Distributed Research Networks and Opioids: A Veterans Health Affairs Perspective

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JASON SIMCAKOSKI MEMORIAL AND PROMISE ACT
LECTURE OBJECTIVES

• Introduction to FDA PMR Study 1A
• Overview: HCSRN Virtual Data Warehouse (VDW) within VHA
• Use of VDW to evaluate Trajectories of Co-Prescribing of Benzodiazepines
DISCLOSURES

• I have no conflicts of interest that could affect the content of my presentation.

• Funded research:
  – Food & Drug Administration PMR Study 3033–1A
    “A prospective investigation of the risks of opioid misuse, abuse, and addiction among patients treated with extended-release/long acting (ER/LA) opioids for the treatment of chronic pain”
  – VA HSR&D Merit Grant I01 HX002314–01A1
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- Paul Chung
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BACKGROUND

RISE IN OPIOID OVERDOSE DEATHS IN AMERICA

A Multi-Layered Problem in Three Distinct Waves

399,000 people died from an opioid overdose (1999-2017)

1990s mark a rise in prescription opioid overdose deaths

2010 marks a rise in heroin overdose deaths

2013 marks a rise in synthetic opioid overdose deaths

Rx OPIOIDS
Include natural, semi-synthetic, and methadone and can be prescribed by doctors

HEROIN
An illegal opioid

SYNTHETIC OPIOIDS
Such as fentanyl and tramadol are very powerful and can be illegally made

Overdose Death Rates Involving Opioids, by Type, United States, 2000-2017

LONG TERM RISKS AND BENEFITS OF OPIOIDS?

- Magnitude of misuse, abuse, and addiction among patients who are treated with opioids for chronic pain?

- Insufficient data to estimate how the risk of these outcomes varies by the presence of risk factors (other substance use and psychiatric disorders), among patients treated with opioids over the long-term?

BACKGROUND

Existing pharmacovigilance framework (i.e. FDA Sentinel Initiative) insufficient.
A prospective investigation of the risks of opioid misuse, abuse, and addiction among patients treated with extended-release/long acting (ER/LA) opioids for the treatment of chronic pain

- Estimate the incidence of misuse, abuse, addiction, overdose, and death associated with long–term use of opioids for chronic pain.

- Evaluate and quantify other risk factors for misuse, abuse, addiction, overdose, and death associated with long–term use of opioids for chronic pain.
Conceptual Model

- Psychologic factors
- Chronic Pain
  - Biologic Factors
  - Social Factors
DATA SOURCES

EHR → Data

Gene6c Samples

Patient Reported Outcomes
### ELIGIBILITY CRITERIA

<table>
<thead>
<tr>
<th>Prospective Study</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Inclusion Criteria</strong></td>
<td></td>
</tr>
<tr>
<td>30 days of new ER/LA opioid use*</td>
<td></td>
</tr>
<tr>
<td>Age 18–79 years at incident prescription</td>
<td></td>
</tr>
<tr>
<td>Enrolled with medical and drug benefit for at least 12 months prior to incident use of opioids (HCSRN and VA only as enrollment is N/A to PBRNs) And</td>
<td></td>
</tr>
<tr>
<td>2+ visits to participating clinic during 12 months prior to incident use of opioids (PBRN, HCSRN, and VA)</td>
<td></td>
</tr>
<tr>
<td>Additional prescription/order for an ER/LA opioid following at least 30 days of new use</td>
<td></td>
</tr>
<tr>
<td>Ability to complete interview/self-administered questionnaires in English</td>
<td></td>
</tr>
<tr>
<td>Willing to provide informed consent</td>
<td></td>
</tr>
<tr>
<td><strong>Exclusion Criteria</strong></td>
<td></td>
</tr>
<tr>
<td>Not using an ER/LA opioid at the time of recruitment (self-report)</td>
<td></td>
</tr>
<tr>
<td>Cognitive impairment that interferes with the ability to consent or participate in the interview, unavailable for 12 months of follow-up, or receiving hospice care as determined at the time of recruitment</td>
<td></td>
</tr>
<tr>
<td>Diagnosis of a terminal illness in the prior 12 months</td>
<td></td>
</tr>
</tbody>
</table>

*New use defined as prescription or prescriptions lasting at least 30 days and no ER/LA opioid use in the prior 12 months. Prior IR opioid use allowed.

**Cross-sectional study** – same eligibility criteria except opioid users for at least 1 year and must include 1+ prescriptions for ER/LA opioid
WHY VA?

• High risk, vulnerable population
• Promotes generalizability
• Lower socioeconomic strata
• High prevalence of chronic pain; mental health and substance use disorders
• Detailed pharmacy data; longitudinal records
• Multi-year, multi-healthcare system collaboration. Data may not be exported outside of VA.
DISTRIBUTED RESEARCH NETWORKS

Sentinel Initiative

health care systems research network

mid-south clinical data research network

PCORnet® The National Patient-Centered Clinical Research Network

Stanford Medicine Anesthesia

VA Department of Veterans Affairs
DISTRIBUTED RESEARCH NETWORK

• Need for an efficient, reusable infrastructure
• Assemble and analyze routinely collected healthcare data
• Rapidly generate reliable information about utilization and outcomes of care needed to support decision making.
• Allows data holders to maintain physical and logical control over their data.

Institute of Medicine. Initial National Priorities for Comparative Effectiveness Research. June 2009
HCSRN EXAMPLE

HMORN Parent Organizations
Care Delivery & Health Plan Data Systems

Site A

Site B

Site C

HMORN Research Organizations
Various ETL processes
VDW data remains at sites

Multisite Project Team
Extraction of Limited or De-identified Data
QA Feedback
DISTRIBUTED RESEARCH NETWORKS

Key Functions:
• Distribute queries through network software;
• Execute the queries against the local data; and
• Return aggregated results to the end-user.
• Support both simple, menu-driven querying and complex queries using customized analysis code.
FRAMEWORK TO POOL DATA USING VDW

1. Cohort Identification and Analysis Dataset Created Using NDC
2. Weekly NDC Maintenance and Cohort Updates
3. Cohort and Analytic Datasets Sent to Group Health from All Sites

Group Health, creating SAS programs that is run by each site on their VDW

KPNW DCC responsible for helping the 3 site create their own VDW, including running the QA results

KPNW
KPSC
Geisinger
Meyers
Henry Ford

PAVA
UF
MMC

PILOT

Anesthesia
INITIAL FOCUS: VDW

- **Virtual Datawarehouse (VDW) development**: A framework to share data with Health Care Systems Research Network healthcare system.
- The data warehouse normalizes VA data elements i.e. PHARMACY with Health Care Systems Research Network data model.
- **Key Tables** such as:
  - Demographics
  - Enrollment
  - Provider
  - Encounter
  - EverNDC
  - Pharmacy
  - Diagnoses
  - Procedures
  - Contact
  - Death
KEY ASPECTS FOR VDW

- Data from October 2015 to present from VA EMR to populate the VDW tables.
- The intent of starting at October 2015 to minimize code complexities due to the switch from ICD–9 to ICD–10.
- ALL patients included, not just those who meet the project eligibility criteria – Entire population be used for reporting purposes.
- Dynamically updated weekly and monthly.
KEY USAGES WITH VDW

- Weekly Workplan process for cohort development with VDW
- Quality assurance (QA) program via SAS for VDW tables at each site
- Monthly descriptive reports on VDW tables to the lead site
- Analytical datasets for the study and FDA reporting.
KEY CONSTRAINTS FOR VDW

- VDW database developed using Microso` SQL
- All data transferred to SAS datasets to be accessible via SAS.
- All centralized QA, cohort iden6fica6on, and analysis programs distributed via SAS.
- A site metadata dic6onary for mapping CDW to VDW
5 Steps for Pharmacy Data from CDW to VDW

1. Target to Source Mapping
2. Data Query
3. Quality Assurance
4. Documentation
5. Submit

CDW EverNDC and RX tables ➔ EverNDC, Pharmacy tables
## Target table - Ever NDC

- The EVERNDC table is a lookup table containing all National Drug Codes (NDC)

<table>
<thead>
<tr>
<th>Target Column</th>
<th>Primary Key</th>
<th>Source Table/View</th>
<th>Source Column</th>
<th>Transforma6on Rule</th>
</tr>
</thead>
<tbody>
<tr>
<td>NDC</td>
<td>PK, FK</td>
<td>RxOut_RxOutpatFill</td>
<td>NDC</td>
<td>straight move</td>
</tr>
<tr>
<td>GENERIC</td>
<td>PK</td>
<td>DIM.National Drug</td>
<td>DrugNameWithDose</td>
<td>na6onalDrug.na6onalDrugSID = RxOut_RxOutpatFill.na6onalDrugSID; na6onalDrug.sta3n = RxOut_RxOutpatFill.sta3n</td>
</tr>
<tr>
<td>BRAND</td>
<td>Src.RxOut_RxOutpat</td>
<td>tradeLabelName</td>
<td>na6onalDrug.na6onalDrugSID = RxOut_RxOutpat.na6onalDrugSID; na6onalDrug.sta3n = RxOut_RxOutpat.sta3n;</td>
<td></td>
</tr>
<tr>
<td>UNIT_OF_MEASURE</td>
<td>dim.drugUnit</td>
<td>drugUnit</td>
<td>na6onalDrug.na6onalDrugSID = RxOut_RxOutpatFill.na6onalDrugSID; Na6onalDrug.Na6onalDrugSID = drugUnit.DrugUnitSID; na6onalDrug.sta3n = RxOut_RxOutpatFill.sta3n = drugUnit.sta3n</td>
<td></td>
</tr>
<tr>
<td>STRENGTH</td>
<td>DIM.National Drug; dim.drugUnit</td>
<td>Strength, drugUnit</td>
<td>na6onalDrug.na6onalDrugSID = RxOut_RxOutpatFill.na6onalDrugSID; Na6onalDrug.Na6onalDrugSID = drugUnit.DrugUnitSID; na6onalDrug.sta3n = RxOut_RxOutpatFill.sta3n = drugUnit.sta3n</td>
<td></td>
</tr>
</tbody>
</table>
**Target table - Pharmacy**

- The PHARMACY file contains data on medications dispensed in the outpatient setting.
- Dispensing in the inpatient setting is not included. Incomplete or unfilled medication orders are also excluded.
- Rows are unique on the combination of patient, NDC, dispense date, and prescribing provider.

<table>
<thead>
<tr>
<th></th>
<th>Foreign Key</th>
<th>Source Column</th>
<th>Transforma6on Rule</th>
</tr>
</thead>
<tbody>
<tr>
<td>MRN</td>
<td>PK, FK</td>
<td>cohortCrosswalk + RxOut_RxOutpatFill</td>
<td>pa6entICN</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>RxOut_RxOutpatFill.pa6entSID = cohortCrosswalk.pa6entSID</td>
</tr>
<tr>
<td>RXDATE</td>
<td>PK</td>
<td>RxOut_RxOutpatFill</td>
<td>releaseDateTime + dispensedate</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Use releaseDateTime. If releaseDateTime is Null, use dispenseDate</td>
</tr>
<tr>
<td>NDC</td>
<td>PK, FK</td>
<td>RxOut_RxOutpatFill</td>
<td>NDC</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>straight move</td>
</tr>
<tr>
<td>RXSUP</td>
<td></td>
<td>RxOut_RxOutpatFill</td>
<td>DaysSupply</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>straight move</td>
</tr>
<tr>
<td>RXAMT</td>
<td></td>
<td>RxOut_RxOutpatFill</td>
<td>QtyNumeric</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>straight move</td>
</tr>
<tr>
<td>RXMD</td>
<td>PK, FK</td>
<td>RxOut_RxOutpatFill</td>
<td>providerSID</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>straight move</td>
</tr>
</tbody>
</table>
## QA Checks

<table>
<thead>
<tr>
<th>QA Checks</th>
<th>Type of check</th>
</tr>
</thead>
<tbody>
<tr>
<td>• dataset exists</td>
<td>Warn/Fail</td>
</tr>
<tr>
<td>• count observations and unique members</td>
<td>Exploratory</td>
</tr>
<tr>
<td>• variables exist</td>
<td>Warn/Fail</td>
</tr>
<tr>
<td>• variable type numeric or char, compare to data dictionary</td>
<td>Warn/Fail</td>
</tr>
<tr>
<td>• variable length, compare to data dictionary</td>
<td>Warn/Fail</td>
</tr>
<tr>
<td>• variable length, site specific</td>
<td>Warn/Fail</td>
</tr>
<tr>
<td>• missing values, all variables</td>
<td>Warn/Fail</td>
</tr>
<tr>
<td>• expected values and frequencies (category checks)</td>
<td>Warn/Fail if defined in DD</td>
</tr>
<tr>
<td>• primary key uniqueness</td>
<td>Warn/Fail</td>
</tr>
<tr>
<td>• primary key linkage to foreign keys</td>
<td>Warn/Fail</td>
</tr>
<tr>
<td>• cross tabs</td>
<td>Exploratory</td>
</tr>
<tr>
<td>• count or percent of observations, by month and year (trend)</td>
<td>Exploratory</td>
</tr>
<tr>
<td>• count or percent of observations by specific groups, by month and year (trend)</td>
<td>Exploratory</td>
</tr>
</tbody>
</table>
Lessons Learnt

• VDW development – federated database challenging and painstaking due to its intensive iterative process
• Discussions needed on documentation early
TRAJECTORIES

• “The course of an outcome or observation over time or age”

• Can approximate how clinicians approach problems:
  – How are they doing now?
  – How did they get here?
  – Where will they go?

Hypertension. 2017;70:508--514
GROUP BASED TRAJECTORY MODELING (GBTM)

- Identifies discrete clusters of individual trajectories within the population

- Distribution of outcome (biomarkers) conditional on time

- Population: a mixture of distinct groups defined by their trajectories

- No assumptions on distribution of trajectories.

- PROC Traj in SAS; R package lcmm
MODEL CHOICE

• Maximize Bayesian Information Criterion (BIC)

\[ BIC = \log L - 0.5k \log N \]

L=value of the model’s maximum likelihood
N=sample size
K=the order of the polynomial used to model each trajectory and the number of groups

• Domain Knowledge
In about one-half of the deaths involving opioid analgesics, more than one type of drug was specified as contributing to the death, with benzodiazepines being the most frequent.

Within the Veterans Health Administration (VHA), benzodiazepines are often co-prescribed for outpatient treatment for patients diagnosed with chronic pain and taking opioids.

Given potential risks for sedation or overdose, gaps remain in understanding the longitudinal patterns of underlying benzodiazepine consumption.

Objectives: 1) patterns of benzodiazepine use within a large tertiary referral center; and 2) subgroups of patients along with their trajectories of overall benzodiazepine use.
METHODS

• **Cohort**: VA Palo Alto: 10/01/2014 to 09/30/2017; >=3 prescriptions for opioids and benzodiazepines + Z-class medications (zolpidem)

• **Outcome**: Valium equivalents (VEQ)

• **Predictors**: Demographics; Medication use; Diagnoses; Comorbidities

• **Analyses**
  – Descriptive statistics
  – Group-based Trajectory Analysis
  – Overdose rates
RESULTS

Total= 2708 patients
   ---75%(benzo): 2031; Z-class: 677

Overall, older (>50), male, white, had a lower comorbidity index, with a high prevalence of mental health diagnoses including depression, post-traumatic stress disorder, chronic pain; and generalized anxiety disorder.
### RESULTS

<table>
<thead>
<tr>
<th>Models</th>
<th>BIC</th>
<th>Group membership (%)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>-112198.6</td>
<td>93.27</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>2</td>
<td></td>
<td>6.73</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Models</th>
<th>BIC</th>
<th>Group membership (%)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>-105034.5</td>
<td>81.39</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>2</td>
<td></td>
<td>16.58</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>3</td>
<td></td>
<td>2.03</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>
## RESULTS

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Odds Ratio</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urban Residence</td>
<td>1.49</td>
<td>0.03</td>
</tr>
<tr>
<td>None-Opioid Analgesics</td>
<td>1.46</td>
<td>0.03</td>
</tr>
<tr>
<td>Post-Traumatic Stress Disorder</td>
<td>0.75</td>
<td>0.07</td>
</tr>
<tr>
<td>Period of Service - Vietnam War</td>
<td>0.71</td>
<td>0.06</td>
</tr>
<tr>
<td>Generalized Anxiety Disorder</td>
<td>0.52</td>
<td>0.01</td>
</tr>
<tr>
<td>Opioid Use Disorder</td>
<td>0.51</td>
<td>0.01</td>
</tr>
</tbody>
</table>
RESULTS

Figure. Trajectories of Daily Valium Use separated by Monthly Morphine Use

<table>
<thead>
<tr>
<th>Groups</th>
<th>BIC</th>
<th>Group membership (%)</th>
<th>p-value</th>
<th>Groups</th>
<th>BIC</th>
<th>Group membership (%)</th>
<th>p-value</th>
<th>Groups</th>
<th>BIC</th>
<th>Group membership (%)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low (0-20 Mmeq) Morphine Equivalent 3-Group</td>
<td>-48615.30</td>
<td>79.15</td>
<td>&lt;.001</td>
<td>Medium (20-100 Mmeq) Morphine Equivalent 2-Group</td>
<td>-54967.81</td>
<td>92.30</td>
<td>&lt;.001</td>
<td>High (&gt;100 Mmeq) Morphine Equivalent 4-Group</td>
<td>-3893.28</td>
<td>83.43</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Group 1</td>
<td></td>
<td></td>
<td></td>
<td>Group 2</td>
<td></td>
<td></td>
<td></td>
<td>Group 3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group 2</td>
<td></td>
<td>19.25</td>
<td>&lt;.001</td>
<td>Group 3</td>
<td></td>
<td>7.699</td>
<td>&lt;.001</td>
<td>Group 4</td>
<td></td>
<td>2.425</td>
<td>0.156</td>
</tr>
<tr>
<td>Group 3</td>
<td></td>
<td>1.602</td>
<td>&lt;.001</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group 4</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
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<td></td>
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</tr>
</tbody>
</table>
CONCLUSIONS

• Majority of our patients on opioid therapy were prescribed benzodiazepines with a significant percentage being prescribed Z-class medications.

• Patients showed stable trajectories overall and when stratified by opioid daily MEQ dosing.

• Within the VHA, intensive management has resulted in stable use over 6me.

• Given ongoing concerns for respiratory depression with concurrent benzodiazepine use, attention may be more directed to opioid dose escalation.
THANK YOU!
RESULTS

Bup/Nal Groups differ
• Age (1=younger)
• Comorbidity levels (1=healthier)
• Depression (2 and 3)
Thank You!

Questions?
References

Background

Age–adjusted rate of drug overdose deaths, by state — 2013 and 2017

Synthetic Opioid** Overdose Death Rate
Age-adjusted deaths per 100,000 population from 2016 to 2017, by county urbanization level

United States*
28,466 Deaths in 2017

Large Central Metro*
8,511 Deaths in 2017

Large Fringe Metro*
8,991 Deaths in 2017

Medium Metro*
6,254 Deaths in 2017

Small Metro*
1,878 Deaths in 2017

Micropolitan*
1,860 Deaths in 2017

Noncore*
972 Deaths in 2017

SOURCE: CDC/NCHS, National Vital Statistics System, Mortality. CDC WONDER, Atlanta, GA:
* Statistically significant at p<0.05 level.
** Excluding methadone
DRN

- What are they?
- Why are they useful?
- Example of one?

The alternative, distributed network configuration leaves the data holder in control of their protected data. The FDA Mini–Sesnnel program (an active surveillance system for monitoring the safety of FDA regulated medical products) is a good example. Queries are sent to each node (organisation) in the network. They each return results (often aggregated) in an agreed common data model, to a coordinating centre. A mapping must be agreed between each node and the common data model and the distributed implementation is more complex than the centralised approach. However, it overcomes many of the privacy issues and the participating organisations maintain operational control of their data (Brown 2015). They may even choose to review each query before releasing the data.
# Domains from CDW

## CDW DOMAIN CHECKLIST

### Production
- Allergy
- Appointment
- Consult
- CPRS Orders
- Data Profiling
- Dental
- Health Factors
- Immunization
- Inpatient
- Lab Microbiology
- LabChem
- Mental Health Assessment
- Non-VA Meds
- Outpatient
- Outpatient Workload
- Patient
- Patient Associated
- Patient Enrollment
- Patient Insurance
- PCMM (Primary Care Management Module)
- Pharmacy BCMA (Bar Code Medication Administration)
- Pharmacy Outpatient
- Pharmacy Patient
- Purchased Care (formerly fee)

### RAW*
- Bill Claims (CBO)
- CAPRI Audit Trail Table
- ClinComp
- Echocardiogram
- Emergency Dept. Int. Software (EDIS)
- Equipment Inventory
- FBCS (Fee Basis Claim System)
- IFCAP (Integrated Funds Control, Accounting, and Procurement)
- Intravenous meds (IV)
- Oncology
- PAID (Personnel and Administration Integrated Data System)
- Prosthetics
- Pulmonary Function Test (PFT)
- Radiology
- RxLAB (Laboratory)
- Surgery Data, select the SQDUG option in DART Reference Page
- Travel
- Unit Dose (Pharmacy)
- VACAA (Veterans Choice Program Eligibility)

*CDW Raw data is data that has been pulled directly
Data Query - Results

Pharmacy Table

EverNDC Table

SQL Query:

```sql
SELECT TOP 1000
  [RXDATE]
  ,[NDC]
  ,[RXSUP]
  ,[RXAMT]
FROM [ORD_Mudumbai_201606025D]
```
### Opioid RX Data for Study

```sql
SELECT TOP 1000 *
FROM ...
```
Start

For 640 and fixed time period, Get the patient MRN list and match it with patientSID in Src.RxOut RxOutputFill table

Get non-null NDC, RXSUP, RXAMT, and RXMD from Src.RxOutputFill

Get ReleaseDateTime, DispenseDate from Src.RxOutputFill

ReleaseDateTime is null

Y

Set RXDate as DispenseDate.

N

Set RXDate as ReleaseDateTime.

Order MRN, NDC, RXSUP, RXAMT, and RXMD, RXDate by RXSUP, RXAMT

Order MRN, NDC, RXSUP, RXAMT, and RXMD, RXDate by RXSUP, RXAMT

Select 1st row to get unique primary key and content

Insert records into Pharmacy table

End
**Data Query - Design**

**Begin EverNDC**

Find NDC Generic Name and others for all -1 and real NationalDrugSIDs for beta.patient cohort and 640 only and fixed time period from Rxout RxOutputFill, by left join Dim.NationalDrug, into temp table #rx.

**Y**

Any NationalDrugSIDs = -1 in #rx

Find NDC Generic Name and others for -1 NationalDrugSIDs for all stations and all time, inner join Dim.NationalDrug, into #rx1.

Order the results in #rx1 to get the 1st NationalDrugSID, sta3n and other info for the same NDC.

Update #rx for the -1 NationalDrugSIDs with the 1st non -1 NationalDrugSID and other info from #rx1.

Any NationalDrugSIDs = -1 in #rx

**Y**

Assign the Generic to be ‘LOCAL’ in #rx

Find BRAND for all NationalDrugSID and sta3n in #rx from RxOut RxOutputPat, into #lab1.

Get Brand names for all NDC in #rmx based on NationalDrugSID; If NationalDrugSID = -1, use LocalDrugName with Does as Brand, into #rx2.

Get drug unit, DosageForm by combining Dim.DrugUnit, Dim.DosageForm, into #rm3.

Get unique record for NDC, Generic, Brand, into #rm4.

Create Table EverNDC, and insert unique records into EverNDC. Primary Key: NDC + Generic

**End EverNDC**
Examples of DRNs

  - Mini–Sen6nel (FDA)
Distributed Research Networks

- A large public–private CER enterprise.
- Support high–efficiency, pragmatic randomized trials
- Require large–scale clinical and administrative data networks that enable observational studies of patient care while protecting patient privacy and data security.

Institute of Medicine. Initial National Priorities for Comparative Effectiveness Research. June 2009
Key Steps to assemble VDW

- IRB and DART Approval
  - VINCI Workspace
  - CDW--Domain Checklist: Used to specify any CDW Production or Raw Domains the study might need to use.
  - Real SSN Access Requests