

Current Data Resources Used to Investigate Drug Products with Properties Intended to Deter Abuse

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Issues Paper Correction

- Treatment Episode Dataset (page 5, section 3.2)
 - The Treatment Episode Data Set (TEDS) is an admission-based **system** that includes data from facilities that receive public funds, are licensed or certified by a **State Substance Abuse Agency** to provide treatment, or are tracked at the state level for other reasons.

Overview

- Summary of Current Data Resources for ADF studies
- General Methodological Considerations
- Outcomes in ADF Opioid Investigations
- Questions for Discussion

SUMMARY OF CURRENT DATA RESOURCES FOR ADF OPIOID STUDIES

Base Populations

- Categories of current data resources generally used to assess misuse and abuse of ADF opioid products
 - Poison Control Center data (convenience sample)
 - Surveys of those being assessed or entering treatment (convenience samples)
 - Population-based surveys (nationally representative and convenience samples)
 - Medical and prescription claims (Medicare/Medicaid and convenience samples)

Poison Control Centers

- Poison Control Centers collect data from calls relating to exposure to substances
 - + Widespread catchment area (57 regional centers)
 - + Often product-specific information
 - + May include individuals that otherwise would not interact with the health-care system
 - Percentage of events that result in a call is unknown
 - Ability to distinguish specific formulations and generic products is unclear
 - Severe overdoses and immediate deaths are unlikely to generate a call – may be underrepresented

Surveys of High-Risk Individuals

- Includes those entering or being assessed for substance use disorder treatment
 - + Captures a hard-to-reach population of high-risk individuals
 - + Can provide product-specific patterns of abuse
 - + Can provide route-specific abuse information
 - Difficult to define underlying population
 - Generalizability of results is unclear
 - Difficult to validate key pieces of information

General Population-Based Surveys

- Population-based surveys
 - + Federal surveys are nationally representative
 - + Captures wide range of abuse behaviors
 - + Can focus on specific populations (i.e. students)
 - Eligibility criteria (e.g., stable residence, school attendance) may exclude individuals with more severe use disorders
 - Inability to capture same level of product and administration detail (e.g. formulation, route of abuse)
 - Most are cross-sectional in nature (although MTF does have a longitudinal component)

Claims-Based Data

- Claims-based data resources
 - + Catchment can range from very large convenience samples to national census
 - + Can be linked to other data sources (i.e., NDI)
 - + Can be longitudinal (e.g., CMS)
 - Claims data by themselves are not sufficient to study prescription drug abuse; validation can be challenging
 - Misuse, abuse, and addiction difficult to define using medical coding or claims
 - Often not possible to determine specific drug product; not useful in determining route of abuse

Additional Data Resources

- Collected from alternate streams
 - Spontaneous adverse event reports
 - Drug diversion data
 - Web-based data collection, including street price
 - Regional cohort studies
- Can provide valuable insights not available through more commonly used “big data” streams
- Can be a challenge to define the relationship between metrics available in these resources and those of interest to the Agency
- Validation and verification can be an issue, particularly for web-based data collection

GENERAL METHODOLOGICAL CONSIDERATIONS

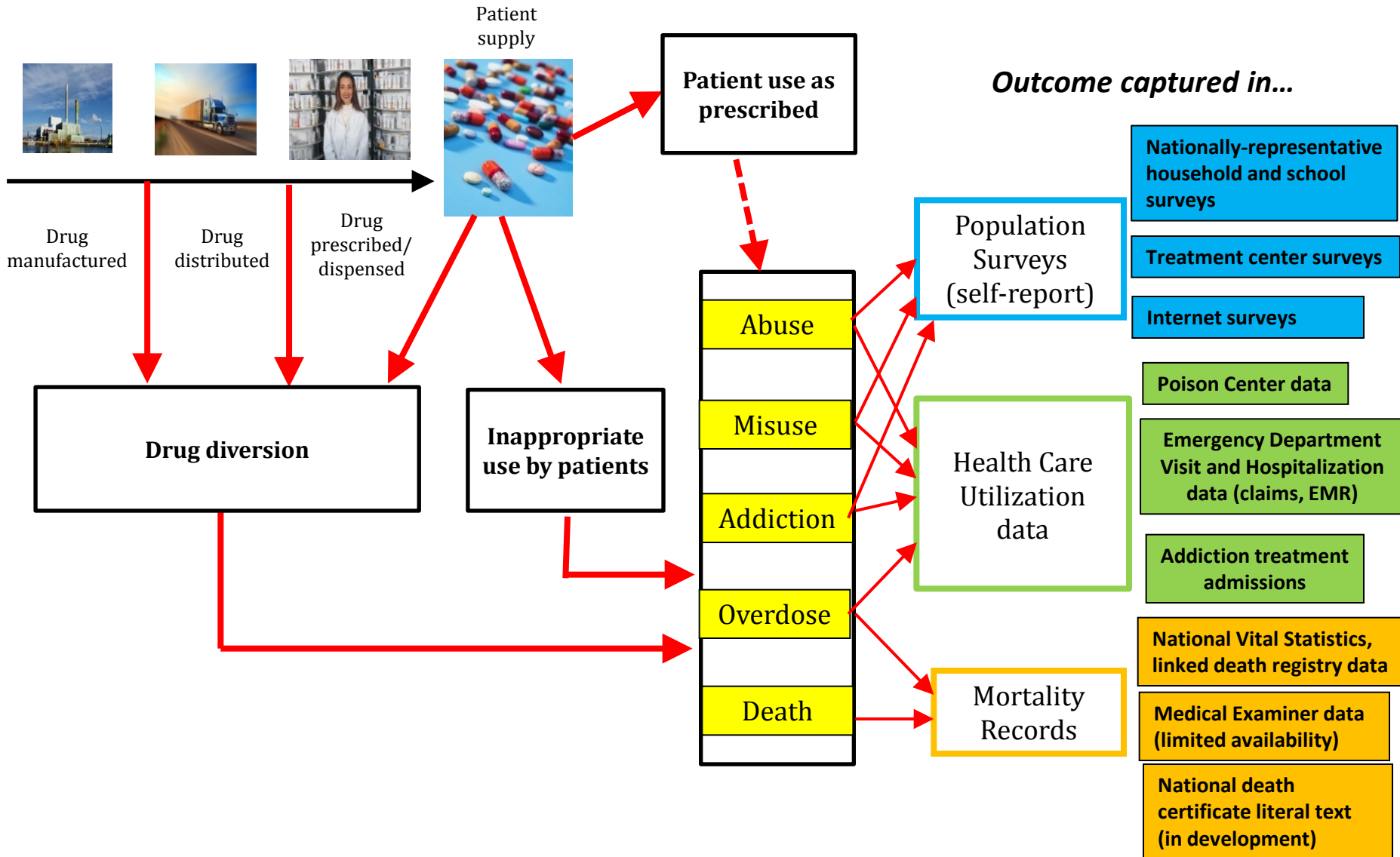
Exposure Definition and Assessment

- Dependent on level of analyses
- Group-based study design (e.g., ecologic)
 - Unit of time (e.g. month, quarter)
 - Other demographic variable
- Individual-based study design
 - Possession of (or prescription for) an ADF opioid (e.g. longitudinal studies)
 - Participation in an activity (e.g., entering substance abuse treatment, completing survey)

Misclassification and Ascertainment

- Can be an important factor in identifying abuse related to ADF products
 - pre- vs. post-transition product identification
 - “Kleenex effect” and/or counterfeiting
 - Data collection methodology (e.g., product order)
- Assessing the extent and nondifferential nature of misclassification important to interpreting analysis results

Pathways to Abuse/Misuse of Prescription Drugs and Related Adverse Outcomes



OUTCOME CONSIDERATIONS

Outcome Measurement

- Multiple data sources are able to assess a variety of outcomes
- Outcomes of interest to Agency: misuse, abuse, addiction, overdose, and death
- Since many technologies focus on non-oral abuse, route-specific outcomes are also of interest
 - Not always available in current data resources

Outcome Measurement

- FDA has definitions of both misuse and abuse, but operationalizing them can be a challenge
 - Data resources have differing definitions
 - Some combine the concepts of misuse and abuse
 - Difficult to measure in claims-based resources
 - Ascertaining specific products abused can be difficult
 - Multiple product abuse adds to complexity
 - Misclassification is a significant issue

Outcome Measurement

- Addiction is a complex and nuanced concept
 - Similar to misuse and abuse, data resources do not often capture components used to assess addiction
- Overdose and mortality are easier to define
 - Few data resources can connect abuse and outcome data
 - Difficult to attribute to a specific product

Additional Outcomes

- Doctor and/or Pharmacy Shopping
 - Not straightforward to define
 - Three ER/LA PMR Studies to define, and assess in relation to misuse and abuse
- Proxy clinical outcomes (e.g. hepatitis, HIV)
 - Challenge to relate to specific ADF products
- Drug seizure levels, changes in street price
 - How to relate to outcomes of interest to FDA?

QUESTIONS FOR DISCUSSION

Questions for Discussion

- Discuss the ability of currently available abuse-related data resources to adequately characterize the underlying population of those who misuse and abuse drugs
 - How well do they capture
 - Occasional/recreational use?
 - Severe/advanced opioid use disorder?
 - Individuals in between these two extremes?

Questions for Discussion

- Discuss the ability of current data sources to distinguish ADF opioid molecules and formulations
- Discuss the ability of currently available data sources for collecting information on routes of abuse

Questions for Discussion

- Discuss the important exposures and outcomes to consider when conducting ADF opioid investigations. How well are these factors measured in currently existing data sources?

Questions for Discussion

- Discuss the best practices for measuring misuse, abuse, addiction, overdose, and mortality
 - What are the best practices for validating misuse, abuse, and addiction?
- Are there additional outcome and/or exposure measures that could be used in these studies?

BACKUP SLIDES

Abuse

- “The intentional, non-therapeutic use of a drug product or substance, even once, to achieve a desirable psychological or physiological effect”
 - “Abuse-Deterrent Opioids —Evaluation and Labeling Guidance for Industry”

Misuse

- “The intentional therapeutic use of a drug product in an inappropriate way, specifically excluding abuse”
 - From “Abuse-Deterrent Opioids —Evaluation and Labeling Guidance for Industry”