AvertD™
Genetic Risk Assessment Test for Opioid Use Disorder

October 20, 2022

Clinical Chemistry and Clinical Toxicology Devices Panel

SOLVD Health

AvertD™
Genetic Risk Assessment Test for Opioid Use Disorder

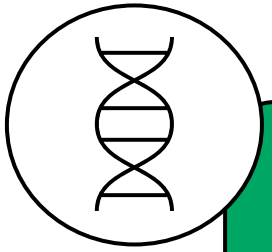
Keri Donaldson, MD, MSCE
Chief Executive Officer
SOLVD Health

Opioid Epidemic is a Public Health Emergency in the United States

- Despite efforts to reduce prescription opioid use, people are still becoming addicted[1]
- Need additional measures to develop safer prescribing practices
- Current risk assessment tools have limitations
- No FDA-approved test to assess genetic risk of developing OUD

1. CDC 2020

AvertD: Innovative Genetic Risk Assessment Test



Uses genetic polymorphisms involved in brain reward pathways

- Specifically designed and trained for OUD
- Includes genes associated with brain reward pathways and addiction

Assesses genetic risk of developing OUD after taking prescription oral opioids for acute pain

- Machine learning algorithm specifically trained to classify individuals with and without OUD

Key Components of AvertD

- Sample Collection Kit
  - Instructions for Use / Patient information label sheet
  - 2 flocked swabs
  - 2 vials with DNA stabilizing solution
- Multiplex PCR instrument (510(k) cleared)
  - Amplification Mix
  - Reagent Module
  - Microarray
  - Proprietary software

AvertD Testing is Simple
Step 1: Sample Collected and Mailed to CLIA-Certified Lab

Step 1

Sample collected and mailed to CLIA-certified lab

Step 2: CLIA-certified Lab Processes Sample and Generates Report

Step 1
Sample collected and mailed to CLIA-certified lab

Step 2
Lab receives and processes the sample

1. DNA extraction using standard qualified method
2. Multiplex PCR DNA amplification using assay PCR amplification mix
3. Allele specific primer extension with fluorescent label using assay reagent module on analyzer
4. Hybridization and immobilization of extended oligonucleotides to Microarray on analyzer
5. Microarray chip washed and dried to remove unbound material
6. Signal detection and analysis using assay-specific software on analyzer

Step 3: AvertD Results Considered in Conjunction with Clinical Evaluation for Individually Tailored Pain Management Decision

Step 1
Sample collected and mailed to CLIA-certified lab

Step 2
Lab receives and processes the sample

Step 3
Results used with clinical evaluation for individually tailored pain management decision making

Key Elements of Proposed Indication

- AvertD is a genotyping test
  - Detects 15 clinically relevant SNPs to identify patients at increased genetic risk for OUD
- ≥18 years of age, being prescribed oral opioids for acute pain
- Facilitates shared (patient/provider) informed decision making
- Intended for use as part of a clinical evaluation and assessment

Regulatory History

2018	Breakthrough Device designation granted
2019	Clinical study conducted
2020	Initial De Novo application submitted
2021	De Novo request declined
2022	Resubmitted De Novo request with additional data and analyses to address uncertainty around study population and applicability of study results to intended use population

AvertD is Effective Risk Assessment Test to Help Identify Those Who May Be at Increased Risk of OUD

- Met specificity and sensitivity performance goals
- Those identified as high genetic risk are 18 times more likely to develop OUD (high diagnostic odds ratio)

AvertD used in conjunction with a complete clinical evaluation will further enhance shared, informed decision-making regarding use of prescription oral opioids for acute pain

Agenda

Epidemiology, Current Practice Guidelines and Unmet Need	**Joseph Garbely, DO, DFASAM, FAPA** Distinguished Fellow of the American Society of Addiction Medicine Fellow of the American Psychiatric Association Faculty, Penn State University and Drexel University College of Medicine National Director and Board Member of Physician In-Training Committee, ASAM
Study Design and Results	**Keri Donaldson, MD, MSCE** Chief Executive Officer SOLVD Health
Additional Analyses Performed to Address FDA Questions	**Christine Brauer, PhD** Regulatory Affairs Consultant
Clinical Perspective	**Chris Zacko, MD** Spine Surgeon Member of Enhanced Recovery After Surgery (ERAS) Professor and Vice-Chair of Quality, Dept of Neurosurgery Penn State Health Milton S Hershey Medical Center

Epidemiology, Current Practice Guidelines, and Unmet Need

Joseph Garbely, DO, DFASAM, FAPA

Distinguished Fellow of the American Society of Addiction Medicine

Fellow of the American Psychiatric Association

Faculty, Penn State University and Drexel University College of Medicine

Member of Board of Directors and National Director of Physician In-Training Committee, ASAM

OUD is Condition Characterized By Desire to Obtain and Take Opioids Despite Social and Professional Consequences

- Overpowering desire to use opioids
- Increased opioid tolerance
- Withdrawal syndrome when discontinued in commission of active addiction, a chronic brain disease
- Prevalence in general U.S. population ~1%[1, 2]

1. Keyes et al. 2022; 2. https://nida.nih.gov/publications/research-reports/medications-to-treat-opioid-addiction/overview

Opioid Epidemic Began with and Continues to be Fueled by Prescription Oral Opioids

~80% of heroin users reported that they began with prescription opioids[1]

- 13.4 million people self-reported misused prescription opioids during previous year[2]
- Overdose deaths involving prescription opioids increased nearly five times from 1999 to 2020[3]

1. Muhuri et al. 2013; 2. SAMSHA Annual Survey 2020; 2. SAMSHA Annual Survey 2020; 3. CDC 2021

Approaches to Help Prevent Opioid Addiction

- Prescribing guidelines and educational materials
  - Use non-opioid alternatives when appropriate for acute pain
  - Reduce duration and dosage of prescribed opioids
- Risk assessments – *cornerstone of today's clinical practice*
  - Patient interviews
  - Medical record review
  - Risk questionnaires

Limitations of Current Risk Assessments

Currently available risk stratification tools
…show ***insufficient accuracy for classification of patients as at low or high risk for abuse or misuse****.*

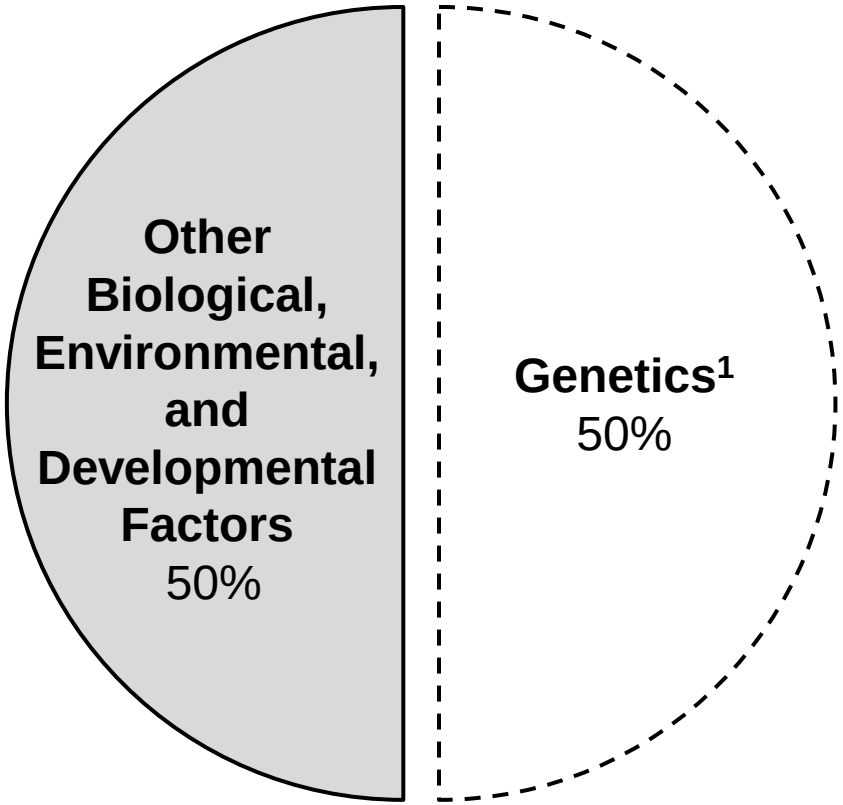
CDC Statement, Dowell et al. 2016

…despite risk assessment tools becoming a widespread aspect of the prescribing of opioids in pain management care environments, they appeared to be ***of little value for identifying patients at high vs low risk***

Klimas 2019

None of the current risk assessment tools assess genetic risk for developing OUD

Genetics Account for ~50% of a Person's Risk for Drug Addiction[1, 2]



Genetic and environmental factors interact with critical developmental stages in a person's life to affect addiction risk

1. NIH: National Institute of Drug Abuse (NIDA); 2. Berrettini et al. 2017

Genetic Variants are Associated with OUD Risk

- Numerous genes identified in both candidate gene and genome-wide association approaches[1, 2, 3, 4]
  - Opioid receptors
    - Mu (OPRM1) and kappa (OPRK1)
  - Delta-opioid receptor (OPRD1)
  - Dopamine receptors
    - DRD1, DRD2, DRD5

1. Crist et al. 2019; 2. Deak and Johnson 2021; 3. Berrettini et al. 2017; 4. Deak et al. 2022

Genetic Predisposition Occurs in Meso-Limbic System

- Chemical messages release dopamine
- Genes control these messages and subsequent release "brain reward pathways"
- Genetic mutations affecting brain reward pathways can result in substance seeking behavior

Unmet Need Summary

- Opioid epidemic began with and continues to be fueled by prescription oral opioids
- Genetics contribute significantly to risk of developing OUD
- Current risk assessment tools do not take into consideration the role of genetics
- Genetic risk assessment test is needed

Study Design and Results

Keri Donaldson, MD, MSCE
Chief Executive Officer
SOLVD Health

Clinical Study Design

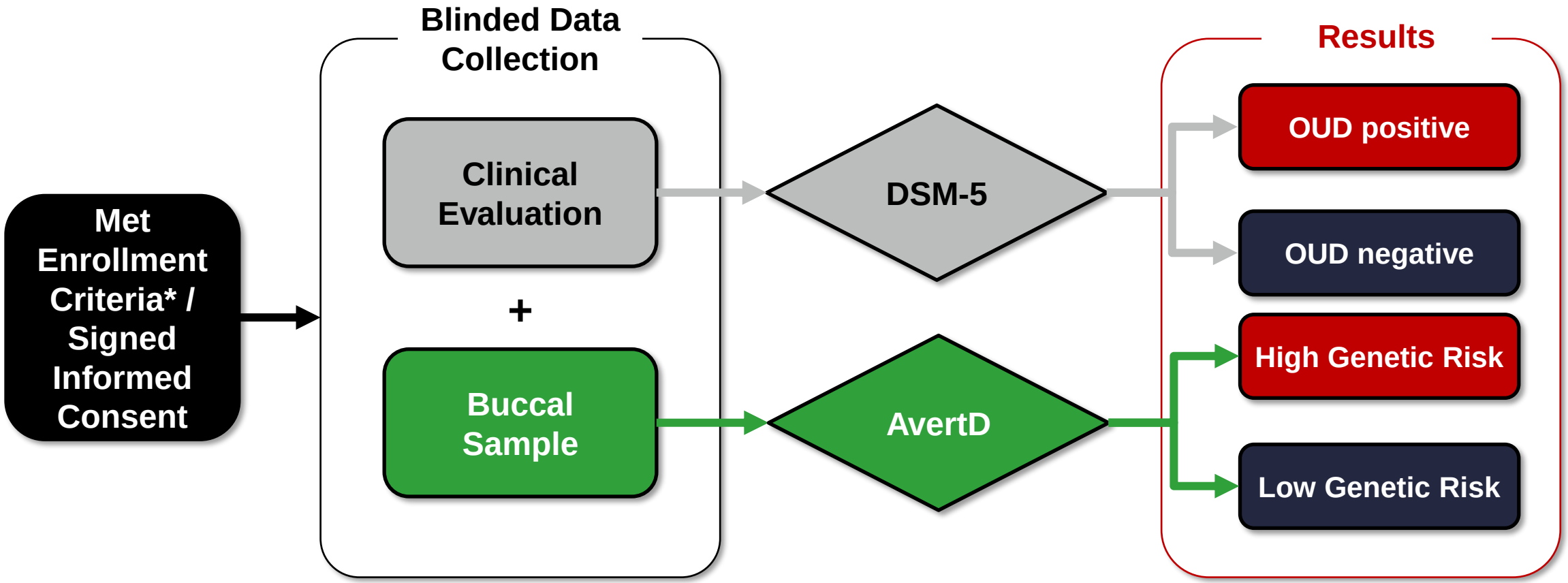
- Blinded, multi-center study
- Differentiate high/low genetic risk for OUD
- Enrolled all participants who met inclusion / exclusion criteria
- 10 geographically diverse private practice sites in U.S.
  - 6 general practice sites
  - 1 research only site
  - 3 sites providing medication assisted OUD treatment
- Prospective study with one retrospective element

Retrospective Design Element: Participants Self-Reported Opioid Exposure

- Adults ≥ 18 interviewed by site personnel for index exposure
  - Oral opioids prescribed and taken ≥ 1 year prior to interview
  - Exposure consistent with acute pain (range of 4–30 days)
- Self-reported opioid use minimizes potential known biases associated with prescription records
  - Many patients may not fill opioid prescriptions, or fill them but do not take them[1, 2, 3]

1. Cramer et al. 1989; 2. Drieling et al. 2016; 3. Hafferty et al. 2017

Study Overview



*Enrollment Criteria

- ≥ 18 years of age
- Prior prescription opioid use
  - At least 1 year prior to enrollment
  - ≥ 4 to ≤ 30 days

Co-Primary Effectiveness Endpoints

- Sensitivity:
  - Proportion with OUD correctly identified by AvertD as high genetic risk
    - Lower limit of 95% CI must exceed Performance Goal of 59.5%
- Specificity:
  - Proportion without OUD correctly identified by AvertD as low genetic risk
    - Lower limit of 95% CI must exceed Performance Goal of 55.5%

Co-Secondary Effectiveness Endpoints

- Positive likelihood ratio (LR+)

$$LR+ = \frac{\text{Sensitivity}}{\text{1-Specificty}}$$

- Negative likelihood ratio (LR-)

$$LR- = \frac{\text{1-Sensitivity}}{\text{Specificity}}$$

Random Representative Sampling Used to Ensure Study Population Represented Intended Use Population

- Blinded, independent statistician randomly selected participants post-enrollment to ensure adequate participants in each strata
  - Sex
  - Age
  - Time from opioid index exposure to enrollment
  - Likelihood of OUD (presence or absence of any SUD)

Study Participants

- 812 participants enrolled
- Blinded statistician determined 689 participants sufficient to meet stratification criteria
- Sample size statistically powered to assess sensitivity and specificity
- 385 participants selected at random to fill strata and ensure
  - Study population represented U.S. prescription opioid population
  - Adequate representation of patients with OUD

Study Population Demographics and Clinical Characteristics

		N = 385
Sex	Male	58%
	Female	42%
Race*	White	92%
	Non-white	6%
Ethnicity	Hispanic	24%
	Non-Hispanic	76%
OUD Status	Positive	45%
	Negative	55%

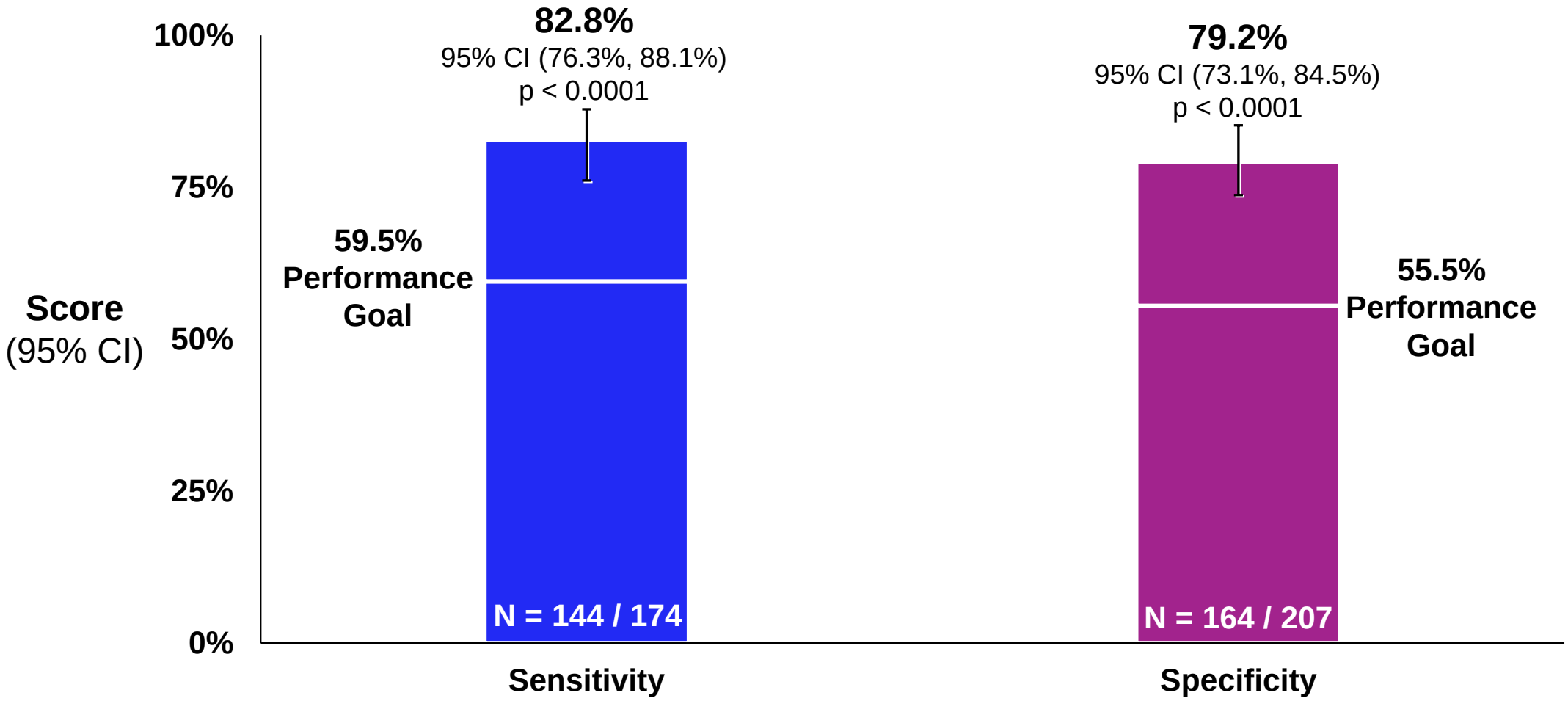
* Unknown = 2%

Study Population Stratification

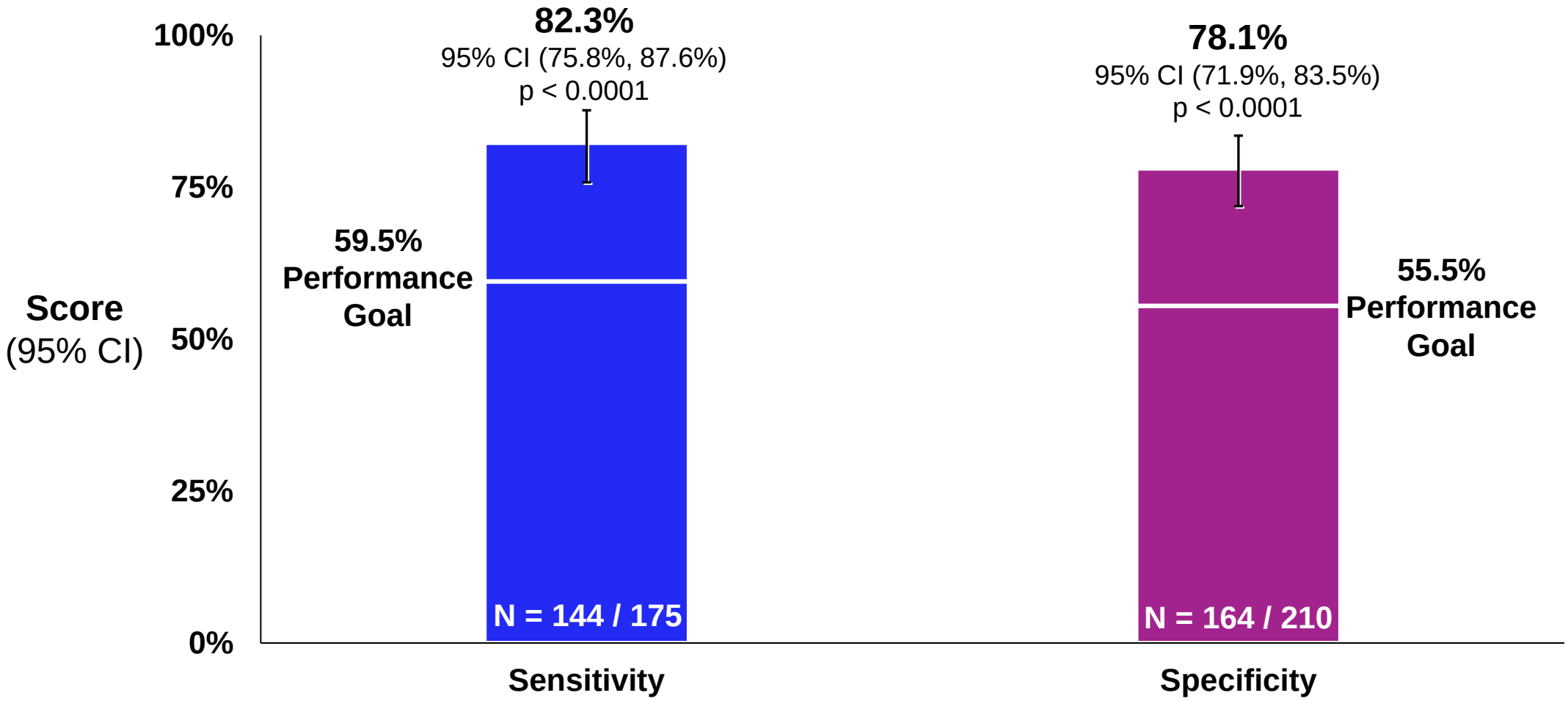
		N = 385
Sex	**Male**	**58%**
	Female	**42%**
Age at Enrollment	**18 – 34**	**36%**
	35 – 49	**32%**
	50 – 64	**20%**
	≥ 65	**12%**
Prospective Prognostic Enrichment *Likelihood of OUD based on presence/absence of SUD*	**High**	**53%**
	Low	**47%**
Time from Opioid Index Exposure to Enrollment	**≥ 4 Years**	**78%**
	1 – 3 Years	**22%**

Primary Efficacy and Subgroup Analysis

AvertD Met Prespecified Efficacy Endpoints for Performance Goals

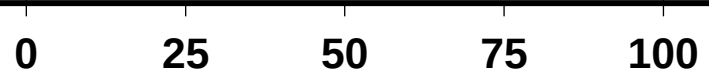


Worst-Case Imputation for Missing Data Support the Robustness of the Data



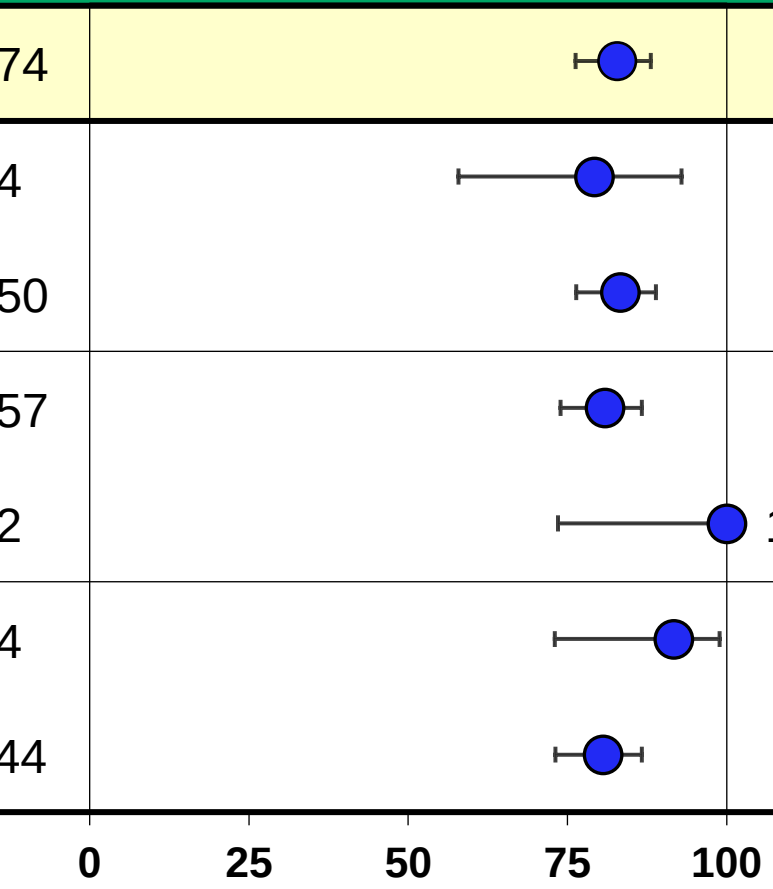
Subgroup Analysis for Sensitivity Results Based on Sex and Age Demonstrate Robustness of Test Accuracy

		n / N	Sensitivity	Point Estimate (95% CI)	Subgroup p-value
Overall		144 / 174		82.8% (76.3 – 88.1)	
Sex	Females	56 / 66		84.9% (73.9 – 92.5)	0.68
	Males	88 / 108		81.5% (72.9 – 88.3)	
Age	18 – 34	61 / 74		82.4% (71.8 – 90.3)	0.90
	35 – 49	52 / 61		85.3% (73.8 – 93.0)	
	50 – 64	20 / 25		80.0% (59.3 – 93.2)	
	≥ 65	11 / 14		78.6% (49.2 – 95.3)	



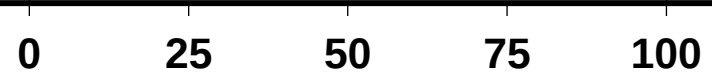
Subgroup Analysis for Sensitivity Results Related to Opioid Exposure, Race, and Ethnicity Demonstrate Robustness of Test Accuracy

		n / N	Point Estimate (95% CI)	Subgroup p-value
Overall		144 / 174	82.8% (76.3 – 88.1)	
Time from Opioid Index Exposure to Enrollment	1 – 3 yrs	19 / 24	79.2% (57.9 – 92.9)	0.57
	4+ yrs	125 / 150	83.3% (76.4 – 88.9)	
Race and Ethnicity	White	127 / 157	80.9% (73.9 – 86.7)	0.13
	Non-White	12 / 12	100.0% (73.5 – 100.0)	
	Hispanic	22 / 24	91.7% (73.0 – 98.9)	0.26
	Non-Hispanic	116 / 144	80.6% (73.1 – 86.7)	



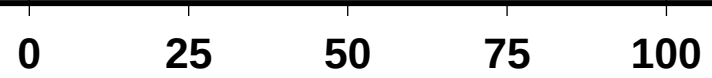
Subgroup Analysis for Specificity Results Based on Sex and Age Demonstrate Robustness of Test Accuracy

		n / N	Specificity	Point Estimate (95% CI)	Subgroup p-value
Overall		164 / 207		79.2% (73.1 – 84.5)	
Sex	Female	75 / 96		78.1% (68.5 – 85.9)	0.73
	Male	89 / 111		80.2% (71.5 – 87.1)	
Age	18 – 34	51 / 62		82.3% (70.5 – 90.8)	0.24
	35 – 49	51 / 61		83.6% (71.9 – 91.9)	
	50 – 64	40 / 51		78.4% (64.7 – 88.7)	
	≥ 65	22 / 33		66.7% (48.2 – 82.0)	



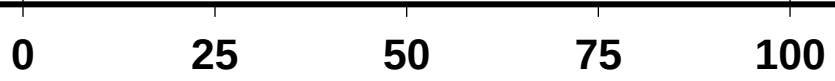
Subgroup Analysis for Specificity Results Related to Opioid Exposure, Race, Ethnicity Demonstrate Robustness of Test Accuracy

		n / N	Specificity	Point Estimate (95% CI)	Subgroup p-value
Overall		164 / 207		79.2% (73.1 – 84.5)	
Time from Opioid Index Exposure to Enrollment	1 – 3 yrs	47 / 60		78.3% (65.8 – 87.9)	0.85
	4+ yrs	117 / 147		79.6% (72.2 – 85.8)	
Race and Ethnicity	White	155 / 194		79.9% (73.6 – 85.3)	0.71
	Non-White	9 / 12		75.0% (42.8 – 94.5)	
	Hispanic	47 / 66		71.2% (58.8 – 81.7)	0.066
	Non-Hispanic	117 / 141		83.0% (75.7 – 88.8)	



Subgroup Analysis for Sensitivity and Specificity Results Based on Age Demonstrate Robustness of Test Accuracy

		n / N	Sensitivity	Point Estimate (95% CI)	Subgroup p-value
Overall		144 / 174		82.8% (76.3 – 88.1)	
Age	< 18	42 / 53		79.3% (65.9 – 89.2)	0.51
	≥ 18	102 / 121		84.3% (76.6 – 90.3)	



		n / N	Specificity	Point Estimate (95% CI)	Subgroup p-value
Overall		164 / 207		79.2% (73.1 – 84.5)	
Age	< 18	27 / 32		84.4% (67.2 – 94.7)	0.64
	≥ 18	137 / 175		78.3% (71.4 – 84.2)	

Similar Performance Across Severity of OUD

- Analysis based on OUD severity requested by FDA
- Prevalence of OUD severity in acute pain not well-characterized in literature

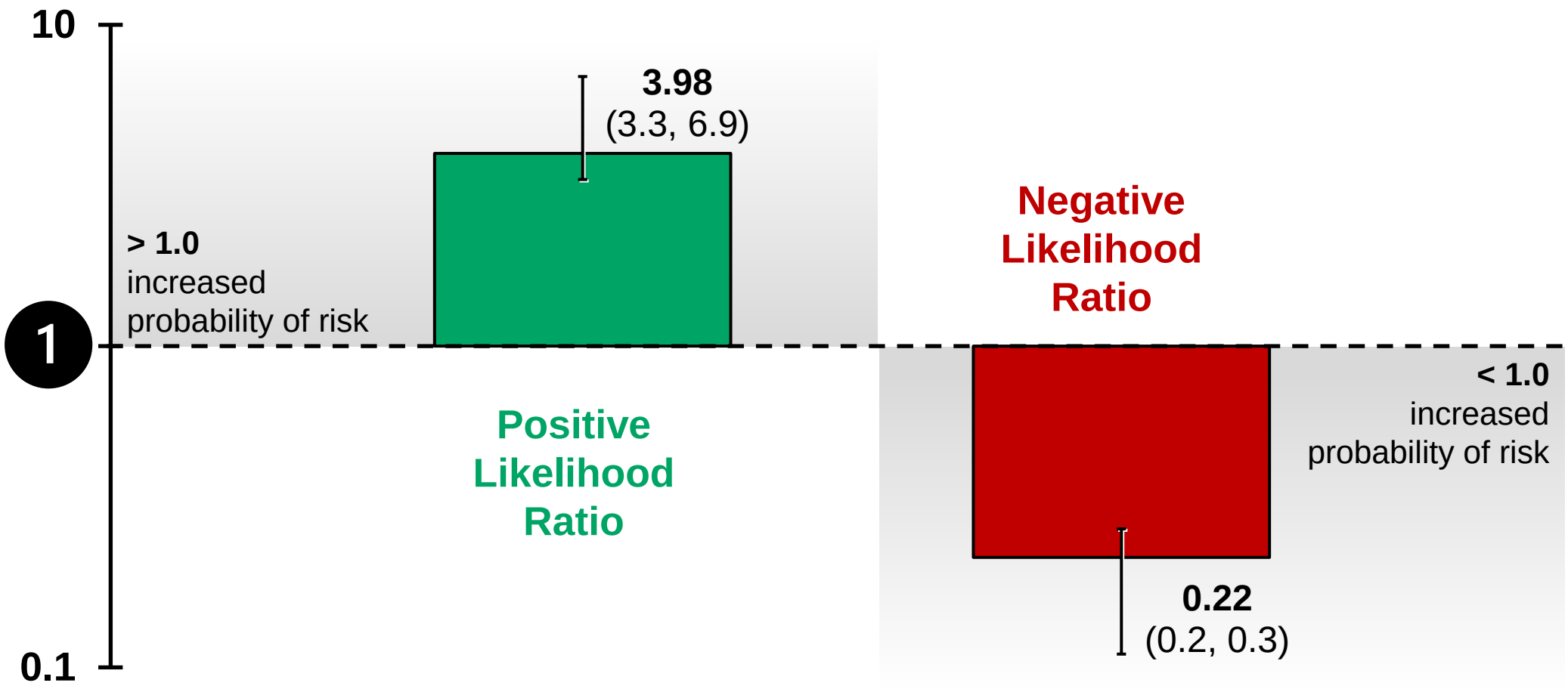
	AvertD Result			P-value (1-tailed)	
OUD Severity	No	Yes	Sensitivity	Mild vs. Moderate / Severe	Mild / Moderate vs. Severe
Mild	1	12	92.3%		
Moderate	10	21	67.8%	0.32	0.97
Severe	18	111	86.0%		

Secondary Endpoint Results
Positive and Negative Likelihood Ratios

Likelihood Ratios

- LR+ = True positive rate / false positive rate
  - Values > 1 indicate increase probability of risk
- LR- = False negative rate / true negative rate
  - Values < 1 indicate a decreased probability of risk

Secondary Effectiveness Results for Likelihood Ratios Support Primary Results



Diagnostic Odds Ratio for Overall Diagnostic Performance

$$\text{Diagnostic Odds Ratio} = \frac{\text{LR+}}{\text{LR-}}$$

$$18.1 = \frac{3.98}{0.22}$$

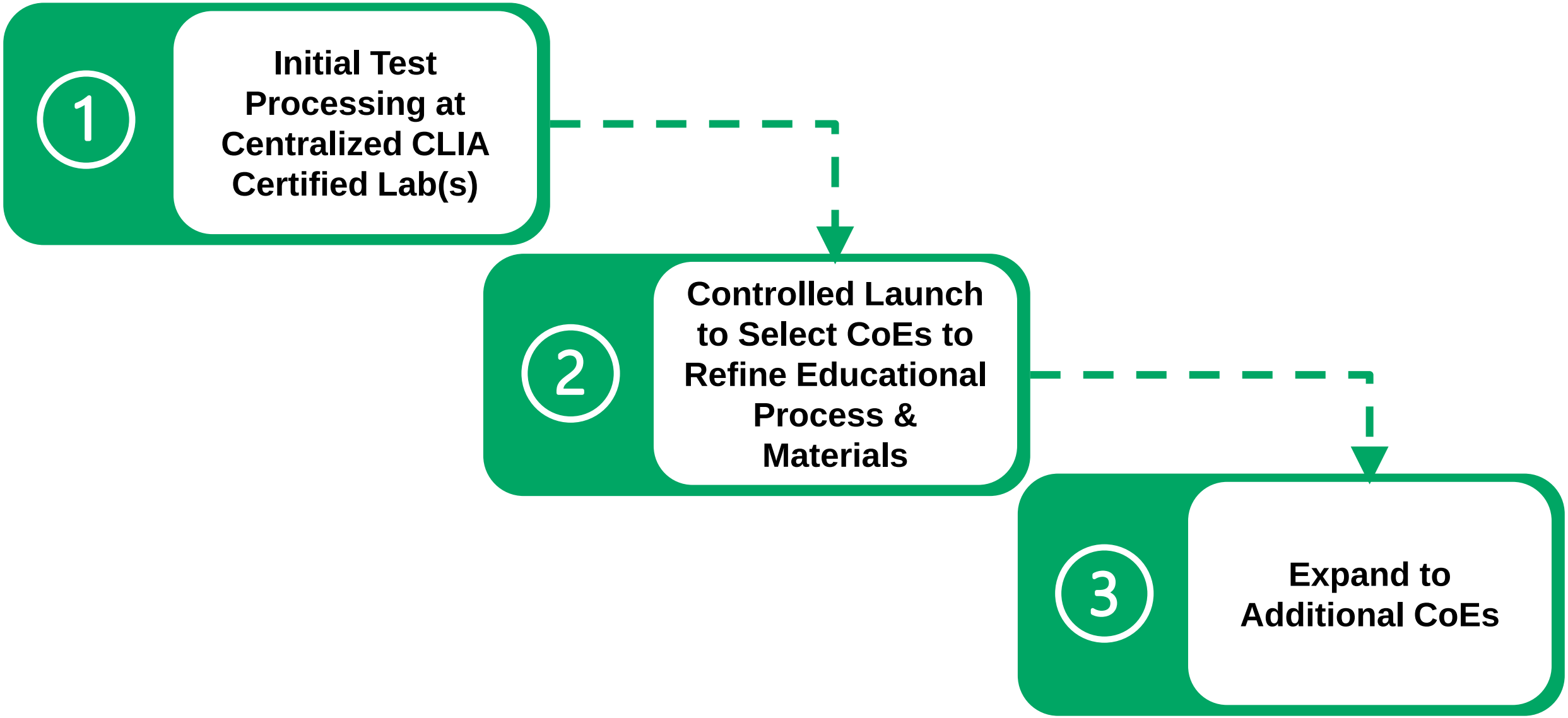
Those with high genetic risk have 18-fold increased risk of OUD compared to those at low risk

Education Program and Materials

Educational Materials to Support Appropriate and Personalized Pain Management Plan

- Genetics are one risk factor for developing OUD
- AvertD assesses genetic risk, does not diagnose OUD
- Prescription-only
  - Administered by an HCP
  - Discussed between HCP and patient
  - Used in conjunction with complete clinical evaluation and current opioid prescribing guidelines

Controlled Launch to Obtain and Incorporate Feedback from Centers of Excellence (CoEs)



Study Design and Results Summary

AvertD Provides Valid Scientific Evidence in Detecting Those Who May be at High Genetic Risk for OUD

- Co-primary endpoint analyses demonstrate sensitivity and specificity
- Results not impacted by age, sex, time from index exposure, race, or ethnicity
- Likelihood ratios support primary findings
- AvertD provides valuable information to clinicians and patients to help with assessment of risk

Additional Analyses Performed to Address FDA Questions

Christine Brauer, PhD
Regulatory Affairs Consultant

Remaining FDA Questions

1. Potential impact of multiple CRF versions
2. Uncertainty around self-reporting to capture opioid exposure
3. Uncertainty in applicability of results from study population to intended use population
   - Difference in study site results
   - Mental health comorbidities

Potential Impact of Multiple CRF Versions

Final CRF Version to Ensure Study Population Met Inclusion/Exclusion Criteria

- All sites were trained on study protocol
- Inclusion/exclusion criteria specified in study protocol used to enroll participants
- Changes to CRFs had no impact on enrollment or outcomes
- CRFs used to capture data evolved throughout the study, e.g.
  - Added State of residence
  - Minimum and maximum days of opioid exposure
- Final CRF version confirmed all 385 participants met the study inclusion/exclusion criteria

Self-Reported Data of Index Exposure to Prescription Oral Opioid

Sites Collected Data to Corroborate Patient Self-Reported Opioid Exposure

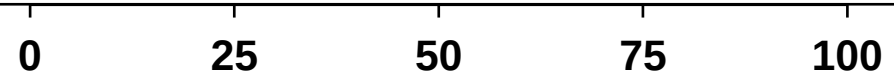
- Information from medical records at sites 1 year before and after self-reported index exposure
  - Documentation of surgical procedure or event (e.g., accident) that may result in oral opioid prescription
  - Documentation of oral opioid prescription
  - Physical presence of opioid prescription itself (physical copy, electronic copy, scan or photograph)

Established Systematic Classification for Documenting Robustness of Data on Index Procedure

	Key Criteria to Meet Classification	Observed n (%)
Tier 1	**Met inclusion / exclusion criteria**	**381 (100%)**
Tier 2	**Tier 1 + Documentation of surgery, procedure, or accident in medical record where opioids may be prescribed** *Within 1 year of the self-reported exposure*	**361 (95%)**
Tier 3	**Tier 2 + Medical records noted opioid prescription written** *Within 1 year of the self-reported exposure*	**318 (83%)**
Tier 4	**Tier 3+ Medical records included a physical copy, electronic copy, scan or photograph of actual prescription**	**133 (35%)**

Results from Reanalysis Are Consistent With Primary Results

		N	Point Estimate (95% CI)
Sensitivity	**Overall**	**381**	82.8% (76.3 – 88.1)
	Tier 1	381	82.8% (76.3 – 88.1)
	Tier 2	361	82.7% (76.0 – 88.2)
	Tier 3	**318**	**82.5% (75.1 – 88.4)**
	Tier 4	133	70.7% (54.5 – 83.9)
Specificity	**Overall**	**381**	79.2% (73.1 – 84.5)
	Tier 1	381	79.2% (73.1 – 84.5)
	Tier 2	361	78.9% (72.6 – 84.4)
	Tier 3	**318**	**79.6% (72.9 – 85.2)**
	Tier 4	133	84.8% (75.8 – 91.4)



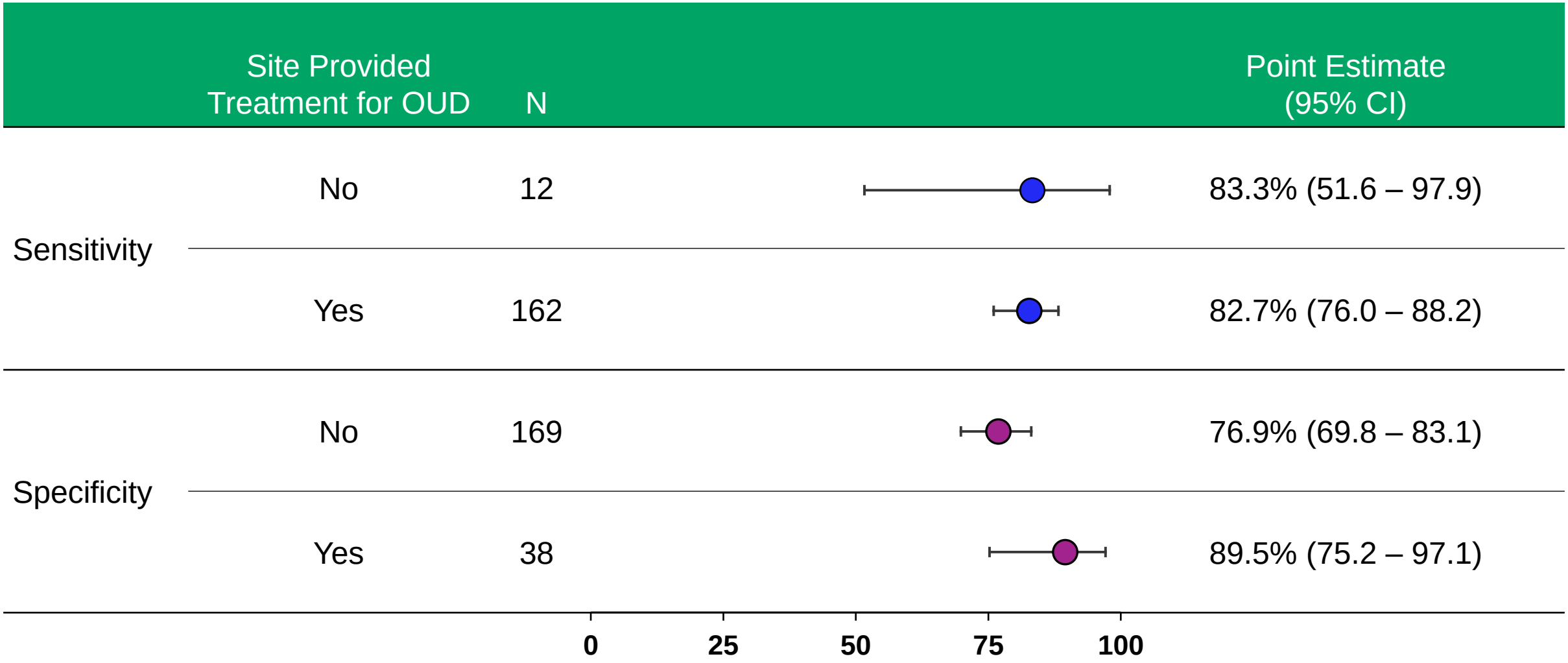
Sensitivity and Specificity by Site Specialization

3 Sites Provided Treatment for OUD

- Prescribed medical assisted therapy medication and had providers with SAMHSA Drug Addiction Treatment Act of 2000 waiver certifications
- Remaining 7 sites did not provide treatment for OUD

SAMHSHA = Substance Abuse and Mental Health Services Administration

Sensitivity and Specificity by Site Specialization



Prevalence of Mental Health Comorbidities

Study Population Not Enriched and Consistent with Prevalence Rates in the United States

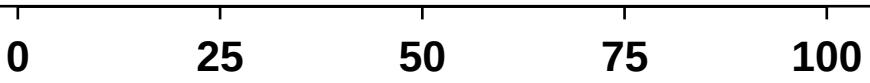
History of	Study Participants at Index Exposure (N = 377*) Overall Population n (%)		DSM-5 OUD Negative n (%)		DSM-5 OUD Positive n (%)		US Prevalence Data
Depression	38	**10%**	17	**8%**	21	**12%**	**8.1%[1]**
Anxiety	36	**10%**	16	**8%**	20	**11%**	**3.1 – 9.1%[2]**
Alcohol Use Disorder	27	**7%**	17	**8%**	10	**6%**	**6.2%[3]**
Bipolar Disorder	13	**3%**	2	**1%**	11	**6%**	**2.8% – 4.4%[4]**
Other SUD	10	**3%**	0	**-**	10	**6%**	**3.9%[5]**
Cannabis Use Disorder	7	**2%**	1	**< 1%**	6	**3%**	**1.5%[6]**

*** Data not available (n=8)**

1. **https://www.cdc.gov/nchs/covid19/pulse/mental-health.htm**
2. **https://adaa.org/understanding-anxiety/facts-statistics**
3. **https://www.apa.org/topics/substance-use-abuse-addiction/alcohol-disorders**
4. **https://www.nimh.nih.gov/health/statistics/bipolar-disorder**
5. **https://www.samhsa.gov/data/sites/default/files/reports/rpt29393/2019NSDUHFFRPDFWHTML/2019NSDUHFFR090120.htm**
6. **https://pubmed.ncbi.nlm.nih.gov/31586809**

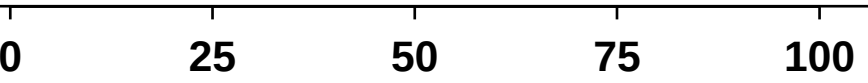
Strong Sensitivity Results for AvertD Regardless of Mental Health Status at Time of Index Exposure

	History of	n / N	Sensitivity	Point Estimate (95% CI)	P-value
Depression	No	123 / 152		80.9% (73.8 – 86.8)	0.28
	Yes	20 / 21		95.2% (76.2 – 99.9)	
Anxiety	No	127 / 153		83.0% (76.1 – 88.6)	0.80
	Yes	16 / 20		80.0% (56.3 – 94.3)	
Alcohol Use Disorder	No	135 / 163		82.8% (76.1 – 88.3)	0.74
	Yes	8 / 10		80.0% (44.4 – 97.5)	
Bipolar Disorder	No	136 / 162		84.0% (77.4 – 89.2)	0.26
	Yes	7 / 11		63.6% (30.8 – 89.1)	
Other SUD	No	134 / 163		82.2% (75.5 – 87.8)	1.00
	Yes	9 / 10		90.0% (55.5 – 99.8)	
Cannabis Use Disorder	No	139 / 167		83.2% (76.7 – 88.6)	0.40
	Yes	4 / 6		66.7% (22.3 – 95.7)	

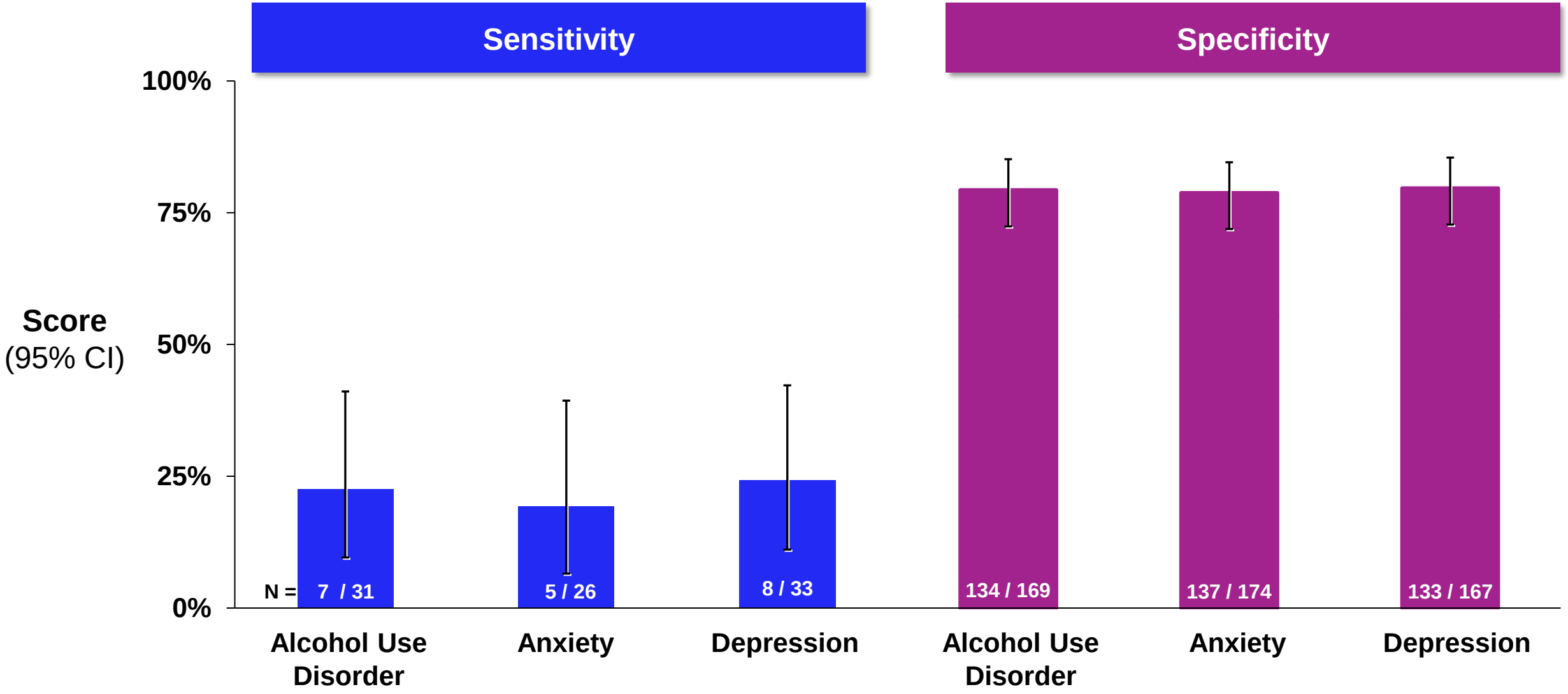


Strong Specificity Results for AvertD Regardless of Mental Health Status at Time of Index Exposure

	History of	n / N	Specificity	Point Estimate (95% CI)	P-value
Depression	No	145 / 183		79.2% (72.6 – 84.9)	0.91
	Yes	13 / 17		76.5% (50.1 – 93.2)	
Anxiety	No	144 / 184		78.3% (71.6 – 84.0)	0.76
	Yes	14 / 16		87.5% (61.7 – 98.5)	
Alcohol Use Disorder	No	147 / 184		79.9% (73.4 – 85.4)	0.57
	Yes	11 / 16		68.8% (41.3 – 89.0)	
Bipolar Disorder	No	157 / 198		79.3% (73.0 – 84.7)	0.59
	Yes	1 / 2		50.0% (1.3 – 98.7)	
Other SUD	No	158 / 200		79.0% (72.7 – 84.4)	1.00
	Yes	0 / 0		--	
Cannabis Use Disorder	No	157 / 199		78.9% (72.6 – 84.4)	1.00
	Yes	1 / 1		100% (2.5 – 100.0)	



AvertD Performance Specific to OUD Classification



Data have not been reviewed by FDA

Overall Conclusions of Additional Analyses Performed by SOLVD

- Clinical study population matched intended use population
  - Allowed interpretation of results and demonstrated applicability to intended use population
- Self-reported oral opioid exposure consistent with corroborating documentation in medical record
- Consistent sensitivity and specificity across sites
- Study population not enriched for mental health and non-opioid use disorder comorbidities
- AvertD performance remained same in presence or absence of comorbidities

Clinical Perspective

Chris Zacko, MD
Spine Surgeon
Member of Enhanced Recovery After Surgery (ERAS)
Professor and Vice-Chair of Quality, Dept of Neurosurgery
Penn State Health Milton S Hershey Medical Center

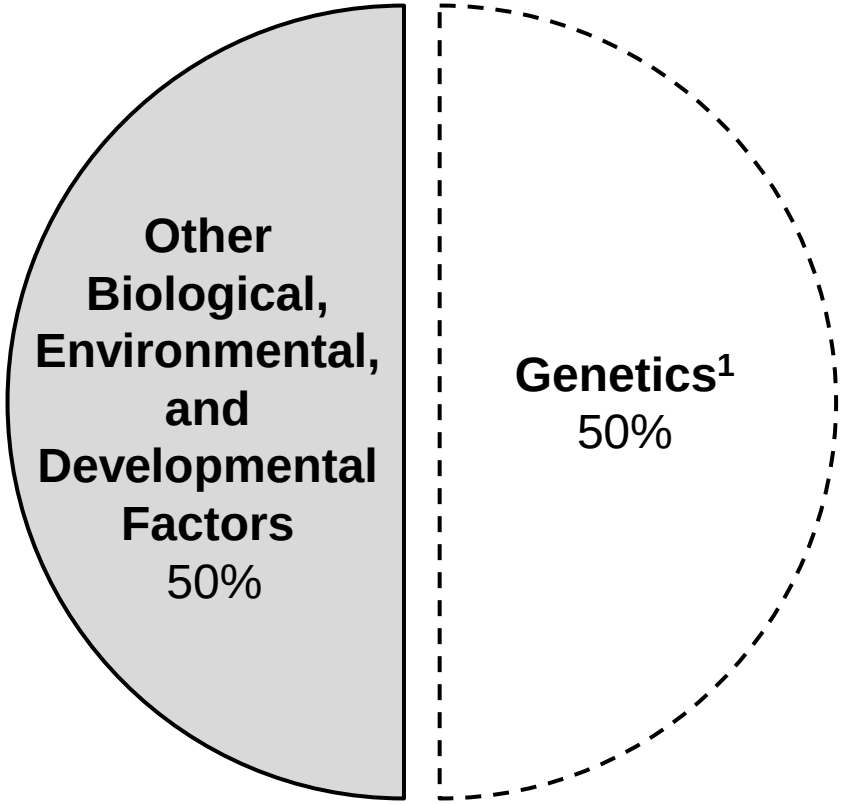
Many Patients with OUD Start with an Oral Opioid Prescription

- Prescribing guidelines attempt to reduce opioid addiction and illicit use
  - Limiting duration and dosage of exposure
  - Risk assessment
- Most guidelines include risk assessment prior to prescribing opioids to determine patient risk of developing OUD
- Current risk mitigation strategies are not working

Limitations of Existing Risk Assessment Tools

- Risk assessments identify OUD through a retrospective lens
- Risk assessments do not prospectively evaluate predisposition to addiction
- Risk questionnaires designed to assess future risk are not sufficient on their own
  - Subjective
  - Do not account for genetic risk which is a significant component

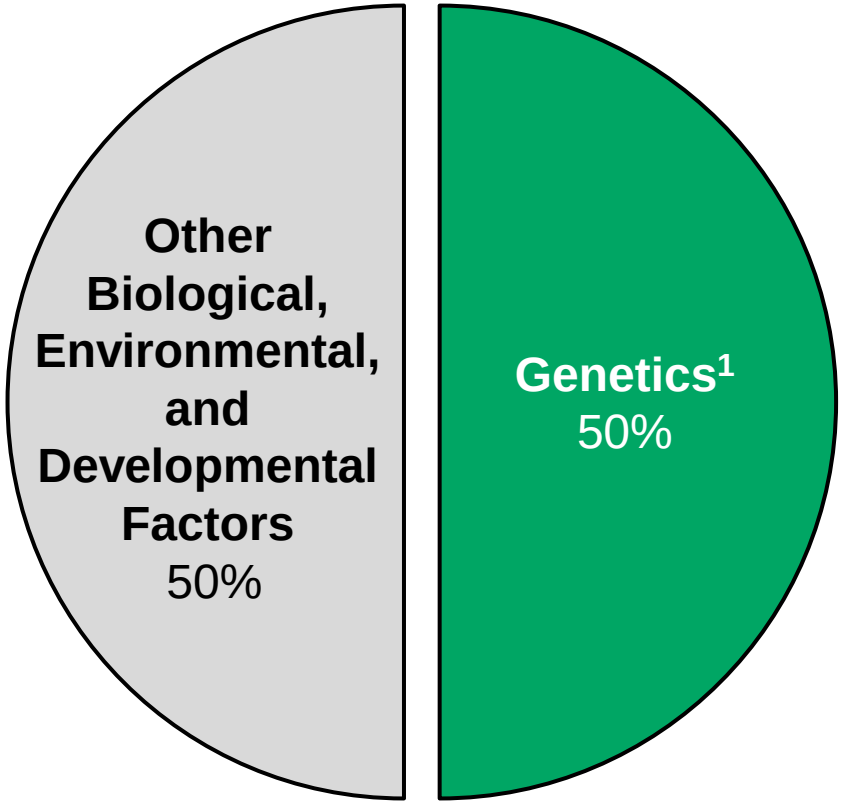
Current Risk Assessments Fail to Assess for Genetics



Genes can account for ~50% of risk for addiction[1]

1. Berrettini 2017

AvertD Would Enable Physicians to Factor in Genetic Component of OUD Risk



AvertD assesses genetic risk of a patient developing OUD with high diagnostic odds ratio (18 X)

1. Berrettini 2017

Potential Risks of AvertD Can Be Mitigated Through Proper Use, Labeling, and Education

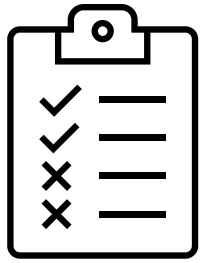
False Negative	False Positive	Overreliance, Misinterpretation, Incorrect Action
▪ Clinicians following current standard of care for prescribing oral opioids ▪ Mitigated through proper use, labeling, and education	▪ Sufficient non-opioid alternatives exist for managing acute pain ▪ If pain management with non-opioid alternatives is insufficient, decision to avoid opioids could be reassessed	▪ Proposed labeling and educational materials describe how test results should be interpreted and used

Individualized Assessment of Risks/Benefits of Surgical Intervention Must Include Post-Operative Pain Control

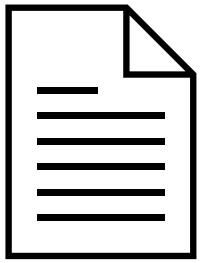
- Many patients inquire about personal risks of opioid usage
- Currently limited in ability to assess risks
- Prescribing guidelines advise to minimize opioid exposure
- Genetic risk information is increasingly used to present comprehensive precision-medicine solutions to patients
  - Oncologists use BRCA1 / BRCA2
  - Neurologists use APOe4

AvertD Would Enhance Ability to Assess a Patient's Risk of Developing OUD

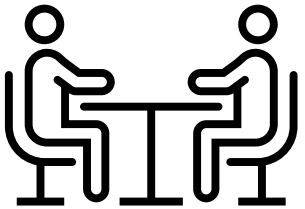
Patient undergoes risk assessment for OUD, including AvertD, as part of complete clinical evaluation



AvertD test results returned to provider



Provider and patient discuss overall risk of developing OUD, including genetics



If low risk

Follow current standard of care guidelines for acute pain

If high risk

Develop personalized pain management plan to minimize or avoid use of opioids

AvertD™
Genetic Risk Assessment Test for Opioid Use Disorder

October 20, 2022

Clinical Chemistry and Clinical Toxicology Devices Panel

SOLVD Health