

The background features a repeating pattern of the letters 'U', 'S', and 'U' in a light blue color on a white background. In the center, there is a maroon shield containing a white caduceus (a staff with two snakes) and a white silhouette of a person's head and shoulders.

Medication Misuse in US Service Members

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Disclosures

- US Navy Wounded Warrior Fund grant W47
- Prescription Medication Misuse Educational Project
- No personal benefits
- No off label usage

Agenda

- Definition
- Epidemiology
- Screening
- Risk Stratification
- Mitigation

Prescription Medication Misuse Definition

- Taking medications for non-intended uses, differently than prescribed, without a prescription or with interacting substances.
- Contrast to
 - Non-Medical Use of Pharmaceuticals
 - Prescription drug abuse
 - NIDA definition

Drugs frequently misused

- Analgesics
 - Most commonly misused
 - Oxycodone
 - Methadone
 - Vicodin
- Tranquilizers
 - Valluim
- Stimulants
 - Adderal
 - Ritalin
- Sedatives
 - Lunesta
 - Ambien

Epidemiology



Epidemiology of PMM

- Patterns in Service Members compared to the US population
 - Age matched
 - Employment matched
 - Gender matching
 - Limits to comparisons
- Rates for different groups of Service Members
 - Age specific rate among Service Members
 - Rates for different ranks of Service Members
 - Other demographic groupings of Service Members
- Increase in incidence over time among Service Members
- Sources of misused medications
- Proportions of medications misused in both populations

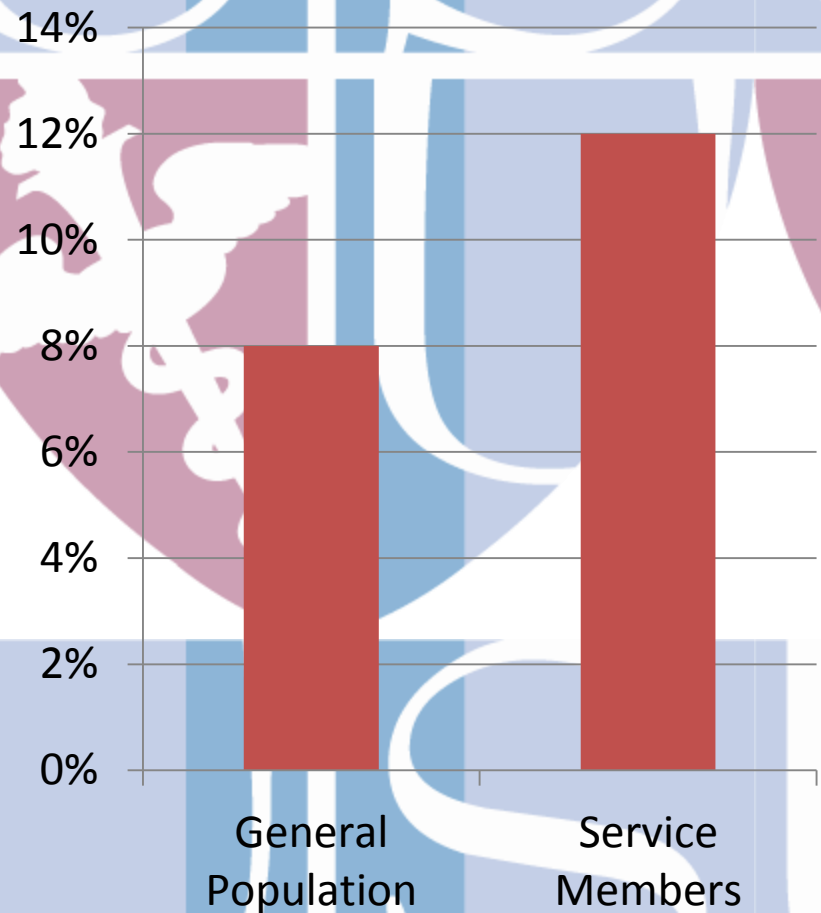
Civilian vs. Military Incidence of PMM

Age Matched Comparison

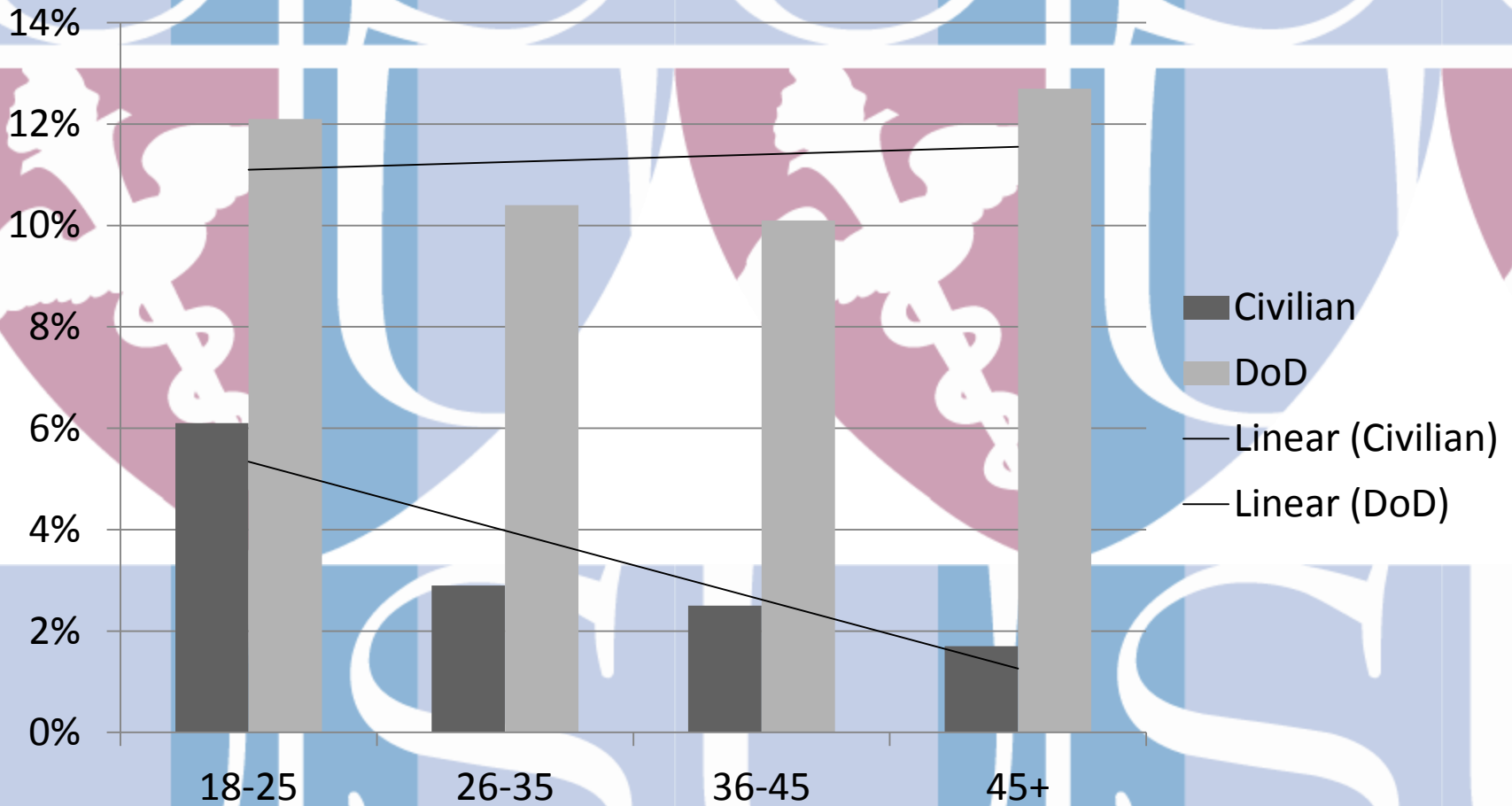
- Civilian Incidence
 - 2.5% PMM in past 30 days, 4.4% among members of general population age matched with Service Members
 - Substance Abuse and Mental Health Services Administration. Results from the 2009 National Survey on Drug Use and Health: National Findings. Rockville: Office of Applied Studies 2009.
 - 2008 Department of Defense survey of health related behaviors among military personnel, Research Triangle Institute, Research Triangle Park NC 2009
- Incidence in Service Members
 - 11.1% 30 days incidence of PMM
 - 18.4% in the past 12 months (23.1% in Army)
 - 2008 Department of Defense survey of health related behaviors among military personnel, Research Triangle Institute, Research Triangle Park NC 2009

Rates Matched for Employment Status (PMM or ISA)

- Higher rate of all substance misuse or abuse in Service Members when compared to fully employed civilians
 - Substance Abuse and Mental Health Services Administration. Results from the 2008 National Survey on Drug Use and Health: National Findings (Office of Applied Studies, NSDUH Series H-36, HHS Publication No. SMA 09-4434). Rockville, MD. 2009.
 - 2008 Department of Defense Survey of Health Related Behaviors among Active Duty Military Personnel. Research Triangle Institute, Research Triangle Park NC. 2009.



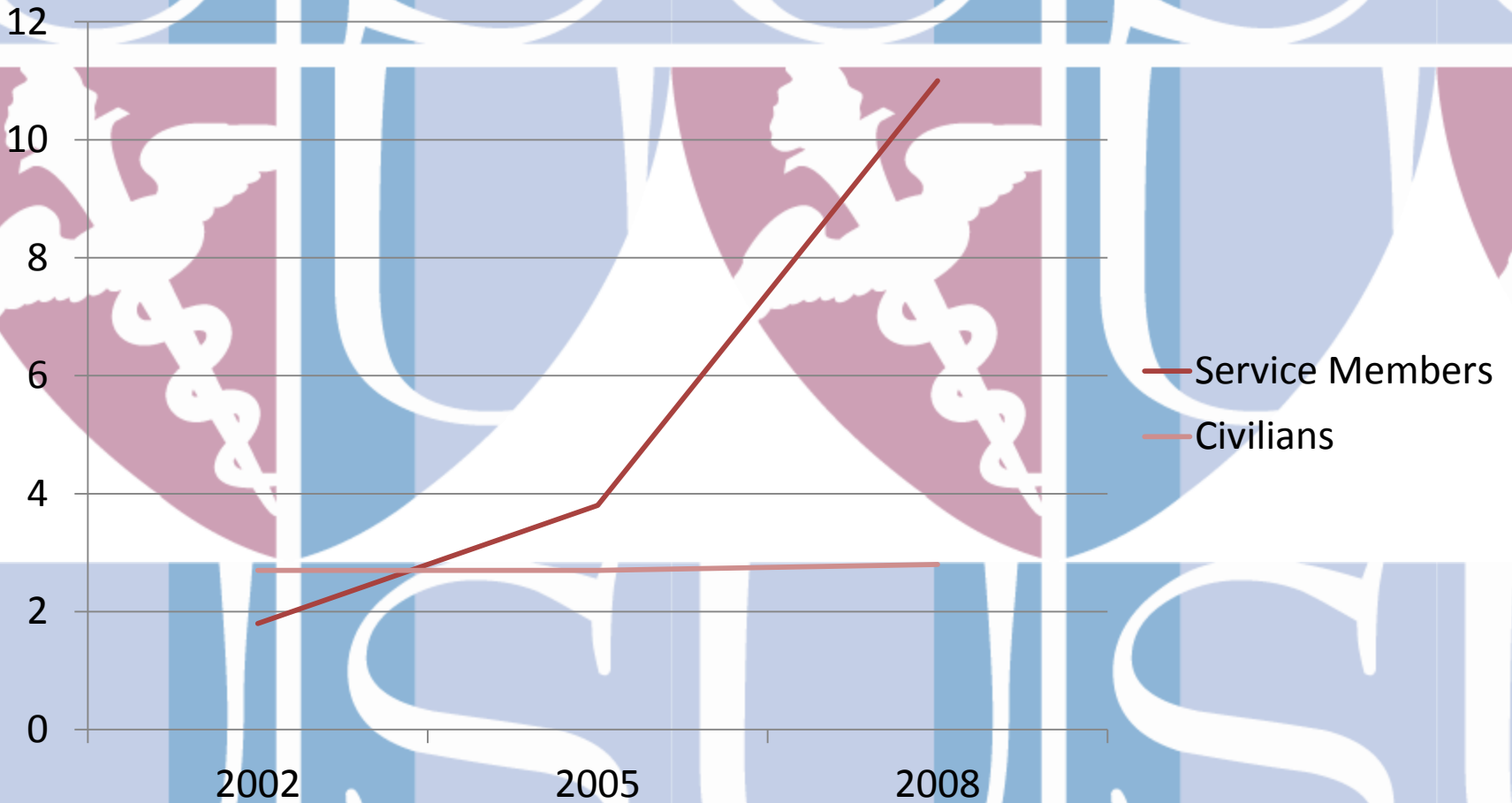
PMM by Age Group Service Members Vs. Civilian



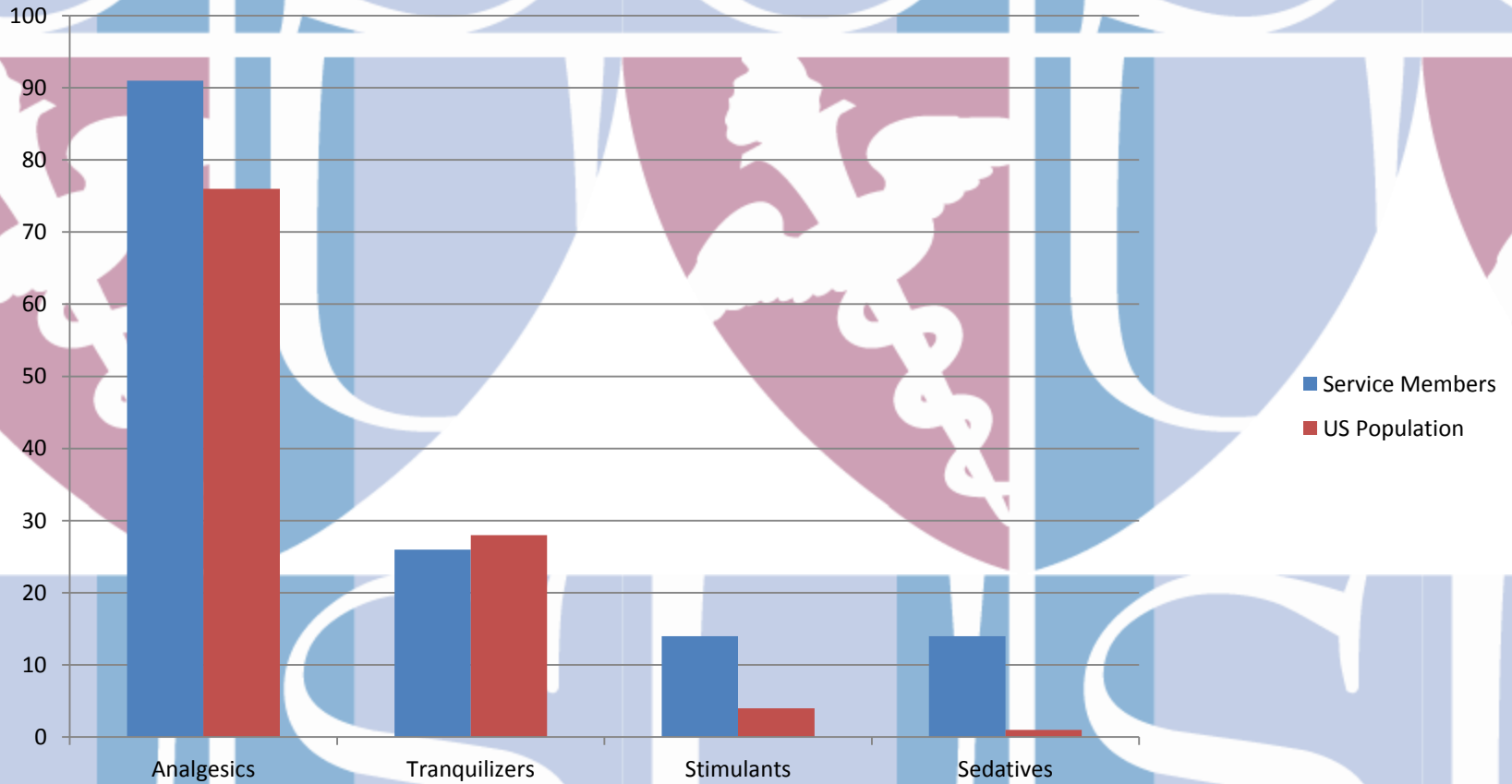
PMM Incidence – Gender Comparison Service Members Vs. US Population

- US population – males have higher incidence
 - Males – 4.6% 30 day incidence
 - Females – 3.2% 30 day incidence
- Service Members – females have higher incidence
 - Males – 11.4% 30 day incidence
 - Females – 13.2% 30 day incidence

Increasing Rate of PMM SM vs. Civ



Misusers by Medication Category/ Total Misusers in Each Group



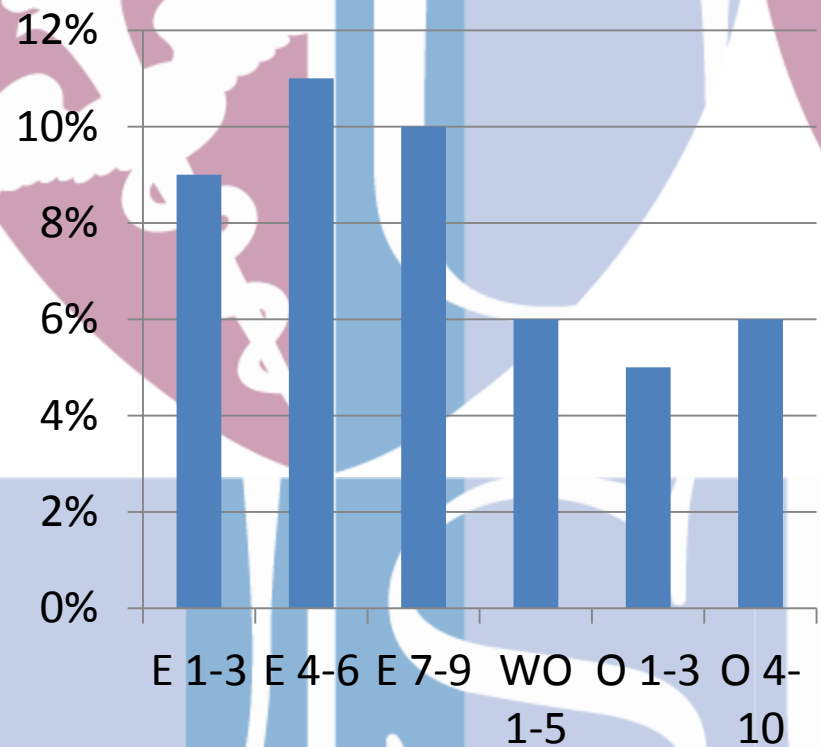
Sources of Misused Medications

- 22% obtained through prescription
- Friends or relatives were the most common sources
 - 47% obtained them from a friend or relative for free
 - 13% purchased
 - 2/3 purchased from a friend or relative.
 - Partnership for a Drug-Free America, Partnership Attitude Tracking Study
 - Schepis T and Krishnan-Sarin S. Sources of Prescriptions for Misuse by Adolescents: Differences in Sex, Ethnicity, and Severity of Misuse in a Population-Based Study. *J Am Acad Child Adolesc Psychiatry.* 2009; 48: 828-36.
- Corroborated by data from National Survey on Drug Use and Health (NSDUH) performed for Substance Abuse and Mental Health Administration (SAMHSA)
 - 18% of medications misused obtained with a prescription
 - Majority from friend or relative
- No Service Member specific data
 - 14% of Army received a prescription for an opioid
 - US Army Suicide Report
 - Media reports have documented sharing
 - Personal reports of card games with oxycontin

PMM by Military Rank

- Rates vary more by military rank (enlisted vs. officer) than by age

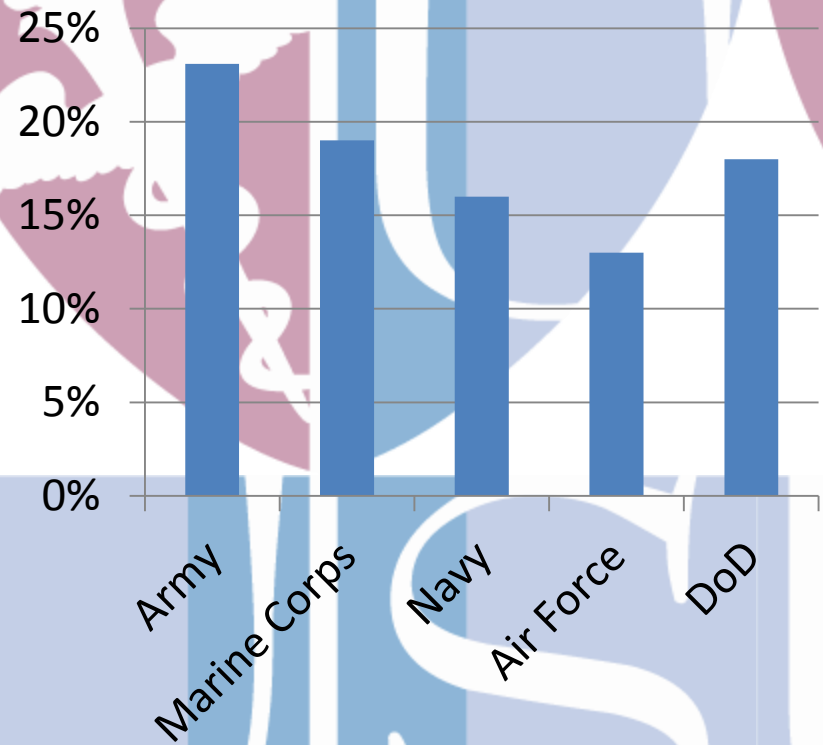
Incidence in previous 30 days



PMM by Service

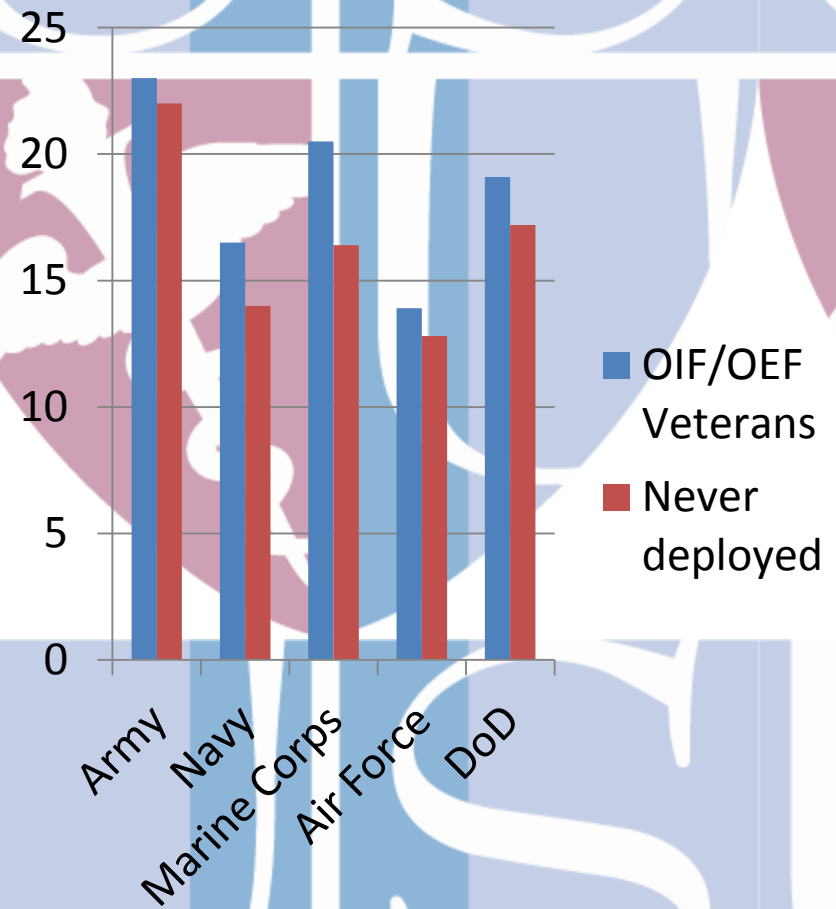
- Highest rates in the Army and Marine Corps
- Differences achieved statistical significance

PMM Rates in Previous 12 Months



PMM – Impact of Deployment

- 19.1 % of OIF/OEF deployed endorsed in previous 12 months
- 17.0 % for never deployed
- Mild increased incidence in every service
 - 2008 DoD Survey of Health Related Behaviors



Screening for Medication Misuse



Risk factors for misuse

- Illicit drug use
- Previous substance use issues
 - History of substance abuse (particularly multi-substance)
 - Positive abnormal urine drug screen previously
 - History of legal problems (e.g. DUI/DWI)
- Family history of drug abuse
- Psychiatric Dysfunction
 - PTSD
 - Depression
 - Anxiety disorder
 - Schizophrenia
- Younger age (less than 30, greater when less than 25)
- History of physical, emotional, or sexual abuse
- Smoking
- Chronic pain

Odds Ratios for PMM

- | | |
|------------------------------|------------------|
| • History of nonopioid abuse | 2.34 (1.75-3.14) |
| • History of Alcohol abuse | 2.6 (1.12-6.26) |
| • History of Cocaine abuse | 4.3 (1.76-10.4) |
| • Smoking | 1.4 (1.1-1.8) |
| • DUI or drug conviction | 2.58 (1.01-6.59) |
| • Probable Depression | 2.4 (1.6-3.4) |
| • Mood disorder | 3.5 (3.1-3.9) |
| • MDD | 3.2 (2.9-3.6) |
| • Bipolar disorder, type I | 4.7 (3.8-5.7) |
| • Anxiety disorder | 2.4 (2.2-2.8) |
| • PTSD | 2.45 (1.88-3.19) |
| • Chronic Pain | 1.9 (1.4-2.5) |
- Edlund MJ, Steffick D, Hudson T, Harris KM, Sullivan M. Risk factors for clinically recognized opioid abuse and dependence among veterans using opioids for chronic non-cancer pain. *Pain*. 2007;129:355-62.
 - Ives TJ, Chelminski PR, Hammitt-Stabler CA, Malone RM, Perhac JS, Potisek NM, Shilliday BB, DeWalt DA, Pignone MP. Predictors of opioid misuse in patients with chronic pain: a prospective cohort study. *BMC Health Serv Res*. 2006;6:46.
 - Becker W, Fiellin D, Gallagher R, Barth K, Ross J, Oslin D. The association between chronic pain and prescription drug abuse in Veterans. *Pain Medicine* 2009; 10: 531-536.
 - Martins S, Keyes K, Storr C, Zhu H, Chilcoat H. Pathways between nonmedical opioid use/dependence and psychiatric disorders: Results from the National Epidemiologic Survey on Alcohol and Related Conditions Drug and Alcohol Dependence. 2009: 16–24.
 - White AG, Birnbaum HG, Shiller M, Tang J, Katz NP. Analytic models to identify patients at risk for prescription opioid abuse. *Am J Manag Care*. 2009; 15: 897-906.

Direct Comparison of Screening Tools for Future Misuse

- Clinical history focusing on risk factors - sensitivity of 0.77
- SOAPP-R 0.72
- ORT 0.45
 - Moore TM, Jones T, Browder J, Daffron S, and Passik SD. A Comparison of Common Screening Methods for Predicting Aberrant Drug-Related Behavior among Patients Receiving Opioids for Chronic Pain Management. *Pain Medicine* 2009; 10: (8) 1426-1433

Tools to Screen for Current Misuse

- PDUQ
- COMM
- All tools for this purpose targeted patients already prescribed frequently misused medications – no study in the general population

PDUQ – Most Predictive Points

- Patient believes he/she addicted
- Physician believes patient is addicted
- Multiple prescription providers
- Increases analgesic dose/frequency
- Early prescription refills
- Use analgesics for other symptoms
- Save/hoard unused medication
- Supplement with alcohol/psychoactive drugs
- Prescription forgery
- Patient has a route of administration preference
- Emergency room visits for analgesics
- Obtained analgesic from street source
- MD/DDS limited care
- Family believes patient addicted
- Family interaction sustaining patient analgesic use
- All of the above had a $P < 0.05$ for predicting misuses
 - Compton, P., J. Darakjian, et al. Screening for Addiction in Patients with Chronic Pain and "Problematic" Substance Use: Evaluation of a Pilot Assessment Tool. *J Pain Symp Man.* 1998. 16(6): 355-363.

Risk Stratification



Patient Risk Stratification

Risk Categories

- Modification of originally described categories
 - Gourlay D, Heit H, Almahrezi A. Universal Precautions in Pain Medicine: A rational Approach to the Treatment of Chronic Pain. Pain Med. 2005, 6: 107-112.
- Included category for actively addicted to denote need for highly structured care

PMM Risk Categories

- Low risk
 - No psychopathology or other risk factors
 - May be managed by primary care providers when potentially misused medications are indicated
- Intermediate risk
 - Well treated psychopathology, family history of substance abuse, younger age, and smokers
 - May be managed by primary care providers but PCM should consider psychiatric or pain management consultation as indicated
- High risk
 - Active psychopathology or a history of substance abuse
 - Should only be managed through coordinated efforts of primary care providers, psychiatrists, pain management physicians and addiction medicine physicians
- Actively addicted
 - Should only be managed by multidisciplinary teams of specialists in highly structured environments

When to Consult a Specialist

- High risk patients or intermediate risk patients when PCM comfort level exceeded
- Addiction medicine consultation – when addiction is suspected
- Psychiatric consultation – when taking prescription medications with active psychiatric disorder
- Pain medicine consultation – when basic medication regimens fail to treat pain or improve function
- Admission and withdrawal or monitoring – for violation of a treatment agreement or there is evidence of diversion
- Legal “consultation” – when diversion or misuse is suspected

The background features a repeating pattern of the letters 'USU' in a white, serif font on a blue background. Interspersed within this pattern are red and white crests, each containing a caduceus (a staff with two snakes and wings), which is a common medical symbol. The text 'Mitigation of PMM' is centered in the middle of the image.

Mitigation of PMM

Mitigation of PMM

- Most recommendations are expert opinion rather than evidence based
- Unethical to deviate from standard practice when caring for patients abusing or misusing
- Difficult to accurately detect and prospectively evaluate the following recommendations

PMM Mitigation Tools

- Informed consent
- Treatment agreements
- Prescribing practices
 - Frequent refills
 - Long acting medication
- Administrative oversight of patients
 - Sole provider programs
 - Pill count
 - Random urine drug tests
 - Supervised administration
- Treating comorbid disorders
- Consultative co-management

Informed Consent

- Respect patient autonomy
- 2 parts – Information and consent

INFORMED Consent – Part 1a

- Risks
 - E.g. Opioids
 - Constipation, nausea
 - Tolerance, addiction, dependence
 - Hyperalgesia, decreased pain relief
 - Hypogonadism
 - Respiratory depression, death
- Patients also need to be informed of legal ramifications of misusing or diverting medications
- Patients need to know the risks to others if they divert their medications or allow them to be diverted

INFORMED Consent – Part 1b

- Realistic discussion of benefits
 - For pain medication
 - Moderate reduction in pain scores
 - Kalso E, Edwards J, Moore R, McQuay H. Opioids in chronic non-cancer pain: systematic review of efficacy and safety. *Pain*. 2004; 112: 372-380.
 - Return of function is an attainable goal, not complete relief of pain
 - Anxiety medication
 - Improved functioning not loss of consciousness

Informed ***CONSENT***– Part 2

- Consent – patients need to understand and agree to enacting the treatment plan

Treatment Agreements

- State goals of therapy and conditions for continuation (mutual respect, honesty, and a bidirectional responsibility)
- Identify a sole provider or sole clinic for prescriptions
- Prohibit escalation above prescribed dose
- Prohibit misuse or diversion
- Identify penalties for misuse or diversion
 - legal (police report)
 - medical (forced detox, forced taper, or cessation of medical treatment based on the clinical scenario)
- Should be readable, reasonable and FLEXIBLE – use the word “may” rather than “will” to retain flexibility

Treatment Agreement References

- Fishman SM, Kreis PG. The opioid contract. Clin J Pain. 2002; 18: S70-5.
- Federation of State Medical Boards. Model policy for the use of controlled substances for the treatment of pain. J Pain Palliat Care Pharmacother. 2004; 19: 73-78.
- Chou R. 2009 Clinical Guidelines from the American Pain Society and the American Academy of Pain Medicine on the use of chronic opioid therapy in chronic noncancer pain: what are the key messages for clinical practice. Pol Arch Med Wewn. 2009; 119:469-77.

Best Prescribing Practices

- Minimize pill burden
 - Short duration of prescription
 - frequent refills
- Long acting or sustained release medications for long term therapy

Minimize Pill Burden

- Less medication to divert or misuse
- Short duration of prescription - two weeks or less based on risk of misuse
- Allows for more frequent reassessment 📌
- A recommended practice without significant evidence in the literature to support

Prescribing Long Acting or Sustained Release Medications

- Higher troughs – less craving
- Lower peaks – less euphoria
- Stimulant abuse pattern provides moderate evidence based support for this theory – faster release, shorter acting adderal and ritalin are more frequently abused
 - Teter CJ, McCabe SE, LaGrange K, et al. Illicit use of specific prescription stimulants among college students: prevalence, motives, and routes of administration. *Pharmacotherapy*. 2006; 26: 1501–1510.
 - Williams RJ, Goodale LA, Shay-Fiddler MA, et al. Methylphenidate and dextroamphetamine abuse in substance abusing adolescents. *Am J Addict*. 2004; 13: 381–389.
- No clinical evidence of effect in opioid therapy

Administrative Tools for Mitigation

- Pill counting
- Drug testing
- Supervised administration
- Sole provider program



Pill Counting

- Must be random, short notice pill counts
- Less pills than expected indicates diversion or use in excess of prescribed amount
- Requires investment of personnel
- Establishes trust in patient by provider
- Recommended practice based on expert opinion

Random Drug Testing

- Urine testing most common
- Used to establish trust between provider and patient
- DoD drug testing not sufficient
 - Significant number not tested - 14% not tested in 2009
 - US Army Health Promotion Risk Reduction Suicide Prevention Report 2010.
 - Only active duty military tested
 - Most only tested once per year
 - Only 20% of samples are tested for prescription medications
 - Positives evaluated by Medical Review Officer (MRO)
 - Any prescription in past for drug tested excuses the positive result regardless of current clinical picture – old prescriptions saved

Urine Drug Testing

- Immunoassay most common initial test
 - IA performed by DoD labs unless otherwise specified
- Mass Spectroscopy or Gas Chromatography
 - Can detect all substances including ones missed by IA
 - Can be used to determine concentration present
 - Must be specially ordered for medication prescribed or drug suspected
 - Not part of routine hospital lab drug screening

Urine Drug Testing – Negative Results

- Negatives
 - Could indicate diversion
- False negatives
 - Might be the result of ultra rapid metabolizers or timing of medication administration
 - Semisynthetic and synthetic narcotics (fentanyl, methadone, oxycodone) are poorly or not detected by IA – specific IA or GC/MS must be ordered

Urine Drug Testing – Positive Results

- An expectedly positive result can help establish trust in the patient
- Does not ensure compliance – IA testing only signifies presence of compound, does not rule out self escalation of dose
- IA testing for classes of medications does not rule out misuse or abuse of other medications of the same class
 - E.g. – Positive for opioids could mean taking morphine which was prescribed and another opioid not prescribed

Urine Drug Testing – Unexpected Positive Results

- Positive for not prescribed substances
- False positives for not prescribed substances may occur, particularly with IA testing
 - Quetiapine can yield a false positive for methadone.
 - Cherwinski K, Petti TA, Jekelis A. False methadone-positive urine drug screens in patients treated with quetiapine. *J Am Acad Child Adolesc Psychiatry*. 2007; 46: 435-6.
 - Venlafaxine can yield a false positive for phenylcyclidine (PCP)
 - Santos P, Lopez-Garcia P, Navarro J, Fernandez A, Sadaba B, and Vidal J. False positive phencyclidine results caused by venlafaxine. *Am J Psychiatry*. 2007; 164: 349.
 - Efavirenz for benzodiazepines
 - Blank A, Hellstern V, Schuster D, Hartmann M, Matthée AK, Burhenne J, Haefeli WE, Mikus G. Efavirenz treatment and false-positive results in benzodiazepine screening tests. *Clin Infect Dis*. 2009; 48: 1787-9.
- Should be confirmed with GC/MS or specific IA testing

Supervised Administration

- Ensure compliance in high risk patients with legitimate and significant indication for a potentially misused medication
- Manpower intensive
- Alternative is to admit for withdrawal
- Should always be done in conjunction with other providers and legal authorities

Conclusion

- Definition
- Epidemiology
- Screening
- Risk Stratification
- Mitigation Strategies
- Future directions
 - Drug formulations
 - Pharmacogenetics
 - Novel μ agonists