Drugs and workplace safety

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What is ICADTS?

• ICADTS is an independent nonprofit body whose only goal is to reduce the mortality and morbidity brought about by misuse of alcohol and drugs by operators of vehicles in all modes of transportation.

• The Council sponsors international and regional conferences.
Illegal Drugs and Driving
Alcohol Ignition Interlocks
Alcohol Biomarkers
Prescribing Guidelines for Medicinal Drugs and Driving
Clinical Signs of Impairment for Drugs Other than Alcohol
Young Drivers
Standardization of Reporting Alcohol and Drug Involvement in Fatal Crashes
Low and Middle Income Countries
Designer Drugs and Driving
Young Scientists
Upcoming International Conference
www.t2019.org
www.icadtsinternational.com

T2019
Edmonton, Alberta, Canada
August 18 - 21, 2019

22ND INTERNATIONAL COUNCIL ON ALCOHOL, DRUGS AND TRAFFIC SAFETY CONFERENCE
Rotterdam, The Netherlands
Drugs and work

1. Worry about what?
2. Is alcohol a useful model? Where is the good data?
3. The problem with cannabis!
4. What to do about ICE
5. Medication and driving
How big is the drug problem in Australia?

Figure 1. Number of prevalent cases and 95% UIs by each mental and substance use disorder in 2015 in Australia.

= 1.2 million Australians

 WHICH DRUG SHOULD WE WORRY ABOUT?

Use of drugs of abuse in less than 30-year old drivers killed in a road crash in France: A spectacular increase for cannabis, cocaine and amphetamines

JG Ramaekers: Drug effects on driving - perspectives from experimental studies

Tove Heit and Inger Marie Bernhoff: Risk of serious injury and death for drivers positive for drugs

Acute cannabis consumption and motor vehicle collision risk: systematic review of observational studies and meta-analysis

Risk of road accident associated with the use of drugs: A systematic review and meta-analysis of evidence from epidemiological studies

Motor vehicle collision risk and driving under the influence of cannabis: Evidence from adolescents in Atlantic Canada

Mark Asbridge, Christiane Poulin, Arnaud Vigneau
Is alcohol a useful model?

- Ethanol is a simple molecule
- Taken in gram quantities
- Zero-order pharmacokinetics
- Risks studied for 150 years
How much matters?

If you can measure the alcohol there is an effect
Other drugs are not so simple

- Complex pharmacodynamics (e.g. cannabis)
- Long half life (e.g. methamphetamine)
- Complex relationship between dose and risk
  - Exponential - sedatives like alcohol, benzodiazepines
  - Quadratic - cannabis, opiates, antidepressants
- Drug interactions
  - Symbiotic
  - Antagonistic
  - Complex

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So where do we look for good data?

- Epidemiology
- National Household Drug Survey
- Police data
  - Random Drug Testing
  - Drug screening post collision
  - DUI (drive under the influence)
- Responsibility studies
- Case matched studies
Responsibility analysis

1. Injury Collision
   - Police
   - Blood Token
   - Hospital

2. Collision Report
   - Toxicology
   - Decedent
   - Responsibility Analysis
     - Not Responsible
     - Contributory
     - Responsible

3. Odds Ratio
   - Relative Risk

Condition of the road
Condition of the vehicle
Driving conditions
Type of crash
Witnesses' observations
Road law obedience
Difficulty of task
Level of fatigue
The involvement of drugs in drivers of motor vehicles killed in Australian road traffic crashes.

The odds of responsibility for fatal and non-fatal collisions are different

Meta-analysis of risk

Combining psychotropic drugs

**DRUG & ALCOHOL FREE**
- Not responsible: 30%
- Contributory: 70%

**USING 1 DRUG**
- Responsible: 70%
- Contributory: 30%

**USING 2 DRUGS**
- Responsible: 80%
- Contributory: 20%

**3 DRUGS**
- Responsible: 90%
- Contributory: 10%

**4 OR MORE DRUGS**
- Responsible: 100%
# Odds Ratios for Drug Classes

<table>
<thead>
<tr>
<th>Drug Class</th>
<th>Odds Ratio</th>
<th>Alcohol</th>
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</thead>
<tbody>
<tr>
<td>THC (Cannabis)</td>
<td>1.05</td>
<td>0.05%</td>
</tr>
<tr>
<td>Antidepressants</td>
<td>0.87</td>
<td>2.07</td>
</tr>
<tr>
<td>Narcotic Analgesics</td>
<td>1.14</td>
<td>0.08%</td>
</tr>
<tr>
<td>Sedatives</td>
<td>1.27</td>
<td>0.10%</td>
</tr>
<tr>
<td>Stimulants</td>
<td>0.94</td>
<td>0.15%</td>
</tr>
<tr>
<td>Illegal Drugs</td>
<td>1.04</td>
<td>0.18%</td>
</tr>
<tr>
<td>Legal Drugs</td>
<td>1.03</td>
<td>0.20%+</td>
</tr>
</tbody>
</table>

(Adjusted for Demographic Variables: Age, Gender And Race/Ethnicity)

Cannabis

Figure 59: THC smoking <9 mg, time-dependent impairment.

Berghaus, G., et al., Meta-analysis of empirical studies concerning the effects of medicines and illegal drugs including pharmacokinetics on safe driving. 2011, University of Würzburg.
Subjective high, time course and impairment not related
Rapid Change in Legal Status of Marijuana Raises Important Issues

- Changes in use patterns
- More prevalence in traffic
- More prevalence in crash-involved drivers
- But does it pose greater risk?
U.S. Example: Washington State

- Following legalisation the proportion of drivers in fatal crashes with detectable THC doubled
  - 8.3% in 2013
  - 17.0% in 2014.
- Does not necessarily indicate impairment or that THC was causal in the crash.

THC- Positive Drivers Involved in Fatal Crashes

- had neither alcohol nor other drugs: 39.0%
- had detectable alcohol in addition to THC: 34.0%
- had other drugs in addition to THC: 16.5%
- had both alcohol and other drugs in addition to THC: 10.5%

Acute impairment due to THC

• Consistent evidence of impairment in many domains of cognition
  – Psychomotor speed
  – Attention
  – Visual processing
  – Perception
  – Executive function?
  – Verbal fluency ok; working memory impaired

  ▪ Naïve or less regular users less impaired
  ▪ Abstinence in heavier users causes larger impairments

Head Movements & Jerks
Acute effects on coordination
How well can per se laws work?

• THC concentration alone
  • misclassified a substantial number of drivers as impaired
  • misclassified a substantial number of drivers as unimpaired

• Simple THC levels cannot be scientifically supported

• THC impairment matters!
Interpreting THC


\[
\text{time} = 10^{(-0.698 \times \log[THC] + 0.687)}
\]

\[
\text{time} = 10^{(0.576 \times \log([THCCOOH]/[THC]) - 0.176)}
\]


Prediction based on THC alone


Ogden, E., et al. (2007). Validation of a model for estimating time of last cannabis use from known concentrations of tetrahydrocannabinol and the major metabolite. ICADTS, Seattle.
Case Study

• 7.15 am offending driver crossed to incorrect side of highway
  – Had driven 42 km
• Killed drivers of two cars and injured passengers
• Denied drug use
• Blood sample at 9.00 am
  – THC 10 ng/ml
  – TCH-COOH 40 ng/ml
• Mathematical model predicts smoking within 4 hours of blood test – immediately before or whilst driving
Medicinal Marijuana: The cart before the horse

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The cart IS before the horse

Human studies tells us ...

• There is **good evidence** for use in
  • chronic pain, multiple sclerosis, nausea

• There is **limited evidence** for use in
  • improving weight loss in HIV, tics in Tourette Syndrome, PTSD
  • Decrease in inflammatory markers

• There is **evidence that it is ineffective in**
  • Dementia, cancers, glioma

Medical marijuana?
Alcohol + Cannabis

- **Alcohol impairs**
  - Thinking
  - Planning
  - Reaction time
  - Multitasking
- **So the driver relies on habit**
- **Cannabis impairs**
  - Habituated responses

So the driver relies on **thinking**

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Conclusion

• We should not rely on Canada and USA for data
  – We need more work on cannabis and impairment
  – What about ‘medical marijuana’ impairment?
  – All the work concentrates on THC. What about the 100+ other cannabinoids

• Should we measure THC-COOH?
  – Validation of interpretation of levels
  – How would that look in legislation?
Methamphetamine is a powerful CNS stimulant derived from ephedrine and closely related to adrenaline

- First synthetized 1919
- Patented 1920
Natural rewards

**FOOD**

- 0% Basal DA Output
- % of Basal DA Output
- Time (min)

**SEX**

- DA Concentration (% Baseline)
- Copulation Frequency

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Di Chiara et al., Neuroscience, 1999.

Di Chiara and Imperato, PNAS, 1988
Effects of Drugs on Dopamine Release

**Di Chiara and Imperato, PNAS, 1988**
Effects of Drugs on Dopamine Release

**Methamphetamine**

![Graph showing the effects of methamphetamine on dopamine release](image)

**Cocaine**

![Graph showing the effects of cocaine on dopamine release](image)

**Nicotine**

![Graph showing the effects of nicotine on dopamine release](image)

**Morphine**

![Graph showing the effects of morphine on dopamine release](image)

Di Chiara and Imperato, PNAS, 1988

Amphetamines

- **Low doses**
  - Improve concentration
  - Reduce fatigue
  - Improve driving (esp. with ADD)

- **High doses**
  - Brain overload
  - Tunnel vision
  - Psychosis
Amphetamine misuse

• **Withdrawal**
  – Fatigue
  – Sudden onset of sleep

• **Abuse**
  – Cyclic pattern of use
    • Intoxicated
    • Crash
  – Psychosis
Opiates and opioids

Painkiller deaths on the rise

Amy Cody
Published: October 4, 2012 - 3:28PM

Older patients ingesting painkilling medication have driven more than 20 deaths, experts say.

Preliminary figures indicate that deaths from the drugs in the National Drug and Alcohol Research Centre's State of the Nation Drug and Alcohol Research Report.

Medicines killing hundreds

KATE HAGAN

Prescription drugs caused or contributed to the deaths of 310 of the 371 people who died in Victoria from drug overdoses last year, prompting calls for greater controls on medication.

Victoria's 374 drug overdose deaths exceeded the state's road toll of 242 last year.

In many cases illicit drugs and alcohol also contributed to the prescription drug deaths, but in 143 cases the deaths were due to prescription drug use alone.

Prescription drugs contributed to 83 percent of drug overdoses.

Illicit drugs contributed to 164 deaths and were the sole cause of death in 52 cases.

Deaths, commonly known as Valium, are the drug that caused or contributed to death.

DEATH BY OVERDOSE 2013

Prescription drugs

Illegal drugs

Alcohol

143 (82.3%) Prescription drugs only
86 (22%) Prescriptions & illegal
56 (13%) Prescriptions & alcohol

Alarm over opioid doses for patients with chronic pain

With Australian prescription of opioids reaching record levels, the risk of overdose from prescription painkillers is rising, with the potential for significant harm.

Prescriptions for opioids in Australia have more than doubled in the past five years, with a significant number of patients prescribed opioids for chronic pain.

While opioids can be effective in managing pain, they can also lead to addiction and other serious health problems.

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The medical opioid epidemic

Sources: International Narcotics Control Board; WHO population data; Pain & Policy Study Group, University of Wisconsin/WHO Collaborating Center, 2017
Oxycodone in Victoria

Addiction is not tolerance or dependence

- **Addiction is compulsive drug seeking** knowing the negative health and social consequences
- **Tolerance is a consequence of neuroadaption** and is almost invariable long term
- **Dependence result in withdrawal syndrome**
Addiction is NOT simply bad patient choices

• **Addiction can be the result of bad doctor choices**
  – High doses
  – Long-acting formulation
  – Combination of opioids with benzodiazepines
  – Long-term use (> 3 months)
  – Not recognising substance-use disorder
  – Adolescence
The risk of addiction in acute pain

- The likelihood of chronic opioid use increases with each additional day of medication supplied starting with the third day.
- Sharpest increase occurs after the fifth day.

Avoid too many tablets on discharge


N=1,294,247
Opiate Replacement Therapy

• Methadone
  • No difference in traffic violation rate
  • No difference in accident rate
  • Infrequent in fatal drivers - 0.1%


• Buprenorphine
  • Less impairment than methadone

Assessing fitness to drive

• Australian national standard on opiates
  • ... Cognitive performance is reduced early in treatment, largely due to their sedative effects, but neuroadaptation is rapidly established. This means that patients on a stable dose of an opioid may not have a higher risk of a crash. This includes patients on buprenorphine and methadone for their opioid dependency, providing the dose has been stabilised over some weeks and they are not abusing other impairing drugs. ...


• Impairment reflects the OTHER DRUGS TAKEN not the ORT!
Tranquilisers

- 2 to 5% of Australians used a tranquiliser in the past 2 weeks
  - Anxiety
  - Insomnia
  - Muscles relaxant
  - Epilepsy
  - Intoxication

- Often used with other drugs

- 23 tablets/year for every person over 15 years old in Australia
Benzodiazepines

- 184 (10.2%) drivers tested positive for a benzodiazepine
- 83.7% responsible for or contributed to collision

What is the value of adding warning labels?

- Labelling promotes responsible use of medicine
  - Informed decision making
  - Understanding and management of risk

- Poor labelling has unintended consequences
  - “Do not drive” = stop medicine
  - “Avoid alcohol’ = stop medicine

ICADTS Working Party on medication and driving

**Category 0**
Presumed to be safe or unlikely to produce an effect on fitness to drive.

- Confirm that the medicine will be safe for driving, provided that combinations with alcohol and other psychotropic medicines are excluded.

**Category 1**
Likely to produce minor adverse effects on fitness to drive.

- Inform the patient that impairing side effects may occur especially during the first days and that they have a negative influence on his/her driving ability.
- Give the patient the advice not to drive if these side effects occur.

**Category 2**
Likely to produce moderate adverse effects on fitness to drive.

- Inform the patient about the possible impairing side effects and the negative influence on his/her driving ability.
- Advise the patient not to drive during the first few days of the treatment.
- If possible prescribe a safer medicating, if effective and acceptable to the patient.

**Category 3**
Likely to produce severe effects on fitness to drive or presumed to be potentially dangerous.

- Inform the patient about the possible impairing side effects and the negative influence on his/her driving ability.
- Urgently advise the patient not to drive.
- Consider prescribing a safer medicine, if acceptable to the patient.

**Warning level 1**
Do not drive without having read the relevant section on driving impairment in the package insert.

- Be careful
- Read the patient information leaflet before driving

**Warning level 2**
Do not drive without advice of a health care professional. Read the relevant sections on driving impairment in the package insert before consulting the physician or pharmacist.

- Be very careful
- Don’t drive without the advice of your GP or pharmacist

**Warning level 3**
Do not drive. Seek medical advice after a period of treatment about the conditions to restart driving again.

- Attention: danger
- Do not drive. Seek medical advice before driving again
SafeScript

Is real time prescribing information possible nationally?
### Medical standards for licensing – Alcohol and other substance use disorders

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<thead>
<tr>
<th>Condition</th>
<th>Private standards</th>
<th>Commercial standards</th>
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| **Substance use disorder** *(For withdrawal seizures refer to Acute Symptomatic Seizures, page 86 and 90)* | A person is not fit to hold an unconditional licence:  
- if there is an alcohol or other substance use disorder, such as substance dependence or heavy frequent alcohol or other substance use that is likely to impair safe driving.  
A conditional licence may be considered by the driver licensing authority subject to periodic review, taking into account the nature of the driving task and information provided by the treating doctor as to whether the following criteria are met:  
- the person is involved in a treatment program and has been in remission* for at least one month; and  
- there is an absence of cognitive impairments relevant to driving; and  
- there is absence of end-organ effects that impact on driving (as described elsewhere in this publication). | A person is not fit to hold an unconditional licence:  
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Remission

Guidelines define remission as

- **Abstinence** from use of impairing substance/s
- **Reduced frequency of use** - unlikely to cause impairment
- **Confirmed by biological monitoring** for presence of drugs

Oxford Dictionary defines remission as

- A temporary diminution of the severity of disease or pain
Is ‘remission’ genuine?

Applicants are highly motivated to under-report use

- Minimise perception of problems
- Maximise chance of licence

Self report is unreliable at best

- Meta-analysis - 42% reported use when drugs were found on test
Which matrix for testing?

- BLOOD
- ORAL FLUID
- URINE
- SWEAT
- HAIR & NAILS

Minutes | Hours | Days | Weeks | Months | Years
### Which matrix?

<table>
<thead>
<tr>
<th>MATRIX</th>
<th>HAIR</th>
<th>BLOOD</th>
<th>URINE</th>
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</thead>
<tbody>
<tr>
<td>Collection</td>
<td>Non-invasive</td>
<td>Invasive</td>
<td>Non-invasive</td>
</tr>
<tr>
<td></td>
<td>Easy to transport</td>
<td>Biohazard</td>
<td>Transport issues</td>
</tr>
<tr>
<td></td>
<td>Easy to collect</td>
<td>Requires refrigeration</td>
<td>Requires refrigeration</td>
</tr>
<tr>
<td>Detection Window</td>
<td>&gt; 3 days to 6 months</td>
<td>1 – 2 days</td>
<td>2 hours to a week</td>
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</tbody>
</table>
Urine

Easy to collect
Non-invasive
Cheap to analyse

Cheating ...
Devices and artificial urine
Hair is the obvious choice
but ...

• Four ways to beat a hair follicle drug test
  – Shave it all off
  – A new industry
    • “Detox products that work”
    • “Personalized detox program”
    • Do-it-yourself detox
Absence of cognitive impairments

Clinical tests are crude

- Mini-mental state
- MoCA useful

Specialised test batteries sensitive but time consuming

- Vienna Test Battery (Schufreid)
- CANTAB (Cambridge Automated Neuropsychological Test Battery)
- CDR – Computerised assessment system
Driving

Simulated driving

• Safer

• No agreed standards

On-road assessment

• Inherent risk

• Requires skilled assessor
Medical & psychological assessment

Knowledge
↓
Insight
↓
Understanding
↓
Change
↓
Positive assessment

→ Licence back
Getting it right

Precision = true positives as percentage of positives
Accuracy = percentage correctly classified
Principles for better outcomes

Safety at work is not optional

Drug-impairment is just as important as alcohol-impairment

Professionals can help responsible workers to remain safe

They can identify problems by seeking them out

We must offer long term treatment for those who need it
If you drive on drugs, you’re out of your mind.