Psychiatry and Behavioural Disorders Research Review™

Making Education Easy

Issue 1 2014

In this issue:

Abbreviations used in this issue:

ADD = attention deficit disorder
ADHD = attention deficit/hyperactivity disorder
CBT = cognitive-behavioural therapy
CGI = Clinical Global Impression
OCD = obsessive-compulsive disorder

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Welcome to a combined review of Psychiatry and Behavioural Disorders Research Review.

This issue will review papers from each discipline, with Associate Professors David Menkes and Wayne Miles commenting on psychiatry papers, while Dr Craig Immelman and Giles Bates provide commentary on behavioural disorders.

A large study published recently in the *BMJ* has reported finding that several anxiolytic and hypnotic medications are linked to an increased risk of death. This adds to the evidence that these drugs must be used with care and preferably for as short a time as possible.

In a European clinical trial, an oral preparation of lavender oil was associated with anti-anxiety and antidepressant effects, as well as improvements in general mental health and health-related quality of life in patients with generalised anxiety disorder. Moreover, this natural medication appeared to be as effective as paroxetine, without the unwanted sedative or drug-specific effects commonly reported with benzodiazepines and selective serotonin reuptake inhibitors/serotonin-norepinephrine reuptake inhibitors (SSRIs/SNRIs) in the treatment of comorbid anxiety and depression.

An Australian group of researchers describe their development of a robust predictive model incorporating information-rich administrative electronic medical records, which could improve risk stratification of patients presenting with potential suicidal behaviour. This model showed greater predictive ability than clinical assessment using a checklist to identify high-risk patients.

We hope you enjoy this new combined review – please feel free to send us your comments, feedback and suggestions.

Kind regards

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Effect of anxiolytic and hypnotic drug prescriptions on mortality hazards

Authors: Weich S et al.

Summary: Practice records from the UK General Practice Research Database were used to identify 34,727 patients aged ≥16 years first prescribed anxiolytic or hypnotic drugs, or both, between 1998 and 2001, and 69,418 patients with no prescriptions for such drugs matched by age, sex, and practice (controls). Benzodiazepines were the most commonly prescribed drug class (63.7%), including diazepam and temazepam, followed by Z drugs (zaleplon, zolpidem and zopiclone; 23.0%) and other study drugs (13.4%). Co-prescribing was common, particularly for benzodiazepines and Z drugs (18.2%); 5% of patients were co-prescribed drugs from all 3 classes. The age-adjusted hazard ratio for mortality for use of any study drug in the first year after recruitment was 3.46 (95% CI, 3.34 to 3.59) and 3.32 (3.19 to 3.45) after adjusting for other potential confounders. Dose-response associations were found for all 3 classes of study drugs. After excluding deaths in the first year, there were approximately 4 excess deaths linked to drug use per 100 people followed for an average of 7.6 years after their first prescription.

Comment (DM): This ambitious study from the UK indicates an important association between hypnosedative prescription and mortality. As the authors acknowledge, observational studies such as this cannot establish causality, but the careful control of confounders helps to keep prescription (and, by implication, over-prescription) of these drugs in the frame as preventable causes of morbidity and mortality. Attempts to limit prescription in the UK are roughly similar to those in New Zealand and of only limited success. Here, for example, prescription rates are relentlessly increasing year-on-year, notably for lorazepam and zopiclone. PHARMAC's decision in 2010 to relax restrictions on funding of repeat monthly dispensing could be interpreted as giving the wrong message to prescribers (http://journal.nzma.org.nz/journal/124-1345/4936/content.pdf), particularly as these drugs are generally contraindicated for use beyond a fortnight.

Reference: BMJ 2014;348:g1996
Abstract

About Research Review

Research Review is an independent medical publishing organisation producing electronic journals in several specialist areas. These journals provide summaries of the 'must see' studies from the most respected medical journals in the world together with a local specialist commentary indicating why they matter. Research Review publications are intended for New Zealand medical professionals.

Depression and clinical inertia in patients with uncontrolled hypertension

Authors: Moise N et al.

Summary: This analysis of data from 158 adult patients with uncontrolled hypertension attending two US-based hospital-based primary care clinics reports that "clinical inertia", i.e., a lack of treatment intensification in individuals not at evidence-based goals for care, referral to a hypertension specialist, or work-up for identifiable hypertension, was more likely among patients with a diagnosis of depression than in those without depression (70% vs 51% of patients, respectively; p=0.02). This difference remained significant after accounting for potential confounders (relative risk 1.49; 95% CI, 1.06 to 2.10).

Comment (DM): This novel study from New York sheds light on a possible contributory mechanism for the cardiovascular mortality gap between those with and without depression. The study population, mainly older Hispanic women, is hardly representative of New Zealand, but it seems the underlying mechanisms might well be applicable here. Beyond depression, a more general mortality gap between those with and without mental illness (for example a WA study by Lawrence et al., reviewed previously in Psychiatry Research Review, Issue 37, 2013) needs to be addressed as a matter of urgency. ***Equally Well***, a government-sponsored call to action regarding physical health of those with mental disorders, is due shortly for release across the sector. Interested readers are also referred to a major meta-analysis recently published in World Psychiatry (2014;13(2):153-60; http://onlinelibrary.wiley.com/doi/10.1002/wps.20128/abstract).

Reference: JAMA Intern Med 2014;174(5):818-9
Abstract

Lavender oil preparation Silexan is effective in generalized anxiety disorder – a randomized, double-blind comparison to placebo and paroxetine

Authors: Kasper S et al.

Summary: In this trial, 539 adults with generalised anxiety disorder were randomised to receive orally administered lavender oil (Silexan) 80 mg/day or 160 mg/day, paroxetine 20 mg/day, or placebo, once daily for 10 weeks. A baseline Hamilton Anxiety Scale (HAMA) total score ≥18 points was required. At 10 weeks, the HAMA total score was decreased from baseline by a mean 14.1 points with the Silexan 160 mg dose and by 12.8 points with the Silexan 80 mg dose, by 11.3 points with paroxetine and 9.5 points with placebo. Both doses of Silexan were superior to placebo in reducing the HAMA total score (p<0.01); paroxetine showed a trend towards significance (p=0.10). In the Silexan 160 mg/day group, HAMA total score was reduced by ≥50% from baseline in 60.3% of patients and 46.3% had a total score <10 points at treatment end, compared to 51.9% and 33.3% for Silexan 80 mg/day, 43.2% and 34.1% for paroxetine, and 37.8% and 29.6% for placebo, respectively. Silexan also showed a pronounced antidepressant effect and improved general mental health and health-related quality of life. Adverse event rates for Silexan were comparable to placebo and lower than those associated with paroxetine.

Comment (DM): This combined Austrian-German study is notable for its ample sample size, methodological precision and straightforward data analysis. The results are encouraging both in terms of efficacy and tolerability. Given its broad clinical spectrum of action, including a distinct antidepressant effect, efforts are under way to identify the active principle(s) in lavender oil that underlie these pharmacological effects. Like Hypericum perforatum (St John's wort), this herbal preparation seems to perform better in Central European clinical hands than elsewhere, possibly because of better chemical quality and standardisation of doses in the German-speaking world. It will be of interest as to how soon comparable high-quality and standardised preparations are available in New Zealand.

Reference: Int J Neuropsychopharmacol 2014;17(6):859-69
Abstract

For more information, please go to http://www.medsafe.govt.nz/

Risk stratification using data from electronic medical records better predicts suicide risks than clinician assessments

Authors: Tran T et al.

Summary/Comment (WM): This "title says it all" article comes from an Australian group of experts in data analysis working with mental health clinicians. They report the process by which they developed a computer-based programme that uses available electronic medical records (cross-health, not just mental health-specific). They then compare the accuracy of the predictive model they developed with the accuracy of prediction by clinicians (aided by an 18-point rating scale utilised by the mental health services). The modelling process and the research comparing the model against clinician prediction is all based on retrospective analysis of accumulated electronic medical records. The study found that the predictive model was superior to the clinician rating (even with the assistance of the rating check list) in the accuracy of risk prediction.

I found this a very interesting study that does suggest a possible way forward for clinicians to be assisted in the difficult task of making valid calls regarding ongoing suicide risk. As we move to an era where most clinical records are electronically stored and aggregated analysis is increasingly possible, good models for prediction could be expected to emerge. This study looked at clinical data from a standard health care setting so its translation capacity is enhanced. Clearly it is too early for this fledgling model to be widely adopted. There needs to be testing of the model across different populations and in different settings. There needs to be review over longer periods of time to ensure that the accuracy is sustained. It does, however, give a strong signal that further work in this area is highly desirable.

Reference: BMC Psychiatry 2014;14:16
Abstract

Change in mental health after smoking cessation

Authors: Taylor G et al.

Summary: This systematic review and meta-analysis investigated change in mental health after smoking cessation compared with continuing to smoke, using data from 26 studies that assessed mental health with questionnaires designed to measure anxiety, depression, mixed anxiety and depression, psychological quality of life, positive affect, and stress. Follow-up mental health scores were measured between 7 weeks and 9 years after baseline. Compared with continuing to smoke, quitting smoking was associated with significant decreases from baseline in anxiety, depression, mixed anxiety and depression, and stress: standardised mean differences were anxiety –0.37 (95% CI, –0.70 to –0.03); depression –0.25 (95% CI, –0.37 to –0.12); mixed anxiety and depression –0.31 (95% CI, –0.47 to –0.14); and stress –0.27 (95% CI, –0.40 to –0.13). Both psychological quality of life and positive affect significantly increased between baseline and follow-up in quitters compared with continuing smokers 0.22 (95% CI, 0.09 to 0.36) and 0.40 (95% CI, 0.09 to 0.71), respectively. The effect size appeared to be no different for those with psychiatric disorders and those without.

Comment (WM): This group of public health physicians and psychiatrists from the UK conducted a careful literature review to examine the evidence in support of changes in mental health after smoking cessation. I was particularly drawn to this report after the experience locally with attempts to have psychiatric facilities become smoke-free environments. I am sure that many clinicians reading this review will have been drawn in to the debates about freedom to choose, rights violation and the like. Those debates have largely focussed on the benefits for physical health status of not smoking. The opponents of no smoking environments often use the negative impact on the person's mental health as an argument against smoke-free environments for psychiatric inpatients.

The review included both clinical and non-clinical populations. Data re previous and continued exposure was required, as were outcome measures before and after quitting. There was requirement for a satisfactorily robust design. The reviewers give a thorough account of their review methodology, largely informed by Cochrane practice. Studies where there was uncertainty regarding the duration of quitting (mostly the point prevalence type) were not included as the authors felt that recent quitters might still have withdrawal. They also looked for biological verification of abstinence. The reviewers also considered the possible psychotherapeutic component of cessation programmes for possible confounding of any mental health change.

The review confirms that quitters have significant decreases in stress, depression and anxiety as compared with those continuing to smoke. Indicators of positive affect and measures of psychological quality of life are also higher in those who quit. When looking at the effects in the non-clinical population versus those with a clinical condition there were no differences.

These findings should give some reassurance to the clinician who is encouraging patients to quit smoking, and for those advocating for reduction in exposure to smoking. Critics of the review will point to the fact that we cannot assume that correlation of improvement is causally connected to stopping smoking; things such as different life style, more exercise and the like will be raised. Whatever the reason, anything that allows psychiatrists to advocate for improved physical health as well as mental health in people with mental illness should be gratefully accepted.

Reference: BMJ 2014;358:g1151
Abstract

The prognosis of common mental disorders in adolescents: a 14-year prospective cohort study

Authors: Patton GC et al.

Summary: This study was conducted between August 1992 and January 2008 in a random sample of 1943 adolescents from 44 secondary schools across the state of Victoria, Australia. Common mental disorder was assessed at 5 points in adolescence and 3 in young adulthood, commencing at a mean age of 15.5 years and ending at a mean age of 29.1 years. Adolescent disorders were defined on the Revised Clinical Interview Schedule (CIS-R), with a primary cut-off score of ≥12 representing a level at which a family doctor would be concerned. The study sought to describe the patterns and predictors of mental disorder persisting into adulthood. Twenty-nine percent of male participants and 54% of female participants reported high symptoms on the CIS-R (≥12) at least once during adolescence, and almost 60% reported a further episode as a young adult. Among adolescents with one episode lasting less than 6 months, just over half had no further common mental health disorder as a young adult. Longer duration of mental health disorders in adolescence was the strongest predictor of clear-cut young adult disorder (odds ratio [OR] for persistent young adult disorder vs none, 3.16). Girls (OR 2.12) and adolescents with a background of parental separation or divorce (OR 1.62) were more likely to have ongoing disorder into young adulthood than those without such a background. A sharp fall in rates of adolescent onset disorder by the late 20s (OR 0.57) suggested that many patients experience further symptom resolution.

Comment (GB): Youth are at increased risk of mental health problems at a time when their minds and bodies are rapidly changing. This large, robust, prospective, longitudinal study from Australia found that over half of the young female participants and nearly a third of the male participants had at least one episode of depression or anxiety during adolescence, as measured by the CIS-R. Just over 50% of those affected went on to have another episode but there were lower rates of mental health disorders when they became adults. Those particularly at risk of developing adult illness had more prolonged episodes of anxiety and/or depression and/or came from a background of parental separation or divorce. It was unclear whether information was collected about past or present abuse and parental psychotherapy, factors that are known to have a significant effect on adolescent mental health. There have been whole school intervention studies using psychoeducation, CBT and relaxation that have shown overall reductions in anxiety. One hopes that a large randomised intervention trial is in the making.

Reference: Lancet 2014;383(9926):1404-11
Abstract

What does risperidone add to parent training and stimulant for severe aggression in child attention-deficit/hyperactivity disorder?

Authors: Aman MG et al.

Summary: This study involved 168 children aged 6–12 years with attention deficit/hyperactivity disorder (ADHD) and severe physical aggression who were randomised to a 9-week trial of parent training, psychostimulant and placebo (Basic treatment; n=84) or parent training, psychostimulant and risperidone (Augmented treatment; n=84). A total of 124 children also had oppositional-defiant disorder and 44 had conduct disorder. The children were given titrated doses of a psychostimulant (usually Osmotic Release Oral System methylphenidate) for 3 weeks while their parents received PT consisting of behaviour management techniques. If there was room for improvement at the end of week 3, placebo or risperidone was added. Compared with Basic treatment, Augmented treatment was associated with significantly greater improvements on the Nisonger Child Behavior Rating Form (NCBRF) Disruptive-Total subscale, the NCBRF Social Competence subscale and the Antisocial Behavior Scale Reactive Aggression subscale. Improvements in Clinical Global Impression (CGI) scores were substantial in both groups, with no significant differences between them.

Comment (GB): Severe aggression in kids is difficult to manage, for parents, schools and clinicians. Although some cases of childhood onset conduct disorder remit, the overall outcome is not good. Hence, the stakes are high and may justify using higher doses of medication with greater potential for side effects when parent training and other interventions are not enough.

This Ohio study was conducted across 4 sites and funded by grants from the NIMH. Children were randomised to placebo or risperidone in addition to parent training and methylphenidate. The doses of medications used were high, up to 54 mg of Concerta in kids under 25 kg, up to 2.5 mg/day risperidone in children under 25 kg and up to 3.5 mg/day in those heavier children, with the average dose of risperidone being 1.6 mg/day. Over the 9-week trial, the intervention group had significantly more gastrointestinal side effects, while serum prolactin was above the normal limit in 65%. Weight gain was greater with risperidone but it was more due to the Concerta-only group not gaining adequate weight. Parent training and stimulants alone produced significant improvements, while risperidone added a smaller additional benefit, reducing the impulsive reactive aggression but having little impact on planned callous aggression. As a clinician, you have to balance the potential benefits and harm of medication in light of the severity of the child's suffering, remembering the potential of other long-term side effects.

Reference: J Am Acad Child Adolesc Psychiatry 2014;53(1):47-60
Abstract

Psychiatry and Behavioural Disorders
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Independent commentary by Associate Professor David Menkes

David Menkes is an academic psychiatrist with a background in psychology and pharmacology (PhD 1983, Yale). Since completing specialist training in Dunedin (FRANZCP 1989) he has worked as an academic liaison psychiatrist in NZ and the UK. He has a continuing interest in the pharmacology, toxicology and sociology of drug treatments in psychiatry, is a member of www.healthyskepticism.org, and works closely with the International Society of Drug Bulletins (www.isdbweb.org).

He also provides expert commentary for the Psychiatry Research Review.

Independent commentary by Associate Professor Wayne Miles

Dr Wayne Miles did his basic medical training in Dunedin and Christchurch, graduating MBChB in 1972. Specialty training in psychiatry resulted in MRANZCP in 1982. Assisted by a Medical Research Council of New Zealand Training Fellowship he also obtained an Otago MD in 1982, his research area being psychoendocrinology. From 1990 until 2003 he was Director of Mental Health Services for the Waitemata area. He continued a clinical research interest in psychiatry and addiction, being principal investigator of a number of research trials as well as providing supervision for other researchers. He has continued an association with the Auckland University School of Medicine and is currently Clinical Associate Professor.

Wayne has had an interest in and commitment to service improvement through promotion of evidence-based practice so was keen to accept the offer to develop the Knowledge Centre as a hub for the facilitation of new knowledge and the translation of this knowledge into practice.
Dr Miles provides expert commentary for NZ Psychiatry Research Review.

Independent commentary by Dr Craig Immelman

Dr Craig Immelman is a Child & Adolescent, and General Psychiatrist in private practice in Auckland, and an Honorary Lecturer at the Department of Psychological Medicine at the University of Auckland. He is a graduate of the University of Witwatersrand, Johannesburg, completed his post-graduate training in psychiatry in Auckland in 2001 and is a Fellow of the Royal Australian & New Zealand College of Psychiatry. Dr Immelman has broad clinical interests, is a Fellow of the Faculty of Child & Adolescent Psychiatry as well as a Member of the Section of Forensic Psychiatry (RANZCP). His special interests include Fetal Alcohol Syndrome, Eating Disorders and Youth Justice. He also consults to a number of District Health Boards. He provides expert opinion to Courts, and holds the designation of Specialist Assessor relating to Intellectual Disability.

Dr Immelman provides expert commentary for Behavioral Disorders Review.

Independent commentary by Dr Giles Bates

Dr Giles Bates graduated in 1987 with a MB ChB from Otago University and completed his RACP (Paediatrics) in 1997. He trained in Community Paediatrics in Melbourne and has been a Consultant Paediatrician at MidCentral Health for 12 years. Dr Bates started working 1 day per week at the Child, Adolescent and Family Mental Health Service 8 years ago and this extended to half-time at the end of 2008, with the rest of the time working as a Community Paediatrician, overlapping with Child Protection work. Previously he worked with children with development problems. Within the CAFMHS service, his role has been to see the children with ADHD and overlapping developmental problems, issues related to abuse and conduct disorder. As well, he is part of the eating disorder team.

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Establishing a link between attention deficit disorder/attention deficit hyperactivity disorder and childhood physical abuse

Authors: Fuller-Thomson E et al.

Summary: Data were analysed from 13,054 respondents aged ≥18 years from the 2005 Canadian Community Health Survey, which contained questions on ADHD/attention deficit disorder (ADD) and physical abuse. In logistic regression analyses using ADD/ADHD as the criterion variable, respondents who reported they had been abused in childhood were 7 times more likely to be diagnosed with ADD/ADHD compared with those who were not abused. These analyses controlled for several potential mediating factors, including age, race, gender, and 3 other adverse childhood experiences (parental divorce, parental addictions, and long-term parental unemployment).

Comment (GB): The Adverse Childhood Experiences (ACE) Study of Vincent J. Felliti et al. from 20 years ago helped open the eyes of the world to the fact that many physical and mental health illnesses are influenced by negative events in childhood. As the number of adverse events increased, including physical, verbal and sexual abuse, there was an almost exponential increase in the risk of depression, drug abuse, cardiovascular disease and so on.

This Canadian study asked adults to list medical conditions, including ADD/ADHD, and recall childhood experiences. There was a strong link between childhood physical abuse and ADD/ADHD when controlling for some parental factors. This does not say what came first, the ADHD or physical abuse. Hyperactive kids are more likely to get a hostile physical response from their parents, especially if they themselves are impulsive. However, there is increasing evidence about the negative effects on the young brain of growing up in a violent, threatening environment without much warmth. Many kids who end up in CYF care are impulsive and reactive, with their minds switched to a hyper-alert defensive state.

Reference: J Aggression, Maltreatment Trauma 2014;23(2):188-98
Abstract

Family-based treatment of early childhood obsessive-compulsive disorder: the Pediatric Obsessive-Compulsive Disorder Treatment Study for Young Children (POTS Jr)

Authors: Freeman J et al.

Summary: This US-based study enrolled 127 children aged 5–8 years with a primary diagnosis of obsessive-compulsive disorder (OCD) and a Children's Yale-Brown Obsessive Compulsive Scale (Y-BOCS) total score of ≥16. Participants were randomly assigned to 14 weeks of either family-based cognitive-behavioural therapy (FB-CBT) involving exposure plus response prevention, or to an FB relaxation treatment (FB-RT) control condition. At 14 weeks, 72% of children in the FB-CBT cohort met response criteria (CGI–Improvement scale score of 1 [very much improved] or 2 [much improved]) compared with 41% of children in the FB-RT cohort. The number needed to treat (NNT) with FB-CBT vs FB-RT was estimated as 3.2. The effect size difference between FB-CBT and FB-RT on the Children's Y-BOCS at week 14 was 0.84 (95% CI, 0.62 to 1.06).

Comment (CI): This is good evidence that working psychologically with children and families produces results. From a less optimistic place, it seems that there are two main issues in this well-designed and implemented NIMH-funded study. The first relates to how easy it would be to apply Family-Based CBT in the New Zealand context (workforce, capability, pressured iCAMHS and so on). Second, whether the "lack of socioeconomic diversity in the sample" diminishes the study's applicability in NZ. But I don't think these allow us to dismiss this important study. Nor do I think our usual clinical practice (from my experience) needs major changes, because this study provides further evidence supporting the efficacy of psychological and family interventions as first-line, before considering (adjuvant) medications such as SSRIs. Although methodological issues could always be commented on (such as whether the sample is really representative, not just to a NZ-based population, considering 452 participants were present at the start, and only 127 randomised), the take-home message for me is to continue to support the application of family-based interventions including the specific focus of CBT in (ever-younger) populations. This ties in nicely with early intervention, helping develop more helpful synaptic pathways and parental support (who may well have also benefitted from learning CBT skills – albeit indirectly).

Reference: JAMA Psychiatry 2014;71(6):689-98
Abstract

Early prevention of antisocial personality: long-term follow-up of two randomized controlled trials comparing indicated and selective approaches

Authors: Scott S et al.

Summary: Outcomes are reported from two follow-up studies of randomised trials of group parent training. One involved 120 clinic-referred 3- to 7-year-olds with severe antisocial behaviour for whom treatment was indicated, 93 of whom were reassessed between ages 10 and 17 (indicated sample). The other involved 109 high-risk 4- to 6-year-olds with elevated antisocial behaviour who were selectively screened from the community, 90 of whom were reassessed between ages 9 and 13 (selective high-risk sample). In the indicated sample, antisocial behaviour and antisocial character traits were improved in the early intervention group at long-term follow-up. Reading ability was also improved, parental expressed emotion was warmer and supervision was closer. However, teacher-rated and self-rated antisocial behaviour were unchanged. No such improvement in long-term outcomes resulted from early intervention in the selective high-risk sample.

Comment (CI): For us in NZ, the message is "keep supporting families (including hard-to-reach families) to attend the Incredible Years programme as early as possible because it persistently leads to less disruptive behaviour as well as less antisocial attitudes". Intuitively, this is probably not news to any of us working with young people. Perhaps harking back to Harlowe's poor monkeys and our modern need for there to be scientific data for almost everything it is nonetheless reassuring to have strong and well-implemented studies. Acknowledging but not entering into the philosophical debate about antisocial personality, anything that could make a difference to our burgeoning criminal justice system and the costs thereof (personal, societal and financial), would be welcome. Again we have it: early intervention, when brain development shows more plasticity, when the ability to feel empathy is still developing, and when supportive parenting relates to increased brain growth in emotion processing areas. And in this case, with severely antisocial children, possibly preventing the development of antisocial personality in adolescence and improving academic performance.

Reference: Am J Psychiatry 2014;171(6):649-57
Abstract

References: 1. NICE Guidelines on Diagnosis and Management of ADHD in Children, Young People and Adults, NCP Guideline, Number 72, 2009. **2.** Markowitz JS, et al. Clin Pharmacokinet 2003; 42 (4): 393-401. **3.** Lopez F, et al. Pediatr Drugs 2003; 5(8):545-555. **4.** Ritalin LA Data Sheet, Novartis New Zealand Limited. **5.** Silva R, et al., J Child Adolesc Psychopharmacology 2005; 15:637-654. **6.** Lyseng-Williamson K. & Keating G. Drugs 2002;62(15): 2251-2259. **7.** Huss M. Presentation: Challenged by ADHD Treatments? 17 August 2010. **8.** Huss M et al. Adv Ther 2014;31:44-65. **9.** Kooij S, et al. BMC Psychiatry 2010, 10:67.

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