Pharmaceutical drugs: maintaining appropriate use while preventing diversion

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Clinical drug use decisions

benefits

Risks
• Patient-centred
Clinical drug use decisions

Benefits

Risks
• Patient-centred
• Population level
Heterogeneous population

- Addicted (SUD)
- Substance abusers
- Recreational users
- Self-treaters
- Nonmedical opioid users
- Adherent
- Chemical copers
- Substance abusers
- Addicted (SUD)
- Pain patients

Heterogeneous population

Addicted (SUD)  Substance abusers  Recreational users  Self-treaters  Adherent  Chemical copers  Substance abusers  Addicted (SUD)

Nonmedical opioid users  Pain patients  hidden population

At-risk cohorts

- Mental health disorders – 20% of adult population
- Substance use disorders – personal, family – 7% of adult population
- Comorbidity prevalent
- Abusive childhood prevalent
Opioid base supply: Australia, 1991-2009

- Morphine
- Oxycodone
- Methadone
- Codeine
- Pethidine
Opioid base supply:
USA 1997-2006

Source: ARCOS Automated Reports and Consolidated Orders. DEA, US DoJ.
Consequences of increased supply

“...very strong correlation between therapeutic exposure to opioid analgesics.....and their abuse”

“..suggest..non-medical use of opioids is predictable based on potency and extent of prescriptive use.”

“...linear relationship between total opioid analgesic sales and drug poisoning mortality.”
Unintentional drug overdose deaths by major type of drug, U.S., 1999-2006

Unintentional drug overdose deaths by major type of drug, U.S., 1999-2006


Chain of supply: to Australia

Licit import

Illicit import

Internet
Post
import freight
import personal
Licit chain of supply: within Australia

- Port
- Warehouse
- Factory
- Pharmacy, Hospital, ER
- Patient
- Prescriber

Flow direction:
- Port to Warehouse
- Warehouse to Factory
- Factory to Pharmacy, Hospital, ER
- Pharmacy, Hospital, ER to Patient
- Patient to Prescriber

Flow direction:
- Patient to Prescriber
- Prescriber to Pharmacy, Hospital, ER
- Pharmacy, Hospital, ER to Patient
- Port to Warehouse
- Warehouse to Factory
Diversion

Warehouse

- Pilfer
- Theft
- False invoice
- Armed robbery
- Diversion in transit
Diversion

Prescriber

- Inappropriate prescribing
- Identity fraud
- False representation of disease “doctor shopping”
- Across State borders
- Stolen prescription stationery, forgery, alteration of scripts
- Intimidation, threat
- Self-administration
Diversion

Forged prescription

Altered prescription

False representation of disease "pharmacy shopping"

Robbery, theft, ram raid

Intimidation, threat: outside pharmacy, General threat
Patient

- Theft from & within home
- Friends, family share, sell
- Patient on-selling
- Intimidation, threat: outside pharmacy, General threat
- Inject, snort tablets

Diversion
High risk - low value drugs: characteristics

- Euphorogenic, sedating
- Intoxicating
- Rapid onset of effect
- Low margin – therapeutic & toxic dose
- Low therapeutic advantage
- Formulation problem - high dose, gelcap
High risk - low value drugs: removed

- chloral hydrate
- barbiturates
- methaqualone
- temazepam gelcaps (UK, Australia)
- flunitrazepam 2 mg
- dextromoramide
- propoxyphene (UK, NZ)
High risk - low value drugs: current concerns

- Compound analgesics
  - opioid + simple analgesic
- midazolam oral tablets
- quetiapine (antidepressant)
- alprazolam (e.g. Xanax®)
- propoxyphene
- pethidine (meperidine)
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<thead>
<tr>
<th>Problem</th>
<th>Countermeasure</th>
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<tbody>
<tr>
<td>High risk, low value drugs</td>
<td>• Registration process – assess diversion risk</td>
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<td>• Enhanced information systems to monitor drugs subject to diversion</td>
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<tr>
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<td>• Early identification of adverse trends</td>
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<td>• Agile and adaptable regulatory system</td>
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<td>• Review and remove</td>
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<td>• Reschedule to more restrictive</td>
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High risk - high value drugs: characteristics

- Clinically important
- Commonly misused, diverted
- Dependence-producing, intoxicating effect
- Criminal activity - to obtain & under-the-influence
- Contribute to severe morbidity, mortality
- Heterogeneous, hidden sub-populations
  - Include non-injectors, not from drug subculture
High risk - high value drugs: categories

- Opioids
- Benzodiazepines & other sedatives
- Antipsychotic, antidepressant drugs
- Pharmacotherapies (opioid dependence)
- Precursor drugs
- Other (e.g. anti-Parkinson’s drugs, appetite suppressants, stimulants)
- Performance-enhancing - veterinary & human
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| Regulatory control           | • Appropriate regulatory control  
|                              | • Prescription - quantities in words & figures  
|                              | • Pharmacist to know handwriting or contact prescriber  
|                              | • Special prescription pads  
|                              | • Oversight - problematic prescribing  
|                              | • National uniformity |

Toolbox HRHV drugs
## Toolbox HRHV drugs

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| Insufficient information about HRHV drug supply to individuals -> unsafe supply | • Coordinated medication management  
• Real time, for prescribers, pharmacists, at time of prescribing, dispensing  
• available to regulators – detect injudicious supply, diversion  
• Automated real-time analysis  
• Software to detect forged or altered scripts, drug-seeker, at-risk individuals  
• Privacy safeguards, audit trail of access  
• Encryption  
• Unique health-care identifiers  
• National – across State/Provinces  
• Include OTC high risk drugs |
Coordinated medication mgmt
“Prescription monitoring”

- **1st generation**: inspecting pharmacies
- **2nd generation**: paper based scripts to central point
- **3rd generation**: electronic transmission
- **4th generation**: real time information for prescribers, pharmacists, regulators
Coordinated medication mgmt
“Prescription monitoring”

- 3rd generation deficiencies
  - Historical, after-the-event
  - Limited capacity to identify individuals
  - Responsibility of operators to notify on limited information – How? Criteria? Delay
  - Difficult access for professionals needing immediate information for safe supply decisions
Coordinated medication mgmt
“Prescription monitoring”

- 2nd generation deficiencies
  - As for 3rd generation, PLUS
  - ‘chilling’ effect on appropriate prescribing.

- NY triplicate prescription program 1989:
  - ~60% reduction in benzodiazepine scripts
  - Increased prescribing of older, more toxic sedatives
  - Greater impact on non-problematic use

Wintraub et al. JAMA 1991;266:2392-7 plus others
Forged benzodiazepine scripts: 1995

Total forged items 223. Bzds 115 (49%)
Forged benzodiazepine scripts: to May 2001

- Temazepam caps: 69%
- 85% Temazepam
- Flunitrazepam: 10%
- Diazepam: 1%
- Oxazepam: 4%
- Temazepam (not specified): 16%
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<tr>
<td>Forged, altered prescriptions</td>
<td>• Tamper-proof, dedicated prescriptions for HRHV drugs</td>
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<tr>
<td></td>
<td>• Secure storage</td>
</tr>
<tr>
<td></td>
<td>• Software programs to detect at time of supply</td>
</tr>
<tr>
<td></td>
<td>• Electronic prescribing</td>
</tr>
<tr>
<td></td>
<td>• Specify number of items on script</td>
</tr>
<tr>
<td></td>
<td>• Words and figures</td>
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<td>• Cross out unmarked space</td>
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To be considered Tamper Resistant, a prescription must contain at least one of the following three characteristics:

1. one or more industry-recognized features designed to prevent unauthorized copying of a completed or blank prescription form;

2. one or more industry-recognized features designed to prevent the erasure or modification of information written on the prescription by the prescriber;

3. one or more industry-recognized features designed to prevent the use of counterfeit prescription forms.
In 2007-2008 Where Pain Relievers Were Obtained for Most Recent Nonmedical Use: Ages 12+

Source Where Respondent Obtained

- One Doctor: 81.7%
- More than One Doctor: 2.4%
- Bought/Took from Friend/Relative: 14.3%
- Drug Dealer/Stranger: 4.3%
- Bought on Internet: 0.4%
- Other: 4.8%
- Free from Friend/Relative: 55.9%

Source Where Friend/Relative Obtained

- One Doctor: 81.7%
- More than One Doctor: 3.4%
- Free from Friend/Relative: 6.2%
- Bought/Took from Friend/Relative: 5.4%
- Drug Dealer/Stranger: 1.6%
- Other: 1.6%
- Bought on Internet: 0.1%
- Other: 0.1%

Note: Totals may not sum to 100% because of rounding or because suppressed estimates.

1 The Other category includes the sources: “Wrote Fake Prescription,” “Stole from Doctor’s Office/Clinic/Hospital/Pharmacy,” and “Some Other Way.”
# Toolbox HRHV drugs

## Patient selection
- Identify higher risk patients – MHD, SUD-personal or family history
- Examination for evidence of SUD
- Screening tools
- Universal precautions
- Inherited patients special precautions – confirm with previous prescriber directly

## Management of request
- Borrowed protection
- Scripted responses
- Broken record, use “we”
Pharmacy robbery
OxyContin in time-delay safe
Ram raid

Damage $5000, theft $100

POLICE are seeking witnesses to a ram raid robbery on the Whits Road Pharmacy on Wednesday morning.

Less than $100 worth of temazepam capsules were stolen in the robbery, which caused more than $5000 damage to the shopfront (pictured).

It is the fourth time in six months there has been a robbery or attempted robbery on the Hamlyn Heights pharmacy.

Detective Sergeant Garry Arnold of Geelong's Criminal Investigation Unit said it appeared a white Ford Laser had driven through the shopfront about 2.30am.

He said a small amount of medication was stolen.

Anyone with information is asked to telephone Det Sgt Arnold at Geelong CIB on 5273 5779 or Crimestoppers on 1800 333 000.
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<td>Crime to obtain: pharmacy, warehouse, transit, domestic robbery</td>
<td>• Requirement to keep in original pack</td>
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<td></td>
<td>• Indelibly marked or embossed blister packs</td>
</tr>
<tr>
<td></td>
<td>• Hotline for law enforcement to track to whom dispensed, by whom prescribed and dispensed</td>
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<td></td>
<td>• ‘Pedigree’ chain records</td>
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<td>Theft, robbery</td>
<td>• time-release safes, segmented</td>
</tr>
<tr>
<td></td>
<td>• Mandatory high quality CCTV</td>
</tr>
<tr>
<td></td>
<td>• indelibly labelled blister packs</td>
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Blister pack
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<tr>
<td>Identity fraud</td>
<td>• unique health-care identifiers</td>
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<tr>
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<td>• ‘inherited’ patients: special precautions</td>
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| Patient on-selling | • Requirement to keep in original indelibly marked or embossed pack  
|                  | • Coordinated medication management system to detect unusually high doses     |
|                  | • Pill counts                                                                  |
|                  | • Urine drug screen                                                            |
## Toolbox HRHV drugs

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<td>Trafficking, brokering</td>
<td>• Requirement to keep in original indelibly marked or embossed pack</td>
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<td>• Supported by hotline for law enforcement</td>
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<tr>
<td></td>
<td>• Penalty for unauthorised possession, or not in original pack</td>
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<tr>
<td></td>
<td>• Coordinated medication management system to detect unusually high dose supply, potential on-selling</td>
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<td>Sharing, domestic source, medicine cabinet</td>
<td>• Patient information – risks, safe storage</td>
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<tr>
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<td>• Limited quantity of supply</td>
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<tr>
<td></td>
<td>• Return unused HRHV medicines</td>
</tr>
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<td></td>
<td>• Safe storage</td>
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<td>Poisoning risk</td>
<td>• Patient information – risks, safe use, storage</td>
</tr>
<tr>
<td></td>
<td>• Labelling, package inserts, leaflets, advice – prescribers &amp; pharmacists</td>
</tr>
<tr>
<td></td>
<td>• Information about recognition of coma</td>
</tr>
<tr>
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<td>• Advice about use of other CNS depressants</td>
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Enhanced data systems

Poisoning deaths
Coroner etc.

Poisoning hospitalisations

ED treatment

Poisons information systems

Prison, police custody, law enforcement

Forged prescriptions

AOD treatment

Injecting drug user surveys

School children surveys

Population survey - dependence, abuse (DSM-IV)

Population surveys: initiation & illicit use
Enhanced data systems

- Provide real-time data
- Unaggregated drug data
  - data aggregated (ICD-10), can’t identify individual drugs, formulations, brands
- Automated analysis
- Early identification of emerging trends, effects of controls
- Agile, targeted & tailored response
Abuse-resistant formulations

- Different targets for a heterogeneous cohorts of non-medical users:
  - IDU – incorporate antagonist
  - Different routes: nasal – irritant
  - Excessive oral intake – sorbitol or other agent active in high dose only
DEMAND CONTROL

- Prescriber/pharmacist education about optimal use of high risk high value drugs
- Patient information about safe use, risks
- Reconfigure services to attract and retain individuals in treatment
- Reconfigure treatment regimes tailored to needs.
- Integrated multi-disciplinary care
Heath Ledger

"died as the result of acute intoxication by the combined effects of oxycodone, hydrocodone, diazepam, temazepam, alprazolam, and doxylamine,"