Online clinical resources: To pay or not to pay?

Free references invaluable in many clinical situations

Simon Kung, MD
Assistant professor of psychiatry

Maria I. Lapid, MD
Assistant professor of psychiatry

Mayo Clinic College of Medicine
Rochester, MN

Why pay for diagnostic, treatment, and research information when the Internet offers scores of free resources? Which free references are best, and when are they more clinically beneficial than paid information?

This article reviews select free online references and—where applicable—compares them with fee-based resources.

DIAGNOSTIC RESOURCES

We often don't look past DSM-IV-TR guidelines when forming a diagnosis. In such cases, BehaveNet's simple yet comprehensive list of DSM-IV-TR criteria is handy (www.behavenet.com, click on "Diagnoses and criteria by category").

For in-depth diagnostic guidelines, American Psychiatric Publishing (www.appi.org) offers its DSM-IV-TR Quick Reference for $29, and Skyscape (www.skyscape.com) offers the full DSM-IV-TR at $77. Both personal digital assistant (PDA)-based programs come in Palm OS and Pocket PC versions.

TREATMENT DECISION AIDS

Free drug information references such as PDR.net (www.pdr.net) and Epocrates (www.epocrates.com) can help with medication choices. Both services let you check interactions on several drugs at once, which is important when treating patients who are taking multiple medications.

PDR.net is free for U.S.-based physicians and prescribers and requires registration. Epocrates can be used without registering, but going through the free registration process will provide additional features such as medication cost estimates. For a fee, Epocrates will throw in premium features such as pill identification, clinical tables and guidelines, and medical calculators.

Both PDR.net and Epocrates offer free PDA versions (Epocrates started as a PDA-based service). Other PDA-based drug references charge for access, but in some cases the information is more comprehensive and accurate.

For cytochrome P-450 metabolism information, you could reference the metabolism sections of each drug information sheet. Alternatively:

- Indiana University offers a good free drug interaction table showing substrates, inhibitors, and inducers of CYP-450 isoenzymes (http://medicine.iupui.edu/flockhart).
- http://mhc.com/Cytochromes offers similar

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highest dose of oral olanzapine (15±2.5 mg/d). In controlled clinical trials of intramuscular olanzapine for injection, there were no statistically significant differences from placebo in occurrence of any treatment-emergent extrapyramidal symptoms, assessed by either rating scales incidence or spontaneously reported adverse events.

Other Adverse Events: Dose-relatedness of adverse events was assessed using data from this same clinical trial involving 3 fixed oral dosage ranges (5±2.5, 10±2.5, or 15±2.5 mg/d) compared with placebo. The following treatment-emergent events showed a statistically significant trend: asthenia, dry mouth, nausea, somnolence, tremor.

In an 8-week, randomized, double-blind study in patients with schizophrenia, schizophreniform disorder, or schizoaffective disorder comparing fixed doses of 10, 20, and 40 mg/d, statistically significant differences were seen between doses for the following: baseline to endpoint weight gain, 10 vs 40 mg/d; incidence of treatment-emergent prolactin elevations >24.2 ng/mL (female) or >18.77 ng/mL (male), 10 vs 40 mg/d and 20 vs 40 mg/d; fatigue, 10 vs 40 mg/d and 20 vs 40 mg/d; and dizziness, 20 vs 40 mg/d.

Vital Sign Changes—Oral olanzapine was associated with orthostatic hypotension and tachycardia in clinical trials. Intramuscular olanzapine for injection was associated with bradycardia, hypotension, and tachycardia in clinical trials (*see* PRECAUTIONS).

Weight Gain—In placebo-controlled 6-week schizophrenia studies, weight gain was reported in 5.6% of oral olanzapine patients (average 2.8-kg gain) compared to 0.8% of placebo patients (average 0.4-kg loss); 29% of olanzapine patients gained >7% of their baseline weight, compared to 3% of placebo patients. During continuation therapy (238 median days of exposure), 56% of patients met the criterion for having gained >7% of their baseline weight. Average gain during long-term therapy was 5.4 kg.

Laboratory Changes—Olanzapine is associated with asymptomatic increases in SGPT, SGOT, and GGT and with increases in serum prolactin and CPK (*see* PRECAUTIONS). Asymptomatic elevation of eosinophils was reported in 0.3% of olanzapine patients in premarketing trials. There was no indication of a risk of clinically significant neutropenia associated with olanzapine in the premarketing database.

In clinical trials among olanzapine-treated patients with baseline random triglyceride levels of <150 mg/dL (N=659), 0.5% experienced triglyceride levels of ≥500 mg/dL anytime during the trials. In these same trials, olanzapine-treated patients (N=1185) had a mean triglyceride increase of 20 mg/dL from a mean baseline of 175 mg/dL. In placebo-controlled trials, olanzapine-treated patients with baseline random cholesterol levels of <200 mg/dL (N=1034) experienced cholesterol levels of ≥240 mg/dL anytime during the trials more often than placebo-treated patients (N=602; 3.6% vs 2.2% respectively). In these same trials, olanzapine-treated patients (N=2528) had a mean increase of 0.4 mg/dL in cholesterol from a mean baseline of 203 mg/dL, which was significantly different compared to placebo-treated patients (N=1415) with a mean decrease of 4.6 mg/dL from a mean baseline of 203 mg/dL.

ECG Changes—Analyses of pooled placebo-controlled trials revealed no statistically significant olanzapine/placebo differences in incidence of potentially important changes in ECG parameters, including QT, QTc, and PR intervals. Olanzapine was associated with a mean increase in heart rate of 2.4 BPM compared to no change among placebo patients.

Other Adverse Events Observed During Clinical Trials—The following treatment-emergent events were reported with oral olanzapine at multiple doses ≥1 mg/d in clinical trials (8661 patients, 4165 patient-years of exposure). This list may not include events previously listed elsewhere in labeling, those events for which a drug cause was remote, those terms which were so general as to be uninformative, and those events reported only once or twice which did not have a substantial probability of being acutely life-threatening. *Frequent* events occurred in ≥1/100 patients; *infrequent* events occurred in 1/100 to 1/1000 patients; *rare* events occurred in <1/1000 patients. ***Body as a Whole***—*Frequent:* dental pain, flu syndrome; *Infrequent:* abdomen enlarged, chills, face edema, intentional injury, malaise, moniliasis, neck pain, neck rigidity, pelvic pain, photosensitivity reaction, suicide attempt; *Rare:* chills and fever, hangover effect, sudden death. ***Cardiovascular***—*Frequent:* hypotension; *Infrequent:* atrial fibrillation, bradycardia, cerebrovascular accident, congestive heart failure, heart arrest, hemorrhage, migraine, pallor, palpitation, vasodilatation, ventricular extrasystoles; *Rare:* arteritis, heart failure, pulmonary embolus. ***Digestive***—*Frequent:* flatulence, increased salivation, thirst; *Infrequent:* dysphagia, esophagitis, fecal impaction, fecal incontinence, gastritis, gastroenteritis, gingivitis, hepatitis, melena, mouth ulceration, nausea and vomiting, oral moniliasis, periodontal abscess, rectal hemorrhage, stomatitis, tongue edema, tooth caries; *Rare:* aphthous stomatitis, enteritis, eructation, esophageal ulcer, glossitis, ileus, intestinal obstruction, liver fatty deposit, tongue discoloration. ***Endocrine***—*Infrequent:* diabetes mellitus; *Rare:* diabetic acidosis, goiter. ***Hemic and Lymphatic***—*Infrequent:* anemia, cyanosis, leukocytosis, leukopenia, lymphadenopathy, thrombocytopenia; *Rare:* normocytic anemia, thrombocythemia. ***Metabolic and Nutritional***—*Infrequent:* acidosis, alkaline phosphatase increased, bilirubinemia, dehydration, hypercholesteremia, hyperglycemia, hyperlipemia, hyperuricemia, hypoglycemia, hypokalemia, hyponatremia, lower extremity edema, upper extremity edema; *Rare:* gout, hyperkalemia, hypernatremia, hypoproteinemia, ketosis, water intoxication. ***Musculoskeletal***—*Frequent:* joint stiffness, twitching; *Infrequent:* arthritis, arthrosis, leg cramps, myasthenia; *Rare:* bone pain, bursitis, myopathy, osteoporosis, rheumatoid arthritis. ***Nervous System***—*Frequent:* abnormal dreams, amnesia, delusions, emotional lability, euphoria, manic reaction, paresthesia, schizophrenic reaction; *Infrequent:* akinesia, alcohol misuse, antisocial reaction, ataxia, CNS stimulation, cogwheel rigidity, delirium, dementia, depersonalization, dysarthria, facial paralysis, hypesthesia, hypokinesia, hypotonia, incoordination, libido decreased, libido increased, obsessive compulsive symptoms, phobias, somatization, stimulant misuse, stupor, stuttering, tardive dyskinesia, vertigo, withdrawal syndrome; *Rare:* circumoral paresthesia, coma, encephalopathy, neuralgia, neuropathy, nystagmus, paralysis, subarachnoid hemorrhage, tobacco misuse. ***Respiratory***—*Frequent:* dyspnea; *Infrequent:* apnea, asthma, epistaxis, hemoptysis, hyperventilation, hypoxia, laryngitis, voice alteration; *Rare:* atelectasis, hiccup, hypoventilation, lung edema, stridor. ***Skin and Appendages***—*Frequent:* sweating; *Infrequent:* alopecia, contact dermatitis, dry skin, eczema, maculopapular rash, pruritus, seborrhea, skin discoloration, skin ulcer, urticaria, vesiculobullous rash; *Rare:* hirsutism, pustular rash. ***Special Senses***—*Frequent:* conjunctivitis; *Infrequent:* abnormality of accommodation, blepharitis, cataract, deafness, diplopia, dry eyes, ear pain, eye hemorrhage, eye inflammation, eye pain, ocular muscle abnormality, taste perversion, tinnitus; *Rare:* corneal lesion, glaucoma, keratoconjunctivitis, macular hypopigmentation, miosis, mydriasis, pigment deposits lens. ***Urogenital***—*Frequent:* vaginitis*; *Infrequent:* abnormal ejaculation,* amenorrhea,* breast pain, cystitis, decreased menstruation,* dysuria, female lactation,* glycosuria, gynecomastia, hematuria, impotence,* increased menstruation,* menorrhagia,* metrorrhagia,* polyuria, premenstrual syndrome,* pyuria, urinary frequency, urinary retention, urinary urgency, urination impaired, uterine fibroids enlarged,* vaginal hemorrhage*; *Rare:* albuminuria, breast enlargement, mastitis, oliguria. (*Adjusted for gender.)

The following treatment-emergent events were reported with intramuscular olanzapine for injection at one or more doses ≥2.5 mg/injection in clinical trials (722 patients). This list may not include events previously listed elsewhere in labeling, those events for which a drug cause was remote, those terms which were so general as to be uninformative, and those events reported only once or twice which did not have a substantial probability of being acutely life-threatening. ***Body as a Whole***—*Frequent:* injection site pain; *Infrequent:* abdominal pain, fever. ***Cardiovascular***—*Infrequent:* AV block, heart block, syncope. ***Digestive***—*Infrequent:* diarrhea, nausea. ***Hemic and Lymphatic***—*Infrequent:* anemia. ***Metabolic and Nutritional***—*Infrequent:* creatine phosphokinase increased, dehydration, hyperkalemia. ***Musculoskeletal***—*Infrequent:* twitching. ***Nervous System***—*Infrequent:* abnormal gait, akathisia, articulation impairment, confusion, emotional lability. ***Skin and Appendages***—*Infrequent:* sweating.

Postintroduction Reports—Reported since market introduction and temporally (not necessarily causally) related to olanzapine therapy: allergic reaction (eg, anaphylactoid reaction, angioedema, pruritus or urticaria), diabetic coma, jaundice, neutropenia, pancreatitis, priapism, rhabdomyolysis, and venous thromboembolic events (including pulmonary embolism and deep venous thrombosis). Random cholesterol levels of ≥240 mg/dL and random triglyceride levels of ≥1000 mg/dL have been reported.

DRUG ABUSE AND DEPENDENCE: Olanzapine is not a controlled substance.

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information and links to more CYP-450 resources.

Clinical trials. Numerous Web sites offer free access to evidence-based findings and randomized clinical trials. The National Institute of Mental Health, for example, offers free online information on:

- Sequenced Treatment Alternatives to Relieve Depression (STAR*D, www.nimh.nih.gov/healthinformation/stard.cfm)
- Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE, www.nimh.nih.gov/healthinformation/catie.cfm).

The sites describe these medication trials in a lucid question-and-answer format. Clinicians can use the study results to guide medication choices. The STAR*D site also lists percentages of treatment success and describes duration-of-treatment trials.

Online algorithms. Free drug treatment algorithms and guidelines based on literature reviews and expert consensus are available online:

- The Texas Medication Algorithm Project (www.dshs.state.tx.us/mhprograms/TMAPtoc.shtm) addresses depression, bipolar disorder, and schizophrenia treatment.
- The Harvard Psychopharmacology Algorithm Project (http://mhc.com/Algorithms) covers depression, schizophrenia, and anxiety in patients with substance abuse.
- The International Psychopharmacology Algorithm Project (www.ipap.org) covers schizophrenia, posttraumatic stress disorder, and generalized anxiety disorder.

Free psychiatric rating scales—such as the Patient Health Questionnaire-9 (PHQ-9, www.depression-primarycare.org/clinicians/toolkits/materials/forms/phq9)—can help you efficiently monitor the progress of patients who complete the self-report forms.

The Psychiatric Rating Scales Index (www.neurotransmitter.net/ratingscales.html) lists links to other rating scales and descriptions, and notes which scales are free and which must be purchased.

ACCESS TO CLINICAL ARTICLES

Online abstracts. By subscribing to Medline services, academic institutions provide students and faculty access to journal articles.

If you don't have Medline access, use the free National Institutes of Health PubMed database (www.pubmed.gov) to search for abstracts on a given topic. You can view abstracts to all types of articles or click on the "review" tab on the search results page to view only reviews.

Although abstracts are free, full-text access usually is not unless your institution has a site license for that journal or you have purchased online access to that publication. By reading the abstract, you often can tell whether the full article contains information relevant to your practice.

Evidence-based medicine. The Centre for Evidence Based Mental Health (www.cebmh.com, click on "Research") lists links to reviews, clinical trial information, and resources for learning about evidence-based medicine. CEBMH posts references to articles but does not offer full-text access.

The Cochrane Collaboration (www.cochrane.org/reviews/en/topics/index.html) offers free online abstracts of systematic reviews of psychiatric treatments, but you need a paid subscription to access full articles.

News sites such as *Psychiatric News* (http://pn.psychiatryonline.org), *Psychiatric Times* (www.psychiatrictimes.com), *Clinical Psychiatry News* (www.clinicalpsychiatrynews.com), and Medscape Psychiatry (www.medscape.com/psychiatry) offer free full-text access to news updates and summaries of recent major papers and presentations. These summaries help you stay abreast of the literature, but they are not as detailed as the original sources.

You don't need a subscription to request free electronic tables of contents (e-TOCs) from selected journals. Some e-TOCs list links to abstracts of all articles in the current issue.

Online clinical textbooks and journals. American Psychiatric Publishing's online DSM Premium package (www.psychiatryonline.com) includes access to the *Textbook of Clinical Psychiatry*, 5 psychiatry journals, American Psychiatric Association (APA) practice guidelines, and the DSM Library. DSM Premium Plus also includes access to 3 PDA-based eBooks (DSM-IV-TR Quick Reference, DSM-IV-TR Differential Diagnosis, and APA Practice Guidelines Quick Reference). Packages cost $229 to $399 annually, depending on which package you choose and whether you are an APA member.

Open-source book technology allows users to contribute to and edit an online volume. Wikipedia (http://en.wikipedia.org), the prototypical open-source site, hosts a free online encyclopedia.

Giles[1] in 2005 found the accuracy of science entries in Wikipedia comparable to similar entries in Encyclopaedia Britannica. Among 42 entries from both encyclopedias, researchers found on average 4 errors per entry with Wikipedia and 3 with Encyclopaedia Britannica.

One sister Wiki project, Wikibooks (http://en.wikibooks.org), is designed to encourage production of open-source textbooks. This has led to one fledgling psychiatry textbook (http://en.wikibooks.org/wiki/Psychiatry) and others soon could follow. The clinical accuracy of this Wiki-based psychiatry textbook is variable, though this could improve if more psychiatrists become involved with Wikibook peer review.

Reference

1. Giles J. Internet encyclopaedias go head to head. *Nature* 2005;438 (7070):900-1. Available at: http://www.nature.com/news/2005/051212/full/438900a.html. Accessed February 14, 2007.

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