Translating research into clinical practice & back again: Challenges for the AoD sector

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Why do we not always provide the interventions that are known to work?

Why do we provide interventions that are known to not work?

(How) Can we improve?
Overview

• Origins of ‘decision making’ in AoD treatment
• Early approaches to evidence based medicine (EBM)
• Translational Research: Evidence is not enough
• Future approaches to EBM and their application in AoD treatment
Origins of ‘decision-making’ in AoD treatment

- Treatment in AoD sector historically aligned to ‘belief systems’ re: the cause and nature of addiction (“mad, bad, dangerous”)
  - Legal: incarceration
  - Moral: proliferation of faith-based / spiritual approaches
  - Sickness: psychological and medical responses

- Combination of all three

- Not just historical: ‘political imperatives’ still apply today
The purpose of this communication is to evaluate critically some of the current ideas about the treatment of alcohol intoxication and the withdrawal syndrome. .... This literature with relatively few exceptions, is characterised not only by its immense bulk, but also by its inordinately uncritical quality. Some of the shortcomings are perfectly evident and require little comment. Reference is made here to the innumerable claims for the therapeutic value of a particular drug or some other method of treatment unsupported by any meaningful data. Some of these claims are so illogical and extravagant that one wonders how they have ever found a place in what is euphemistically termed scientific literature.
The emergence of evidence based medicine (EBM)

Originated in UK in 1990’s amongst a group of cardiologists who were no longer content providing care based on “established wisdom”
What is the evidence – and how is this constructed

Table I: Designations of levels of evidence [1]

<table>
<thead>
<tr>
<th>Level of evidence</th>
<th>Study design</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Evidence obtained from a systematic review of all relevant randomised controlled trials</td>
</tr>
<tr>
<td>II</td>
<td>Evidence obtained from at least one properly-designed randomised controlled trial</td>
</tr>
<tr>
<td>III-1</td>
<td>Evidence obtained from well-designed pseudorandomised controlled trials (alternate allocation or some other method)</td>
</tr>
<tr>
<td>III-2</td>
<td>Evidence obtained from comparative studies (including systematic reviews of such studies) with concurrent controls and allocation not randomised, cohort studies, case-control studies, or interrupted time series with a control group</td>
</tr>
<tr>
<td>III-3</td>
<td>Evidence obtained from comparative studies with historical control, two or more single arm studies, or interrupted time series without a parallel control group</td>
</tr>
<tr>
<td>IV</td>
<td>Evidence obtained from case series, either post-test or pre-test/post-test</td>
</tr>
</tbody>
</table>
Figure 2. Improvement in Pain

<table>
<thead>
<tr>
<th>Improvement in Pain With Cannabinoid vs Placebo by Study</th>
<th>Cannabinoid Events</th>
<th>Placebo Events</th>
<th>Odds Ratio (95% CI)</th>
<th>Weight, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tetrahydrocannabinol (smoked)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abrams et al., 2007</td>
<td>13</td>
<td>25</td>
<td>3.43 (1.03-11.48)</td>
<td>6.51</td>
</tr>
<tr>
<td>Nabiximols</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GW Pharmaceuticals, 2005</td>
<td>54</td>
<td>149</td>
<td>0.86 (0.54-1.37)</td>
<td>19.02</td>
</tr>
<tr>
<td>Johnson et al., 2010</td>
<td>23</td>
<td>53</td>
<td>2.81 (1.27-6.50)</td>
<td>10.87</td>
</tr>
<tr>
<td>Langford et al., 2013</td>
<td>84</td>
<td>167</td>
<td>1.25 (0.81-1.91)</td>
<td>20.19</td>
</tr>
<tr>
<td>Nurmiikko et al., 2007</td>
<td>16</td>
<td>63</td>
<td>2.00 (0.81-4.96)</td>
<td>9.84</td>
</tr>
<tr>
<td>Portenoy et al., 2012</td>
<td>22</td>
<td>90</td>
<td>0.90 (0.46-1.76)</td>
<td>14.04</td>
</tr>
<tr>
<td>Selvarajah et al., 2010</td>
<td>8</td>
<td>15</td>
<td>0.63 (0.14-2.82)</td>
<td>4.63</td>
</tr>
<tr>
<td>Serpell et al., 2014</td>
<td>34</td>
<td>123</td>
<td>1.97 (1.05-3.70)</td>
<td>14.01</td>
</tr>
<tr>
<td>Subtotal</td>
<td>241</td>
<td>660</td>
<td>1.32 (0.94-1.86)</td>
<td>93.49</td>
</tr>
<tr>
<td>Overall</td>
<td>254</td>
<td>685</td>
<td>1.41 (0.99-2.00)</td>
<td>100.00</td>
</tr>
</tbody>
</table>

Odds indicate 30% or greater improvement in pain with cannabinoid compared with placebo, stratified according to cannabinoid. The square data markers indicate odds ratios (ORs) from primary studies, with sizes reflecting the statistical weight of the study using random-effects meta-analysis. The horizontal lines indicate 95% CIs. The blue diamond data markers represent the subtotal and overall OR and 95% CI. The vertical dashed line shows the summary effect estimate, the dotted shows the line of no effect (OR = 1).
Assessing / ranking the evidence

<table>
<thead>
<tr>
<th></th>
<th>Effectiveness</th>
<th>Appropriateness</th>
<th>Feasibility</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Excellent</strong></td>
<td>• Systematic review</td>
<td>• Systematic review</td>
<td>• Systematic review</td>
</tr>
<tr>
<td></td>
<td>• Multi-centre studies</td>
<td>• Multi-centre studies</td>
<td>• Multi-centre studies</td>
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<tr>
<td><strong>Good</strong></td>
<td>• RCT</td>
<td>• RCT</td>
<td>• RCT</td>
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<tr>
<td></td>
<td>• Observational studies</td>
<td>• Observational studies</td>
<td>• Observational studies</td>
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<tr>
<td><strong>Fair</strong></td>
<td>• Uncontrolled trials</td>
<td>• Descriptive studies</td>
<td>• Descriptive studies</td>
</tr>
<tr>
<td></td>
<td>with dramatic results</td>
<td>• Focus groups</td>
<td>• Focus groups</td>
</tr>
<tr>
<td></td>
<td>• Before and after</td>
<td></td>
<td>• Action research</td>
</tr>
<tr>
<td></td>
<td>studies</td>
<td></td>
<td>• Before and after</td>
</tr>
<tr>
<td></td>
<td>• Non-randomized</td>
<td></td>
<td>• Focus groups</td>
</tr>
<tr>
<td></td>
<td>controlled trials</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Poor</strong></td>
<td>• Descriptive studies</td>
<td>• Expert opinion</td>
<td>• Expert opinion</td>
</tr>
<tr>
<td></td>
<td>• Case studies</td>
<td>• Case studies</td>
<td>• Case studies</td>
</tr>
<tr>
<td></td>
<td>• Expert opinion</td>
<td>• Studies of poor</td>
<td>• Studies of poor</td>
</tr>
<tr>
<td></td>
<td>• Studies of poor</td>
<td>methodological quality</td>
<td>methodological quality</td>
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<tr>
<td></td>
<td>methodological quality</td>
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</tbody>
</table>

*Figure 1 Hierarchy of evidence: ranking of research evidence evaluating health care interventions.*
Our health care system today

Figure 1 | Health-care system today. The current health-care system has important shortcomings and inefficiencies. Insights from research are poorly managed, the available evidence is poorly used, and the care experience is poorly captured, resulting in missed opportunities, wasted resources, and potential harm to patients. Reprinted with permission from Best Care at Lower Cost: The Path to Continuously Learning Health Care in America (2013) by the National Academy of Sciences, courtesy of the National Academies Press, Washington, D.C.

Examples of EBM ‘gone wrong’ in AoD sector

- The ‘opioid wars’
- Baclofen for alcohol dependence
- Take home naloxone
- Medical cannabis
The ‘opioid wars’: Antagonists (rapid detox, implants & depot NTX)

• Rapid detox:
  • Promoted as major advance in treating ‘addicts’
  • Evidence: safety & cost concerns with no better outcomes

• Long-acting NTX products:
  • Evidence re: safety and effectiveness still emerging
  • No licensed products in Australia
  • In USA: poor uptake of Vivitrol (depot injection): expensive and ‘not that popular’
The ‘opioid wars’: heroin assisted treatment

- Evidence from RCTs suggests some role as second line treatment for those not responding to conventional treatment approaches
- Expensive to provide
- ‘Not that popular’
- No licensed products in most parts of the world.
Baclofen: the controversial pill that could 'cure' alcoholism
Baclofen for alcohol dependence

• Baclofen: a GABA-B agonist used to treat MS spasticity
• Popularised by French doctor’s own personal experience (Dr Olivier Ameisen “The Last Glass”)
• Widespread uptake across France, and promoted in parts of Australia despite
  (a) limited and conflicting evidence,
  (b) serious concerns re: safety;
  (c) no licensed indication or recommending guidance by authoritative bodies

• Meanwhile disulfiram, the medication shown to be most effective in treating alcohol dependence is largely ignored in Australian clinical practice.
Take home naloxone for at-risk opioid users

• Conventional evidence of safety / efficacy difficult to establish
• Consensus approach to evidence as a public health measure
• Barriers to uptake in Australia
  • Attitudes of health workers and opioid users
  • Regulatory & funding models for medication & service providers
  • A ‘prevention’ not a ‘treatment’ intervention: changing paradigms
• Yet to see the ‘enablers of practice change’ routinely seen in clinical change management (e.g. professional guidance, training, industry support)
Medical cannabis: a contemporary challenge to ‘EBM’

• Historical evidence of cannabis use as a medicine
• Preclinical evidence supportive of cannabinoids for many conditions
• High levels of positive patient reported experiences and outcomes
• Clinical trials: hampered by quality concerns

• Poor consensus on what the evidence is telling us
  • support in some quarters (community, politicians, industry, some clinicians)
  • resistance in others (medical establishment)
“FPM does not recognise a need for greater availability of medicines in general and in particular **does not endorse the use of cannabinoids in chronic non-cancer pain until such time as a clear therapeutic role for them is identified in the scientific literature.**”

“With the possible exception of pain and spasticity in multiple sclerosis, there is **little evidence for the effectiveness of cannabinoids in chronic non-cancer pain situations**, whether or not the pain attracts the descriptor “neuropathic”.”
Ware & Desroches (2014). *What does the practicing pain clinician need to know?*

“... the response ... that there is ‘not enough information’ is disingenuous at best, and at worst, an abnegation of clinical responsibility.”

“Careful consideration of cannabis use in pain medicine provides an opportunity to deepen and refine our pain-management toolbox, understand our patients’ needs and wishes, strengthen our relationships, and improve the quality of our care, while we wait for more long-term RCTs to provide more definitive evidence.”
Medical cannabis and the addictions
Could medical cannabis have a role in addiction treatment?

• Arguments against ...
  • Cannabis is an addictive harmful drug causing mental health, cognitive, physical and social harms
  • Prohibition must be upheld ... now is not the time to “go soft on the war on drugs”

• Arguments for ..... 
  • Research increasingly highlighting that many people use cannabis as a means of substitution from more harmful substances (e.g. heroin, alcohol, BZDs)
  • Many people with SUDs have a range of comorbidities for which cannabis may have potential benefits (e.g. chronic pain, sleep disorders, PTSD)
  • Medical cannabis is the ‘backdoor approach’ to drug law reform
Figure 2. Barriers to evidence uptake. Innovation and change in clinical practice at the individual, departmental, and institutional levels are contingent on 3 key sources of behavior change: knowledge, attitudes, and behavior. However, a series of complex barriers exists for each of these dimensions, some of which are illustrated here. Adapted from Cabana et al.33
Figure 1. A model for closing the evidence-to-practice gap. This schematic demonstrates 4 stages of moving from research to practice-altering outcomes. The first stage involves getting the evidence straight, illustrated by increasingly more applicable forms of information drawn from valid and important clinical research and represented in the 4S pyramid. The evidence-to-practice pipeline, also shown, reveals the dissipation of useful conclusions from clinical research, thus failing to make it into practice. The 3 remaining disciplines of knowledge translation can facilitate evidence uptake and help close the gap between research and practice. Adapted from Glasziou and Haynes. EBM, Evidence-based medicine; CQI, continuous quality improvement.
The goals of translation research

1. Changing practitioner behaviour in the direction of applying evidence-based interventions and strategies to patient care

2. Demonstrating improved patient outcomes
Translational research framework

Enhancing Translational research and EBM in Australian AoD sector

• Increasing our ability to conduct translational clinical research: Establishing a national clinical research network in AoD

• Developing the next generation of clinical information systems that enables data informed services and continuous improvement
Towards a national clinical research network in AoD

• To develop & conduct research that is informed by, and in turn impacts upon, clinical practice
• Research done ‘with’ - not ‘to’ patients and clinicians
• Identify relevant clinical research questions, research projects and have the network that allows multisite studies to occur
• Bring together relevant stakeholders:
  • Clinical services with research capacity
  • Consumers
  • Academics
  • Governments & other ‘purchasers’ of services
• Has the time come for a National Clinical Research Network?
• NSW D&A Clinical Research & Improvement Network established 2018
Clinical information systems: ‘data driven’ services

• Building systems that enable ‘real world’ and ‘real time’ data from clinical services
• Developments with electronic clinical information systems, computer power & data linkage is transforming service delivery in many sectors of health care
• Triangulation of patient, service and outcome level data.
<table>
<thead>
<tr>
<th>Data sources</th>
<th>Analytics</th>
<th>Applications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Administrative</td>
<td>Combined data sources into an analytical platform</td>
<td>Predicing risk and resource use</td>
</tr>
<tr>
<td>Clinical registry</td>
<td>Analytical methods (e.g. data mining, machine learning, traditional statistical methods)</td>
<td>Population management</td>
</tr>
<tr>
<td>Electronic health record</td>
<td></td>
<td>Drug and medical device surveillance</td>
</tr>
<tr>
<td>Biometric</td>
<td></td>
<td>Disease and treatment heterogeneity</td>
</tr>
<tr>
<td>Patient-reported</td>
<td></td>
<td>Precision medicine and decision support</td>
</tr>
<tr>
<td>Internet</td>
<td></td>
<td>Quality of care and performance measurement</td>
</tr>
<tr>
<td>Medical imaging</td>
<td></td>
<td>Public health</td>
</tr>
<tr>
<td>Biomarker</td>
<td></td>
<td>Research applications</td>
</tr>
</tbody>
</table>

Figure 2 | **Overview of big data analytics and applications.** Examples of the inputs (data sources) and outputs (analytical methods and applications) of big data analytics that can potentially improve cardiovascular quality and outcomes of care.
NSW Health AoD Clinical Outcomes & Quality Indicator (COQI) Project

- Opportunity of introduction of electronic clinical information system (eMR) across NSW Health AoD treatment services
- Identify and build ‘data items’ that are embedded in ‘routine care’ & enable outcomes and quality indicators to be examined
- Aims to address 2 key questions:
  - “Do patients get better” (Clinical outcomes)
  - “Did we deliver treatment well?” (Quality indicators)
Measuring Outcomes

• Combination of
  • Process measures (treatment completion, safety measures)
  • Patient and clinician reported outcomes
    • Change in substance use
    • Physical health, psychological health, quality of life
• Vary according to type of treatment service
  • Inpatient detox / counselling / resi rehab / methadone
Quality Indicators

• ‘Service level’ indicators: accreditation, incident reporting, systems to enhance staff and consumer engagement

• ‘Patient level’ indicators: PREMs

• ‘Episode level’ indicators: Clinical care standards identified:
  • Intake
  • Assessment
  • Global care plan
  • Managing risk (child protection, DV, homelessness, suicide, BBV ....)
  • Monitoring treatment outcomes over time
  • Transfer of care / discharge
How will we use our own data to inform practice?

- “What services are used and what are the outcomes for homeless clients attending our services?”
- “Do older clients have different health problems or treatment outcomes than younger clients?”
- “Who was treated with baclofen, naltrexone or disulfiram, and did it make any difference?”
- “How did the group of clients recruited to the RCT compare with clients in our service?”
The opportunity to become data informed services

The more you know, the harder it is to take decisive action.

Once you become informed, you start seeing complexities and shades of gray.

You realize that nothing is as clear and simple as it first appears. Ultimately, knowledge is paralyzing.

Being a man of action, I can't afford to take that risk.

You're ignorant, but at least you act on it.
Conclusions

• Services for clients with AoD problems are subject to ‘interference’ from a range of political and social forces, both patients and services must negotiate discrimination and stigma, and there is considerable nihilism in the community and amongst health providers regarding the role of AoD treatment

• We must get better at demonstrating our services provide EB interventions and result in positive client outcomes

• Translational research approaches require a shift in the relationship between clients, services and researchers

• The promise of a national clinical research network & ‘smart’ clinical information systems