EVIDENCE-BASED PRACTICE:
From Concepts to Reality

LINDA GOWING

A great and increasing challenge facing all practitioners, regardless of their discipline or background, is how to keep abreast of new research findings. This is particularly relevant in the AOD field as there have been substantial expansions in our scientific knowledge base over the past 10 to 20 years. There is growing pressure on the AOD workforce to function from an evidence-based perspective. This paper examines the basic concepts of evidence-based practice and some of the basic tools and techniques involved.

All clinicians would like to think that they are following best practice and that their practice is based on evidence. However, evidence-based practice means more than practicing with an awareness of research evidence. A widely accepted definition of evidence-based medicine is a *"conscientious, explicit and judicious use of current best evidence in making decisions about individual patients"* (Sackett et al, 1996). This is reflected in Figure 1, which depicts clinical decisions taking account of research evidence, clinical expertise and patient preference (Haynes et al, 1996).

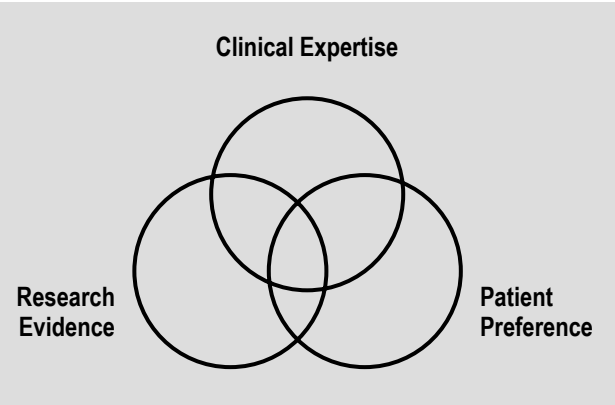

Figure 1: A Model for Evidence-Based Clinical Decisions

The concept of evidence-based practice is also applicable at a broader level of health care decision making.

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Silagy and Haines (1998) describe evidence-based health care as an approach that *"takes account of evidence at a population level as well as encompassing interventions concerned with the organisation and delivery of health care"*. This is reflected in Figure 2, which shows different types of evidence on the effects of care feeding into policies and health care decisions.

The consistent point with these models of clinical decisions and health care is that research evidence is a component of the decision-making process, but it is not the only component. Other aspects (clinical expertise, patient preference, needs, priorities and resources) are also important considerations. Nonetheless the models demonstrate that, if we are to achieve evidence-based practice, we need to incorporate research evidence into decisions.

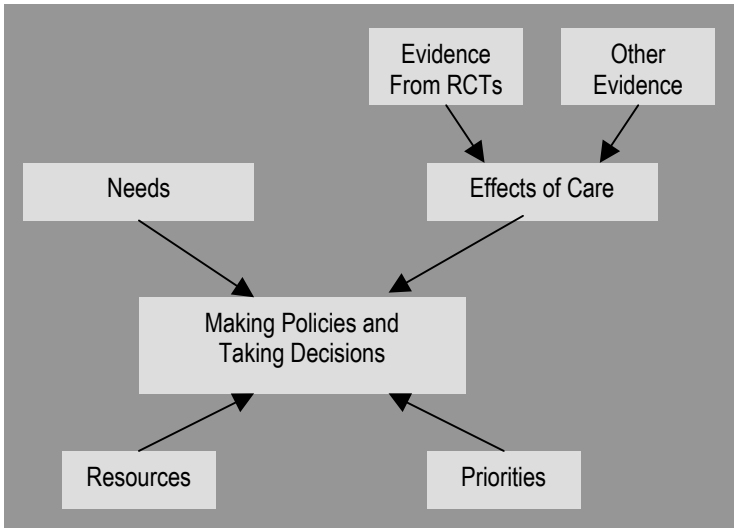

Figure 2: Evidence-Based Practice in Health Care

WHAT IS EVIDENCE?

The concept of incorporating research evidence into decisions seems simple, but complexities arise as soon as you start to consider what is meant by "research evidence". The above definition of evidence-based medicine refers to "judicious use of current best evidence". This raises questions of what is "current" and "best", how do we find it, and what sort of judgements need to be applied in using it "judiciously".

Then there is the sheer scale of research literature. It is estimated that there are 3,000 new medical articles published every day. Of these, 1,000 will be included in Medline and 46 will be randomised controlled trials. Furthermore, the volume of information has been steadily increasing. For example, in 1976 Medline contained 3,810 articles on hypertension, in 1996 there were 7,591. Clearly it is impossible for any one person, or even a small team of people, to monitor this volume of literature, let alone use it "judiciously".

This situation of information overload necessitates strategies that make good quality research evidence readily available. Hence promoting evidence-based practice entails:

- location of evidence
- critical appraisal
- synthesis of findings
- dissemination.

This paper focuses on two aspects - critical appraisal and synthesis of findings. Research on interventions for the management of opioid withdrawal will be used as an example to consider how the implementation of evidence-based practice can be limited by the realities of available research.

CRITICAL APPRAISAL

If we are to identify "best" evidence and use it judiciously, we must critically appraise the evidence, and not simply accept it on face value. Critical appraisal means considering research in terms of:

- quality (the methods used to minimise bias in a study design)
- relevance (the outcome measures used and the applicability of study results to other treatments, settings and patients)
- strength (the magnitude, precision and reproducibility of the intervention effect).

Levels of evidence (see Box 1 below) provide some indication of the degree to which bias has been eliminated by study design (NHMRC, 1999) but levels of evidence place a particular emphasis on whether participants were allocated randomly to study groups. While randomisation is an important measure for controlling bias, it addresses only one type of bias, namely selection bias.

Studies may be exposed to:

- selection bias (systematic differences in comparison groups)
- performance bias (systematic differences in care provided apart from the intervention being evaluated)
- attrition bias (differences in withdrawals from the trial)
- detection bias (systematic differences in outcome assessment).

Critical appraisal needs to consider the extent to which all of these sources of bias have been controlled for in the design and conduct of research studies. This means considering the use of random allocation (control of selection bias), blinding or masking of study participants and observers (control of detection bias) as well as assessing the way in which the study was carried out. It is also worth noting that there is currently vigorous debate about the emphasis that is placed on randomised controlled trials, and whether this emphasis is unreasonably detrimental to approaches such as comparative cohort studies and longitudinal studies which may be a more appropriate approach for investigating particular research questions. Interest in the use of alternative study designs is particularly marked in areas in which there are social and psychological dimensions to be considered in addition to clinical aspects of treatment, such as alcohol and other drug dependence.

Box 1
Levels of Evidence

I	Systematic review of RCTs
II	At least one properly designed RCT
III-1	Well-designed pseudo-RCTs
III-2	Comparative (non-randomised) studies with concurrent controls, case-control studies or interrupted time series with control group
III-3	Comparative studies with historical control, two or more single-arm studies or interrupted time series without parallel control group
IV	Case series, either post-test or pre-test and post-test

SYNTHESISING RESEARCH EVIDENCE

The development of the techniques of systematic reviews and meta-analysis has arisen from the need to summarise large amounts of research information concisely and accurately.

The strengths of systematic reviews are that they:

- use scientific strategies to limit bias
- summarise the accumulated state of knowledge
- highlight important unresolved issues
- gain power from combining multiple studies
- address questions in a timeframe not achievable through single studies
- quantify outcomes.

The systematic review process entails:

- precise formulation of the objective
- study retrieval and selection
  - inclusion/exclusion criteria
  - assessment of methodologic quality
  - assessment of combinability
- data extraction
- analysis.

Box 2
Definitions

- Systematic review - the application of scientific strategies that limit bias to the systematic assembly, critical appraisal, and synthesis of all relevant studies on a specific topic
- Meta-analysis - a systematic review that employs statistical methods to combine and summarise the results.

It is important to note that the review objective and the inclusion/exclusion criteria should be defined before searching for research evidence. This ensures objectivity in the preparation of systematic reviews, with studies being assessed on the basis of set criteria and not subjective judgements of what is "good" or "useful". Defining the review criteria before searching the literature means that it is possible that no literature will be found. This in itself is a useful finding if the objective of the systematic review has been defined on the basis of perceived clinical need or policy importance, as it identifies a significant gap in research.

The preparation of systematic reviews is a time-consuming process and is not something that everyone will want to embark upon. However, as with any form of evidence, it is important that you critically appraise systematic reviews before using the findings. To assess the quality of a systematic review you should consider:

- is it a review of randomised trials of the treatment you are interested in?
- does it include a methods section that describes how all the relevant trials were found?
- did the authors assess the trials' individual validity?
- were the results consistent from study to study?

THE COCHRANE COLLABORATION

The Cochrane Collaboration was established for the purpose of "preparing, maintaining and disseminating systematic reviews of the effects of health care". It was inspired by an English epidemiologist, Archie Cochrane:

> *"It is surely a great criticism of our profession that we have not organised a critical summary, by specialty or sub-specialty, adapted periodically, of all relevant randomized controlled trials."*

The work of the Cochrane Collaboration is undertaken through around 50 Collaborative Review Groups, supported by Cochrane Centres around the world (the Australasian Cochrane Centre is in Melbourne). For more information see http://www.cochrane.org.

The Drug and Alcohol Services Council, South Australia is associated with the Cochrane Drugs and Alcohol Group. The scope of this group is active interventions (prevention, treatment, rehabilitation) aimed at reducing the potential for harm or the actual harm directly related to the use of different dependence producing substances. Tobacco is excluded as this is covered by a separate collaborative review group. The coordinator of the Cochrane Drugs and Alcohol Group is based at the Agenzia di Sanita Pubblica Regione Lazio, Rome, Italy.

THE GOAL OF META-ANALYSIS

The power of a systematic review with meta-analysis is illustrated in the Cochrane review of nicotine replacement therapy (Silagy et al, 1998). A major outcome considered by the review, namely abstinence from smoking after at least six months of follow-up, is detailed in Box 3 below. The data combine the results of 88 separate trials. Meta-analysis enables this data to be condensed into a simple tabulation of outcomes for the different types of nicotine replacement therapy, and for any type of nicotine replacement therapy compared to placebo or no treatment.

However, meta-analysis is only valid where:

- the primary literature is of good quality (ie there is low risk of bias)
- heterogeneity in the response to treatment of the tested population is small and well understood
- interest centres on estimation of a specific, critical parameter of outcome (Bailar, 1995).

In the above meta-analysis of nicotine replacement therapy, these conditions are met by:

Box 3
Nicotine Replacement Therapy (NRT) for Smoking Cessation

Odds ratios (95% CI) for abstinence with NRT compared to control

• gum	1.63 (1.49 – 1.79)
• patches	1.73 (1.56 – 1.93)
• nasal spray	2.27 (1.61 – 3.20)
• inhaled nicotine	2.08 (1.43 – 3.04)
• sublingual tablet	1.73 (1.07 – 2.80)
• all NRT	1.71 (1.6 – 1.8)

- limiting the review to randomised controlled trials that compared nicotine replacement therapy with placebo or no treatment, or different doses of nicotine replacement therapy
- undertaking subgroup analyses to explore heterogeneity (the effect of setting, intensity of additional support and the severity of dependence)
- defining the major outcome as abstinence of smoking after at least six months follow up with biochemically validated rates wherever possible.

OPIOID WITHDRAWAL LITERATURE: A CASE ILLUSTRATION OF EVIDENCE-BASED PRACTICE

The meta-analysis from the Cochrane review of nicotine replacement therapy prepared by Silagy et al (1998) is the sort of outcome that we would have liked to achieve for the management of opioid withdrawal. However, in attempting to achieve this goal, we encountered a range of limitations. These are discussed in this section, on the basis of the three aspects of meta-analysis validity identified above.

Study Quality

Systematic searching of the research literature resulted in the identification of a total of 716 references relating to opioid dependence and withdrawal. Of these:

- 110 were randomised controlled trials
- 54 were non-randomised controlled trials
- four were crossover studies.

Hence, controlled studies (of all types of intervention) constitute less than one quarter of the research literature. Furthermore, studies generally used small group sizes meaning they were also exposed to random error.

Sources of Heterogeneity

1. Treatment Regimens

There is considerable diversity in the type of treatment regimens used to manage opioid withdrawal. The use of placebo or no-treatment comparisons is rare, and probably unethical - in the absence of active treatment, opioid dependent people undergoing withdrawal rapidly develop marked symptoms, become distressed and either drop-out or are transferred to active treatment. Either way, the use of placebo or no-treatment comparisons is untenable, meaning that most studies now compare different active treatment regimens. This in itself is not problematic except that the diversity of treatment regimens extends to both experimental and control arms of studies. Adjunct treatments (pharmacological and psychosocial) are also variable and often not documented in detail. This diversity in approach complicates attempts to combine the findings of multiple studies.

The main types of treatment regimen used for the management of opioid withdrawal are:

- reducing doses of opioid agonist (usually methadone)
- symptom amelioration with α_2-adrenergic agonists (mainly clonidine, but with increasing use of lofexidine)
- induction of withdrawal with opioid antagonists (naloxone or naltrexone), sometimes in conjunction with heavy sedation or anaesthesia
- symptom amelioration with buprenorphine.

These approaches formed the basis for the preparation of four Cochrane reviews on the management of opioid withdrawal.

2. Treatment Setting

There are no studies that compare identical treatment regimens delivered in inpatient and outpatient settings. Therefore, to gain some idea of the impact of setting we combined data from all studies (including single group studies) where groups of participants were treated entirely in either an inpatient or an outpatient setting, using either reducing doses of methadone, or clonidine to manage withdrawal. This produced the data shown in Box 4. Because of the method used to calculate the completion rates, the data is subject to bias, making the accuracy of the calculated rates uncertain.

Box 4
Effect of Treatment Setting on Completion of Withdrawal

Regimen	Completion Rate	
	Inpatient	Outpatient
Methadone	78% (n=740)	31% (n=1,144)
Clonidine	70% (n=663)	52% (n=842)

Nonetheless it indicates that rates of completion of withdrawal are consistently higher when withdrawal occurs in an inpatient, compared to an outpatient, setting. Hence the treatment setting is a source of heterogeneity that needs to be considered when combining the findings of multiple studies. However, there are insufficient follow-up data available to form a view on how long the advantage offered by inpatient treatment is maintained.

3. Drug of Dependence

There are very few studies that compare withdrawal according to the main drug from which participants are withdrawing. Consequently, the data shown in Box 5 are again derived by combining data from all studies where there were participants identified as withdrawing from either heroin or methadone, with withdrawal managed with either reducing doses of methadone or an α_2-adrenergic agonist (usually clonidine or lofexidine). As with the analysis of the impact of treatment setting, these data are also subject to bias making the accuracy of the calculated completion rates uncertain. However, these data again indicate that the nature of the drug from which participants are withdrawing affects the rate of completion of withdrawal and is another source of heterogeneity to be considered in any meta-analysis.

The data indicate that completion of withdrawal is somewhat more likely for people withdrawing from methadone, compared to heroin. This is despite evidence that withdrawal from methadone is more severe and more prolonged than withdrawal from heroin. This would be expected to reduce, not increase, the likelihood of completion of withdrawal.

Box 5
Effect of Drug of Dependence on Completion of Withdrawal

Regimen	Completion Rate Heroin	Methadone
Methadone	36% (n=578)	55% (n=563)
Adrenergic agonist	58% (n=572)	73% (n=410)

People withdrawing from methadone may have been obtaining methadone illicitly, have been prescribed methadone for a short period of time (a few days to a few weeks) in preparation for detoxification, or they may have been receiving methadone maintenance treatment.

Participation in methadone maintenance treatment would be expected to help people to stabilise in health and social terms and hence to be better prepared for withdrawal. It seems likely that it is the impact of methadone maintenance treatment that is resulting in the higher rates of completion for withdrawal from methadone, compared to withdrawal from heroin. It would be of interest to confirm whether this is the case, but there are insufficient data available to investigate this issue further.

Outcome Indicators

1. Completion of Withdrawal

Withdrawal occurs when the drug of dependence is eliminated from the body, and any physical adaptation that has occurred as a consequence of dependent drug use is reversed. Detoxification entails the provision of interventions to ensure that withdrawal can be completed with safety and comfort.

Because detoxification addresses only the physical adaptation, and not the social dimensions of dependence, detoxification is not in itself a treatment for dependence (Lipton and Maranda, 1983; Mattick and Hall, 1996). Rather, detoxification is generally regarded as a necessary stepping stone to drug-free treatment. Given this, it is questionable whether completion of withdrawal constitutes a specific, critical parameter of outcome. Indeed, it could be argued, on the basis of detoxification being a stepping stone to treatment, that a more appropriate outcome indicator would be engagement and retention in further treatment. However, engagement and retention in further treatment is very rarely used as an outcome indicator. Of the studies we assessed, 78% included no information on post-detoxification outcomes. Only 3% had some information on the nature of post-detoxification treatment and 18% included information on drug use at follow-up (most

commonly one month after detoxification). Consequently we were forced to accept completion of withdrawal as a significant parameter of outcome.

Assessing completion of withdrawal is also problematic. The definition of completion varied between studies (see Box 6) with the result that differences between studies can often, in part, be attributed to differing definitions. The best indicator of completion would be a combination of subsidence of withdrawal signs and symptoms and objective confirmation that drug use has ceased. As this was rarely possible we were forced to accept whatever was stated by authors as the number of study participants who had completed withdrawal.

2. Severity and Adverse Effects

The stated aim of detoxification services is generally to ensure that withdrawal can be completed in safety and comfort. Hence withdrawal severity and the occurrence of adverse events are important outcomes to consider when comparing different approaches to the management of opioid withdrawal.

There was huge diversity in methods of assessment and reporting of withdrawal severity. We identified more than 70 different rating scales for the 151 references that used at least one. This diversity complicated the comparison of findings from different studies, and generally made meta-analysis of withdrawal severity impossible.

Box 6
Defining Completion of Withdrawal

	Studies
Urine screening	14%
Naloxone challenge	8%
Maintenance dose naltrexone	7%
Signs and symptoms	8%
Scheduled discharge	17%
Prescription of medication	7%
Subjective or not defined	39%

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