Abstracts

Fundamentals of Life: Disorders of Sleep, Eating and Sex

Given space limitations and varying reprint permission policies, not all of the influential publications the editors considered reprinting in this issue could be included. This section contains abstracts from additional articles the editors deemed well worth reviewing.

Treatment-Emergent Sexual Dysfunction Related to Antidepressants: A Meta-Analysis
Serretti A, Chiesa A
Journal of Clinical Psychopharmacology 2009 Jun;29(3):259–66

Background: Sexual dysfunction (SD) is an important underestimated adverse effect of antidepressant drugs. Patients, in fact, if not directly questioned, tend to scarcely report them. The aim of the present meta-analysis was to quantify SD caused by antidepressants on the basis of studies where sexual functioning was purposely investigated through direct inquiry and specific questionnaires. **Methods:** A literature search was conducted using MEDLINE, ISI Web of Knowledge, and references of selected articles. Selected studies performed on patients without previous SD were entered in the Cochrane Collaboration Review Manager (RevMan version 4.2). Our primary outcome measure was the rate of total treatment-emergent SD. Our secondary outcome measures were the rates of treatment-emergent desire, arousal, and orgasm dysfunction. **Results:** Our analyses indicated a significantly higher rate of total and specific treatment-emergent SD and specific phases of dysfunction compared with placebo for the following drugs in decreasing order of impact: sertraline, venlafaxine, citalopram, paroxetine, fluoxetine, imipramine, phenelzine, duloxetine, escitalopram, and fluvoxamine, with SD ranging from 25.8% to 80.3% of patients. No significant difference with placebo was found for the following antidepressants: agomelatine, amineptine, bupropion, moclobemide, mirtazapine, and nefazodone. **Discussion:** Treatment-emergent SD caused by antidepressants is a considerable issue with a large variation across compounds. Some assumptions, such as the inclusion of open-label studies or differences in scales used to assess SD, could reduce the significance of our findings. However, treatment-emergent SD is a frequent adverse effect that should be considered in clinical activity for the choice of the prescribed drug.

The Impact of Mental Illness and Psychotropic Medications on Sexual Functioning: The Evidence and Management
Clayton AH, Balon R
J Sex Med 2009 May;6(5):1200–11; quiz 1212–3

Background: Sexual dysfunction (SD) occurs frequently in patients with psychiatric illness. **Methods:** The published literature on SD in patients with a psychiatric illness and/or taking psychotropic medications was reviewed. **Results:** SD prevalence and type was found to vary with the specific psychiatric illness and medication treatment. Assessment is complicated by the presence of preexisting or comorbid sexual disorders or medical illness affecting sexual function. Direct questioning about sexual function before treatment and throughout the course of therapy is essential to establish baseline sexual functioning, patient preferences regarding medication side effects, and to identify medication-associated SD. A limited number of management strategies for SD in psychiatric patients have been systematically studied. **Conclusions:** SD with psychiatric illness and its treatment requires early identification, and incorporation of patient preferences for successful management.

Evidence-Based Recommendations for the Assessment and Management of Sleep Disorders in Older Persons
Bloom HG, Ahmed I, Alessi CA, Ancoli-Israel S, Buysse DJ, Kryger MH, Phillips BA, Thorpy MJ, Vitiello MV, Zee PC
J Am Geriatr Soc 2009 May;57(5):761–89

Sleep-related disorders are most prevalent in the older adult population. A high prevalence of medical and psychosocial comorbidities and the frequent use of multiple medications, rather than aging per se, are major reasons for this. A major concern, often underappreciated and underaddressed by clinicians, is the strong bidirectional relationship between sleep disorders and serious medical problems in older adults. Hypertension, depression, cardiovascular disease, and cerebrovascular disease are examples of diseases that are more likely to develop in individuals with sleep disorders. Conversely, individuals with any of these diseases are at a higher risk of developing sleep disorders. The goals of this article are to help guide clinicians in their general understanding of sleep problems in older persons, examine specific sleep disorders that occur in older persons, and suggest evidence- and expert-based recommendations for the assessment and treatment of sleep disorders in older persons. No such recommendations are available to help clinicians in their daily patient care practices. The four sections in the beginning of the article are titled, Background and Significance, General Review of Sleep, Recommendations Development, and General Approach to Detecting Sleep Disorders in an Ambulatory Setting. These are followed by overviews of specific sleep disorders: Insomnia, Sleep Apnea, Restless Legs Syndrome, Circadian Rhythm Sleep Disorders, Parasomnias, Hypersomnias, and Sleep Disorders in Long-Term Care Settings. Evidence- and expert-based recommendations, developed by a group of sleep and clinical experts, are presented after each sleep disorder.

Sexual Dysfunction in Patients Treated with Atypical Antipsychotics
Meyer JM
Journal of Clinical Psychiatry 2008 Nov 24;69(9):e26

Atypical antipsychotics can provide improvement in schizophrenic symptomatology but also may cause side effects, such as erectile dysfunction and decreased libido, which can be problematic for patients. In order to keep patients symptomatically stable and to help alleviate these side effects, clinicians should alter the treatment strategy, possibly by switching medications, to encourage adherence to the medication as well as optimize patients' outcomes. To establish clinically useful standards for switching agents, more studies are needed that focus on gradual cross-titration methods to achieve therapeutic doses for patients.

Bulimia Nervosa
Hay PJ, Bacaltchuk J
Clin Evid (Online) 2008 Jun 12;2008

Introduction: Up to 1% of young women may have bulimia nervosa, characterised by an intense preoccupation with body weight, uncontrolled binge-eating episodes, and use of extreme measures to counteract the feared effects of overeating. People with bulimia nervosa may be of normal weight, making it difficult to diagnose. After ten years, about half of people with bulimia nervosa will have recovered fully, a third will have made a partial recovery, and 10–20% will still have symptoms. **Methods and Outcomes:** We conducted a systematic review and aimed to answer the following clinical questions: What are the effects of treatments for bulimia nervosa in adults? What are the effects of discontinuing treatment in people with bulimia nervosa in remission? We searched: Medline, Embase, The Cochrane Library and other important databases up to June 2007 (Clinical Evidence reviews are updated periodically, please check our website for the most up-to-date version of this review). We included harms alerts from relevant organisations such as the US Food and Drug Administration (FDA) and the UK Medicines and Healthcare products Regulatory Agency (MHRA). **Results:** We found 26 systematic reviews, RCTs, or observational studies that met our inclusion criteria. We performed a GRADE evaluation of the quality

of evidence for interventions. **Conclusions:** In this systematic review we present information relating to the effectiveness and safety of the following interventions: cognitive behavioural therapy (alone or plus exposure response prevention enhancement); cognitive orientation therapy; dialectical behavioural therapy; discontinuing fluoxetine in people with remission; guided self-help cognitive behavioural therapy; hypnobehavioural therapy; interpersonal psychotherapy; mirtazapine; monoamine oxidase inhibitors (MAOIs); motivational enhancement therapy; pharmacotherapy plus psychotherapy; pure or unguided self-help cognitive behavioural therapy (CBT); reboxetine; selective serotonin reuptake inhibitors (SSRIs); topiramate; tricyclic antidepressants (TCAs); and venlafaxine.

Treatment of Narcolepsy and Other Hypersomnias of Central Origin
Wise MS, Arand DL, Auger RR, Brooks SN, Watson NF; American Academy of Sleep Medicine
Sleep 2007 Dec 1;30(12):1712–27

Objective: The purpose of this paper is to summarize current knowledge about treatment of narcolepsy and other hypersomnias of central origin. **Methods:** The task force performed a systematic and comprehensive review of the relevant literature and graded the evidence using the Oxford grading system. This paper discusses the strengths and limitations of the available evidence regarding treatment of these conditions, and summarizes key information about safety of these medications. Our findings provide the foundation for development of evidence-based practice parameters on this topic by the Standards of Practice Committee of the American Academy of Sleep Medicine. **Results:** The majority of recent papers in this field provide information about use of modafinil or sodium oxybate for treatment of sleepiness associated with narcolepsy. Several large randomized, placebo-controlled studies indicate that modafinil and sodium oxybate are effective for treatment of hypersomnia due to narcolepsy. We identified no studies that report direct comparison of these newer medications versus traditional stimulants, or that indicate what proportion of patients treated initially with these medications require transition to traditional stimulants or to combination therapy to achieve adequate alertness. As with the traditional stimulants, modafinil and sodium oxybate provide, at best, only moderate improvement in alertness rather than full restoration of alertness in patients with narcolepsy. Several large randomized placebo-controlled studies demonstrate that sodium oxybate is effective for treatment of cataplexy associated with narcolepsy, and earlier studies provide limited data to support the effectiveness of fluoxetine and tricyclic antidepressants for treatment of cataplexy. Our findings indicate that very few reports provide information regarding treatment of special populations such as children, older adults, and pregnant or breastfeeding women. The available literature provides a modest amount of information about improvement in quality of life in association with treatment, patient preferences among the different medications, or patient compliance. **Conclusion:** Several recent studies provide evidence that modafinil and sodium oxybate are effective for treatment of hypersomnia due to narcolepsy. No studies were identified that report direct comparison of these newer medications with traditional stimulants. Despite significant advances in understanding the pathophysiology of narcolepsy, we do not have an ideal treatment to restore full and sustained alertness. Future investigations should be directed toward development of more effective and better tolerated therapies, and primary prevention.

Clinical Effectiveness of Treatments for Anorexia Nervosa in Adolescents: Randomised Controlled Trial
Gowers SG, Clark A, Roberts C, Griffiths A, Edwards V, Bryan C, Smethurst N, Byford S, Barrett B
British Journal of Psychiatry 2007 Nov;191:427–35

Background: Treatment guidelines identify few adequately powered trials to guide recommendations for anorexia nervosa. AIMS: To evaluate the effectiveness of three readily available National Health Service treatments for adolescents (aged 12–18 years) with anorexia nervosa. **Method:** Multicentre randomised controlled trial of 167 young people comparing in-patient, specialist out-patient and general child and adolescent mental health service (CAMHS) treatment. **Results:** Each group made considerable progress at 1 year, with further improvement by 2 years. Full recovery rates were poor (33% at 2 years, 27% still with anorexia nervosa). Adherence to in-patient treatment was only 50%. Neither in-patient nor specialist out-patient therapy demonstrated advantages over general CAMHS treatment by intention to treat,

although some CAMHS out-patients were subsequently admitted on clinical grounds. In-patient treatment (randomised or after out-patient transfer) predicted poor outcomes. **Conclusions:** First-line in-patient psychiatric treatment does not provide advantages over out-patient management. Out-patient treatment failures do very poorly on transfer to in-patient facilities.

The Efficacy and Safety of Drug Treatments for Chronic Insomnia in Adults: A Meta-Aanalysis of RCTs

Buscemi N, Vandermeer B, Friesen C, Bialy L, Tubman M, Ospina M, Klassen TP, Witmans M
J Gen Intern Med 2007 Sep;22(9):1335–50

Background: Hypnotics have a role in the management of acute insomnia; however, the efficacy and safety of pharmacological interventions in the management of chronic insomnia is unclear. **Objective:** The objective of this paper is to conduct a systematic review of the efficacy and safety of drug treatments for chronic insomnia in adults. **Data Sources:** Twenty-one electronic databases were searched, up to July 2006. **Study Selection:** Randomized double-blind, placebo-controlled trials were eligible. Quality was assessed using the Jadad scale. Data were pooled using the random effects model. **Data Synthesis:** One hundred and five studies were included in the review. Sleep onset latency, as measured by polysomnography, was significantly decreased for benzodiazepines (BDZ), (weighted mean difference: −10.0 minutes; 95% CI: −16.6, −3.4), non-benzodiazepines (non-BDZ) (−12.8 minutes; 95% CI: −16.9, −8.8) and antidepressants (ADP) (−7.0 minutes; 95% CI: −10.7, −3.3). Sleep onset latency assessed by sleep diaries was also improved (BDZ: −19.6 minutes; 95% CI: −23.9, −15.3; non-BDZ: −17.0 minutes; 95% CI: −20.0, −14.0; ADP: −12.2 minutes; 95% CI: −22.3, −2.2). Indirect comparisons between drug categories suggest BDZ and non-BDZ have a similar effect. All drug groups had a statistically significant higher risk of harm compared to placebo (BDZ: risk difference [RD]: 0.15; non-BDZ RD: 0.07; and ADP RD: 0.09), although the most commonly reported adverse events were minor. Indirect comparisons suggest that non-BDZ are safer than BDZ. **Conclusions:** Benzodiazepines and non-benzodiazepines are effective treatments in the management of chronic insomnia, although they pose a risk of harm. There is also some evidence that antidepressants are effective and that they pose a risk of harm.

Olanzapine Therapy in Anorexia Nervosa: Psychobiological Effects

Brambilla F, Garcia CS, Fassino S, Daga GA, Favaro A, Santonastaso P, Ramaciotti C, Bondi E, Mellado C, Bordello R, Monteleone P
Int Clin Psychopharmacol 2007 Jul;22(4):197–204

Dopamine impairments occur in anorexia nervosa. The aim of this study was to see whether treatment with the atypical dopamine antagonist antipsychotic olanzapine improves the disorder. Thirty anorexics, 18 restricted and 12 bingeing-purging, underwent a 3-month course of cognitive behavioral therapy, plus at random and double-blinded oral olanzapine (2.5 mg for 1 month, 5 mg for 2 months) in half and oral placebo in the other half of them. BMI, psychopathological aspects (eating disorder inventory, Hamilton Rating Scale, Buss-Durkee Rating Scale, Yale Brown Cornell for Eating Disorders Rating Scale, temperament-character inventory), and homovanillic acid blood concentrations for dopamine secretion, were monitored at baseline and then monthly during the trial. At the end of the trial BMI, total eating disorder inventory, total Yale Brown Cornell for Eating Disorders Rating Scale, Buss-Durkee Rating Scale, Hamilton Rating Scale scores and in olanzapine-treated patients the subitems of eating disorder inventory ineffectiveness and maturity fear, of Buss-Durkee Rating Scale direct aggressiveness, of temperament-characteristic inventory persistence had improved significantly. When stratified for anorexia nervosa subtype, BMI changes were significant among anorexia nervosa bingeing-purging patient, "depression' (Hamilton Rating Scale) and "direct aggressiveness' (Buss-Durkee Rating Scale) among anorexia nervosa bingeing-purging patients, "persistence' (temprerament-characteristic inventory), among anorexics restricted patients, with a trend toward significance for obsessivity-compulsivity (Yale Brown Cornell for Eating Disorders Rating Scale), homovanilic acid blood levels increased significantly in the cognitive behavioral therapy+olanzapine group. No correlations were observed between homovanilic acid concentrations and psychopathological parameters. The pharmacological treatment can significantly improve specific aspects of anorexia nervosa.

Anorexia Nervosa Treatment: A Systematic Review of Randomized Controlled Trials
Bulik CM, Berkman ND, Brownley KA, Sedway JA, Lohr KN
Int J Eat Disord 2007 May;40(4):310–20

Objective: The RTI International-University of North Carolina at Chapel Hill Evidence-based Practice Center (RTI-UNC EPC) systematically reviewed evidence on efficacy of treatment for anorexia nervosa (AN), harms associated with treatments, factors associated with treatment efficacy, and differential outcome by sociodemographic characteristics. **Method:** We searched six major databases for studies on the treatment of AN from 1980 to September 2005, in all languages against a priori inclusion/exclusion criteria focusing on eating, psychiatric or psychological, or biomarker outcomes. **Results:** Thirty-two treatment studies involved only medications, only behavioral interventions, and medication plus behavioral interventions for adults or adolescents. The literature on medication treatments and behavioral treatments for adults with AN is sparse and inconclusive. Cognitive behavioral therapy may reduce relapse risk for adults with AN after weight restoration, although its efficacy in the underweight state remains unknown. Variants of family therapy are efficacious in adolescents, but not in adults. **Conclusion:** Evidence for AN treatment is weak; evidence for treatment-related harms and factors associated with efficacy of treatment are weak; and evidence for differential outcome by sociodemographic factors is nonexistent. Attention to sample size and statistical power, standardization of outcome measures, retention of patients in clinical trials, and developmental differences in treatment appropriateness and outcome is required.

Bulimia Nervosa Treatment: A Systematic Review of Randomized Controlled Trials
Shapiro JR, Berkman ND, Brownley KA, Sedway JA, Lohr KN, Bulik CM
Int J Eat Disord 2007 May;40(4):321–36

Objective: The RTI International-University of North Carolina at Chapel Hill Evidence-based Practice Center systematically reviewed evidence on efficacy of treatment for bulimia nervosa (BN), harms associated with treatments, factors associated with treatment efficacy, and differential outcome by sociodemographic characteristics. **Method:** We searched six major databases published from 1980 to September 2005 in all languages against a priori inclusion/exclusion criteria; we focused on eating, psychiatric or psychological, and biomarker outcomes. **Results:** Forty-seven studies of medication only, behavioral interventions only, and medication plus behavioral interventions for adults or adolescents met our inclusion criteria. Fluoxetine (60 mg/day) decreases the core symptoms of binge eating and purging and associated psychological features in the short term. Cognitive behavioral therapy reduces core behavioral and psychological features in the short and long term. **Conclusion:** Evidence for medication or behavioral treatment for BN is strong, for self-help is weak; for harms related to medication is strong but either weak or nonexistent for other interventions; and evidence for differential outcome by sociodemographic factors is nonexistent. Attention to sample size, standardization of outcome measures, attrition, and reporting of abstinence from target behaviors are required. Longer follow-up intervals, innovative treatments, and attention to sociodemographic factors would enhance the literature.

Insomnia: Pathophysiology and Implications for Treatment
Roth T, Roehrs T, Pies R
Sleep Med Rev 2007 Feb;11(1):71–9

Interest in developing a greater understanding of the pathophysiogical mechanisms underlying primary insomnia has increased. Recent evidence indicates that there may be some neuroendocrine and clinical similarities between primary insomnia and major depressive disorder, that abnormal corticotropin releasing factor (CRF) activity occurs in major depression, and that CRF hyperactivity appears to mediate the hyperarousal seen in primary insomnia. These findings all point to the possibility of hypothalamic-pituitary-adrenal (HPA) axis and CRF overactivity in both disorders. More recent findings have strengthened the evidence that primary insomnia may be linked with mood disorders and is associated with HPA axis overactivity and excess secretion of CRF, adrenocorticotropin releasing hormone, and cortisol. These insights have implications for managing chronic primary insomnia, such as use of antiglucocorticoid agents.

Individual Psychotherapy in the Outpatient Treatment of Adults with Anorexia Nervosa
Hay P, Bacaltchuk J, Claudino A, Ben-Tovim D, Yong PY
Cochrane Database Syst Rev 2003;(4):CD003909

Background: Anorexia nervosa is a disorder of high morbidity and significant mortality. It is commonest in young adult women, in whom the incidence may be increasing. The focus of treatment has moved to an outpatient setting and a number of differing psychotherapies are presently used in treatment. **Objectives:** The aim of the present review was to evaluate the evidence from randomised controlled trials for the efficacy of outpatient psychotherapies used in the treatment of older adolescents and adults with anorexia nervosa. **Search Strategy:** The strategy comprised database searches of MEDLINE, EXTRAMED, EMBASE, PSYCLIT, CURRENT CONTENTS, Cochrane Collaboration Controlled Trials Register and the Depression and Anxiety Neuroses Cochrane Group (CCDAN), a hand-search of The International Journal of Eating Disorders, and he reference lists of all papers selected. Personal letters were sent to identified notable researchers published in the area, requesting information on trials that are unpublished or in progress. **Selection Criteria:** All randomised controlled trials of adult individual outpatient therapy for anorexia nervosa as defined by the DSM-IV or similar international criterion. Quality ratings were made according to the CCDAN criteria and in addition, whether the trial had examined treatment integrity. **Data Collection and Analysis:** A range of outcome variables were selected, including physical state, severity of eating disorder attitudes and beliefs, interpersonal function, and general psychiatric symptom severity. Continuous outcome data comparisons were made with the standardized mean difference statistic, and binary outcome comparisons made with the relative risk statistic. Reliability of data extraction and quality ratings were made with the kappa statistic. Sensitivity analyses to evaluate the effects of trial quality and subgroup analyses to explore specific questions of treatment effects from different settings, frequency and duration of therapies were planned. **Main Results:** Six small trials only, two of which included children or adolescents, were identified from the search and aggregation of data was not possible. Bias was possible due particularly to lack of blinding of outcome assessments. The results in two trials suggested that "treatment as usual" or similar may be less efficacious than a specific psychotherapy. No specific treatment was consistently superior to any other specific approach. Dietary advice as a control arm had a 100% non-completion rate in one trial. **Reviewer's Conclusions:** No specific approach can be recommended from this review. It is unclear why "treatment as usual" performed so poorly or why dietary advice alone appeared so unacceptable as the reasons for non-completion were not reported. There is an urgent need for large well-designed trials in his area.

NOTES