=0.43, adjusted-*OR*=0.89]. In addition, ambiguity tolerance measured in this manner remained a significant predictor in the extended model that included the clinical variables [*B*=2.55, *SE*=0.99, *t*(537)=2.58, *P*=0.01, adjusted-*OR*=1.43]. Note that we did not

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perform these analyses in the full dataset with the model-based measures as these measures either could not be estimated or had extreme values in many of the poor-quality data cases.

Clinic Records and Study Definitions of Treatment Adherence and Illicit Opioid Use

Patients provided consent for the review of their clinic records. We accessed patients' Addiction Management System (AMS) record and toxicology reports from their chart to obtain information on treatment adherence and opioid use corresponding to each study session completed. AMS is a state-wide treatment access and dosage registry system, sponsored by the New York State's Office of Alcoholism and Substance Abuse Services (OASAS), that provides a time-stamped record of clients' medication dispensation, and information regarding randomly scheduled urine toxicology testing.

Treatment Adherence. Our measure of treatment adherence was based on the AMS medication dispensation record. For each patient, the system reports the date and time that opioid maintenance medication was dispensed. Methadone was provided in liquid form and buprenorphine (Suboxone) was provided in sublingual tablet form. In both cases the patient is asked to pick up and ingest the medication onsite and submit an empty container to the clinic's dispensation nurse before it is recorded on AMS. Most of our patient participants were receiving methadone (87.7%) as their maintenance medication and almost all were on a 6 days/week pickup schedule with one take-home dose for the duration of the study. We computed adherence as the percentage of confirmed dispensed doses out of the number prescribed. For example, adherence over a period of one week spanning the time between two consecutive study sessions would correspond to the number of doses dispensed on AMS for that patient divided by 7. If out of 7 doses the patient was only confirmed to have received 5, adherence would be 71.4%. For interpretability in our analyses of predictors of opioid use we coded this variable as the inverse, nonadherence, or 100% – adherence.

Illicit Opioid Use. To determine whether illicit opioid use had occurred between two consecutive study sessions for a given patient participant, we proceeded as follows. AMS was accessed to determine if the system had randomly programmed a urine toxicology test for the period between the sessions and whether that sample was successfully "submitted" or "scheduled but refused or not completed". Patients would approach the clinic's dispensation window and be informed of whether the system had scheduled a urine sample for that day which would need to be submitted after receiving their medication. They would be provided with a cup and a tube and asked to collect the sample and then submit it by depositing it into a container located at the

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nurse's station. If a patient formally refused to provide a sample or skipped clinic attendance that day, the record was labeled "scheduled but refused or not completed" in AMS. After confirming a sample was in fact "submitted", we accessed the patient's hospital laboratory results to confirm whether it was positive or negative for opioids other than methadone. Substances tested for by the laboratory include methadone, opiates, cocaine, alcohol, benzodiazepines, barbiturates, and tetrahydrocannabidiol (THC). Finally, to cross-reference the objective urine test data and better align opioid use events to our study sessions, we collected the calendar-based Time Line Follow Back (TLFB) at each session, surveying self-reported use in the period since the last completed session. The TLFB is a standard tool for tracking substance use in addiction studies and is often used in conjunction with toxicology reports in longitudinal research[1].

We formally defined a positive opioid use event as any illicit opioid use self-reported on the TLFB or a positive urine toxicology result (including a "scheduled but not completed or refused" urine test) in the period since the last completed study session. While a positive toxicology report for opioids other than methadone was sufficient to identify a session as positive for recent opioid use, when this result was negative, we cross-referenced it with the corresponding TLFB. This was necessary given that the testing window for urine tests is ~72 h from the date of administration, while use could have occurred anytime between sessions. Given that a common reason for "scheduled but refused or not completed" tests in the context of opioid treatment is illicit use, it is standard clinical research practice to treat these tests as positive (e.g. [2]). Nevertheless, from all tests reviewed for our study, only 7.3% were "scheduled but not completed or refused", and further about a third (33.3%) of those could be directly confirmed as positive by patient self-reported admission of use on the TLFB. That is, 4.8% of all events and 10.2% of all positive opioid use events were imputed as positive on the basis of a "scheduled but not completed or refused" urine test. We note that our results were unchanged if we performed our analysis excluding these sessions (eTable 3).

We formally defined a negative opioid use event as one where a patient denied any opioid use on the TLFB and urine toxicology results that were all negative in the period since the last completed study session.

A special case pertained to determining the presence/absence of opioid use following the final completed study session. For these cases, we relied exclusively on the urine toxicology tests/clinic records given that no TLFB data could be consulted at an immediately following session; therefore, here applied slightly different criteria. In addition to the criteria outlined above for defining positive use, we also treated formal clinic dropouts as positive. A third

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"unknown status" category was also used to identify a subset of cases/sessions which included instances where there was no scheduled test or available clinic record for review at the close of data collection, or when a patient briefly discontinued treatment (but was not deemed dropped out), transferred to another clinic, was hospitalized, or was incarcerated (eFigure 3).

While substance use other than opioids was tolerated and not uncommon, patients were required to be seeking treatment at the current clinic specifically for opioids and needed to have an expressed desire to reduce their opioid use (which was also a requirement of the clinic). Thus, there was variability in whether or not a secondary substance was endorsed (see Table 1 in the main text), whether patients had a desire to quit use of that substance, and whether use of other substances occurred on occasions on which opioids were not also used.

Strategies Employed to Enhance Veracity of Self-Reports. Although the veracity of self-reported substance use has been questioned, this is of particular concern for negative reports rather than positive reports, as participants, particularly those in treatment, may feel inclined to under-report their use. Our coding scheme for negative opioid use events which required both self-reported lack of use and a negative urine test was used to provide some protection against this possibility. In addition, we employed the following steps to minimize biased reporting on the TLFB: we explicitly informed participants that (1) their toxicology records would be reviewed (and asked them as part of consent to provide us with permission to do so); (2) their answers were confidential, would not be communicated to clinic staff, and would therefore have no bearing (good or bad) on their treatment; and (3) their answers would have no bearing (good or bad) on their participation in the study. From all events identified as positive via urine tests (including "scheduled but refused or not completed"), 52.5% were corroborated by the TLFB, and from all events identified as negative, 86.9% were corroborated by the TLFB, for an overall concordance rate of 73.9%.

Identifying Substance Use in Controls. To confirm the absence of any illicit substances in controls, at each session, we administered a commercial multi-panel rapid drug test (T-Cup™). The substances assessed were methadone, opiates, oxycodone, buprenorphine, propoxyphene (PPX), cocaine, benzodiazepines, barbiturates, amphetamine, methamphetamine, methylenedioxymethamphetamine (MDMA), phencyclidine (PCP), tricyclic antidepressants, and THC. Control participants also completed the TLFB.

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eResults

Intraclass Correlation Coefficients (ICCs) for the Decision-Making Task Parameters in Opioid Use Disorder Participants

Community controls completed the risky decision-making task up to 5 times as a means to obtain a normative estimate of measurement test-retest reliability [here, '1-k' intraclass correlation coefficient (ICC)]. We could however also compute ICCs in patients to understand how the changing levels of the task parameters in this group interacted with ICCs, that is, how variable the presence of opioid use disorder and/or opioid use vulnerability might render these parameters. Considering the same timeframe examined in controls (first 5 sessions), we find moderate within-subject pairwise correlations across sessions in patients for both parameters [r range: 0.09–0.71, M=0.35 (SE=0.04)]. The ICC for known-risk tolerance, computed for the n=45 patients with data for all five sessions, was 0.70 (95% CI: [0.53, 0.82]), and for ambiguity tolerance it was 0.72 (95% CI: [0.57, 0.83]). This indicates that, as might be expected, the ICCs were on average lower in patients than in controls, although they suggest at least moderate (ICC>0.5) to good (ICC>0.75) reliability in both groups. More specifically, the ICC values indicate that, within both groups separately, there was more between-person variability than there was within-person variability (i.e., session-to-session) in these parameters. Critically, our main results would suggest that some of the additional variability in the parameters in patients could reflect clinically meaningful information about opioid use vulnerability rather than necessarily increased measurement noise in the patient group relative to the control group.

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Supplemental References

1. Hjorthoj CR, Hjorthoj AR, Nordentoft M. Validity of Timeline Follow-Back for self-reported use of cannabis and other illicit substances--systematic review and meta-analysis. *Addict Behav.* 2012;37(3):225-233.

2. Lee JD, Nunes EV, Jr., Novo P, Bachrach K, Bailey GL, Bhatt S, Farkas S, Fishman M, Gauthier P, Hodgkins CC, King J, Lindblad R, Liu D, Matthews AG, May J, Peavy KM, Ross S, Salazar D, Schkolnik P, Shmueli-Blumberg D, Stablein D, Subramaniam G, Rotrosen J. Comparative effectiveness of extended-release naltrexone versus buprenorphine-naloxone for opioid relapse prevention (X:BOT): a multicentre, open-label, randomised controlled trial. *Lancet.* 2018;391(10118):309-318.

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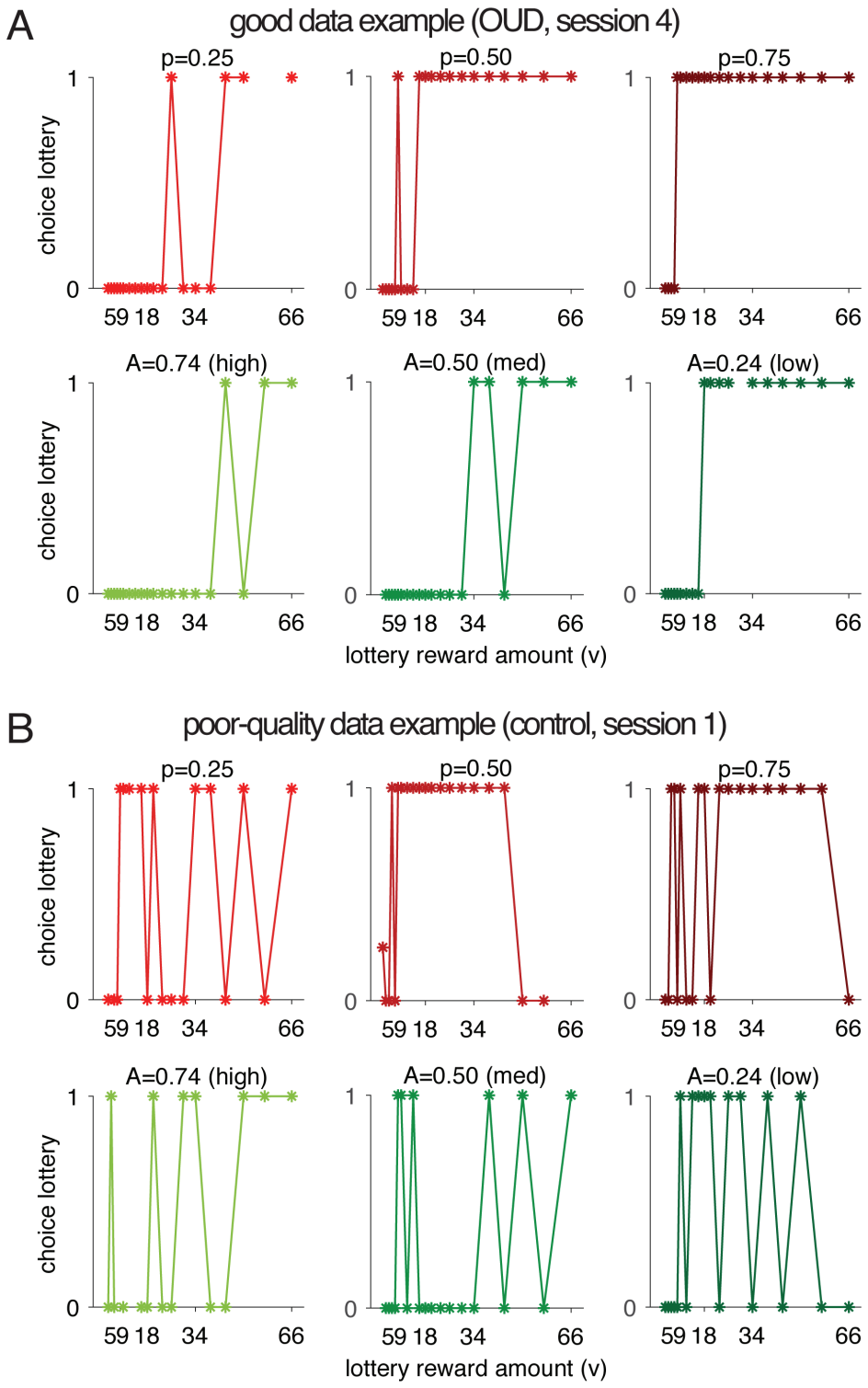

eFigure 1. *Examples of Acceptable and Poor-Quality Behavioral Data*

Raw choice data by probability level, ambiguity level, and lottery amount for two example participants, where (**A**) shows an example of data that have overall tolerable levels of noise and (**B**) shows an example of data that are of overall poor-quality with excessive levels of noise. Choice lottery = 0 indicates the participant chose the guaranteed $5 instead of the lottery (thus

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rejecting the lottery) and choice lottery = 1 indicates the participant chose the lottery instead of the guaranteed $5. The reward amount offered by the lottery increases from left to right along the x-axis. In the participant's data depicted in (**A**), the lottery is more likely to be chosen as the amount that could be won from the lottery increases, as the winning probability increases (from p=0.25 to p=0.50 to p=0.75), and as the ambiguity level decreases (from A=0.74 to A=0.50 to A=0.24). By contrast, the participant's data depicted in (**B**) does not reveal a clear transition between rejection and acceptance of the lottery, in particular as a function of the probability of winning and/or ambiguity level associated with the lottery.

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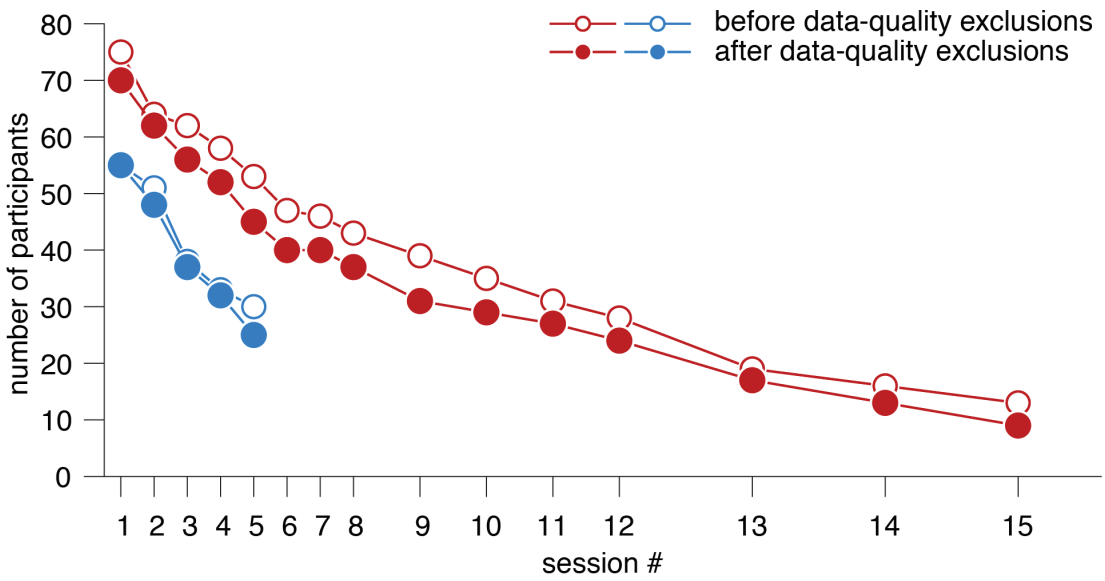

eFigure 2. *Participants Remaining in the Study by Session Number*

Participant numbers by increasing session number for both groups, individuals with opioid use disorders (OUD, red) and controls (blue), before and after data-quality exclusions. A total of 10.4% of all completed sessions across groups were excluded due to data-quality considerations.

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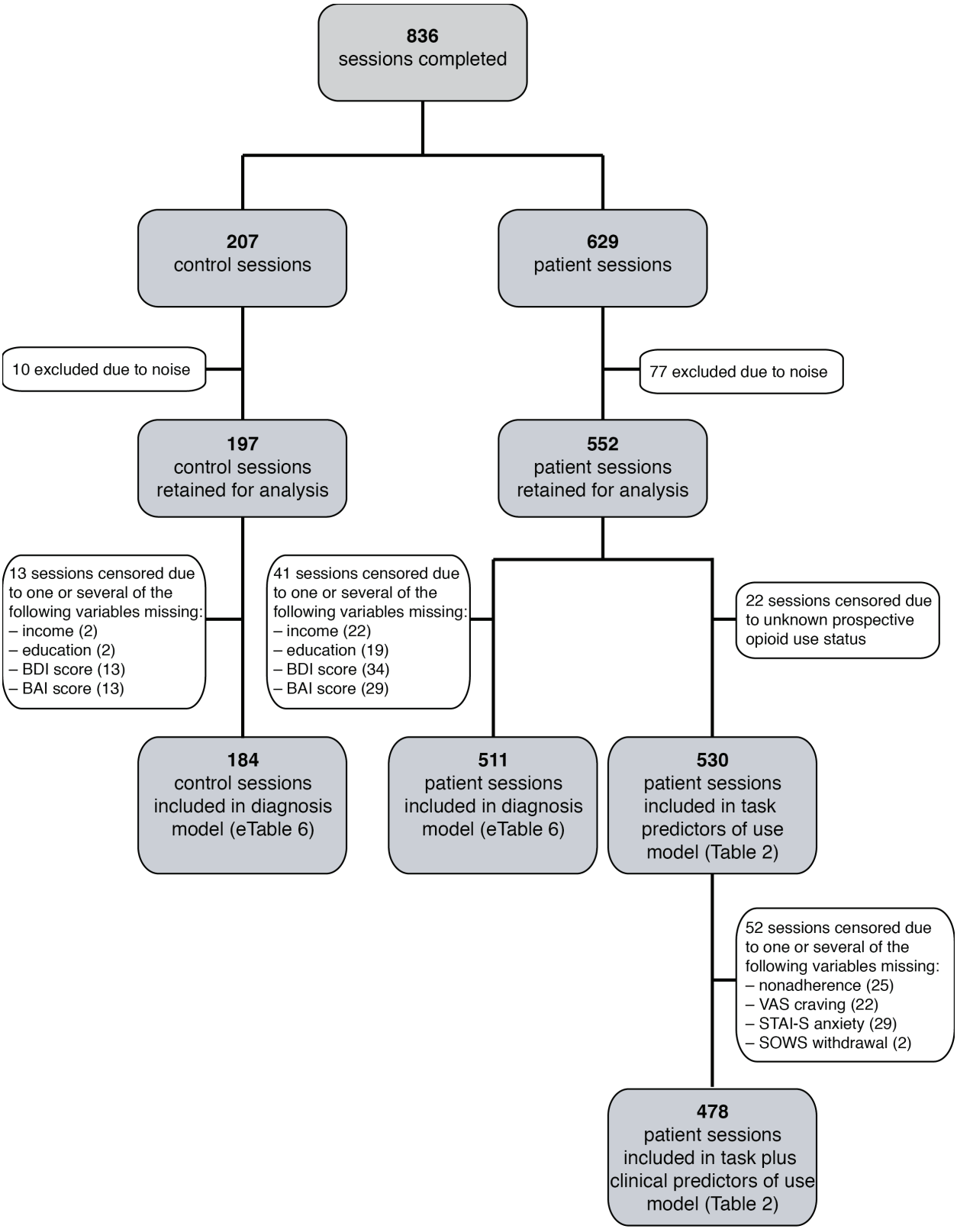

eFigure 3. *CONSORT Diagram of Sessions Excluded and Retained for Analysis*

Flow diagram showing number of sessions collected by diagnostic group, excluded due to poor-quality behavioral data and model fit, and retained for analysis including analysis with additional

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predictors. Reasons for incomplete/missing clinical variable information include running out of time to complete a particular questionnaire, removal of a patient's record from the clinic tracking system before it could be reviewed by the study team (adherence), experimenter error in not administering a questionnaire, and some questionnaires (VAS craving and STAI-S anxiety) being added to the study after the first participants had already initiated the study. "Unknown prospective use status" is used to identify a subset of cases/sessions which included instances where there was no scheduled test or available clinic record for review at the close of data collection, or when a patient briefly discontinued treatment (but was not deemed dropped out), transferred to another clinic, was hospitalized, or was incarcerated.

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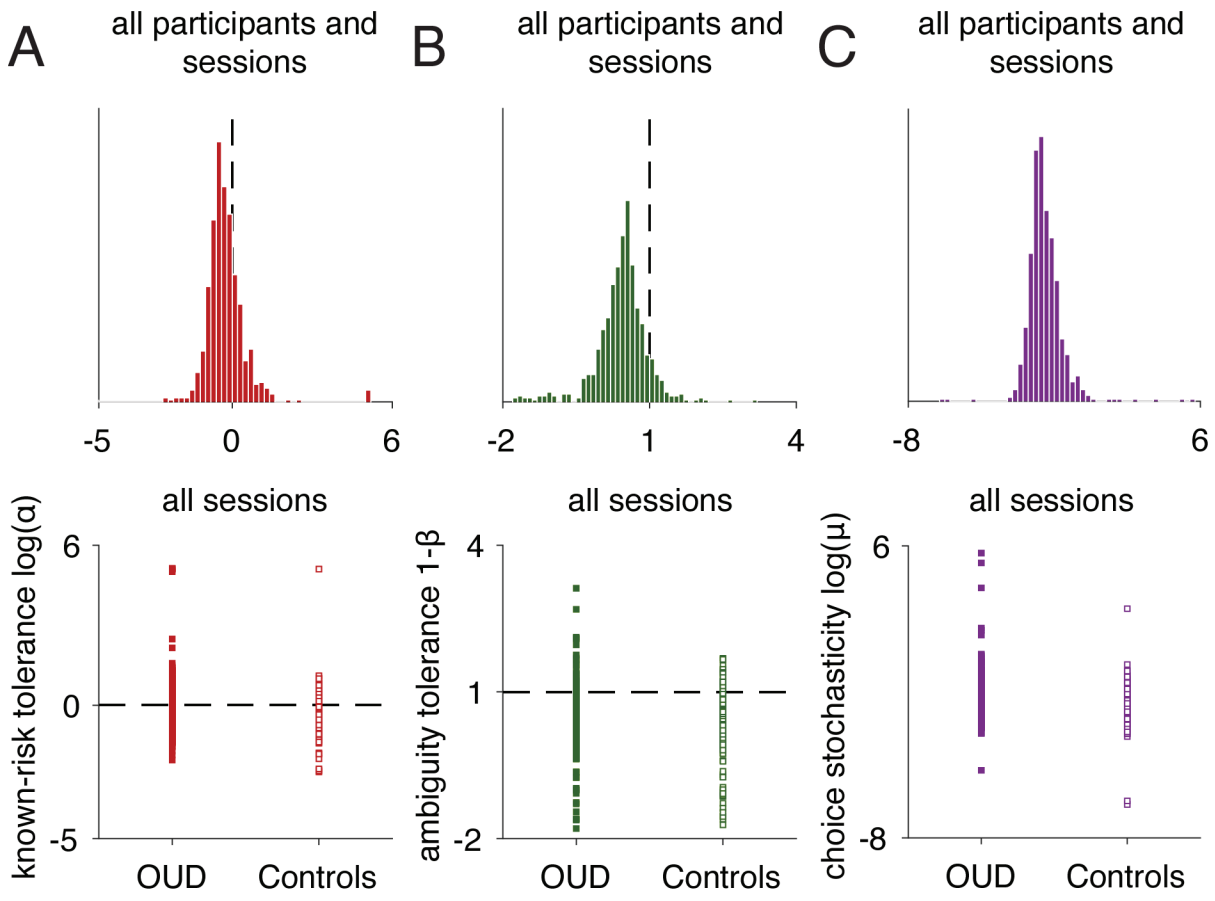

eFigure 4. *Distribution of Decision-Making Task Parameters by Diagnostic Group*
Distribution of (**A**) known-risk tolerance, (**B**) ambiguity tolerance, and (**C**) choice stochasticity across all sessions and participants (top) and across all sessions in individuals with opioid use disorders (OUD) and controls (bottom). Dashed lines represent neutrality such that values to the left (or below) indicate known-risk and ambiguity averse attitudes and values to the right (or above) of the line indicate known-risk and ambiguity seeking attitudes. The data shown for known-risk tolerance excludes one outlier.

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eTable 1. *Time-Lagged Association of Task Variables with Prospective Opioid Use, First 8 Study Sessions Only* [A]

Model: Decision-Making Parameters (First 8 Sessions)							
Num. Observations [B]	378						
Degrees of Freedom	374						
AIC	464.1						
BIC	487.7						
Log–Likelihood	–226.0						
	B	***SE***	**95% CI**		***t*–stat**	***p*–value**	**standardized odds ratio** [C]
(Intercept)	–0.489	0.433	[–1.342	0.362]	–1.131	0.259	0.867
Known-Risk Tolerance: log(α)	–0.172	0.298	[–0.758	0.413]	–0.579	0.563	0.892
Ambiguity Tolerance: 1–β	0.612	0.311	[0.001	1.224]	1.969	0.049	1.351
Choice Stochasticity: log(μ)	0.003	0.275	[–0.538	0.544]	0.010	0.992	1.002

[A] Results of time-lagged linear mixed-effects logistic regressions including random intercepts for participant and session and the listed predictors as fixed effects;
[B] Number of observations reflects total number of task sessions available for analysis (n=387) minus n=9 sessions that were censored due to unknown prospective opioid use status;
[C] Unstandardized odds ratios can be computed from the regression coefficient B as Exp(B). Standardized values provided are from the same model using z-scored continuous predictors.

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eTable 2. *Time-Lagged Association of Task Variables with Prospective Opioid Use, Controlling for Medication Type and Dose* [A]

Model: Decision-Making Parameters and Medication Type (All Participants)							
Num. Observations [B]	530						
Degrees of Freedom	525						
AIC	636.6						
BIC	666.5						
Log–Likelihood	–311.3						
	B	***SE***	**95% CI**		***t*–stat**	***p*–value**	**standardized odds ratio** [C]
(Intercept)	–1.154	0.709	[–2.548	0.241]	–1.625	0.105	0.369
Medication: Methadone	1.008	0.689	[–0.346	2.363]	1.463	0.144	2.741
Known-Risk Tolerance: log(α)	–0.029	0.236	[–0.493	0.435]	–0.122	0.903	0.979
Ambiguity Tolerance: 1–β	0.594	0.254	[0.096	1.093]	2.341	0.019	1.345
Choice Stochasticity: log(μ)	0.086	0.224	[–0.353	0.525]	0.385	0.701	1.067
Model: Decision-Making Parameters and Medication Dose (Methadone-Maintained Participants Only)							
Num. Observations [B]	451						
Degrees of Freedom	446						
AIC	548.7						
BIC	577.4						
Log–Likelihood	–267.3						
	B	***SE***	**95% CI**		***t*–stat**	***p*–value**	**standardized odds ratio** [C]
(Intercept)	0.881	0.581	[–0.261	2.022]	1.516	0.130	1.046
Methadone Dose: mg	–0.012	0.005	[–0.021	–0.002]	–2.453	0.015	0.634
Known-Risk Tolerance: log(α)	0.044	0.250	[–0.448	0.536]	0.175	0.861	1.034
Ambiguity Tolerance: 1–β	0.735	0.287	[0.171	1.299]	2.561	0.011	1.431
Choice Stochasticity: log(μ)	0.064	0.237	[–0.401	0.529]	0.269	0.788	1.051

[A] Results of time-lagged linear mixed-effects logistic regressions including random intercepts for participant and session and the listed predictors as fixed effects;
[B] Number of observations reflects total number of task sessions available for analysis (n=552) minus n=22 sessions that were censored due to unknown prospective opioid use status (all participants model) and an additional n=49 due to buprenorphine maintenance medication (methadone participants only model);
[C] Unstandardized odds ratios can be computed from the regression coefficient B as Exp(B). Standardized values provided are from the same model using z-scored continuous predictors.

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eTable 3. *Time-Lagged Association of Task Variables with Prospective Opioid Use, Without Positive Sessions Based on Urine Test Samples "Scheduled but Refused or Not Completed"* [A]

Model: Decision-Making Parameters (Subset of Sessions)							
Num. Observations [B]	503						
Degrees of Freedom	499						
AIC	570.9						
BIC	596.2						
Log–Likelihood	–279.4						
	B	***SE***	**95% CI**		***t*–stat**	***p*–value**	**standardized odds ratio** [C]
(Intercept)	–0.357	0.416	[–1.174	0.460]	–0.858	0.391	0.719
Known-Risk Tolerance: log(α)	–0.070	0.258	[–0.577	0.438]	–0.269	0.788	0.947
Ambiguity Tolerance: 1–β	0.572	0.283	[0.016	1.128]	2.023	0.044	1.333
Choice Stochasticity: log(μ)	0.176	0.252	[–0.318	0.671]	0.701	0.483	1.160

[A] Results of time-lagged linear mixed-effects logistic regressions including random intercepts for participant and session and the listed predictors as fixed effects;
[B] Number of observations reflects total number of task sessions available for analysis (n=552) minus n=22 sessions that were censored due to unknown prospective opioid use status and an additional n=27 that were identified as positive based on "scheduled but refused or not completed" urine tests;
[C] Unstandardized odds ratios can be computed from the regression coefficient B as Exp(B). Standardized values provided are from the same model using z-scored continuous predictors.

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eTable 4. *Comparison of "Full" Clinical Model to the Same Model Including Ambiguity Tolerance in the Time-Lagged Association with Prospective Opioid Use* [A]

Model	Degrees of Freedom	AIC	BIC	Log–Likelihood	*LR*–stat	*p*–value
"Full" Clinical Model	8	560.9	594.2	–272.4	4.188	0.041
"Full" Clinical Model and Ambiguity Tolerance	9	558.7	596.2	–270.3		

[A] "Full" model includes the time-varying clinical variables (anxiety, craving, withdrawal, nonadherence, and recent use).

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eTable 5. *Comparison of "Best" Clinical Model to the Same Model Including Ambiguity Tolerance in the Time-Lagged Association with Prospective Opioid Use* [A]

Model	Degrees of Freedom	AIC	BIC	Log–Likelihood	*LR*–stat	*p*–value
"Best" Clinical Model	6	568.3	593.5	–278.2	3.618	0.057
"Best" Clinical Model and Ambiguity Tolerance	7	566.7	596.1	–276.4		

[A] "Best" model includes only the significant time-varying clinical variables (craving, nonadherence, and recent use).

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eTable 6. *Diagnostic Group Differences in Decision-Making Task Parameters* [A]

Model: Known-Risk Tolerance						
Num. Observations [B]	695					
Degrees of Freedom	686					
AIC	1979.1					
BIC	2033.7					
Log–Likelihood	–977.6					
	B	***SE***	**95% CI**		***t*–stat**	***p*–value**
(Intercept)	0.217	1.029	[–1.803	2.238]	0.211	0.833
Diagnosis: OUD	0.559	0.261	[0.047	1.071]	2.145	0.032
Education	0.019	0.049	[–0.076	0.115]	0.395	0.693
Race: Caucasian	–0.093	0.676	[–1.420	1.233]	–0.138	0.890
Race: African–American	–0.409	0.687	[–1.758	0.940]	–0.595	0.552
Ethnicity: Hispanic	0.003	0.232	[–0.452	0.458]	0.014	0.988
Income	–0.013	0.050	[–0.112	0.085]	–0.265	0.791
Anxiety: BAI [C]	–0.016	0.012	[–0.039	0.008]	–1.321	0.187
Depression: BDI [D]	–0.004	0.013	[–0.029	0.021]	–0.339	0.735
Model: Ambiguity Tolerance						
Num. Observations [B]	695					
Degrees of Freedom	686					
AIC	932.1					
BIC	986.6					
Log–Likelihood	–454.04					
	B	***SE***	**95% CI**		***t*–stat**	***p*–value**
(Intercept)	0.084	0.471	[–0.842	1.009]	0.178	0.858
Diagnosis: OUD	0.141	0.119	[–0.093	0.374]	1.183	0.237
Education	0.031	0.022	[–0.013	0.074]	1.382	0.167
Race: Caucasian	0.017	0.310	[–0.592	0.627]	0.056	0.956
Race: African–American	–0.020	0.316	[–0.639	0.599]	–0.064	0.949
Ethnicity: Hispanic	–0.149	0.106	[–0.357	0.059]	–1.410	0.159
Income	–0.001	0.023	[–0.046	0.045]	–0.029	0.977
Anxiety: BAI [C]	0.003	0.006	[–0.008	0.013]	0.476	0.634
Depression: BDI [D]	–0.0003	0.006	[–0.012	0.011]	–0.048	0.962
Model: Choice Stochasticity						
Num. Observations [B]	695					
Degrees of Freedom	686					
AIC	1463.4					
BIC	1518.0					
Log–Likelihood	–719.7					
	B	***SE***	**95% CI**		***t*–stat**	***p*–value**
(Intercept)	–1.413	0.677	[–2.742	–0.085]	–2.089	0.037
Diagnosis: OUD	0.307	0.171	[–0.029	0.643]	1.789	0.074
Education	–0.014	0.032	[–0.076	0.049]	–0.435	0.664
Race: Caucasian	0.168	0.446	[–0.707	1.043]	0.377	0.706
Race: African–American	0.506	0.453	[–0.384	1.395]	1.117	0.265
Ethnicity: Hispanic	0.297	0.152	[–0.0005	0.595]	1.960	0.050
Income	–0.006	0.033	[–0.070	0.059]	–0.169	0.865
Anxiety: BAI [C]	–0.0001	0.008	[–0.016	0.015]	–0.012	0.990
Depression: BDI [D]	–0.004	0.008	[–0.019	0.013]	–0.420	0.675

[A] Results of linear mixed-effects regressions including random intercepts for participant and session and the listed predictors as fixed effects;

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[B] Number of observations reflects total number of task sessions available for analysis (*n*=749) minus *n*=54 sessions (41 for OUD participants and 13 for controls) that were censored due to missing data on any one of the covariates listed (see eFigure 3);
[C] Beck Anxiety Inventory (BAI);
[D] Beck Depression Inventory (BDI).

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