USING PREDICTIVE MODELS AND LINKED DATASETS TO UNDERSTAND

RISK OF FATAL OPIOID OVERDOSE

by
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A dissertation submitted to Johns Hopkins University in conformity with the requirements
for the degree of Doctor of Public Health

Baltimore, Maryland
August 2019

Abstract

Problem Statement

The opioid crisis has had a devastating impact on the United States that will span generations. Public health agencies are increasingly looking toward data-driven solutions to understand risk factors, identify high-risk individuals, and direct interventions. Leveraging data captured by public health, healthcare, and other social and human service agencies will be increasingly common, as will applying sophisticated risk modeling to predict outcomes. This dissertation examines risk factors and models in the literature, compares multivariate predictive models with existing threshold-based risk identification, and measures the impact patient matching algorithms have on understanding risk when linking disparate patient-level datasets together.

Methods

A comprehensive review of the literature from 2008-2018 examined predictive model variables and performance related to opioid overdose using prescription history and other data sources. Using 2015 Maryland Prescription Drug Monitoring Program (PDMP) data and 2015-2016 death data, multiple risk identification methods for fatal opioid overdose were quantified and compared, including a multivariate risk model and common prescription-based thresholds. Finally, criminal justice data from 2013-2015 were matched with PDMP data at the patient-level using three matching algorithms to understand the impact on risk indicator prevalence and performance of a risk model.

Results

Risk models are increasingly being explored in the literature in recent years, although most use a payer-specific cohort and risk factor and measure definitions were inconsistent. Generally, risk models identified more individuals at risk of a fatal opioid overdose than simple risk thresholds, however, there may be value in combining the risk model with simple thresholds to identify high-risk individuals. Finally, the probabilistically matched population resulted in the highest degree of matching with arrest and death data, although risk model performance was comparable across all algorithms.

Conclusions

These results illustrate the ways predictive models based on PDMP data can assist with identifying high-risk individuals as a standalone tool or in combination with other risk stratification methods. The matching technique used to link person-level data across disparate data together affects the risk prevalence and factors, although model performance indicates a basic deterministic matching algorithm may be a suitable approach depending on resource constraints and scope of analysis.

Thesis Advisors

Jonathan Weiner, DrPH

Brendan Saloner, PhD

Hadi Kharrazi, MD PhD

Elizabeth Stuart, PhD

Amanda Latimore, PhD

Acknowledgements

I want to first acknowledge the humanity behind the data in this analysis. The outcome being analyzed, fatal opioid overdose, are lives that have been lost to a devastating addiction. I am hopeful that the many brilliant and passionate people focused on addressing this issue will alleviate some of the pain felt by so many people, families, and communities.

To my husband, Tim, for his love, patience, and support throughout the six years I worked toward one of my longest-standing life goals. I could not have asked for a more thoughtful, understanding, and hard-working human being to spend life with and cannot wait to see what the future holds. Thank you for everything you have done while I buried my head in research and writing – I love you with all my heart!

To my mother, Linda, who has been one of the greatest influences on my life. Watching you push through the rigors of a Ph.D. during my childhood seeded my passion to pursue an advanced degree. Thank you for everything you sacrificed over the years to give me (and Rob) every opportunity to pursue our goals and mature as human beings. It is wonderful to see you so happy with Les, who I am thankful to have as part of our family.

To my brother, Rob, who I have looked up to since I came into this world. I could not have asked for a better best friend, teacher, and role model in life. Thank you for the words of encouragement, thoughtful review and discussion of my work, and motivational photos. I am still your biggest fan! And one of the smartest things you have ever done was to fall in love with and marry Jenny, who I love dearly and am lucky to call my sister-in-law.

To my father, Joe, who I wish I could have shared every step of this experience with. I love you and miss you every day. Thank you for instilling a sense of curiosity and drive in me. You are one of the most brilliant minds I have ever known, and I am lucky to have had you in my life.

Thank you to my friends and extended family for checking in on me, being incredibly patient, and offering reassurance during this long and intense process. I cannot thank my CRISP and Ai work families enough for taking my mind off school during the day, frequent trips to Aida's, and unquestionable patience and support in my pursuit of this degree. A big thank you to my colleagues who had direct involvement in helping to make my research possible, especially Aya Watanabe and Raina Sharma. Thank you to my partners at the Maryland Department of Health for your expertise and support, particularly Kate Jackson and Casey Lyons. None of this would have been possible without you.

My utmost appreciation goes to my advisor, Dr. Jonathan Weiner. I am very lucky to have stumbled across your faculty page as an MPH student in 2010 and am so thankful you took a chance on me. You always found the right balance of providing direction versus freedom and encouragement or a nudge. Thank you for guiding me through this intense journey!

Thank you so much to my incredible committee members, Drs. Hadi Kharrazi, Brendan Saloner, Liz Stuart, and Amanda Latimore. I could not have asked for a more brilliant, dedicated, and kind group of people to guide me through the dissertation process. I sincerely appreciate all the time and effort you put into providing feedback and helping me work through my analyses and interpretations. You all have been instrumental in shaping my dissertation and I could not have arrived at the end-product without your expert input!

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Introduction

Opioid addiction and overdose have taken a substantial toll on the health and welfare of the United States population. Between 1999 and 2017, the number of prescription opioid-related deaths grew over five-fold, reaching epidemic proportions.[3] In 2017, the total number of deaths due to drug overdose in the U.S. was 70,237, of which 47,600 (67.8%) involved opioids.[1] It is estimated that the aggregate societal cost of prescription opioid use disorder, including health care utilization, criminal justice spending, and lost work productivity, is $78.5 billion (2013 dollars).[4] The devastating impact of opioid abuse on individuals, families, and institutions has substantially increased the need for effective data-driven solutions for the purpose of deploying evidence-based interventions.

Addressing the epidemic requires a multi-faceted approach. According to the Centers for Disease Control and Prevention (CDC), overdose deaths are best prevented though improved prescribing of opioids, preventing individuals from developing an opioid use disorder, reversing overdoses through the use of naloxone, and providing treatment to individuals with opioid use disorder.[5] Public health strategies build upon these concepts by highlighting the importance of capturing data across service systems, engaging and reforming criminal justice to offer treatment in jails and prisons, expanding programs that divert individuals to treatment instead of incarceration, and aligning regulations with evidence-based best practices.[6] Deploying evidence-based strategies to combat the opioid epidemic rely upon data inputs to identify underlying risk factors and appropriately respond to the unique conditions of the target population.

Historically, data analyses have largely utilized payer claims or electronic health record (EHR) datasets when evaluating risk factors due to ease of accessibility and availability.[7-10]

However, use of statewide datasets will allow for a more complete picture of risk. State Prescription Drug Monitoring Programs (PDMPs), which collect controlled substance histories from in-state and mail-order pharmacies, are increasingly being leveraged as a source of data to understand risk factors.[11] Operationally, many PDMP programs have existing processes to identify high risk patients that meet simple thresholds, such as exceeding average daily morphine milligram equivalents or interacting with multiple unique prescribers and dispensers in a specific time period. The identities of patients identified as high risk according to the thresholds are communicated by the PDMP program to the healthcare practitioners interacting with the patient to bring attention to potential misuse or abuse. Advancing this concept, predictive models are being explored in the literature as a way to compound multiple risk factors for an individual into a calculated score that is quantifiable and comparable for a particular outcome.[7-12] The potential for predictive models to accurately identify high-risk populations holds promise for better direct interventions to those in need.

Efforts to combat the crisis have evolved to encompass more multidisciplinary interventions, increasing the need to share person-level data maintained by various public health, health, and human service agencies. Statutory mandates that require multiple agencies to share and analyze person-level data to better understand risk, inform policy decisions, and direct interventions have begun to emerge in states, as seen with the Massachusetts Chapter 55 and Maryland Chapter 211 efforts.[13,14] Utilizing risk factors and outcomes from multiple datasets is also present in the literature, often combining prescription history (PDMP or claims) with death data and/or hospital data.[11,15,16]

With the emergence of national guidelines and policy initiatives supportive of increased data exploration and sharing across disciplines, attention will need to be paid to the risk identification strategies and how person-level data are combined for analysis. Results of this study will provide public health insight into opioid overdose predictive model variables and performance, compare different techniques to identify individuals at risk of fatal opioid overdose; and provide insight into the importance of how datasets from multiple domains come together.

Thesis Contributions

Public health's ability to identify individuals at risk to better direct resources is crucial to curbing fatal opioid overdose. The epidemic requires a data-driven public health response that considers the unique circumstances of a geographically defined population. The availability of statewide datasets, such as PDMPs, and the push toward cross-disciplinary data sharing has advanced this cause. Public health has the opportunity to apply sophisticated approaches to risk identification and data matching that can maximize available resources and deploy interventions in the most efficient manner. Understanding the impact of different approaches in these domains is vital when making critical decisions in a resource-constrained environment. The primary objectives of this study are to: 1) summarize and quantify predictive models based on opioid-related overdose risk factors in the literature; 2) compare the performance of multiple risk identification methods for fatal opioid overdose, including a sophisticated predictive risk model and several simplistic threshold-based risk indicators; and 3) quantify the impact of using a probabilistic versus two variations of deterministic matching algorithms has on identifying persons at risk of fatal opioid overdose when combining disparate person-level datasets together.

References

1. CDC National Center for Health Statistics. Wide-ranging online data for epidemiologic research (WONDER). http://wonder.cdc.gov. Updated 2016.

2. Scholl L, Seth P, Kariisa M, Wilson N, Baldwin G. Drug and opioid-involved overdose deaths — United States, 2013–2017. 2019;67:1419–1427.

3. Florence CS, Zhou C, Luo F, Xu L. The economic burden of prescription opioid overdose, abuse, and dependence in the united states, 2013. *Med Care*. 2016;54(10):901-906.

4. Centers for Disease Control and Prevention. Overdose prevention. https://www.cdc.gov/drugoverdose/prevention/index.html. Updated August 31, 2017.

5. Saloner B, McGinty EE, Beletsky L, et al. A public health strategy for the opioid crisis. *Public Health Reports*. 2018;133(1_suppl):24S-34S.

6. Bohnert AS, Logan JE, Ganoczy D, Dowell D. A detailed exploration into the association of prescribed opioid dosage and overdose deaths among patients with chronic pain. *Med Care*. 2016;54(5):435-441.

7. Liang Y, Goros MW, Turner BJ. Drug overdose: Differing risk models for women and men among opioid users with non-cancer pain. *Pain Med*. 2016;17(12):2268-2279.

8. Zedler B, Saunders WB, Joyce AR Vick CC, Murrelle EL. Validation of a screening risk index for serious prescription opioid-induced respiratory depression or overdose in a US commercial health plan claims database. *Pain Med*. 2018;19(1):68-78.

9. Zedler B, Xie L, Wang L, Joyce A, Vick C, Brigham J, Kariburyo F, Baser O, Murrelle L. Development of a risk index for serious prescription opioid-induced respiratory depression or overdose in veterans' health administration patients. *Pain Med*. 2015;16(8):1566-1579.

10. Geissert P, Hallvik S, Van Otterloo J, O'Kane N, Alley L, Carson J, Leichtling G, Hildebran C 3rd, Wakeland W, Deyo RA. High-risk prescribing and opioid overdose: Prospects for prescription drug monitoring program–based proactive alerts. *Pain*. 2018;159(1):150-156.

11. Boscarino JA, Kirchner HL, Pitcavage JM, Nadipelli VR, Ronquest NA, Fitzpatrick MH, Han JJ. Factors associated with opioid overdose: A 10-year retrospective study of patients in a large integrated health care system. *Subst Abuse Rehabil*. 2016;7:131-141.

12. Massachusetts Department of Public Health. Chapter 55. https://chapter55.digital.mass.gov/#chapter55.

13. Del. Kipke. Maryland department of health - "pill mill" tip line and overdose report. 2018:7.5-701.

14. Brady JE, Giglio R, Keyes KM, DiMaggio C, Li G. Risk markers for fatal and non-fatal prescription drug overdose: A meta-analysis. *Injury Epidemiology*. 2017;4(1):24.

15. Binswanger IA, Blatchford PJ, Mueller SR, Stern MF. Mortality after prison release: Opioid overdose and other causes of death, risk factors, and time trends from 1999 to 2009. *Ann Intern Med*. 2013;159:592–600.

Paper 1: Using Electronic Pharmacy and Health Care Data to Identify Persons at Risk of Opioid-Related Overdose – A Review of the Predictive Modeling Literature

Abstract

Background: The opioid crisis has taken a substantial toll on the U.S. population. As clinical and public health professionals gain access to increasing volumes of electronic patient data, more sophisticated approaches to identifying individuals at risk of overdose should be explored. Predictive models leverage multiple variables in an individual's historical data to distill risk into a consumable message that can assist agencies and providers with better directing resources and interventions to those at highest risk in a data rich world. Understanding the landscape of literature on models predictive of opioid overdose is a necessary step prior to using one operationally.

Objective: The aim of this review is to synthesize and compare predictive model variables and performance in a variety of ways and discuss practical implications.

Data Sources and Eligibility: PubMed, Embase, and PsychINFO databases were searched for studies conducted July 2008-2018 that identify risk factors and predictive models based on electronic prescription history and other medical record or claims data to identify U.S. patients at risk of nonfatal or fatal drug- or opioid-related overdose. Studies were reviewed to identify risk factors, analytic model approach, and validation performance.

Article Review Process: For those articles meeting the defined criteria, the following items were extracted: details on the data source, time period, study design, target population and size for the derivation and validation cohorts, outcome, key strengths and limitations, patient matching methods (if applicable), risk factors and effect sizes, and model performance measures.

Synthesis Results: Of the 2,806 studies identified and screened, nine studies with seven unique models met the inclusionary criteria and were included in the full review. All studies used different outcome definitions, except two published by the same author. Most studies used payer-based populations and subpopulations. Only two studies externally validated the model; one of which saw improved performance with adjustments to accommodate the population and data source. Model area under the curve statistics ranged from 0.71-0.90.

Conclusions: Most models were developed using payer-specific cohorts, which have implications on selection of variables, performance, and generalizability. More statewide databases should be leveraged to develop and validate overdose predictive models. If implementing a model, adaptations should be considered for the target population, data source and variables available, and outcome of interest.

Introduction

The number of opioid-related overdoses has quintupled between 1999 and 2016, reaching an average of 115 daily opioid-overdose deaths per day nationally.[1] The country has experienced three overlapping waves of opioid-related epidemics: prescription opioids beginning in the 1990s, heroin beginning after 2010, and most recently from synthetic opioids (i.e., illicit fentanyl).[1] The economic cost to society of overdose mortality and other associated harms reached $504.0 billion in 2015, representing 2.8% of the national GDP.[2]

Addressing the prescription opioid epidemic requires a comprehensive response,[3] a portion of which will need to rely upon a better understanding risk factors associated with negative opioid-related outcomes at a more localized level. Health insurance claims data have been a common source for identifying risk factors for opioid use disorder and overdose, but more recently, electronic health record (EHR) and statewide prescription drug monitoring programs (PDMPs) have become an important source of data.[4-6] PDMPs collect controlled substances dispensed in a state across all payers for monitoring, analysis, and reporting purposes and have been adopted by all states (except Missouri, which is a county-level PDMP), the District of Columbia, and Guam.[7,8] Public health officials, prescribers, and other healthcare professionals play an important role in monitoring for signs of misuse or abuse using monitored prescription opioids data.[9] Approaches to transforming the substantial volume of data into actionable information that can guide overdose prevention efforts, such as classifying individuals into certain levels of risk, are increasingly needed.

While much of the literature that identifies risk factors for opioid overdose are descriptive, a subset has developed predictive models. Predictive models are statistical algorithms designed to predict future outcomes using historical data.[10] The hallmark of predictive models is that

they can provide the quantitative basis for assigning risk scores to individual subjects, and these diagnostics can be statistically assessed for sensitivity, specificity, and other predictive properties. Predictive analytics have historically been utilized in many applications in healthcare, including risk assessment, disease management, and billing anomalies.[11] Applying predictive modeling to the opioid epidemic to identify those at risk can support clinical and public health interventions, including informed prescribing, co-prescribing of naloxone, enrollment in treatment, and improved targeting of public health programs.[9] This review aims to synthesize and compare predictive model variables and performance and discuss practical implications of deploying the models in real world setting.

Methods

Search Strategy

Searches were performed in the PubMed, PsychINFO, and Embase databases on July 30, 2018 for the period July 2008 through July 2018. Key term searches were conducted and were evaluated by an informationist from the Johns Hopkins Bloomberg School of Public Health. Where possible, both Medical Subject Heading (MeSH) terminology and key terms were searched (Appendix A). The first search focused on opioids, including terms such as "analgesic, opioid", "prescription drug", and "narcotic". The second search focused on identifying risk factors and predictive models in the literature by searching on terms such as "risk", "risk factor", and "predictive modeling" or "prediction." The third search focused on the outcome of overdose, with terms including "overdose", or "respiratory depression." The search strings were combined, and studies were reviewed that met all three term searches.

Study Selection

All titles returned from the database searches were reviewed for relevance. Titles and abstracts that indicated risk identification for opioid overdose or severe respiratory depression among humans were retained for full review. During the full-text review, studies were selected if they included the development and/or validation of a risk model for opioid overdose or severe respiratory depression. Studies were excluded if they were conducted on populations outside the United States, were literature reviews, used data before July 2008, did not analyze risk factors, did not contain prescription history data as variables, only reported univariate results, or were based on self-reported data (i.e. surveys, interviews, questionnaires). Articles that were commentary of other studies, not accessible online, not available in English, not human-based research, or not related to opioid overdose were also excluded. Predictive model studies were selected based on evidence of evaluating the performance of a predictive model in the form of area under the receiver operating characteristic curve (AUC) or using a machine learning technique aimed at predicting or identifying individuals at risk of opioid overdose.

Data Extraction and Synthesis

General information extracted from each study included: data source, time period, study design, target population, size of the derivation and validation cohorts, outcome, key strengths and limitations, and whether multiple datasets were linked together. The target populations were extracted to assess implications for generalizability to other populations and model performance overall. Population denominators can affect model performance, for example, some populations may have higher underlying risk than others, making it more challenging to differentiate those at highest risk from others in the sample from relatively lower risk individuals. Analytic details were also extracted, including the statistical method and measure of association used, the model lookback time period, , risk factor details, and

model performance measures. Measure performance in the form of area under the curve (AUC) was extracted, which defines the ability of the model to discriminate between patients who truly experienced an outcome event from those who did not experience the event.[12]

Results

Study Selection

A total of 2,806 articles qualified across the three database searches, 449 of which were duplicates. Of the remaining 2,357 non-duplicate studies screened, 2,254 were excluded based on the title and/or abstract. Full text reviews were performed on the remaining 103 studies, 26 of which met the inclusion criteria for the review (Figure 1.1). Of the 26 studies included for review, nine evaluated the performance of the risk model. Two of the studies used the same model and population and thus were omitted from the synthesis to reduce duplicative results (Zedler et al. 2015 was summarized and Zedler et al. 2014 was omitted; Zedler et al. 2018 was summarized and Nadpara et al. 2017 was omitted), resulting in seven models synthesized in this review.

Figure 1.1: PRISMA flow chart of study selection.
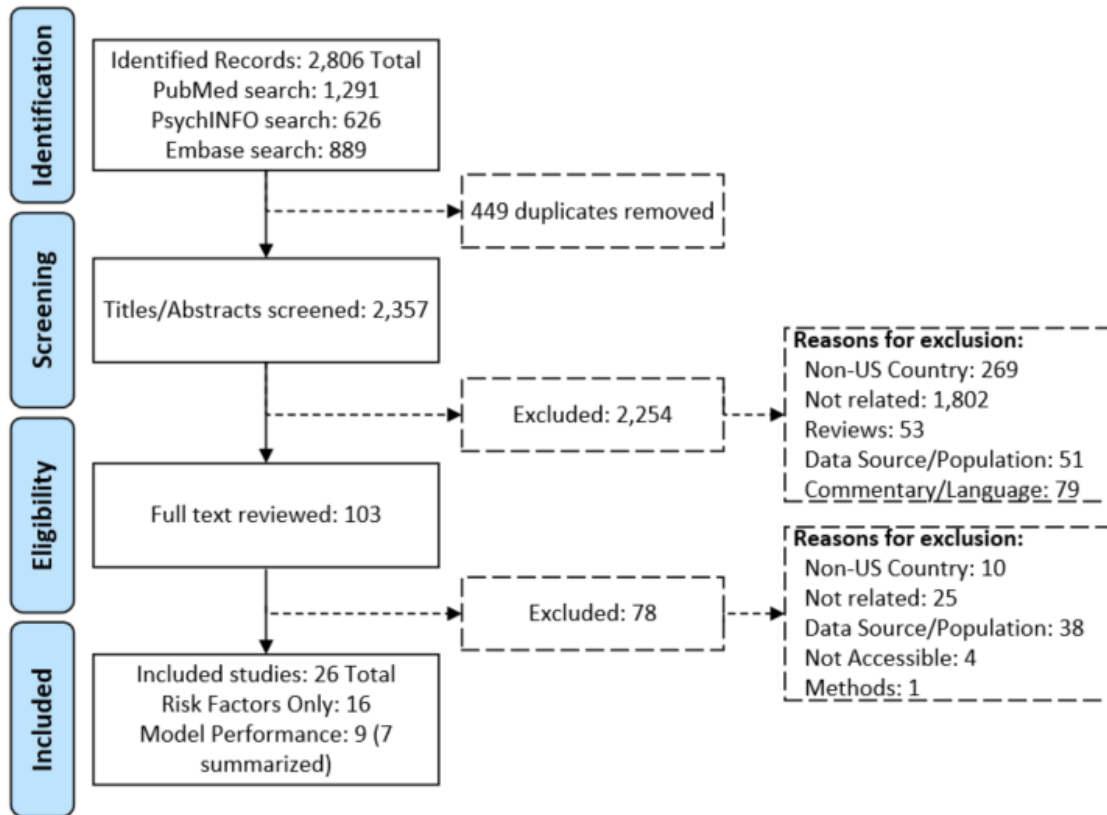
Data Sources and Outcome Definitions

Overall, several studies linked claims or EHR data to death data to examine an outcome of fatal and/or non-fatal opioid overdose (Table 1.1).[13-15] Zedler et al. (2018) leveraged a standalone claims or EHR database for opioid- or drug-related overdoses while Geissert et al. (2018) combined PDMP data, death data, and EHR data together for an outcome of fatal or non-fatal overdose. Boscarino et al. (2016) did not cite or describe the source of their overdose outcome definition,[14] while the remaining studies based their definition on a previous study's, or a synthesis of definitions from past publications and/or national guidelines for overdose coding, reporting and syndromic surveillance.

All studies used the International Classification of Disease (ICD) version 9 or 10 codes to define the outcome, however, aside from studies building on previous work (Zedler et al.

2015; Zedler et al. 2018), the codes used to define the outcome were different in each study. Only studies linked claims or EHR data to death records examined fatalities, each with a different definition. Bohnert et al. (2016) looked at unintentional fatal opioid overdoses, including alcohol.[13] Two studies combined both non-fatal and fatal overdoses together, but Geissert et al. (2018) focused specifically on prescription overdose whereas Glanz et al. (2018) focused on any opioid overdose and both included codes with different intentionality (i.e. unintentional, intentional and undetermined intent).[15,16] Although Boscarino et al. (2016) linked EHR data to death data, cause of death was not included, therefore only the model predicting non-fatal opioid overdose was included in this analysis. Finally, Liang et al. (2017) examined unintentional and intentional drug overdoses without mention of fatal or non-fatal result.

Table 1.1: Summary of model studies.

Source	Population	Data Source	Cohort	Outcome	Model	Performance
Bohnert et al. 2016	VHA patients with opioid prescription & chronic pain diagnosis	EHR Death	D: 211 cases, 211 controls V: Not defined	Fatal opioid overdose (unintentional)	Logistic regression	AUC: 0.71 (0.66–0.76)
Boscarino et al. 2016	Medical IP, OP, or ED patients 10-95 years with multiple overdose events	EHR Deaths	D: 2,039 cases, 1,174,120 patients V: Not defined	Non-fatal opioid overdose (undetermined) [b]	Logistic regression	AUC: 0.71
Geissert et al. 2018	Oregon residents 12+ years with opioid prescription	PDMP Deaths EHR	D (2013 data): 1,409 cases, 879,402 patients V (2012 data): similar population	Prescription opioid overdose (non-fatal & fatal combined) (unintentional & intentional)	Logistic regression	d-AUC: 0.8198 v-AUC: 0.8236 Sens.: 63.2% Spec.: 82.1% PPV: 0.006
Glanz et al. 2018	Kaiser Permanente Colorado patients 18+ years with chronic opioid therapy.	EHR Deaths	D: 121 cases, 42,828 patients V: 118 cases, 10,708 patients	Opioid overdose (non-fatal & fatal combined) (unintentional, intentional, undetermined)	Cox prop. hazards	Internal v-AUC: 0.75 (0.70–0.79), Sens.: 66.1%, Spec.: 66.6%, PPV: 0.56% External v-AUC: 0.75 (0.70–0.80), Sens.: 82.2%, Spec.: 49.5%, PPV 1.8%
Liang et al. 2016 [a]	Privately insured 18-64 years, non-cancer pain, 2+ Schedule II/III opioid prescriptions.	Claims	D: Split half: 1,386 cases 206,869 patients (89,397 men; 117,472 women) V: same	Drug overdose (unintentional & intentional)	Logistic regression	Women final model: d-AUC: 0.8 v-AUC: 0.8 Men final model: d-AUC: 0.79 v-AUC: 0.8
Zedler et al. 2015	VHA patients with an opioid prescription.	EHR	D: 817 cases, 8,170 controls V: Not defined	Opioid overdose & adverse events (unintentional)	Logistic regression	d-AUC: 0.88
Zedler et al. 2018	Commercially insured patients 18+ years with opioid pharmacy claim.	EHR	D (VHA): 817 cases, 8,170 controls V (CIP data): 7,234 cases, 28,932 controls	Opioid overdose & adverse events (unintentional)	Logistic regression	VHA model on CIP v-AUC: 0.85 adjusted VHA model on CIP v-AUC: 0.90

Abbreviations: VHA=Veteran's Health Administration, CIP=Commercial Insurance Payer, IP=inpatient, OP=outpatient, ED=emergency department, EHR=electronic health record, PDMP=prescription drug monitoring program, , PPV=positive predictive value, D=derivation, V=validation, AUC=area under the curve d-AUC=derivation AUC, v-AUC=validation AUC, Sens.=sensitivity, Spec=specificity

[a] Other versions of sex-specific models are not represented; only the final reduced model is summarized.

[b] Fatalities were studied but cause of death was not available and was therefore omitted from this study.

Target Populations

Most studies defined population based on insurance (five studies). The Veterans Health Administration (VHA) was the most studied population (three studies),[13] while other studies developed models using commercially or privately insured payer populations,[18] or a single-state integrated health system population (Kaiser Permanente Colorado).[15] Zedler et al. (2015) developed a risk model for unintentional opioid overdose among a VHA population, then performed external validation of the original and updated version of the model on a population of commercially insured health plan patients with at least one opioid dispense.[18] The only two studies with non-payer populations used individuals with a prescription in the statewide Oregon PDMP[16] and individuals with an inpatient, outpatient, or emergency room (ER) visit for overdose at a single health system.[14]

Beyond payer-based populations, many studies focused on subpopulations based on various criteria. The most common denominator were individuals with at least one prior opioid prescription, regardless of formulation.[16,18,19] However, other subpopulations included individuals with a pain or chronic pain diagnosis,[13] receiving chronic opioid therapy (three prescriptions within 90 days),[15] or a prior overdose event.[14] Nearly all studies examined individuals aged 18 or older, including the VHA populations, although VHA populations were heavily skewed toward the older adult population (65 years or older). Exceptions to this included Boscarino et al. (2016), which purposefully examined patients aged 10 to 95 years with the reasoning of remaining consistent with national studies of drug misuse, and Geissert et al. (2018), which looked at patients aged 12 years or older.

Model Predictors

A comprehensive summary of the categories of predictors found in the models included in this review is summarized in Table 1.2 (a detailed account of risk and protective factors is in Appendix 1.2). The predictors used in the models fell into one of four general categories: 1) demographics, 2) diagnoses, 3) prescription variables, or 4) healthcare utilization. Age, medical or mental/behavioral health diagnoses, types of non-opioid prescriptions, and opioid prescription formulation and dose were the most common predictors included in the models. Of the included predictors, several in each category stood out as the strongest candidates if implementing a model for applied use, as described below and in Table 1.3.

Demographics. Age was the most commonly explored demographic, however, age and age groups were defined and applied differently, with mixed findings. Two studies using privately insured health data or integrated health system data found each year increase in age to be a slightly protective factor.[15,20] Geissert et al. (2018) demonstrated monotonically increasing risk with every 10-years of age using a statewide population and two studies found older individuals to be at higher risk.[18] Only Zedler et al. (2018) included sex as a variable in the multivariate model, although it was not found to be statistically significant.[18] Liang et al. (2016) created sex-specific models and therefore did not use sex as a predictor and Boscarino et al. (2016) used sex descriptively but not in the model.

Diagnoses. Approximately 64 different clinical, mental/behavioral health, and pain-related diagnoses were evaluated across six studies, with 55 diagnoses represented in the final models. The mental health/behavioral health diagnoses variables yielded the greatest risk of overdose, specifically substance use disorder or alcohol abuse,[15,18,20] bipolar disorder or schizophrenia,[18] or a mental health disorder diagnosis broadly.[15] Clinical diagnoses with the

strongest effect sizes using multivariate analysis included non-malignant pancreatic disease and heart failure.[18]

Prescription. Patients with a buprenorphine prescription were at highest risk for fatal opioid overdose, according to one study, which likely reflects the history of opioid use disorder that is common in this population.[14] Maximum morphine equivalent daily dose (MMEDD) was one of the most commonly evaluated prescription dose predictors (six studies), however, only four included dose in the final model.[13,15,18,19] The second most common prescription variable included in the risk models were extended release/long-acting opioids,[15,16,18,19] three of which demonstrated increased risk of opioid overdose.[16,18,19] Finally, methadone[18,19] and benzodiazepine (prescription or total days' supply)[16,18-20] prescriptions had the next highest odds of overdose in several studies.

Other. Only two studies included all-cause utilization in a risk model, however, both ≥1 hospitalization days and ≥1 ER visits significantly increased risk of opioid overdose.[18,19]

Risk Factors Not Included Models

A review of the literature for risk factors beyond those included in the predictive models was also conducted to determine if studies contained other variables of interest than included in this review. The descriptive studies evaluated only a handful of associations for diagnosis and prescription-based variables that did not appear in any risk models, including a composite score for total number of diagnoses,[21,22] prescription fill frequency,[23,24] multiple provider episodes (number of unique prescribers and dispensers within a specific timeframe), patterns within the prescription history,[25,26] method of payment for prescriptions,[26] and indicator of out-of-state prescriber or pharmacy.[27]

Table 1.2 - Categories of predictors used in risk model studies.	Risk Model Studies (n=7)		
Predictor Category	**In Final Model**	**Evaluated, Omitted**	**Not Evaluated**
Demographics			
Age	6[14-16,18-20]	0	1[13]
Geographic Region/Setting	2[18,19]	2[16,20]	3[13-15]
Sex [a]	2[14,18]	0	5[13,15,16,19,20]
Race/Ethnicity	1[19]	1[14]	5[13,15,16,18,20]
Marital status	1[19]	1[14]	5[13,15,16,18,20]
Employment status	0	1[14]	6[13,15,16,18-20]
Education status	N/A	N/A	N/A
Diagnoses			
Diagnoses - total number chronic conditions	N/A	N/A	N/A
Diagnoses - clinical	4[14,15,18,19]	0	3[13,16,20]
Diagnoses - mental/behavioral health	4[15,18,19,28]	1[14]	2[13,16]
Diagnoses - pain-related	2[18,19]	2[14,20]	3[13,15,16]
Prescription			
Prescription type - nonopioid	4[14,16,18,19]	1[15]	2[13,20]
Prescription type - opioid	2[18,19]	2[14,15]	3[13,16,20]
Prescription dose (MMED daily, true peak)	4[13,18-20]	2[15,16]	1[14]
Prescription formulation (ER/LA) [b]	4[15,16,18,19]	0	3[13,14,20]
Prescription route	2[18,19]	0	6[13-16,20]
Prescription fill days (by drug type or number)	1[20]	0	6[13-16,18,19]
Prescription overlap	0	1[16]	6[13-15,18-20]
Number of pharmacies	1[16]	0	6[13-15,18-20]
Number of prescribers	1[16]	0	6[13-15,18-20]
Number of prescriptions (total, by drug class)	1[19]	1[16]	5[13-15,18,20]
Other			
All-cause healthcare utilization	2[18,19]	0	5[13-16,20]
Other - prior risk indicators (overdose/suicide/treatment)	0	0	6[13-16,18,19]

Abbreviations: MMED=Maximum Morphine Equivalent Dose, ER/LA=extended release/long-acting.

[a] Liang et al. developed sex-specific models and therefore was not used as a predictor

[b] Garg et al. 2017 limited the opioid drug formulation to schedule II prescriptions only

Table 1.3: Risk factors for use in a multivariable model based on literature data availability.

Category	Risk Factor	Effect Size	Author
Demographics	Age or age group	**aOR/OR 1.16-4.99 (1.04-4.02, 1.29-6.19)**	Boscarino 2016; Geissert 2018; Glanz 2018; Liang 2016; Zedler 2015, Zedler 2018
	Sex	OR 1.03-1.40 (0.95, 1.11)	Boscarino 2016; Zedler 2018;
Diagnosis-MH/BH	Opioid dependence	**OR 4.54 (3.12, 6.63)**	Zedler 2015
	Alcohol or substance use disorder or dependence [a]	**aHR 3.47-12.74 (2.25-11.46, 5.36-14.16)**	Glanz 2018; Liang 2016; Zedler 2018
	Mental health diagnosis	**aHR 3.39 (2.32, 4.96)**	Glanz 2018
	Depression or psychotic disorder	**aOR 3.04-3.23 (2.27-2.41, 3.82-4.54)**	Liang 2016
	Bipolar disorder/schizophrenia	**OR 1.95-2.85 (1.43-2.44, 2.67-3.32)**	Zedler 2015; Zedler 2018
Diagnosis-clinical	Liver disease (mild)	**OR 2.42 (1.39, 4.19)**	Zedler 2015
	Non-malignant pancreatic disease	**OR 2.07-2.13 (1.06-1.56, 2.75-4.25)**	Zedler 2015, Zedler 2018
	Heart failure	**OR 2.06 (1.74, 2.44)**	Zedler 2018
Prescription	Prescription: Buprenorphine prescription	**OR 12.30 (5.92, 25.53)**	Boscarino 2016
	Dose: MMED prescribed (mg/day)	**aOR/OR 1.49-4.96 (1.19-3.24, 2.12-7.61)**	Bohnert 2016; Liang 2016; Zedler 2015, Zedler 2018
	Long-acting/extended-release opioid prescription	**aOR/OR 1.73-4.41 (1.51-3.93, 1.99-4.94)**	Geissert 2018; Zedler 2015, Zedler 2018; Glanz 2018
	Methadone prescription	**OR 2.42-2.80 (1.61-2.22, 3.51-3.66)**	Zedler 2015, Zedler 2018
	Benzo/sedative prescription or days' supply	**OR/aOR 1.49-2.75 (1.22-2.23, 1.83-3.64)**	Geissert 2018; Liang 2016; Zedler 2015, Zedler 2018
Utilization	All-cause utilization ≥1 day of hospitalization	**OR 1.12-2.20 (1.02-1.76, 1.23-2.76)**	Zedler 2015, Zedler 2018
	All-cause utilization ≥1 ER visit	**OR 1.52-2.88 (1.41-2.34, 1.65-3.54)**	Zedler 2015, Zedler 2018

Abbreviations: MH/BH=Mental Health/Behavioral Health; MMED=Maximum Morphine Equivalent Dose; Benzo=benzodiazepine; ER=Emergency Room, OR=odds ratio, aOR=adjusted odds ratio
Bold indicates statistical significance.
[a] The definition of substance use disorder may differ between studies; results have been consolidated for simplification purposes

Cross-Dataset Patient Matching Techniques

The method of matching patient-level datasets together can influence the ability to achieve a comprehensive picture of risk for an individual. Of the five studies that utilized two or more disparate datasets, only three described the patient matching approach. Two studies used deterministic matching, which relies upon exact matching of some combination of the names, dates of birth, sex, zip, and social security number.[13,15] Glanz et al. (2017) used the social security number, date of birth, and partial or whole name to perform the matching, while Bohnert et al. (2016) established two definitions using various combinations of patient demographic information. Geissert et al. (2018) used probabilistic software (Link King v7.1) to match patients in three disparate PDMP, EHR, and death datasets based on name, date of birth, and zip.[29] Probabilistic matching applies a weighted score to each portion of demographics compared to determine an overall match "score" that will combine the data together at the person-level if a pre-defined threshold is met.[30] Boscarino et al. (2016) linked EHR and death data, but did not describe how the connections were established.[14]

Model Development, Validation, and Performance

Two studies internally validated a newly developed risk model[16,20] and two studies performed external validation.[15,18] Liang et al. (2016) used the split half technique,[20] which randomly selects half of the sample for model derivation and half for model validation.[31] Liang et al. (2016) developed multiple sex-specific models, of which the final reduced model performed modestly well for both women and men in the derivation and validation cohorts (AUC of 0.79 or 0.80). Geissert et al. (2018) took a different approach of developing the model on 2013 data (AUC: 0.82) and validating on 2012 data (AUC: 0.82).

Of the studies performing external validation, Glanz et al. (2018) developed and internally validated (AUC: 0.75) the model using Harrell bootstrap resampling on data from an integrated health system and externally validated (AUC: 0.75) the model on a separate cohort served by a safety-net health system within the same state. Zedler et al. (2015) developed a model (AUC: 0.88), which was later externally validated in two phases.[18] The first phase applied the model developed on the VHA population to a commercially insured population (AUC: 0.85), then adjusted the VHA model to improve the performance within the commercially insured population (AUC: 0.90).[18] The remaining two studies developed, but did not validate, the risk model and had modestly performing models (AUC: 0.71[13,14]).

Only four studies included other model performance indicators, such as sensitivity (ability to identify individuals truly at risk), specificity (ability to identify individuals truly not at risk) and positive predictive value (PPV; probability the patient is at risk of the outcome when the model classifies the patient as at risk).[32] Only Glanz et al. (2018) and Geissert et al. (2018) reported the sensitivity, specificity, and PPV for the validated model. Geissert et al. (2018) had a very low PPV of 0.006 and Glanz et al. (2018) also had a low PPV of 0.018. Bohnert et al. (2016) reported sensitivity and specificity according to the prescribed morphine equivalent milligrams (ranging from 10-200 milligrams).

Discussion

Identifying individuals at risk of opioid overdose using a predictive model has the potential to be an important tool for addressing the opioid crisis. Applying a predictive model to the population can serve as resource to public health when making programmatic, policy, and budget decisions to create the infrastructure needed in a comprehensive response. Predictive models can also be useful in broader harm reduction efforts, such as prioritized naloxone

distribution, or fine-tuned for resource-intensive interventions such as treatment or specialized care coordination.[33] However, based on the literature reviewed in this study, many considerations must be taken into account with the practical application of a predictive model. Models should be adapted based on the population of interest, available data sources and variables, and desired outcome.

Most studies leveraged payer-specific datasets because of easy access to electronic payer-based data for analyses. However, using a payer-based data source raises concerns about the generalizability of the models to other populations, as they will likely not have a complete picture of a patient's medical or prescription history. For example, self-pay (when patients purchase medications fully out-of-pocket) and out-of-network care will not be represented in the data. To increase generalizability of a model built on a specific population, validating the model on an external dataset can aid in understanding whether the model can be used in other settings. Only two studies externally validated the model to quantify the ability for the model to be applied to a population in a different setting. Zedler et al. (2015) developed a model on a VHA population that was subsequently externally validated against a commercially insured population after adjusting the model variables to account for differences in the populations, drug formularies, and clinical practice.[18] Alternatively, the model Glanz et al. (2018) externally validated resulted in poorer calibration, citing the differences in the cohort as a limitation.[15] These findings suggest that published models have the potential to be applied to different populations; however, models require modifications to accommodate differences in the applied population.[18] More studies need to leverage all-payer, statewide, or national datasets, externally validate published models while adjusting for any underlying population demographics and availability of predictors, and provide more performance analyses that can be used to better deploy the risk model in an applied setting.

While the specific variables used in the risk models varied across the studies, a handful surfaced as the strongest candidates for the practical application of a predictive model, whether customizing from the literature or developing *de novo*. The predictors included in a risk model will need to be adapted depending on what data are available, however, the variables described represent risk factors that are either readily available in datasets (age, sex), most commonly used in models in the literature (prescription dose, formulation), or have the highest effect size in the model. Generally, predictors used in the models were simple, such as a binary variable indicating the presence of a type of drug (i.e. benzodiazepine prescription). Complex variables that require multiple calculations and dependencies on other variables in the data were generally avoided in final models. An example of this is overlapping prescriptions, which require calculating the duration of the prescription using the date dispensed and days' supply compared against other prescriptions in the patient's history, occasionally across multiple drug classes. Geissert et al. (2018) originally included variables for several versions of overlapping prescriptions, but specifically chose to replace the variables with a simple indicator of certain types of drug fills, citing simple indicators will ease the implementation of the model in an applied setting. Complex variables should therefore be carefully considered as to whether it should be included in a model, especially if simple alternative variables exist.

Finally, nearly all models used different, but similar, outcome definitions. Some definitions were based on studies conducted in part or wholly from nearly a decade prior, despite multiple published definitions from the Centers for Disease Control (CDC), Substance Abuse and Mental Health Services Administration (SAMHSA), and Safe States Alliance Injury Prevention Workgroups (ISW) in the same time period of the study. Because coding practices by medical examiners can vary between states, any program or organization

deciding to implement a validated risk model should pay close attention to the outcome definition. Having multiple definitions of fatal opioid overdose in play in a given region can cause confusion for public health officials examining the results of the model, or clinicians viewing a risk score for an individual. Modifications may need to be made to the model to establish consistency with fatal opioid overdose definitions already in play in a region or state. As future studies evaluate predictive models for overdose, attempts should be made to incorporate the currently published national guidelines on overdose coding, as well as state-level definitions that consider local coding anomalies and circumstances.

Conclusion

As the need for more comprehensive and scalable approaches to identifying individuals at risk increases, predictive models that can be applied in a practical setting will become more relevant. Several key considerations for real-world application emerged in the literature, however. Most models were developed using payer-specific cohorts, which have implications on selection of variables, performance, and generalizability. Using all-payer, statewide databases should be prioritized when applying a predictive model, as it gives a more complete picture of risk. However, based on the literature, generalizability across populations may be possible with proper modifications to the model to fit the population and available data variables. Caution should be paid to the outcome the model is predicting, as many definitions exist in the literature or are available in the data. Future research should be performed on adjusting and validating the existing models within the relevant population. In addition to referencing prior studies, using the most up-to-date national overdose coding definitions should be explored to ensure the model is targeting individuals at risk of the outcome of highest interest.

References

1. Centers for Disease Control and Prevention. Understanding the epidemic. https://www.cdc.gov/drugoverdose/epidemic/index.html. Updated August 30, 2017. Accessed August 1, 2018.

2. The Council of Economic Advisers. The underestimated cost of the opioid crisis. November 2017.

3. Alexander GC, Frattaroli S, Gielen AC, eds. The prescription opioid epidemic: An evidence-based approach. 2015.

4. Evans E, Grella CE, Murphy DA, Hser YI. Using administrative data for longitudinal substance abuse research. *J Behav Health Serv Res.* 2010;37(7):252-271.

5. Weiner J, Bao Yl, Meisel Z. Prescription drug monitoring programs: Evolution and evidence. . *LDI Issue Briefs.* 2017.

6. Wu LT, Gersing KR, Swartz MS, Burchett B, Li TK, Blazer DG. Using electronic health records data to assess comorbidities of substance use and psychiatric diagnosis and treatment settings among adults. *J Psychiatr Res.* 2013;47(4):555-563.

7. Prescription Drug Monitoring Program (PDMP) Center of Excellence at Brandeis. History of prescription drug monitoring programs. 2018.

8. Prescription Drug Monitoring Program (PDMP) Center of Excellence at Brandeis. Status of prescription drug monitoring programs (PDMPs). https://www.pdmpassist.org/pdf/PDMP_Program_Status_20170824.pdf. Updated 2017. Accessed August 1, 2018.

9. Kolodny A, Courtwright DT, Hwang CS, Kreiner P, Eadie JL, Clark TW, Alexander GC. The prescription opioid and heroin crisis: A public health approach to an epidemic of addiction. *Annu. Rev. Public Health.* 2015;36:559-574.

10. Raghupathi W RV. Big data analytics in healthcare: Promise and potential. *Health Inf Sci Syst.* 2014;2:3-13.

11. Simpao AF, Ahumada LM, Gálvez JA, Rehman MA. A review of analytics and clinical informatics in health care. *J Med Syst.* 2014;38(4):1-45.

12. Cook NR. Statistical evaluation of prognostic versus diagnostic models: Beyond the ROC curve. *Clin Chem.* 2008;54:17-23.

13. Bohnert AS, Logan JE, Ganoczy D, Dowell D. A detailed exploration into the association of prescribed opioid dosage and overdose deaths among patients with chronic pain. *Med Care.* 2016;54(5):435-441.

14. Boscarino JA, Kirchner HL, Pitcavage JM, Nadipelli VR, Ronquest NA, Fitzpatrick MH, Han JJ. Factors associated with opioid overdose: A 10-year retrospective study of patients in a large integrated health care system. *Subst Abuse Rehabil.* 2016;7:131-141.

15. Glanz JM, Narwaney KJ, Mueller SR, Gardner EM, Calcaterra SL, Xu S, Breslin K, Binswanger IA. Prediction model for two-year risk of opioid overdose among patients prescribed chronic opioid therapy. *J Gen Intern Med.* 2018.

16. Geissert P, Hallvik S, Van Otterloo J, O'Kane N, Alley L, Carson J, Leichtling G, Hildebran C 3rd, Wakeland W, Deyo RA. High-risk prescribing and opioid overdose: Prospects for prescription drug monitoring program–based proactive alerts. *Pain.* 2018;159(1):150-156.

17. Ohman EM, Granger CB, Harrington RA, Lee KL. Risk stratification and therapeutic decision making in acute coronary syndromes. *JAMA.* 2000;284(7):876-878.

18. Zedler B, Saunders WB, Joyce AR Vick CC, Murrelle EL. Validation of a screening risk index for serious prescription opioid-induced respiratory depression or overdose in a US commercial health plan claims database. *Pain Med.* 2018;19(1):68-78.

19. Zedler B, Xie L, Wang L, Joyce A, Vick C, Brigham J, Kariburyo F, Baser O, Murrelle L. Development of a risk index for serious prescription opioid-induced respiratory depression or overdose in veterans' health administration patients. *Pain Med.* 2015;16(8):1566-1579.

20. Liang Y, Goros MW, Turner BJ. Drug overdose: Differing risk models for women and men among opioid users with non-cancer pain. *Pain Med.* 2016;17(12):2268-2279.

21. Campbell CI, Bahorik AL, VanVeldhuisen P, Weisner C, Rubinstein AL. Ray GT. Use of a prescription opioid registry to examine opioid misuse and overdose in an integrated health system. *Prev Med.* 2018;110:31-37.

22. Turner BJ, Liang Y. Drug overdose in a retrospective cohort with non-cancer pain treated with opioids, antidepressants, and/or sedative-hypnotics: Interactions with mental health disorders. *J Gen Intern Med.* 2015;30(8):1081-1096.

23. Bohnert AS, Valenstein M, Bair MJ, Ganoczy D, McCarthy JF, Ilgen MA, Blow FC. Association between opioid prescribing patterns and opioid overdose-related deaths. *JAMA.* 2011;305(13):1315-1321.

24. Sun EC, Dixit A, Humphreys K, Darnall BD, Baker L C, Mackey S. Association between concurrent use of prescription opioids and benzodiazepines and overdose: Retrospective analysis. *BMJ.* 2017;356:760.

25. Cochran G, Gordon AJ, Lo-Ciganic WH, Gellad WF, Frazier W, Lobo C, Chang CH, Zheng P, Donohue JM. An examination of claims-based predictors of overdose from a large medicaid program. *Med Care.* 2017;55(3):291-298.

26. Rose AJ, Bernson D, Chui KKH, Land T, Walley AY, LaRochelle MR, Stein BD, Stopka TJ. Potentially inappropriate opioid prescribing, overdose, and mortality in massachusetts, 2011–2015. *J Gen Intern Med.* 2018;33(9):1512-1519.

27. Carey CM, Jena AB, Barnett ML. Patterns of potential opioid misuse and subsequent adverse outcomes in medicare, 2008 to 2012. *Ann Intern Med.* 2018;168(12):837-845.

28. Liang Y TB. Assessing risk for drug overdose in a national cohort: Role for both daily and total opioid dose? *J Pain.* 2015;16(4):318-325.

29. Campbell KM, Deck D, Krupsi A. Record linkage software in the public domain: A comparison of link plus, the link king, and a 'basic' deterministic algorithm. *Health Informatics J.* 2008;14(1):5-15.

30. Zhu Y MY, Ohashi Y SS. When to conduct probabilistic linkage vs. deterministic linkage? A simulation study. *Journal of Biomedical Informatics.* 2015;56:80-86.

31. Arlot S CA. A survey of cross-validation procedures for model selection. *Statistics Surveys.* 2010;4:40-79.

32. Altman DG, Bland JM. Diagnostic tests 2: Predictive values. *BMJ: British Medical Journal.* 1994;309(6947):102-102.

33. Centers for Disease Control and Prevention. Evidence-based strategies for preventing opioid overdose: What's working in the United States. 2018.

Paper 2: Comparing the Performance of a Predictive Risk Model with Prescription-Based Thresholds in Identifying Patients at Risk of Fatal Opioid Overdose

Abstract

Background: Nearly every U.S. state and territory have laws establishing Prescription Drug Monitoring Programs (PDMPs) that collect dispensed controlled substance prescriptions to identify patients with patterns indicative of potential misuse and abuse. Many PDMPs use "unsolicited reporting" to notify prescribers and pharmacists when patients have exceeded numerical thresholds. However, the degree to which these thresholds are identifying patients at highest risk of fatal opioid overdose has not been compared with one another or with a multi-factor predictive risk model.

Objective: To compare multiple methods of identifying individuals at risk of fatal opioid overdose, including common unsolicited reporting algorithms and a multivariate predictive model, using PDMP data.

Methods: The study population included individuals with one prescription opioid fill between April-June 2015 present in the Maryland PDMP data. The performance of a multivariable logistic regression predictive model and three simple PDMP thresholds were evaluated: (1) multiple provider episodes; (2) high daily average morphine milligram equivalents; and (3) overlapping opioid and benzodiazepine prescriptions. An overlap analysis of individuals identified by at least one risk identification method and prevalence of death among the high-risk populations were compared.

Results: Approximately 30% (n=50,501) of the validation cohort (n=170,438) was identified by one or more risk identification methods, of which, 73.0% (n=178) of the total deaths (n=244) were captured. Across nearly all comparative analyses, the comprehensive multivariate predictive risk models performed equal to or better than the PDMP thresholds in identifying individuals at risk of a fatal opioid overdose. Analysis showed the risk model in combination with other PDMP thresholds were also effective in certain circumstances.

Conclusions: PDMP programs have the opportunity to leverage an improved method of identifying individuals at risk of fatal opioid overdose as compared with the PDMP thresholds commonly used for unsolicited reporting today. Consideration should be made as to the balance between sensitivity and specificity and the intended use of the model in a resource-constrained environment.

Introduction

In an effort to combat the epidemic, states are increasingly utilizing statewide Prescription

Drug Monitoring Programs (PDMPs), which collect data on controlled dangerous

substances (CDS) prescriptions as part of state-mandated program.[1] Commonly collected

data includes the patient's basic demographic information (i.e. name and date of birth),

medication characteristics, and identifiers for prescribers and dispensers of the prescription.

PDMPs in some form have existed as early as 1918 and were historically established as a law

enforcement or regulatory tool.[2] Over time, PDMPs have been recognized as a powerful

public health and clinical tool that could be leveraged to combat opioid use disorder and

other adverse outcomes.[2] States have established laws defining who is authorized to use the

PDMP information, including prescribers, pharmacists, law enforcement, public health

agencies, licensing boards, and others.[3] These users may solicit information (i.e., proactively

query) on a patient being treated or investigated as authorized by law, or the users may

receive an "unsolicited" (i.e., reactive) report from the State PDMP program for particular

high-risk prescription patterns or thresholds.[4] Scope of state PDMP unsolicited reporting is

generally defined by statute and may focus on identifying patients with inappropriate

prescription patterns or a prescriber or dispenser that falls outside their respective standard

of practice to reduce opioid use disorder, overdoses, diversion, and fatalities.[2] The thresholds

utilized by state PDMP programs to identify high-risk patients ("PDMP thresholds") have

been shared across the country and similar practices have been adopted by the PDMP

community. The PDMP thresholds are often simple and target a smaller subset of the

highest risk individuals to accommodate a resource-constrained environment.

While the PDMP thresholds are the most commonly used approach to identify high-risk

patients in practice, other risk identification techniques may yield better results. A handful of

studies have developed more comprehensive multivariate predictive models as a method to identify patients at future risk of negative outcomes related to opioid prescriptions.[5-11] Predictive models are typically developed and validated within real patient populations to assess their predictive ability in finding individuals at risk of a future outcome. By considering multiple factors present within the patient's prescription history and being trained to a particular outcome, predictive models are likely to identify different populations of high-risk individuals compared with PDMP thresholds. Predictive models also have flexibility with the risk score cutoff point of who is considered "high-risk" since all individuals are assigned a risk score on a spectrum, rather than a binary indication, as is the case with PDMP thresholds. Although these various risk identification approaches are either in operation or emerging in the literature, to date, no study has compared the different methods. The objective of this study is to compare the populations and performance of common unsolicited reporting PDMP thresholds and a predictive model in identifying individuals at risk of opioid overdose using prescription drug monitoring program data.

Background

Unsolicited reporting is an established best practice among state PDMPs. As of 2015, 44 states and the District of Columbia have legislation enacted that authorizes the PDMP to engage in unsolicited reporting, of which 40 states allow the unsolicited reports to be sent to prescribers directly.[2] The method of unsolicited reporting delivery varies by state; they can be delivered electronically or via paper-based methods, such as mailed letters.[3] Typically, the unsolicited report directed toward a prescriber or dispenser indicates that the patient has met the program's criteria for inappropriate prescription patterns and provides supporting information.

Each state may employ different criteria and thresholds of risk. Examples of unsolicited reporting criteria include identifying patients with high average daily morphine milligram equivalents (MME) or overlapping opioids and other controlled substances, such as benzodiazepines or stimulants. One of the most common criteria used by state PDMPs is multiple provider episodes (MPEs), in which patients have prescriptions from a certain number of unique prescribers and unique dispensers within a defined time period determined by the PDMP program. Based on a recent questionnaire sent to all state and U.S. territory PDMP programs by the PDMP Training and Technical Assistance Center (TTAC) at Brandeis University, 20 states of the 34 respondents indicated sending unsolicited reports for MPEs, five states for high MME, and eight states for some form of overlapping or combinations of prescriptions.[2]

Ideally, state PDMP programs would notify providers of all patients meeting a high-risk criterion. However, if manual or paper processes are in place, the threshold may be determined based on the operational capacity of the program to notify providers. As a result, a more limited process may be selected, in which a higher threshold is chosen to ensure a small number of high-risk individuals, resulting in a smaller volume of letters needing to be produced to inform the relevant prescribers and dispensers. These thresholds may be adjusted over time as the outliers are addressed. For example, as the patients with the highest number of multiple provider episodes are addressed through raising awareness to the prescribers and dispensers interacting with the high-risk patient, the threshold may be adjusted to a smaller number of multiple providers, although it is generally accepted by PDMP programs that a minimum of four or five unique providers is considered to be beyond reasonable clinical circumstances.[12-15] The PDMP TTAC questionnaire results indicated that the lookback period, or timeframe/amount of data used to identify the high-

risk pattern, varied across PDMP programs, ranging from one month to six months of data.[2] From a practical standpoint, shorter lookback periods are generally preferred so that providers may intervene sooner, with more PDMP programs attempting to use the most recent one month of data for unsolicited reporting practices.[2]

Multiple states have evaluated the impact of unsolicited reporting on the prescriptions dispensed to patients, such as the number of prescriptions per patient, number of prescribers, pharmacies, average dosage units, and days' supply.[16-19] A study performed in Massachusetts found that patients about whom prescribers were sent an unsolicited report resulted in a statistically significant decrease in the number of opioid prescriptions, dosage units, average daily and total MME, total days' supply, and number of prescribers and pharmacies used.[19] Similar to a PDMP, a New York Managed Care Organization sent unsolicited reports to providers for patients who had three or more unique opioid prescribers and three or more unique opioid dispensers in the prior three months and demonstrated a statistically significant decrease in the average number of opioid prescribers and dispensers over time.[16] One study found Nevada providers who received an unsolicited report about patients receiving prescriptions from 4+ unique prescribers and 4+ unique dispensers in the prior six months were more likely to discontinue future prescribing to identified patients, although patients often were able to replace the prescribers and dispensers.[20] Importantly, all of these studies focus on the patients' prescriptions, but not on the downstream impact on overdose fatality or other adverse outcome.

Despite evidence that proactively informing providers of patients with high risk patterns results in prescribing changes, to date, no known literature has been published examining the performance of unsolicited reporting related to fatal opioid overdose as an outcome. There

is also no known literature on a PDMP program implementing a predictive model that incorporates multiple factors to identify patients at risk. Thus, there is a lack understanding of who is identified by each risk identification method, the overlap between them, and how well each approach identified individuals at risk of fatal opioid overdose.

Methods

Study Design, Population, and Data Sources

A retrospective analysis was performed using PDMP data for Maryland residents aged 18 to 80 years with an opioid fill during 2015. The Maryland PDMP collects controlled dangerous substance, Schedule II-V prescriptions dispensed to Maryland residents from all Maryland pharmacies, dispensing prescribers, and mail-order pharmacies. Facilities performing direct administration of controlled substances in an inpatient setting, pharmacies dispensing exclusively to assisted living facilities, and opioid treatment programs protected under the Federal rule 42 CFR Part 2 are exempted from reporting controlled substance prescription fills.[21] The outcome of interest was fatal opioid overdose originating from the Office of the Chief Medical Examiner (OCME) database, which contains all investigated deaths in Maryland.[22] The OCME and PDMP data were matched at a person-level by processing demographic data, including name, date of birth, gender, full address, phone number, and social security number, using a probabilistic algorithm before removing patient identifiers for the purposes of this study. The matching was performed by Maryland's State-designated health information exchange, CRISP, which links data from multiple sources that do not share a common identifier.

One predictive model and three unsolicited reporting thresholds were compared: (1) multiple provider episodes; (2) high morphine milligram equivalents (MME); and (3)

overlapping opioid and benzodiazepine prescriptions. This study used three months of data for the primary analysis, with individuals having at least one opioid fill between April-June 2015, to effectively simulate a PDMP program deciding to send unsolicited reports out on July 1, 2015. The study was approved by the Johns Hopkins University Institutional Review Board (IRB) and the Maryland Department of Health (MDH) IRB Committee.

Variables

The target outcome was fatal opioid overdose occurring between July 1, 2015 and December 31, 2016. Fatal opioid overdoses included any patients determined to have a cause of death involving any type of licit or illicit opioid, including prescription opioids, heroin, hydrocodone, hydromorphone, methadone, morphine, oxycodone, oxymorphone, tramadol, or fentanyl. Unintentional, undetermined and intentional deaths were not distinguished in the data analysis.

All independent risk factor variables were derived from the PDMP dataset. The model predictors were selected based on a literature review, availability in the PDMP database, and expert consensus.[5-8,11,23,24] Predictors included: sex, age group, prescription method of payment, numbers of opioid prescribers, opioid dispensers, methadone fills, long-acting opioid fills, opioid use disorder fills (buprenorphine indicated for opioid use disorder); short-acting schedule II opioid fills, short-acting schedule III/IV opioid fills, opioid supply ≥90 days, overlapping opioids and benzodiazepines, benzodiazepine fills, muscle relaxant fills, and stimulant fills. Model predictors were purposefully kept simple to ensure that PDMP users would be able to readily interpret and act upon them.[7]

PDMP threshold variables (Table 2.1) were constructed to represent the unsolicited reporting criteria commonly used by PDMP programs and the most recently published

Centers for Disease Control and Prevention (CDC) guidelines for prescribing opioids.[25]

MPEs was defined as patients with five unique prescribers and five unique dispensers within

the three-month period. Individuals were flagged as having a high daily average MME if the

patient met ≥90 mg/day MME and had ≥60 days' supply of opioids within the three-month

time period (additional detail available in Appendix 2.1).[26] Overlapping opioid and

benzodiazepines was defined as prescriptions that overlapped 25% or more of the days

prescribed, with the initial dispensed prescription having five days' supply or longer[27] and

only for patients with ≥60 days' supply of opioids within the three-month period.[26]

Table 2.1: Summary of PDMP Risk Identification Methods.	
Risk Identification Method	**Definition/Detail**
Predictive Risk Model (PRM)	Full model: 26 variables
Multiple Provider Episode (MPE)	Five unique prescribers, five unique dispensers in three months.
High average Morphine Milligram Equivalents (MME) daily dose	≥90 mg/day average daily dose for patients with ≥60 days' supply opioids within three-months.
Overlapping opioid and benzodiazepine prescriptions	Opioid and benzodiazepine prescriptions overlapping by 25% or more of the days' supply (for days' supply>5 days) based on month the prescription was dispensed and if patient has ≥60 days' supply opioids within three-months.

Statistical Analysis

An adaptation of a logistic regression predictive model that was previously developed and

validated to forecast fatal opioid overdoses was run against the 2015 data using split half

technique (60% development, 40% validation using random selection).[28,29] The predictive

model's odds ratios and model discrimination in the form of the Area Under the Curve

(AUC) were calculated and the predictive risk score was generated for the validation cohort.

Using the validation cohort, individuals meeting the PDMP thresholds were identified and

assigned a binary indication. Therefore, all analyses were performed on the validation cohort as identified by the predictive model's random selection.

Two types of analyses were performed to compare performance. First, the populations identified by each risk identification method (risk model, MPEs, high MMEs, overlapping opioid and benzodiazepine prescriptions) were compared with each other using the model's risk score cutoff that maximized sensitivity and specificity. Comparisons included a descriptive analysis and an overlap analysis of individuals identified by each risk identification method (broken into mutually exclusive groups). Those who experienced fatalities within each high-risk group were captured as well, and a logistic regression for fatal opioid overdose was performed on the mutually exclusive groups to determine the odds ratio and 95% CI's. Further, the PDMP thresholds were then compared with the predictive model as a binary indication at three different risk score cutoff points using several performance indicators such as odds ratios and 95% confidence intervals (CI's), area under the curve, sensitivity (ability of the risk identification method to identify individuals truly at risk of the outcome), and specificity (ability of the risk identification method to identify individuals truly not at risk of the outcome).

Second, each individual PDMP threshold was compared directly against the risk model. The model's risk score cutoff was modified to identify an "equivalently sized" population of high-risk individuals as each PDMP threshold. The "equivalently sized" population was accomplished by sorting the risk score from highest to lowest and assigning a binary indicator of being "at risk" to an equal number of individuals that each PDMP threshold identified. The result was three populations identified by the PDMP thresholds (MPE, high MME, overlapping opioids/benzodiazepines) and three populations identified by the risk

model (one the same size as the MPE, one the same size as high MME, and one the same size as overlapping opioids/benzodiazepines). The risk model binary indicator was applied to the highest risk individuals, regardless of whether the patient also met the PDMP threshold. An overlap analysis was conducted between the PDMP threshold and corresponding risk model populations of equivalent size for each mutually exclusive group: individuals only identified by the PDMP threshold, individuals only identified by the risk model, and individuals identified by both. Chi-square tests were performed to test the probability of independence of each unique group. Logistic regression for fatal opioid overdose was performed to determine the odds ratio and 95% CI's and deaths per 1,000 high risk individuals were calculated.

Results

Study Population

Descriptive statistics for the full validation, risk model, and PDMP threshold cohorts, are summarized in Table 2.2. The validation cohort had 170,438 Maryland residents aged 18-80 years with at least one opioid fill, of which, 244 experienced a fatal opioid overdose. Among those, a total of 50,501 (30%) individuals were identified by at least one risk identification method, of which a total of 178 (73% of all decedents) experienced a fatal opioid overdose. A summary of the full risk model performance can be found in Table 2.3. The risk model cutoff point that maximized sensitivity and specificity, was found to be 0.0015 (Appendix 2.2). This resulted in the largest number of individuals being classified as high-risk, with 39,220 total individuals. The overlapping opioid/benzodiazepine prescription population was next in size with 17,440 total individuals, followed by the high MME population of 14,675. The MPE threshold identified the fewest individuals as high risk (398 total).

Characteristics of the populations identified by a single threshold only were also analyzed and compared and can be found in Appendices 2.3 and 2.4.

Risk Population Overlap

There was a fair amount of population overlap between the risk model, high MME threshold, and overlapping opioid/benzodiazepine threshold. Figure 2.1 is a graphical representation of the overlap of high-risk individuals and high-risk individuals who died across the different risk identification methods. The predictive model had 23,588 (60%) individuals identified by the risk model alone, with 15,632 (40%) individuals identified by at least one of the other PDMP thresholds. The MPE had the highest degree of overlap with 368 (92.5%) individuals being identified by another risk identification method while only 30 (7.5%) individuals were identified by the MPE threshold alone.

The number of high-risk individuals and deaths among each mutually exclusive group is represented in Table 2.4/Figure 2.2. The risk model alone or in combination with other PDMP thresholds identified the most deaths among high-risk individuals. The two highest death rates were for individuals who met all risk identification methods (24.7 deaths per 1,000) and individuals who were identified by the risk model and MPE threshold (17.2 deaths per 1,000), although that was due to two deaths being captured within a very small number of high-risk individuals. Interestingly, the other combinations in which MPE was involved and MPE alone did not capture any deaths. The risk model in combination with high MME and/or overlapping opioid/benzodiazepines resulted in the next highest deaths rates and odds of death (PRM + high MME + opioid/benzo: 8.0 deaths per 1,000, OR 14.6 [9.6-22.3]; PRM + opioid/benzo: 6.0 deaths per 1,000, OR 11.0 [7.1-16.2]; PRM + high MME: 4.1 deaths per 1,000, OR 7.4 [4.4-12.5]). Individuals identified by the risk model alone

captured highest number of deaths (72 deaths; 29.5% of total deaths) but the death rate of

3.1 deaths per 1,000 was average due to the large number of high-risk individuals

(n=23,588). The PDMP thresholds that captured deaths without the risk model were high

MME and overlapping opioid/benzodiazepine (2.4 deaths per 1,000, OR 4.4 [1.4-13.9]), high

MME only (1.0 deaths per 1,000) and overlapping opioid/benzodiazepine prescriptions only

(0.6 deaths per 1,000), although the odds of death for the latter two were not statistically

significant.

Risk Identification Method Performance

Results from the comparative analysis between the PDMP thresholds and the risk model as a

binary indicator at several cutoff points are represented in Table 2.5. The cutoff point that

maximized sensitivity plus specificity was 0.0015 and resulted in the highest sensitivity

(68.4%) and specificity (77.1%) compared with any PDMP thresholds. It captured 68.4% of

the total deaths and although it also identified the largest number of high-risk individuals

(n=39,220), the death rate (4.26 per 1,000 high-risk) was comparable to that of the

overlapping opioid/benzodiazepine prescriptions (4.64 per 1,000 high-risk) and high MME

(4.09 per 1,000 high-risk) thresholds. When the risk model cutoff is modified to be 0.0030 to

identify a more comparable number of high-risk individuals (n=15,881) to that of the

overlapping opioid/benzodiazepine prescriptions (n=17,440) and high MME (n=14,675)

thresholds, the risk model still captures far more deaths (n=113; 46.3% of total deaths) and

has a higher death rate (7.12 per 1,000 high-risk) than the thresholds (overlapping

opioid/benzodiazepine: 81 deaths, 33.2% of total deaths; high MME: 60 deaths, 24.6% of

total deaths). The risk model also had a higher sensitivity (46.3%) than the overlapping

opioid/benzodiazepine prescriptions (33.2%) and high MME (24.6%) with comparable

specificity (risk model: 90.7%; overlapping opioid/benzodiazepine: 89.8%; high MME:

91.4%). The MPE threshold had a high death rate (10.1 per 1,000) but captured only four deaths (1.6% of total deaths) due to a low number of high-risk individuals (n=398) and had extremely low sensitivity (1.64%) and high specificity (99.8%).

Equivalently Sized Population Comparative Analysis

Results from the comparative analysis that examined the degree of overlap in the individuals identified by both the risk model and PDMP threshold of equivalent size are represented in Table 2.6 (characteristics of the equivalent sized populations can be found in Appendix 2.5). While varied, the individuals identified by the PDMP threshold and/or risk model represented only a modest degree of overlap. Overlapping opioid and benzodiazepines had the highest degree of overlap (45.0% overlap; n=17,440), high MME had the second highest degree of overlap (32.3% overlap; n=14,675) and MPE had the smallest overlap (9.6% overlap; n=398). Similar to some of the mutually exclusive population comparisons, individuals identified by both the risk model and threshold had the highest rate of deaths per 1,000 high-risk individuals (Figure 2.3). For high MMEs, the risk model captured a higher percentage of total deaths (27.9%; n=39) as compared to individuals identified by the threshold only (8.6%; n=21) and individuals identified by both (16.0%; n=68). For overlapping opioid and benzodiazepines, the highest proportion of deaths was the population identified by both the PDMP threshold and the risk model (25.8%; n=63) compared with the population identified by the threshold only (7.4%; n=18) or identified by the risk model only (20.9%; n=51).

Discussion

To date, this study is the first to evaluate the extent to which individuals are identified by one or more risk identification methods and how well each approach captured fatal overdose

deaths. There are several key findings to note. First, the overlap analysis demonstrates that while there are groups of people that fall into multiple high-risk definitions, there are some differences in the populations that should be explored. Second, the risk models did a better job of identifying individuals at risk of fatal opioid-overdose. Finally, combining the risk model with other PDMP thresholds can be successful in identifying individuals at risk of fatal opioid overdose, although a large enough pool of high-risk individuals must be maintained to ensure enough individuals at high-risk of death are being properly captured.

As seen with the overlap analysis, there are variations in the population being captured by each of the risk identification methods, even if ignoring the risk model results. With the wide range of thresholds used in practice, there may be populations affected by the opioid crisis that are not being captured if one methodology is being used but not another. Understanding who is being captured by each respective risk identification approach can help understand the impact of identifying one population over another and which high-risk individuals remain unidentified if the risk identification approach is not being utilized. Perhaps some interventions, such as a concerted effort of deprescribing, are better suited toward a particular risk identification method. This concept should be explored further in future research.

The comparative analysis of the risk model at several cutoff points and the equivalently sized population allowed for a direct comparison of the predictive risk model and the thresholds. Across nearly all comparisons, the comprehensive multivariate predictive risk models performed equal to or better than the PDMP thresholds in identifying individuals at risk of a fatal opioid overdose. Should a PDMP program decide to use a predictive model, a challenge facing administrators will be selecting a risk score cutoff to determine who is considered

"high-risk." Selecting a cutoff involves weighing sensitivity versus specificity, or tolerance of false positives (identifying an individual as high risk when they are not) and false negatives (identifying an individual as not at risk when they are). Setting the risk score to a cutoff point that maximizes sensitivity and specificity may be acceptable for more broadly applied harm reduction programs, such as naloxone kit distribution, but if the intervention needs to target a smaller, higher-risk group, the risk score cutoff can be adjusted. For example, if attempting to identify the highest risk individuals for enrollment into intensive one-on-one care management, the risk score cutoff could be adjusted to maximize specificity to reduce the chance of false positives, which inherently reduces the number of high-risk individuals identified.

Another interesting result from the overlap analyses for both the mutually exclusive and equivalent size populations is that risk models could be used in conjunction with other risk identification methods effectively. Rather than selecting only one approach, the PDMP thresholds and risk models could be combined in certain circumstances to identify a high risk population (such as individuals with high MMEs) and then narrow the pool to the highest risk individuals using the predictive model to capture those at highest risk of deaths. While there should be some caution to not narrow the number of high-risk individuals too much, as seen with individuals that met all four risk identification methods or when the risk model was combined with the small number of high-risk individuals identified by the MPEs, the risk model in combination with PDMP thresholds that identified a larger pool of high-risk individuals was successful at identifying individuals at risk of fatal opioid overdose, as seen with high MME and/or overlapping opioid/benzodiazepine prescription. In fact, although the risk model captured the highest number of deaths among the high-risk population, it was at the expense of including a very large number of high-risk individuals.

By combining the risk model with high MME, overlapping opioid/benzodiazepine, or both thresholds, the proportion of deaths among the high-risk individuals increased. This analysis highlights how single or multiple risk identification approaches can be better tailored to circumstance where resources must be distributed or deployed in a manner that will have the highest impact.

Limitations and Additional Considerations

Several study limitations should be noted. The analyses were based on a denominator of patients that had an opioid fill in the PDMP. Therefore, it does not include individuals outside this cohort, including more than half of all opioid overdose decedents in Maryland during that period available in the death dataset. The PDMP data used in this study only contains controlled substances dispensed within or into Maryland. If a Maryland patient were to fill a controlled substance in another state, that would not be represented in the Maryland PDMP, resulting in an incomplete prescription history. Although access to other state data was not available for this analysis, as reference, there were 145,131 (7.66%) non-Maryland residents who filled 434,135 prescriptions (4.62%) in the 2015 Maryland PDMP data. Additionally, only one outcome was analyzed. The individuals identified by the PDMP threshold and risk model that did not experience a fatal opioid overdose may be experiencing other negative outcomes related to opioids not being captured in this analysis, such as non-fatal overdoses or substance use disorder.

This study only examined a standard logistic model, which may not be optimal for predicting fatal opioid overdose. More advanced logistic regression models may result in even more accurate results.[30] This analysis also does not take into consideration natural changes in high-risk behaviors over time (i.e., regression to the mean)[31] or in response to program policies

(e.g., unsolicited reporting). Finally, these data represent a relatively narrow period and does not capture long-term risk patterns and related outcomes. Future research should be conducted to understand whether individuals are consistently meeting the threshold over long periods of time versus a single point in time and whether risk differences exist for those populations.

Conclusion

This study is the first to compare the population overlap and ability to capture fatal opioid overdose events between multiple risk identification methods, including common unsolicited reporting PDMP thresholds and a comprehensive, multivariate risk model for identifying individuals at risk of fatal opioid overdose within a large patient population. The risk model captured a larger number of individuals at risk of fatal opioid overdose as compared with the PDMP thresholds, demonstrating the possibility for improved methods of identifying individuals at risk by PDMP programs. In certain circumstances, the risk model could be combined with one or more PDMP thresholds, provided the number of high-risk individuals was not too restrictive. Working within a naturally resource-constrained circumstance of addressing an epidemic of large proportion, methods to better target individuals at risk for negative outcomes, such as fatal overdoses, are extremely valuable. Understanding the different characteristics of populations identified through various risk identification approaches, the impact of combining multiple together, and the appropriate targeted intervention will assist with refining existing approaches to proactively identify individuals at risk.

References

1. Prescription Drug Monitoring Program (PDMP) Center of Excellence at Brandeis. Status of PDMPs. http://www.pdmpassist.org/pdf/PDMP_Program_Status_20180801.pdf. Updated August 2018.

2. Prescription Drug Monitoring Program (PDMP) Center of Excellence at Brandeis. Questionnaire results from state PDMP programs sent by PDMP TTAC for the purposes of this analysis. February 2019.

3. Prescription Drug Monitoring Program (PDMP) Center of Excellence at Brandeis. Guidance on PDMP best practices: Options for unsolicited reporting. May 2016.

4. Gudoski AJ. Prescription drug monitoring programs: Combating prescription drug misuse. *The Nurse Practitioner*. 2015;40(11):28-33.

5. Bohnert AS, Logan JE, Ganoczy D, Dowell D. A detailed exploration into the association of prescribed opioid dosage and overdose deaths among patients with chronic pain. *Med Care*. 2016;54(5):435-441.

6. Boscarino JA, Kirchner HL, Pitcavage JM, Nadipelli VR, Ronquest NA, Fitzpatrick MH, Han JJ. Factors associated with opioid overdose: A 10-year retrospective study of patients in a large integrated health care system. *Subst Abuse Rehabil*. 2016;7:131-141.

7. Geissert P, Hallvik S, Van Otterloo J, O'Kane N, Alley L, Carson J, Leichtling G, Hildebran C 3rd, Wakeland W, Deyo RA. High-risk prescribing and opioid overdose: Prospects for prescription drug monitoring program–based proactive alerts. *Pain*. 2018;159(1):150-156.

8. Glanz JM, Narwaney KJ, Mueller SR, Gardner EM, Calcaterra SL, Xu S, Breslin K, Binswanger IA. Prediction model for two-year risk of opioid overdose among patients prescribed chronic opioid therapy. *J Gen Intern Med*. 2018.

9. Liang Y, Goros MW, Turner BJ. Drug overdose: Differing risk models for women and men among opioid users with non-cancer pain. *Pain Med*. 2016;17(12):2268-2279.

10. Oliva, EM, Bowe T, Tavakoli S, Martins S, Lewis ET, Paik M, Wiechers I, Henderson P, Harvey M, Avoundjian T, Medhanie A, Trafton JA. 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. *Psychol Serv*. 2017;14(1):34-49.

11. Zedler B, Saunders WB, Joyce AR Vick CC, Murrelle EL. Validation of a screening risk index for serious prescription opioid-induced respiratory depression or overdose in a US commercial health plan claims database. *Pain Med*. 2018;19(1):68-78.

12. Bureau of Justice Assistance. Program performance report: Prescription drug monitoring program (PDMP). 2013.

13. Ferries EA, Gilson, AM, Aparasu RR, Chen H, Johnson ML, Fleming ML. Prevalence and factors associated with multiple provider episodes in texas: An epidemiological analysis of prescription drug monitoring program data. *painmedicine*. 2016;18(10):1941-1951.

14. Hall AJ, Logan JE, Toblin RL, Kaplan JA, Kraner JC, Bixler D, Crosby AE, Paulozzi LJ. Patterns of abuse among unintentional pharmaceutical overdose fatalities. *JAMA*. 2008;300(22):2613-2620.

15. Katz N, Panas L, Kim M, Audet AD, Bilansky A, Eadie J, Kreiner P, Paillard FC, Thomas C, Carrow G. Usefulness of prescription monitoring programs for surveillance: Analysis of schedule II opioid prescription data in massachusetts, 1996–2006. *Pharmacoepidemiol Drug Saf*. 2010;19:115–23.

16. Gonzalez AM KA. Impact of a managed controlled-opioid prescription monitoring program on care coordination. *Am J Manag Care*. 2012;18(9):516-524.

17. Simeone R HL. An evaluation of prescription drug monitoring programs. 2006.

18. Sorg MH, LaBrie S, Parker W. Analysis and evaluation of participation by prescibers and dispensers in the maine state prescription monitoring program. *Anthropology Faculty Scholarship*. 2009;19.

19. Young LD, Kreiner PW, Panas L. Unsolicited reporting to prescribers of opioid analgesics by a state prescription drug monitoring program: An observational study with matched comparison group. *Pain Medicine*. 2017;0:1-12.

20. McDonald DC, Carlson KE, Jalbert SK. Unsolicited reporting by a prescription drug monitoring program in reducing inappropriate acquisition of opioids. *Pain Medicine*. 2018;00:1-11.

21. State of Maryland Code of Maryland Regulations (COMAR). 03 dispenser reporting. 10.47.07.03.

22. Maryland Department of Health. Office of the chief medical examiner. https://health.maryland.gov/ocme/Pages/Home.aspx.

23. Liang Y TB. Assessing risk for drug overdose in a national cohort: Role for both daily and total opioid dose? *J Pain*. 2015;16(4):318-325.

24. Zedler B, Xie L, Wang L, Joyce A, Vick C, Brigham J, Kariburyo F, Baser O, Murrelle L. Development of a risk index for serious prescription opioid-induced respiratory depression or overdose in veterans' health administration patients. *Pain Med*. 2015;16(8):1566-1579.

25. Dowell D, Haegerich TM, Chou R. CDC guideline for prescribing opioids for chronic pain — united states, 2016. *MMWR Recomm Rep*. 2016;65(No. RR-1):1-49.

26. Centers for Disease Control and Prevention. Quality improvement and care coordination: Implementing the CDC guideline for prescribing opioids for chronic pain. 2018.

27. Paulozzi LJ, Kilbourne EM, Shah NG, et al. A history of being prescribed controlled substances and risk of drug overdose death. *Pain Med*. 2012;13(1):87-95.

28. Picard RR BK. Data splitting. *American Statistician*. 1990;44(2):140-147.

29. Ferris LM, Saloner B, Krawczyk N, Schneider KE, Jarman M, Jackson K, Lyons BC, Eisenberg M, Richards TM, Lemke KW, Weiner JP. Predicting opioid overdose deaths using prescription drug monitoring program data. *Am J Prev Med*. Accepted July 2019, awaiting publication.

30. Kan HJ, Kharrazi H, Chang HY, Bodycombe D, Lemke K., Weiner JP. Exploring the use of machine learning for risk adjustment: A comparison of standard and penalized linear regression models in predicting health care costs in older adults. *PloS one*. 2019;14(3):e0213258.

31. Kelly C PT. Correcting for regression to the mean in behavior and ecology. *Am Nat*. 2005;166(6):700-707.

Tables and Figures

Table 2.2: Characteristics of study population based on various risk identification methods. *					
	Full Cohort	**Risk Model Cohort**	**MPE Cohort**	**High MME Cohort**	**Op/Ben Overlap Cohort**
# individuals	170,438	39,220	398	14,675	17,440
Sex – Male, n (%)	69,580 (40.8)	25,527 (65.1)	145 (36.4)	6,772 (46.2)	5,657 (32.4)
Age 18-34 years	32,619 (19.1)	8,819 (22.5)	117 (29.4)	1,093 (7.5)	1,273 (7.3)
Age 35-49 years	41,699 (24.5)	16,179 (41.3)	166 (41.7)	4,027 (27.4)	4,121 (23.6)
Age 50-64 years	60,697 (35.6)	13,965 (35.6)	96 (24.1)	7,092 (48.3)	7,924 (45.4)
Age 65-80 years	35,423 (20.8)	257 (0.7)	19 (4.8)	2,463 (16.8)	4,122 (23.6)
Region of Patient Residence, n (%)					
Baltimore City	22,301 (13.1)	5,830 (14.9)	70 (17.6)	12 (0.1)	1,693 (9.7)
Capital	46,539 (27.3)	8,834 (22.5)	105 (26.4)	1,643 (11.2)	3,492 (20.0)
Central	63,601 (37.3)	15,004 (38.3)	158 (39.7)	2,696 (18.4)	7,265 (41.7)
Eastern	15,637 (9.2)	3,468 (8.8)	19 (4.8)	6,476 (44.1)	1,902 (10.9)
Southern	12,182 (7.2)	3,205 (8.2)	32 (8.0)	1,464 (10.0)	1,387 (8.0)
Western	10,014 (5.9)	2,857 (7.3)	14 (3.5)	1,435 (9.8)	1,693 (9.7)
Unknown	164 (0.1)	22 (0.1)	0 (0)	949 (6.5)	8 (0.1)
Method of Payment, n (%)					
Private Pay	19,114 (11.2)	5,798 (14.8)	23 (5.8)	742 (5.1)	916 (5.3)
Medicaid	26,023 (15.3)	12,877 (32.8)	148 (37.2)	1,912 (13.0)	3,096 (17.8)
Medicare	19,430 (11.4)	4,208 (10.7)	44 (11.1)	2,506 (17.1)	3,181 (18.2)
Commercial Insurance	101,813 (59.7)	15,086 (38.5)	182 (45.7)	9,013 (61.4)	9,771 (56.0)
Military/VA	1,661 (1.0)	793 (2.0)	0 (0)	176 (1.2)	177 (1.0)
Indian	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Other/Unknown	2,397 (1.4)	458 (1.2)	1 (0.3)	326 (2.2)	299 (1.7)
# prescribers, mean (SD)	1.5 (0.9)	2.1 (1.3)	7.0 (2.8)	2.1 (1.3)	2.4 (1.3)
# dispensers, mean (SD)	1.3 (0.7)	1.7 (1.0)	6.2 (1.9)	1.8 (1.1)	1.8 (1.1)
# deaths, n (%)	244 (0.1)	167 (68.4)	4 (1.6)	60 (24.6)	81 (33.2)
Abbreviations: PDMP=Prescription Drug Monitoring Program; PRM=predictive risk model; MPE=Multiple Provider Episodes (5 unique prescriber and 5 unique dispensers); MME=morphine milligram equivalents; Op/Ben=opioid/benzodiazepine, VA=Veterans Affairs; SD=standard deviation. * Maryland residents 18-80 years with at least one opioid fill for full populations and individuals identified by a single risk identification method only within the validation population using 3 months of data (April-June 2015). Note: Cohorts have overlapping individuals represented.					

Table 2.3: Multivariate risk model for individuals at risk of fatal opioid overdose. *		
Predictor	**Odds Ratio (95% Confidence Interval)**	**p-value**
Male	**2.45 (1.96-3.06)**	**0.000**
Age 35-49 years	1.11 (0.83-1.49)	0.497
Age 50-64 years	**0.64 (0.47-0.87)**	**0.004**
Age 65-80 years	**0.11 (0.06-0.22)**	**0.000**
Method of Payment: Self-pay	**1.64 (1.13-2.38)**	**0.009**
Method of Payment: Medicaid	**2.35 (1.82-3.03)**	**0.000**
Method of Payment: Medicare	**2.12 (1.47-3.06)**	**0.000**
Method of Payment: Military/Veteran's Affairs (VA)	**2.83 (1.24-6.47)**	**0.014**
Method of Payment: Other/unknown payer	1.16 (0.43-3.14)	0.772
Opioid prescribers 2	**1.59 (1.19-2.13)**	**0.002**
Opioid prescribers ≥3	1.47 (0.99-2.19)	0.057
Opioid dispensers 2	**1.44 (1.07-1.93)**	**0.015**
Opioid dispensers ≥3	**1.60 (1.06-2.42)**	**0.026**
Methadone fills ≥1	1.52 (0.90-2.57)	0.114
Opioid long acting fills ≥1	0.91 (0.66-1.26)	0.572
Opioid use disorder (OUD) fills ≥1	**2.29 (1.23-4.24)**	**0.009**
Opioid short acting, schedule II fills 1	0.86 (0.55-1.34)	0.498
Opioid short acting, schedule II fills 2-3	0.93 (0.57-1.52)	0.764
Opioid short acting, schedule II fills ≥4	1.16 (0.66-2.06)	0.603
Opioid other short acting, schedule III-IV fills ≥1	0.72 (0.50-1.03)	0.076
Opioid supply ≥91 days	**1.68 (1.23-2.30)**	**0.001**
Overlapping opioid/benzodiazepine prescriptions	0.92 (0.60-1.40)	0.692
Benzodiazepine fills 1	**1.66 (1.09-2.55)**	**0.020**
Benzodiazepine fills ≥2	**3.11 (2.06-4.70)**	**0.000**
Muscle relaxant fills ≥1	0.99 (0.55-1.79)	0.983
Sedative fills ≥1	1.04 (0.72-1.52)	0.823
Note: bolded values indicate statistical significance (p<0.05). The cutoff point that maximized sensitivity and specificity for the 3-month risk model was 0.0015. Reference categories include: female sex, age 18-34, commercial insurance (modal), 1 opioid prescriber, 1 opioid dispenser, 0-90 days' supply, no concomitant opioid/benzodiazepines, and no other controlled substance fills. Model performance: derivation AUC=0.814; validation AUC=0.798. * Maryland residents 18-80 years with at least one opioid fill using 3 months of data (April-June 2015).		

Figure 2.1: Overlap analysis of individuals identified by a risk identification method.*

Figure 2.1.1: Number of individuals identified as high-risk
(n=50,501; 30.0%)
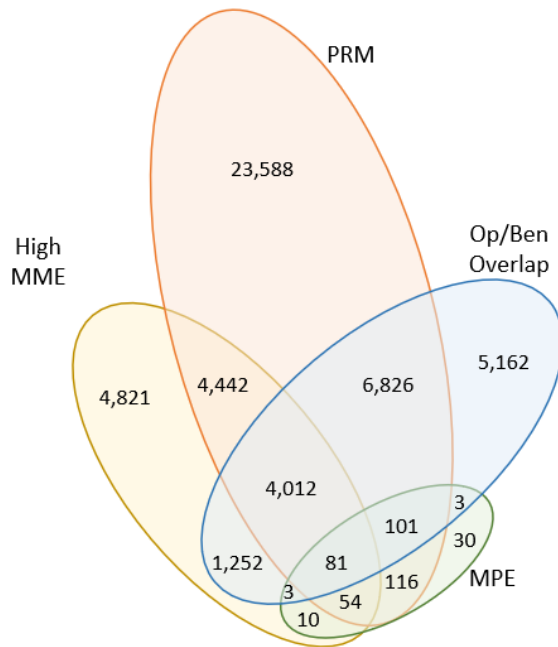
Figure 2.1.2: Number of deaths among high-risk individuals
(n=178; 73.0%)
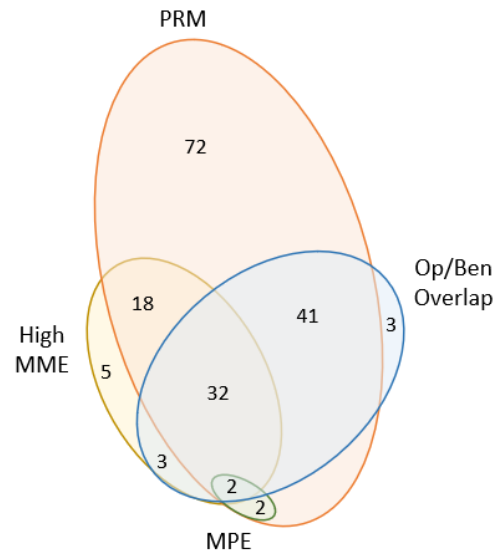
Abbreviations: PRM=predictive risk model; MME=morphine milligram equivalents; MPE=multiple provider episodes (5 unique prescribers and 5 unique dispensers); op/ben=opioid/benzodiazepine.

*Maryland residents 18-80 years with at least one opioid fill for full populations and individuals identified by a single risk identification method only within the validation population using 3 months of data (April-June 2015). Total validation cohort is 170,438 individuals with a total of 244 deaths. Total validation cohort size is 170,438 individuals with a total of 244 deaths (2015-2016). PRM cohort=39,220 individuals; High MME cohort=14,675 individuals; Op/Ben overlap=17,440 individuals; MPE=398 individuals.

Table 2.4: Mutually exclusive populations of high-risk individuals. *					
Risk Populations	**# High-Risk Individuals**	**# Deaths**	**Deaths per 1,000**	**% Total Deaths**	**Odds Ratio (95% CI)**
All	81	2	24.7	0.8%	**46.0 (11.1-191.0)**
PRM + MPE	116	2	17.2	0.8%	**31.9 (7.7-131.7)**
PRM + High MME + Op/Ben Overlap	4,012	32	8.0	13.1%	**14.6 (9.6-22.3)**
PRM + Op/Ben Overlap	6,826	41	6.0	16.8%	**11.0 (7.4-16.2)**
PRM + High MME	4,442	18	4.1	7.4%	**7.4 (4.4-12.5)**
PRM Only	23,588	72	3.1	29.5%	**5.6 (4.0-7.8)**
High MME + Op/Ben Overlap	1,252	3	2.4	1.2%	**4.4 (1.4-13.9)**
High MME Only	4,821	5	1.0	2.0%	1.9 (0.8-4.7)
Op/Ben Overlap Only	5,162	3	0.6	1.2%	1.1 (0.3-3.4)
MPE + Op/Ben Overlap	3	0	0.0	0.0%	-
MPE + High MME + Op/Ben Overlap	3	0	0.0	0.0%	-
MPE + High MME	10	0	0.0	0.0%	-
MPE Only	30	0	0.0	0.0%	-
PRM + MPE + High MME	54	0	0.0	0.0%	-
PRM + MPE + Op/Ben Overlap	101	0	0.0	0.0%	-
Abbreviations: MPE=multiple provider episodes (5 unique prescribers and 5 unique dispensers); PRM=predictive risk model; MME=morphine milligram equivalents; Op/Ben=opioid/benzodiazepine; CI=confidence interval * Maryland residents 18-80 years with at least one opioid fill for full populations and individuals identified by a single risk identification method only within the validation population using 3 months of data (April-June 2015).					

Figure 2.2: Death data analysis for mutually exclusive populations of high-risk individuals. *
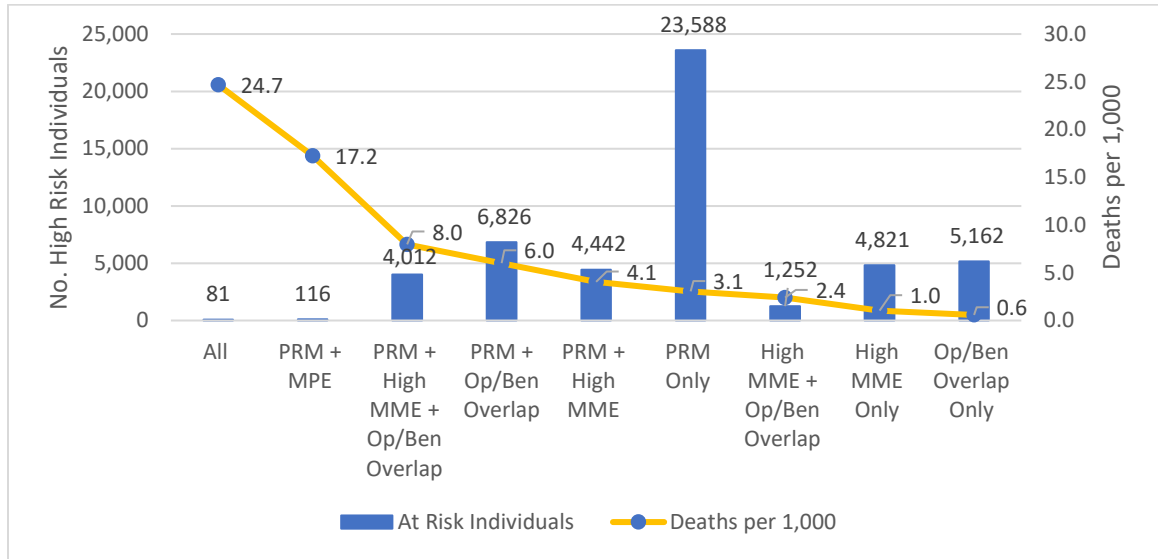
* Maryland residents 18-80 years with at least one opioid fill for full populations and individuals identified by a single risk identification method only within the validation population using 3 months of data (April-June 2015). Total validation cohort is 170,438 individuals with a total of 244 deaths.

Table 2.5: Performance of each PDMP threshold and the risk model at three different cutoff points.						
Performance Indicator	PRM (0.0015 cutoff)	Opioid/ Benzo overlap	PRM (0.0030 cutoff)	High MME	PRM (0.0085 cutoff)	MPE
No. of High Risk	39,220	17,440	15,881	14,675	3,102	398
% of total population	23.0	10.2	9.3	8.6	1.8	0.2
No. of Deaths	167	81	113	60	35	4
% of Total deaths	68.4	33.2	46.3	24.6	14.3	1.6
Deaths per 1,000 high risk	4.26	4.64	7.12	4.09	11.28	10.05
Chi square	284.7	140.3	395.8	78.3	214.5	20.73
p-value	0.000	0.000	0.000	0.000	0.000	0.000
Odds Ratio (95% CI)	7.28 (5.56, 9.54)	4.38 (3.35, 5.71)	8.45 (6.57-10.87)	3.47 (2.59, 4.65)	9.13 (6.37, 13.08)	7.18 (2.66, 19.39)
AUC	0.728	0.615	0.685	0.580	0.563	0.507
Sensitivity (%)	68.44	33.20	46.31	24.59	14.34	1.64
Specificity (%)	77.05	89.80	90.67	91.41	98.20	99.77
PPV (%)	0.43	0.46	0.71	0.41	0.88	1.01
NPV (%)	99.94	99.89	99.92	99.88	99.89	99.86
Abbreviations: PRM=predictive risk model; Benzo=Benzodiazepine; MME=morphine milligram equivalents (≥90 mg/day); MPE=multiple provider episode (5 unique prescribers and 5 unique dispensers); CI=confidence interval; AUC=area under the curve; PPV=positive predictive value; NPV=negative predictive value Total number of high-risk individuals was 170,438 and total deaths was 244 in the validation sample.						

Table 2.6: Overlap analysis of PDMP threshold and equivalent size risk model populations. *

Variable, n (%)	MPE vs. Risk Model			High MME vs. Risk Model			Opioid/Benzo Overlap vs. Risk Model		
	MPE Only	Both	PRM Only	High MME Only	Both	PRM Only	Op/Benzo Only	Both	PRM Only
Total high-risk patients	398 (0.2)			14,675 (8.6)			17,440 (10.2)		
Total high-risk patient deaths	7 (1.8)			128 (0.9)			132 (0.8)		
High risk patients	360 (90.5)	38 (9.6)	360 (90.5)	9,937 (67.7)	4,738 (32.3)	9,937 (67.7)	9,586 (55.0)	7,854 (45.0)	9,586 (55.0)
Deaths among high-risk	3 (42.9)	1 (14.3)	3 (42.9)	21 (16.4)	39 (30.5)	68 (53.1)	18 (13.6)	63 (47.7)	51 (38.6)
# deaths per 1,000 high risk patients	8.3	26.3	8.3	2.1	8.2	6.8	1.9	8.0	5.3
% of total deaths	1.2	0.4	1.2	8.6	16	27.9	7.4	25.8	20.9
Risk of death, OR (95% CI)	6.0 (1.9, 18.9)	19.3 (2.6, 141.4)	6.0 (1.9, 18.9)	2.6 (1.7, 4.2)	10.4 (7.2, 15.0)	8.7 (6.4, 11.7)	2.4 (1.5, 4.0)	10.4 (7.6, 14.1)	6.8 (4.9, 9.5)

Abbreviations: MPE=multiple provider episodes (5 unique prescribers and 5 unique dispensers); PRM=predictive risk model; MME=morphine milligram equivalents; op/benzo=opioid/benzodiazepine
* Maryland residents 18-80 years with at least one opioid fill for full populations and individuals identified by a single risk identification method only within the validation population using 3 months of data (April-June 2015).

Figure 2.3: Death analysis of PDMP threshold and equivalent size risk model populations.
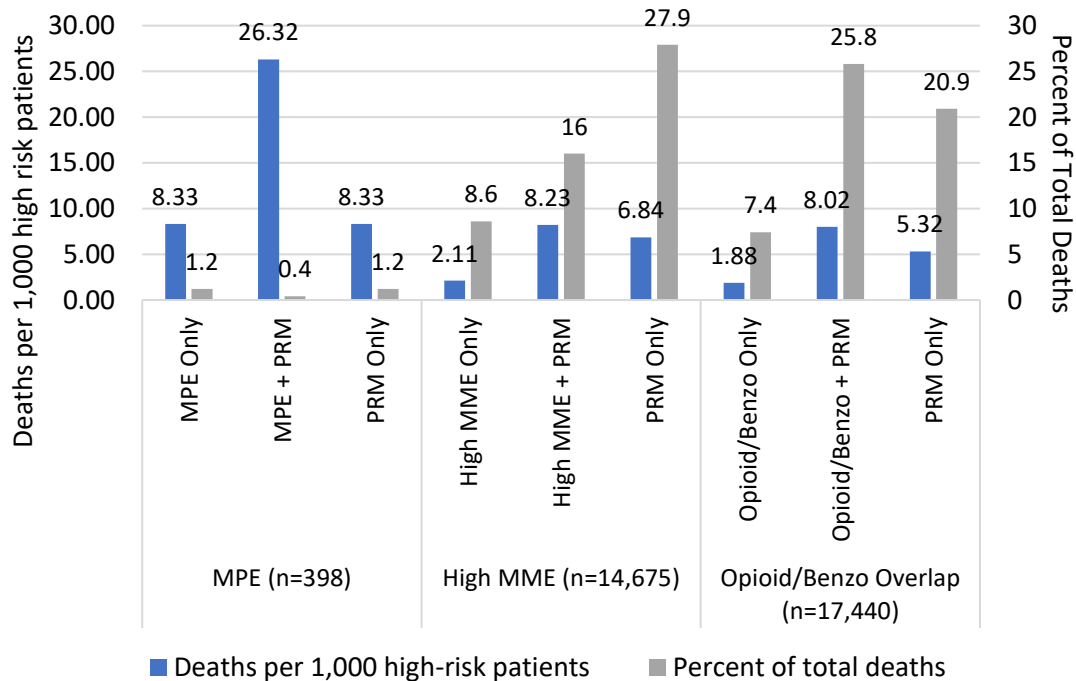
Paper 3: Assessing the Impact of Algorithms for Matching Persons Across State Datasets to Identify Risk of Fatal Opioid Overdose

Abstract

Background: The opioid epidemic in the United States has precipitated a need for public health agencies to better understand risk factors associated with fatal overdoses. Matching person-level information stored in public health, medical, and human services datasets can enhance the understanding of opioid overdose risk factors and interventions. A major impediment to using datasets from separate agencies has been the lack of a cross-organization unique identifier. Although different matching techniques that leverage patient demographic information can be used, the impact of using a particular matching approach is not well understood.

Objective: This study compares the impact of using probabilistic versus deterministic matching algorithms to link disparate person-level datasets together for identifying persons at the highest risk of a future fatal opioid overdose.

Methods: This study used person-level data from three agencies in Maryland: Prescription Drug Monitoring Program data, arrest data, and death data. Individuals with at least one controlled substance filled during 2015 were linked with drug- or property-related arrests (2013-2015) and opioid-related overdose death data (2015-2016) using a probabilistic matching algorithm and two deterministic matching algorithms. Impact of the person-level matching was assessed by comparing the prevalence of key risk indicators, the outcome, and the performance of a multivariate logistic regression for fatal opioid overdose using the combined datasets.

Results: The probabilistically matched population resulted in the fewest unique identities (n=1,859,445) as compared with the deterministic-basic algorithm (n=1,910,741) and the deterministic+zip algorithm (n=2,065,019) and had the highest degree of matching with arrest and death data. Model area under the curve performance was comparable across the three algorithms (probabilistic: 0.847; deterministic-basic: 0.854; and deterministic+zip: 0.826), however, the optimal model cutoff points differed, resulting in tradeoffs between sensitivity and specificity.

Conclusions: The probabilistic algorithm enabled a more comprehensive understanding of risk prevalence for fatal opioid overdose among all individuals within and across disparate datasets. However, model performance based on area under the curve indicates the deterministic-basic matching could be a suitable option for understanding high-level risk. Consideration must be made as to the intent of matching the datasets together, as probabilistic algorithms can be more resource-intensive and costly to maintain compared with the deterministic algorithms.

Introduction

Individuals at risk of adverse opioid-related outcomes often interact with multiple human service sectors, including health care, public health, social and human service agencies. As individuals interact with each sector, information about their complex needs, characteristics and service provisions are recorded in electronic databases. If these databases were linked, thoughtful analysis of an integrated database encompassing relevant cross-sector factors could improve the understanding and identification of individuals at risk for adverse outcomes related to opioid use. Although the ease of collecting and matching electronic data has improved for single datasets, matching person-level data across distinct agencies remains a major impediment.[1] Most human service datasets remain siloed without a common identifier to efficiently match separate person-level datasets in a way that supports a more comprehensive understanding of an individual's risk.[2] Social security numbers are usually not collected by electronic systems and in the health care realm, the United States Congress overruled the mandate for a unique patient identifier in the Health Insurance Portability and Accountability Act (HIPAA) of 1996, citing privacy concerns.[3]

Absent a nationwide unique identifier for patients, alternative analytic techniques are often used to match person-level data from different sources together using personal demographics and identifiers. Most often, either "deterministic" and/or "probabilistic" matching algorithms are utilized. Deterministic matching relies on exact matches of combinations of direct and indirect identifiers to determine a match, while probabilistic matching uses a weighted analytic algorithm applied to key demographic (e.g., age, gender) and personal information (e.g., name, address) to derive a score that determines whether a certain match threshold was reached.[4]

Within the health care industry, probabilistic matching is a fairly common applied technique, particularly within Health Information Exchanges (HIEs) and large multi-system health organizations.[5] The performance of probabilistic algorithms have been found to have a higher degree of matching accuracy than deterministic algorithms[6] and a strong potential to link individuals across datasets in the absence of a common identifier available for exact matching.[7] A handful of studies examining opioid overdose outcomes have used probabilistic algorithms to link cross-domain datasets (e.g., electronic health records [EHRs], Prescription Drug Monitoring Program [PDMP] and death) together with public domain software applying both deterministic and probabilistic algorithms.[8,9]

Despite the improved performance, access to a probabilistic matching is not always available and exact matching must be used. A handful of studies have linked death data with prison/corrections data to examine fatal overdose events,[10-14] the majority of which have applied deterministic algorithms techniques to link datasets together.[15-19] Exact match on the individual's name and date of birth are most commonly used, with some studies also using sex, county of residence, and social security number as additional matching criteria.[15-19] The largest scale example of combining data from multiple agencies was a statewide opioid overdose analysis performed by Massachusetts state government that linked fifteen datasets together using a series of deterministic algorithms.[20]

As matching person-level data across sectors to understand risks related to opioids becomes more common, additional research needs to be done to understand the impact of data matching techniques. A recent analyses examined the impact of a deterministic matching algorithm against a proprietary probabilistic algorithm on the prevalence of key high-risk indicators within PDMP data, and demonstrated that the degree of the impact varied based

on the measure.[21] This study, using statewide Maryland data, builds on these concepts by comparing two deterministic record matching algorithms with probabilistic matching (operational standard) to quantify the effect the record linkage approaches on patient risk measures using PDMP, criminal justice, and death data.

Methods

Study Design

A retrospective cohort analysis was performed using 2015 PDMP data as the anchor database. Individuals with one or more controlled substance prescription fills were included. The Maryland PDMP collects schedule II-V controlled substances (i.e. opioids, sedatives, stimulants, and other drugs for medicinal use with potential for abuse) dispensed to Maryland residents by pharmacists, dispensing prescribers, and mail-order pharmacies. The data collected by PDMP includes: (1) patient identifying information; (2) prescription number, date written, date filled, refill information, payment method, National Drug Code (NDC) of the drug dispensed, quantity dispensed, and days' supply; (3) the prescriber's Drug Enforcement Agency (DEA) number and last name; and, (4) the dispenser's DEA number.[22] The PDMP data is collected by a vendor's software that has its own native matching algorithm to determine unique identities (totaling 3,304,446 in 2015) prior to being processed by the probabilistic or deterministic algorithms. The matching algorithms were applied to the PDMP dataset starting with the vendor-defined identities such that individuals were matched within the dataset before being matched with external datasets. After applying the matching algorithms to each row within the PDMP database, matching was performed across the other datasets. This resulted in a newly created unique identifier being assigned to each identity included in the study specific to the matching algorithm. The final limited dataset for research contained only the unique identifiers and IRB-approved variables for

analysis. See Appendix 3.1 for graphical and numerical representations of the dataset overlap.

Population & Data Sources

Arrest and death data were layered onto the PDMP anchor dataset and were only included if matched with an individual with a controlled substance dispensed in 2015. Individuals with property- or drug-related arrests with Maryland's criminal justice system occurring between 2013-2016 from the Department of Public Health Safety and Correctional Services (DPSCS) were matched with the individuals in the PDMP data, however; only arrest events for 2013-2015 that matched with an individual in the PDMP dataset were included in the analysis. Arrests prior to 2015 were included because historical arrests were relevant to future fatal opioid-related outcomes and ensured a large enough sample size. Arrests from 2016 were omitted to align with the PDMP anchor dataset timeframe. DPSCS contains administrative data for individuals arrested for drug or property crimes (except for pre-trial) and uses a State Identification Number to positively identify unique individuals within their Offender Case Management System using the arrestee's fingerprints. The DPSCS data consisted of 38,004 unique identities from 2013-2016.

Death data were provided by the Office of the Chief Medical Examiner (OCME) and contained case investigation data for all drug and alcohol overdose deaths in Maryland. Data included, but was not limited to, identifying information for the decedent, date of death, and cause of death. Deaths across all dates (2012-2016) were matched with the PDMP data (all-cause: n=22,829; opioid-related overdose deaths: n=4,551), but only the outcome-of-interest of opioid-related overdose deaths occurring in 2015-2016 that were matched with an individual in the PDMP dataset were included in the analysis. The OCME data was

inherently based on a final biological event and therefore each individual is represented only once and did not require within-dataset matching.

IRB approval was obtained from the Johns Hopkins Bloomberg School of Public Health (IRB #00007542) and the Maryland Department of Health. Strict guidelines were followed to maintain data security and confidentiality. All personal identifiers were maintained separately from the risk information, and the risk information was in a database only with anonymous unique identifiers specific to this study to ensure no re-identification of the records could occur. See Appendix 3.2 for the data linking process using identifiable data prior to delivering the research dataset.

Variables

The target outcome of interest was fatal opioid overdose. Fatal opioid overdose was defined as having a cause-of-death indicator in the OCME database involving illicit or licit opioids, including any of the following substances: prescription opioids, hydrocodone, hydromorphone, methadone, morphine, oxycodone, oxymorphone, tramadol, heroin, or fentanyl. Intentional, unintentional, and undetermined intent were not distinguished in the data analysis.

Independent/predictive variables for the risk model were derived from the PDMP data and were based on common risk indicators found in the literature[8,16,23,24] or established as national clinical quality improvement outcome measures.[25] The model variables included sex, age group, method of payment for prescriptions (modal), number of unique opioid prescribers and dispensers, and number of prescriptions for methadone, long-acting opioids, buprenorphine opioids, shorting-acting schedule II opioids, short-acting schedule III and IV opioids, benzodiazepines, other non-benzodiazepine sedatives, and muscle relaxants.

Prevalence of several more complex variables were also analyzed independently and/or were included in the model based on thresholds commonly used by PDMP programs to identify individuals at risk:[26] (1) multiple provider episodes (MPEs), defined as five unique prescribers and five unique dispensers for all controlled substances within a rolling three-month window for the duration of the study period; (2) high daily average morphine milligram equivalents (MMEs), defined as ≥90 mg/day average daily dose for patients with ≥60 days' supply opioids within a rolling three-month window for the duration of the study period; and (3) overlapping opioid and benzodiazepine prescriptions, where overlap occurs for 25 percent or more of the days' supply (for days' supply>5 days) based on month the prescription was dispensed and if patient had ≥60 days' supply opioids within a rolling three-month window for the duration of the study period. A variable was also constructed for any individual with at least one arrest in the DPSCS dataset.[27]

Person-level Matching Techniques

Prior to removing personal identifiers from the research database, the data files were linked together using a probabilistic matching algorithm and two different deterministic matching algorithms. The matching algorithms relied on a set of core identifiable personal and demographic data available for use, including first name, last name, DOB (date of birth), sex, street address, city, zip code, phone number, and SSN (social security number), if available.

Probabilistic linkage: The probabilistic matching algorithm served as the operational standard in this study and has been functioning in Maryland to deliver information to clinicians at the point of care and support statewide analytic initiatives for a decade. The probabilistic matching services were executed by Maryland's state-designated, non-profit health information exchange (HIE), CRISP (Chesapeake Regional Information System for

our Patients), using master patient index (MPI) technology (IBM InfoSphere®, v10.1; IBM, Armonk, North Castle, NY). The CRISP MPI supports HIE technology in Maryland, West Virginia, and the District of Columbia and contains approximately 19 million unique master identities. The MPI is pinged by user queries ~2.16 million times per day (multiple calls per patient search possible) and processes ~1.7 million new clinical data elements per day from HIE participants.[28]

By adopting conservative scoring methodologies and thresholds, the CRISP MPI algorithm was designed to reduce the risk of false positives (i.e., matching records of separate persons incorrectly together) to a near-zero level; while at the same time ensuring limited false negatives (i.e., not matching the same person's records together if the identifier information is slightly different on each record). The estimated false positive rate is 0.9 percent, as measured by a comparative analysis performed in 2019 with a subset of a major stakeholder's data.[28] As a high-level summary, the probabilistic matching algorithm reaches a final matching score using the demographic inputs by bucketing the data values together for fast comparison after basic standardization steps. The standardization functions include removing special characters, applying truncations, converting name to all upper-case, and applying two address standardization arguments for postal codes and unit information. The bucketing processes included name (first name + last name), name phonetic + DOB, name phonetic + zip code, SSN, phone, zip code, MRN (master record number), plus some special attributes specific to MD data providers (e.g., hospitals). The comparison step applies a score based on whether the bucketed information matched exactly (full score) or had minor discrepancies (partial score), such as misspellings, nicknames, and transposed numbers, or risk of a false positive. The final score is tallied and if it passes the CRISP-defined threshold for a match (≥13.1), the records are considered part of the same master

patient identity and are linked together. Any records that did not meet the threshold remain as separate records. Matching improves over time as more sources of data provide the MPI with more comprehensive and updated patient information. Past phone numbers, addresses, and names (including maiden names) are factored into the matching, increasing the likelihood that data from different sources are appropriately associated with a single identity. See Appendix 3.3 for further detail on the probabilistic algorithm functions and configurations.

Deterministic linkage: Two levels of deterministic matching algorithms were applied to the data based on availability of the demographic elements and common approaches taken in previously published literature.[17,20] The first deterministic algorithm ("deterministic-basic") linked patients using an exact match on first name, last name, gender, and DOB. The second deterministic algorithm ("deterministic+zip") took a more stringent approach to matching and linked patients using an exact match on the same elements as the first algorithm (name, gender, date of birth), plus zip code. Gender was normalized to Male, Female, or Unknown. Minor adjustments to first name were also made to ensure there were no middle initials or middle names included in the first name field. No close-match, near-match, or phonetic matching logic was applied to remain conservative.

Processing the data using the deterministic algorithms began with an empty master patient list. The PDMP dataset was processed first by comparing each identity within the dataset with the master patient list. If a new identity was found in the dataset that did not exist in the master patient list, it was added to the master patient list with a new deterministic identifier (ID). If an exact match occurred between the master patient list and an identity in the dataset, the identity in the dataset with assigned the deterministic ID in the master list. Next,

the DPSCS and OCME files were processed in the same manner, comparing the identities in

the dataset with the master patient list. Because the master patient list was for all unique

individuals, if there were multiple records with matching demographics within a single

database, the deterministic ID would be applied across all records, therefore matching

records within a single database (not just across). For transaction-level databases (PDMP and

DPSCS), identities with the same dataset-defined patient identifier within a single database

was checked to ensure the same deterministic ID was applied. This process was repeated for

both deterministic algorithms, resulting in two separate sets of master deterministic IDs. See

Appendix 3.4 for a detailed description of the deterministic matching steps.

Statistical Analysis

Each matching algorithm requires the demographic data to be at a high enough quality level

to facilitate sufficient matching. Prior to data linkage, the demographic variables used for

matching in each dataset were assessed for data completeness. Completeness was calculated

by computing the number of occurrences of missing data values for each data field per

dataset.[29] Post data linkage, the characteristics of the population linked by the different

matching algorithms were described. A multivariate logistic regression analysis for risk of

fatal opioid overdose was performed on the population as defined by each matching

algorithm to assess the impact of data matching on predicting patient-level risk. Model

performance was measured using sensitivity, specificity, and area under the receiver

operating characteristic curve (AUC), measuring the ability of the model to discriminate

between individuals truly at risk (sensitivity) from individuals truly not at risk (specificity),

ranging from 0 to 1. Percentage bias was calculated for each model variable by taking the

difference in the coefficients (log odds) of each predictor for the deterministically linked

population (comparison) against the coefficients of the model from the probabilistically

linked population (reference) serving as the operational standard using the formula:[30]

$$[(logit_{reference} - logit_{comparison} / logit_{reference})]*100$$

Finally, the number of unique individuals with a high-risk indicator identified by a single

matching algorithm only (i.e. not identified by other matching algorithms) and death rates

per 1,000 for individuals with a predictor or high-risk indicator were also calculated for the

population matched by each algorithm.

Results

Quality of Matching Fields

All datasets (PDMP, DPSCS, and OCME) contained the common matching fields (i.e.,

name, date of birth, sex, address, city, state and zip) with high completeness rates varying

between 93.8% and 100% (Table 3.1). The PDMP and OCME files had no SSN's available

for matching and DPSCS file had only 61.0% completeness for SSN. Thus, SSN was

excluded from the study's deterministic algorithms, but was used by the probabilistic

algorithm when furnished. The address was not standardized in any dataset, limiting the

potential for exact matches, and was therefore not leveraged for the deterministic matching.

However, the address fields were well-populated (completeness ranging from 95.9% to

100%), which could be leveraged by the probabilistic algorithm.

Study Population

Using the probabilistic algorithm, a total of 1,859,445 unique individuals were identified

within the PDMP dataset. Of the probabilistically linked records across all three data

sources, 1,318 (0.07%) individuals experienced a fatal opioid overdose and 8,712 (0.47%)

had an arrest record. The deterministic-basic algorithm resulted in a total of 1,910,741

unique individuals (2.8% more identities than probabilistic matching), of which, 1,167 (0.06%) experienced a fatal opioid overdose and 8,589 (0.45%) had an arrest record. The deterministic+zip algorithm resulted in a total of 2,065,019 unique individuals (11.1% more identities than probabilistic matching), of which, 605 (0.03%) experienced a fatal opioid overdose and 3,839 (0.19%) had an arrest record (Table 3.2).

Population Characteristics

The characteristics of probabilistically-linked population were consistent with the two deterministically-linked populations for the full cohort; however, some differences were more pronounced in the death cohorts given the lower number of deaths linked to the PDMP data and higher number of unique individuals deterministically identified in the PDMP dataset (Table 3.2): the number of individuals who were male was 2.98% higher and who used Medicaid as a method of payment was 2.42% higher in the population linked by the deterministic-basic algorithm than the probabilistically linked population. For the deterministic+zip algorithm, the number of individuals in the 50-64 age group was 3.58% higher and the method of payment of self-pay (modal) was 3.31% higher than the probabilistically linked population. The percentage of individuals in the death cohort with a high number of opioid prescribers and dispensers was one of the most distinguishable differences between the deterministic and probabilistic algorithms. For the population linked by the deterministic-basic algorithm, the number of individuals with ≥3 opioid prescribers and ≥3 opioid dispensers decreased by 2.81% and 2.54%, respectively, as compared with the probabilistically linked population. Similarly, for the population linked with the deterministic+zip algorithm, individuals with ≥3 opioid prescribers and ≥3 opioid dispensers decreased by 7.57% and 7.93%, respectively.

The statistically significant predictors in the risk model were relatively consistent between the probabilistic algorithm and the deterministic algorithms, with a few exceptions (Table 3.3). Self-pay was found to be a predictor of fatal opioid overdose for the model applied to the population linked with the deterministic-basic (Odds Ratio [OR] 1.39, 95% Confidence Interval [CI] 1.08-1.78) and the deterministic+zip (OR 1.64, 95% CI 1.19-2.27) algorithms but was not a predictor for the probabilistically linked population. The risk model found high MME to be a statistically significant predictor when run on the population that was probabilistically matched (OR 1.36, 95% CI 1.02-1.80) or matched using the deterministic+zip algorithm (OR 1.75, 95% CI 1.15-2.68), but not the deterministic-basic algorithm. Finally, the population linked using the deterministic algorithm-basic did not find the ≥3 opioid prescribers or ≥1 methadone fill variables to be statistically significant predictors, despite being a predictor for the population linked using the probabilistic algorithm and deterministic-basic algorithm. Nearly all statistically significant predictors in the model run on the population matched using the deterministic-basic algorithm displayed some level of bias as compared with population linked probabilistically, other than the male (bias: 0.0), ≥1 methadone fills (bias: 0.0), and any arrest (bias: -0.1) variables. The degree of bias varied for the other statistically significant variables, with one of the largest calculated bias being ≥1 muscle relaxant fills (deterministic-basic bias: -79.5; deterministic+zip bias: -121.6).

The performance of the predictive model in the form of AUC was comparable across the three matching algorithms at different cutoff points where sensitivity and specificity were maximized (Table 3.4). The deterministic-basic algorithm (derivation AUC: 0.860, validation AUC: 0.854) slightly outperformed the probabilistic algorithm (derivation AUC: 0.858,

validation AUC: 0.847), which slightly outperformed deterministic+zip algorithm (derivation

AUC: 0.837, validation AUC: 0.826). The cutoff point for the probabilistic algorithm was

0.0010, resulting in a total of 104,293 individuals being flagged as high risk, of which, 362

died from a fatal opioid overdose (3.47 deaths per 1,000 high risk individuals). This is in

comparison with the deterministic-basic algorithm's cutoff point of 0.0005, resulting in

229,646 individuals flagged as high risk with 384 deaths (1.67 deaths per 1,000 high risk

individuals), and the deterministic+zip algorithm, which had an optimal cutoff point of

0.00025, resulting in 275,352 individuals flagged as high risk with 195 deaths (0.71 deaths per

1,000 high risk individuals). The probabilistic algorithm had a lower sensitivity (67.54%) and

higher specificity (84.29%) relative to the deterministic-basic algorithm (sensitivity: 87.47%,

specificity: 66.26%) and deterministic+zip algorithm (sensitivity: 85.53%, specificity:

62.17%), demonstrating that the probabilistic algorithm is tuned to minimize the potential

for false positives, although at the expense of potential false negatives. See Appendix 3.5 for

classification tables of the model run on the population linked by the three matching

methods.

Risk Indicator and Death Rate Statistics

Examining the quantity of individuals with certain high-risk indicators that were identified by

only one of the matching algorithms further demonstrates the impact the matching can have

on understanding patient-level risk (Table 3.5). The probabilistic algorithm uniformly yielded

the highest number of individuals identified as having a high-risk indicator that were not

otherwise identified by one of the deterministic algorithms. This was consistent for the

PDMP-based risk indicators as well as the indicators that relied upon cross-sector variables

from the DPSCS and OCME files. The most pronounced differences included multiple

provider episodes (probabilistic: n=963 [19.68%]; deterministic-basic: n=420 [9.45%];

deterministic+zip: n=3 [0.12%]); and opioid overdose deaths (probabilistic: n=327 [24.81%]; deterministic-basic: n=153 [13.11%]; deterministic+zip: 0 [0.00%]). The deterministic+zip algorithm identified an almost negligible number of individuals (MPE: 3 [0.02%], High MME: 2 [0.00%], overlapping opioid/benzodiazepines: 205 [0.23%], arrest: 11 [0.29%], opioid overdose death: 0 [0.00%]) with high risk indicators as compared with the probabilistic and deterministic-basic algorithms.

Finally, death rate per 100,000 in the denominator was calculated for each of the variables included in the multivariable model (Table 3.6 & Figure 3.1). The population linked using the probabilistic algorithm universally resulted in capturing the highest death rates per predictor as compared with the deterministic algorithms. The highest death rates per 100,000 involved individuals who had any arrest (probabilistic: 1 per 1,309; deterministic-basic algorithm: 1 per 1,246; deterministic+zip algorithm: 1 per 703) or any arrest and opioid prescription (probabilistic: 1 per 1,247; deterministic-basic algorithm: 1 per 1,170; deterministic+zip algorithm: 1 per 718). Individuals with multiple provider episodes (probabilistic: 1,074; deterministic-basic algorithm: 1,058, deterministic+zip algorithm: 431) had a death rate similar in scale to the population with an arrest. All predictors had a higher death rate than the Maryland average death rate (49 per 100,000) for the population linked via the probabilistic and deterministic-basic algorithms. The deterministic+zip algorithm had two predictors that were lower than the Maryland average, including ≥1 schedule III or IV opioid prescriptions (30 per 100,000) and ≥1 schedule II opioid prescriptions (41 per 100,000).

Discussion

Patient matching, both within and across datasets, is critical to constructing a complete picture of risk. Absent a common identifier that can be used to stitch together the electronic data captured in fragmented human service datasets, other methods to match person-level data together must be utilized. Understanding how the matching method impacts the results of subsequent risk analyses is important when making decisions related to how to respond to the opioid crisis.

The greatest impact on matching is the quality of the patient's demographic data inputs for the algorithms. Given the nature of the datasets included in this study, the data completeness was not a barrier to matching. The PDMP program requires basic patient information be supplied per state regulations and the nature of arrest and death data inherently ensures accurate patient information is captured as a matter of the law. The high degree of data completeness of the patient demographics used in this study nearly eliminates matching errors due to missing data, leaving only the potential for more nuanced matching errors (e.g. minor typos such as "Jhon" versus "John," causing two records for the same person to not match if using exact matching, or more common names, such as John Smith with the same date of birth, may be incorrectly matched together), and providing a solid foundation for the multivariate predictive model, risk indicator, and death rate analyses.

Model performance, defined in this study as how accurately the model was able to predict fatal opioid overdose, did not vary greatly across the three matching algorithms with regards to the AUC at the optimal risk model cutoff. However, the sensitivity and specificity of the model were inversed when run on the probabilistically matched dataset versus the deterministically matched dataset. The risk model for the probabilistically matched dataset

had a lower sensitivity and higher specificity, consequently capturing fewer than half of the population identified as high risk as the model run on the deterministically linked population. Balancing sensitivity versus specificity is common practice with risk modeling and has practical implications for applied use of the model. When resources are scarce, such as the number of treatment beds, emphasis may want to be made on a higher specificity, where there is a lower likelihood of capturing individuals at high-risk when they are not, therefore reserving beds for individuals at highest risk for future fatal opioid overdose. However, if the intervention allows for more latitude with who receives a service or resource, such as naloxone distribution, a higher sensitivity may be desired to cast a wider net, even if some individuals were incorrectly classified as high risk.

As the results of this study suggests, using probabilistic versus deterministic matching within and across datasets may consequently predetermine the suitability of the applied uses of a risk model. If using deterministic matching, risk models may best be used for low-cost, broad interventions based on the higher sensitivity at the optimal cutoff. It may also support the model serving as an analytic tool to understand risk factors and their effect sizes at a population-level, with the understanding that bias may exist with some of the statistically significant predictors as compared to the operational standard. Alternatively, the higher specificity of the probabilistic model demonstrated aptness toward correctly classifying individuals at high risk for fatal opioid overdose, with the tradeoff that some individuals will be incorrectly classified as not at high-risk. However, if scarce resources are being distributed, the model being run on a probabilistically matched dataset outperformed the model being run on the deterministically matched dataset.

Beyond the multivariate analysis, the probabilistic algorithm was the most successful in matching individuals in the PDMP dataset with the arrest and death data. The probabilistically matched dataset also uniformly identified the highest number of individuals with a high-risk indicator (other than high MMEs) and individuals with high-risk indicators not identified by one of the other matching methods, demonstrating the benefits of a probabilistic model both within a primary dataset and across disparate datasets. The death rate analysis reflects these concepts, particularly when comparing the probabilistic matching with the deterministic+zip matching algorithm. As fewer individuals were found to have a particular characteristic and fewer arrests and deaths were linked, the death rates per 100,000 high-risk individuals are drastically deflated when using the deterministic+zip algorithm as compared with the probabilistic algorithm. If using the deterministic+zip algorithm alone to match individuals across datasets, the results of the analysis will fairly drastically underestimate prevalence of risk for the population. The deterministic-basic algorithm is closer to the death rates demonstrated by the probabilistically linked population; however, it underestimates prevalence of risk indicators as well.

While the results of the analysis points toward the benefits of using a probabilistic algorithm in many cases, consideration must be made on the cost and complexity of establishing and maintaining a probabilistic algorithm versus a deterministic algorithm. The benefit of the deterministic matching is in its simplicity; no real long-term maintenance and quick to implement.[4] Probabilistic algorithms can be very complex and take in a larger number of data elements, which leaves a higher opportunity for missing data to impact matching. Some publicly available probabilistic software exist, including Link Plus and The Link King,[6] and several software companies sell probabilistic matching master data management solutions. Organizations that choose to leverage probabilistic MPIs for operational purposes often

have dedicated staff that monitor the quality of the data processed through the MPI, perform clean up steps to continuously improve the matching rate, resolve issues, and assess the weighting rules for continuous improvement. Because of this, probabilistic MPIs are often used for ongoing clinical or analytic purposes that require continuous use. If the matching is only needed periodically, it may not make financial sense to invest in a robust probabilistic matching solution.

Strengths and Limitations

Most of the existing literature that has evaluated alternative matching and data linkage approaches performed "manual" reviews of the matches where a human assessed how often the algorithm to correctly or incorrectly classify two individuals as a match or non-match.[7,31,32] Although the data were linked together in an identifiable manner, this study only used de-identified linked records for analysis. Using the probabilistic algorithm as the operational standard for comparison against the deterministic matching was logical given it contains a robust collection of demographics for Maryland residents over a long period of time, which was this study's target population. While using a robust operational MPI is strength, it is also a limitation for generalizability. One of the benefits of the MPI is that it links records using historical addresses and names in addition to the most recently processed information. The degree to which the MPI contains historical data from individuals for improved matching must be factored in if replicating this process elsewhere since robust historical data expectedly improves the rate of matching for the study that would not have been achieved with an empty MPI.

While the PDMP data from 2015 were able to be both probabilistically and deterministically matched together for this study, the timing of when the data was extracted for the

probabilistic matching versus deterministic matching was different. This resulted in a slight difference in total number of prescriptions in one data extract from another. The number of prescriptions was normalized between the two extracts prior to person-level analysis. Additionally, although the individuals within the PDMP data were matched using both probabilistic and deterministic algorithms, the arrest data was probabilistically linked within the dataset, then the deterministic identifiers were applied as a one-to-one swap. This was because the de-identified DPSCS arrest data was linked using the probabilistic algorithm and was delivered for analysis prior to this study. Deterministic matching was therefore only applied when matching the DPSCS dataset with the PDMP and OCME datasets. The OCME data was also a one-to-one swap, but was inconsequential to the study given it is a person-level dataset and not transactional, as the other two datasets were. Finally, only two deterministic algorithms were analyzed, despite many other algorithm options, such as using partial name matches (i.e. first several digits of the first and last name).[33] The demographic elements used for the matching was largely influenced by the data availability in the datasets used for this study. Other datasets may have fields that are very helpful with exact matching, such as SSN.

Conclusion

Combining PDMP and criminal justice data can lead to an improved understanding of risk of fatal opioid overdose among vulnerable populations, increased pathways for cross-discipline partnerships, and more targeted program delivery. With the lack of a common identifier, linking multiple datasets from different domains need to rely upon matching algorithms applied to patient demographic data. The probabilistic algorithm enabled a more comprehensive understanding of risk indicator prevalence within and across datasets and may be best suited for costly, resource-limited interventions. Based on the intended applied

use of the model and operational simplicity, however, the risk model performed well on the population linked using the deterministic-basic algorithm (exact match on name, date of birth, and gender) and may be a suitable matching method for low-cost, broad interventions and generally understanding risk factors at a population-level, although some bias is introduced compared to the probabilistic matching approach.

Moving forward, the frequency with which cross-sector datasets will be used to gain a comprehensive understanding of an individual's risk of negative outcomes related to opioid use will only increase. Similar approaches will, and should, also be used to address other public health challenges. Advanced methods for matching person-level datasets from across organizations and programs, such as those explored in this study, will provide essential tools for facilitating the use of multiple datasets to better identify individuals at high risk and design public health programs and interventions that benefit the community.

References

1. Kharrazi H WJ. IT-enabled community health interventions: Challenges, opportunities, and future directions. *EGEMS (Wash DC)*. 2014;2(3):1117.

2. Gliklich RE, Dreyer NA, Leavy MB, editors. Registries for evaluating patient outcomes: A user's guide [internet]. *Agency for Healthcare Research and Quality (US)*. 2014;3rd edition(Apr).

3. Centers for Disease Control and Prevention. The national committee on vital and health statistics, 1996-98. 1999.

4. Zhu Y MY, Ohashi Y SS. When to conduct probabilistic linkage vs. deterministic linkage? A simulation study. *Journal of Biomedical Informatics*. 2015;56:80-86.

5. Office of the National Coordinator for Health Information Technology. Master data management within HIE infrastructures: A focus on master patient indexing approaches. 2012.

6. Campbell KM, Deck D, Krupski A. Record linkage software in the public domain: A comparison of link plus, the link king, and a `basic' deterministic algorithm. *Health Informatics J*. 2008;14(1):5-15.

7. Aldridge RW, Shaji K, Hayward AC, Abubakar I. Accuracy of probabilistic linkage using the enhanced matching system for public health and epidemiological studies. *PLoS One*. 2015;10(8):e0136179.

8. Geissert P, Hallvik S, Van Otterloo J, et al. High-risk prescribing and opioid overdose: Prospects for prescription drug monitoring program-based proactive alerts. *Pain*. 2018;159(1):150-156.

9. Paulozzi LJ, Kilbourne EM, Shah NG, et al. A history of being prescribed controlled substances and risk of drug overdose death. *Pain Med*. 2012;13(1):87-95.

10. Binswanger IA, Blatchford PJ, Lindsay RG, Stern MF. Risk factors for all-cause, overdose and early deaths after release from prison in Washington state. *Drug and Alcohol Dependence*. 2011;117(1):1-6.

11. Binswanger IA, Blatchford PJ, Mueller SR, Stern MF. Mortality after prison release: Opioid overdose and other causes of death, risk factors, and time trends from 1999 to 2009. *Ann Intern Med*. 2013;159:592–600.

12. Binswanger IA, Stern MF, Deyo RA, Heagerty PJ, Cheadle A, Elmore JG, Koepsell TD. Release from prison — A high risk of death for former inmates. *N Engl J Med*. 2007;356(2):157-165.

13. Binswanger IA, Stern MF, Yamashita TE, Mueller SR, Baggett TP, Blatchford PJ. Clinical risk factors for death after release from prison in Washington state: A nested case-control study. *Addiction*. 2016;111(3):499-510.

14. Degenhardt L, Larney S, Kimber J, Gisev N, Farrell M, Dobbins T, Weatherburn DJ, Gibson A, Mattick R, Butler T, Burns L. The impact of opioid substitution therapy on mortality post-release from prison: Retrospective data linkage study. *Addiction*. 2014;109(8):1306-1317.

15. Dasgupta N, Funk MJ, Proescholdbell S, Hirsch A, Ribisl KM, Marshall S. Cohort study of the impact of high-dose opioid analgesics on overdose mortality. *Pain Med*. 2016;17(1):85-98.

16. Glanz JM, Narwaney KJ, Mueller SR, et al. Prediction model for two-year risk of opioid overdose among patients prescribed chronic opioid therapy. *J Gen Intern Med*. 2018;33(10):1646-1653.

17. Gwira Baumblatt JA, Wiedeman C, Dunn JR, Schaffner W, Paulozzi LJ, Jones TF. High-risk use by patients prescribed opioids for pain and its role in overdose deaths. *JAMA Intern Med*. 2014;175(5):796-801.

18. Holt CT, McCall KL, Cattabriga G, Tu C, Smalley EK, Nichols SD. Using controlled substance receipt patterns to predict prescription overdose death. *Pharmacology*. 2018;101(3-4):140-147.

19. Nechuta SJ, Tyndall BD, Mukhopadhyay S, McPheeters ML. Sociodemographic factors, prescription history and opioid overdose deaths: A statewide analysis using linked PDMP and mortality data. *Drug Alcohol Depend*. 2018;190:62-71.

20. Massachusetts Department of Public Health. An assessment of fatal and nonfatal opioid overdoses in Massachusetts (2011 – 2015). 2017.

21. Kreiner P. Approaches to patient record linking: How much difference can it make? 2017.

22. State of Maryland Code of Maryland Regulations (COMAR). .03 dispenser reporting. 10.47.07.03.

23. Oliva EM, Bowe T, Tavakoli S, Martins S, Lewis ET, Paik M, Wiechers I, Henderson P, Harvey M, Avoundjian T, Medhanie A, Trafton JA. 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. *Psychol Serv*. 2017;14(1):34-49.

24. Zedler B, Saunders WB, Joyce AR Vick CC, Murrelle EL. Validation of a screening risk index for serious prescription opioid-induced respiratory depression or overdose in a US commercial health plan claims database. *Pain Med*. 2018;19(1):68-78.

25. Centers for Disease Control and Prevention. Quality improvement and care coordination: Implementing the CDC guideline for prescribing opioids for chronic pain. 2018.

26. Prescription Drug Monitoring Program (PDMP) Center of Excellence at Brandeis. Questionnaire results from state PDMP programs sent by PDMP TTAC for the purposes of this analysis. February 2019.

27. Krawczyk N, Schneider KE, Eisenberg MD, Richards TM, Ferris LM, Lyons BC, Jackson K, Weiner JP, Saloner B. Drafted, unpublished. Retrieved March 2019.

28. Pokharel S. Personal communication at CRISP. April 17, 2019.

29. Measure Evaluation. Data quality audit tool – guidelines for implementation. 2008.

30. Hagger-Johnson G, Harron K, Goldstein H, Aldridge R, Gilbert R. Probabilistic linking to enhance deterministic algorithms and reduce linkage errors in hospital administrative data. *Journal of innovation in health informatics*. 2017;24(2):891.

31. Baldwin E, Johnson K, Berthoud H, Dublin S. Linking mothers and infants within electronic health records: A comparison of deterministic and probabilistic algorithms. *Pharmacoepidemiol Drug Saf*. 2014;24:45– 51.

32. Durojaiye AB, Puett LL, Levin S, Toerper M, McGeorge NM, Webster KLW, Deol GS, Kharrazi H, Lehmann HP, Gurses AP. Linking electronic health record and trauma registry data: Assessing the value of probabilistic linkage. *Methods Inf Med*. 2018;57(05/06):261-269.

33. Brady JE, Giglio R, Keyes KM, DiMaggio C, Li G. Risk markers for fatal and non-fatal prescription drug overdose: A meta-analysis. *Injury Epidemiology*. 2017;4(1):24.

34. IBM. Default algorithm for InfoSphere MDM probabilistic matching engine. 2015.

35. IBM. Probabilistic matching in IBM InfoSphere master data management. http://www-01.ibm.com/support/docview.wss?uid=swg27043172. Accessed February 17, 2019.

Tables and Figures

Dataset	# Native Dataset IDs	First Name	Last Name	Sex	DOB	Address	City	Zip	SSN
Table 3.1: Data completeness of identifiable demographic data elements. [a]									
PDMP [b]	3,304,446	3,304,440 (100)	3,304,363 (100)	3,304,000 (100)	3,303,391 (100)	3,303,546 (100)	3,304,171 (100)	3,303,515 (100)	0 (0.0)
DPSCS Arrest [c]	118,218	118,218 (100)	118,218 (100)	118,218 (100)	118,218 (100)	114,311 (96.7)	114,087 (96.5)	113,806 (96.3)	72,093 (61.0)
OCME [d]	22,829	22,828 (100)	22,827 (100)	22,791 (99.8)	22,704 (99.8)	21,888 (95.9)	21,747 (95.3)	21,404 (93.8)	0 (0.0)

Abbreviations: IDs=identities, PDMP=Prescription Drug Monitoring Program, DPSCS=Department of Public Health Safety and Correctional Services, OCME=Office of Chief Medical Examiner, DOB=Date of Birth, SSN=Social Security Number.
[a] Demographic data were used by the health information exchange to match identities within and across datasets prior to removing patient identifiers from final analytic dataset. This table reflects the completeness of the demographic data (based on missing values) used for matching. All demographic fields were utilized for the probabilistic matching. Deterministic matching only relied upon first name, last name, sex, date of birth, and zip.
[b] PDMP data consists of all controlled substance prescriptions dispensed in 2015.
[c] DPSCS data consists of drug and property arrests from 2013-2016 (narrowed to arrests in 2013-2015 for analyses).
[d] OCME data consists of outcome of all investigated deaths from 2012-2016 (narrowed to opioid-related overdose deaths in 2015-2016 for analyses).

Table 3.2: Characteristics of study population for each matching algorithm.[a]						
	Probabilistic		**Deterministic-basic[b]**		**Deterministic+zip[b]**	
Characteristic, n (%)	Full (n=1,859,445)	Deaths (n=1,318)	Full (n=1,910,741)	Deaths (n=1,167)	Full (n=2,065,019)	Deaths (n=605)
Demographic Variables						
Male	775,716 (41.72)	849 (64.37)	794,564 (41.61)	788 (67.35)	856,100 (41.47)	393 (64.96)
Age ≤18 years	140,648 (7.56)	0 (0)	142,288 (7.45)	0 (0)	152,207 (7.37)	0 (0)
Age 18-34 years	410,834 (22.09)	378 (28.68)	418,770 (21.93)	338 (28.89)	461,323 (22.35)	165 (27.27)
Age 35-49 years	427,737 (23.00)	488 (37.03)	440,897 (23.09)	437 (37.35)	485,742 (23.53)	212 (35.04)
Age 50-64 years	520,899 (28.01)	419 (31.79)	537,772 (28.16)	370 (31.62)	579,104 (28.05)	214 (35.37)
Age 65-80 years	294,854 (15.86)	33 (2.50)	303,760 (15.91)	25 (2.14)	317,083 (15.36)	14 (2.31)
Age ≥80 years	64,473 (3.47)	0 (0)	66,096 (3.46)	0 (0)	68,959 (3.34)	0 (0)
Prescription Variables						
MP: Self-Pay	291,474 (15.68)	135 (10.24)	302,575 (15.85)	125 (10.68)	320,322 (15.52)	82 (13.55)
MP: Medicaid	268,537 (14.44)	475 (36.04)	271,363 (14.21)	450 (38.46)	311,520 (15.09)	213 (35.21)
MP: Medicare	150,139 (8.07)	123 (9.26)	154,659 (8.10)	99 (8.46)	165,832 (8.03)	59 (9.75)
MP: Commercial	1,103,135 (59.33)	559 (42.41)	1,131,679 (59.26)	484 (41.37)	1,213,700 (58.79)	246 (40.66)
MP: Military/VA	10,673 (0.57)	18 (1.37)	11,599 (0.61)	4 (0.34)	12,392 (0.60)	2 (0.33)
MP: Workers Comp	9,383 (0.50)	2 (0.15)	10,443 (0.55)	3 (0.26)	11,232 (0.54)	3 (0.50)
MP: Unknown/Other	26,104 (1.40)	7 (0.53)	27,265 (1.43)	5 (0.43)	29,420 (1.43)	0 (0)
Opioid prescribers ≥3	172,105 (9.26)	420 (31.87)	171,963 (9.00)	340 (29.06)	164,913 (7.99)	147 (24.30)
Opioid dispensers ≥3	78,961 (4.25)	305 (23.14)	74,073 (3.88)	241 (20.60)	58,138 (2.82)	92 (15.21)
Methadone fills ≥1	10,194 (0.55)	57 (4.32)	10,606 (0.56)	46 (3.93)	12,069 (0.58)	24 (3.97)
Opioid LA fills ≥1	70,589 (3.80)	190 (14.42)	73,696 (3.86)	158 (13.50)	80,657 (3.91)	83 (13.72)
Opioid OUD fills ≥1	28,339 (1.52)	200 (15.17)	28,453 (1.49)	181 (15.47)	34,326 (1.66)	78 (12.89)
Opioid SA-2 fills ≥4	885,205 (47.61)	877 (66.46)	908,770 (47.56)	772 (65.98)	968,287 (46.89)	396 (65.45)
Opioid other SA-3,4 fills ≥1	458,851 (24.68)	376 (28.53)	465,086 (24.34)	315 (26.92)	479,594 (23.22)	143 (23.64)
Benzodiazepine fills ≥2	463,008 (24.90)	639 (48.48)	471,180 (24.66)	551 (47.09)	500,000 (24.21)	285 (47.11)
Muscle relaxant fills ≥1	19,300 (1.04)	65 (4.93)	19,789 (1.04)	57 (4.87)	21,295 (1.03)	31 (5.12)
Sedative fills ≥1	138,643 (7.46)	187 (14.19)	141,174 (7.39)	150 (12.82)	148,940 (7.21)	79 (13.06)
High MME (≥90 mg/day)	57,314 (3.08)	226 (17.15)	59,423 (3.11)	178 (15.21)	63,454 (3.07)	95 (15.70)
Overlapping Opioid/Benzo	87,805 (4.72)	311 (23.60)	88,373 (4.63)	244 (20.85)	90,476 (4.38)	126 (20.83)
Criminal Justice Variable						
Has any arrest	8,825 (0.47)	113 (8.57)	8,589 (0.45)	107 (9.15)	3,839 (0.19)	27 (4.46)

Abbreviations: MME=Morphine Milligram Equivalent, OUD=opioid use disorder (buprenorphine), SA=short-acting, LA=long-acting

[a] Population consists of drug and property arrests from 2013-2015, PDMP data from 2015, and an outcome of fatal opioid overdose in 2015 or 2016.

[b] Deterministic-basic algorithm matched first name, last name, date of birth. Deterministic+zip algorithm matched first name, last name, date of birth, zip code.

[c] % difference is the probabilistic algorithm minus the deterministic algorithm percentage for the full and death cohorts.

Table 3.3: Odds Ratios and bias for populations matched by each matching algorithm. [a]							
	Probabilistic (N=1,859,445)		Deterministic-basic[b] (N=1,910,753)			Deterministic+zip[b] (N=2,065,023)	
	n	OR (95% CI)	n	OR (95% CI)	bias[c]	n	OR (95% CI)	bias[c]
Demographic Variables								
Male	774,868 (41.70)	**2.86 (2.45-3.32)**	794,564 (41.61)	**2.85 (2.44-3.34)**	0.0	856,100 (41.47)	**2.90 (2.34-3.60)**	-1.4
Age ≤18 years	140,648 (7.57)	-	142,288 (7.45)	-		152,207 (7.37)	-	
Age 18-34 years	410,456 (24.83)	reference	418,770 (21.93)	reference		461,323 (22.35)	reference	
Age 35-49 years	427,249 (25.85)	1.01 (0.85-1.21)	440,897 (23.09)	1.04 (0.87-1.25)	-289.6	485,742 (23.53)	1.02 (0.79-1.32)	-64.2
Age 50-64 years	520,480 (31.49)	**0.69 (0.58-0.84)**	537,772 (28.16)	**0.77 (0.63-0.93)**	26.0	579,104 (28.05)	0.82 (0.63-1.07)	45.8
Age 65-80 years	294,821 (17.84)	**0.09 (0.06-0.16)**	303,760 (15.91)	**0.07 (0.04-0.13)**	-12.0	317,083 (15.36)	**0.06 (0.02-0.14)**	-22.7
Age ≥80 years	64,473 (3.47)	-	66,096 (3.46)	-		68,959 (3.34)	-	
Prescription Variables								
MP: Self-Pay	291,339 (15.68)	1.23 (0.96-1.57)	302,575 (15.85)	**1.39 (1.08-1.78)**	-60.6	320,322 (15.52)	**1.64 (1.19-2.27)**	-144.9
MP: Medicaid	268,062 (14.43)	**2.55 (2.15-3.01)**	271,363 (14.21)	**2.99 (2.51-3.54)**	-17.1	311,520 (15.09)	**2.68 (2.11-3.41)**	-5.7
MP: Medicare	150,017 (8.07)	**2.46 (1.87-3.23)**	154,659 (8.10)	**2.70 (2.03-3.58)**	-10.2	165,832 (8.03)	**2.92 (2.01-4.24)**	-19.1
MP: Commercial	1,102,576 (59.34)	reference	1,131,679 (59.26)	reference	0.0	1,213,700 (58.79)	reference	
MP: Military/VA	10,655 (0.57)	**3.25 (1.81-5.81)**	11,599 (0.61)	0.66 (0.17-2.68)	193.6	12,392 (0.60)	0.60 (0.08-4.27)	144.0
MP: Workers Comp	9,381 (0.50)	0.28 (0.04-2.01)	10,443 (0.55)	0.59 (0.15-2.39)	58.7	11,232 (0.54)	1.01 (0.25-4.11)	101.1
MP: Unknown/Other	26,097 (1.40)	0.28 (0.07-1.13)	27,265 (1.43)	0.45 (0.14-1.41)	37.4	29,420 (1.43)	-	100.0
Opioid prescribers ≥3	171,685 (9.24)	**1.53 (1.23-1.91)**	171,963 (9.00)	**1.47 (1.17-1.85)**	10.0	164,913 (7.99)	1.31 (0.95-1.81)	36.2
Opioid dispensers ≥3	78,656 (4.23)	**1.83 (1.45-2.30)**	74,073 (3.88)	**1.57 (1.24-2.00)**	24.9	58,138 (2.82)	**1.56 (1.09-2.23)**	26.4
Methadone fills ≥1	10,137 (0.55)	**2.05 (1.40-3.00)**	10,606 (0.56)	**2.04 (1.36-3.08)**	0.0	12,069 (0.58)	1.57 (0.86-2.89)	36.6
Opioid Long-Acting fills ≥1	70,399 (3.79)	1.06 (0.80-1.39)	73,696 (3.86)	1.36 (0.94-1.68)	-333.1	80,657 (3.91)	1.27 (0.85-1.90)	-343.4
Opioid OUD fills ≥1	28,139 (1.51)	**4.88 (3.93-6.04)**	28,453 (1.49)	**5.10 (4.09-6.37)**	-2.1	34,326 (1.66)	**5.58 (4.07-7.65)**	-8.5
Opioid SA-2 fills ≥4	884,329 (47.59)	**1.38 (1.16-1.65)**	908,770 (47.56)	**1.63 (1.36-1.96)**	-52.2	968,287 (46.89)	**1.59 (1.24-2.04)**	-43.2
Opioid other SA-3,4 fills ≥1	458,475 (24.67)	1.03 (0.87-1.23)	465,086 (24.34)	1.05 (0.88-1.26)	-61.4	479,594 (23.22)	1.16 (0.90-1.50)	-344.5
Benzodiazepine fills ≥2	462,369 (24.88)	**2.08 (1.74-2.48)**	471,180 (24.660)	**2.34 (1.96-2.80)**	-16.7	500,000 (24.21)	**2.24 (1.74-2.88)**	-10.3
Muscle relaxant fills ≥1	19,235 (1.04)	**1.49 (1.04-2.14)**	19,789 (1.04)	**2.05 (1.46-2.89)**	-79.5	21,295 (1.03)	**2.43 (1.55-3.81)**	-121.6
Sedative fills ≥1	138,456 (7.45)	**1.69 (1.38-2.08)**	141,174 (7.39)	**1.59 (1.27-1.97)**	12.3	148,940 (7.21)	**1.57 (1.15-2.14)**	15.0
High MME (≥90 mg/day)	57,088 (3.07)	**1.36 (1.02-1.80)**	59,423 (3.11)	1.22 (0.90-1.66)	33.3	63,454 (3.07)	**1.75 (1.15-2.68)**	-84.5
Overlapping Opioid/Benzo	87,494 (4.71)	**1.57 (1.23-2.01)**	88,373 (4.63)	1.21 (0.94-1.56)	58.2	90,476 (4.38)	1.15 (0.79-1.67)	69.5
Criminal Justice Variable								

Has any arrest	8,712 (0.47)	**4.59 (3.52-6.00)**	8,589 (0.45)	**4.58 (3.46-6.06)**	-0.1	3,839 (0.19)	**5.01 (2.86-8.76)**	-5.6

Abbreviations: MME=Morphine Milligram Equivalent, Benzo=Benzodiazepine, VA=Veteran's Affairs, OUD=opioid use disorder (buprenorphine), SA=short-acting, OR=odds ratio, CI=confidence interval

[a] Population consists of drug and property arrests from 2013-2015, PDMP data from 2015, and an outcome of fatal opioid overdose in 2015 or 2016.

[b] Deterministic-basic algorithm matched first name, last name, date of birth. Deterministic+zip algorithm matched first name, last name, date of birth, zip code.

[c] Bias refers to the difference in log odds coefficients in each multivariable model, compared to the reference (probabilistic) standard model using the equation: $[(logit_{reference} - logit_{comparison} / logit_{reference})]*100$.

Table 3.4: Model performance for opioid overdose death for populations matched by each algorithm. [a]

Model Performance	Probabilistic (Operational standard)	Deterministic-basic Algorithm [b]	Deterministic+zip Algorithm [b]
Optimal Cutoff point	0.0010	0.0005	0.00025
Derivation AUC	0.858	0.860	0.837
Validation AUC	0.847	0.854	0.826
Sensitivity	67.54	87.47	60.96
Specificity	84.29	66.26	42.54
# of high-risk patients	104,293	229,646	275,352
% of validation cohort	15.8	33.78	37.85
# of deaths among high risk patients	362	385	195
Deaths per 1,000 high risk patients	3.47	1.67	0.71

Abbreviations: AUC – area under the curve

[a] Population consists of drug and property arrests from 2013-2015, PDMP data from 2015, and an outcome of fatal opioid overdose in 2015 or 2016.

[b] Deterministic-basic algorithm matched first name, last name, date of birth. Deterministic+zip algorithm matched first name, last name, date of birth, zip code.

Table 3.5: Risk indicator comparison for each matching algorithm cohort and those identified only by a single algorithm. [a]

High Risk Indicators	Identified by Probabilistic Algorithm		Identified by Deterministic-basic Algorithm [a]		Identified by Deterministic+zip Algorithm [a]	
	Full Cohort	Not identified by other matching methods	Full Cohort	Not identified by other matching methods	Full Cohort	Not identified by other matching methods
Multiple Provider Episode	4,893 (100)	963 (19.68)	4,443 (100)	420 (9.45)	2,552 (100)	3 (0.12)
High MME (≥90 mg/day)	57,314 (100)	664 (1.16)	59,422 (100)	274 (0.46)	63,453 (100)	2 (0.00)
Overlapping Opioid/Benzo	87,805 (100)	2,252 (2.56)	88,371 (100)	738 (0.84)	90,474 (100)	205 (0.23)
Has any arrest	8,825 (100)	1,682 (19.06)	8,584 (100)	1,279 (14.90)	3,839 (100)	205 (0.23)
Opioid overdose death	1,318 (100)	327 (24.81)	1,167 (100)	153 (13.11)	605 (100)	0 (0.00)

Note: All chi2 tests were significant at the p<0.001 level

Abbreviations: MME=morphine milligram equivalents, Benzo=benzodiazepine

[a] Deterministic-basic algorithm matched first name, last name, date of birth. Deterministic+zip algorithm matched first name, last name, date of birth, zip code.

Variables	Probabilistic Death Rate (per 100,000)	Deterministic-basic Algorithm [b] Death Rate (per 100,000)	Deterministic+zip Algorithm [b] Death Rate (per 100,000)
Table 3.6: Opioid overdose death comparison for populations linked by each algorithm. [a]			
Maryland average	49	49	49
Opioid other SA-3,4 fills ≥1	82	68	30
Has any opioid	84	73	35
Opioid SA-2 fills ≥4	99	85	41
Sedative fills ≥1	135	106	53
Benzodiazepine fills ≥2	138	117	57
Opioid prescribers ≥3	245	198	89
Opioid LA fills ≥1	270	214	103
Muscle relaxant fills ≥1	338	288	146
Overlapping Opioid/Benzo	355	276	139
Opioid dispensers ≥3	389	325	158
High MME (≥90 mg/day)	396	300	150
Methadone fills ≥1	562	434	199
Opioid OUD fills ≥1	711	636	227
Multiple Provider Episode	1,074	1,058	431
Any Opioid + Arrest	1,247	1,170	718
Has any arrest	1,309	1,246	703

Abbreviations: MME=Morphine Milligram Equivalent, Benzo=Benzodiazepine, OUD=opioid use disorder (buprenorphine), LA=long-acting, SA=short-acting

Maryland average death rate was estimated by dividing the number of any opioid-related fatal overdose in 2015 and 2016 by the estimated Maryland Census population.

[a] Population consists of drug and property arrests from 2013-2015, PDMP data from 2015, and an outcome of fatal opioid overdose in 2015 or 2016.

[b] Deterministic-basic algorithm matched first name, last name, date of birth. Deterministic+zip algorithm matched first name, last name, date of birth, zip code.

Figure 3.1: Death rate comparison for populations matched by alternate algorithms.

Death Rates (per 1,000) for Probablistic and Deterministic Algorithms among Subpopulations
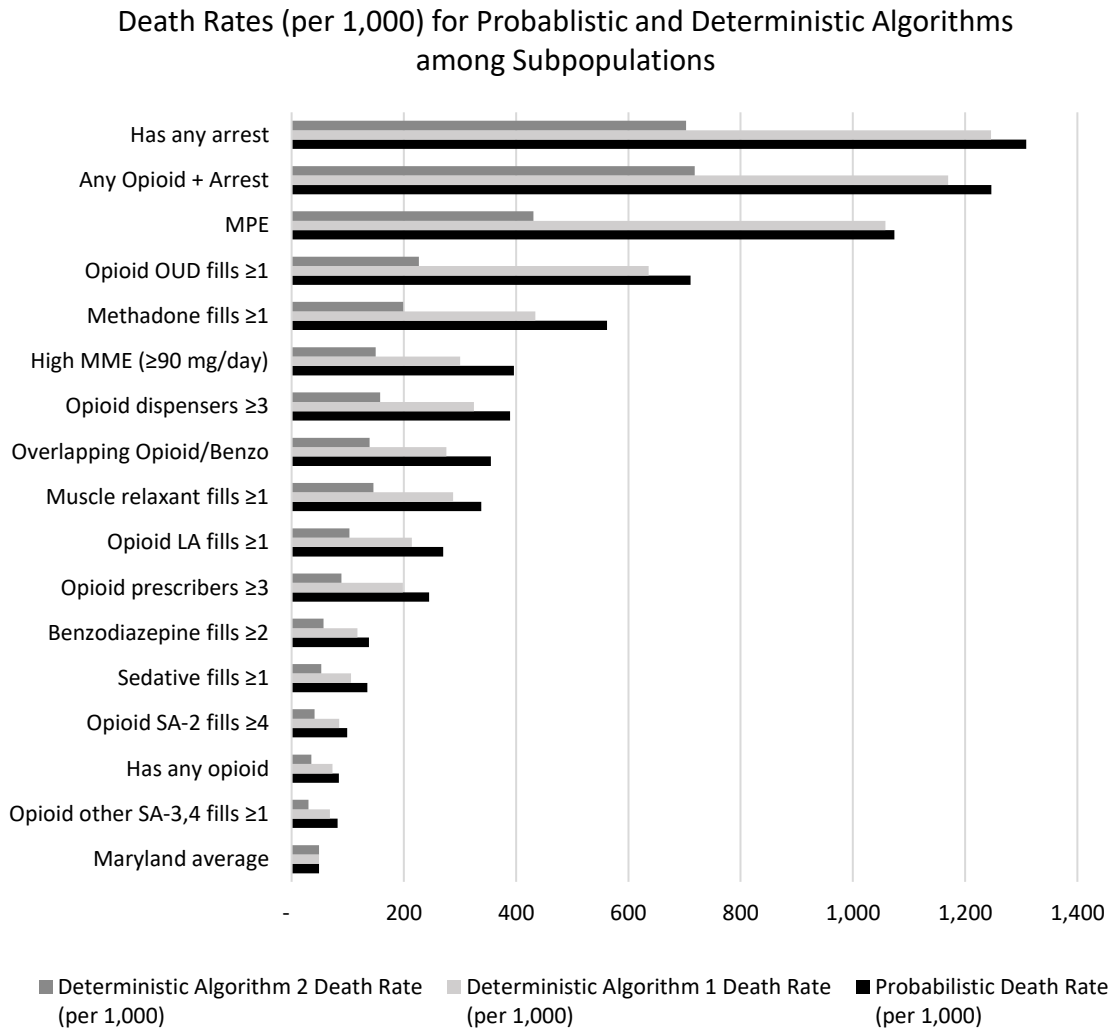
Abbreviations: MPE=multiple provider episodes, OUD=opioid use disorder (buprenorphine), MME=morphine milligram equivalents, mg/day=milligram per day, Benzo=Benzodiazepine, LA=long-acting, SA-2=short-acting, schedule II, SA-3,4=short-acting, schedule III or I

Implications for Public Health Practice and Policy

Central to this analysis is the pursuit of understanding risk within a statewide PDMP dataset and across datasets from other sectors. There is increasing interest in public health practice to utilize risk scores to identify individuals at highest risk and provide the appropriate intervention based on the specific patient's needs and wants. As public health practice looks to such solutions, understanding how to explore available data based on prior literature and the data available for operational use will be vital to the process. The first paper's systematic review provides foundational knowledge around which risk factors have been explored, nuances around the variable and outcome definitions, and range of model performance. Public health practitioners can adapt an existing model in the literature or choose to create a model unique to their population and data sources. This analysis could drive policy changes to require certain fields of interest as a variable or outcome to be submitted by dispensers required to report to the PDMP through legislative or regulatory changes.

Another core implication to public health practice covered by these analyses is how predictive risk models can be applied in practice, particularly in context of existing PDMP program risk identification processes many states already execute. The practical implications outlined in the second paper are compelling. The risk model did a better job of identifying individuals at risk of fatal opioid overdose than the PDMP thresholds commonly used by PDMP programs today. Combining the risk model with other common PDMP thresholds may also improve the identification of individuals at risk of fatal opioid overdose. Predictive models are specifically designed to identify high-risk individuals for a specific outcome, in this case fatal opioid overdose, based on a multitude of factors. As part of that process, however, the models often identify a larger denominator of individuals than simple PDMP

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thresholds. Thus, the predictive model must be applied thoughtfully and in a way that allows for ease of operational use. Based on the intervention intended for those identified as high-risk, additional tailoring or partnering with other risk identification techniques may be beneficial to ensure individuals are not being identified for a resource that cannot meet the resulting demand. This paper also covered key considerations that must be followed if pursuing the application of a risk model in conjunction with a PDMP threshold. As more criteria are added, the denominator will narrow and should be considered to ensure enough of a denominator of high-risk individuals are captured. Additionally, finding the optimal cutoff point for a risk model that strikes the appropriate balance of sensitivity and specificity in alignment with the intended intervention should be determined by the public health agency. Ultimately, risk models are a promising option for public health practitioners, such as PDMP programs, in fine-tuning intervention and program decisions in a resource-constrained environment while maintaining or improving ability to identify those at risk for fatal opioid overdose. Risk models in conjunction with other risk identification methods or standalone can drive policy and programmatic changes based on the populations identified, perhaps by forming a new intervention for a specific high-risk population or geographic region, or partnerships with other disciplines aimed at improving patient outcomes for individuals with an opioid addiction.

Finally, in the context of an increasing need for cross-disciplinary collaboration and data-driven solutions, the third paper addressed some of the impacts of how data from multiple disparate dataset comes together absent a unique identifier. The method to which person-level data are matched within and across datasets impacts the risk indicators for individuals and general understanding of risk. This includes the use of common PDMP thresholds or risk models. Using the probabilistic matching operational standard in Maryland led to

improved matching within the PDMP dataset and with external arrest and death datasets, which consequently resulted in a higher prevalence for fatal opioid overdose and arrests among the PDMP patients in the study. Despite the probabilistic algorithm performing better than deterministic algorithms, the nature of the analysis must be considered prior to pursing a probabilistic matching algorithm. In Maryland, the resources involved in maintaining the probabilistic algorithm is extensive, however, it is being used daily and therefore warrants that level of investment as it directly impacts patient safety and care. If the analysis being performed involving matched datasets is infrequent and is for a higher-level understanding of risk, the risk model run on the population matched using the basic deterministic matching algorithm (based on name, DOB, and gender) was fairly comparable to the probabilistic algorithm. Deterministic matching is a straightforward, simple way to bring variables from disparate datasets together. Caution should be made that there may be some variation in the risk factors and their effect sizes, as seen with the percent bias, however, as long as the intervention is not needed on a daily basis, such as for displaying a risk score to clinicians at the point of care, using the deterministic algorithm can be a viable option. If there is an increasing need to link multiple datasets together that do not have a common identifier, policy changes to ensure the completeness of all relevant demographic elements and/or standardization of certain fields may be necessary to improve patient-level matching. Operationalizing the cross-domain datasets in an applied setting must also be analyzed for potential policy changes, depending on the audience or manner in which the cross-domain data are used. There are often clear pathways for cross-domain analysis for research purposes, but an applied setting with identifiable data requires an in-depth legal review and discussion.

Appendix

I. Additional information for Paper 1: Using Electronic Pharmacy and Health Care Data to Identify Persons at Risk of Opioid-Related Overdose – A Review of the Predictive Modeling Literature

Appendix 1.1: Database Search Strategies

Database: PubMed
Search performed: 7/29/2018
Results: 1291 articles
Filters: published in the last 10 years (2008-2018); English language

#	Search Terms [type]
1	(opioid*[tw]) OR (analgesics, opioid[MeSH Terms]) OR (controlled substance*[tw]) OR (analgesics, narcotic[MeSH Terms]) OR (narcotic*[tw]) OR (control, narcotic[MeSH Terms]) OR (prescription drug&[tw]) OR (drug prescription[MeSH Terms]) OR (opioid prescription*[tw])
2	(overdose[tw]) OR (overdose[MeSH Terms]) OR (respiratory depression[MeSH Terms]) OR (respiratory depression[tw])
3	(risk factor*[tw]) OR (risk factor[MeSH Terms]) OR (risk[tw]) OR (prediction model[tw]) OR (predictive modeling[tw]) OR (logistic models[MeSH Terms]) OR (logistic model[MeSH Terms]) OR (risk assessment[MeSH Terms])
4	1 AND 2 AND 3

Database: PsychINFO
Search performed: 7/29/2018
Results: 626 articles
Filters: published in the last 10 years (2008-2018); English language; academic journals

#	Search Terms [type]
1	opioid OR analgesics, opioid OR controlled substances OR narcotics OR prescription OR prescription drugs OR prescription opioids
2	overdose OR overdose death OR (overdose or poisoning) OR respiratory depression OR (respiratory depression and opioids)
3	risk OR risk factors OR risk assessment OR prediction OR predictive analytics OR predict OR predictive OR prediction model OR predictive model OR predictive modeling
4	1 AND 2 AND 3

Database: Embase
Search performed: 7/29/2018
Results: 889 articles
Filters: published in the last 10 years (2008-2018); publication type=article

#	Search Terms [type]
1	'opiate agonist':ti,ab,kw OR 'opiate':ti,ab,kw OR 'analgesic agent':ti,ab,kw OR 'controlled substance':ti,ab,kw OR 'narcotic analgesic agent':ti,ab,kw OR 'narcotic agent':ti,ab,kw OR 'prescription':ti,ab,kw OR 'prescription drug':ti,ab,kw
2	'intoxication':ti,ab,kw OR 'drug overdose':ti,ab,kw OR 'respiration depression':ti,ab,kw OR 'death':ti,ab,kw
3	'risk':ti,ab,kw OR 'risk factor':ti,ab,kw OR ('prediction':ti,ab,kw AND 'forecasting':ti,ab,kw) OR 'predictive value':ti,ab,kw OR 'predictor variable':ti,ab,kw OR 'predictive validity':ti,ab,kw
4	1 AND 2 AND 3

Appendix 1.2: Risk factors and effect sizes for models in literature.

Appendix B.1: Risk factors found to be statistically significant in predicting adverse outcomes

Category	Risk Factor	Effect Size	Author
Demographics	Geographic region: Midwest or West	OR 1.20-1.56 (1.08-1.23, 1.33-2.2)	Zedler 2015; Zedler 2018
Demographics	Marital status: Never Married or Widowed	OR 1.48-2.12 (1.11-1.46, 1.97-3.08)	Zedler 2015
Demographics	Race: Non-Hispanic White or Other[a]	OR 1.56-1.71 (1.1-1.27, 2.2-2.31)	Zedler 2015
Dx-clinical	Chronic pulmonary disease	OR 1.57-1.72 (1.27-1.56, 1.89-1.94)	Zedler 2015; Zedler 2018
Dx-clinical	Heart failure	OR 2.06 (1.74, 2.44)	Zedler 2018
Dx-clinical	Liver disease (mild)	OR 2.42 (1.39, 4.19)	Zedler 2015
Dx-clinical	Non-malignant pancreatic disease	OR 2.07-2.13 (1.06-1.56, 2.75-4.25)	Zedler 2015; Zedler 2018
Dx-clinical	Renal disease or renal disease with renal impairment	OR 1.59-2.17 (1.17-1.83, 2.17-2.57)	Zedler 2015; Zedler 2018
Dx-clinical	Serious autoimmune rheumatologic disease	OR 1.47 (1.23, 1.77)	Zedler 2018
Dx-clinical	Skin (pressure) ulcers	OR 1.50-2.31 (1.18-1.48, 1.90-3.61)	Zedler 2015; Zedler 2018
Dx-clinical	Sleep apnea	OR 1.33-1.34 (1.03-1.15, 1.52-1.75)	Zedler 2015; Zedler 2018
Dx-MH/BH	Bipolar disorder/schizophrenia	OR 1.95-2.85 (1.43-2.44, 2.67-3.32)	Zedler 2015; Zedler 2018
Dx-MH/BH	Depression or psychotic disorder	aOR 3.04-3.23 (2.27-2.41, 3.82-4.54)	Liang 2016 (men & women)
Dx-MH/BH	Mental health diagnosis	aHR 3.39 (2.32, 4.96)	Glanz 2018
Dx-MH/BH	Opioid dependence	OR 4.54 (3.12, 6.63)	Zedler 2015
Dx-MH/BH	Alcohol or substance use disorder or dependence[b]	aHR 3.47-12.74 (2.25-11.46, 5.36-14.16)	Glanz 2018; Liang 2016; Zedler 2018
Dx-MH/BH	Tobacco use or tobacco abuse/dependence diagnosis	aHR 1.53 (1.03, 2.28)	Glanz 2018
Dx-pain	Traumatic Injury	OR 1.48-1.53 (1.18-1.41, 1.65-1.87)	Zedler 2015; Zedler 2018
Other	Length of follow-up (years)	aOR 1.38-1.57 (1.2-1.42, 1.58-1.74)	Liang 2016 (men & women)
Prescription	Days' supply: Antidepressant days 1-60; 61-180	aOR 1.98 (1.32, 2.9) (men); aOR 1.41 (1.11, 1.8) (women)	Liang 2016
Prescription	Days' Supply: Benzodiazepine days 1-30; 31-90	aOR 2.75 (2.07, 3.64) (men); aOR 2.35 (1.88, 2.93) (women)	Liang 2016
Prescription	Days' Supply: Zolpidem days 91-180	aOR 1.74 (1.26, 2.35) (women)	Liang 2016
Prescription	Dose: MMED (mg/day) prescribed 20-49; 50-99; ≥100	OR 1.59 (1.19, 2.12); OR/aOR 1.96-2.51 (1.29-1.73, 2.66-3.63); OR/aOR 1.79-4.96 (1.35-3.24, 2.24-7.61)	Liang 2016; Zedler 2015; Zedler 2018
Prescription	Number of unique pharmacies or unique prescribers[c]	aOR 1.11-1.15 (1.06-1.12, 1.16-1.18)	Geissert 2018
Prescription	Anticonvulsant prescription	OR 1.96 (1.23, 3.14)	Boscarino 2016
Prescription	Antidepressant prescription	OR 1.98-2.19 (1.63-2.03, 2.36-2.41)	Zedler 2015; Zedler 2018

Prescription	Benzodiazepine/sedative prescription	**OR/aOR 1.49-2.50 (1.22-2.23, 1.83-2.79)**	Zedler 2015; Zedler 2018; Geissert 2018
Prescription	Buprenorphine prescription	**OR 12.30 (5.92, 25.53)**	Boscarino 2016
Prescription	Carisoprodol prescription	**aOR 1.63 (1.25, 2.13)**	Geissert 2018
Prescription	Methadone prescription	**OR 2.42-2.80 (1.61-2.22, 3.51-3.66)**	Zedler 2015; Zedler 2018
Prescription	Oxycodone prescription	**OR 1.32 (1.03-1.19, 1.45-1.69)**	Zedler 2015; Zedler 2018
Prescription	Route: oral prescription	**OR 1.90 (1.54, 2.34)**	Zedler 2018
Utilization	All-cause utilization ≥1 day of hospitalization	**OR 1.12-2.20 (1.02-1.76, 1.23-2.76)**	Zedler 2015; Zedler 2018
Utilization	All-cause utilization ≥1 ER visit	**OR 1.52-2.88 (1.41-2.34, 1.65-3.54)**	Zedler 2015; Zedler 2018

Abbreviations: Dx=diagnosis MH/BH=Mental Health/Behavioral Health; MMED=Maximum Morphine Equivalent Dose; ER=Emergency Room, OR=Odds Ratio, aOR=adjusted Odds Ratio
[a] Other race is defined as races other than non-Hispanic black, non-Hispanic white, or Hispanic.
[b] The definition of substance use disorder may differ between studies; results have been consolidated for simplification purposes
[c] Number of unique prescribers and number of unique dispensers were considered separate variables

Appendix B.2: Protective factors found to be statistically significant in predicting adverse outcomes

Category	Risk Factor	Effect Size	Author
Demographics	Age, per year increase	**aOR/aHR 0.93-0.98 (0.89-0.98, 0.98-0.99)**	Glanz 2018; Liang 2016
Prescription	Prescription: migraine prescriptions	**OR 0.46 (0.28, 0.75)**	Boscarino 2016
Utilization	All-cause healthcare utilization ≥1 prescription fill	**OR 0.48 (0.28, 0.85)**	Zedler 2015

Appendix B.3: Risk factors found to not be statistically significant in predicting adverse outcomes

Category	Risk Factor	Effect Size	Author
Demographics	Geographic region: North Central, South, Other*	OR 0.63-1.29 (0.36-0.99, 1.11-1.84)	Zedler 2015; Zedler 2018
Demographics	Male sex	OR 1.03 (0.95, 1.11); OR 1.40 (p=0.136)	Zedler 2018; Boscarino 2016
Demographics	Marital status: separated/divorced	OR 1.16 (0.94, 1.44)	Zedler 2015
Demographics	Race: Hispanic	OR 1.53 (0.9, 2.59)	Zedler 2015
Dx-clinical	Any malignancy, including leukemia and lymphoma	OR 1.09-1.28 (0.93-0.95, 1.29-1.72)	Zedler 2015; Zedler 2018
Dx-clinical	Chronic hepatitis/cirrhosis	OR 1.39 (0.96, 2.00)	Zedler 2018
Dx-clinical	Congestive heart failure	OR 1.05 (0.64, 1.72)	Zedler 2015
Dx-clinical	Peripheral vascular disorder	OR 0.91-1.14 (0.72-0.78, 1.14-1.67)	Zedler 2015; Zedler 2018
Prescription	Route: parenteral or transdermal	OR 3.08 (0.58, 16.48)	Zedler 2015
Prescription	Formulation: proportion of opioids ER/LA	OR 0.65 (0.28, 1.54)	Zedler 2015

Abbreviations: Dx=diagnosis, ER/LA=extended release/long-acting, OR=Odds Ratio, aOR=adjusted OR
*Other defined as not the Northeast, North Central, South, or West geographic region of the United States.

Appendix B.4: Risk factors with mixed results for statistical significance and/or increased risk versus protective effects in predicting adverse outcomes

Category	Risk Factor	Effect Size	Author
Demographics	Age 35-44y; 45-54y; 55-64y; 65-74y; 75y+	**aOR 1.47 (1.15, 1.88); 1.95 (1.57, 2.44); 2.82 (2.29, 3.48); 3.68 (2.97, 4.57); 4.99 (4.02, 6.19)**	Geissert 2018
	Age 35-44y; 45-54y; 55y+ Age 35-54y; 55y+ Age (years)	OR 1.24 (0.65, 2.35); **1.97 (1.15, 3.37); 2.57 (1.55, 4.26)** OR 1.05 (0.95, 1.15); **1.16 (1.04, 1.29)** OR 1.00 (p=0.230)	Zedler 2015 Zedler 2018 Boscarino 2016
Dx-clinical	Cardiovascular disease	OR 1.2 (0.77, 1.88); OR 0.98 (0.81, 1.20); **OR 0.28 (0.12, 0.69)**	Zedler 2015; Zedler 2018; Boscarino 2016
Dx-clinical	Cerebrovascular disease	OR 0.66 (0.41, 1.06); **OR 2.52 (2.18, 2.92)**	Zedler 2015; Zedler 2018
Dx-clinical	Metastatic solid tumor	**OR 1.88 (1.04, 3.41);** OR 0.95 (0.73, 1.23)	Zedler 2015; Zedler 2018
Dx-clinical	Rheumatologic disease (serious autoimmune)	**OR 0.32 (0.12, 0.89); OR 1.47 (1.23, 1.77)**	Zedler 2015; Zedler 2018
Dx-clinical	Skin infections/abscesses	**OR 0.46 (0.28, 0.76);** OR 1.14 (1.00, 1.30)	Zedler 2015; Zedler 2018
Dx-clinical	Warfarin treatment	OR 1.27 (0.91, 1.79); **OR 0.79 (0.55, 0.95)**	Zedler 2015; Zedler 2018
Dx-clinical	Headache/migraine	OR 1.25 (0.9, 1.74); **OR 1.73 (1.57, 1.90)**	Zedler 2015; Zedler 2018
Prescription	Formulation: long-acting or extended-release opioid	**aOR 4.41 (3.93, 4.94); OR 2.48 (1.27, 4.88); OR 1.73 (1.51, 1.99);** aHR 1.99 (1.00, 3.93)	Geissert 2018; Zedler 2015; Zedler 2018; Glanz 2018
Prescription	Fentanyl prescription	OR 0.63 (0.11, 3.76); **OR 3.72 (3.10, 4.46)**	Zedler 2015; Zedler 2018
Prescription	Hydrocodone prescription	OR 0.87 (0.7, 1.08); **OR 1.30 (1.20, 1.41)**	Zedler 2015; Zedler 2018
Prescription	Hydromorphone prescription	OR 1.85 (0.96, 3.58); **OR 1.50 (1.38, 1.64)**	Zedler 2015; Zedler 2018
Prescription	Morphine prescription	OR 1.28 (0.77, 2.14); **OR 2.93 (2.49, 3.43)**	Zedler 2015; Zedler 2018
Prescription	Tramadol prescription	**OR 0.69 (0.52, 0.92);** OR 1.19 (1.08, 1.31)	Zedler 2015; Zedler 2018

Abbreviations: Dx=diagnosis, OR=Odds Ratio, aOR=adjusted Odds Ratio. Note: Bold indicates statistical significance

Appendix B.5: Risk factors evaluated but not included in the final multivariable model.

Category	Risk Factor	Effect Size	Author
Demographics	Geographic Region-Rural	aOR 0.94 (0.84-1.04)	Geissert 2018
Dx-clinical	Chronic pain	aOR 1.33 (0.93, 1.85) (women); **aOR 1.7 (1.07, 2.61) (men)**	Liang 2016
Dx-clinical	Hepatitis C diagnosis	HR 2.82 (1.04, 7.63)	Glanz 2018
Dx-MH/BH	Anxiety or post-traumatic stress disorder	aOR 1.02-1.26 (0.67-0.97, 1.48-1.61)	Liang 2016
Dx-pain	Back pain	aOR 1.35 (0.09, 1.68) (women); **aOR 1.4 (1.05, 1.86) (men)**	Liang 2016
Dx-pain	Musculoskeletal conditions	aOR 0.75-0.87 (0.7-0.75, 1-1.08)	Liang 2016
Dx-pain	Neuropathy	aOR 1.8 (0.53, 4.55) (women); **aOR 4.04 (1.36, 9.52) (men)**	Liang 2016
Prescription	Dose: Daily opioid dose (per 10 mg MMED)	HR 1.01 (0.99, 1.03)	Glanz 2018
Prescription	Dose: MMED daily ≥ 90 mg	**aOR 1.52 (1.25-1.83)**	Geissert 2018
Prescription	Number of prescriptions	aOR 0.99 (0.98, 0.99)	Geissert 2018
Prescription	Overlapping long acting/short acting opioids	**aOR 2.70 (2.16, 2.86)**	Geissert 2018
Prescription	Overlapping opioid-benzodiazepine/sedative	**aOR 2.13 (1.89, 2.39)**	Geissert 2018
Prescription	Overlapping opioid-benzodiazepine-carisoprodol	**aOR 1.59 (1.08, 2.32)**	Geissert 2018
Prescription	Overlapping opioid-opioid	**aOR 2.48 (2.16, 2.86)**	Geissert 2018
Prescription	Prescription: opioid prescriptions in the year prior to initiating chronic opioid therapy	HR 1.43 (1.00, 2.05)	Glanz 2018
Prescription	Psychotropic prescription	HR 2.82 (1.88, 4.25)	Glanz 2018

Abbreviations: Dx=diagnosis; MMED=Maximum Morphine Equivalent Dose, OR=Odds Ratio, aOR=adjusted Odds Ratio. Note: Bolded indicates statistical significance

II. Additional information for Paper 2: Comparing the Performance of a Predictive Risk Model with Prescription-Based Thresholds in Identifying Patients at Risk of Fatal Opioid Overdose

Appendix 2.1: Average daily morphine milligram equivalents (MME) calculation

Average daily MME was calculated for each month by:

(1) calculating how many days' supply of a prescription were in each month based on the date written, quantity dispensed, days' supply, and days in the given month;

(2) calculating the total MME for each opioid prescription in the month by multiplying the strength per unit for the drug by the CDC MME conversion factor and the number of days the prescription was active in a given calendar month; and,

(3) adding up all MME calculations for a given month and taking the average based on the number of days in the given calendar month. Buprenorphine prescriptions indicated for opioid use disorder were omitted from the calculation.

Appendix 2.2: Classification table for fatal opioid overdose predictive model. *										
Model Risk Score Cut-off	Sens.	Spec.	Sens. + Spec.	PPV	NPV	Acc.	# high-risk	% of Total	# Deaths among high-risk	Deaths per 1,000 high-risk
0.0005	91.08	40.09	131.17	0.22	99.97	40.16	102,192	57.44	224	2.19
0.0010	78.69	64.66	143.35	0.32	99.95	64.68	60,346	33.92	192	3.18
0.0015	**68.44**	**77.05**	**145.49**	**0.43**	**99.94**	**77.04**	**39,220**	**22.05**	**167**	**4.26**
0.0020	59.43	84.23	143.66	0.54	99.93	84.19	26,991	15.17	145	5.37
0.0025	50.41	87.94	138.35	0.60	99.92	87.89	20,643	11.60	123	5.96
0.0030	46.31	90.74	0.63	0.71	99.92	90.67	15,881	8.93	113	7.12
0.0035	40.16	92.53	132.69	0.77	99.91	92.46	12,806	7.20	98	7.65
0.0040	36.07	93.76	129.83	0.82	99.90	93.67	10,713	6.02	88	8.21
0.0045	31.56	94.75	126.31	0.85	99.90	94.64	9,042	5.08	77	8.52
0.0050	27.87	95.39	123.26	0.88	99.89	95.39	7,750	4.36	68	8.77
0.0055	24.18	96.19	120.37	0.90	99.89	96.08	6,550	3.68	59	9.01
0.0060	22.15	96.70	118.85	0.95	99.88	96.60	5,667	3.19	54	9.53
0.0065	20.49	97.13	117.62	1.01	99.89	97.02	4,930	2.77	50	10.14
0.0070	18.85	97.45	116.30	1.05	99.88	97.34	4,383	2.46	46	10.50
0.0075	16.80	97.73	114.53	1.05	99.88	97.62	3,896	2.19	41	10.52
0.0080	15.16	97.98	113.14	1.07	99.88	97.86	3,471	1.95	37	10.66
0.0085	14.34	98.20	112.54	1.13	99.88	98.09	3,102	1.74	35	11.28
Abbr.: Acc.=accuracy, NPV=negative predictive value, PPV=positive predictive value, Sens.=sensitivity, Spec.=specificity Bold indicates risk model cutoff that maximizes sensitivity plus specificity. * Maryland residents 18-80 years with at least one opioid fill for full populations and individuals identified by a single risk identification method only within the validation population using 3 months of data (April-June 2015).										

Appendix 2.3: Characteristics of individuals identified by a single risk identification method. *

	Risk Model Only	MPE Only	High MME Only	Op/Ben Overlap Only
# individuals	23,588	30	4,821	5,162
Sex – Male, n (%)	17,722 (75.1)	4 (13.3)	1,461 (30.3)	933 (18.1)
Age, mean (SD)	41.79 (11.8)	48.8 (15.0)	58.57 (11.1)	64.80 (10.0)
18-34	7,020 (29.8)	8 (26.7)	162 (3.4)	67 (1.3)
35-49	10,358 (43.9)	5 (16.7)	632 (13.1)	236 (4.6)
50-64	6,185 (26.2)	10 (33.3)	2,431 (50.4)	1,735 (33.6)
65-80	25 (0.1)	7 (23.3)	1,596 (33.1)	3,124 (60.5)
Region of Patient Residence, n (%)				
Baltimore City	4,036 (17.1)	8 (26.7)	558 (11.6)	430 (8.3)
Capital	5,919 (25.1)	4 (13.3)	895 (18.6)	1,159 (22.5)
Central	8,419 (35.7)	12 (40.0)	2,122 (44.0)	2,047 (39.7)
Eastern	1,934 (8.2)	3 (10.0)	535 (11.1)	625 (12.1)
Southern	1,751 (7.4)	3 (10.0)	423 (8.8)	358 (6.9)
Western	1,518 (6.4)	0 (0)	285 (5.9)	540 (10.5)
Unknown	11 (0.1)	0 (0)	3 (0.1)	3 (0.1)
Method of Payment, n (%)				
Private Pay	4,889 (20.7)	2 (6.7)	169 (3.5)	320 (6.2)
Medicaid	8,952 (38.0)	1 (3.3)	142 (3.0)	181 (3.5)
Medicare	1,860 (7.9)	3 (10.0)	779 (16.2)	1,254 (24.3)
Commercial Insurance	7,151 (30.3)	24 (80.0)	3,578 (74.2)	3,285 (63.6)
Military/VA	572 (2.4)	0 (0)	47 (1.0)	41 (0.8)
Indian	0 (0)	0 (0)	0 (0)	0 (0)
Other/Unknown	164 (0.7)	0 (0)	106 (2.2)	81 (1.6)
# prescribers, mean (SD)	1.9 (1.0)	6.1 (1.9)	1.6 (0.9)	1.9 (1.0)
# dispensers, mean (SD)	1.5 (0.8)	5.5 (1.0)	1.4 (0.7)	1.3 (0.6)
# deaths, n (%)	72 (0.3)	0 (0)	5 (0.1)	3 (0.1)

Abbreviations: PDMP=Prescription Drug Monitoring Program; PRM=predictive risk model; MPE=Multiple Provider Episodes (5 unique prescriber and 5 unique dispensers); MME=morphine milligram equivalents; Op/Ben=opioid/benzodiazepine, VA=Veterans Affairs; SD=standard deviation.
* Maryland residents 18-80 years with at least one opioid fill for full populations and identified by a single risk identification method only within the validation population using 3 months of data (April-June 2015).

Appendix 2.4: Key characteristics of individuals identified by single risk identification method. *
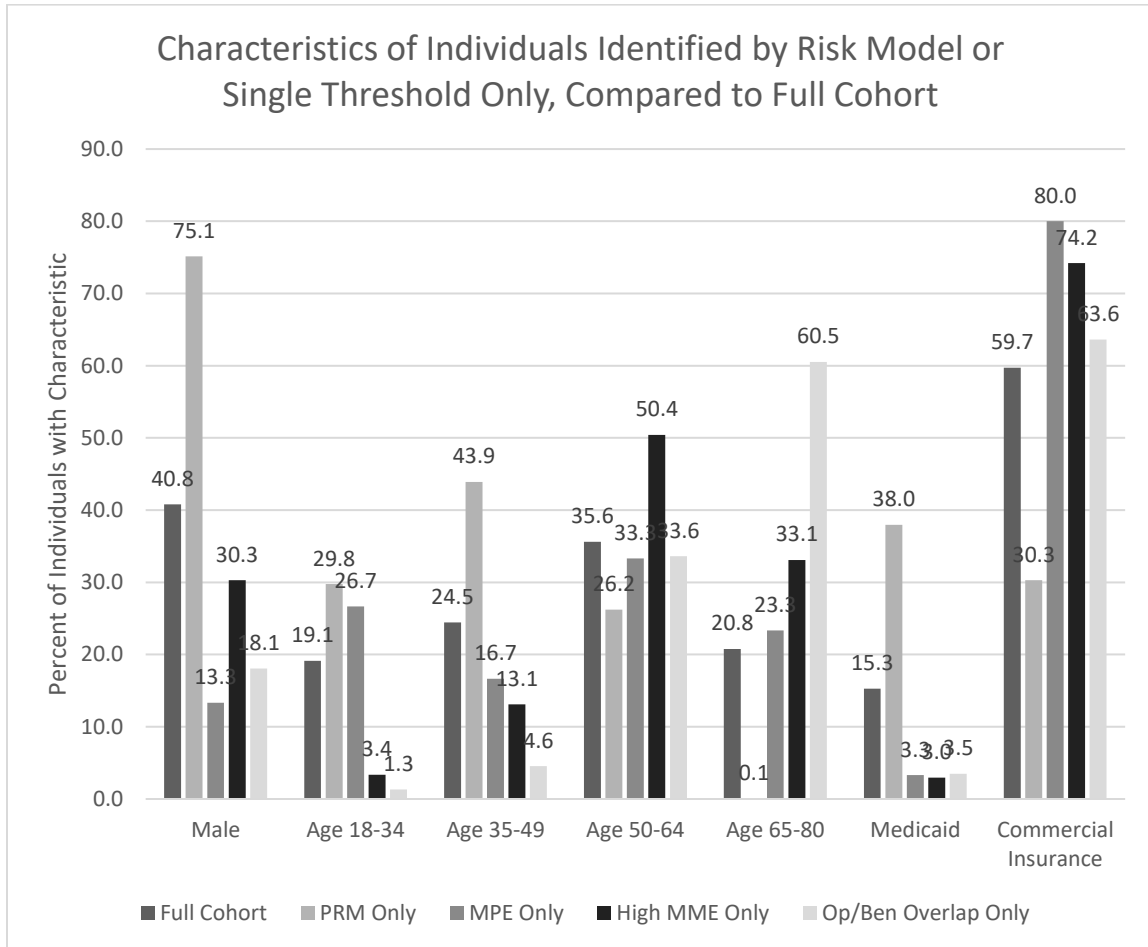
Characteristics of Individuals Identified by Risk Model or Single Threshold Only, Compared to Full Cohort

* Maryland residents 18-80 years with at least one opioid fill for full populations and individuals identified by a single risk identification method only within the validation population using 3 months of data (April-June 2015)

Abbreviations: PRM=predictive risk model; MPE=multiple provider episodes (5 unique prescribers and 5 unique dispensers), MME=Morphine Milligram Equivalents, Op/Ben=opioid/benzodiazepine

Appendix 2.5: Characteristics of study populations of equivalent size. *						
	Full Cohort**	Equivalent Populations - MPE		Equivalent Populations - High MME		Equivalent Populations - Opioid/Benzo Overlap	
		Threshold	PRM	Threshold	PRM	Threshold	PRM
# individuals	170,438	398	398	14,675	14,675	17,440	17,440
Male sex, n (%)	69,580 (40.8)	145 (36.4)	376 (94.5)	6,772 (46.2)	9,552 (65.1)	5,657 (32.4)	11,165 (64.0)
Age 18-34 years	32,619 (19.1)	117 (29.4)	89 (22.4)	1,093 (7.5)	2,594 (17.7)	1,273 (7.3)	3,012 (17.3)
Age 35-49 years	41,699 (24.5)	166 (41.7)	238 (59.8)	4,027 (27.4)	6,691 (45.6)	4,121 (23.6)	7,862 (45.1)
Age 50-64 years	60,697 (35.6)	96 (24.1)	71 (17.8)	7,092 (48.3)	5,352 (36.5)	7,924 (45.4)	6,518 (37.4)
Age 65-80 years	35,423 (20.8)	19 (4.8)	0 (0)	2,463 (16.8)	38 (0.3)	4,122 (23.6)	48 (0.3)
Private Pay	19,114 (11.2)	23 (5.8)	19 (4.8)	742 (5.1)	1,131 (7.7)	916 (5.3)	1,488 (8.5)
Medicaid	26,023 (15.3)	148 (37.2)	283 (71.1)	1,912 (13.0)	5,999 (40.9)	3,096 (17.8)	6,749 (38.7)
Medicare	19,430 (11.4)	44 (11.1)	71 (17.8)	2,506 (17.1)	2,210 (15.1)	3,181 (18.2)	2,492 (14.3)
Commercial Insurance	101,813 (59.7)	182 (45.7)	15 (3.8)	9,013 (61.4)	4,865 (33.2)	9,771 (56.0)	6,120 (35.1)
Military/VA	1,661 (1.0)	0 (0)	10 (2.5)	176 (1.2)	289 (2.0)	177 (1.0)	390 (2.2)
Indian	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Other/ Unknown	2,397 (1.4)	1 (0.3)	0 (0)	326 (2.2)	181 (1.2)	299 (1.7)	201 (1.2)
MPE	398 (0.2)	398 (100)	38 (9.6)	148 (1.0)	298 (2.0)	188 (1.1)	303 (1.7)
High MME	14,675 (8.6)	148 (37.2)	186 (46.7)	14,675 (100)	4,738 (32.3)	5,348 (30.7)	5,415 (31.1)
Op/benzo overlap	17,440 (10.2)	188 (47.2)	347 (87.2)	5,348 (36.4)	7,045 (48.0)	17,440 (100)	7,854 (45.0)
Any 1 high risk pattern	26,913 (15.8)	398 (100)	359 (90.2)	14,675 (100)	9,016 (61.4)	17,440 (100)	10,249 (58.78)
Any 2 high risk patterns	5,516 (3.2)	252 (63.3)	202 (50.8)	5,412 (36.9)	2,989 (20.4)	5,452 (31.3)	3,246 (18.6)
All 3 high risk patterns	84 (0.1)	84 (21.1)	10 (2.5)	84 (0.6)	76 (0.5)	84 (0.5)	77 (0.4)

* Maryland residents 18-80 years with at least one opioid fill using 3 months of data (April-June 2015).

**"Full Cohort" indicates the full validation cohort

Abbreviations: SD=standard deviation; VA=Veteran's Affairs; MPE=multiple provider episodes (5 unique dispensers and 5 unique prescribers); MME=morphine milligram equivalents; LA=long-acting; SA=short-acting; PRM=predictive risk model; Benzo=benzodiazepine.

III. Additional information for Paper 3: Assessing the Impact of Algorithms for Matching Persons Across State Datasets to Identify Risk of Fatal Opioid Overdose

Appendix 3.1: Graphical and Numerical Results of the Dataset Overlap Analysis.

Probabilistic Matching Overlap Analysis:
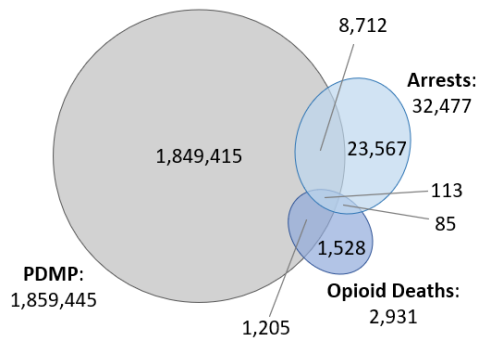
Deterministic-basic Matching Overlap Analysis:
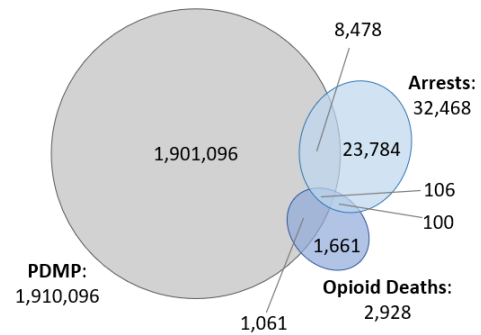
Deterministic+zip Matching Overlap Analysis:
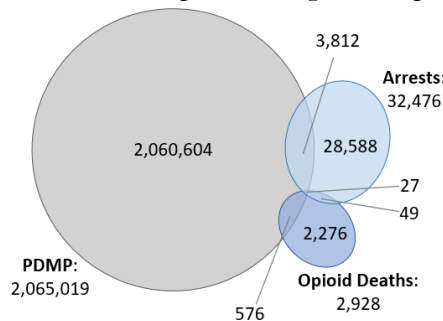
Analytic Dataset:
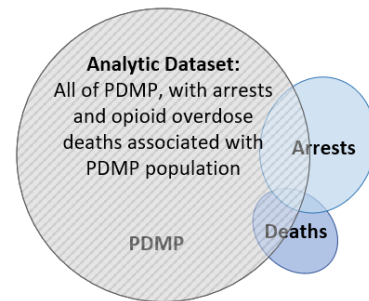
	Probabilistic	Deterministic-basic	Deterministic+zip
Within Dataset Matching*			
PDMP Dataset (No. native identities: 3,304,446)	1,859,445	1,910,741	2,065,019
Arrest Dataset (No. native identities: 38,004)	37,903	41,637	46,730
OCME Dataset (No. native identities: 22,829)	22,829	22,829	22,829
Across Dataset Matching*			
PDMP Only	**1,849,415**	**1,901,096**	**2,060,604**
Arrests Only	23,567	23,784	28,588
Opioid Overdose Deaths Only	1,528	1,661	2,276
PDMP + Arrests	**8,712**	**8,478**	**3,812**
PDMP + Opioid Overdose Deaths	**1,205**	**1,061**	**576**
Arrests + Opioid Overdose Deaths	85	100	49
PDMP + Arrests + Opioid Overdose Deaths	**113**	**106**	**27**

Bold indicates the population used for this study's analysis.
*Within dataset matching timeframes and scope: PDMP=2015, Any property or drug arrest=2013-2016, Any investigated death=2012-2016.
**Across dataset matching timeframes and scope: PDMP=2015, Any property or drug arrest=2013-2015, opioid-related overdose deaths=2015-2016

Appendix 3.2: Identifiable and Limited Dataset Management Process Flow

An explicit process for handling the OCME and DPSCS datasets was established where the grant administrator, the Maryland Department of Health (MDH), served as the broker between the parties involved in the study. The agency would provide the full dataset to the grant administrator, including patient-identifiable demographic information. To link the datasets, the grant administrator securely transferred only the demographic data from each of the datasets to CRISP to process and assign a master identifier to each identity, which was then encrypted. The encrypted identifier was appended to the agency's patient-identifiable demographic file and was provided back to the grant administrator. The grant administrator would append the encrypted identifier to the dataset, remove all identifiable data not approved by the IRB, and supply the de-identified dataset with the encrypted identifier to the researchers.
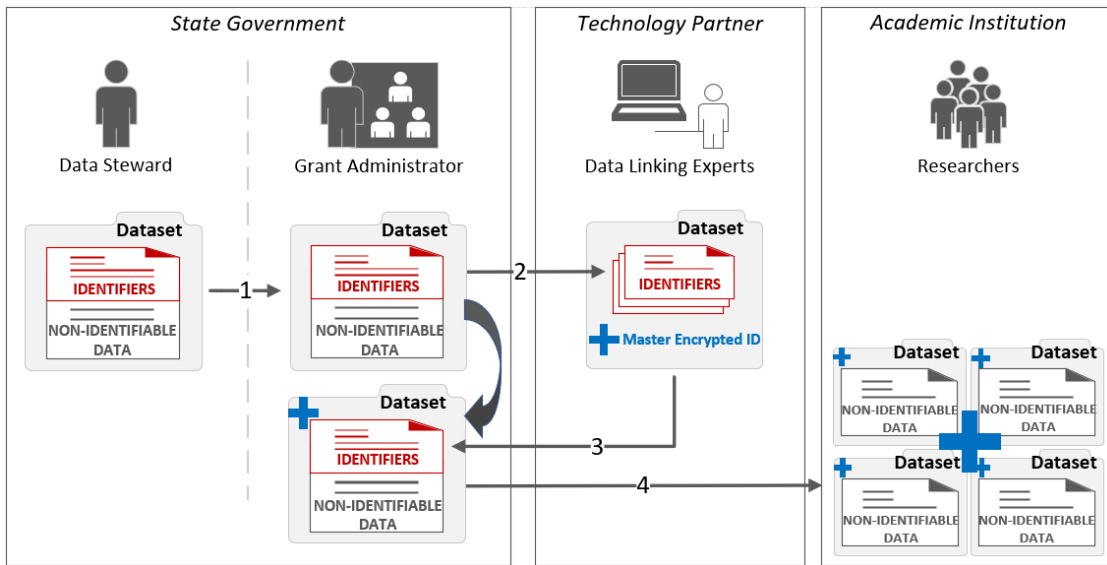
Using the grant administrator (MDH) as a data broker facilitated three key functions. It eased the burden on the data stewards from having to perform any de-identification steps post processing through the MPI by allowing the data steward the option to pass along the

fully identifiable dataset to a fellow state agency to manage. It allowed for a control step that ensured only identifiers were passed to the HIE and only identifiable data approved by the IRB would be shared with researchers. Finally, it removed the potential for unintended legal consequences resulting from matching identities recorded as separate individuals within the criminal justice datasets.

The HSCRC and PDMP dataset were already processed through the Master Patient Index as part of CRISP's operational responsibilities. CRISP supplied the final HSCRC limited dataset for 2012-2016 hospital visits with the encrypted identifier applied. CRISP supplied the crosswalk of PDMP ID to the encrypted identifier used for the study to the PDMP program. The PDMP program then supplied the PDMP limited dataset to the researchers. CRISP processed the OCME, DPSCS, and other relevant dataset demographic data, applied the encrypted identifier, and supplied it to grant administrators. The grant administrators married the encrypted identifier with the full dataset then supplied the limited datasets to researchers. The new datasets were processed after going through basic data cleaning to separate full names into separate First Name and Last Name fields. The OCME, DPSCS, and other relevant datasets followed the external dataset process depicted below:
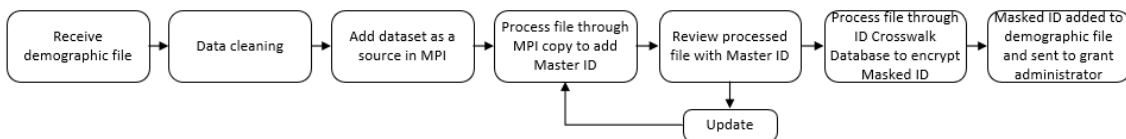
Appendix 3.3: MPI Probabilistic Matching Algorithm Functions and Configuration

The probabilistic matching algorithm can be broken into five basic functions:
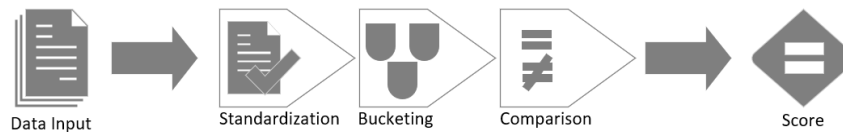
Data Input: The MPI algorithm uses demographic data elements normalized into different "attributes". The algorithm attributes used to link individuals included name, date of birth, gender, address, phone number, and social security number. Each unique attribute was used to create a match score to represent the degree of certainty for an exact match.

Standardization: Standardization represents the conversion of the data into its simplest form to allow for easy comparison. The standardization steps used included removing false or anonymous values, such as phone numbers entered as (000) 000-0000, removing any special characters and applying truncations, such as (123) 456-7890 to 4567890, and converting the name to all upper case.[34] Two types of address standardization arguments were employed: 1) postal codes patterning, and 2) type of words or characters used for unit information (floor, suite, unit, etc.).[34]

Bucketing: Bucketing organizes common data values together using single or multiple attributes to create unique combinations that are more easily recalled during searching and matching. Theoretically, each identity needs to be compared with every previously processed identity, which would be far too consuming without a mechanism to limit it only logical comparisons.[35] The bucketing processes employed by the MPI used in this study included Name (First Name + Last Name), Name Phonetic + DOB, Name Phonetic + Zip Code, SSN, Phone, Zip Code, MRN, plus some special attributes specific to Maryland stakeholders.

Comparison: The individuals sharing buckets together are then compared and scored using predefined probabilistically generated weights. Each comparison function for the different attributes generates a score that can be positive or negative. Full points were awarded for exact matches and partial points were given for common but minor data discrepancies, such as the use of nicknames, misspellings, and transposed dates, names, and numbers. The comparison function incorporates various approaches to processing information that inherently have data quality challenges:

- Initials and full word comparison: match on initials or full word are assessed and scored.
- Enhanced soundex: words with similar phonetic sounds receive a higher score
- Frequency indexing: common words and names yield lower scores; uncommon words and names yield higher scores.

- Nickname tables: tables that equate formal and informal names and cross-compare the exact and phonetic names.
- Edit distance calculations: the number of changes needed for two values to be equivalent, the lower the number of changes the more likely the records are a match. Prefix and compound comparisons are also employed where matches may be missed by the edit-distance calculation, for example, Belair and Bel Air would be compared.
- Acronym comparison: for example, D.C. would be compared with District of Columbia.
- Attribute weights: for example, phone number receives a higher weight than gender.
- Historical values in matching: the use of previous addresses or names (maiden names) as part of the matching technology improves the matching capability.
- False positive filter: applies deterministic logic to specific false positive matches and uses the result to apply a penalty score.

Score: The final score is a sum of scores from the comparison functions in the algorithm and reflects the degree of match certainty between the two individuals being compared. The patient was a "match" if above the CRISP-defined threshold (score≥13.1), "potential match" if the individuals are close but not strong enough to be linked together (score between 13.1 and 10.2), or "not matched" (score≥10.1). The attributes configured for comparison and MPI weight distributions include:

Attribute	Max Weight	Min Weight
Name/ Previous Name (1 attribute)	4.08 (max 7.00)	Invalid Names: -2.35; Other: -1.45
Date of Birth (1 attribute)	4.75	-3.92
Gender (1 attribute)	M: 0.23; F: 0.38; Other: 0.23	-2.03
SSN – Full (1 attribute)	3.66	-5.37
SSN - Last four (1 attribute)	1.85	-1.00
Patient Address and Phone Combinations (2 attributes)		
Patient Address - Missing & Phone - Missing	0	N/A
Patient Address - Match & Phone - Missing	5.01	N/A
Patient Address - Missing & Phone - Match	4.79	N/A
Patient Address - Match & Phone - Match	5.24	N/A
Patient Address - Non-Match & Phone - Missing	4.03	-2.83
Patient Address - Missing & Phone - Non-Match	4.75	-3.61
Patient Address - Non-Match & Phone - Non-Match	4.95	-2.19
False Positive filter (4 attributes)		
Name: matching, Gender: missing, DOB: apart >15 years, SSN: missing		-3.00
Name: matching, Gender: missing, DOB: apart >15 years, SSN: not missing		-5.00
Name: partial matching, Gender: missing, DOB: apart >15 years, SSN: missing		-3.00
Name: partial matching, Gender: missing, DOB: apart >15 years, SSN: not missing		-5.00
Name: not matching, Gender: missing, DOB: matching		-5.00
Name: not matching, Gender: missing, DOB: apart >15 years		-5.00

Name: matching, Gender: matching, DOB: apart >15 years, SSN: missing		-3.00
Name: matching, Gender: matching, DOB: apart >15 years, SSN: not missing		-5.00
Name: partial matching, Gender: matching, DOB: matching, SSN: missing		-2.00
Name: partial matching, Gender: matching, DOB: matching, SSN: matching		-2.00
Name: partial matching, Gender: matching, DOB: matching, SSN: edit distance	-2.50	-5.00
Name: partial matching, Gender: matching, DOB: apart >15 years, SSN: missing		-3.00
Name: partial matching, Gender: matching, DOB: apart >15 years, SSN: not missing		-5.00
Name: not matching, Gender: matching, DOB: matching, SSN: missing		-4.00
Name: not matching, Gender: matching, DOB: matching, SSN: matching		-3.50
Name: not matching, Gender: matching, DOB: matching, SSN: edit distance	-4.00	-5.00
Name: not matching, Gender: matching, DOB: apart >15 years		-5.00
Name: matching, Gender: not matching, DOB: apart >15 years, SSN: missing		-3.00
Name: matching, Gender: not matching, DOB: apart >15 years, SSN: not missing		-5.00
Name: partial matching, Gender: not matching, DOB: matching, SSN: missing or not matching		-2.50
Name: partial matching, Gender: not matching, DOB: apart >15 years, SSN: missing		-3.00
Name: partial matching, Gender: not matching, DOB: apart >15 years, SSN: not missing		-5.00
Name: not matching, Gender: not matching, DOB: matching		-5.00
Name: not matching, Gender: not matching, DOB: apart >15 years		-5.00

An example scoring of two individual's test demographics (fake patient) processed through the operational MPI's probabilistic algorithm is represented below:

Comparison	Grape, Gilbert, PDMP:9900991	Gilbert, Grape, DPSCS: 55324343	Weight
XNM	GRAPE|GILBERT|	GILBERT|GRAPE|	6.84
Date of Birth	19840101	19840101	4.75
Gender	F	F	0.23
Address	4145|EARL|C|ADKINS|DR|RIVER|WV|26000	4145|EARL|C|ADKINS|DR|RIVER|WV|26000	5.01
Phone	301-222-2999		
SSN	X16326289	X214024632	-2.66
False Positive Filter	19840101	19840101	0
Total Match Score			**14.17**

Appendix 3.4: Deterministic algorithm matching

Two deterministic, exact-match algorithms were applied to each dataset, starting with PDMP data.

The matching process consisted of the following steps:

1. Start with an empty master patient list.
2. Begin processing the identities in each file using the defined algorithm (i.e. first name, last name, gender, date of birth), comparing each identity in the database to the identities in the master patient list.
    a. If any exact matches occurred between the master list of the unique identities and the dataset, the identity in the dataset was assigned the deterministic ID in the master list.
    b. If no match exists, the identity is added to the master patient list and assigned its own unique deterministic ID (note: this applies to the very first identity processed – the identity was added since there was no exact match to be made with an empty list.)
3. Steps 2a and 2b were repeated for the remaining datasets, one dataset at a time.

Note: The steps outlined above were repeated for each dataset. Because the master list of identities was for all unique individuals, if there were multiple records within a single database with matching demographics, the deterministic ID would be applied across all records, therefore matching records within a single database as well (not just across). For transaction-level databases (PDMP and DPSCS), identities that had the same dataset-defined patient identifier within a single database was checked to ensure the same deterministic ID was applied. Any identities in the dataset that did not have an assigned database-level unique patient identifier were removed before the processing began.

Appendix 3.5: Predictive model classification tables for each matching algorithm.

Model Risk Score Cutoff	Sens.	Spec.	Sens. + Spec.	PPV	NPV	Acc.	# high-risk patients	% of validation cohort	# Deaths among high-risk	Deaths per 1,000 high-risk
Appendix Table 3.5.1: Probabilistic Algorithm - validation cohort (N=661,451)										
0.00025	95.51	38.15	133.66	0.12	99.99	28.19	409782	62.0%	511	1.25
0.0005	87.87	61.37	149.24	0.18	99.98	61.40	256,047	38.7%	471	1.84
0.0010	**67.54**	**84.29**	**151.83**	**0.35**	**99.97**	**84.28**	**104,293**	**15.8%**	**362**	**3.47**
0.0015	56.16	90.78	146.94	0.49	99.96	90.76	61,286	9.3%	301	4.91
0.0020	48.88	93.79	142.67	0.63	99.96	93.76	41,325	6.2%	262	6.34
0.0025	44.59	95.11	139.70	0.73	99.95	95.07	32,564	4.9%	239	7.34
0.0030	36.75	96.45	133.20	0.83	99.95	96.40	23,695	3.6%	197	8.31
0.0035	33.21	96.99	130.20	0.88	99.94	96.93	20,122	3.0%	178	8.85
0.0040	29.29	97.53	126.82	0.95	99.94	97.47	16,506	2.5%	157	9.51
0.0045	25.75	97.86	123.61	0.96	99.94	97.80	14,304	2.2%	138	9.65
0.0050	24.44	98.07	122.51	1.02	99.94	98.01	12,897	1.9%	131	10.16
0.0055	22.39	98.32	120.71	1.07	99.94	98.25	11,263	1.7%	120	10.65
0.0060	19.96	98.52	118.48	1.08	99.93	98.46	9,886	1.5%	107	10.82
0.0065	16.98	98.85	115.83	1.18	99.93	98.78	7,721	1.2%	91	11.79
0.0070	16.04	98.94	114.98	1.22	99.93	98.88	7,072	1.1%	86	12.16
0.0075	15.30	99.02	114.32	1.25	99.93	98.96	6,541	1.0%	82	12.54
0.0080	14.37	99.08	113.45	1.26	99.93	99.02	6,133	0.9%	77	12.56
0.0085	12.87	99.18	112.05	1.25	99.93	99.11	5,518	0.8%	69	12.50
0.0090	11.75	99.26	111.01	1.27	99.93	99.19	4,971	0.8%	63	12.67
0.0095	11.01	99.32	110.33	1.29	99.93	99.25	4,570	0.7%	59	12.91
Abbreviations: Acc.=accuracy, NPV=negative predictive value, PPV=positive predictive value, Sens.=sensitivity, Spec.=specificity, pts=patients										

Appendix Table 3.5.2: Deterministic-basic Algorithm - validation cohort (N=679,925)										
Model Risk Score Cutoff	Sens.	Spec.	Sens. + Spec.	PPV	NPV	Acc.	# high-risk	% of validation cohort	# Deaths among high-risk	Deaths per 1,000 high-risk
0.00025	94.97	45.54	140.51	0.11	99.99	44.58	377229	55.48	415	1.10
0.0005	**87.47**	**66.26**	**153.73**	**0.17**	**99.99**	**66.27**	**229,646**	**33.78**	**384**	**1.67**
0.0010	66.74	85.99	152.73	0.31	99.98	85.98	95,460	14.04	293	3.07
0.0015	57.63	91.03	148.66	0.41	99.97	91.01	61,202	9.00	253	4.13
0.0020	47.15	94.30	141.45	0.53	99.96	94.27	38,923	5.72	207	5.32
0.0025	39.18	95.79	134.97	0.60	99.96	95.75	28,805	4.24	172	5.97
0.0030	35.99	96.77	132.76	0.71	99.96	96.73	22,120	3.25	158	7.14
0.0035	33.03	97.37	130.40	0.80	99.96	97.32	18,042	2.65	145	8.04
0.0040	31.44	97.70	129.14	0.88	99.95	97.66	15,759	2.32	138	8.76
0.0045	26.88	98.00	124.88	0.86	99.95	97.96	13,680	2.01	118	8.63
0.0050	23.69	98.44	122.13	0.97	99.95	98.39	10,684	1.57	104	9.73
0.0055	22.32	98.60	120.92	1.02	99.95	98.55	9,600	1.41	98	10.21
0.0060	19.13	98.80	117.93	1.02	99.95	98.75	8,241	1.21	84	10.19
0.0065	15.95	98.96	114.91	0.98	99.95	98.90	7,164	1.05	70	9.77
0.0070	15.26	99.06	114.32	1.04	99.94	99.01	6,427	0.95	67	10.42
0.0075	13.67	99.17	112.84	1.06	99.94	99.12	5,676	0.83	60	10.57
0.0080	13.21	99.24	112.45	1.12	99.94	99.19	5,199	0.76	58	11.16
0.0085	12.76	99.30	112.06	1.17	99.94	99.25	4,788	0.70	56	11.70
0.0090	12.30	99.36	111.66	1.22	99.94	99.30	4,416	0.65	54	12.23
0.0095	12.07	99.41	111.48	1.31	99.94	99.36	4,051	0.60	53	13.08
Abbreviations: Acc.=accuracy, NPV=negative predictive value, PPV=positive predictive value, Sens.=sensitivity, Spec.=specificity, pts=patients										

Appendix Table 3.5.3: Deterministic+zip Algorithm - validation cohort (N=727,565)										
Model Risk Score Cutoff	Sens.	Spec.	Sens. + Spec.	PPV	NPV	Acc.	# high-risk	% of validation cohort	# Deaths among high-risk	Deaths per 1,000 high-risk
0.00025	**85.53**	**62.17**	**147.70**	**0.07**	**99.99**	**62.18**	**275,352**	**37.85**	**195**	**0.71**
0.0005	60.96	84.37	145.33	0.12	99.99	84.37	113,791	15.64	139	1.22
0.0010	42.54	94.30	136.84	0.23	99.98	94.29	41,531	5.71	97	2.34
0.0015	34.21	96.98	131.19	0.35	99.98	96.96	22,074	3.03	78	3.53
0.0020	26.32	98.00	124.32	0.41	99.98	97.97	14,629	2.01	60	4.10
0.0025	22.37	98.55	120.92	0.48	99.98	98.53	10,580	1.45	51	4.82
0.0030	17.98	98.94	116.92	0.53	99.97	99.92	7,727	1.06	41	5.31
0.0035	14.91	99.22	114.13	0.60	99.97	99.19	5,713	0.79	34	5.95
0.0040	10.53	99.38	109.91	0.53	99.97	99.35	4,515	0.62	24	5.32
0.0045	9.21	99.49	108.70	0.56	99.97	99.46	3,761	0.52	21	5.58
0.0050	8.77	99.58	108.35	0.65	99.97	99.55	3,075	0.42	20	6.50
0.0055	7.46	99.63	107.09	0.63	99.97	99.60	2,686	0.37	17	6.33
0.0060	7.46	99.69	107.15	0.31	99.97	99.66	2,301	0.32	17	7.39
0.0065	6.14	99.72	105.86	0.69	99.97	99.69	2,041	0.28	14	6.86
0.0070	5.26	99.77	105.03	0.73	99.97	99.74	1,654	0.23	12	7.26
0.0075	3.95	99.80	103.75	0.61	99.97	99.77	1,483	0.20	9	6.07
0.0080	3.95	99.81	103.76	0.66	99.97	99.78	1,358	0.19	9	6.63
0.0085	3.51	99.83	103.34	0.65	99.97	99.80	1,225	0.17	8	6.53
0.0090	3.51	99.85	103.36	0.74	99.97	99.82	1,082	0.15	8	7.39
0.0095	3.07	99.86	102.93	0.70	99.97	99.83	993	0.14	7	7.05
Abbreviations: Acc.=accuracy, NPV=negative predictive value, PPV=positive predictive value, Sens.=sensitivity, Spec.=specificity, pts=patients										

Curriculum Vitae

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PERSONAL DATA:

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Place of Birth: Bloomfield Hills, Michigan
Year of Birth: 1983

EDUCATION:

2013-2019	**Johns Hopkins Bloomberg School of Public Health,** Baltimore, MD Doctor of Public Health Candidate, Healthcare Management & Leadership, Informatics Track
2010-2011	**Johns Hopkins Bloomberg School of Public Health,** Baltimore, MD Master of Public Health
2001-2005	**Carnegie Mellon University**, Pittsburgh, PA Bachelor of Science in Chemistry Minor in Business Administration; Graduated with Research Honors in Chemistry

WORK EXPERIENCE:

Chesapeake Regional Information System for our Patients (CRISP), Program Director, HIE Projects, Columbia, MD, June 2012-Current
Audacious Inquiry, Senior Director, Catonsville, MD, June 2012-Current

Contracted full time in a senior leadership role overseeing all public health and other new HIE-related projects at CRISP, the Health Information Exchange (HIE) serving Maryland, DC and partnered with WV. Manage a team of seven project/program management personnel, contribute to company strategy, staffing plans, policy-based discussions, and goal setting. Responsibilities include:

- **Prescription Drug Monitoring Program (PDMP):** oversaw original implementation in 2013 as the program manager for Maryland's statewide PDMP in partnership with Maryland Department of Health. Manage the budget, relationship with the state, and oversee the management and operation of the PDMP, including through the mandated registration and use laws.

- **Medicaid APD Manager & Public Health Lead:** manage the reporting, budgeting, invoicing, and resource allocation for CRISP HIE services funded by the Centers for Medicare & Medicaid Services (CMS) to Maryland Medicaid. The grant is for $31 million over two years for a range of projects/services.

- **Opioid and Behavioral Health-related Efforts:** manage team working to capture suspected overdoses occurring within hospital Emergency Departments for viewing while providers consult the PDMP and Emergency Medical Services (EMS) data to capture overdose events occurring outside the hospital setting. Oversee the work to expand CRISP services to the behavioral health community and understand the 42 CFR Part 2 federal rule about patient consent for sharing substance use disorder treatment data.

- **Harold Rogers PDMP Grant:** collaborate on efforts between CRISP, MDH, and the Johns Hopkins Center for Population Health Information Technology (CPHIT). Oversaw the data linking efforts at CRISP related to the Grant for a Practitioner/Researcher partnership to create a predictive risk model opioid overdose.

CodeRyte/3M, Client Engagement Executive, Bethesda, MD, June 2011-June 2012
- Coordinated between multiple divisions (technical team, coding analysts, sales) at CodeRyte and the client.
- Brought 5 clients live with the Natural Language Processing-driven computer assisted coding software.
- Designed a critical comparison report that reflected CodeRyte/Coder results with Practitioner-selected codes to determine financial impact of software at a major healthcare system.
- Worked with additional 10 existing CodeRyte clients on optimization of the coding software to maximize Return on Investment (ROI) and managed overall relationships.
- Worked with Sales team members on expanding the product suite to additional specialties at existing client sites, and managed enhancement requests.
- Analyzed and presented the impact of industry-driven events, such as meaningful use, accountable care organizations, and ICD-10 on CodeRyte and its clients.

Epic Systems Corporation, Project Manager, Madison, WI, July 2005 – June 2010
- Installed pharmacy and oncology portions of Epic's electronic medical record (EMR) software for seven projects across six clients and managed six Epic employees.
- For each project, collected organization-specific information, translated client information into the software, demonstrated workflows for stakeholder validation, tailored documentation supplied to clients, assisted in testing and training, and managed project timelines, budgets, scope, and outcomes.
- Completed evaluation of over 10 customer systems post go-live to determine user efficiency, satisfaction and potential improvements/optimization.
- Continually volunteered to support users during point of software induction for Epic teams outside of my customers, allowing familiarization of workflows and policies for over 20 health systems in the US and one in Holland. Customers, projects, and dates of engagement include:

  Cleveland Clinic Health System, Pharmacy, July 2005 – July 2008
  Cleveland Clinic Health System, Oncology, September 2006 – June 2010
  Dartmouth Hitchcock Medical Center, Pharmacy, March 2009 – June 2010
  Northwestern Medical Faculty Foundation, Oncology, July 2009 – June 2010
  Aurora Advanced Healthcare, Oncology, October 2009 – June 2010
  Nemours - Alfred I. duPont Hospital for Children, Pharmacy, June 2007 – May 2009
  Buffalo Medical Group, Oncology, May 2008 – December 2008

OTHER EXPERIENCE:

Project Management Professional, Baltimore, MD October 2013-Current
Passed the Project Management Professional exam in October of 2013, which is a globally recognized test to demonstrate my experience, education and competency to lead and direct projects.

Certified in Public Health, Baltimore, MD May 2011-Current
Passed the National Board of Public Health Examiners' (NBPHE) Certified in Public Health exam in May of 2011, which is a test to demonstrate my mastering the foundational competencies in public health learned from a CEPH-accredited school.

Certificate in Public Health Informatics, Baltimore, MD, June 2010-June 2011
Graduated with a certificate in public health informatics offered at Johns Hopkins after completing the required 21 course credits, informatics related capstone, and practicum experience.

Teaching Assistant, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD 2011-2017
Lead Teaching Assistant for Dr. Weiner's Population Health Informatics online course. Mentored students, graded midterms and finals, created quiz questions, assisted in Live Talks, managed online course content.

Crew Chief of Race Across America (RAAM), Oceanside, CA to Annapolis, MD 2016
Served as crew chief for my brother's solo RAAM challenge, which is a 3,089-mile bike race from Oceanside, CA to Annapolis, MD. Orchestrated a 12-person team and made all critical decisions to support his race, seeing him across the finish line in 10 days, 21 hours, and 43 minutes.