Comparative Assessments of the Prescription Drug Abuse Climate in Europe and the United States: Scientific, Regulatory, and Cultural Factors

RADARS System: International Pre-Symposium
May 11, 2017

Scott P. Novak, Ph.D.
Director
Prescription Drug Abuse Clinical Research and Public Policy Institute
Center for Public Health Research and Translational Science
Battelle Memorial Institute
Baltimore, Maryland  USA
Previous Conflicts of Interest/Disclosure

• Scott Novak has received direct funds through paid consultancy through:
  ▪ Daiichi Sankyo
  ▪ Endo
  ▪ Indivior
  ▪ Reckitt Benckiser
  ▪ Pfizer
  ▪ Zogenix

• Scott Novak has received grant/contract support through organizational arrangements with:
  ▪ Eli Lilly
  ▪ Indivior
  ▪ Reckitt Benckiser
  ▪ Pfizer
  ▪ Shire
Acknowledgements

- The data are from public source documents, and any interpretation are solely the author and neither the funder(s) nor any government agency
Goals of Today’s Talk

• Identify the prevalence of nonmedical prescription drug in the E.U.

• Compare E.U. data to the U.S.

• Assess cultural and regulatory differences across countries
Surveillance Systems in the U.S.

• The U.S. has numerous government sponsored systems to monitor drug abuse
  ▪ National Survey on Drug Use and Health (SAMHSA)*
  ▪ Monitoring the Future (NIDA/NIH)
  ▪ Behavioral Risk Factor Surveillance Survey (BRFSS)
  ▪ MEDWATCH/Adverse event systems

• Commercial Systems in the U.S.
  ▪ RADARS System
  ▪ Others

*NSDUH is a congressionally mandated system ($45 million per year)
Surveillance Systems in the E.U.

• The European Monitoring Centre for Drugs and Drug Addiction (EMCDDA)
  - Established in 1993, ratified in Lisbon in 1995
  - Decentralized agency, comprised of volunteer member states
  - Serve a data clearinghouse to capture secondary data sources
  - Typically doesn’t fund primary data collection

• Types of Surveillance data collected by EMCDDA
  - Population-based surveys (Occasionally)
  - Drug trafficking/arrests
  - Drug Treatment Admissions
  - Groundwater analyses for discarded medications
The European Medicine Study

• What is the prevalence of non-medical drug use in the European Union, as reported by the general population?

• Definitional Challenges
  ▪ Non-medical use:
    – self-treat without a prescription
    – Use for euphoria

  ▪ Types of drugs approved in each country
    – Different types of drugs approved in each country
    – Different levels of prescriptive authority (pharmacist-approved codeine)
The European Medicine Study

• Which countries do you choose?
  ▪ 28 member countries* (minus UK/Great Britain)

• How’s the best the way to reach the population?
  ▪ Internet Survey
  ▪ Mail Survey
  ▪ Telephone Survey

• At what cost?
  ▪ $1 to $2 million versus $45 million (or equivalent Euros)
The European Medicine Study

• Funded by Shire to investigate prevalence of nonmedical prescription drug use for lifetime and past year prevalence:
  - Prescription Stimulants
  - Prescription Benzodiazepines
  - Prescription Opioids

• Purposively selected 5 E.U. countries
  - Denmark
  - Germany
  - Great Britain
  - Spain
  - Sweden
Data Collection Design

• Wanted a hybrid model to capture youth (ages 12-17) and adults (ages 18 or older)

• Need ability to capture data in-person, especially for high-risk groups for methodological validity

• Balance costs against scientific rigor
The E.U. Landscape

In 1993, 12 Countries
After 1992, 28 Countries*

Over 500 million residents

4 administrative bodies covering Judicial and political aspects
Country Selection

• Five key countries represent a target population of 160,360,360 of the entire EU population of 507,416,607, corresponding to approximately 32% of the EU population and 27% of the total land mass

• Represent significant geographic and cultural diversity across the region

• Hypothesized that G.B./U.K. would be most similar to U.S.
Hybrid Data Collection

• Multi-Stage Quota Sampling and post-hoc weights to generalize to each country’s population
  ▪ Step 1: Identify 4-5 key population characteristics (i.e., demographics) to recruit proportionate to size
  ▪ Step 2: Identify 1-2 related drug abuse characteristics (i.e., cannabis, cocaine) with high correlations to Rx Abuse (r=0.6 or more)
  ▪ Recruit to fill quotas
Hybrid Data Collection

• Theory behind weighting in Step 2.
  - In typical sampling and weighting, use post-hoc weights to balance sample based on some neglected characteristic (i.e., Hispanic males less likely to be in survey)
  - But, if you know the correlation between your desired outcome (i.e. Rx abuse) and a highly correlated instrument (i.e. cigarette use) then you can weight on instrument and adjust based on Corr X and Y.
Weighting Scheme Illustrated
Solving for Y using X, Z, and bivariable correlations
Sampling and Data Collection

• Contracted with several web-panels in the E.U. to select participants aged 18-49
  - Peak age of onset for Rx abuse
  - Peak age of use of Internet

• Contracted with local market research firms
  - In-house survey administration
  - Collect data onsite to verify consent and answer questions
  - Collect data on ages 12-17, for parental consent
  - Collect data on high-risk groups (street intercept sampling in high-risk areas)
Final Sampling Catchment Areas

5 Countries

29 Cities

Data Collected May to Sept through 2014

6 IRB’s:

RTI International and 1 per country
EU-Meds Co-Investigator Team

Lead Country Investigators

Anders Hakasson, MD, PhD (Denmark, Sweden)
Internal Medicine, Unit for Psychosocial Interventions and for Addiction, Lund University

Jose Martinez-Raga, MD, PhD (Spain)
Prof. Asociado, Hospital Universitario Dr. Peset and University of Valencia

Jens Reimer, MD (Germany)
Psychiatrist, Center for Interdisciplinary Addiction Research at the University of Hamburg
### Sampling Results (n=22,075)

<table>
<thead>
<tr>
<th>Youth Study (ages 12-17)</th>
<th>Enrolled*</th>
<th>Completed</th>
<th>Refused #</th>
<th>Incomplete Interviews</th>
<th>Total Enrolled</th>
<th>Total Refuse</th>
</tr>
</thead>
<tbody>
<tr>
<td>Germany (n=500 target)</td>
<td>524</td>
<td>498</td>
<td>2</td>
<td>24</td>
<td>524</td>
<td>2</td>
</tr>
<tr>
<td>Spain (n=500 target)</td>
<td>524</td>
<td>492</td>
<td>0</td>
<td>23</td>
<td>524</td>
<td>0</td>
</tr>
<tr>
<td>Denmark (n=250 target)</td>
<td>234</td>
<td>219</td>
<td>0</td>
<td>15</td>
<td>234</td>
<td>0</td>
</tr>
<tr>
<td>Sweden (n=250 target)</td>
<td>263</td>
<td>241</td>
<td>2</td>
<td>16</td>
<td>263</td>
<td>2</td>
</tr>
<tr>
<td>Great Britain (n=500 target)</td>
<td>592</td>
<td>532</td>
<td>2</td>
<td>54</td>
<td>592</td>
<td>2</td>
</tr>
<tr>
<td>Totals (n=2000 target)</td>
<td>2137</td>
<td>1982</td>
<td>6</td>
<td>132</td>
<td>2137</td>
<td>6</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Adult Study (Ages 18-49)</th>
<th>Enrolled*</th>
<th>Completed</th>
<th>Refused #</th>
<th>Incomplete Interviews</th>
<th>Total Enrolled</th>
<th>Total Refuse</th>
</tr>
</thead>
<tbody>
<tr>
<td>Germany (n=5000 target)</td>
<td>6354</td>
<td>5013</td>
<td>332</td>
<td>769</td>
<td>6354</td>
<td>332</td>
</tr>
<tr>
<td>Spain (n=5000 target)</td>
<td>6371</td>
<td>5015</td>
<td>123</td>
<td>796</td>
<td>6371</td>
<td>123</td>
</tr>
<tr>
<td>Denmark (n=2500 target)</td>
<td>3550</td>
<td>2516</td>
<td>357</td>
<td>573</td>
<td>3550</td>
<td>357</td>
</tr>
<tr>
<td>Sweden (n=2500 target)</td>
<td>3249</td>
<td>2509</td>
<td>124</td>
<td>435</td>
<td>3249</td>
<td>124</td>
</tr>
<tr>
<td>Great Britain (n=5000 target)</td>
<td>6681</td>
<td>5040</td>
<td>230</td>
<td>1005</td>
<td>6681</td>
<td>230</td>
</tr>
<tr>
<td>Totals (n=20000 target)</td>
<td>26205</td>
<td>20093</td>
<td>1166</td>
<td>3578</td>
<td>26205</td>
<td>1166</td>
</tr>
</tbody>
</table>

# Weighting Validation Check

<table>
<thead>
<tr>
<th>Age</th>
<th>Denmark Target</th>
<th>Denmark EU-Meds</th>
<th>Germany Target</th>
<th>Germany EU-Meds</th>
<th>Great Britain Target</th>
<th>Great Britain EU-Meds</th>
<th>Spain Target</th>
<th>Spain EU-Meds</th>
<th>Sweden Target</th>
<th>Sweden EU-Meds</th>
</tr>
</thead>
<tbody>
<tr>
<td>12-17</td>
<td>17%</td>
<td>9%</td>
<td>12%</td>
<td>9.2%</td>
<td>16%</td>
<td>9.9%</td>
<td>14%</td>
<td>9.1%</td>
<td>14%</td>
<td>8.9%</td>
</tr>
<tr>
<td>18-30</td>
<td>33%</td>
<td>37%</td>
<td>32%</td>
<td>34.7%</td>
<td>34%</td>
<td>35.7%</td>
<td>35%</td>
<td>32.7%</td>
<td>35%</td>
<td>34.3%</td>
</tr>
<tr>
<td>31-49</td>
<td>50%</td>
<td>54%</td>
<td>56%</td>
<td>56.1%</td>
<td>50%</td>
<td>54.4%</td>
<td>51%</td>
<td>58.2%</td>
<td>51%</td>
<td>45.8%</td>
</tr>
<tr>
<td>Sex</td>
<td>Male</td>
<td>49%</td>
<td>52%</td>
<td>53%</td>
<td>49%</td>
<td>36%</td>
<td>48%</td>
<td>40%</td>
<td>51%</td>
<td>47%</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>51%</td>
<td>48%</td>
<td>47%</td>
<td>51%</td>
<td>64%</td>
<td>52%</td>
<td>60%</td>
<td>49%</td>
<td>53%</td>
</tr>
<tr>
<td>Marital</td>
<td>Married</td>
<td>35%</td>
<td>43%</td>
<td>34%</td>
<td>47%</td>
<td>38%</td>
<td>44%</td>
<td>38%</td>
<td>32%</td>
<td>28%</td>
</tr>
<tr>
<td></td>
<td>(18+)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Education</td>
<td>Secondary</td>
<td>74%</td>
<td>52%</td>
<td>50%</td>
<td>61%</td>
<td>61%</td>
<td>58%</td>
<td>52%</td>
<td>69%</td>
<td>65%</td>
</tr>
<tr>
<td>Cigarettes</td>
<td>Past 30 Day</td>
<td>33%</td>
<td>30%</td>
<td>39%</td>
<td>34%</td>
<td>28%</td>
<td>33%</td>
<td>33%</td>
<td>22%</td>
<td>29%</td>
</tr>
</tbody>
</table>

## EU Meds Study and EMCDDA Study

<table>
<thead>
<tr>
<th>DRUG</th>
<th>COUNTRY</th>
<th>EMCDDA YEAR</th>
<th>AGE RANGE</th>
<th>EU Meds % (se)</th>
<th>EMCDDA %</th>
<th>Diff</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cannabis</td>
<td>Denmark</td>
<td>2010</td>
<td>16-34</td>
<td>43.6 (1.5)</td>
<td>44.5</td>
<td>-0.9</td>
</tr>
<tr>
<td></td>
<td>Germany</td>
<td>2009</td>
<td>18-34</td>
<td>35.2 (0.9)</td>
<td>38.5</td>
<td>-3.3</td>
</tr>
<tr>
<td></td>
<td>Great Britain</td>
<td>2011</td>
<td>16-34</td>
<td>41.2 (1.2)</td>
<td>37.3</td>
<td>4.9</td>
</tr>
<tr>
<td></td>
<td>Spain</td>
<td>2011</td>
<td>15-34</td>
<td>47.1 (1.3)</td>
<td>39.6</td>
<td>7.5</td>
</tr>
<tr>
<td></td>
<td>Sweden</td>
<td>2011</td>
<td>16-34</td>
<td>27.5 (1.4)</td>
<td>21.4</td>
<td>6.1</td>
</tr>
<tr>
<td>Cocaine</td>
<td>Denmark</td>
<td>2010</td>
<td>16-34</td>
<td>13.7 (1.1)</td>
<td>8.9</td>
<td>4.8</td>
</tr>
<tr>
<td></td>
<td>Germany</td>
<td>2009</td>
<td>18-34</td>
<td>6.2 (0.4)</td>
<td>5.0</td>
<td>1.2</td>
</tr>
<tr>
<td></td>
<td>Great Britain</td>
<td>2011</td>
<td>16-34</td>
<td>15.4 (1.0)</td>
<td>13.6</td>
<td>1.8</td>
</tr>
<tr>
<td></td>
<td>Spain</td>
<td>2011</td>
<td>15-34</td>
<td>10.2 (0.8)</td>
<td>11.1</td>
<td>-0.9</td>
</tr>
<tr>
<td></td>
<td>Sweden</td>
<td>2011</td>
<td>15-34</td>
<td>5.3 (0.7)</td>
<td>4.6</td>
<td>0.7</td>
</tr>
</tbody>
</table>

Lifetime and Past-Year: 2015 EU-Meds Study
Nonmedical Prescription Opioid Use-Ages 12-49

<table>
<thead>
<tr>
<th>Country</th>
<th>Lifetime %</th>
<th>Past Year %</th>
</tr>
</thead>
<tbody>
<tr>
<td>U.S.*</td>
<td>12.6</td>
<td>6.1</td>
</tr>
<tr>
<td>Denmark **</td>
<td>11.6</td>
<td>4.4</td>
</tr>
<tr>
<td>Germany **</td>
<td>9.6</td>
<td>2.9</td>
</tr>
<tr>
<td>G.B./U.K. **</td>
<td>14.6</td>
<td>6.2</td>
</tr>
<tr>
<td>Spain **</td>
<td>18.3</td>
<td>6.8</td>
</tr>
<tr>
<td>Sweden **</td>
<td>11.3</td>
<td>3.8</td>
</tr>
</tbody>
</table>

*Source: 2015 National Survey on Drug Use and Health Public Use File (SAMHDA Archives)

Lifetime and Past-Year: 2015 EU-Meds Study
Nonmedical Prescription Stimulant Use-Ages 12-49

*Source: 2015 National Survey on Drug Use and Health Public Use File (SAMHDA Archives)
Lifetime and Past-Year: 2015 EU-Meds Study
Nonmedical Prescription Sedative Use-Ages 12-49

**Source: 2015 National Survey on Drug Use and Health Public Use File (SAMHDA Archives)**

Methods of Acquisition: 2015 EU-Meds Study
Nonmedical Prescription Opioid Use-Ages 12-49

- Category 1: Shared: Friend/Family (44)
- Category 2: Taken/Stolen (15)
- Category 3: Doctor/Pharmacy Shopping (13)
- Category 4: Bought Friends/Dealer (4)
- Category 5: Internet Pharmacy (26)

Methods of Acquisition: 2015 NSDUH
Nonmedical Prescription Opioid Use-Ages 12-49

- Category 1: Shared: Friend/Family: 55%
- Category 2: Taken/Stolen 4.8%
- Category 3: Bought Friends/Dealer (11.4%)
- Category 4: Prescribed/Dr. Shopping
- Category 5: Other

Source: SAMHSA, 2015 National Survey on Drug Use and Health Public Use Files (SAMHDA Data Archive)
## Predictors of Nonmedical Use

Odd Ratios of Past-Year Use of Selected Prescription Drug

<table>
<thead>
<tr>
<th>Predictors</th>
<th>Opioids O.R.</th>
<th>Stimulants O.R.</th>
<th>Sedatives O.R.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female (v. male)</td>
<td>0.7**</td>
<td>0.5***</td>
<td>0.8**</td>
</tr>
<tr>
<td>18y-29, (v. 12-17)</td>
<td>3.4***</td>
<td>3.6***</td>
<td>5.5***</td>
</tr>
<tr>
<td>30y-49, (v. 12-17)</td>
<td>3.6***</td>
<td>2.5***</td>
<td>5.4***</td>
</tr>
<tr>
<td>Had Prescription</td>
<td>8.8***</td>
<td>7.8***</td>
<td>10.5***</td>
</tr>
<tr>
<td>Mental Dx</td>
<td>3.2***</td>
<td>4.5***</td>
<td>4.2***</td>
</tr>
<tr>
<td>STD/STI</td>
<td>4.6***</td>
<td>7.2***</td>
<td>3.9***</td>
</tr>
<tr>
<td>HIV</td>
<td>18.9***</td>
<td>15.1***</td>
<td>12.2***</td>
</tr>
<tr>
<td>Arrested&lt;15</td>
<td>2.9***</td>
<td>2.6***</td>
<td>2.1***</td>
</tr>
<tr>
<td>ADHD/ADD Dx</td>
<td>3.5***</td>
<td>9.5***</td>
<td>5.1***</td>
</tr>
</tbody>
</table>

*p<.05, **p<.01, ***p<.001

Study Conclusions

• Prevalence of nonmedical use similarly high across E.U. and U.S., risk factors more strongly related to NMPDU.

• Primary difference between E.U. and U.S. is the prevalence of harms associated with opioid abuse in the U.S. that is not present in E.U.

• What can account for differences in harm, given similar levels of exposure:
  ▪ Availability of OTC codeine (mid-level product)
  ▪ Opioids “last-line of defense”
  ▪ Patient culture not focused on “immediate gratifications” like in the U.S.
Study Limitations

- Rapid method with high degree of reliability with other national studies, but limitations are:

  - Larger standard errors compared to stratified random, address-based sampling limit comparison across rare events or cell sizes
  
  - With Internet panel studies, often concern of “gaming” but identity was confirmed for payment, and addressed checked
  
  - Due to methodological differences in survey sampling, administration, and coding cannot directly compare NSDUH and EU Meds
NSDUH Survey Recodes (ages 12+)

Ever used for any reason in Lifetime

<table>
<thead>
<tr>
<th>Survey Answer-Life</th>
<th>Opioids*</th>
<th>Stimulants*</th>
</tr>
</thead>
<tbody>
<tr>
<td>1=Answered YES</td>
<td>22.59%</td>
<td>4.92%</td>
</tr>
<tr>
<td>2=Answered NO</td>
<td>42.88%</td>
<td>86.25%</td>
</tr>
<tr>
<td>5=Logically Assigned</td>
<td>33.65%</td>
<td>8.34%</td>
</tr>
<tr>
<td>94=Don’t Know</td>
<td>0.73%</td>
<td>0.32%</td>
</tr>
<tr>
<td>97=Refused</td>
<td>0.04%</td>
<td>0.04%</td>
</tr>
<tr>
<td>98=Blank</td>
<td>0.11%</td>
<td>0.13%</td>
</tr>
</tbody>
</table>

Source: Public Use File, 2015 NSDUH; Unweighted estimates presented
Overall Conclusions

• Web panels can be very helpful for monitoring trends, even in the E.U.

• Modifications can help improve precision of estimates

• Is the E.U. on the same trajectory as U.S., circa 1995-2000?

• How does the flow of information across the Internet and travel create new opportunities
Thank You

Scott P. Novak, Ph.D.
NOVAKS@Batelle.org