Addiction Treatment Research NEWS

NEWSLETTER OF THE ADDICTION TREATMENT RESEARCH INTEREST GROUP

June 2012 ISSN 1177-8083 Vol 16 No 2

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MESSAGE FROM THE ATRIG CHAIRPERSON

I would like to use my space in this edition of the ATRN to promote the initiatives of the Addiction Treatment Research Interest Group (ATRIG) and the addiction research field more widely by endorsing a couple of events that are occurring over the next few months.

The first is the Cutting Edge Conference, the national addiction treatment conference. This year the theme is Cutting Edge - 20/20: both the vision and the thinking for planning our services in 2020 and will be held at the Convention Centre, Wellington in September. So not only do I want to promote a great opportunity for hearing about addiction initiatives from both formal presentations and informal networking, but I would also like to encourage and promote the Addiction Treatment Research Interest Group. ATRIG is an incorporated society set up in 1996 to:

- To foster interest in scientific research on treatment of people with addiction related problems in Aotearoa/New Zealand;
- To disseminate and promote research findings related to effective treatment of people with addiction related problems in Aotearoa/New Zealand;
- To support the development of improved treatment services for people with addiction related problems in Aotearoa/New Zealand.

With this in mind, ATRIG is again supporting the Young Researcher's Award. This award is for the best oral or poster research presentation by a young or emerging presenter. Now to the clinicians out there who don't deem themselves to be academics – please don't get scared off by this. It really is an opportunity for you to showcase your work, with a research slant to it. Whilst the call for abstracts has gone out there may be an opportunity for a dedicated research stream in which we can foster that interest and work to disseminate and promote effective treatment findings. For more information on this, call or email Catherine Lowry Hanlon of Waitemata DHB (Catherine.Lowry-Hanlon@waitematadhb.govt.nz) or myself (Klare.braye@matuaraki.org.nz) and we can fill you in on any details.

The conference is also the time for the ATRIG AGM. And while AGMs don't typically inspire attendance or interest, if you are at all interested in the research field this is a really good opportunity to meet those of a like mind and find out more about us.

The other venture that I would like to push is the next Addiction Research Symposium. This was initiated by the University of Auckland in 2010, and was subsequently held in Christchurch in 2011. The next symposium is planned for Wellington prior to Cutting Edge. Its aims are to:

- Provide a forum for New Zealand addiction researchers to meet and share their work
- Provide an opportunity for research students (PhD, Masters) to present and be supported by more experienced colleagues
- Allow for focused discussions on issues of common interest to addiction researchers, including potential collaborations.

Again, this is a great opportunity to share your research, promote your findings, pick the brains of others or simply find out more about the addiction research field.

If you want to find out how you can be more involved or what it is about, please feel free to contact anyone on the ATRIG executive and we will be more than happy to try and answer your queries.

Klare Braye
ATRIG Chairperson

ABACUS REPORT

What works best? A guide for best problem gambling therapy

"Better a diamond with a flaw than a pebble without".
Confucius

Treatment of problem gambling in New Zealand essentially commenced in the early 1990s with the funding of the Gambling Helpline, followed quickly by the offer of face-to-face therapy to meet the sudden demand for this 'new' problem. Twenty years on, problem gambling treatment is widespread, with a range of approaches adopted to address what is now accepted as a mainstream addiction. There is a greater understanding of the harm to families and society as a whole that problem gambling causes, with the federal Australian Productivity Commission estimating that 1% of problem gamblers in Australia contribute 41% of the total gambling expenditure (Productivity commission, 2010).

In New Zealand, there has been a recent focus on aligning addiction treatments, and integrating the treatment of problem gambling with coexisting mental health problems. As with substance addictions, problem gamblers are more likely than non-problem gamblers to report a range of other mental health problems during their lives (Petry et al., 2005). A recent meta-analysis of the prevalence of mental health disorders with coexisting problem gambling identified high coexistence of nicotine dependence (60.1%), (other) substance use disorder (57.5%), mood disorders (37.9%), and anxiety disorders (37.5%) (Lorains et al., 2011). This high correlation, whether these disorders and the problem gambling are independent or related, has formed the consensus by treatment providers that effective treatment must take into account the presence of such coexisting mental health problems (Winters & Kushner, 2003). This is also influenced by the finding that where such coexisting mental health problems are present, the problem gambling problems will be more severe than where problem gambling alone is present (Stinchfield et al., 2005).

Current treatment approaches in NZ

Since the passing of the Gambling Act in 2003, there has been a greater standardisation of screening tools used for presenting problem gamblers and their families, and the recording of data enabling profiles of these clients to be

drawn. The coexisting problem (CEP) screens used in gambling assessment suggest that there is a need to address coexisting issues alongside those of problem gambling.

Despite the need for evidence-based support for best practice treatment, little research has been conducted worldwide specifically upon treatment approaches where such problem gambling and other mental health problems coexist (Problem Gambling Research & Treatment Centre, 2011). The vast majority of treatment research focuses only upon the problem gambling. Yet the New Zealand adoption of the broad addiction and coexisting problem (CEP) strategy has strong face validity, and the support of addiction clinical and expert opinion (Todd, 2010).

An Australian guideline for PG treatment

Recently, Monash and Melbourne Universities published evidence-based guidelines for the screening, assessment, and treatment of problem gambling (PG), using evaluation criteria from the National & Medical Research Council (Problem Gambling Research & Treatment Centre, 2011). This guideline for PG treatment is an important development for the field, and is the first for both Australia and New Zealand (although evaluation of services has previously occurred) (AUT Gambling & Addictions Research Centre, 2009).

Elusive evidence for screening and assessment

However, despite an extensive review of research, no evidence-based recommendations could be made for either screening or assessment of PG, and only consensus-based (clinical and expert support where insufficient evidence) support could be made for these topics. Within this limitation, the panel recommended the screening for PG in primary care settings of those presenting with (other) mental health problems. A practice point offered to practitioners is that those presenting with anxiety disorders, depression (assess for suicidal ideation), alcohol or other drug dependence, impulse control disorders, personality disorders and family violence, could also be advantageously screened for PG.

This may in practice be less likely as many of these conditions or issues appear to be risk factors for each other, and PG may be considered to be less prevalent and less 'mainstream' than these issues. One NZ answer may be regular screening of all primary care clients using the Case-finding & Help Assessment Tool (CHAT) (Good-Year, 2008) screen, which covers all these risk factors (other than personality disorders, which appear to be under review anyway) (APA DSM-V).

Evidence for treatment

Potential levels of support raised in the Guideline could vary according to strength, ranging through A (evidence can be trusted to guide practice), B (trusted in most situations), C (some support but care should be taken) and D (evidence weak and apply with caution). There are seven recommendations made for treatment approaches, all applying either levels B or C.

Both CBT and MI were recommended to reduce gambling behaviour and its severity, with CBT also supported for coexisting psychological distress. Practitioner-delivered psychological interventions were also recommended, compared with self-help manuals, or a control group. Evidence level of B was applied for each of the three – 'body of evidence can be trusted to guide practice *in most situations'*.

Group psychological interventions for PG were also recommended to reduce PG behaviour or severity, albeit with a reduced level of C – '*some support but care should be taken*'.

The use of anti-depressant medications alone were not recommended to reduce gambling severity (recommendation level B), with the finding that these, from the evidence, indicated that they were no better than placebos. However, a notation was given that this recommendation was based on studies without CEP, such as depression and anxiety, and mainly SSRI antidepressants. In light of research suggesting most PGs will be affected by CEP, some care may need to be taken in this conclusion.

The final recommendation was that naltrexone could be used to reduce PG severity (recommendation level C) and that further research should be considered. This opioid antagonist is not funded in Australia or NZ for this purpose, but is used with some success in alcohol and opioid interventions.

Conclusions for NZ

While not demonstrating strong conclusions, the Australian research is a welcomed example of a systematic, comprehensive review of the available evidence upon which to base future PG treatment directions. The conclusions may not be surprising, but they do suggest there is support for treatment approaches that are amongst more widely used NZ therapies. Motivational Interviewing is widely used in NZ PG interventions, and while support exists for CBT, fewer opportunities exist here for training. Currently in NZ, PG practitioners can elect their psychotherapeutic intervention, with few services requiring specific approaches.

The Australian findings may provide a useful guide for future treatment directions for PG, even though the limited and sometimes mixed research has not enabled strong recommendations to be made for this developing field of treatment. Fortunately, the strong NZ acceptance of Motivational Interviewing for PG treatment appears to be on the right track.

Sean Sullivan
Abacus Counselling Training & Supervision Ltd

Please contact editor for full list of references – ria.schroder@otago.ac.nz

IBOGAINE – OPENING THE DOOR TO POSSIBILITY

The discussion regarding ibogaine in addiction treatment in New Zealand has recently gained momentum. Medsafe's 2010 gazetting of the psychotropic plant derivative as a non-approved prescription medicine, under Section 25 of the Medicines Act 1981, has further animated this debate. New Zealanders have been made aware of ibogaine through entertainment media (e.g. *Law and Order: SVU* Season 11 Episode 7) and New Zealand websites (e.g. http://ibogaine.org.nz). For the treatment sector the New Zealand Drug Foundation (NZDF) has previously voiced concerns over ibogaine (Scoop Independent News, 2009). Subsequently a broader analysis by the NZDF presented both pros and cons of treatment (NZDF, 2011). At least one scholarly discussion of these issues has been presented in a New Zealand healthcare journal (Galea et al., 2011), with those authors likewise urging caution.

A psychoactive indole alkaloid present in the West African shrub *Tabernanthe iboga*, ibogaine has been recognised for addiction-interrupting and psychotherapeutic qualities (Lotsof, 1995; Popik et al., 1995; Naranjo, 1969). Its administration, principally to facilitate rapid detoxification for opioid dependence, is garnering greater attention in academic literature; for example Alper et al. (2008) report on ibogaine's use in 3414 cases up to 2006. Pre-clinical and Phase I human trials have provided evidence of ibogaine's efficacy and its principal metabolite's (noribogaine) in attenuating opioid withdrawal (Mash et al., 2000; Mash et al., 2001). This is reflected in anecdotal evidence, e.g. Alper et al. (1999) note a case series where 76% of 33 heroin-dependent patients in withdrawal showed no symptoms at 24 and 48 hours post-treatment. Attenuation of craving post single-dose treatment is also commonly reported. Mash et al. (2000) observe that in their study of 27 opioid and cocaine-dependent subjects, participants self-reported significant ($p < .05$) reductions in opioid craving across all five subscales of the Lower Heroin Craving Questionnaire (HCQN), immediately post-treatment and after 14 days. While the reduction of withdrawals and cravings are prominent clinical phenomena, ibogaine's psychotropic effects are also of significance, with individuals reporting powerful dream (oneiric) and evaluative states lasting several hours, which are claimed to provide insight into one's reasons for drug use or other issues (e.g. Naranjo, 1969). Galea et al. (2011) also note the potential for a residual stimulation stage potentially lasting up to 72 hours following ingestion.

Nonetheless, there do remain concerns over safety. Animal studies show the potential for neurotoxicity with damage to cerebellar Purkinge cells observed in rats (O'Hearn & Molliver, 1993; O'Hearn et al., 1993), albeit beyond typical therapeutic dosages of between 5-25 mg/kg (Popik et al., 1995; Mash et al., 2000). Moreover, nineteen deaths occurring up to 72 hours following treatment have been reported between 1990-2008 (Alper et al., 2012). However, rather than neurotoxicity, evidence from this latter study implicated advanced pre-existing medical comorbidities (particularly cardio-vascular) in being associated with mortality. Other risk factors included seizures due to alcohol and benzodiazepine withdrawal, and the uninformed or inexperienced use of this indigenous ethnopharmaceutical beyond its traditional context (Alper et al., 2012).

Thus, there appear clear grounds for concern where ibogaine therapy might be proposed and yet optimism on the part of potential beneficiaries of treatment, as well as some researchers, clinicians and potential treatment providers. Indeed, the documented enthusiasm of the ibogaine 'underground' (see e.g. Alper et al., 2008) may well have been a factor prompting Medsafe to formalise New Zealand legislation dealing with ibogaine. This was initiated in November 2009, following Medsafe's receipt of a number of enquiries about importing ibogaine into New Zealand (Medsafe, 2009). In gazetting ibogaine as a prescription medicine, Medsafe's Medicines Classification Committee compared the drug's putative harms against perceived benefits. While noting concerns over fatalities, data provided to the Committee suggested "that the number of deaths due to methadone, the most controlled substance, were a little higher that those associated with ibogaine, which is unregulated" (Medsafe, 2009). When considering this along with ibogaine's limited potential for recreational abuse, e.g. expense and negative side effects including nausea, vomiting, diarrhoea and ataxia, the Committee decided that a medically controlled pathway to treatment would further limit the dangers of lay access, thereby reducing harms overall while retaining therapeutic advantages.

Certainly the potential for harm to result from treatment is a concern for physicians approached to prescribe ibogaine. One might argue, however, that after due diligence regarding ibogaine treatment has been done by a physician, to not support an individual in their desire for treatment could also result in exposure to avoidable risks.

Those dependent on opioids are constantly facing harms, these being both acute, e.g. risk of overdose, or chronic, e.g. exposure to blood borne viruses (HCV or HIV), vein and other damage associated with long-term injecting, problems with legal authorities and general lifestyle (poor nutrition, exposure to crime, poverty). Broadly, opioid using populations, whether in treatment (e.g. OST) or not, suffer greater mortality than the general population, with death rates exceeding ten times that of non-users (Bargagli et al., 2006). While those in treatment fare better, both groups are at risk of overdose, a common cause of death (Degenhardt et al., 2010). In New Zealand the most common drug associated with overdose, both in treatment and outside of it, is methadone (Reith et al., 2005; Rix-Trott, 2011).

As with so much in the field of addiction treatment, the above presents an array of options and some difficult choices. Medsafe's decision reflects this and while it may have created yet further complexity where clinicians are concerned, it has also opened the door to opportunity. Here one option concerns the possibilities for research. While not unique, by allowing medically supported treatment the New Zealand legislation does provide a rare chance to collect data on ibogaine's efficacy. The significant lack of outcome data for ibogaine treatment no doubt contributes to clinicians' wariness regarding use of the drug as a treatment option. An appropriately undertaken outcomes study may contribute to the limited body of knowledge about ibogaine, thereby facilitating clinical decisions and the development of a further string to the bow of addiction treatment.

Finally, just as the new legislation has made prescribed treatments an option and prepared the ground for much needed research, it also implies the presence of treatment providers. Ibogaine's long-lasting psychotropic and related physical effects (e.g. ataxia) require an extended period of closely monitored care by appropriately experienced personnel. It would seem unlikely that prescribing physicians could be in attendance throughout the duration of a treatment. This suggests the need for a close association between physicians and treatment providers, with open communication and professional backing, i.e. the medically supported treatment model presumably envisaged by Medsafe. One might hope the nurturing of these relationships would extend to developing national guidelines for treatment, informed by clinicians, experienced ibogaine treatment practitioners and consumer advocates.

Geoff Noller
Independent Researcher
Substance Use and Policy Analysis
Dunedin

In 2011 Geoff Noller received funding to carry out an observational study of ibogaine treatment outcomes for opioid-dependent individuals. The study gained final ethical approval in February 2012.

Please contact editor for full list of references – ria.schroder@otago.ac.nz

I'VE BEEN READING …

Oxycodone:

This article is a summary of a presentation I made at Cutting Edge and NAOTP in 2011.

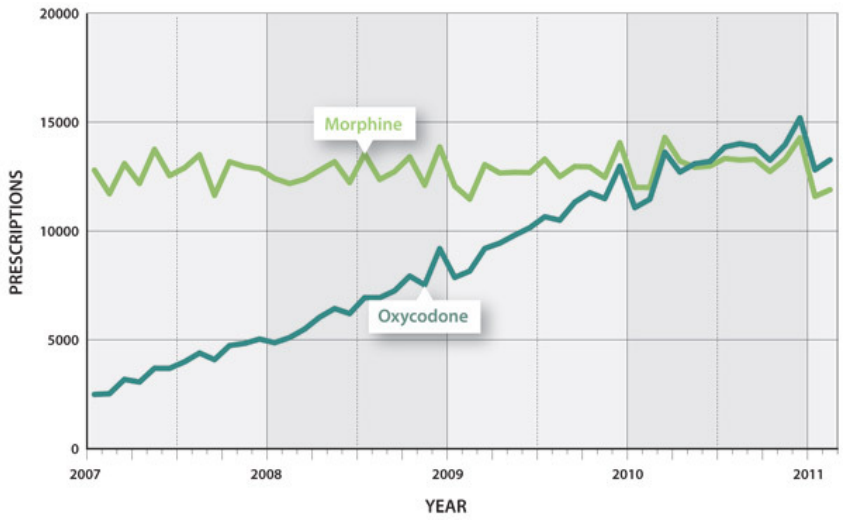
Background:

Oxycodone is a potent opiate analgesic that is rapidly changing the landscape of opiate prescribing in this country. In the USA there has been a marked rise in oxycodone prescribing, which has worryingly resulted in a corresponding increase in opiate-related overdose and death. Indeed, the number of deaths from prescribed opiates in the USA now exceeds that due to cocaine and heroin. The same prescribing pattern and subsequent rise in emergency department presentations with overdose has now been witnessed in Australia (Dobbin, 2011) and prompted the publication of a "Prescription Opioid Policy" in 2009 by the combined Australian Colleges of Physicians, General Practitioners and Psychiatrists (The Royal Australasian College of Physicians, 2009).

The emerging picture of oxycodone prescribing in New Zealand appears to be following a similar pattern, raising concerns that a rise in oxycodone related deaths will surely follow. Interestingly, analysis of the rise in oxycodone prescribing in NZ by BPAC shows it has ***not*** been matched with a commensurate drop in morphine prescribing, which suggests that a new cohort of patients has been created (BPJ, Nov 2009). This trend is at variance with published advice from Medicine's Control and BPAC (BPJ, Nov 2009; BPJ, June 2009), which recommend using oxycodone only as a second choice agent after morphine in patients with significant renal impairment (GFR < 40) or previous intolerance to morphine. The preference for oxycodone among prescribers is somewhat puzzling in the light of this advice, especially when one considers it is no more effective than morphine.

Oxycodone:

Although they are very similar, there are some important differences between oxycodone and morphine. Firstly, oxycodone is twice as strong in terms of milligram dose i.e. 10mg oxycodone = 20 mg morphine. Secondly, it is twice as expensive as morphine. Thirdly, it appears to have greater abuse potential because it is more easily injected than morphine, it is readily smoked, and (anecdotal reports suggest) it has a more euphoric effect than morphine. These are characteristics in common with heroin. One advantage of oxycodone is its greater safety in patients with *significant* renal impairment (GFR < 40), where use of morphine can lead to accumulation of morphine metabolites and overdose.



So why is this happening ?

1. "Honey Moon Phase"
   Every new medication that arrives on the market goes through an initial popular phase with prescribers, and oxycodone is no exception. Doctors have a strong desire to keep up to date, and there is an inherent assumption that newer medications will be safer and more effective than existing ones. However, this does not always prove to be the case, and there have been many instances in the past where longer term problems and side effects have become apparent down the track and caused a U turn in prescribing (e.g. HRT, calcium supplements, Selegiline in Parkinson's Disease). Oxycodone may be another such example.

2. Effective Marketing
   Without doubt the pharmaceutical manufacturer of oxycodone (Mudipharma) has waged a very effective marketing campaign to establish oxycodone's impressive market share. They have emphasised its advantage in renal impairment, yet this only really applies to a small number of patients (GFR<40). Case presentations used in the company's promotional material typically involve people with osteoarthritis in their 60s, yet the use of strong opiates for this condition has traditionally rarely been indicated or appropriate. In fact, the use of strong opiates in *any* chronic non-malignant pain should be avoided. It is noteworthy that there are ***no*** longitudinal RCTs on the long-term effectiveness and consequences of opioid use in chronic non malignant pain (The Royal Australasian College of Physicians, 2009).

3. Lack of Resources
   Managing patients with chronic pain is a challenge for any doctor, and requires a great deal of time and effort to grapple with the complex problems involved. GPs in particular lack ready access to the resources required. Physiotherapists, psychologists and occupational therapists are expensive in the private sector and hard to access in the public system, where specialist multidisciplinary pain teams struggle to cope with the demand.

4. What's in a Name ?
   It is my opinion that the name "oxycodone" has itself played a part in this drug's popularity. Patients (and perhaps some doctors) may not appreciate the drug is as powerful (in fact twice as powerful mg for mg) as morphine because the name bears a resemblance to codeine. This contrasts with the term "morphine" which has very strong connotations that immediately arouse concern for doctor and patient alike regarding overdose and addiction, in a similar way to the word 'heroin'.

And Another Thing … COST !

Oxycodone is twice as expensive as morphine. Total expenditure on oxycodone increased between 2009 to 2010 by more than one million dollars. First funded in NZ in 2005, oxycodone expenditure has now surpassed morphine:

Cost of morphine 2010	$ 3,235,862
Cost of oxycodone 2010	$ 5,167,500

Considering it is twice as expensive, yet no more effective than morphine, it is uncharacteristic that PHARMAC decided to fully fund oxycodone. It is unclear why oxycodone was not reference-priced to morphine, with a part charge passed on to the patient, as has been done in the past with other new medications. Another strategy PHARMAC elected not to use was to create a Special Authority mechanism to limit oxycodone use to patients with renal impairment or documented previous intolerance to morphine. PHARMAC's rationale for funding oxycodone was to provide an alternative to morphine, which is reasonable. A similar case could be made to fund buprenorphine to provide an alternative to methadone.

What to do?

My message to anyone about to prescribe oxycodone is first STOP and THINK, have I exhausted the alternatives? Consider:

- non-pharmacological interventions (activity programmes, psychologist etc.)
- referral to multi-disciplinary pain team
- referral to musculoskeletal, orthopaedic, rheumatology specialists
- non-opiate medications (NSAID, Tramadol, TCA, Gabapentin)
- weaker opiates (codeine, transdermal Buprenorphine)

Check for "red flags":

- past history of addiction/substance abuse disorder
- family history of addiction/substance abuse disorder
- Hep C (strongly indicates past intravenous drug use)
- aberrant behaviour

Remember the principle of 'Universal Precautions', as not all risks are apparent and any patient prescribed opiates may develop addiction problems, not just those with obvious red flags (Darke, 2011). Medication can also be diverted or stolen and ultimately end up in the wrong hands.

Obtain a second opinion before prescribing a strong opiate for chronic non-malignant pain. Ideally seek advice from a pain specialist, but even one's peers can provide good guidance. It may also be medico-legally prudent to document that proper consideration has been given.

Have a full discussion with the patient to clarify the goals of treatment and, crucially, ensure that the patient's expectations are realistic (the pain is, after all, very unlikely to be cured). A patient contract is useful to spell out the dose and dispensing arrangements, and when and how treatment will be reviewed and/or terminated.

If a strong opiate must be prescribed, PRESCRIBE MORPHINE. This should be the first choice unless the patient has significant renal impairment (GFR < 40) or has previously been intolerant of morphine.

Finally, if oxycodone is required, rather than tell the patient it's "like morphine", try saying it's "like heroin".

Dr Alistair Dunn
Northland Addiction Service

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Addiction Treatment Research News is the official newsletter of the **Addiction Treatment Research Interest Group (ATRIG).**

ATRIG was established in 1997 to promote research in the addiction treatment field in New Zealand.

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- To disseminate and promote research findings related to effective treatment of people with addiction related problems in Aotearoa NZ.
- To support the development of improved treatment services for people with addiction related problems within Aotearoa NZ.

The **executive committee** are:
Klare Braye (Chairperson), Simon Adamson, Janie Sheridan, Robin Shepherd, Ria Schroder (ATRN Editor), Catherine Lowry-Hanlon, Lindsay Atkins (Secretary)

Please direct **enquiries to**
Lindsay Atkins,
ATRIG Secretary
PO Box 4345,
Christchurch 8140
Phone (03) 364 0480,
Email: lindsay.atkins@otago.ac.nz

Contact Person for ATRN:
Ria Schroder
Ph: 03 364 0480
Email: ria.schroder@otago.ac.nz

ATRN is the official newsletter of the Addiction Treatment Research Interest Group (ATRIG)

ATRIG is sponsored by
The National Addiction Centre
Dept of Psychological Medicine
University of Otago, Christchurch
Enquiries to Lindsay Atkins
ATRIG Secretary
PO Box 4345
Christchurch 8140

Phone: 03 364 0480
Fax: 03 364 1225
www.addiction.org.nz

Addiction Treatment Research Interest Group (ATRIG)

MEMBERSHIP/RENEWAL FORM

Please note all individuals wishing to be a member of ATRIG must join by completing this form regardless of current membership status.

Membership in ATRIG entitles you to the following:

- three issues of the Addiction Treatment Research News via email
- membership in the ATRN email discussion group

PLEASE ENROL ME AS A MEMBER OF ATRIG (ADDICTION TREATMENT RESEARCH INTEREST GROUP). I HAVE READ AND SIGNED THE DECLARATION BELOW.

Surname _____ First Names _____

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(NB - You must provide an email address if you wish to receive a copy of ATRN)

The objectives of ATRIG are:

- *To foster interest in scientific research on treatment of people with addiction related problems in Aotearoa New Zealand.*
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- *To support the development of improved treatment services for people with addiction related problems in Aotearoa New Zealand.*

Declaration

I support the objectives of ATRIG and wish to be a member of ATRIG for the 2012 calendar year. I understand membership fee is $20.

Signed _____ Date _____

Please make cheques payable to: ATRIG

I am interested in participating in an email discussion group around ATRN ☐

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