



Fourth Quarter 2015 Newsletter

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RADARS System Quarterly Technical Report

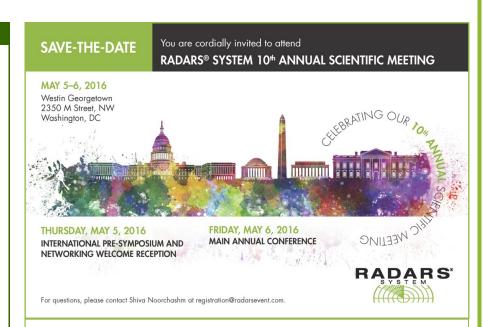
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Rocky Mountain Poison and Drug Center and Denver Health and Hospital Authority

Did You Know?

Did you know the RADARS® System piloted the Survey of Non-Medical Use of Prescription Drugs in Singapore in 2015?



The RADARS® System Annual Scientific Meeting encourages prescription drug abuse experts, representatives from the pharmaceutical industry, medical professionals, and federal regulatory agencies to discuss current trends in prescription drug abuse research and to develop strategies to ensure the safe and proper use of prescription medications.

Thursday, May 5, 2016

1:00pm: International Pre-Symposium 5:00pm: Networking Welcome Reception

Friday, May 6, 2016

8:30 am: Main Annual Conference

Registration will open in the near future - subscribe now to receive registration information by email!

Featured Publication by RADARS® System

RADARS® System Published in Pain Medicine:

Diversion and Illicit Sale of Extended Release Tapentadol in the United States

Dart RC, Surratt HL, Le Lait MC, Stivers Y, Bebarta VS, Freifeld CC, Brownstein JS, Burke JJ, Kurtz SP, Dasgupta N. Diversion and illicit sale of extended release tapentadol in the United States. *Pain Medicine*. 2015; advance online publication. DOI: http://dx.doi.org/10.1093/pm/pnv032

Prescription opioids, including the extended release tapentadol, are commonly prescribed for moderate to severe pain. In some cases, these prescribed opioids are diverted for abuse purposes. The RADARS® System assessed the amount of diversion and related costs of purchasing immediate release and extended release tapentadol, as well as other prescription opioids, in street transactions in the United States. Results are reported in the *Pain Medicine* publication "Diversion and Illicit Sale of Extended Release Tapentadol in the United States".

According to data from the RADARS® System Drug Diversion Program and StreetRx Program, extended release tapentadol is rarely sold on the streets in the United States, and when it is sold on the streets, it costs less than other prescription opioids. Since its introduction in 2011, diversion rates and street price have remained relatively low despite increasing numbers of prescriptions for the drug. While substantial diversion and abuse of extended release tapentadol in the United States has not emerged, ongoing surveillance of this and other prescription opioids is warranted due to changes that may occur in supply and demand of prescription opioids.

Pain Medicine Advance Access published December 14, 2015

Pain Medicine 2015; 0: 1–7 doi: 10.1093/pm/pnv032



Original Research Article

Diversion and Illicit Sale of Extended Release Tapentadol in the United States

Richard C. Dart, MD, PhD,*,† Hilary L. Surratt, PhD,‡ Marie-Claire Le Lait, MS,* Yami Stivers, BA,‡ Vikhyat S. Bebarta, MD,§ Clark C. Freifeld, PhD,¶ John S. Brownstein, PhD,¶ John J. Burke, AS,∥ Steven P. Kurtz, PhD,‡ and Nabarun Dasgupta, PhD¶

Recent Journal Article of Interest

A recent article published in the Journal of Child & Adolescent Substance Abuse (December 2015) highlights prescription opioid abuse in the adolescent population and their progression to addiction as well as describes the association between adolescent prescription opioid addiction and heroin abuse.

In 2010, a questionnaire was administered to 31 adolescents with a history of prescription opioid abuse who were in recovery at two Recovery High Schools in Massachusetts. Most respondents initiated prescription opioid abuse out of curiosity, with fifty-eight percent (n=18) becoming addicted. While the majority received or stole the prescription opioids from family or friends, a subgroup indicated that they were written legitimate opioid prescriptions for pain. Sixteen percent (n=5) indicated that they had abused heroin and all believed that RXO abuse was related in some way to the initiation of their heroin use. All but one of those who moved on to heroin were addicted to prescription opioids prior to the onset of heroin abuse.

Participants were also asked about what their prescription opioid abuse behavior would have been if there had been an abuse-deterrent formulation (ADF) on the market. Approximately one-third of the participants felt that ADFs would have reduced their prescription opioid abuse and approximately fifteen percent felt that they would have been less likely to become addicted to prescription opioids or less likely to try heroin if an ADF had been on the market.

While a small sample size, this study identifies other potential research opportunities including the use of ADFs to disrupt the transition from prescription opioid addiction to heroin abuse, adolescent pain management, adolescent coping mechanisms and the study of different drug combinations.

Vosburg SK, Eaton TA, Sokolowska M, Osgood ED, Ashworth JB, Trudeau JJ, Muffett-Lipinski M, Katz NP. (2015) "Prescription Opioid Abuse, Prescription Opioid Addiction and Heroin Abuse among Adolescents in a Recovery High School: A Pilot Study." *Journal of Child & Adolescent Substance Abuse*, DOI: 10.1080/1067828X.2014.918005.

RADARS® System Accomplishments In 2015

2015 was a year of continued growth and expansion for the RADARS® System. We are pleased to have expanded RADARS® System domestic and international programs in the following ways:

- Expanded the Poison Center Program participation by two new poison centers (Arkansas Poison and Drug Information Center and New Mexico Poison and Drug Information Center), bringing the total number of participating United States poison centers to 50
- Launched Drug Diversion Program and Survey of Key Informants' Patients Program pilots in Ontario,
 Canada
- Survey of Non-Medical Use of Prescription Drugs launched in Singapore and the second survey launched in the United Kingdom
- 5 manuscripts published and 39 abstracts submitted
- Attendance at 15 domestic and international meetings
- Another excellent RADARS® System annual meeting!

RADARS® System Abstracts RADARS System Conference Attendance: October 2015–December 2015

Canadian Centre on Substance Abuse (CCSA) Issues of Substance Conference Montreal, Quebec

November 16, 2015 – November 18, 2015



Partnership. Knowledge. Change.

The Canadian Centre on Substance Abuse (CCSA) Issues of Substance (IOS) is Canada's only national conference that brings together addictions workers, healthcare professionals, researchers, policy makers and knowledge brokers from across the country. This premier learning event provides an unparalleled opportunity to share new developments and best practices, and to get practical training related to addictions prevention, treatment and recovery. IOS is also a forum for showcasing new research and knowledge mobilization efforts in the addictions field.

RADARS® System actively participated in this year's CCSA IOS with two abstract presentations highlighting our integral research on prescription drug abuse in other countries. Data from the Survey of Non-Medical Use of Prescription Drugs (United Kingdom) and StreetRx (Canada) were presented.

Please see following pages to learn more about our presentation.



Chronic Pain and Non-Medical Use of Prescription Opioids in a United Kingdom National Survey

Janetta L Iwanicki, MD¹, Andrea C Besharat, MPH¹, Erin M Goodman, MS¹, Paul I Dargan, MD², David M Wood MD², Richard C Dart, MD, PhD¹, Jody L Green, PhD¹

¹Rocky Mountain Poison & Drug Center, Denver Health, Denver, CO, USA

² Clinical Toxicology, Guy's and St. Thomas' NHS Foundation Trust and King's Health Partners, London, UK

Background

- Data on non-medical use (NMU) of prescription opioids in patients with chronic pain are limited.
- Given the high prevalence of chronic pain, it is important to understand NMU in these individuals.

Objectives

 Compare prescription opioid use and NMU in those with and without chronic pain as reported to an online United Kingdom (UK) national survey.

Methods

- The online survey was launched in July 2014 via a survey administration company.
- Lifetime reports of chronic pain ("pain lasting at least 3 months occurring constantly or flaring up frequently") and prevalence of lifetime prescription opioid use and NMU (without doctor's prescription or for any reason other than recommended by doctor) were analysed.
- · Odds ratios (ORs) were calculated by active pharmaceutical ingredient (API).

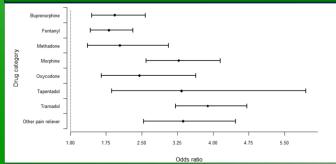
Results

- Of 2,499 respondents, 1,132 (45.3%) reported chronic pain.
- Opioid use was more common in those with chronic pain (1,031 [41.3%]) than without (890 [35.6%]) (Table 1).
- Among respondents reporting opioid use:
 - Those with chronic pain were older (52.0 years \pm 14.8 versus 46.2 \pm 15.8) (Table 2).
- Chronic pain was more common in females (52.2%) than males (47.8%) (Table 2).
- Opioid use was two to four times more likely in those with chronic pain (ORs by API=1.8-3.9, p<0.05) (Figure 1).
- Of opioid users, NMU was reported by 507 (26.4%) with chronic pain and 461 (24.0%) without (p=0.2517) (Table 3).

Conclusions

- Opioid use is common in respondents.
- NMU appears common though unrelated to chronic pain; approximately one-quarter of respondents both with and without chronic pain reported NMU.
- Feasibility of evaluating this topic via an online survey is demonstrated, providing groundwork for future studies in Canada.

Figure 1. Ratio of <u>Use</u> Among Those With Chronic Pain to Those Without



The RADARS System is supported by subscriptions from pharmaceutical manufacturers for surveillance, research and reporting services. RADARS System is the property of Deriver Health and Hospital Authority, a political subdivision of the State of Colorado. Deriver Health relains exclusive ownership of all data, databases and systems. Subscribers do not participate in data

Table 1. Opioid <u>Use</u> and Chronic Pain

| | Chronic Pain | | |
|-------------------|----------------|---------------|----------------|
| | Yes n=1,132 | No n=1,367 | p-value |
| Opioid Use (n, %) | | | |
| Yes | 1,031 (41.3) | 890 (35.6) | <0.0001 |
| No | 101 (4.0) | 477 (19.1) | ~0.0001 |

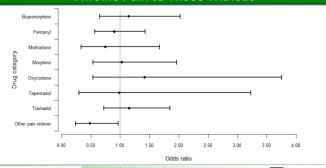
Table 2. Respondent Demographics Among Those Reporting Opioid <u>Use</u>

| | | Chronic Pain | | |
|---------------|------------|----------------|-------------|--|
| | | Yes n=1,031 | No n=890 | |
| Gender (n, %) | | | | |
| | Male | 493 (47.8) | 483 (54.3) | |
| | Female | 538 (52.2) | 407 (45.7) | |
| Age | | | | |
| (1 | Mean ± SD) | 52.0 ± 14.8 | 46.2 ± 15.8 | |

Table 3. Opioid Non-Medical Use and Chronic Pain

| | Chronic Pain | | |
|-------------------------------|----------------|-------------|---------|
| | Yes n=1,031 | No n=890 | p-value |
| Opioid Non-Medical Use (n, %) | | | |
| Yes | 507 (26.4) | 461 (24.0) | 0.2517 |
| No | 524 (27.3) | 429 (22.3) | 0.2517 |

Figure 2. Ratio of Non-Medical Use Among Those With Chronic Pain to Those Without













Monitoring the Street Price of Diverted Opioids in Canada with StreetRx.com

Richard C. Dart¹, Erin Goodman¹, Karin McBride¹, Zachary Margolin¹, Nabarun Dasgupta², Christopher Menone², Jody L. Green¹, Janetta Iwanicki¹

¹Rocky Mountain Poison & Drug Center - Denver Health, Denver, CO, USA

²Epidemico, Inc., Boston, MA, USA

Background

- Prescription drug misuse and abuse in Canada can be monitored by examining prices paid for prescription opioid analgesics on the street.
- StreetRx.com is a website that enables users to anonymously report street prices paid for diverted prescription drugs.

Objectives

To determine street prices of prescription opioid analgesics in Canada.

Methods

- Data gathered from StreetRx.com are summarized as median price per milligram by pharmaceutical ingredient for the period 2nd quarter 2011 through 2nd quarter 2015.
- Poisson regression was used to calculate number of visits and site submissions (Figure 1).

Results

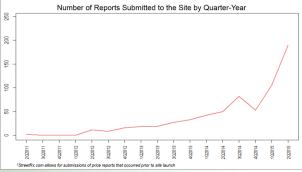
- Rank orders of prescription opioid tablets/capsules pricing are similar in Canada and the United States (US), and provided using each country's currency (Table 1).
- In Canada, the highest median price per milligram is \$2.50 CAD for hydromorphone, and the lowest is \$0.11 CAD for tapentadol.
- Hydromorphone is also \$2.50 USD on the street in the US.
- In Canada, crushable forms of oxycodone (generic immediate release or extended release) cost \$1.00 CAD/mg compared to \$0.63 CAD/mg for crush-resistant formulations.
- Similarly, in the US, crushable oxycodone costs \$1.00 USD/mg while the crush-resistant formulation costs \$0.63 USD/mg.
- The highest number of submissions in Canada involved oxycodone and hydromorphone compared to hydrocodone and oxycodone in the US.
- · Tablet forms of hydrocodone are not approved in Canada.
- For every month increase in time, number of visits to StreetRx.com/Canada increased by 32% (p<0.0001) and number of submissions increased by 31% (p<0.0001) (Figure 1).

Conclusions

- Numbers of visits and submissions to StreetRx.com/Canada are steadily increasing (for reports by province, see Figure 2).
- Our results suggest oxycodone and hydromorphone are the pharmaceutical ingredients most commonly trafficked in the Canadian black market.

Figure 1. Visits and Reports by Quarter-Year





streetrx.com/canada

Figure 2. Number of Reports by Province



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| Table 1. Canada Drug Rankings by Price per Milligram Compared with US | | | | | |
|---|-----|-------------------------|--------------------|--------|-------------------------|
| Canada | | United States | | | |
| Drug | N | Median (IQR) CAD | Drug | N | Median (IQR) USD |
| Hydromorphone | 305 | \$2.50 (\$1.25, \$3.75) | Hydromorphone | 2,061 | \$2.50 (\$1.50, \$5.00) |
| Hydrocodone | 2 | \$2.20 (\$0.40, \$4.00) | Hydrocodone | 12,980 | \$0.80 (\$0.50, \$1.00) |
| Buprenorphine | 2 | \$1.88 (\$1.25, \$2.50) | Buprenorphine | 325 | \$2.50 (\$1.25, \$3.75) |
| Oxycodone | 275 | \$1.00 (\$0.67, \$2.00) | Oxycodone* | 18,171 | \$1.00 (\$0.50, \$1.25) |
| Crushable | 161 | \$1.00 (\$1.00, \$2.00) | Crushable | 10,095 | \$1.00 (\$0.60, \$1.60) |
| Form not indicated | 99 | \$1.00 (\$0.54, \$1.25) | Form not indicated | 5,391 | \$1.00 (\$0.60, \$1.00) |
| Non-crushable | 15 | \$0.63 (\$0.38, \$1.00) | Non-crushable | 2,589 | \$0.63 (\$0.38, \$1.00) |
| Methadone | 2 | \$0.75 (\$0.50, \$1.00) | Methadone | 970 | \$1.00 (\$0.50, \$1.00) |
| Morphine | 51 | \$0.50 (\$0.30, \$1.00) | Morphine | 2,044 | \$0.33 (\$0.20, \$0.67) |
| Tramadol | 11 | \$0.27 (\$0.13, \$0.88) | Tramadol | 1,537 | \$0.06 (\$0.02, \$0.10) |
| Oxymorphone | 1 | \$0.25 (\$0.25, \$0.25) | Oxymorphone | 608 | \$1.38 (\$0.88, \$2.50) |
| Tapentadol | 2 | \$0.11 (\$0.02, \$0.20) | Tapentadol | 94 | \$0.13 (\$0.09, \$0.24) |

For the U.S., price per milligram could not be calculated for 96 reports of oxycodone as price or dosage was not provided.

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RADARS® System Abstracts RADARS System Conference Attendance: October 2015–December 2015

Asian Pacific Association of Medical Toxicology (APAMT)

Perth, Australia

December 1st, 2015 – December 4th, 2015



Online survey of prescription medicine misuse: what is the evidence for misuse of benzodiazepines and 'Z drugs' in Singapore?

Chan WL, Wood DM, Besharat AC, McDaniel HA, Green J, Dargan PI

American Academy of Addiction Psychiatry (AAAP) Huntington Beach, CA

December 3rd, 2015 – December 6th, 2015



Abuse and diversion of buprenorphine/naloxone oral film relative to other buprenorphine formulations

Severtson SG, Bucher Bartelson B, McDaniel HA, Green JL, Besharat AC, Cicero T, Ellis M, Kurtz SP, Rosenblum A, Dart RC

<u>Unintentional exposures to buprenorphine/naloxone tablets and oral film among children less than</u>
<u>six years old October 2010 through June 2015</u>

Severtson SG, Bucher Bartelson B, McDaniel HA, Green JL, Besharat AC, Dart RC

Upcoming RADARS® System Conference Attendance: January 2016 – March 2016

32nd American Academy of Pain Medicine (AAPM) Annual Meeting Palm Springs, CA

February 18th, 2016– February 21st, 2016

The Changing Landscape of Prescription Opioid Abuse in the United States

Richard C. Dart, MD, PhD



Abuse-Deterrent Formulations Summit Alexandria, VA

March 9th, 2016– March 10th, 2016

Investigate Challenges and Opportunities in Post Marketing Surveillance of ADFs

Richard C. Dart, MD, PhD



American College of Medical Toxicology (ACMT) Annual Scientific Meeting Huntington Beach, CA

March 18th, 2016- March 20th, 2016

Prescription Opioid Death Rates are Greater for Females than Males

Iwanicki JL, LeLait MC, Severtson SG, Bucher-Bartelson B, Dart RC



Learn More About Our Domestic and International Services...

Please click below for our Domestic Services:



The Researched Abuse, Diversion and Addiction-Related Surveillance (RADARS®) System is a surveillance system that collects product- and geographically-specific data on abuse, misuse and diversion of

The RADARS® System provides prescription drug abuse data to a variety of organizations, offering surveillance and consulting vices that have helped dozens of clients meet their business and regulatory requirements

Who We Are

RADAR/88 System data have been used by manufacturers, regulatory agencies as well as medical and public health officials to characterize and manifor prescription drug obuse, misuse and diversion. The data have been used for an array of purposes including submission of reports to the U.S. Food and Drug Administration (FDA), new drug applications, labeling claims, post market requirements and filts: Evaluation and Mitigation Strategies (REM) assessment. Data can also be used for the development and evaluation of interventions (i.e. abuse deterent formulations), and to monitor ever-changing market trends.

The RAD ARS® System is a nonprofit operation of the Pocky Mountain Poison & Drug Center RMPDC1, a division of Denver Health

Services

- Surveillance data for risk management activities

- Field research and largeted investigations of emerging topics FDA Advisory Committee preparation and/or presentation Development and execution of publication is stategies Review of materials for regulatory submissions
- Consultation with experts on the RADARS® System Scientific Advisory Board
- Coordination of Industry Advisory Board to gather stakeholder needs and harmonize surveillance strategy
- Annual site visits by RADARS® System Clinicians and Scientists

 - Uterature surveillance
 - Drug information and safety reporting contact
- Adverse event and periodic safety reporting
 Advisory Board participation and general consulting

RADARS® System Programs: Mosaic Approach

The RADARS® System utilizes a mosaic strategy to detect misuse, abuse and diversion at all phases of the

Data from all RADARS® System programs are triangulated to provide a more complete picture of prescription drug suse, abuse and dive

This approach has been used in many fields of research and is especially useful in the study of hard to reach or hidden populations, such as those who use, misuse, or divert prescription drugs. It is not abute, misure, or divert prescription drugs. Il is not hypically possible to study such behavior in controlled settings (e.g., randomized, controlled froits). Instead, researchers often rely on multiple convenience samples, each abtained from a different perspective on the hidden population being studied. No single on the hidden population being studied, No single data source is expected to provide complete and representative information about the covert behaviors but, considered together, multiple data sources strengthen the credibility of findings, reduce the risk of folse interpretations, and provide a more complete and comprehensive perspective.

The RADARS® System is composed of a mosaic of WADANCH SYSTEM CONTRACTOR OF THE SYSTEM CONTRA

Mosaic Approach on allowing for early and ongoing monitoring of newly approved drugs as well as those air

Please click below for our International Services:



International Surveillance of Prescription Drug Misuse, Abuse, and Diversion

Who We Are

The Researched Abuse. Diversion and Addiction-Related Surveillance (RADARS®) System international surveillance services are intended to monitor rates of misuse, abuse and diversion of prescription drugs and provide experienced and expert analysis interpretation of the data. Our consulting services are customized to the business and regulatory requirements of our clients.

The RADARS® System is a nonprofit operation of the Rocky Mountain Poison & Drug Center (RMPDC), a division of Denver Health

International Services

- Surveillance data for risk management activities Development and execution of publication strategies
- Field research and targeted investigations of emerging topics

 Other traditional post-market surveillance services
- Preparation and/or presentation for meetings with regulatory agencies
- Literature surveillance Drug information and safety reporting contact center
- Adverse event and periodic safety reporting

International Programs: Mosaic Approach

The RADARS® System utilizes a mosaic strategy to detect misuse, abuse and diversion at all phases of the drug abuse pathway.

Data from all RADARS® System programs are triangulated to provide a more complete picture of prescription drug misuse, abuse and diversion.

This approach has been used in many fields of research and is especially useful in the study of hard to reach or hidden populations, such as those who abuse populations, such as those who abuse, misuse, or divert prescription drugs. It is not typically possible to study such behavior in controlled settings (e.g. randomized, controlled trails). Instead, researchers often rely on multiple convenience samples, each obtained from a different perspective on the hidden population being studied. No single data source is expected to provide complete and representative information about the covert behaviors but, considered together, multiple data sources strengthen the credibility of findings, reduce the risk of false interpretations, and provide a more complete and comprehensive



The RADARS® International System is composed of a mosaic of programs which target diverse populations throughout Europe Canada and Australia. They are product-specific and sensitive to geographic location allowing for early and ongoing monitoring of newly approved drugs as well as those already on the market.

RADARS® System Quarterly Technical Report Fourth Quarter 2015 Edition

Number of Prescription Opioid Tablets/Capsules Ingested in Intentional Abuse Exposures Cases Reported to Poison Centers

RADARS® System in Social Media – Get Connected!



Follow us at @RADARS System. You can find news relating to prescription drug surveillance and abuse in the US and abroad. RADARS® System tweets include publication announcements, conference attendance, program updates and more.



Publication and conference attendance news can be found on our LinkedIn site (www.linkedin.com/company/radars-system).



Visit www.RADARS.org for active links to presentations, conference and manuscript abstracts.

RADARS® System Mission Statement

The RADARS® System provides timely, product specific and geographically-precise data to the pharmaceutical industry, regulatory agencies, policymakers and medical/public health officials to aid in understanding trends in the abuse, misuse, and diversion of prescription drugs.

Contact Information

Account, Subscription, Program or Data Inquiries:

business@radars.org (303) 389-1233

Rocky Mountain Poison and Drug Center and Denver Health and Hospital Authority

The RADARS® System is a governmental nonprofit operation of the Rocky Mountain Poison and Drug Center (RMPDC), an agency of Denver Health. The RMPDC has been in operation for more than 50 years, making it one of the oldest poison control centers in the nation. Denver Health is the safety net hospital for the City and County of Denver and is the Rocky Mountain region's academic Level I trauma center and includes Denver Public Health, Denver's 911 emergency medical response system, nine family health centers, 12 school-based clinics, NurseLine, correctional care, Denver CARES, the Denver Health Medical Plan, and the Rocky Mountain Center for Medical Response to Terrorism, Mass Casualties and Epidemics.







RADARS® System • 777 Bannock Street • Mail Code 0180 Denver, CO 80204-4507 Questions or comments?

Email the RADARS® System at <u>business@radars.org</u>.

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777 Bannock Street ● Mail Code 0180 Denver, Colorado 80204-4507