Associations Between Family Factors and the Impact of a Digital Health Intervention on Adolescent Perceived Risk of Opioid-related Harm

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Abstract

Adolescent opioid misuse remains a critical public health concern, and family environment may shape how youth respond to prevention interventions. Family-related risk and protective factors, including food insecurity, household substance use exposure, parental monitoring, and family norms surrounding substance use, may influence adolescents' perceived risk of opioid-related harm. Given the established inverse relationship between perceived risk of harm and actual substance use, identifying family factors associated with changes in perceived risk over time is important for informing targeted prevention strategies.

PlaySmart is a videogame intervention designed to promote mental health and increase perceived risk of opioid misuse. This study analyzed longitudinal assessment data from a randomized sample of 532 adolescents collected at baseline, end of gameplay, and 3-, 6-, and 12-month follow-up assessments. Measures included family history of substance misuse, food insecurity, household substance use exposure, help-seeking behaviors, and attitudes toward opioid misuse. Initial ordinary least squares models demonstrated violations of modeling assumptions, motivating a transition to LASSO-regularized logistic regression and longitudinal three-way interaction models examining relationships between family predictors, intervention assignment, and time.

Findings identified beliefs about the safety of using opioids from a family medicine cabinet and anticipation of parental consequences for opioid misuse as consistent predictors of perceived risk in simple models. Longitudinal interaction analyses further showed that food insecurity was associated with increased odds of high perceived risk over time among intervention participants (OR $= 1.849$, $p < 0.05$), while household substance use exposure demonstrated a positive association at the trend level (OR $= 2.075$, $p < 0.1$).

These findings suggest that family context may be associated with differential adolescent responsiveness to digital opioid prevention interventions and may help identify subgroups most likely to benefit from targeted prevention efforts.[1]

Introduction

Adolescent opioid misuse is a critical public health concern. While adolescent prescription opioid misuse has declined modestly over the past decade, 12% of U.S. high school students had ever misused prescription opioids and 4% reported current (past-30-day) misuse in 2023, with higher rates among female, racial/ethnic minority, and LGBTQ+ youth (CDC, 2024). Further,

[1]Note: This thesis presents a novel statistical analysis of data from the *PlaySmart* videogame intervention, focusing specifically on family factors to build on research on overall game outcomes. For completeness, my paper briefly describes data and previous work completed in the play2PREVENT Lab before discussing statistical methods and results of this independent study.

opioid misuse is strongly associated with increased risk of substance use disorders, long-term addiction, and is also closely linked to co-occurring mental health conditions, including depression and anxiety, which have worsened in recent years, particularly following the COVID-19 pandemic. Together, these trends underscore the urgent need for effective early prevention strategies that reduce initiation of substance use and mitigate longer-term health consequences.

Adolescents' perceived risk of harm from opioid misuse continue to be low and vary across substances. Data from the "Monitoring the Future" (MTF) study indicate that only 28% of 10th graders perceive trying a prescription opioid once or twice as posing great risk of harm (Miech et al., 2024). In general, there is an established inverse relationship between perceived risk of harm from drug use and actual drug use, such that lower perceived risk is associated with higher likelihood of use (Bachman et al., 1988; Boomer et al., 2026). Empirical evidence further suggests that adolescents with low perceived risk of harm are substantially more likely to engage in non-medical opioid misuse (Boomer et al., 2026). These findings highlight perceived risk of harm as a strategically important target for and indicator of prevention efficacy.

Family factors represent central influences on adolescent substance use, shaping perceptions, behaviors, and vulnerability to risk. Positive family connectedness, including parental monitoring, emotional support, and routine engagement such as frequent family meals, is consistently associated with reduced substance use behaviors, improved mental health, and greater resilience (Luo et al., 2023; Rahal et al., 2025).

Parental monitoring, defined as an active and multidimensional process involving boundary-setting and open communication about adolescents' activities and peers, has been linked to reduced intentions to engage in substance use and broader protective health behaviors (Dittus et al., 2023). Importantly, adolescents' perceptions of monitoring appear especially influential with higher perceived monitoring associated with lower risk for negative outcomes including sexual behaviors, substance use, violence, and showing indicators of poor mental health (Dittus et al., 2023).

Routine family interactions, such as frequent family meals, provide additional opportunities for communication, behavioral modeling, and emotional support for adolescents (Rahal et al., 2025). More frequent family meals are shown to be associated with better mental health outcomes and lower rates of substance use in female adolescents (Rahal et al., 2025). On the other hand, adolescents of all genders with low vs. high frequency of family meals are 27% more likely to misuse substances and are generally more likely to experience negative mental health outcomes (Luo et al., 2023). This highlights the importance of consistent family engagement in shaping adolescent health behaviors.

However, not all family environments or influences are protective. Adolescents with immediate family members with substance misuse are exposed to additional environmental risk, experience greater stressors, and are at greater risk for early initiation of substance use (Charles et al., 2015). These risks may be driven by the normalization of substance use, heightened

stress exposure, and the development of behavioral tendencies such as impulsivity and reward sensitivity (Charles et al., 2015). While family history of substance misuse is associated with increased risk, family environmental factors including occupation, socioeconomic status, food insecurity, parent marital status, and peer groups appear especially important for early initiation of substance use, whereas genetic influences may play a larger role in later progression (Khoddam et al., 2015). Further, protective family dynamics such as high parental support and clear disapproval of substance use may mitigate these risks and promote more adaptive outcomes (Barry et al., 2025; Dittus et al., 2023).

To address gaps in the prevention of adverse outcomes from opioids, ranging from opioid initiation to overdose, the National Institute on Drug Abuse (NIDA) Helping to End Addiction Long-term (HEAL) Prevention Initiative has supported the development of innovative interventions, specifically for younger individuals, ages 16–30 (Ridenour et al., 2023). Among such interventions is *PlaySmart*, a digital behavioral health game developed by the play2PREVENT Lab for adolescents aged 16–19. *PlaySmart* leverages high engagement with video games to promote mental health awareness and increase perceived risk of opioid misuse (Pendergrass Boomer et al., 2023). With over 85% of adolescents reporting video gameplay, this modality meets adolescents in an engaging and familiar context and delivers promising intervention. The effectiveness of *PlaySmart* has been evaluated through a two-arm, parallel and superiority randomized control trial (Boomer et al., 2026).

Beyond overall efficacy, it is critical to understand how mechanisms such as family-based protective and risk factors influence intervention effects. Prior literature suggests that adolescents who perceive high parental monitoring and support are more likely to internalize risk messaging, while those exposed to parental substance misuse and other environmental stressors may experience reduced internalization and therefore increased risk (Wills & Yaeger, 2003). This study therefore examines whether *PlaySmart* differentially impacts adolescents' perceived risk of harm based on family context, and whether these factors moderate the magnitude of intervention effects over time. Baseline predictor selection and longitudinal classification analyses are conducted as supporting methodological steps to identify stable family-related variables for moderation analyses. Understanding these mechanisms can improve prevention strategies, guide targeted interventions, and inform digital health programming.

Methods

Participants and Setting

Participants were recruited from 15 high schools in Connecticut. Eligible students were 16–19 years of age, had no prior history of opioid misuse, and were identified as high risk based on substance use or mental health screening measures. All participants provided informed assent,

and parental consent was obtained for those under 18 years of age. Participants completed supervised 60-minute gameplay sessions in after school settings one to two times per week over approximately six weeks (Boomer et al., 2026).

Intervention

PlaySmart is a videogame intervention designed to promote mental health and increase perceived risk of opioid misuse (Boomer et al., 2026). Based on a theoretical foundation and co-developed with youth to ensure authenticity and engagement, *PlaySmart* comprises up to six hours of unique gameplay. Within the game, players navigate decisions related to peer pressure, stress, and substance use, particularly opioids, while addressing co-occurring risk factors such as mental health challenges and other substance misuse (Pendergrass Boomer et al., 2023). Over the course of six weeks of gameplay in school, students experience six main storylines and an additional six integrated minigames that reinforce core prevention skills such as refusal, decision-making, and coping strategies (Pendergrass Boomer et al., 2023). Participants assigned to the control condition had access to nine videogames, including commercially available games such as *The Sims* and *Can you Escape*, that contained no relevant content, serving as the attention and time control (Pendergrass Boomer et al., 2023).

Data Collection

Assessment data were collected at five time points (baseline (bsl), end of gameplay (eog), and 3, 6, and 12 months post-baseline) from a randomized sample of 532 adolescents, capturing family history of substance misuse, food insecurity, mental health, substance use behaviors, and help-seeking attitudes (Pendergrass Boomer et al., 2023).

Measures

Pertaining to family factors of interest, assessment questions of interest were mapped to two primary domains, risk (e.g., family history of substance misuse, access to prescription medications at home, food insecurity, and paid work) and protective (e.g., positive family bonds, parental monitoring, help-seeking behaviors, and family meals). Risk factors were hypothesized to show a negative relationship with perceived risk of opioid-related harm, while protective factors were hypothesized to show a positive relationship with perceived risk of opioid-related harm.

Demographics

Demographic characteristics were collected only at baseline and include family history of significant drinking or drug use problems, student employment status, and food security at

home. Family history was assessed through the question "Have any of your blood-related relatives had a significant drinking or drug use problem that did or should have led to treatment?" Participants could select from a list of relatives and responses were categorized into binary yes/no for immediate and extended family. Employment status was obtained through the yes/no question "Are you currently working at a paid job (including self-employment)?" and food insecurity was categorized by three questions pertaining to worries of food running out at home and receiving free or reduced-price lunches at school. Initially the question "Did you worry that food at home would run out before your family got money to buy more?" provided options *A lot*, *Sometimes*, *Never*, however analysis revealed a very small sample size for *A lot* (Appendix Fig. 1, $n = 16$ overall, $n = 3$ in intervention group). As a result, we grouped *A lot* and *Sometimes* together, resulting in a binary yes/no structure. The subsequent school lunch questions are both binary yes/no.

Social Exposure

Social exposure to substances was assessed with the base question: "What is the most often that one person who lives with you…" with 3 descriptors asking about alcohol, marijuana, and heroin. 4 possible answer choices ranged from *Never* to 4–7 days a week. These responses were then summed to create a composite score.

Knowledge Questions

Participant knowledge of opioid misuse and its risks were assessed through 30 statements with answer choices of *true*, *false*, or *not sure*. 2 in particular apply to this study: "It is ok and safe to take prescription opioids if they are in your family's medicine cabinet," and "A person is less likely to misuse opioids and other substances if they have protective factors like strong and positive family bonds."

Attitudes Toward Misuse

Attitudes toward misuse of opioids were assessed by having participants indicate how much they agree or disagree with several statements. All statements have the base: "If I used/took a prescription opioid, or painkiller or heroin, I would [prompt]" For the purposes of this study, the prompt of interest is "Get in trouble with my parents." Five answer choices were presented that range from strongly disagree to strongly agree and categorized into a five point scale.

Help Seeking Questions

Participants were asked about both their past help-seeking behaviors and general help-seeking behaviors. Past help-seeking was assessed by presenting the participant with a list of 13 different

people they may seek help or advice from. They were able to check any of those people or resources that they have gone to for advice or help in the past six months. If they sought help from that person/resource, they were then asked to quantify the number of times in the past six months. People of interest in this study include parent/guardian and other family member/relative. Responses were categorized first into binary yes/no for seeking help and then on a 3-point scale for frequency (never, once, multiple times). General help seeking tendencies were assessed through the likelihood that a participant would seek help from a parent/guardian or other relative/family member if (a) experiencing a personal or emotional problem and if (b) experiencing suicidal thoughts. The answer choices were given on a 7-point Likert scale with answers ranging from extremely unlikely to extremely likely.

Perception of Risk of Harm

As mentioned above, perception of risk of harm of opioid misuse is the study's primary outcome. With youth generally indicating a low perception of risk of harm around opioid misuse, perceived risk of harm is the focus as a proximal target underlying the videogame intervention's impact on the more distal outcome of initiation of opioid misuse (Pendergrass Boomer et al., 2023). Perception of risk of harm score was assessed with the stem question: "How much do you think people risk harming themselves (physically or in other ways), if they [prompt]?" with 8 different prompts related to both illegal and legally available opioids. Answers include no risk, slight risk, moderate risk, and great risk, allowing for a score range of 1–4. The composite score for each participant is an equally weighted sum of all eight questions, allowing for a score range of 8–32.

Statistical Analyses

Exploratory Analysis and OLS

Analyses began with exploration of baseline data to identify a precise linear model to understand the impact of relevant family predictors on *PlaySmart* intervention efficacy and support subsequent longitudinal moderation analyses. This first included Ordinary Least Squares regression of the initial 18 predictors on response variable perceived risk of harm of opioid misuse. Residual plots, Q-Q plots, and P-P plots were generated, the distribution of the perceived risk of harm scale was visualized, and a correlation heatmap was used to examine pairwise relationships and potential multicollinearity and heteroskedasticity among predictors.

To reduce model complexity, principal component analysis (PCA) was tested as a data-driven dimensionality reduction approach to identify latent structures among correlated family risk and protective variables. However, PCA components were not easily interpretable in the context of family environment constructs and did not meaningfully improve model performance.

A LASSO penalty was then applied to the initial OLS model as an alternative to reduce model complexity. This data-driven feature selection process allowed for model simplification without imposing arbitrary composite indices. LASSO (L_1 regularization) shrinks less informative coefficients toward zero, effectively performing variable selection while retaining model interpretability. Cross-validation was used to determine the optimal penalty parameter, with additional consideration given to the one-standard-error rule to favor more parsimonious models in certain iterations.

Logistic Model

Data analysis then shifted to a logistic model, motivated by observed non-normality and clustering at the lower end of the outcome distribution, as well as evidence from residual diagnostics indicating violations of linear regression assumptions. To operationalize logistic regression, the continuous perceived risk score was converted into binary outcomes using multiple thresholds. Model performance across thresholds was evaluated using receiver operating characteristic (ROC) curves and area under the curve (AUC) metrics. In addition to clinical distinctions between high and low perceived risk, heatmaps of AUC values across threshold combinations and box and whisker plots of predictor distributions were used to guide threshold selection and assess separability between classes.

LASSO Selection

Once a single threshold of 18 was selected to dichotomize the data, a LASSO penalty was then applied again to the baseline logistic regression, following the same cross-validation process. This model was then generalized and applied across all time points. Initial analyses focus on applying LASSO logistic regression models independently at each time point for the full data set, as well as for both the control and intervention groups separately, to compare stability of selected predictors and changes in effect sizes over time. Distributions of significant predictors and their changes in outcome over time were further visualized to understand underlying patterns.

Holdout Validation

In addition, we conducted a longitudinal holdout validation as a robustness check for the baseline LASSO logistic regression model to determine whether baseline-selected family predictors retained longitudinal relevance before inclusion in interaction models. Specifically, the model trained on baseline data was first applied to control group observations collected at end of gameplay and at 3-, 6-, and 12-month follow-up assessments to evaluate the stability and predictive performance of the model across time. After confirming that the model retained acceptable predictive performance in the control group, the same model was then applied to

intervention group observations across the same follow-up time points to assess whether baseline family predictors are differentially related to perceived risk outcomes following exposure to the intervention.

Interaction Model

To further examine how intervention effects evolved over time, interaction terms were incorporated into the generalized linear model. Specifically, three-way interaction terms were created between each predictor retained through baseline LASSO selection, intervention status, and time. In these models, the reference group consisted of participants with the reference (0) value for each predictor (see Measures section), participants in the control condition, and baseline assessment time. Time included baseline, end of gameplay, and 3-, 6-, and 12-month follow-up assessments.

Time was modeled with particular care because follow-up intervals were not evenly spaced and prior intervention research has suggested that effects may not emerge immediately after exposure. Although immediate intuition suggested that the hypothesized intervention effect would be strongest immediately following gameplay, previous work examining behavioral and mental health interventions has demonstrated the possibility of delayed or "sleeper" effects, in which intervention-related changes become more pronounced over time. Accordingly, two separate interaction modeling approaches were tested.

Time was first treated as a continuous linear variable in the longitudinal interaction model. This specification allowed the generalized linear model to estimate a single overall longitudinal effect for each LASSO-selected predictor in interaction with intervention exposure across the study period. In these models, the three-way interaction term represented the multiplicative product of predictor status, intervention group assignment, and time.

To then verify the assumption of linearity for our three-way interaction, we conducted a formal diagnostic check using orthogonal polynomial contrasts. This approach decomposed the time variable into independent linear and higher-order (e.g., quadratic, cubic) components to evaluate how treatment effects varied across moderator levels over time. A linear trajectory was supported if the linear contrast was statistically significant while the higher-order trends were not.

Then, time was treated as a categorical variable, allowing the effect of each predictor-by-intervention interaction to be estimated independently at each follow-up time point. This approach enabled direct comparison of intervention-associated effects across assessments and allowed for visualization of longitudinal trends among statistically significant predictors. Exploratory visualizations were also used to assess whether a linear, continuous representation of time would be appropriate for the observed data patterns.

Contingency Tables

Finally, contingency tables were generated to examine overall outcome distributions across intervention and control participants at each assessment time point. These descriptive analyses served as an additional validation step to evaluate overall intervention efficacy and confirm that meaningful longitudinal changes in perceived risk outcomes were present, thereby supporting interpretation of the predictor-by-intervention interaction effects observed in the regression models.

Statistical Environments and Packages

All statistical analyses were conducted using Stata (v18/MP, StataCorp, College Station, TX). After initially exploring baseline data in Python, all logic was moved to and re-written in Stata in order to capture formatting of subsequent time points in Stata files. From there, user-contributed SSC packages included *outreg2* for regression table export, *coefplot* for coefficient visualization, and *heatplot*, *colrspace*, *palettes*, and *stripplot* for exploratory and longitudinal visualizations.

Data preparation procedures included variable binarization, harmonization across the five assessment time points, and restructuring from wide to long format using panel specifications indexed within participants (*xtset*). Preliminary analyses included Ordinary Least Squares (OLS) regression with heteroskedasticity-robust standard errors (*VCE(robust)*) and residual diagnostic evaluation. Primary analyses employed LASSO-regularized logistic regression (*lasso logit*) with cross-validation to identify parsimonious baseline predictors of high perceived risk of harm. Baseline-derived models were subsequently evaluated as longitudinal holdout prediction models across intervention and control groups at all follow-up assessments using Receiver Operating Characteristic Area Under the Curve (ROC/AUC) classification metrics and contingency transition analyses to trace categorical shifting over time.

Longitudinal intervention effects were then estimated using mixed-effects multilevel logistic regression models (*melogit*) with participant-level random intercepts to account for repeated observations nested within individuals. Three-way interaction terms between randomized intervention assignment, time, and LASSO-selected baseline moderators (treatment $\times$ moderator $\times$ time) were modeled with contrast hypothesis testing to assess the handling of time. Post-estimation procedures included computation of average marginal effects, exponentiated odds ratios (*eform*), ROC analyses, and Pseudo-R^2 statistics.

Results

Predictor Mapping and Descriptive Statistics

Overall baseline participant characteristics obtained from participant surveys are shown in Table 1.

Baseline Characteristics in intervention and control groups

	Intervention ($N = 269$)	**Control** ($N = 263$)	**Total** ($N = 532$)
Sex (n, %)*			
Female	127 (47%)	121 (46%)	248 (47%)
Male	142 (53%)	142 (54%)	284 (53%)
Age, years (mean ± SD)	16.6 (0.7)	16.6 (0.7)	16.6 (0.7)
Age, years, Group (n, %)			
15-16	146 (54%)	136 (52%)	282 (53%)
17	89 (33%)	94 (36%)	183 (34%)
18	32 (12%)	31 (12%)	63 (12%)
19	2 (1%)	2 (1%)	4 (1%)
Grade (n, %)*			
9th or 10th Grade	44 (16%)	43 (16%)	87 (16%)
11th or 12th Grade	225 (84%)	220 (84%)	445 (84%)
Race (n, %)**			
White	86 (32%)	93 (35%)	179 (34%)
American Indian/Alaskan Native	14 (5%)	8 (3%)	22 (4%)
Asian	19 (7%)	25 (10%)	44 (8%)
Native Hawaiian or Other Pacific Islander	2 (1%)	5 (2%)	7 (1%)
Black/African American	128 (48%)	113 (43%)	241 (45%)
Something else, please specify	50 (19%)	51 (19%)	101 (19%)
No response	–	–	–
Ethnicity (n, %)			
Not Hispanic or Latinx	157 (58%)	155 (59%)	312 (59%)
Hispanic or Latinx	100 (37%)	102 (39%)	202 (38%)
Don't know	10 (4%)	5 (2%)	15 (3%)
Prefer to Not Say	2 (1%)	1 (0%)	3 (1%)
Familial Substance Misuse (n, %)**			
Father	29 (11%)	28 (11%)	57 (11%)
Mother	6 (2%)	10 (4%)	16 (3%)
Brother	3 (1%)	7 (3%)	10 (2%)
Sister	1 (0%)	4 (2%)	5 (1%)

Baseline Characteristics in intervention and control groups

	Intervention ($N = 269$)	**Control** ($N = 263$)	**Total** ($N = 532$)
Grandfather	13 (5%)	24 (9%)	37 (7%)
Grandmother	7 (3%)	12 (5%)	19 (4%)
Another relative	43 (16%)	36 (14%)	79 (15%)
Prefer not to say	25 (9%)	24 (9%)	49 (9%)
None	173 (64%)	164 (62%)	337 (63%)
Food worries at home (n, %)			
Never	185 (69%)	169 (64%)	354 (67%)
Sometimes	81 (30%)	81 (31%)	162 (30%)
A lot	3 (1%)	13 (5%)	16 (3%)
Receives free or reduced lunch at school (n, %)			
No	49 (18%)	55 (21%)	104 (20%)
Yes	192 (71%)	174 (66%)	366 (69%)
Don't know	28 (10%)	34 (13%)	62 (12%)
Whole school receives free or reduced lunch (n, %)			
No	29 (11%)	27 (10%)	56 (11%)
Yes	164 (61%)	161 (61%)	325 (61%)
Don't know	76 (28%)	75 (29%)	151 (28%)
Mental Health-Anxiety			
Minimal	151 (56%)	143 (54%)	294 (55%)
Mild	60 (22%)	78 (30%)	138 (26%)
Moderate	40 (15%)	34 (13%)	74 (14%)
Severe	18 (7%)	8 (3%)	26 (5%)
Mental Health-Depression			
No significant depressive symptoms	109 (41%)	101 (38%)	210 (39%)
Mild	80 (30%)	94 (36%)	174 (33%)
Moderate	57 (21%)	44 (17%)	101 (19%)
Moderately Severe	15 (6%)	16 (6%)	31 (6%)
Severe	8 (3%)	8 (3%)	16 (3%)
Any experience with Alcohol			
No	183 (68%)	174 (66%)	357 (67%)
Yes	86 (32%)	89 (34%)	175 (33%)
Any experience with Marijuana			
No	213 (79%)	217 (83%)	430 (81%)
Yes	56 (21%)	46 (17%)	102 (19%)

Baseline Characteristics in intervention and control groups

	Intervention ($N = 269$)	**Control** ($N = 263$)	**Total** ($N = 532$)

* Used as stratum for randomization

** More than one selection could be made

Table 1. This table presents a comparative demographic and clinical profile of the study participants ($N = 532$) at baseline, demonstrating well-balanced distributions between the intervention and control arms across key stratification variables, family histories, and behavioral health metrics. (From Boomer et al. (2026))

A complete list of the 18 predictors from the questions of interest used for this study are shown in Table 2.

Descriptive Statistics by Time Point

Measure	N bsl	Mean(SD)/n(%) bsl	N eog	Mean(SD)/n(%) eog	N 03m	Mean(SD)/n(%) 03m	N 06m	Mean(SD)/n(%) 06m	N 12m	Mean(SD)/n(%) 12m
Immediate Family Misuse History	532	0.13 (0.33)	0	. (.)	0	. (.)	0	. (.)	0	. (.)
Extended Family Misuse History	532	0.21 (0.41)	0	. (.)	0	. (.)	0	. (.)	0	. (.)
Employment Status (Binary)	532	149 (28.0%)	0	0 (.%)	0	0 (.%)	0	0 (.%)	0	0 (.%)
Food Insecurity	532	162 (36.5%)	0	0 (.%)	0	0 (.%)	0	0 (.%)	0	0 (.%)
Participant Free/Reduced Price School Lunch	532	366 (68.8%)	0	0 (0.0%)	0	0 (0.0%)	0	0 (0.0%)	0	0 (0.0%)
All Free/Reduced Price School Lunch	532	325 (61.1%)	0	0 (.%)	0	0 (.%)	0	0 (.%)	0	0 (.%)
Household Substance Use Exposure	531	138 (110.9)	463	148 (117.5)	465	123 (116.1)	447	123 (107.4)	433	123 (114.3)
Family Medicine Cabinet	532	0.80 (0.40)	532	0.69 (0.46)	532	0.72 (0.45)	532	0.66 (0.48)	532	0.63 (0.48)
Strong Family Bonds	532	0.53 (0.50)	532	0.51 (0.50)	532	0.53 (0.50)	532	0.48 (0.50)	532	0.47 (0.50)
Anticipation of Parental Consequences	531	2.96 (1.45)	462	3.08 (1.37)	465	3.15 (1.33)	447	3.14 (1.31)	431	3.17 (1.32)
Past Help Seeking: Parent/Guardian	528	289 (54.7%)	459	237 (51.6%)	462	217 (47.0%)	444	199 (44.8%)	428	171 (40.0%)
Past Help Seeking: Other Relative	528	175 (33.1%)	458	132 (28.8%)	459	131 (28.5%)	444	100 (22.5%)	429	92 (21.4%)
Past Help Seeking Frequency: Parent/Guardian	527	32 (189.8)	527	34 (192.4)	524	21 (194.1)	530	17 (195.3)	527	15 (197.2)
Past Help Seeking Frequency: Other Relative	526	26 (189.7)	527	22 (192.4)	526	21 (193.7)	531	13 (195.3)	528	14 (197.0)
General Personal/Emotional Help: Parent/Guardian	530	3.45 (2.05)	455	3.34 (2.18)	462	3.36 (2.14)	442	3.39 (2.09)	428	3.34 (2.11)
General Personal/Emotional Help: Other Relative	531	2.73 (2.01)	456	2.54 (2.07)	463	2.57 (1.99)	443	2.55 (2.03)	429	2.51 (2.02)
General Suicidal Help: Parent/Guardian	530	3.32 (2.37)	457	3.15 (2.33)	463	3.24 (2.27)	443	3.16 (2.27)	429	3.15 (2.21)
General Suicidal Help: Other Relative	531	2.58 (2.31)	456	2.46 (2.21)	462	2.44 (2.18)	443	2.52 (2.15)	427	2.35 (2.14)
Perception of Risk of Harm Score	532	24.36 (7.63)	463	25.10 (7.70)	465	25.49 (7.50)	447	26.09 (6.98)	433	26.06 (7.10)

Table 2. This table summarizes sample sizes (N), means, and standard deviations (or frequency counts and percentages for binary variables) for study predictors of interest, and overall perceived harm scores.

Baseline Exploratory Analysis

Initial OLS regression models were fit to examine associations between 18 baseline predictors and perceived risk of harm from opioid misuse. These analyses were conducted to identify family-context variables associated with adolescents' baseline opioid risk perceptions and to determine which factors may moderate the effects of *PlaySmart* over time. Regression outputs are presented in Table 3. There was selection of two significant predictors, believing it is safe to take prescription opioids from the family's medicine cabinet ($\beta = 3.706$, SE $= 1.041$,

p-value < 0.001, 95% CI [1.661, 5.752]) and anticipation of getting in trouble with parents if the youth used opioids ($\beta = 1.356$, SE $= 0.291$, p-value < 0.001, 95% CI [0.785, 1.927]). The emergence of these predictors suggests that adolescents' perceptions of household medication accessibility and parental consequences may be particularly relevant family-context factors in shaping opioid risk perceptions and, therefore, may influence responsiveness to prevention messaging delivered through *PlaySmart*.

Preliminary OLS Model for Baseline Perception of Risk of Harm Scale

VARIABLES	**(1) Coefficient**	**(2) Std. Error**	**(3) p-value**	**(4) 95% CI**
Immediate Family Misuse History	0.799	0.986	0.418	(-1.138, 2.737)
Extended Family Misuse History	0.962	0.758	0.205	(-0.528, 2.452)
Household Substance Use Exposure	0.188	0.218	0.389	(-0.241, 0.617)
Family Medicine Cabinet	3.706***	1.041	0.000	(1.661, 5.752)
Employment Status (Binary)	0.676	0.721	0.349	(-0.740, 2.092)
Food Insecurity	-1.466*	0.754	0.053	(-2.947, 0.016)
Participant Free/Reduced Price School Lunch	-0.616	0.722	0.394	(-2.035, 0.803)
All Free/Reduced Price School Lunch	-0.249	0.698	0.722	(-1.621, 1.123)
Anticipation of Parental Consequences	1.356***	0.291	0.000	(0.785, 1.927)
Strong Family Bonds	-0.192	0.679	0.777	(-1.526, 1.141)
Past Help Seeking: Parent/Guardian	-0.206	0.826	0.803	(-1.830, 1.417)
Past Help Seeking: Other Relative	-0.654	0.776	0.400	(-2.179, 0.871)
Past Help Seeking Frequency: Parent/Guardian	-0.118	0.885	0.894	(-1.857, 1.621)
Past Help Seeking Frequency: Other Relative	-0.615	0.623	0.325	(-1.839, 0.610)
General Personal/Emotional Help: Parent/Guardian	-0.264	0.271	0.331	(-0.796, 0.269)
General Personal/Emotional Help: Other Relative	0.207	0.246	0.400	(-0.276, 0.690)
General Suicidal Help: Parent/Guardian	0.167	0.220	0.448	(-0.266, 0.601)
General Suicidal Help: Other Relative	-0.165	0.219	0.451	(-0.594, 0.265)
Constant	19.672***	1. 1.972	0.000	(15.796, 23.547)
Observations	513			
R-squared	0.171			

*** $p < 0.01$, ** $p < 0.05$, * $p < 0.1$

Note: Robust standard errors are reported.

Table 3. OLS regression output table displaying estimated coefficients (β), robust standard errors, p-values, and 95% confidence intervals. Stars also indicate p-values.

Residual diagnostics (Appendix Fig. 2) and Q-Q/P-P plots (Appendix Fig. 3, Appendix Fig. 4) indicated violations of linear model assumptions, including non-normality and heteroscedasticity.

Visualization of the outcome distribution at baseline (Fig. 1) demonstrated clustering at the lower end of the perceived risk of harm scale, with a notable spike at the minimum value. This distributional pattern was consistent across time points (Appendix Fig. 5) and suggested that a

linear modeling framework may not appropriately capture variation in the outcome perceived risk of harm.

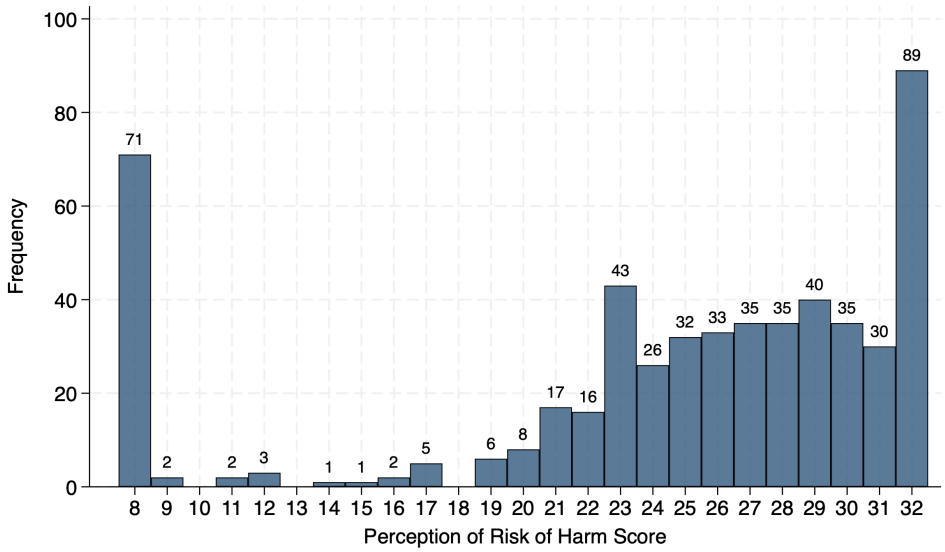

Figure 1. Distribution of Perceived Risk of Harm Outcome Variable at Baseline. The figure displays the distribution of baseline perceived risk of harm scores across study participants prior to dichotomization for logistic regression analyses, with spikes at responses 8 and 32, as well as consistently high levels at higher scores.

A correlation heatmap (Fig. 2) of all 18 predictors of interest revealed modest pairwise correlations among predictors, with no single cluster of highly collinear variables. Principal component analysis (PCA; Appendix Fig. 6) did not yield interpretable components, and therefore did not meaningfully reduce dimensionality.

Logistic Regression and Threshold-Based Classification

Given the non-linear distribution of the outcome, analyses shifted to logistic regression models using dichotomized iterations of perceived risk of harm to increase explanatory power. Multiple thresholds for binary classification were evaluated to assess the robustness of classification performance. Receiver operating characteristic (ROC) analyses demonstrated that model performance varied substantially depending on threshold selection. Models distinguishing very low perceived risk from several other groups achieved higher area under the curve (AUC) values compared to models attempting to separate very high perceived risk from intermediate categories (Appendix Fig. 7). Heatmaps of AUC values across threshold combinations (Fig. 3) indicated that classification performance declined as the lower threshold increased. This pattern suggests reduced separability between moderate and high perceived risk groups.

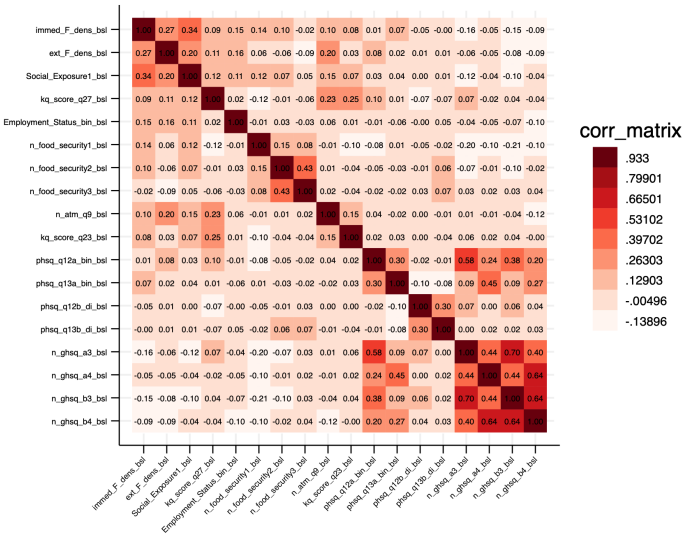

Figure 2. Pairwise Correlation Heatmap of All Predictors of Interest. Standard correlation matrix of predictor variables described in measures. Labels noted by variable names. F_dens refers to family history, kq refers to knowledge questions (q27 refers to the medicine cabinet question and q23 to strong family bonds), food_security1 refers to food insecurity at home and food_security2/3 refer to free/reduced price lunch at school, n_atm refers to attitudes towards misuse, phsq refers to past help seeking, and ghsq refers to general help seeking behaviors.

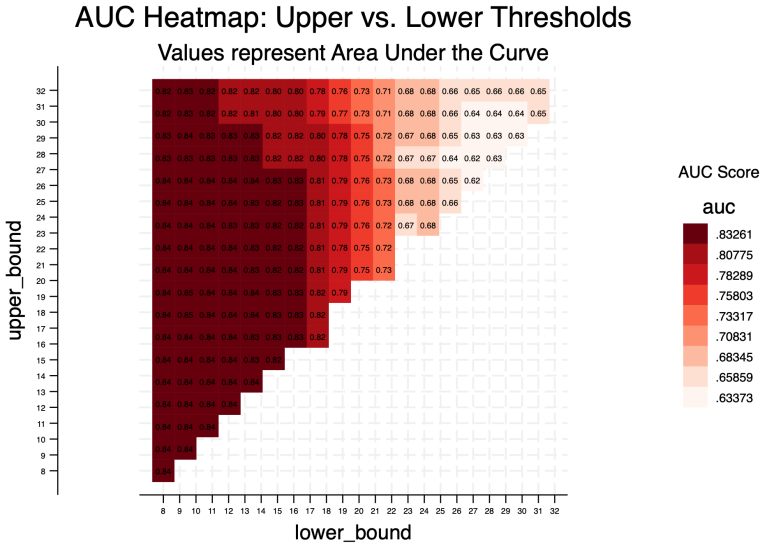

Figure 3. ROC AUC Heatmap Across All Possible Thresholds. All perception of harm values options for both lower and upper bounds for dichotomization in logistic regression models. Higher AUC values noted by darker coloring with exact values displayed inside boxes at the intersection of given combinations.

Further, box and whisker plots of predictor distributions (Fig. 4) revealed that observations in the middle of the perceived risk of harm distribution more closely resembled those at the high end than those at the low end. Additional threshold analyses excluding the lowest values (Appendix Fig. 8, Appendix Fig. 9) did not support a clear distinction between moderate and high perceived risk groups. Instead, results consistently indicated a primary separation between very low perceived risk and all other observations. This, in addition to the distribution of perceived risk of harm (Fig. 1, Appendix Fig. 5), provides justification for a single threshold value at 18 to be used in all regression analyses to understand the impact of family factors on *PlaySmart* efficacy. This threshold therefore operationalizes the primary outcome as whether adolescents fall into the lowest perceived-risk group, which is conceptually aligned with the study's aim of assessing whether family context influences *PlaySmart*'s ability to shift adolescents away from particularly low perceptions of opioid-related harm.

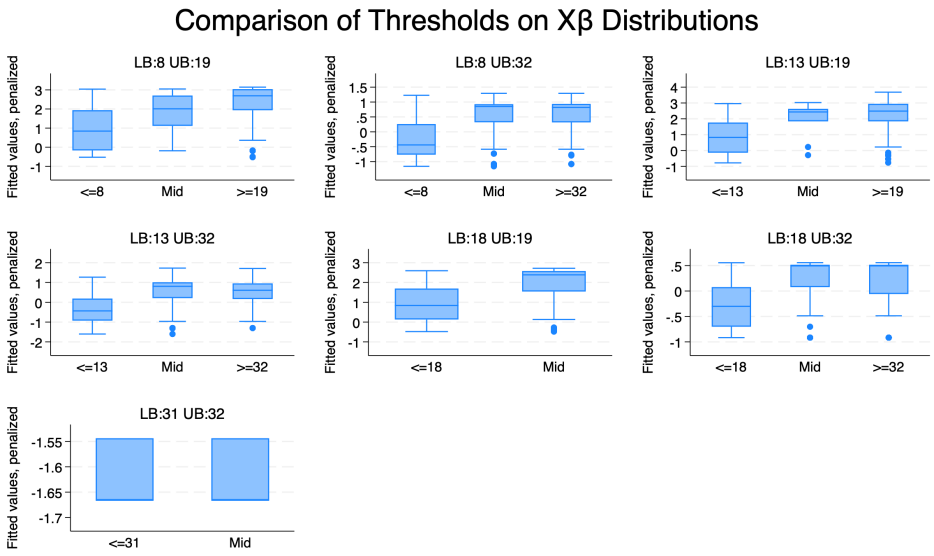

Figure 4. Comparison of Thresholds for Logistic Regression. Each panel displays the distribution of penalized fitted values ($X\beta$) across observations classified below the lower bound (LB), above the upper bound (UB), and within the intermediate ("Mid") range excluded from binary classification. Threshold combinations were evaluated to assess class separability and identify cutoff values that maximized discrimination between low and high perceived risk of harm groups while minimizing overlap in fitted value distributions. In threshold schemes without an excluded middle category, the "Mid" group represents observations above the upper bound.

LASSO Variable Selection

To address model complexity and reduce overfitting, LASSO (L_1) regularization was applied to the regression framework. This approach was used to isolate the subset of family-context

predictors most strongly associated with perceived risk of harm, thereby identifying the variables most likely to moderate intervention-related changes in opioid risk perception over time. At baseline, LASSO reduced the initial 18 predictors to a smaller subset of 9 key variables (1 omitted at baseline but maintained throughout) (Fig. 5). These 9 predictors were then used for all subsequent time points.

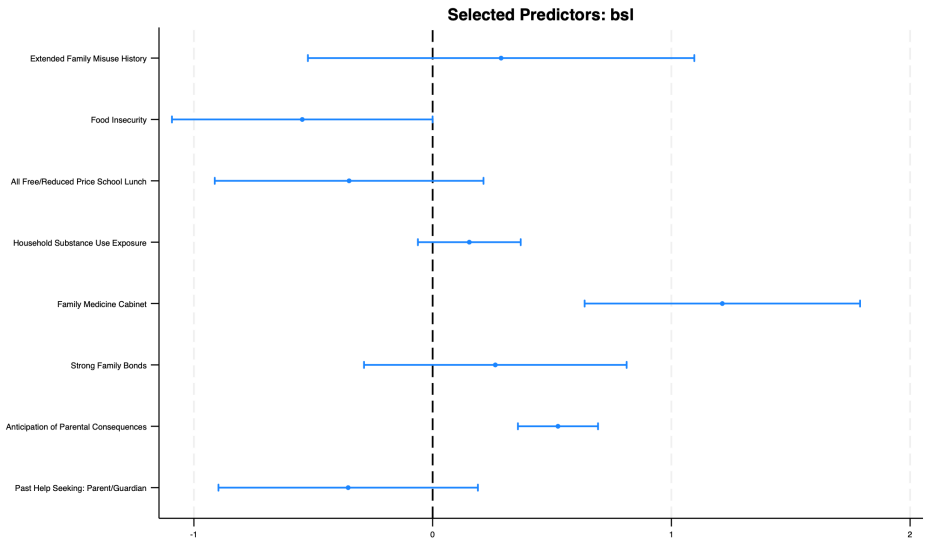

Figure 5. Selected Predictors for LASSO Logistic Regression Model at Baseline. Log-odds coefficients shown by x values of points and 95% confidence intervals shown by extending bars for each of the predictors selected by LASSO regularization in logistic regression with threshold of 18.

Key Predictors in Logistic Regression

Selecting 18 as the optimal threshold for binary classification in this logistic regression (0 or low perception of harm ≤ 18 and 1 or high perception of harm > 18), analyses were performed independently across all time points. Results are shown in Table 4.

The baseline model showed significance of insecurity of enough food at home ($\beta = -0.546$, SE $= 0.279$, p-value < 0.05), believing it is safe to take prescription opioids from the family's medicine cabinet ($\beta = 1.214$, SE $= 0.294$, p-value < 0.01), and anticipation of getting in trouble with parents if the youth used opioids ($\beta = 0.525$, SE $= 0.086$, p-value < 0.01). The latter two of these three are consistent with the OLS model. The consistency of these family-related predictors across modeling approaches further supports their importance as potential moderators of *PlaySmart* efficacy, suggesting that Adolescents' home environments may shape both baseline opioid perceptions and the extent to which prevention messaging is internalized. However, when looking at the outcomes over time for these three significant predictors, it

LASSO Logistic Regression Output Table Over Time

VARIABLES	(1) bsl	(2) eog	(3) 03m	(4) 06m	(5) 12m
Extended Family Misuse History	0.287	-0.045	0.043	0.497	-0.138
	(0.413)	(0.434)	(0.427)	(0.529)	(0.489)
Food Insecurity	-0.546**	-1.050***	-0.972***	-0.845**	-0.374
	(0.279)	(0.320)	(0.316)	(0.334)	(0.367)
All Free/Reduced Price School Lunch	-0.350	-0.164	-0.408	-0.112	-0.884**
	(0.287)	(0.325)	(0.331)	(0.343)	(0.403)
Household Substance Use Exposure	0.154	0.389***	0.218*	0.071	0.163
	(0.110)	(0.143)	(0.124)	(0.129)	(0.135)
Family Medicine Cabinet	1.214***	0.662*	1.065***	0.809**	0.923**
	(0.294)	(0.354)	(0.351)	(0.362)	(0.387)
Strong Family Bonds	0.263	1.566***	1.037***	0.788**	0.069
	(0.281)	(0.352)	(0.334)	(0.362)	(0.395)
Anticipation of Parental Consequences	0.525***	0.388***	0.372***	0.363***	0.630***
	(0.086)	(0.106)	(0.103)	(0.113)	(0.115)
Past Help Seeking: Parent/Guardian	-0.354	-0.491	-0.418	0.359	0.894**
	(0.277)	(0.320)	(0.315)	(0.353)	(0.405)
Past Help Seeking Frequency: Other Relative = 0, omitted	-	-0.463	-0.684	-	-
		(0.959)	(1.254)		
Observations	506	454	456	437	423
Pseudo R-squared	0.210	0.244	0.230	0.180	0.251
AUC	0.812	0.842	0.813	0.794	0.833

Standard errors in parentheses
*** $p < 0.01$, ** $p < 0.05$, * $p < 0.1$

Table 4. Columns include log-odds coefficients with standard errors in parenthesis for each LASSO selected predictor at the given time point. Positive coefficients indicate an increased likelihood of reporting high perceived risk of harm, whereas negative coefficients indicate a decreased likelihood at the following times: baseline (bsl), end of gameplay (eog), and 3-month, 6-month, and 12-month follow-up assessments. AUC values across the bottom indicate strong model performance across all times. Stars indicate p-values showing statistical significance.

appears that very few participants who were initially in the low perceived risk of harm category (0) moved into the high perceived risk of harm category (1). This can be shown for positive predictors significant at the 0.01 level as shown in the low percentage in the top left quadrants of Figures. 6 and 7.

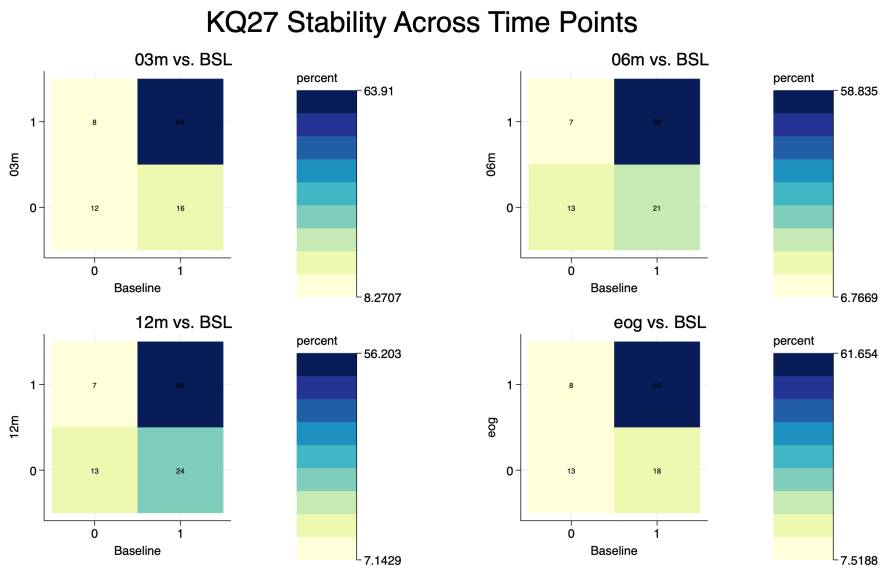

Figure 6. Family Medicine Cabinet (KQ27) Stability Across Time Points. Heatmaps display longitudinal transitions in perceived risk-of-harm classification for the family medicine cabinet (KQ27) variable from baseline to end of gameplay (eog), 3-month, 6-month, and 12-month follow-up assessments. Cells represent the proportion of participants transitioning between low-risk (0) and high-risk (1) classifications over time, with the bottom-left quadrant indicating participants who remained low risk, the top-left indicating movement from low to high risk, the bottom-right indicating movement from high to low risk, and the top-right indicating sustained high-risk classification across assessments.

For subsequent time points, the LASSO reduced model showed several predictors to be statistically significant, including food insecurity, all free/reduced price lunch, household substance use exposure, family medicine cabinet, strong family bonds, anticipation of parental consequences, and past help seeking: parent/guardian (Table 4). This is further visualized in Figure 8. AUC values above 0.79 at all time points also validates efficacy of the logistic regression model (Table 4).

This same process was then repeated for the control and intervention groups independently (first iteration with just control group data, second iteration with just intervention group data). Outputs for the control group can be seen in Table 5, and outputs for the intervention group can be seen in Table 6.

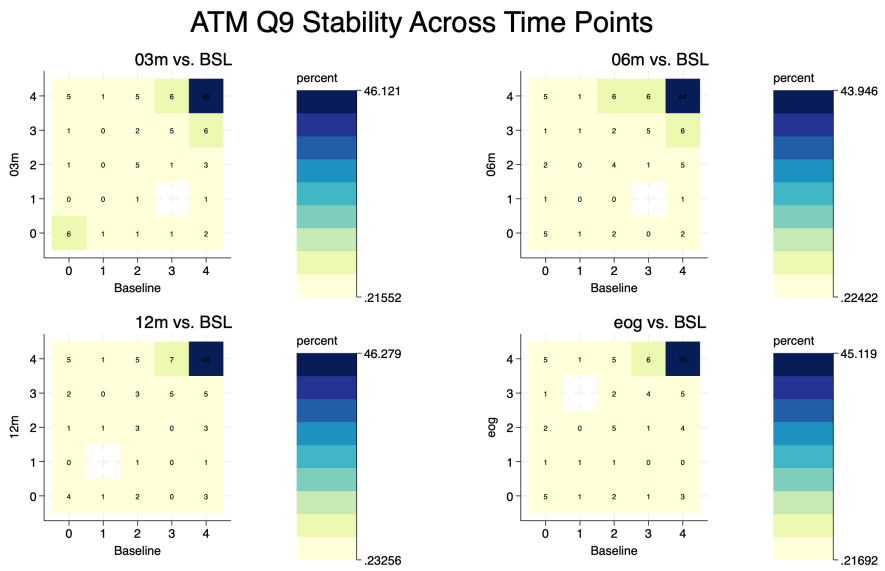

Figure 7. Anticipation of Parental Consequences (ATM Q9) Stability Across Time Points. Heatmaps illustrate longitudinal response stability and transition patterns for anticipation of parental consequences (ATM Q9) from baseline to eog, 3-month, 6-month, and 12-month follow-up assessments. Each cell represents the proportion of participants transitioning between baseline and follow-up response categories, allowing visualization of response persistence, upward and downward category shifts, and overall temporal stability across the five-level outcome scale.

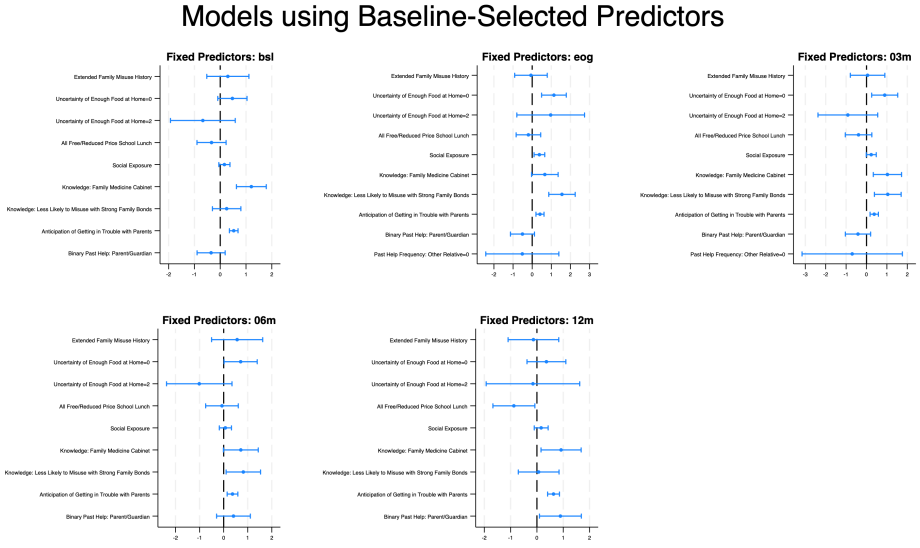

Figure 8. LASSO Logistic Regression Model Coefficients at All Time Points. Log-odds coefficients shown by x values of points and 95% confidence intervals shown by extending bars for each of the predictors selected by LASSO regularization in logistic regression at baseline with threshold of 18. Panels show output for each time point, calculated independently.

LASSO Logistic Regression Output Table Over Time for Control Group

VARIABLES	(1) bsl	(2) eog	(3) 03m	(4) 06m	(5) 12m
Extended Family Misuse History	0.264	-1.076*	-0.398	0.128	-0.751
	(0.592)	(0.554)	(0.559)	(0.652)	(0.591)
Food Insecurity	-0.061	-0.529	-0.648	-0.605	-0.245
	(0.442)	(0.453)	(0.468)	(0.480)	(0.526)
All Free/Reduced Price School Lunch	-1.271**	-0.126	-0.618	-0.247	-1.380**
	(0.524)	(0.465)	(0.503)	(0.498)	(0.662)
Household Substance Use Exposure	0.163	0.588**	0.275	0.687**	0.155
	(0.188)	(0.238)	(0.202)	(0.322)	(0.174)
Family Medicine Cabinet	1.453***	0.489	1.116**	0.903*	0.197
	(0.451)	(0.512)	(0.524)	(0.505)	(0.583)
Strong Family Bonds	0.181	1.534***	1.082**	0.895*	0.822
	(0.434)	(0.520)	(0.503)	(0.524)	(0.561)
Anticipation of Parental Consequences	0.590***	0.491***	0.459***	0.270*	0.622***
	(0.137)	(0.148)	(0.152)	(0.159)	(0.174)
Past Help Seeking: Parent/Guardian	-0.651	-0.903**	-1.073**	-0.275	0.501
	(0.460)	(0.457)	(0.485)	(0.486)	(0.543)
Past Help Seeking Frequency: Other Relative = 0, omitted	-	-	-	-	-
Constant	0.199	0.026	0.380	0.313	0.822
	(0.657)	(0.547)	(0.597)	(0.585)	(0.679)
Observations	246	223	226	216	216
Pseudo R2	0.254	0.262	0.283	0.212	0.240
AUC	0.823	0.847	0.841	0.811	0.830

Standard errors in parentheses

*** $p < 0.01$, ** $p < 0.05$, * $p < 0.1$

Table 5. Table 5 presents the results of LASSO logistic regression models predicting high perceived risk of harm across five assessment periods in the control group: baseline (bsl), end of gameplay (eog), 3-month follow-up (03m), 6-month follow-up (06m), and 12-month follow-up (12m). Coefficients are reported as log-odds estimates with standard errors in parentheses. Positive coefficients indicate an increased likelihood of reporting high perceived risk of harm, whereas negative coefficients indicate a decreased likelihood. AUC values across the bottom indicate strong model performance across all times. Stars indicate p-values showing statistical significance.

LASSO Logistic Regression Output Table Over Time for Intervention Group

VARIABLES	(1) bsl	(2) eog	(3) 03m	(4) 06m	(5) 12m
Extended Family Misuse History	0.278	1.772	0.751	1.074	0.753
	(0.604)	(1.119)	(0.808)	(1.093)	(1.113)
Food Insecurity	-0.817**	-1.557***	-1.213***	-0.924*	-0.388
	(0.374)	(0.521)	(0.456)	(0.543)	(0.594)
All Free/Reduced Price School Lunch	0.095	-0.362	-0.276	-0.251	-0.370
	(0.364)	(0.517)	(0.465)	(0.520)	(0.576)
Household Substance Use Exposure	0.163	0.365*	0.179	-0.195	0.194
	(0.139)	(0.189)	(0.163)	(0.157)	(0.244)
Family Medicine Cabinet	0.977**	0.758	1.229**	0.506	1.639***
	(0.403)	(0.534)	(0.505)	(0.571)	(0.574)
Strong Family Bonds	0.287	1.763***	0.896*	0.961*	-0.502
	(0.376)	(0.530)	(0.459)	(0.549)	(0.602)
Anticipation of Parental Consequences	0.493***	0.365**	0.275*	0.562***	0.691***
	(0.114)	(0.181)	(0.145)	(0.184)	(0.173)
Past Help Seeking: Parent/Guardian	-0.175	-0.113	0.199	0.966*	1.315**
	(0.366)	(0.504)	(0.450)	(0.587)	(0.670)
Past Help Seeking Frequency: Other Relative = 0, omitted	-	-2.358*	-0.834	-	-
		(1.424)	(1.401)		
Constant	-0.445	-0.040	-0.035	0.159	-0.715
	(0.470)	(0.641)	(0.618)	(0.638)	(0.717)
Observations	260	227	228	221	207
Pseudo R2	0.201	0.307	0.215	0.235	0.329
AUC	0.813	0.870	0.792	0.839	0.879

Standard errors in parentheses
*** $p < 0.01$, ** $p < 0.05$, * $p < 0.1$

Table 6. Table 6 presents the results of LASSO logistic regression models predicting high perceived risk of harm across five assessment periods in the intervention group: baseline (bsl), end of gameplay (eog), 3-month follow-up (03m), 6-month follow-up (06m), and 12-month follow-up (12m). Coefficients are reported as log-odds estimates with standard errors in parentheses. Positive coefficients indicate an increased likelihood of reporting high perceived risk of harm, whereas negative coefficients indicate a decreased likelihood. AUC values across the bottom indicate strong model performance across all times. Stars indicate p-values showing statistical significance.

Classification-Based Model Validation

To further validate the logistic regression model (LASSO selected predictors, threshold 18), follow-up data from the control group was used as a natural holdout set to test the logistic regression model trained on baseline data. Across follow-up assessments, participants classified in the high perceived risk group (1) generally exhibited higher predicted probabilities than participants classified in the low perceived risk group (0), indicating sustained predictive discrimination of the baseline model over time. Model discrimination remained acceptable across all holdout waves, with ROC AUC values of 0.795 at end of gameplay, 0.822 at 3 months, 0.700 at 6 months, and 0.765 at 12 months. Although modest attenuation in class separation was observed at the 6-month follow-up, visual inspection of predicted probability distributions demonstrated persistent differentiation between outcome groups across all assessments, supporting the longitudinal robustness of the baseline-selected predictors within the control population (Fig. 9).

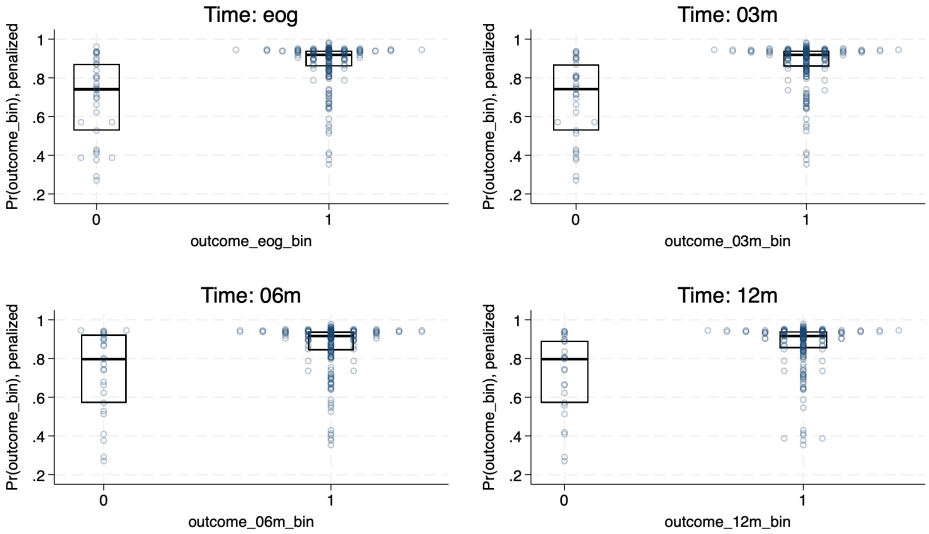

Figure 9. Longitudinal Holdout Validation of Baseline LASSO Logistic Regression Predictions in the Control Group. Boxplots display the distribution of predicted probabilities generated by the baseline-trained LASSO logistic regression model when applied to control group participants at end of gameplay (eog), 3-month, 6-month, and 12-month follow-up assessments. Participants are grouped according to observed binary outcome classification at each timepoint (0 = low perceived risk of harm; 1 = high perceived risk of harm). Individual points represent participant-level predicted probabilities, while boxplots summarize the median, interquartile range, and overall spread of predicted values within each observed outcome category.

The same process was then repeated with the intervention group. Across all follow-up assessments, participants observed in the high perceived risk group (1) consistently demonstrated

elevated predicted probabilities and tighter clustering near the upper end of the probability scale, indicating stable discrimination and predictive separation of the baseline model over time. In contrast, participants classified in the low perceived risk group (0) showed comparatively lower and more variable predicted probabilities across waves. Model discrimination remained acceptable across all holdout assessments, with ROC AUC values of 0.787 at end of gameplay, 0.726 at 3 months, 0.726 at 6 months, and 0.772 at 12 months. Visual inspection of the predicted probability distributions further suggested persistent separation between outcome classes over time (Fig. 10).

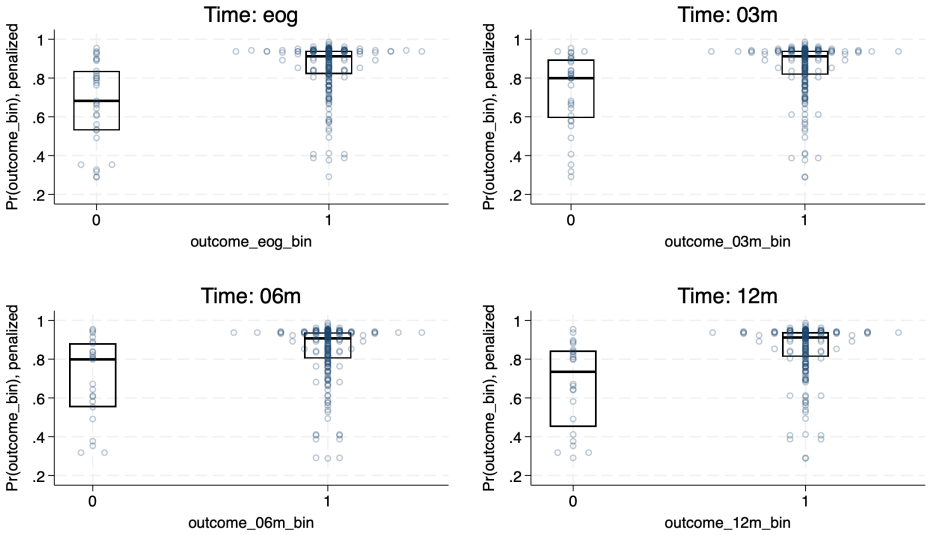

Figure 10. Longitudinal Holdout Validation of Baseline LASSO Logistic Regression Predictions in the Intervention Group. Boxplots display the distribution of predicted probabilities generated by the baseline-trained LASSO logistic regression model when applied to intervention group participants at end of gameplay (eog), 3-month, 6-month, and 12-month follow-up assessments. Participants are grouped according to observed binary outcome classification at each timepoint (0 = low perceived risk of harm; 1 = high perceived risk of harm). Individual points represent participant-level predicted probabilities, while boxplots summarize the median, interquartile range, and overall spread of predicted values within each observed outcome category.

Longitudinal Three-Way Interaction Logistic Regression Model

With this confidence, we then incorporated interaction terms (Intervention $\times$ Predictor $\times$ Time) to this LASSO logistic model to understand the relationships between predictors and the effects of the intervention over time. Maintaining 18 as the optimal threshold and treating time as a continuous linear variable, the results shown in Table 7 were obtained.

LASSO Logistic Regression 3-Way Interaction with Continuous Time Output

VARIABLES	(1) Coefficient	(2) 95% CI
Intervention × Extended Family Misuse History × Time	1.873	(0.810 – 4.330)
Intervention × Food Insecurity × Time	1.849**	(1.059 – 3.229)
Intervention × Free/Reduced Price School Lunch × Time	0.713	(0.400 – 1.270)
Intervention × Household Substance Use Exposure × Time	2.075*	(0.974 – 4.420)
Intervention × Family Medicine Cabinet × Time	1.170	(0.665 – 2.056)
Intervention × Strong Family Bonds × Time	0.635	(0.365 – 1.106)
Intervention × Anticipation of Parental Consequences × Time	1.043	(0.606 – 1.797)
Intervention × Past Help Seeking: Parent/Guardian × Time	0.924	(0.529 – 1.613)
Intervention × Past Help Seeking Frequency: Other Relative × Time	1.522	(0.399 – 5.812)
Observations	2,340	
Number of groups	532	

ciEform in parentheses
*** $p < 0.01$, ** $p < 0.05$, * $p < 0.1$

Table 7. Table 7 presents the results of the LASSO logistic regression model examining three-way interaction effects between intervention status, predictor variables, and continuous time variable on the likelihood of reporting high perceived risk of harm. Coefficients are presented as odds ratios with 95% confidence intervals in parentheses. Odds ratios greater than 1 indicate an increased likelihood of high perceived risk of harm over time among participants in the intervention group relative to the control group at baseline, whereas odds ratios less than 1 indicate a decreased likelihood. Stars indicate p-values showing statistical significance.

Food insecurity emerged as a statistically significant positive predictor over time in this continuous interaction model. For the intervention group, the odds of perceiving a high risk of harm (score > 18) increased by a factor of 1.849 (p-value < 0.05) for every unit increase in time for those who were food insecure compared to those who were food secure at baseline. Household substance use exposure was also positively associated with higher perceived risk of harm over time at the trend level. For the intervention group, the odds of perceiving a high risk of harm (score > 18) increased by a factor of 2.075 (p-value < 0.1) for every unit increase in time and exposure relative to the control group at baseline.

To confirm the appropriateness of modeling time as a continuous linear variable, orthogonal polynomial contrast tests and graphical visualizations were conducted for the significant three-way interactions between time, treatment assignment, and the moderators food insecurity and household substance use exposure. Treating time categorically allowed for hypothesis testing of whether the assumed ordering and spacing of time points in the linear model could be statistically rejected. For food insecurity, orthogonal contrast tests identified a statistically significant linear trend across follow-up assessments ($\chi^2(1) = 5.11,\ p = 0.0238$). In contrast, higher-order polynomial trends, including quadratic ($\chi^2(1) = 0.39,\ p = 0.5334$), cubic ($\chi^2(1) = 0.76,\ p = 0.3822$), and quartic effects ($\chi^2(1) = 0.76,\ p = 0.3827$), were not statistically significant. Although the overall joint test across all polynomial terms was not significant ($\chi^2(4) = 6.58,\ p = 0.1598$), the presence of a significant linear component in the absence of higher-order effects indicates that the observed pattern over time is adequately characterized by a straight-line trajectory. Importantly, these results suggest that the categorical specification of time does not provide sufficient evidence to reject the linear ordering and valuation of time used in the primary model.

The sample size for household substance use exposure was insufficient to conduct equivalent orthogonal contrast testing; however, graphical visualizations demonstrated a consistent upward linear trend when plotting both log-odds and odds-ratio coefficients over time (log-odds shown in Figs. 11 and 12 for interpretability). Together, the statistical tests and graphical evidence support retaining the continuous linear specification of time in the primary three-way interaction models.

This categorical interaction model also shows associations between moderators and the intervention broken out by time, seen in Table 8.

In this case, extended family misuse history, food insecurity, and attending a school where all students receive free or reduced-price lunch emerge as statistically significant factors at specific follow-up times, all at the $p < 0.05$ level. For those in the intervention group with extended family misuse history, the odds of perceiving a high risk of harm (score > 18) increased by a factor of 48.852 at the 12-month follow-up for those with family history relative to those who do not at baseline. For those in the intervention group who were food insecure, the odds of perceiving a high risk of harm (score > 18) increased by a factor of 24.043 at

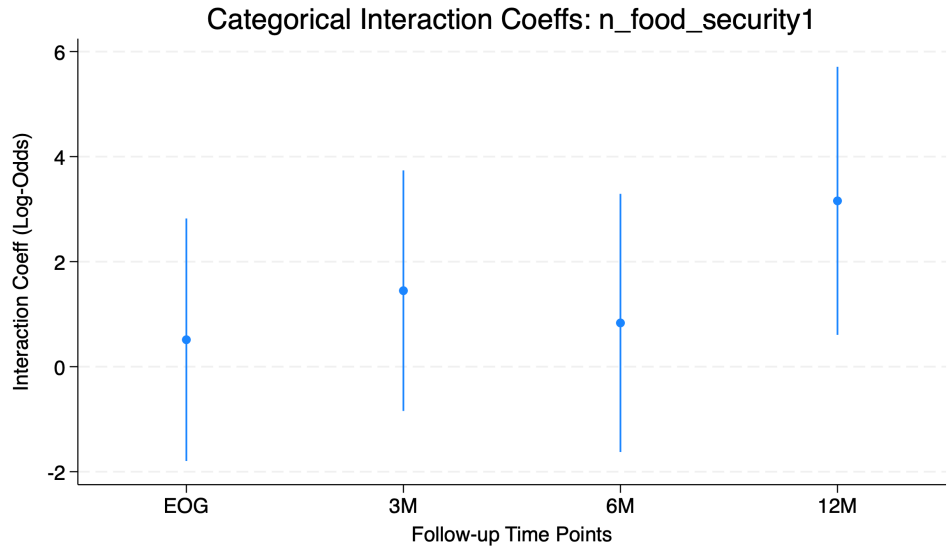

Figure 11. Categorical Interaction Coefficients for Food Insecurity. Figure 11 displays the estimated three-way interaction coefficients between treatment assignment, food insecurity, and categorical follow-up time points on the log-odds scale. Points represent coefficient estimates, and error bars represent 95% confidence intervals for each assessment period relative to baseline.

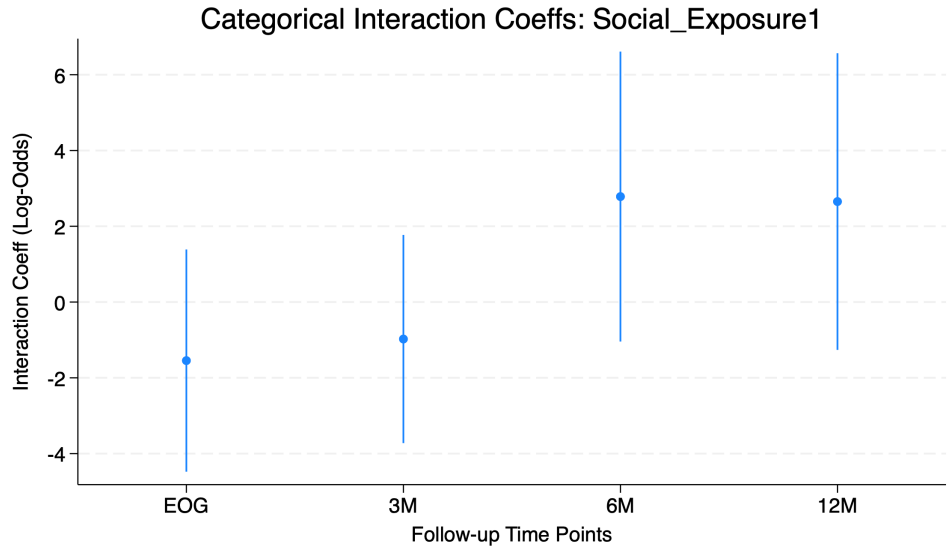

Figure 12. Categorical Interaction Coefficients for Household Substance Exposure. Figure 12 displays the estimated three-way interaction coefficients between treatment assignment, household substance use exposure, and categorical follow-up time points on the log-odds scale. Points represent coefficient estimates, and error bars represent 95% confidence intervals for each assessment period relative to baseline.

LASSO Logistic Regression 3-Way Interaction with Categorical Time Output

VARIABLES	(1) EOG	(2) 03M	(3) 06M	(4) 12M
Intervention × Extended Family Misuse History × Time	21.345	10.879	2.883	48.852**
	(0.526 – 866.889)	(0.391 – 302.992)	(0.061 – 137.100)	(1.096 – 2,177.622)
Intervention × Food Insecurity × Time	2.296	3.747	1.641	24.043**
	(0.206 – 25.572)	(0.340 – 41.343)	(0.123 – 21.949)	(1.692 – 341.653)
Intervention × Free/Reduced Price Lunch × Time	0.074**	0.209	0.065**	0.278
	(0.006 – 0.856)	(0.019 – 2.312)	(0.005 – 0.862)	(0.018 – 4.311)
Intervention × Household Substance Use Exposure × Time	0.213	0.377	16.183	14.185
	(0.011 – 4.006)	(0.024 – 5.881)	(0.353 – 742.569)	(0.283 – 711.403)
Intervention × Family Medicine Cabinet × Time	2.706	0.472	1.431	3.158
	(0.252 – 29.052)	(0.044 – 5.085)	(0.110 – 18.589)	(0.254 – 39.195)
Intervention × Strong Family Bonds × Time	0.683	0.183	0.203	0.193
	(0.069 – 6.814)	(0.018 – 1.821)	(0.017 – 2.378)	(0.017 – 2.245)
Intervention × Anticipation of Parental Consequences × Time	0.800	0.576	2.217	0.915
	(0.083 – 7.761)	(0.060 – 5.515)	(0.193 – 25.465)	(0.079 – 10.559)
Intervention × Past Help Seeking: Parent/Guardian × Time	3.143	1.874	3.062	0.594
	(0.299 – 33.071)	(0.184 – 19.055)	(0.232 – 40.405)	(0.050 – 7.067)
Intervention × Past Help Seeking Frequency: Other Relative × Time	0.042	1.074	5.713	0.964
	(0.000 – 36.435)	(0.002 – 632.138)	(0.013 – 2,601.231)	(0.002 – 588.381)
Observations	2,340		2,340	
Number of groups	532		532	

ciEform in parentheses
Reference: Control. Rows show 3-way interactions.
*** $p < 0.01$, ** $p < 0.05$, * $p < 0.1$

Table 8. Table 8 presents the results of the LASSO logistic regression model examining three-way interaction effects between intervention status, predictor variables, and categorical time variable on the likelihood of reporting high perceived risk of harm. Coefficients are presented as odds ratios with 95% confidence intervals in parentheses. Odds ratios greater than 1 indicate an increased likelihood of high perceived risk of harm over time among participants in the intervention group relative to the control group at baseline, whereas odds ratios less than 1 indicate a decreased likelihood. Stars indicate p-values showing statistical significance.

the 12-month follow-up relative to those who were food secure at baseline. Finally, for the intervention group who attended a school where all students received free or reduced-price lunch, the odds of perceiving a high risk of harm (score > 18) decreased by a factor of 0.074 at end of gameplay and 0.065 at the 6-month follow-up relative to those who did not attend a school with all free or reduced-price lunches at baseline.

Contingency Tables for Overall Validation

As a final validation step to evaluate overall intervention efficacy and confirm that meaningful longitudinal changes in outcomes were present, contingency tables were generated to examine changes in perceived risk of harm classifications over time. As shown in Table 9, across all follow-up periods, the majority of participants in the control group who were classified in the high perceived risk group at baseline remained in the high group at subsequent assessments, with stability rates ranging from approximately 92.50% to 94.68%. Participants initially classified in the low perceived risk group demonstrated greater variability in transitions over time, with the proportion transitioning into the high perceived risk category increasing from 39.39% at end of gameplay to approximately 52% by the 6- and 12-month follow-up assessments, despite a dip to 33.33% at the 3-month follow-up. Pearson chi-square tests were statistically significant across all transition periods (all $p < 0.001$), indicating a significant association between baseline and follow-up classifications over time.

Similarly, Table 10 presents contingency tables for participants in the intervention group comparing baseline classifications with end of gameplay, 3-month, 6-month, and 12-month follow-up outcomes. Participants classified in the high perceived risk group at baseline also demonstrated strong longitudinal stability, with approximately 94.21% to 96.00% remaining in the high group across follow-up assessments. Among participants initially classified in the low perceived risk group, transitions into the high perceived risk category increased over time, ranging from 45.24% at end of gameplay to 60.98% at the 6-month follow-up before slightly decreasing to 56.41% at 12 months. Pearson chi-square tests were statistically significant at each transition period (all $p < 0.001$), further supporting a significant relationship between baseline and follow-up classifications over time. Together, these findings indicate that while perceived risk classifications were generally stable across both groups, participants initially classified in the low perceived risk category demonstrated meaningful upward transitions in perceived risk over the course of the study while those initially in the high perceived risk category were stable.

Contingency Tables for Baseline-to-Follow-Up Outcome Transitions (Control Group)

Baseline		**Follow-Up Outcome**		**Total**
		0	**1**	
Panel A: Baseline vs. EOG		$(\chi^2(1) = 62.58,\ p < 0.001)$		
0	*n* (%)	20 (60.61%)	13 (39.39%)	33 (100.00%)
1	*n* (%)	15 (7.50%)	185 (92.50%)	200 (100.00%)
Total	*n* (%)	35 (15.02%)	198 (84.98%)	233 (100.00%)
Panel B: Baseline vs. 3-Month		$(\chi^2(1) = 84.09,\ p < 0.001)$		
0	*n* (%)	22 (66.67%)	11 (33.33%)	33 (100.00%)
1	*n* (%)	12 (5.97%)	189 (94.03%)	201 (100.00%)
Total	*n* (%)	34 (14.53%)	200 (85.47%)	234 (100.00%)
Panel C: Baseline vs. 6-Month		$(\chi^2(1) = 44.53,\ p < 0.001)$		
0	*n* (%)	15 (48.39%)	16 (51.61%)	31 (100.00%)
1	*n* (%)	12 (6.25%)	180 (93.75%)	192 (100.00%)
Total	*n* (%)	27 (12.11%)	196 (87.89%)	223 (100.00%)
Panel D: Baseline vs. 12-Month		$(\chi^2(1) = 48.81,\ p < 0.001)$		
0	*n* (%)	15 (48.39%)	16 (51.61%)	31 (100.00%)
1	*n* (%)	10 (5.32%)	178 (94.68%)	188 (100.00%)
Total	*n* (%)	25 (11.42%)	194 (88.58%)	219 (100.00%)

Table 9. Table 9 presents contingency tables comparing baseline outcome classifications with classifications at end of gameplay (eog), 3-month, 6-month, and 12-month follow-up assessments for participants in the control group. Frequencies and row percentages are displayed to illustrate patterns of stability and transition in perceived risk of harm classifications over time. Pearson chi-square tests were statistically significant at each transition period ($p < 0.001$), indicating that baseline and follow-up outcome classifications were significantly associated over time.

Contingency Tables for Baseline-to-Follow-Up Outcome Transitions (Intervention Group)

Baseline		**Follow-Up Outcome**		**Total**
		0	**1**	
Panel A: Baseline vs. EOG		$(\chi^2(1) = 71.58,\ p < 0.001)$		
0	*n* (%)	23 (54.76%)	19 (45.24%)	42 (100.00%)
1	*n* (%)	9 (4.79%)	179 (95.21%)	188 (100.00%)
Total	*n* (%)	32 (13.91%)	198 (86.09%)	230 (100.00%)
Panel B: Baseline vs. 3-Month		$(\chi^2(1) = 63.11,\ p < 0.001)$		
0	*n* (%)	22 (53.66%)	19 (46.34%)	41 (100.00%)
1	*n* (%)	11 (5.79%)	179 (94.21%)	190 (100.00%)
Total	*n* (%)	33 (14.29%)	198 (85.71%)	231 (100.00%)
Panel C: Baseline vs. 6-Month		$(\chi^2(1) = 42.05,\ p < 0.001)$		
0	*n* (%)	16 (39.02%)	25 (60.98%)	41 (100.00%)
1	*n* (%)	8 (4.37%)	175 (95.63%)	183 (100.00%)
Total	*n* (%)	24 (10.71%)	200 (89.29%)	224 (100.00%)
Panel D: Baseline vs. 12-Month		$(\chi^2(1) = 50.20,\ p < 0.001)$		
0	*n* (%)	17 (43.59%)	22 (56.41%)	39 (100.00%)
1	*n* (%)	7 (4.00%)	168 (96.00%)	175 (100.00%)
Total	*n* (%)	24 (11.21%)	190 (88.79%)	214 (100.00%)

Table 10. Table 10 presents contingency tables comparing baseline outcome classifications with classifications at end of gameplay (eog), 3-month, 6-month, and 12-month follow-up assessments for participants in the intervention group. Frequencies and row percentages are displayed to illustrate patterns of stability and transition in perceived risk of harm classifications over time. Pearson chi-square tests were statistically significant at each transition period ($p < 0.001$), indicating that baseline and follow-up outcome classifications were significantly associated over time.

Discussion

This study examined whether family factors moderate the impact of *PlaySmart* on adolescents' perceived risk of harm from opioid misuse, and whether these factors are associated with differential changes in perceived risk over time. A secondary aim was to identify which family-based predictors were most strongly associated with perceived risk of harm at baseline, in order to establish a foundation for understanding potential moderation of intervention effects. Throughout the analyses, the central question remained whether adolescents' family environments are associated with differential responsiveness to *PlaySmart*, rather than simply whether family factors predict perceived risk at a single point in time.

The culminating model indicated that food insecurity is a statistically significant moderator and that among those in the intervention group, those who were food insecure at baseline were more likely to report a high perceived risk of harm over time compared to those who were food secure at baseline. Household substance use exposure also showed a positive association at the trend level and among participants in the intervention group, an increase in household substance use exposure was associated with greater odds of reporting a high perceived risk of harm over time.

Initial OLS models on baseline data demonstrated limited explanatory power and clear violations of modeling assumptions, shown by residual diagnostics and outcome distributions. These findings motivated a transition to logistic regression frameworks, which better aligned with the observed structure of the data. The logistic framework estimates the probability that an adolescent falls into a higher risk awareness category, and coefficients are thus interpreted in terms of log-odds, where positive values indicate increased likelihood of higher perceived risk, as well as in terms of odds ratios, where values greater than one indicate increased likelihood of higher perceived risk and values less than one indicate decreased likelihood. LASSO regularization then plays a critical role in improving model robustness, favoring a more parsimonious model with fewer predictors, reducing overfitting and improving generalizability.

Interpretation of Threshold Findings

The threshold analyses were a necessary methodological step toward addressing the central research question. Because the primary outcome, perceived risk of harm, did not follow a normal distribution and exhibited substantial clustering at lower values, selecting an appropriate classification threshold was essential for building a logistic regression framework capable of detecting moderation effects. Through analysis of various thresholds for dichotomization and logistic regression, it became clear that the outcome variable exhibits a clear distinction between very low risk perception and all other levels, rather than a continuum with clearly separable intermediate categories.

Threshold analyses consistently showed that model performance was strongest when distinguishing the lowest end of the distribution from the rest of the sample. Attempts to further subdivide the distribution into low, medium, and high categories resulted in reduced model performance, reflected in declining AUC values and diminished separability. Distributional analyses further indicated that individuals in the middle of the perceived risk scale clustered more closely with those at the high end than those at the low end.

This pattern helps explain the observed decline in classification performance as lower-bound thresholds shift upward. The model is increasingly tasked with distinguishing between moderately and highly risk-aware individuals who are not meaningfully distinct. These findings support a two-step conceptual framework in which the primary distinction lies between very low perceived risk and all other levels, with any further subdivision within the non-low group offering limited statistical utility. With limited responses falling below the perceived risk of harm score of 18, and given the lack of differentiability between observations scoring between 19 and 32, a threshold of 18 was selected as the optimal classification point. This operationalizes the outcome as whether adolescents fall into the lowest perceived-risk group relative to all others, which is directly aligned with the study's goal of assessing whether family context is associated with *PlaySmart*'s ability to shift adolescents away from particularly low perceptions of opioid-related harm.

Interpretation of Key Predictors

Across modeling approaches, two predictors emerged as consistently informative at baseline: belief that it is safe to use opioids from a family medicine cabinet and anticipation of parental consequences for opioid use. The finding that perceived acceptability of accessing medications from a family medicine cabinet is positively associated with perceived risk of harm initially appears counterintuitive. This is considered a risk factor for which one would expect to see a negative association. However, this relationship may reflect a more complex interpretation of household environments, in which medications are more accessible. Exposure to prescription medications in the home may increase familiarity and break down a layer of fear often associated with medication. In contrast, anticipated parental consequences showed a more straightforward, positive relationship with perceived risk, aligning with the framework of a protective factor. Consistent with prior literature and norms, adolescents who expect negative parental responses to substance use may internalize stronger perceptions of harm.

Across modeling approaches, two predictors emerged as consistently associated with perceived risk of harm at baseline: belief that it is safe to use opioids from a family medicine cabinet and anticipation of parental consequences for opioid use. The consistency of these two predictors across both OLS and LASSO logistic models strengthens confidence that they represent meaningful family-context correlates of perceived risk, even as it is important to note

that these are observational associations and do not establish that these factors causally shape perceptions.

The finding that perceived acceptability of accessing medications from a family medicine cabinet was positively associated with higher perceived risk of harm, rather than lower, initially appears counterintuitive. This is considered a risk factor for which one would expect to see a negative association. However, this relationship may reflect a more complex interpretation of household environments, in which medications are more accessible. Exposure to prescription medications in the home may increase familiarity and break down a layer of fear often associated with medication. In contrast, anticipated parental consequences showed a more straightforward positive relationship with perceived risk, consistent with expectations and with prior literature. Adolescents who expect negative parental responses to substance use may be more likely to view opioid misuse as harmful, reflecting internalized family norms around substance use. This association is consistent with a protective factor framework in which strong parental monitoring and clear consequences are associated with more cautious adolescent risk perceptions. Both of these findings are relevant to the study's central question as they identify specific family factors that are associated with where adolescents begin on the perceived risk scale, which in turn shapes the potential for upward movement in risk perception following intervention exposure.

Interpretation of Predictors at Other Time Points

Beyond baseline, the LASSO logistic models showed that several family variables remained associated with perceived risk of harm across follow-up assessments, although the specific predictors varied by time point. Food insecurity, school-level free or reduced-price lunch status, household substance use exposure, family medicine cabinet beliefs, beliefs in the impacts of strong family bonds, anticipated parental consequences, and prior parent or guardian help-seeking each emerged as significant at one or more time points. This variation across time points suggests that family context does not operate as a static moderator but may have time-varying associations with perceived risk. Some factors may be more relevant at certain stages of the intervention or follow-up period, and understanding these patterns can inform when and how family-focused prevention is most useful.

However, given that models here were estimated independently at each time point rather than within a single longitudinal model with time-varying coefficients, observed changes in predictor significance may reflect sampling variability, shifts in the sample due to attrition, unpredictable and variable human behaviors, or genuine changes in the associations between family context and perceived risk over time. These analyses are therefore best understood as exploratory and hypothesis-generating with respect to the study's central question of whether family context moderates *PlaySmart*'s impact over time, with the three-way interaction models providing the most direct test of that question.

Model Testing Using Control and Intervention Holdout Sets

The holdout validation analyses provided further support for the stability and longitudinal relevance of the baseline-selected LASSO predictors, as well as the selected threshold for logistic classification. When the baseline-trained model was applied to follow-up data in both the control and intervention groups, participants observed in the high perceived risk category generally had higher predicted probabilities than those in the low perceived risk category. AUC values in both the control and intervention groups remained in the acceptable range across follow-up waves, though some attenuation was observed at certain time points. This may be due in part to the smaller sample size when using either the control or intervention group rather than the entire data set. These results indicate that the family factors selected at baseline continued to discriminate between perceived risk categories over time, supporting their use in subsequent interaction models designed to test the influence of family factors on *PlaySmart* effects over time.

These holdout analyses should not be interpreted as evidence that *PlaySmart* caused changes in perceived risk. Rather, they demonstrate that the baseline-selected family predictors and generalized linear model retained predictive relevance across time within both the control and intervention groups, which is an important prerequisite for the interaction analyses. If the predictors had lost discriminative validity over time, any apparent moderation effects in the interaction models would be more difficult to interpret. The finding that discrimination remained acceptable across follow-up waves provides support for treating these family-context variables as meaningful moderators in the longitudinal interaction framework.

Interpretation of Three-Way Interaction Model

The three-way interaction models then provide the most direct test of the study's central research question: whether family related factors are associated with differential changes in perceived risk of harm over time among adolescents in the *PlaySmart* intervention group relative to the control group. It is important to emphasize that these analyses are observational and cannot establish that *PlaySmart* caused improvements in perceived risk, or that family factors causally determined intervention response. Rather, the interaction models identify associations between family characteristics, intervention assignment, and perceived risk trajectories, which can inform hypotheses about moderation mechanisms and guide future experimental research.

In the continuous-time model, food insecurity emerged as a significant moderator. Among participants in the intervention group, those who were food insecure at baseline were about two times more likely to report a high perceived risk of harm over time compared to participants who were food secure at baseline (OR $= 1.849$, $p < 0.05$). This association suggests that household economic adversity may be associated with differential responsiveness to *PlaySmart* over time.

Household substance use exposure also showed a positive association at the trend level in the continuous-time model. Among participants in the intervention group, an increase in household substance use exposure was associated with about two times greater odds of reporting a high perceived risk of harm over time compared to participants with lower household substance use exposure (OR $= 2.075$, $p < 0.1$). Although this effect did not meet conventional statistical significance, the direction of the association is consistent with the hypothesis that adolescents with direct household exposure to substance use may be more likely to perceive opioid-related harms over time following intervention exposure, potentially because prevention content connects with their lived experience or because prior to engaging with the intervention, substance use was normalized in their home environments, lowering their overall base perception of harm.

The categorical-time interaction model added specificity to the continuous model, showing that moderation effects varied across follow-up assessments. Food insecurity and extended family misuse history were associated with substantially higher odds of high perceived risk at the 12-month follow-up among intervention participants. These patterns are consistent with the possibility that for adolescents with greater family adversity, changes in perceived risk associated with *PlaySmart* exposure may accumulate over time rather than emerging immediately. However, the very large odds ratios observed at the 12-month follow-up for these variables should be interpreted with caution. The large point estimates in these interaction models with small subgroup sizes are not uncommon, and they may reflect instability due to sparse data rather than true effect magnitudes. These findings are therefore best understood as suggestive of potential delayed moderation effects or "sleeper effects", however they warrant confirmation with larger samples.

The categorical-time model also showed that attending a school where all students received free or reduced-price lunch was associated with slightly lower odds of high perceived risk at end of gameplay and at the 6-month follow-up among intervention participants. This finding appears to contrast with the positive association observed for individual-level food insecurity and warrants careful interpretation. Individual food insecurity captures direct household experience of economic hardship, whereas school-level free or reduced-price lunch status reflects a broader structural context of community-level disadvantage that is not necessarily tied to a specific adolescent's family experience. These two variables may therefore capture distinct dimensions of economic context with different implications for how adolescents engage with and respond to *PlaySmart* prevention messaging. The divergence between individual and structural indicators of socioeconomic context underscores the importance of distinguishing between levels of measurement when examining family and community factors as potential moderators of intervention effects.

Contingency Table Validation

Finally, the contingency table analyses provide descriptive context for understanding the overall pattern of change in perceived risk classifications over time, and complement the regression-based moderation analyses by illustrating the magnitude and direction of transitions at the population level. These analyses are relevant to the analysis of the impact of family factors on intervention effects as they allow a direct examination of whether adolescents who began with very low perceived risk, the group most in need of upward shift, showed meaningful transitions over the course of the study, as well as if those who began with higher perceived risk maintained that positive attitude.

Across both the control and intervention groups, adolescents who began in the high perceived risk category were highly stable over time, with the large majority remaining in that category at each follow-up assessment. This stability is consistent with the regression findings and suggests that perceived risk classifications were not arbitrary but reflected relatively durable characteristics. In contrast, adolescents who began in the low perceived risk category showed greater movement over time, with a meaningful proportion transitioning into the high perceived risk category by later follow-up assessments.

Descriptive comparisons between groups are consistent with the possibility that *PlaySmart* was associated with upward transitions in perceived risk among adolescents who began with very low scores. For example, by the 6-month follow-up, approximately 61% of intervention participants who began in the low perceived risk group had transitioned to the high group, compared with approximately 52% of control participants. While these differences are suggestive, they should be interpreted cautiously. The contingency tables do not adjust for baseline differences between groups, do not account for attrition, and do not directly test group-by-time differences. They are therefore best understood as supportive descriptive evidence rather than confirmatory evidence of intervention efficacy. Additionally, because the low perceived risk group was substantially smaller than the high perceived risk group at baseline, percentage-based comparisons may be sensitive to small absolute changes in frequency, and the threshold used here distinguishes a very low perceived risk minority from all other respondents.

Together, the findings in the contingency tables reinforce the central conclusion that while perceived risk classifications were generally stable across both groups, adolescents who began with very low perceived risk showed meaningful upward transitions over the study period, and the size of those transitions appeared somewhat larger in the intervention group. This pattern is consistent with the hypothesis that *PlaySmart* may be differentially effective for certain subgroups, and that family context may be associated with differential adolescent responsiveness and which are most likely to shift away from very low opioid risk perceptions following exposure to the intervention.

Study Limitations

Several limitations must also be considered in interpreting these findings. Because all analyses are observational and based on naturalistic variation in family characteristics, no causal claims can be made about whether family context determines intervention response. The associations identified in the interaction models reflect correlational patterns that are consistent with moderation hypotheses but require further testing with larger sample sizes to confirm. Further, the *PlaySmart* study was not designed specifically to look at family, therefore the data was not collected with this hypothesis in mind.

The distributional properties of the outcome variable also introduced challenges for both linear and classification-based logistic modeling. Threshold selection in logistic regression introduces subjectivity, though this was mitigated through systematic evaluation of model performance across varying thresholds. The selected threshold of 18 operationalizes the outcome as very low versus all other perceived risk levels, which means that findings are most directly interpretable in terms of whether family context is associated with adolescents remaining in or moving away from the very lowest end of the risk perception distribution. Associations within the non-low group are not captured by this framework. Further, perceived risk of harm questions are not weighted, creating wide variation in the qualitative factors that underlie each score between 8 and 32 and making it difficult to distinguish nuances in the profiles of each participant.

In the case of the three-way interaction models, they involved relatively small subgroup sizes for some combinations of treatment assignment, moderator status, and time point. This may have contributed to large odds-ratio estimates and wide confidence intervals, particularly in the categorical-time models. Results for predictors with low prevalence or sparse cell counts, such as extended family misuse history at the 12-month follow-up, should be interpreted with particular caution. Additionally, although LASSO regularization reduces overfitting and improves parsimony, predictor selection is sample-dependent, and the variables identified in this dataset may not generalize to other adolescent populations or prevention contexts. External validation in independent samples would strengthen confidence in these findings.

Future Directions

Future research should build directly on the central question addressed in this study by testing whether family factors causally moderate *PlaySmart*'s impact in larger samples, allowing for increased confidence in interaction results. From an applied perspective, these findings suggest that pre-screening adolescents using family related risk and protective factors may help identify those most likely to benefit from digital prevention interventions such as *PlaySmart*. Adolescents experiencing food insecurity or household substance use exposure may represent a priority subgroup for targeted outreach. In addition, these findings may inform the expansion of

game development to include families in the intervention process. Future studies should also examine whether the positive association between family medicine cabinet beliefs and perceived risk of harm holds in larger samples and whether it reflects communication patterns, medication presence, or other household characteristics that could be addressed through complementary family-level programming.

Methodologically, future work may benefit from alternative outcome modeling strategies that preserve more information from the original perceived risk scale while accounting for its non-normal distribution. These approaches may help identify qualitatively distinct risk perception profiles among adolescents rather than relying on a single binary threshold, and could reveal moderation patterns that are not captured by the low versus non-low classification used in the current study.

Conclusion

In conclusion, this study provides evidence that family environments may be associated with differences in adolescents' responsiveness to the *PlaySmart* opioid prevention intervention over time. Using longitudinal data from 532 adolescents, LASSO-regularized logistic regression and mixed-effects interaction models identified several family-related factors associated with perceived risk of opioid-related harm, while also demonstrating that the strongest distinction in perceived risk occurred between adolescents with very low risk perception and all other participants.

In the continuous-time interaction models, food insecurity was associated with approximately two times greater odds of high perceived risk over time among intervention participants ($\text{OR} = 1.849$, $p < 0.05$), while higher household substance use exposure was associated with approximately two times greater odds of high perceived risk over time ($\text{OR} = 2.075$, $p < 0.1$). These findings suggest that adolescents experiencing greater household adversity or substance exposure may engage differently with prevention messaging, potentially resulting in greater upward shifts in perceived risk following intervention exposure.

Holdout validation and contingency table analyses further supported the longitudinal relevance and stability of the identified predictors. Although findings are observational and should be interpreted cautiously due to thresholding decisions and small subgroup sizes in some interaction analyses, the results highlight the importance of considering family context in digital opioid prevention research and suggest that targeted or family-informed prevention strategies may improve intervention effectiveness for adolescents at elevated risk.

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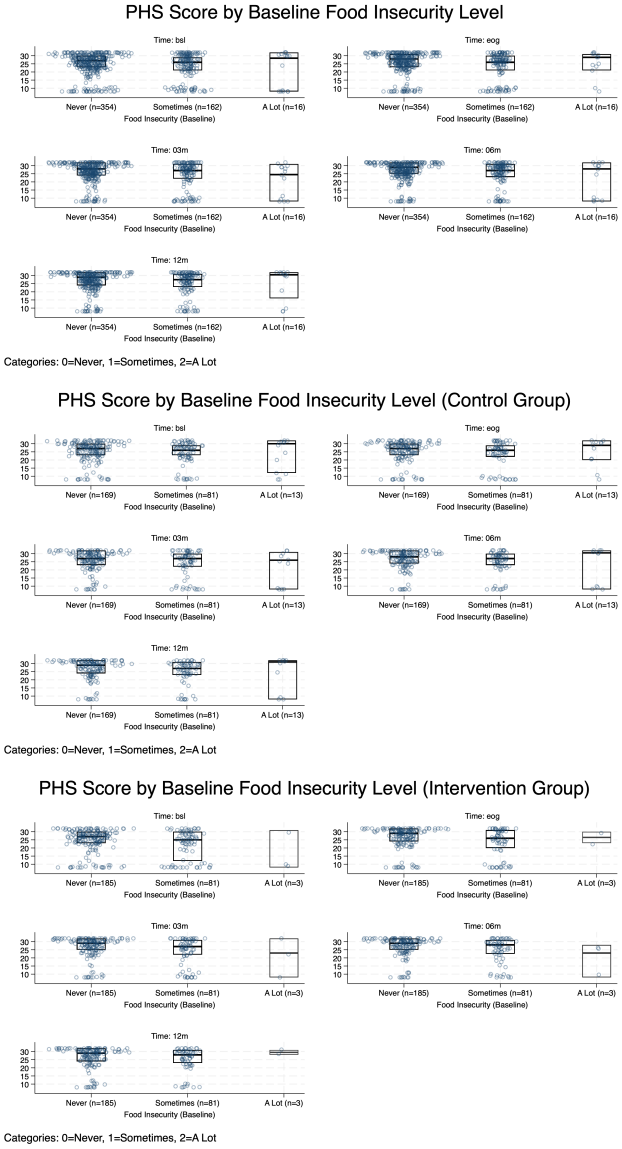
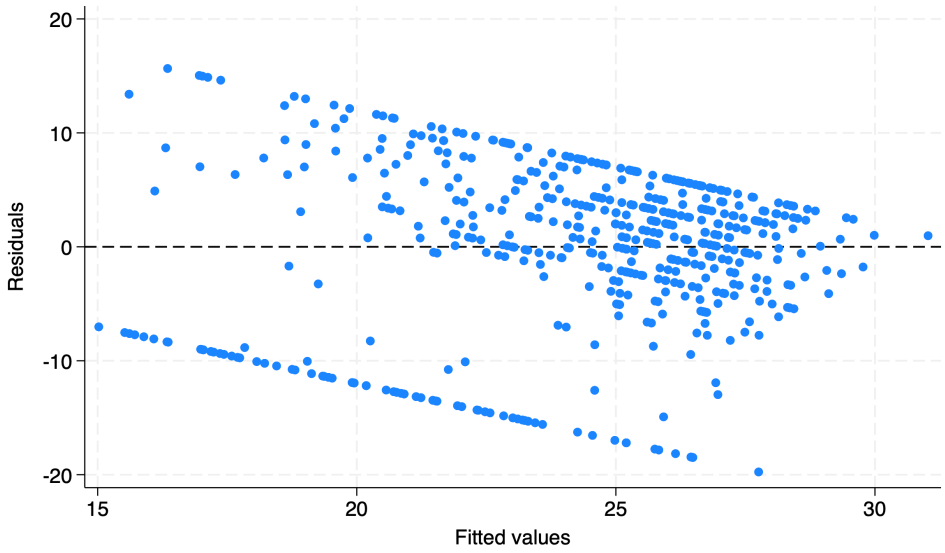
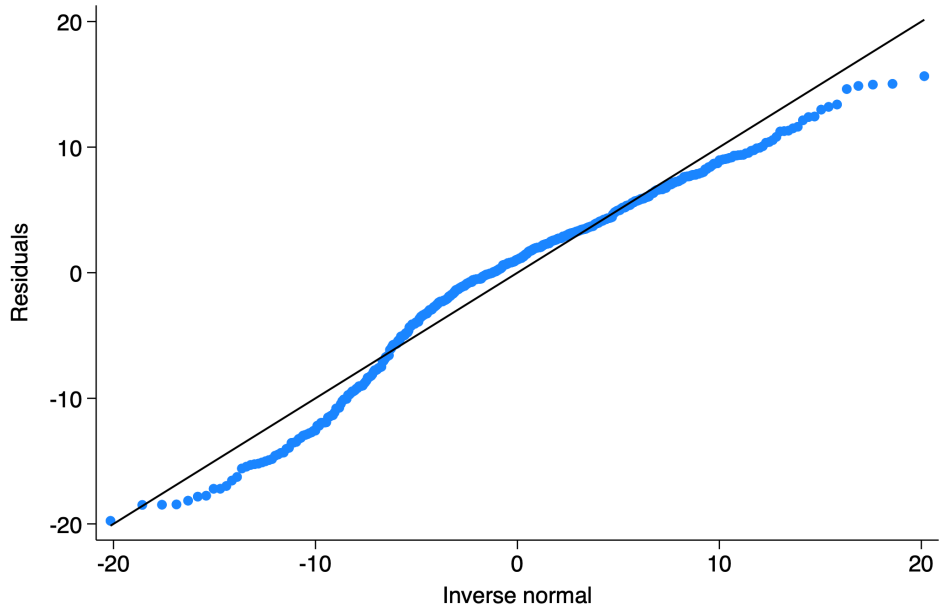
Appendix



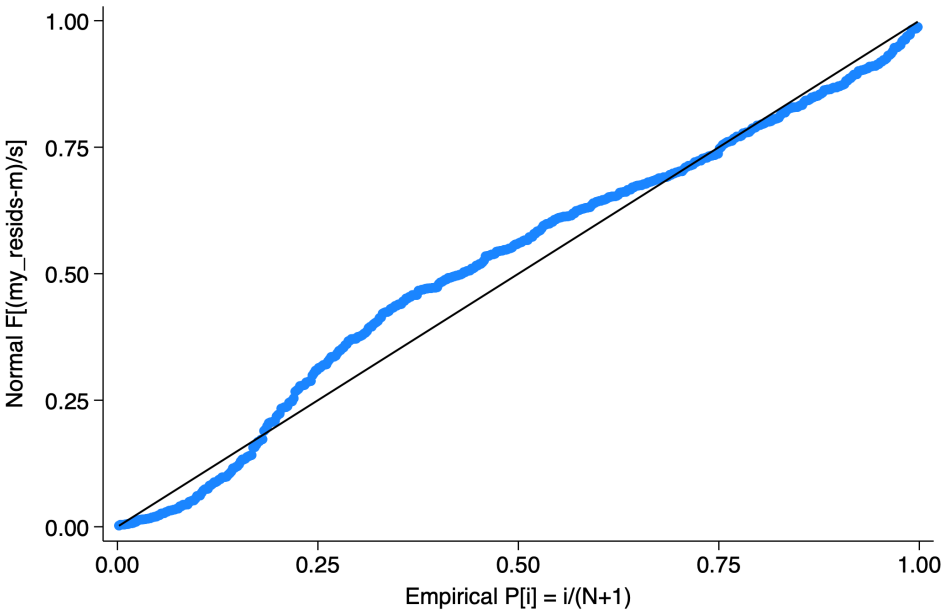
Appendix Figure 1. Food Insecurity Distribution Analysis. Panels show distribution of responses to food insecurity question in complete data set, control group, and intervention group.



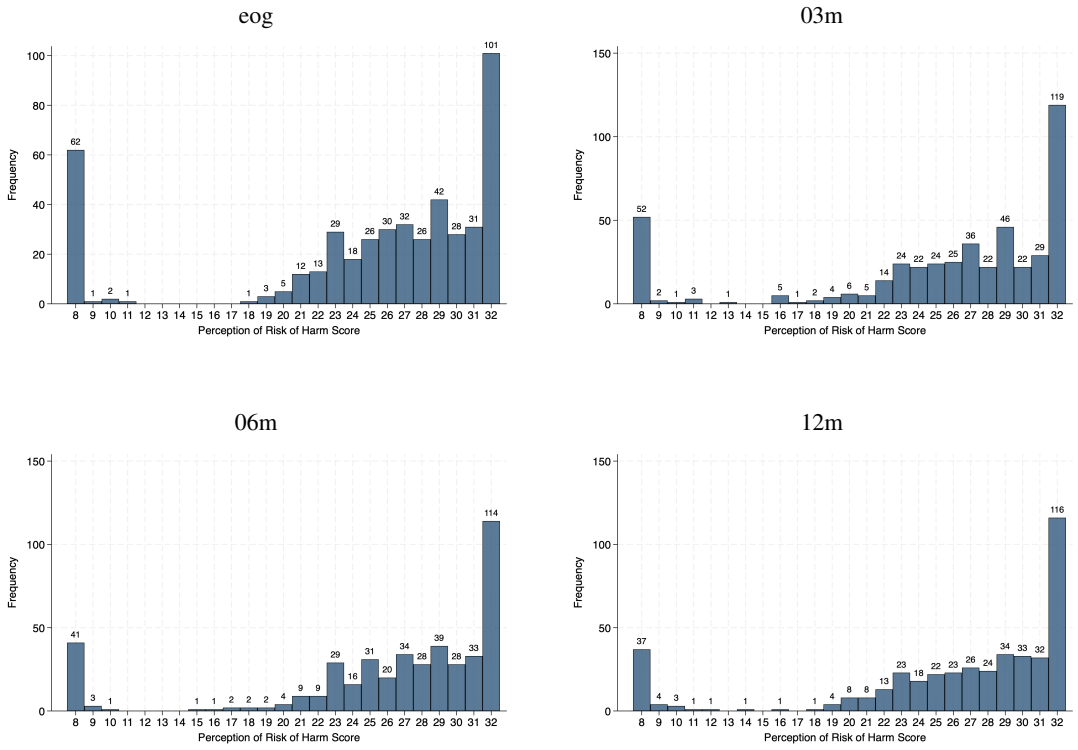
Appendix Figure 2. Residual Plot for Initial OLS Regression. Residual plot shows fitted values vs. residuals and includes all predictors and data.



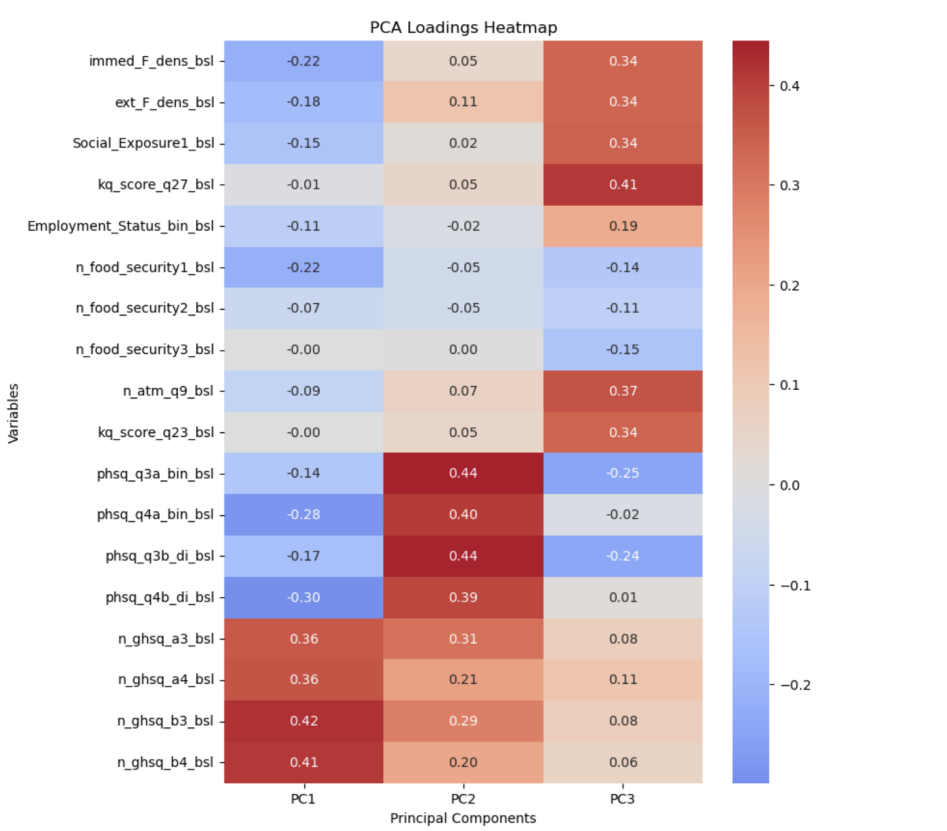
Appendix Figure 3. Q-Q Plot for Initial OLS Regression. Quantile-Quantile plot of the residuals from the initial baseline OLS regression model. The empirical quantiles of the residuals are plotted against a theoretical normal distribution. The distinct S-shaped deviation of the data points from the diagonal reference line indicates a severe violation of the normality assumption, reflecting the highly skewed and bounded nature of the perceived risk of harm outcome variable.



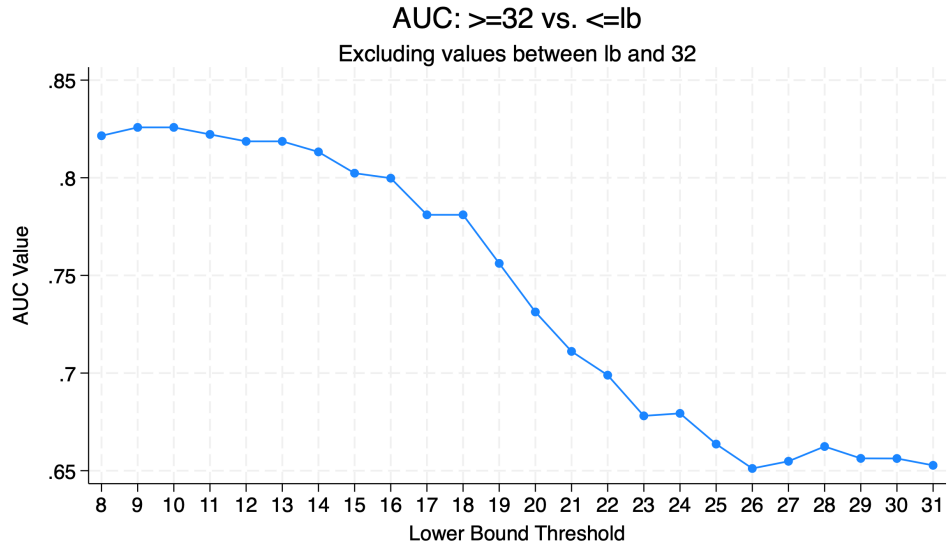
Appendix Figure 4. P-P Plot for Initial OLS Regression. Probability-Probability plot of the residuals from the initial baseline OLS regression model. This plot compares the empirical cumulative distribution function (CDF) of the standardized residuals against the theoretical normal CDF. The pronounced upward bowing of the empirical curve away from the 45-degree reference line confirms a systematic non-normal distribution of errors, providing clear diagnostic justification for transitioning to a threshold-based logistic regression framework.



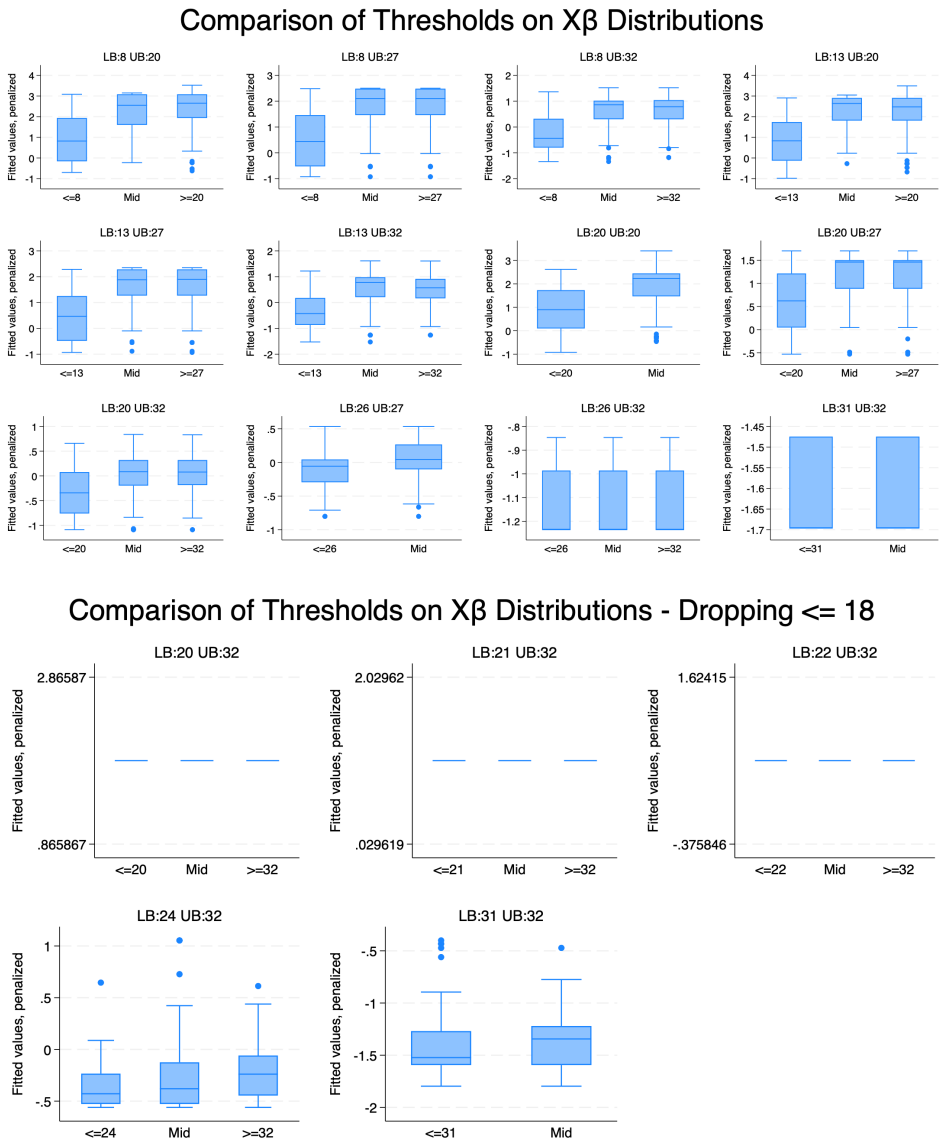
Appendix Figure 5. Distribution of Perceived Risk of Harm Outcome Variable Across Time Points. All panels follow same format as Figure 1. Panels include follow up times (eog through 12m).



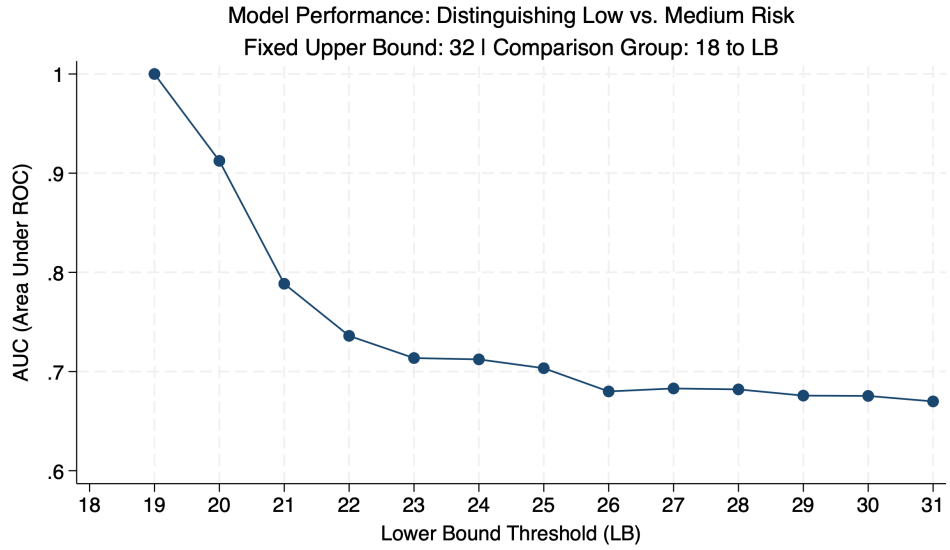
Appendix Figure 6. PCA Loadings Heatmap. Results of initial PCA analysis with full predictor set.



Appendix Figure 7. AUC Plot for Fixed Upper Threshold 32. AUC values plotted for each possible lower threshold with constant upper threshold of 32.



Appendix Figure 8. Additional Threshold Analysis. Panels include plots for various thresholds (labeled above), including subsequent breakdown of 18-32 data in last panel (dropping all data with phs value below 18). Structure matches Figure 4.



Appendix Figure 9. AUC Plot for Fixed Upper Threshold 32, dropping values below 18. AUC values plotted for each possible lower threshold with constant upper threshold of 32. All values below 18 omitted entirely.

Pre-LASSO Logistic Regression Output Table Over Time

VARIABLES	(1) bsl	(2) eog	(3) 03m	(4) 06m	(5) 12m
Immediate Family Misuse History	0.183	0.903	0.846	0.077	-0.086
	(0.515)	(0.808)	(0.696)	(0.700)	(0.649)
Extended Family Misuse History	0.231	-0.048	0.213	0.619	0.146
	(0.428)	(0.465)	(0.504)	(0.540)	(0.536)
Employment Status (Binary)	-0.070	-0.332	-0.484	-0.559	-0.627
	(0.315)	(0.373)	(0.388)	(0.382)	(0.414)
Food Insecurity	-0.592**	-1.132***	-1.102***	-0.799**	-0.387
	(0.288)	(0.346)	(0.347)	(0.349)	(0.395)
Participant Free/Reduced Price School Lunch	-0.144	0.392	-0.093	0.372	0.779*
	(0.341)	(0.393)	(0.432)	(0.418)	(0.453)
All Free/Reduced Price School Lunch	-0.299	-0.457	-0.142	-0.446	-1.495***
	(0.320)	(0.382)	(0.396)	(0.407)	(0.492)
Household Substance Use Exposure	0.163	0.391**	0.229	0.039	0.201

Pre-LASSO Logistic Regression Output Table Over Time (Continued)

VARIABLES	(1) bsl	(2) eog	(3) 03m	(4) 06m	(5) 12m
	(0.118)	(0.152)	(0.144)	(0.131)	(0.140)
Family Medicine Cabinet	1.249***	0.581	1.278***	0.882**	0.811*
	(0.301)	(0.382)	(0.387)	(0.379)	(0.416)
Strong Family Bonds	0.283	1.757***	0.945***	0.811**	-0.020
	(0.286)	(0.389)	(0.365)	(0.376)	(0.411)
Anticipation of Parental Consequences	0.521***	0.327***	0.408***	0.372***	0.617***
	(0.087)	(0.114)	(0.114)	(0.116)	(0.126)
Past Help Seeking: Parent/Guardian	-0.392	-0.846*	-0.642	0.213	0.066
	(0.377)	(0.445)	(0.448)	(0.461)	(0.536)
Past Help Seeking: Other Relative	-0.135	-0.295	0.068	-0.187	0.290
	(0.360)	(0.448)	(0.462)	(0.514)	(0.610)
Past Help Seeking Frequency: Parent/Guardian = 1	0.332	0.044	-0.207	0.351	-
	(1.354)	(0.682)	(1.977)	(1.159)	
Past Help Seeking Frequency: Parent/Guardian = 2, omitted	0.271	-	-0.999	-	-
	(1.238)		(1.563)		
Past Help Seeking Frequency: Other Relative = 1, omitted	-0.068	-0.143	0.232	0.561	-
	(0.666)	(0.708)	(1.656)	(1.193)	
Past Help Seeking Frequency: Other Relative = 2, omitted	-	-	1.327	-	-
			(1.492)		
General Personal/Emotional Help: Parent/Guardian	-0.005	0.245	0.243*	0.322**	0.279*
	(0.108)	(0.150)	(0.143)	(0.144)	(0.149)
General Personal/Emotional Help: Other Relative	0.052	-0.096	-0.191	-0.267*	0.180
	(0.102)	(0.142)	(0.137)	(0.145)	(0.157)
General Suicidal Help: Parent/Guardian	0.020	-0.115	-0.161	-0.072	0.122
	(0.101)	(0.136)	(0.132)	(0.139)	(0.154)
General Suicidal Help: Other Relative	-0.037	0.168	0.207	0.051	-0.195

Pre-LASSO Logistic Regression Output Table Over Time (Continued)

VARIABLES	(1) bsl	(2) eog	(3) 03m	(4) 06m	(5) 12m
	(0.098)	(0.144)	(0.140)	(0.140)	(0.169)
Constant	-0.545	-0.076	-0.488	0.181	-0.666
	(1.311)	(0.522)	(1.580)	(0.538)	(0.550)
Observations	500	433	442	433	390
Pseudo R-squared	0.217	0.270	0.285	0.212	0.300
AUC	0.816	0.851	0.845	0.816	0.867

Standard errors in parentheses

*** p<0.01, ** p<0.05, * p<0.1

Appendix Table 1. Columns include log-odds coefficients with standard errors in parenthesis for each predictor at the given time point. Positive coefficients indicate an increased likelihood of reporting high perceived risk of harm, whereas negative coefficients indicate a decreased likelihood at the following times: baseline (bsl), end of gameplay (eog), and 3-month, 6-month, and 12-month follow-up assessments. AUC values across the bottom indicate strong model performance across all times. Stars indicate p-values showing statistical significance.