Prediction of opioid-related overdose and suicide events using administrative healthcare data

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HEROIC
HEALTH EQUITY AND RURAL OUTREACH INNOVATION CENTER
CHARLESTON VA HSR&D COIN

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Stratification Tool for Opioid Risk Management (STORM)

Psychological Services
2017, Vol. 14, No. 1, 34–49

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Development and Applications of the Veterans Health Administration's Stratification Tool for Opioid Risk Mitigation (STORM) to Improve Opioid Safety and Prevent Overdose and Suicide

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- Clinical decision support tool
- Uses VHA EMR data extracts
- Estimate patient risk for an overdose or suicide-related events
- Provide actionable information for risk-stratified intervention
- Help providers prioritize clinical resources.

Potential limitations:

- Heavy reliance on ICD codes
- Relies on VHA pharmacy data
- Basic statistical modeling approach, combined outcome

ICD codes can lead to under-reporting

- Reliance on International Classification of Disease (ICD) codes to identify disease conditions can lead to under-reporting because:
  - Administrative codes are not consistently recorded, especially for secondary diagnoses
  - Dual-healthcare system users often have fragmented records not fully available within the VA Corporate Data Warehouse (CDW).

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  - Administrative codes are not consistently recorded, especially for secondary diagnoses
  - Dual-healthcare system users often have fragmented records not fully available within the VA Corporate Data Warehouse (CDW).
- Example:
  - Only 46.1% of VISN 7 Veterans with drug overdose from any drug class in 2018 had any prior diagnosis of substance use disorder.
  - Only 10.9% of VISN7 Veterans with opioid overdose in 2018 carried prior ICD-10 codes for opioid use disorder (OUD).

Non-VHA pharmacy data may be helpful

- Dual pharmacy system utilization may be associated with:
  - higher morphine equivalent daily doses (MEDD)[1]
  - higher risk for overdose mortality[2]
    - Dual VHA-Part-D Medicare users had significantly higher odds of death from prescription opioid overdose than those who received opioids from VA only (odds ratio [OR], 3.53 [95% CI, 2.17 to 5.75]; P < 0.001) or Part D only (OR, 1.83 [CI, 1.20 to 2.77]; P = 0.005).

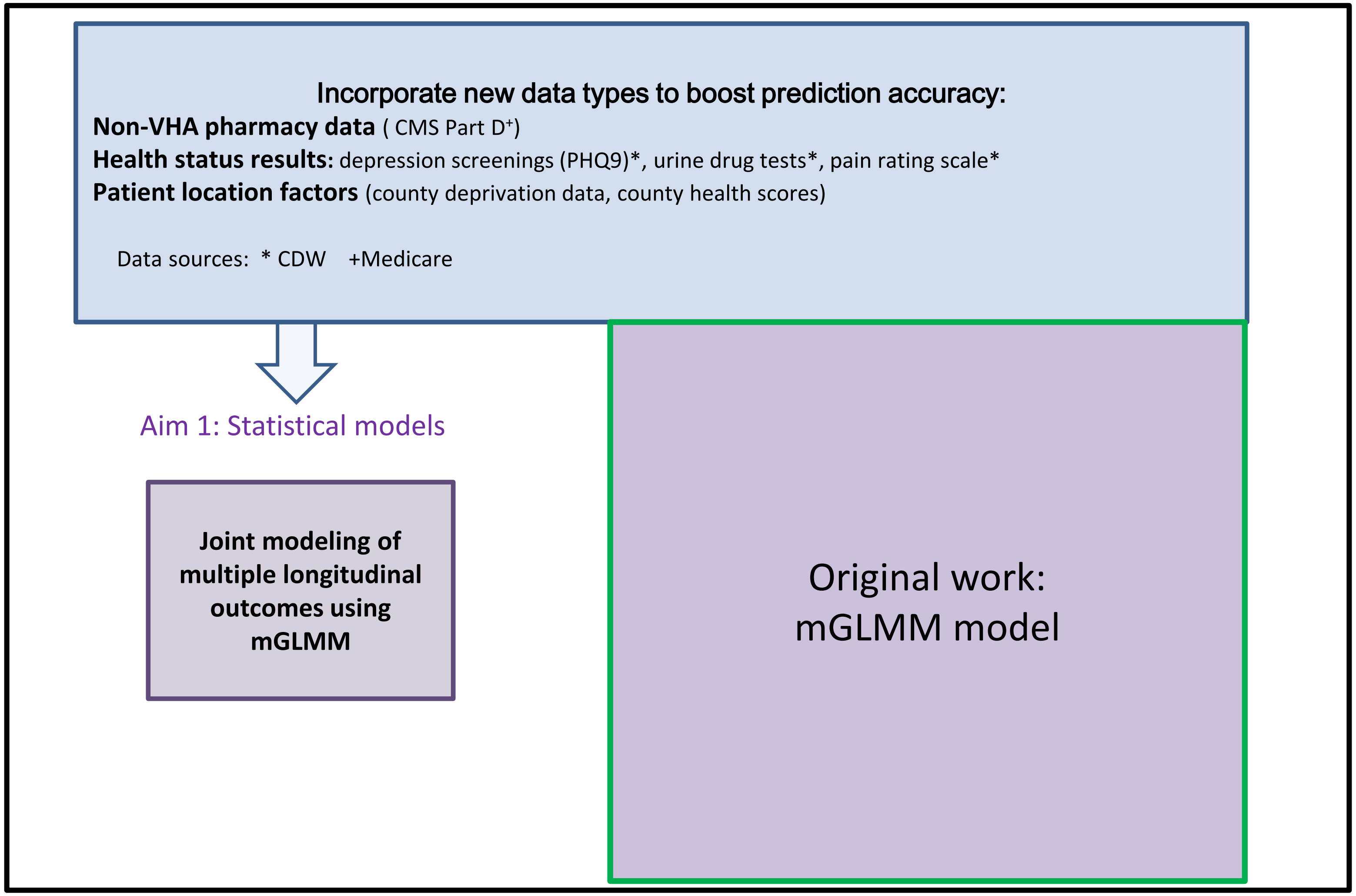
[1]Moyo, P., Zhao, X., Thorpe, C. T., Thorpe, J. M., Sileanu, F. E., Cashy, J. P., Hale, J. A., et al. (2019). Dual Receipt of Prescription Opioids From the Department of Veterans Affairs and Medicare Part D and Prescription Opioid Overdose Death Among Veterans: A Nested Case-Control Study. *Annals of internal medicine*, *170*(7), 433–442.

[2]Gellad, W. F., Thorpe, J. M., Zhao, X., Thorpe, C. T., Sileanu, F. E., Cashy, J. P., Hale, J. A., et al. (2018). Impact of Dual Use of Department of Veterans Affairs and Medicare Part D Drug Benefits on Potentially Unsafe Opioid Use. *American Journal of Public Health*, 108(2), 248–255.

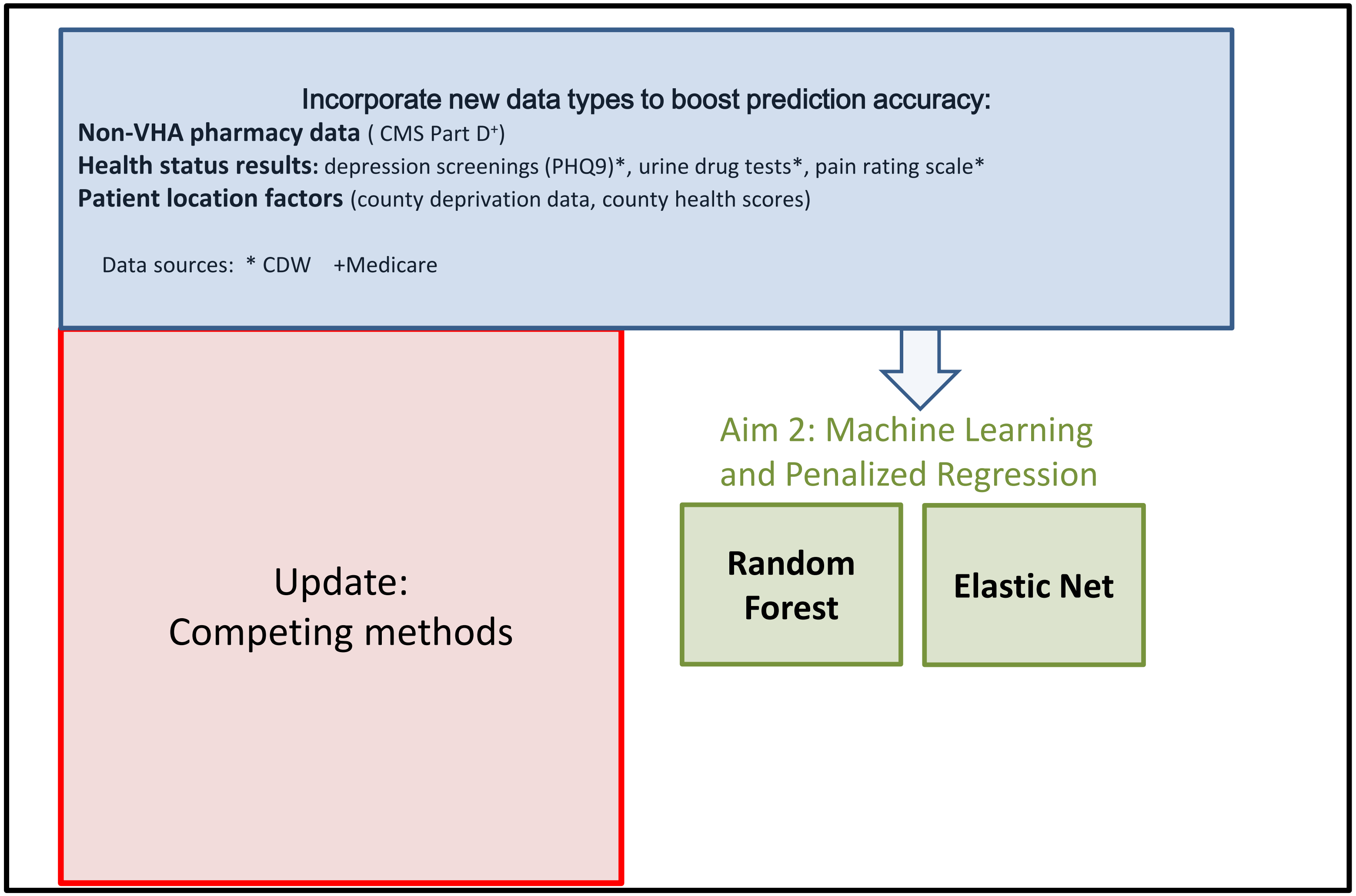
Goals:

Develop improvements to existing prediction models for opioid-related adverse outcomes:

1. Incorporate new predictors available in CDW and Medicare data that are strongly associated with opioid-related outcomes
2. Apply advanced statistical, machine learning and ensemble methods.

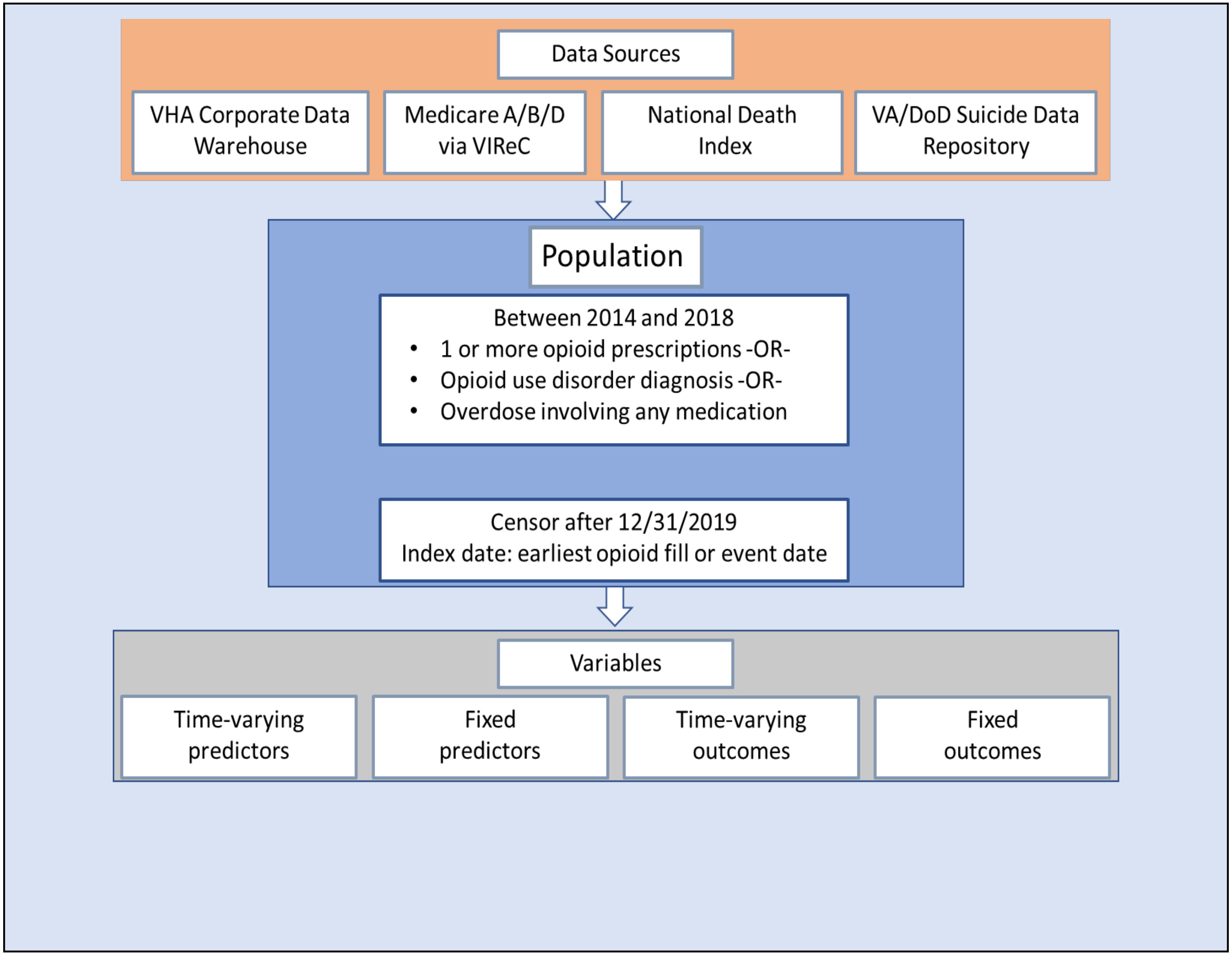


Ward, R., Weeda, E., Taber, D. J., Axon, R. N., & Gebregziabher, M. (2022). Advanced models for improved prediction of opioid-related overdose and suicide events among Veterans using administrative healthcare data. *Health services and outcomes research methodology*, *22*(2), 275–295.



Incorporate new data types to boost prediction accuracy:
Non-VHA pharmacy data (CMS Part D+)
Health status results: depression screenings (PHQ9)*, urine drug tests*, pain rating scale*
Patient location factors (county deprivation data, county health scores)
Data sources: * CDW +Medicare
Update:
Competing methods
Aim 2: Machine Learning and Penalized Regression
Random Forest
Elastic Net

Data sources and cohort description



2017 STORM Model Predictors

Demographic	Sex
	Age
	Location (VISN and Station)
Prior event risk indicators	
	Overdose or suicide event (combined) in year prior
	Falls / accidents in year prior
Prescription related	
	Opioid therapy type (long vs short acting; acute vs long term)
	Morphine equivalent daily dose
	Co-prescription of opioids and sedatives
	Number of sedative classes prescribed
Substance use disorders	
	Opioid use disorder
	Alcohol use disorder
	Tobacco use disorder
	Sedative use disorder
	Stimulant use disorder
	Cannabis/hallucinogen use disorder
	Other SUD
MH disorders	
	PTSD
	Major depressive disorder
	Bipolar disorder
	Other MH disorder
Medical Comorbidities	
	31 Elixhauser comorbidities diagnosed year prior
Treatments	
	Detoxification treatment in year prior
	Inpatient MH treatment in year prior
Utilization	
	ER visit in year prior

2017 STORM Model Predictors		Additional Predictors / Data sources
Demographic	Sex Age Location (VISN and Station)	Race and ethnicity, Service-related disability percentage Marital status, urban-rural location, County and census tract deprivation / socio-economic var.
Prior event risk indicators	Overdose or suicide event (combined) in year prior Falls / accidents in year prior	Separate prior outcomes (SRE and OD)
Prescription related	Opioid therapy type (long vs short acting; acute vs long term) Morphine equivalent daily dose Co-prescription of opioids and sedatives Number of sedative classes prescribed	Opioid classes (long acting and short acting) (9 classes) Positive urine lab results (14 medication classes) Other medication classes (8 classes) **CMS Part D data**
Substance use disorders	Opioid use disorder, Alcohol use disorder, Tobacco use disorder, Sedative use disorder, Stimulant use disorder, Cannabis/hallucinogen use disorder, Other SUD.	
		Lab Results / Health Factors Urine drug tests Numeric pain scale (1-10)
MH disorders	PTSD Major depressive disorder Bipolar disorder Other MH disorder	**Screening results:** Suicide ideation (C-SRRS, PHW2+I9, PTSD-5+I9) Brief addiction measure (BAM) Depression (PHQ9)
Medical Comorbidities	31 Elixhauser comorbidities diagnosed year prior	**Baseline conditions or those developed within 1 year prior** **Chronic pain** **CMS** diagnoses
Treatments	Detoxification treatment in year prior Inpatient MH treatment in year prior	
Utilization	ED visit in year prior	**CMS** ED visits, Inpatient and outpatient utilization (VHA+**CMS**)

Chronic pain algorithm*

(1) Single occurrence of an ICD-9 or ICD-10 code shown to be highly likely to represent chronic pain, **or**

(2) Two or more occurrences of ICD codes shown to be likely to represent chronic pain, separated by at least 30 days, **or**

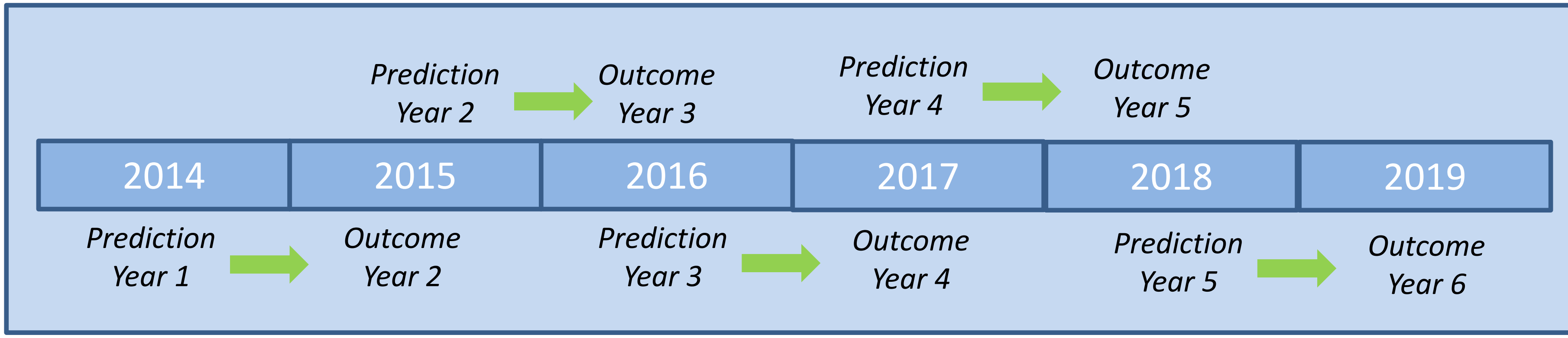
(3) Receipt of at least 90 days of opioid medication, **or**

(4) One occurrence of an ICD code likely to represent chronic pain AND two or more numeric pain scores of 4 or higher more than 30 days apart.

Patients were not considered to have chronic pain until 90 days had passed after any surgery

*Tian, T.Y., Zlateva, I., Anderson, D.R.: Using electronic health records data to identify patients with chronic pain in a primary care setting. *J Am Med Inform Assoc* 20, e275–e280 (2013). https:// doi. org/ 10. 1136/ amiaj nl- 2013- 001856

Longitudinal design: previous year's variables used to predict following year's outcomes



One patient's data (up to 5 rows):

Yearly predictors	Next year outcomes
Year 1	**Year 2**
2	**3**
3	**4**
4	**5**
5	**6**

Aim 1 Method: mGLMM model

$$\log it\left(Y_{ij}^{1}\right) = \beta_0^1 + b_0 + \beta_1^1 t_j + \beta_2^1 x_i,$$

$$\log it\left(Y_{ij}^{2}\right) = \beta_0^2 + b_0 + \beta_1^2 t_j + \beta_2^2 x_i$$

Multivariate generalized linear mixed model

- Two outcomes (1=OD and 2=SRE) modeled jointly
- Shared random intercept (b_0)
- Patient i and year j
- Separate fixed parameter estimates for each outcome
- Assumes a latent relationship between outcomes

Aim 2 Methods: Random Forest algorithm

- 500 independent decision trees used to train a 'forest' to determine which predictors are most important in classifying a known outcome
- In each tree, part of the data is held out (termed 'out of bag') and used to test that tree's predictive performance on new data.
- Inherent ability to handle collinearity and account for interactions
- Out of bag results for the full forest are equivalent to cross validation results
- The 'forest' can then be used to make predictions for new data.

Aim 2 Methods: Elastic net penalized regression

- Method designed to 'shrink' some estimates to 0 based on their lower importance in predicting the outcome of interest.
- Related methods are LASSO and Ridge Regression; each is optimal in certain situations. Elastic net is a compromise between them.
- Model is first 'tuned' using a cross-validation step to find the best performing model parameters

Population summary

Population characteristics		≥1 overdose	≥1 suicide related event	Overall
Group size		165,680(9.5%)	97,688 (5.6%)	**1,744,667**
Race ethnicity	Non-Hispanic White	122,429 (10.2%)	64,073 (5.3%)	1,203,231 (69.0%)
	Non-Hispanic Black	31,688 (8.4%)	23,681 (6.3%)	375,726 (21.5%)
	Hispanic	6,738 (6.9%)	6,207 (6.4%)	97,052 (5.6%)
	Other	4,525 (6.6%)	3,727 (5.4%)	68,658 (3.9%)
Age category	Under 30	3,468 (4.5%)	7,806 (10.1%))	76,982 (4.4%)
	30 - 50	18,185 (5.3%)	27,567 (8.1%)	341,299 (19.6%)
	51- 65	61,206 (9.4%)	43,441 (6.6%)	653,531 (37.5%)
	Over 65	82,521 (12.3%)	18,874 (2.8%)	672,855 (38.6%)
Sex	Female	12,866 (8.0%)	11,772 (7.3%)	160,905 (9.2%)
	Male	152,514 (9.6%)	85,916 (5.4%)	1,583,762 (90.8%)
Marital status	Married	78,081 (9%)	33,570 (3.9%)	867,356 (49.7%)
	Unmarried	87,299 (10%)	64,118 (7.3%)	877,311 (50.3%)
Service related disability	< 50%	87,999 (9.6%)	42,347 (4.6%)	913,268 (52.4%)
	≥50%	77,381 (9.3%)	55,341 (6.7%)	831,399 (47.7%)
Opioid from CMS source	No	134,290 (8.7%)	82,836(5.4%)	1,534,951 (88.0%)
	Yes	31,090 (14.8%)	14,852 (7.1%)	209,716 (12.0%)

Population summary

Population characteristics		≥1 overdose	≥1 suicide related event	Overall
Group size		165,680(9.5%)	97,688 (5.6%)	**1,744,667**
Chronic Pain	Not diagnosed	11,168 (4.3%)	5,096 (1.9%)	272,190 (15.6%)
	Likely	84,331 (7.8%)	46,802 (4.3%)	1,077,561 (61.8%)
	Highly Likely	69,281 (17.5%)	45,790 (11.6%)	394,916 (22.6%)
Prior events	Overdose	52,033 (40.5%)	22,093 (17.2%)	128,479 (7.4%)
	Suicide-related	22,977 (29.7%))	39,087 (50.5%)	77,401 (4.4%)

Prediction performance

Original results:

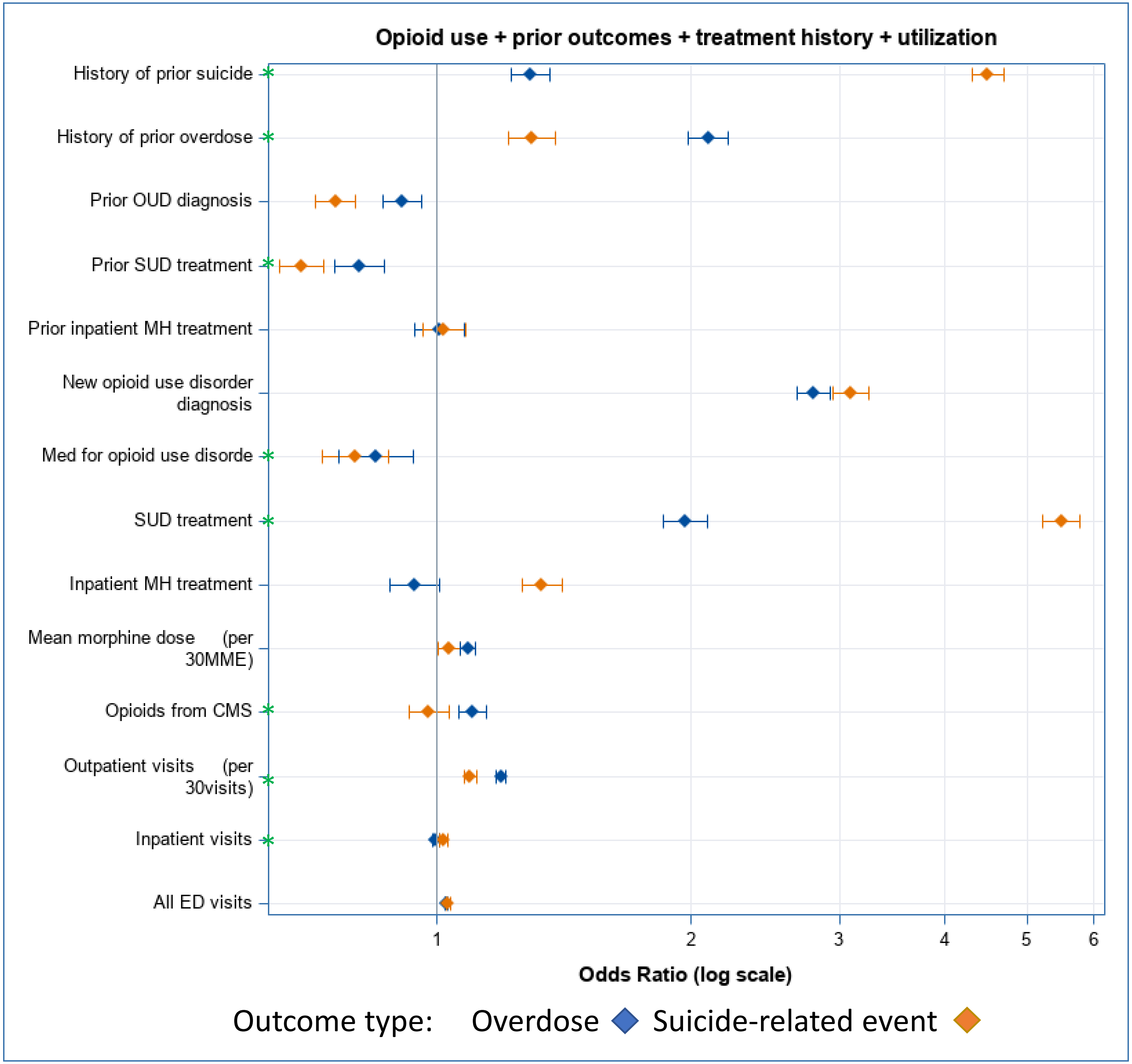
Performance measures using validation data at optimized threshold probability (maximum Youden score)	mGLMM	STORM
Area under the ROC curve (AUC) (95% confidence interval)	0.838 (0.836, 0.840)	0.757 (0.754, 0.760)
Sensitivity	0.71	0.68
Specificity	0.81	0.70
Precision (PPV)	0.09	0.11
Negative predictive value (NPV)	0.99	0.98
Number needed to evaluate	10.79	9.36

Machine Learning and penalized regression results:

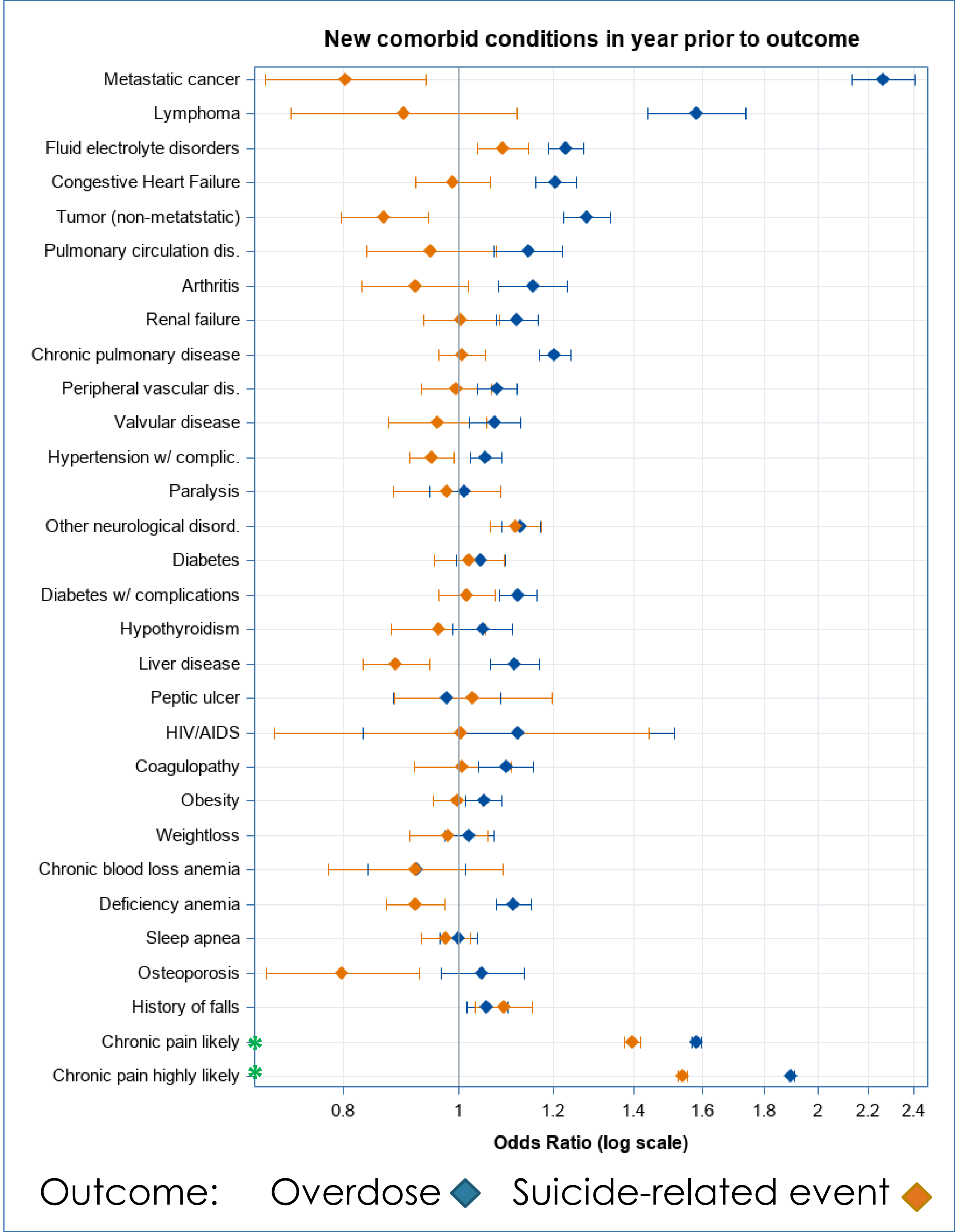
Performance measures using validation data at optimized threshold probability (maximum Youden score)	Random Forest	Elastic Net
Area under the ROC curve (AUC) (95% confidence interval)	0.835 (0.831, 0.838)	0.826 (0.825, 0.827)
Sensitivity	0.76	0.67
Specificity	0.81	0.80
Precision (PPV)	0.07	0.05
Negative predictive value (NPV)	0.99	0.99
Number needed to evaluate	14.4	18.3

mGLMM

* = new predictor

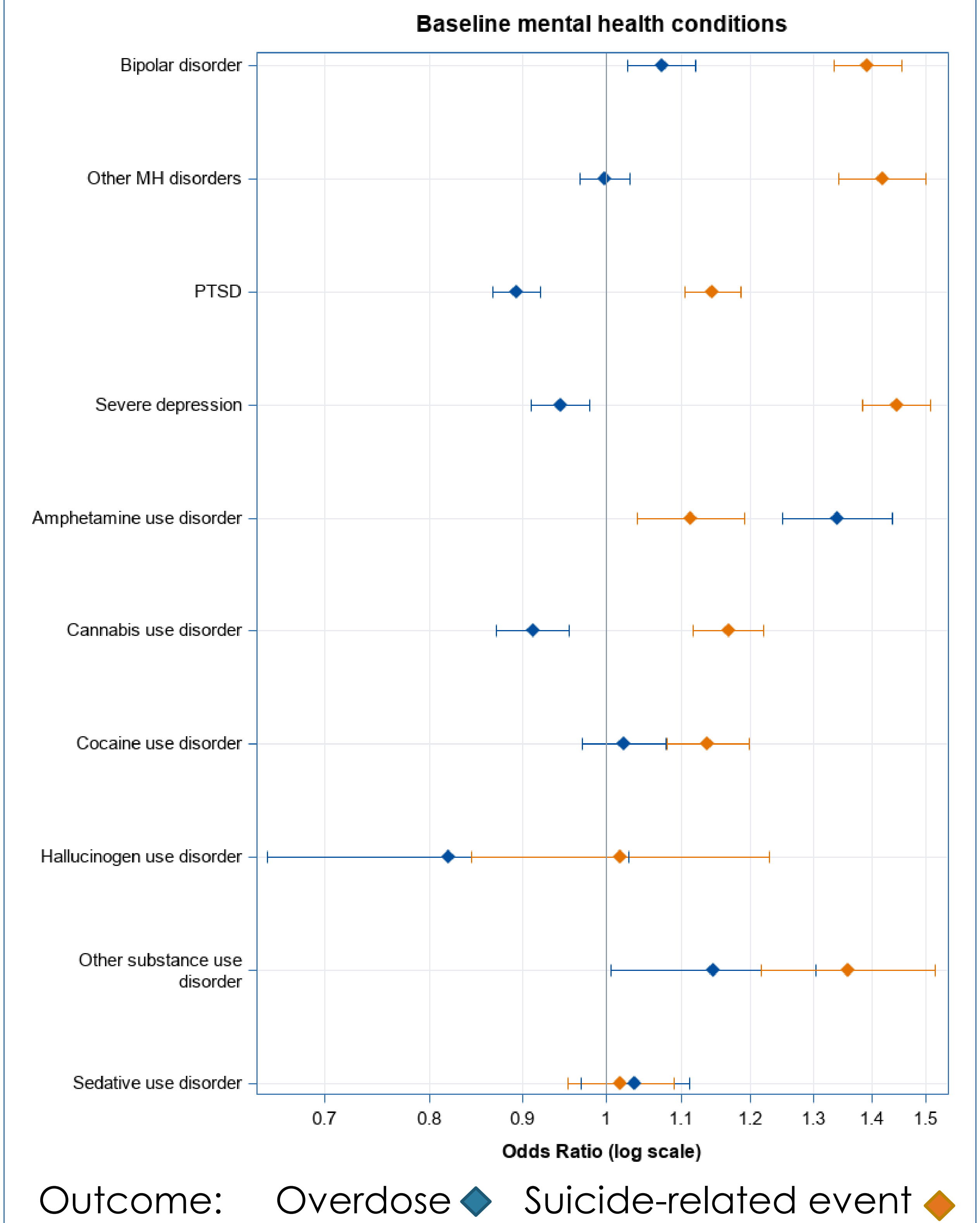


mGLMM



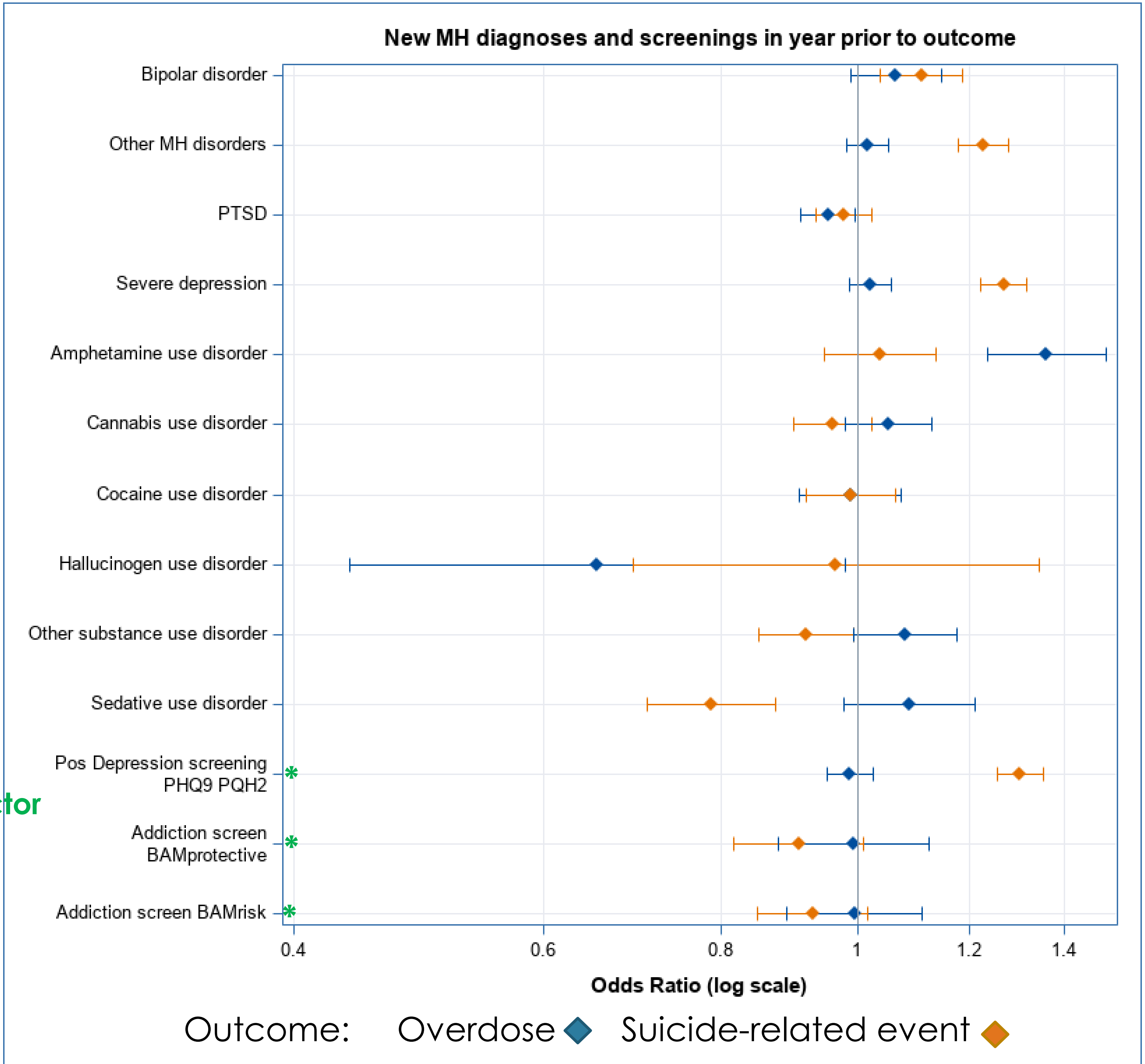
* = new predictor

mGLMM



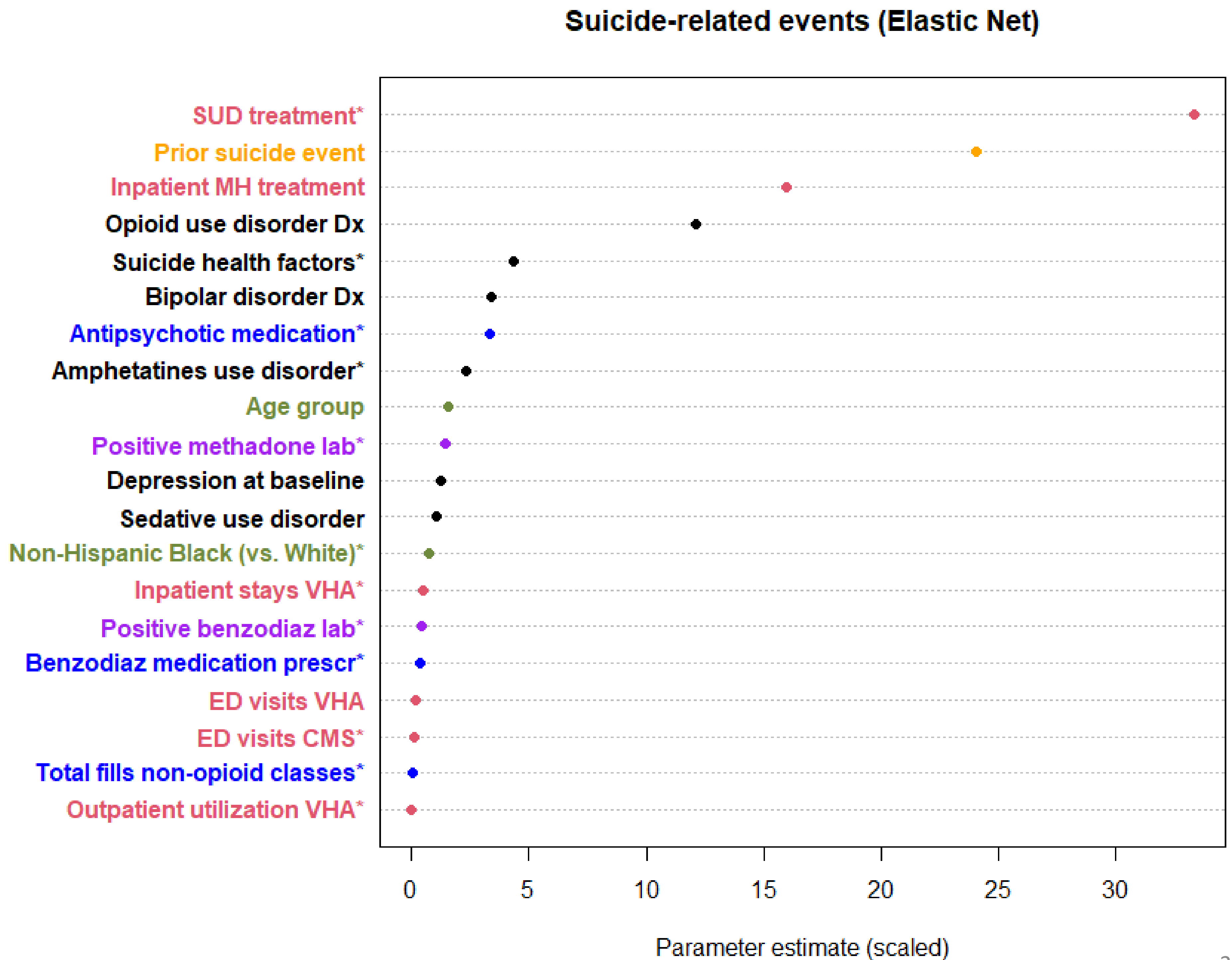
Baseline mental health conditions
Bipolar disorder
Other MH disorders
PTSD
Severe depression
Amphetamine use disorder
Cannabis use disorder
Cocaine use disorder
Hallucinogen use disorder
Other substance use disorder
Sedative use disorder
0.7
0.8
0.9
1
1.1
1.2
1.3
1.4
1.5
Odds Ratio (log scale)
Outcome:
Overdose
Suicide-related event

mGLMM

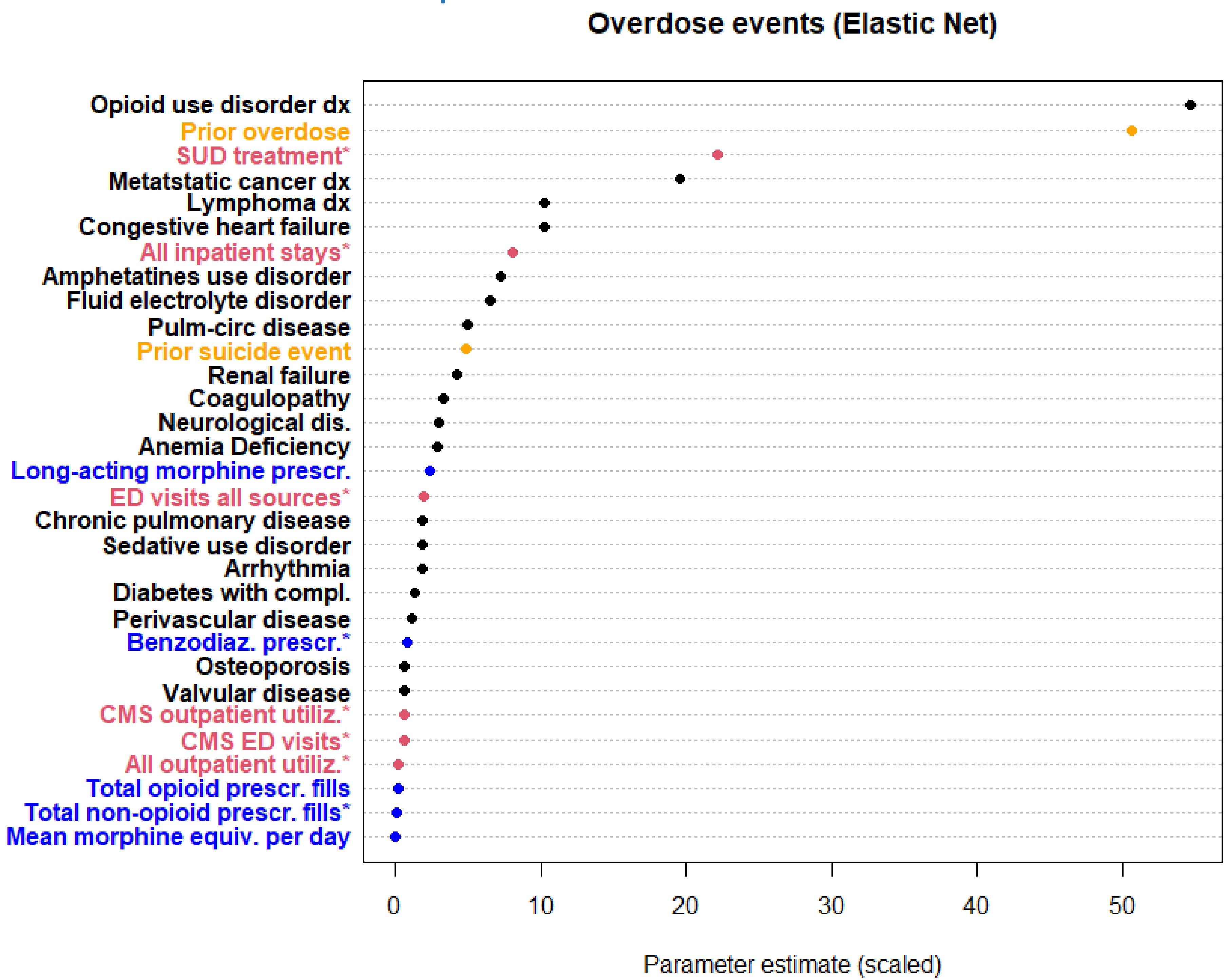


* = new predictor

Elastic Net: Variable importance



Elastic Net Variable importance



Conclusions

- RF and Elastic Net performance similar overall to mGLMM
  - Elastic Net model results may be easier to interpret
- Separate analysis of OD and suicide related outcomes provides new insights how one risk factor can have differing impacts
- Confirmed importance for new predictors and data sources:
  - Screening results for depression /suicide risk
  - Positive urine screening results
  - Opioid types and co-prescribed medication classes
  - Inpatient and outpatient utilization (beyond ED visits)
  - CMS data (especially for OD prediction)

Further challenges

- Implementation (some common reviewer responses)
  - 'Prediction model is a black box: does it make clinical sense?'
  - 'Model is too complex to be clinically useful: could not run it in real time' (not true: original model development is time intensive, but not new predictions from that model)
- Addressing potential subgroup bias: is the model fair to all groups? (we found bias when comparing age group predictions)
- Evolving opioid crisis: opioid related overdoses much more likely to involve illicit & synthetic opioids (fentanyl)
  - Older models may not have continued validity in new risk landscape
  - Pharmacy data could be less important

Questions?

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Back-up slides

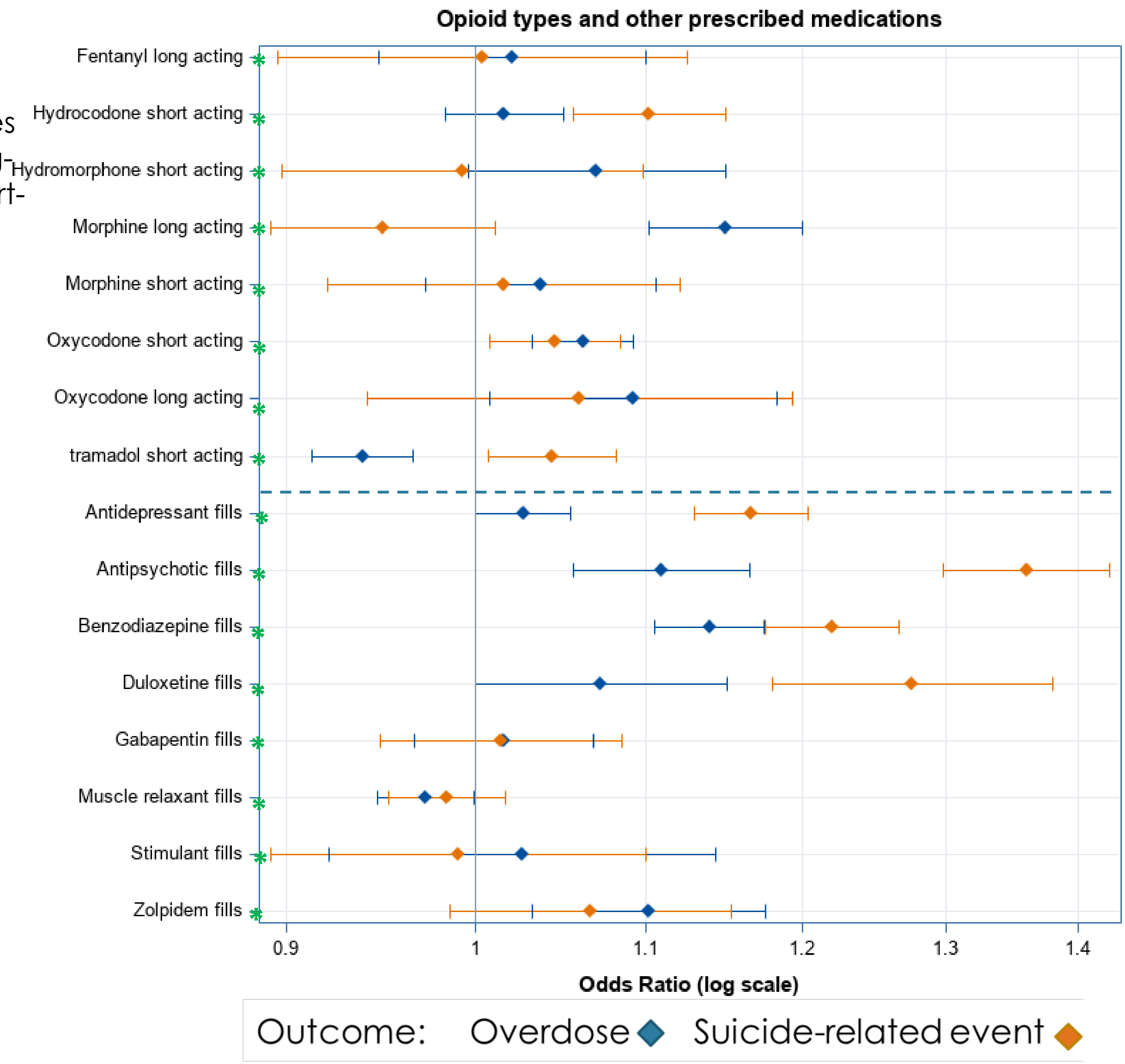
* = new predictor

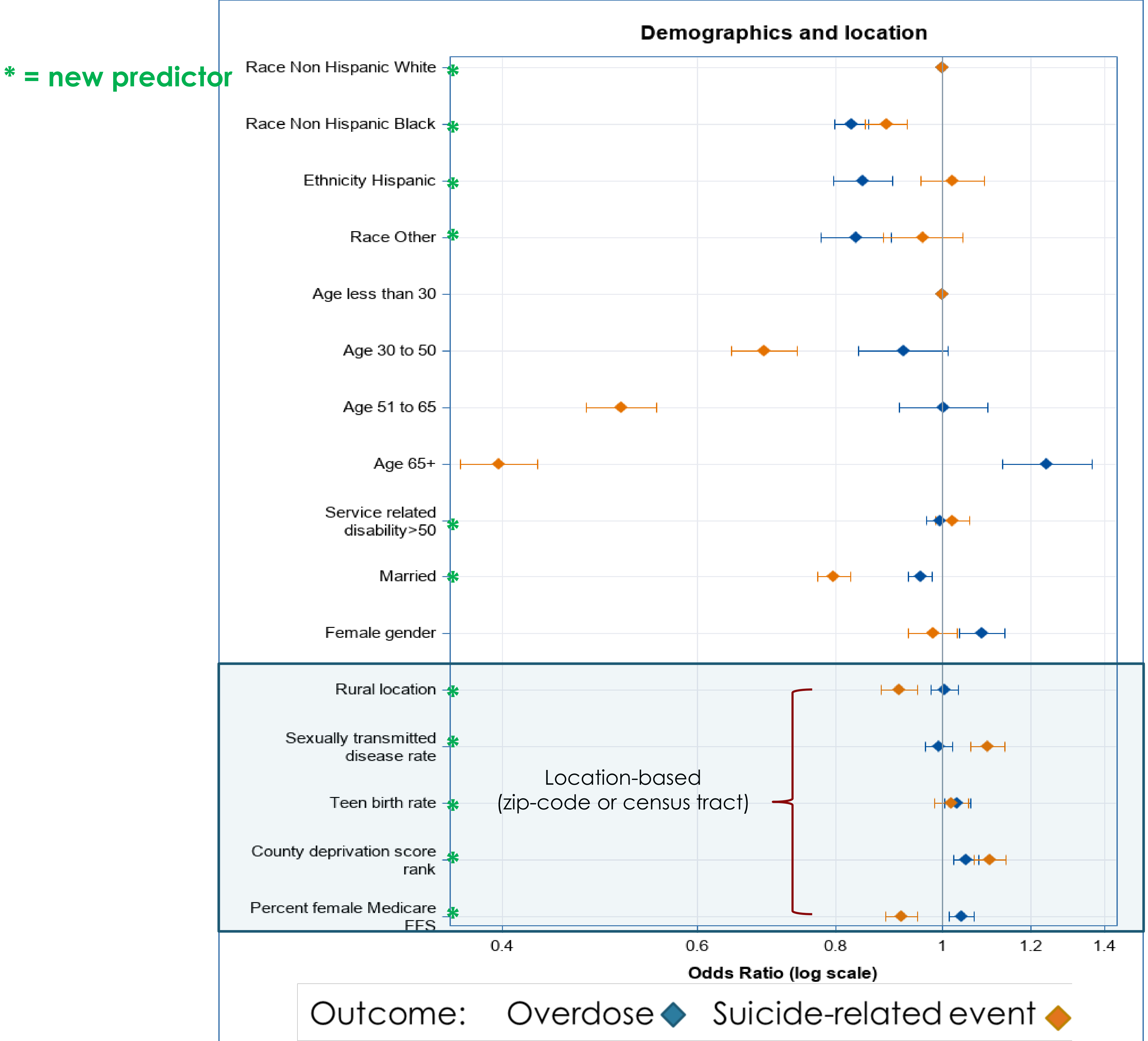
Opioids

STORM categorizes opioid use as long-acting, acute short-acting, chronic short-acting, or tramadol

Other medications

STORM has a single variable that accounts for numbers of sedative classes





* = new predictor
Demographics and location
Race Non Hispanic White
Race Non Hispanic Black
Ethnicity Hispanic
Race Other
Age less than 30
Age 30 to 50
Age 51 to 65
Age 65+
Service related disability>50
Married
Female gender
Rural location
Sexually transmitted disease rate
Teen birth rate
County deprivation score rank
Percent female Medicare FFS
Location-based
(zip-code or census tract)
0.4
0.6
0.8
1
1.2
1.4
Odds Ratio (log scale)
Outcome: Overdose Suicide-related event