Launch of the Initiative to Improve Behavioral Health and Reduce the Use of Antipsychotic Medications in Nursing Homes Residents

A Centers for Medicare & Medicaid Services (CMS)
Video Streaming Event

Premieres Thursday, March 29, 2012
1:00pm EST – 2:00pm EST

On March 29, CMS will launch a new initiative aimed at improving behavioral health and safeguarding nursing home residents from unnecessary antipsychotic drug use. As part of the initiative, CMS is developing a national action plan that will use a multidimensional approach including public reporting, raising public awareness, regulatory oversight, technical assistance/training and research. The action plan will be targeted at enhancing person-centered care for nursing home residents, particularly those with dementia-related behaviors.

Goals for the Video Streaming Event
CMS will provide an overview of the national initiative, resources for technical assistance, and plans for upcoming educational offerings on this topic.

Handouts
Handouts for this broadcast are attached and are also available at the following website:
http://surveyortraining.cms.hhs.gov.

Objectives
Join Patrick Conway, MD, MSc, Chief Medical Officer for the Centers for Medicare & Medicaid Services and Director of the Office of Clinical Standards and Quality, Shari Ling, MD, Centers for Medicare and Medicaid Services, Deputy Chief Medical Officer serving in the Office of Clinical Standards and Quality and Alice Bonner, PhD, RN, Director for the Division of Nursing Homes in the Office for Clinical Standards and Quality in the introduction of this national initiative, discussion of behavioral health opportunities and the announcement of upcoming training sessions.

Target Audience
State Survey Agencies, residents and family members, nursing home staff, clinicians, providers, advocates, CMS Regional Offices, and others (Non-Mandatory)

Registration and Viewing Instructions
Register today at http://surveyortraining.cms.hhs.gov.

Video Streaming Information
This program will be available for viewing up to one year following March 29, 2012, at http://surveyortraining.cms.hhs.gov.

This event is open to the public, so please share this invitation with anyone else who may wish to attend. Thank you for joining CMS in our efforts to improve the quality of care and quality of life for America's nursing home residents.

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Press Releases

Details for: CMS ANNOUNCES PARTNERSHIP TO IMPROVE DEMENTIA CARE IN NURSING HOMES

Return to List

For Immediate Release: Wednesday, May 30, 2012

Contact: CMS Office of Public Affairs
202-690-6145

CMS ANNOUNCES PARTNERSHIP TO IMPROVE DEMENTIA CARE IN NURSING HOMES

GOVERNMENT PARTNERING WITH PROVIDERS, CAREGIVERS, PATIENTS TO ENSURE APPROPRIATE USE OF ANTIPSYCHOTIC MEDICATIONS

CMS ANNOUNCES PARTNERSHIP TO IMPROVE DEMENTIA CARE IN NURSING HOMES

Government partnering with providers, caregivers, patients to ensure appropriate use of antipsychotic medications

Today, Centers for Medicare & Medicaid Services (CMS) Acting Administrator Marilyn Tavenner announced the Partnership to Improve Dementia Care, an initiative to ensure appropriate care and use of antipsychotic medications for nursing home patients. This partnership – among federal and state partners, nursing homes and other providers, advocacy groups and caregivers – has set a national goal of reducing use of antipsychotic drugs in nursing home residents by 15 percent by the end of 2012.

Unnecessary antipsychotic drug use is a significant challenge in ensuring appropriate dementia care. CMS data show that in 2010 more than 17 percent of nursing home patients had daily doses exceeding recommended levels.

"We want our loved ones with dementia to receive the best care and the highest quality of life possible," said Acting Administrator Marilyn Tavenner. "We are partnering with nursing homes, advocates, and others to improve the quality of care these individuals receive in nursing homes. As part of this effort, our partnership has set an ambitious goal of reducing use of antipsychotics in nursing homes by 15 percent by the end of this year."

CMS and industry and advocacy partners are taking several steps to achieve this goal of improved care:

Enhanced training: CMS has developed Hand in Hand, a training series for nursing homes that emphasizes person-centered care, prevention of abuse, and high-quality care for residents. CMS is also providing training focused on behavioral health to state and federal surveyors;

Increased transparency: CMS is making data on each nursing home's antipsychotic drug use available on Nursing Home Compare starting in July of this year, and will update this data;

Alternatives to antipsychotic medication: CMS is emphasizing non-pharmacological alternatives for nursing home residents, including potential approaches such as consistent staff assignments, increased exercise or time outdoors, monitoring and managing acute and chronic pain, and planning individualized activities.

"A CMS nursing home resident report found that almost 40 percent of nursing home patients with signs of dementia were receiving antipsychotic drugs at some point in 2010, even though there was no diagnosis of psychosis," said CMS Chief Medical Officer and Director of Clinical Standards and Quality Patrick Conway, M.D. "Managing dementia without relying on medication can help improve the quality of life for these residents. The Partnership to Improve Dementia Care will equip residents, caregivers, and providers with the best tools to make the right decision."

These efforts will help achieve the 15 percent reduction goal by the end of this year. In addition, to address this challenge in the long-term CMS is conducting research to better understand the decision to use or not to use antipsychotic drugs in residents with dementia. A study is underway in 20 to 25 nursing homes, evaluating this decision-making process. Findings will be used to target and implement approaches to improve the overall management of residents with dementia, including reducing the use of antipsychotic drugs in this population.

Comparative Effectiveness Review
Number 43

Effective Health Care Program

Off-Label Use of Atypical Antipsychotics: An Update

Executive Summary

Background

Antipsychotics medications are approved by the U.S. Food and Drug Administration (FDA) for treatment of schizophrenia and bipolar disorder. These medications are commonly divided into two classes, reflecting two waves of historical development: the conventional antipsychotics and the atypical. The conventional antipsychotics served as the first successful pharmacologic treatment for primary psychotic disorders such as schizophrenia. Having been widely used for decades, the conventional antipsychotics also produced various side effects requiring additional medications, which spurred the development of the atypical antipsychotics.

Currently, nine atypical antipsychotic drugs have been approved by FDA: aripiprazole, asenapine, clozapine, iloperidone, olanzapine, paliperidone, quetiapine, risperidone, and ziprasidone. These drugs have been used off-label (i.e., for indications not approved by FDA) for the treatment of various psychiatric conditions. While it is legal for a physician to prescribe drugs in such a manner, it is illegal for the manufacturer to actively promote such use.

A 2006 study on Efficacy and Comparative Effectiveness of Off-label Use of Atypical Antipsychotics reviewed the scientific evidence on the safety, efficacy, and effectiveness for off-label uses. (Clozapine was excluded because of its association with a potentially fatal blood disorder of bone marrow suppression, and it requires frequent blood tests for safety monitoring.) The 2006 study examined 84 published studies on atypicals and found that the

Effective Health Care Program

The Effective Health Care Program was initiated in 2005 to provide valid evidence about the comparative effectiveness of different medical interventions. The object is to help consumers, health care providers, and others in making informed choices among treatment alternatives. Through its Comparative Effectiveness Reviews, the program supports systematic appraisals of existing scientific evidence regarding treatments for high-priority health conditions. It also promotes and generates new scientific evidence by identifying gaps in existing scientific evidence and supporting new research. The program puts special emphasis on translating findings into a variety of useful formats for different stakeholders, including consumers.

The full report and this summary are available at **www.effectivehealthcare.ahrq.gov/reports/final.cfm.**

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Effective Health Care

most common off-label uses of the drugs were for treatment of depression, obsessive-compulsive disorder (OCD), post-traumatic stress disorder (PTSD), personality disorders, Tourette's syndrome, autism, and agitation in dementia. It concluded that with few exceptions, there was insufficient high-strength evidence to reach conclusions about the efficacy of any off-label uses of these medications. It also found strong evidence that atypicals are associated with increased risk of adverse events such as significant weight gain, sedation, and, among the elderly, increased mortality. Future research areas suggested by the report include safe treatment for agitation in dementia, association between the increased risk of death and antipsychotics drugs, and comparison of the development of adverse effects between patients taking atypical antipsychotics and those taking conventional antipsychotics.

Since publication of that report, important changes have occurred that make the report out of date. Studies have been published on new off-label uses, such as treatment of eating disorders, insomnia, attention-deficit hyperactivity disorder (ADHD), anxiety, and substance abuse. New or increased adverse effects of off-label indications have been observed and new atypicals (asenapine, iloperidone, and paliperidone) have been approved by FDA for the treatment of schizophrenia and bipolar disorder. In addition, the following previously off-label uses have been approved for on-label use by the FDA:

- Quetiapine and quetiapine ER (extended release) as monotherapy in bipolar depression
- Quetiapine ER as augmentation for major depressive disorder (MDD)
- Aripiprazole as augmentation for MDD
- Olanzapine/fluoxetine combination for MDD
- Olanzapine/fluoxetine combination for bipolar depression
- Risperidone and aripiprazole for autism spectrum disorders

An update is needed to better understand the trends in off-label use and the associated risks and benefits. Further, a number of issues remain unclear due to insufficient information in the previous report: subpopulations (i.e., race/ethnicity, gender) that would benefit most from atypical antipsychotics, appropriate dose, and time needed to see clinical improvement. This update will try to address these issues.

This report covers the following off-label uses of atypical antipsychotic medications: anxiety, ADHD, dementia and severe geriatric agitation, major depressive disorder (MDD), eating disorders, insomnia, OCD, PTSD, personality disorders, substance abuse, and Tourette's syndrome. Autism, included in the original systematic review, is now reviewed in a study on the comparative effectiveness of typical and atypical antipsychotics for on-label indications, conducted by another organization.

This report addresses the following Key Questions:

Key Question 1: What are the leading off-label uses of atypical antipsychotics in utilization studies? How have trends in utilization changed in recent years, including inpatient versus outpatient use? What new uses are being studied in trials?

Key Question 2: What does the evidence show regarding the efficacy and comparative effectiveness of atypical antipsychotics for off-label indications?

Sub-Key Question 2: How do atypical antipsychotic medications compare with other drugs, including first-generation antipsychotics, for treating off-label indications?

Key Question 3: What subset of the population would potentially benefit from off-label uses? Do effectiveness and harms differ by race/ethnicity, gender, and age group? By severity of condition and clinical subtype?

Key Question 4: What are the potential adverse effects and/or complications involved with off-label prescribing of atypical antipsychotics? How do they compare within the class and with other drugs used for the conditions?

Key Question 5: What is the effective dose and time limit for off-label indications?

Conclusions

Key Question 1: What are the leading off-label uses of atypical antipsychotics in utilization studies? How have trends in utilization changed in recent years, including inpatient versus outpatient use? What new uses are being studied in trials?

Atypicals have been studied as off-label treatment for the following conditions: ADHD, anxiety, dementia in elderly patients, depression, eating disorders, insomnia, OCD, personality disorder, PTSD, substance use disorders, and Tourette's syndrome.

Off-label use of atypical antipsychotics in various settings has increased rapidly since their introduction in the 1990s; risperidone, quetiapine, and olanzapine are the most common atypicals prescribed for off-label use.

One recent study indicated that the 2005 regulatory warning from the FDA and Health Canada was associated with decreases in the overall use of atypical antipsychotics, especially among elderly dementia patients.

Use of atypicals in the elderly is much higher in long-term care settings than in the community.

Atypicals are frequently prescribed to treat PTSD in the U.S. Department of Veterans Affairs health system.

At least 90 percent of antipsychotics prescribed to children are atypical, rather than conventional antipsychotics. The majority of use is off-label.

No off-label use of the newly approved atypicals (asenapine, iloperidone, and paliperidone) was reported in the utilization literature.

Key Question 2: What does the evidence show regarding the efficacy and comparative effectiveness of atypical antipsychotics, for off-label indications? Sub-Key Question 2: How do atypical antipsychotic medications compare with other drugs, including first-generation antipsychotics, for treating off-label indications?

The efficacy results are summarized in Table A below. It is important to note that no trials of the three most recently FDA-approved atypicals (asenapine, iloperidone, and paliperidone) were found for off-label use. Cells shaded in dark blue indicate areas with the strongest evidence of efficacy, followed by the areas in orange. Areas containing circles indicate areas where no clinical trials exist. Light orange and light blue areas indicate areas where evidence of inefficacy exists. Areas in medium blue indicate mixed results.

Table A. Summary of strength of evidence of efficacy, by drug and condition

	Aripiprazole	Olanzapine	Quetiapine	Risperidone	Ziprasidone
Anxiety					
- generalized anxiety disorder	O	-	++	-	-
Anxiety					
- social phobia	O	+	-	O	O
Attention Deficit/Hyperactivity Disorder					
-no co-occurring disorders	O	O	O	+	O
Attention Deficit/Hyperactivity Disorder					
-bipolar children	-	O	O	O	O
Attention Deficit/Hyperactivity Disorder					
-mentally retarded children	O	O	O	+	O
Dementia overall	++	+	+	++	O
Dementia psychosis	+	+-	+-	++	O
Dementia agitation	+	++	+-	++	O
Depression					
-MDD augmentation of SSRI/SNRI	++	+	++	++	+
Depression					
-MDD: Monotherapy	O	-	++	O	O
Eating Disorders	O	--	-	O	O
Insomnia	O	O	-	O	O
Obsessive Compulsive Disorder					
-augmentation of SSRI	O	+	--	++	-
Obsessive Compulsive Disorder					
-augmentation of citalopram	O	O	+	+	O
Personality Disorder					
-borderline	+	+-	+	O	-

Table A. Summary of strength of evidence of efficacy, by drug and condition (continued)

	Aripiprazole	Olanzapine	Quetiapine	Risperidone	Ziprasidone
Personality Disorder					
-schizotypal	O	O	O	+-	O
Post Traumatic Stress Disorder	O	+-	+	++	O
Substance Abuse alcohol	--	-	-	O	O
Substance Abuse cocaine	O	-	O	-	O
Substance Abuse methamphetamine	-	O	O	O	O
Substance Abuse methadone clients	O	O	O	-	O
Tourette's Syndrome	O	O	O	+	-

++: moderate or high evidence of efficacy
+ : low or very low evidence of efficacy
+- : mixed results
- : low or very low evidence of inefficacy
-- : moderate or high evidence of inefficacy
O : no trials
□: Approved by FDA for the indication

MDD = major depressive disorder; SSRI = selective serotonin reuptake inhibitor; SNRI = serotonin-norepinephrine reuptake inhibitors

Note: Symbols denote strength of evidence, not size of portential effect. For example, in dementia "++" indicates moderate-to-high strength of evidence that there is a beneficial effect; however, the size of the effect is small.

Table B below shows how our current efficacy findings compare with those of our original Comparative Effectiveness Review (CER) submitted to the Agency for Healthcare Research and Quality (AHRQ) in 2006. The evidence that atypicals have efficacy in treating symptoms of dementia has increased in the past few years; this evidence must be weighed against possible harms described in Key Question 4 below. Evidence of efficacy as augmentation for MDD and OCD patients who have not responded adequately to selective serotonin reuptake inhibitors/serotonin-norepinephrine reuptake inhibitors (SSRIs/SNRIs) has also increased. Table B is organized as follows: First, all conditions dealt with in our original CER, in alphabetical order; second, all the new off-label indications in alphabetical order.

Key Question 3: What subset of the population would potentially benefit from off-label uses? Do effectiveness and harms differ by race/ethnicity, gender, and age group? By severity of condition and clinical subtype?

There are insufficient data regarding efficacy, effectiveness, and harms to determine what subset of the population would potentially benefit from off-label uses of atypicals. Only one study conducted a subgroup analysis by gender; there were no studies that stratified by racial or ethnic group. Although many studies specified age in their inclusion criteria, few studies stratified results by age.

Examination of the literature for differing efficacy of atypicals by clinical subsets did not reveal studies reporting subgroup analyses. Our own meta-analysis found efficacy for combat-related PTSD in men but not for PTSD in civilian women, although these data come from separate literatures, and head-to-head comparison of gender effects within study have not been performed. Due to the varying measures utilized in determining severity of illness, it was not possible to analyze treatment effects by severity of illness across any other condition.

Key Question 4: What are the potential adverse effects and/or complications involved with off-label prescribing of atypical antipsychotics? How do they compare within the class and with other drugs used for the conditions?

Table C compares the most important findings regarding adverse events, by age group and study design.

Table B. Summary update: efficacy of atypical antipsychotics for off-label use				
Usage	**Strength of Evidence**	**2006 Findings**	**2011 Findings**	**2011 Conclusions**
Dementia	High	A published meta-analysis of 15 placebo-controlled trials (PCTs) found small but statistically significant effects favoring treatment with risperidone and aripiprazole. There were effects that favored treatment with olanzapine for the BPRS and the NPI, but these differences were not statistically significant. Three studies of quetiapine were considered too clinically dissimilar to pool and results for the individual studies showed, with one exception, trends favoring treatment with quetiapine that did not reach conventional levels of statistical significance.	Overall – In our meta-analysis of PCTs, aripiprazole, olanzapine, and risperidone were superior to placebo as treatment of behavioral symptoms as measured by total scores on BEHAVE-AD, BPRS, and NPI. Effect sizes were generally considered to be "small" in magnitude. Psychosis – In our meta-analysis risperidone was superior to placebo, as measured by the psychosis subscales of the BEHAVE-AD, BPRS, and NPI. Results for aripiprazole did not meet conventional levels of statistical significance. Agitation – In our meta-analysis, aripiprazole, olanzapine and risperidone were superior to placebo, as measured by the agitation subscales of the BEHAVE-AD, BPRS, NPI, and CMAI. Three head to head trials compared atypicals; none was found superior.	Aripiprazole, olanzapine, and risperidone **have efficacy** as treatment for behavioral symptoms of dementia.

Table B. Summary update: efficacy of atypical antipsychotics for off-label use (continued)				
Usage	**Strength of Evidence**	**2006 Findings**	**2011 Findings**	**2011 Conclusions**
Depression – MDD: augmentation of SSRI/SNRI	Moderate – risperidone, aripiprazole, quetiapine Low – olanzapine, ziprasidone	Three trials assessed the combination of olanzapine and fluoxetine, one trial each assessed augmentation of various SRIs with risperidone, ziprasidone, and quetiapine, and one study assessed adding risperidone versus olanzapine to SSRI. The combination of olanzapine and fluoxetine was no better than fluoxetine alone in improvement of depressive symptoms at 8 weeks, but three trials reported more rapid improvement in depressive symptoms (at 2–4 weeks) with combination therapy using olanzapine or quetiapine. The one trial that directly compared augmentation therapy between olanzapine and risperidone reported no differences in outcome.	We conducted a meta-analysis using "response" to treatment and remission as outcome. Pooling trials that reported the HAM-D as outcome, the relative risk of responding for participants taking quetiapine or risperidone was significantly higher than for placebo. Olanzapine had only two trials, so pooling was not performed; the trials reported olanzapine superior to placebo. Other trials reported MADRS scores; the relative risk of responding for participants taking aripiprazole was significantly higher than those taking placebo. Risperidone and ziprasidone were included in two trials and one trial, respectively. These reported the drug superior to placebo. One trial compared ziprasidone at differing levels augmenting sertraline to sertraline alone. This trial found a greater improvement in CGI-S and MADRS scores augmenting with ziprasidone at 160mg than either augmentation with ziprasidone at 80mg or sertraline alone. However, there was no significant difference in HAMD-17, CGI-I or HAM-A scores.	Aripiprazole, quetiapine, and risperidone **have efficacy** as augmentation to SSRIs/SNRIs for major depressive disorder. Olanzapine and ziprasidone **may also have efficacy**.
Depression – MDD: Monotherapy	Moderate	The three olanzapine studies (above) also assessed its efficacy as monotherapy. Olanzapine alone was no better than placebo in improving symptoms at 6 or 12 weeks. Outcomes were too heterogeneous to allow pooling.	In our meta-analysis of five placebo-controlled trials, quetiapine was superior according to relative risk of both responding and remitted as measured by MADRS.	Olanzapine **does not have efficacy** as monotherapy for major depressive disorder. Quetiapine **has efficacy** as monotherapy for major depressive disorder.

Table B. Summary update: efficacy of atypical antipsychotics for off-label use (continued)				
Usage	**Strength of Evidence**	**2006 Findings**	**2011 Findings**	**2011 Conclusions**
Obsessive-compulsive disorder – augmentation of SSRI	Moderate –risperidone Low – olanzapine	Twelve trials used risperidone, olanzapine, or quetiapine as augmentation therapy in patients who were resistant to treatment with SSRI. Nine trials were sufficiently similar clinically to pool. Atypical antipsychotics had a clinically important benefit (measured by the Yale-Brown Obsessive-Compulsive Scale) when used as augmentation therapy. Relative risk of "responding" significant for augmentation with quetiapine and risperidone. There were too few studies of olanzapine augmentation to permit separate pooling of this drug.	Our updated meta-analysis found risperidone superior to placebo, as measured by changed in the Yale Brown Obsessive Compulsive Scale (Y-BOCS). There were too few studies (two) to permit separate pooling for olanzapine; both trials reported olanzapine superior to placebo. One new head to head trial found no difference in effect between olanzapine and risperidone as SSRI augmentation. One new head to head trial found quetiapine more effective than ziprasidone as SSRI augmentation. One new trial compared quetiapine to clomipramine as SSRI augmentation. Quetiapine produced a significant reduction in Y-BOCS score, while clomipramine did not.	Risperidone **has efficacy** in improving OCD symptoms when used as an adjunct to SSRI in treatment refractory patients. Olanzapine may also **have efficacy**. Quetiapine is more **efficacious** than ziprasidone and clomipramine for this purpose.
Obsessive-compulsive disorder – augmentation of citalopram	Low–quetiapine Very low – risperidone	One trial of risperidone reported no differences between groups in achieving a response to therapy, but patients maintained on risperidone had a significantly longer period of time to relapse compared to placebo (102 days vs. 85 days)	Two new trials found quetiapine superior to placebo as augmentation for citalopram, according to Y-BOCS and CGI-I scores.	Quetiapine and risperidone may be **efficacious** as augmentation to citalopram in OCD patients.
Post-traumatic stress disorder	Moderate – risperidone Olanzapine – Low Quetiapine – very low	Four trials of risperidone and two trials of olanzapine, each of at least 6 week duration, treated patients with PTSD. Three trials enrolled men with combat-related PTSD; these showed a benefit in sleep quality, depression, anxiety, and overall symptoms when risperidone or olanzapine was used to augment therapy with antidepressants or other psychotropic medication. Three trials of olanzapine or risperidone as monotherapy for abused women with PTSD were inconclusive regarding efficacy.	Three new trials of risperidone were found, allowing us to conduct a meta-analysis using the Clinician Administered PTSD Scale (CAPS) as outcome. Risperidone was superior to placebo. There were too few olanzapine studies (two) to pool; one reported olanzapine superior to placebo, while one did not. A new trial found a 3-fold decline in CAPS scores in patients treated with quetiapine monotherapy compared to placebo. Exact scores were not reported. We also conducted a meta-analysis by condition; atypicals were efficacious for combat-related PTSD but not PTSD in abused women.	Risperidone is **efficacious** in reducing combat-related PTSD symptoms when used as an adjunct to primary medication.

Table B. Summary update: efficacy of atypical antipsychotics for off-label use (continued)				
Usage	**Strength of Evidence**	**2006 Findings**	**2011 Findings**	**2011 Conclusions**
Personality disorders – borderline	Low – aripiprazole Very low – quetiapine, olanzapine	Three trials provide evidence that olanzapine is superior to placebo and may be superior to fluoxetine. The benefit of adding olanzapine to dialectical therapy in one trial was small. Aripiprazole was superior to placebo in one small trial.	One new trial found aripiprazole superior to placebo in improving SCL-90, HAM-D, and HAM-A scores at 8 months and less self-injury at 18 months. One new trial of ziprasidone found no significant difference in CGI-BPD, depressive, anxiety, psychotic or impulsive symptoms compared to placebo at 12 weeks. Two new trials of olanzapine found no difference from placebo in any outcomes, while another new trial of olanzapine found greater change in ZAN-BPD scores at 12 weeks, compared with placebo. One new trial found quetiapine superior to placebo on BPRS, PANSS scales. Due to heterogeneity of outcomes, we could not perform a meta-analysis.	Olanzapine had **mixed results** in 7 trials, aripiprazole was found **efficacious** in two trials, quetiapine was found **efficacious** in one trial, and ziprasidone was found **not efficacious** in one trial.
Personality disorders – schizotypal	Low	Risperidone was superior to placebo in one small trial.	One new small trial of risperidone found no difference from placebo on a cognitive assessment battery.	Risperidone had **mixed results** when used to treat schizotypal personality disorder in two small trials.
Tourette's syndrome	Low	Risperidone was superior to placebo in one small trial, and it was at least as effective as pimozide or clonidine for 8 to 12 weeks of therapy in the three other trials. One trial of ziprasidone showed variable efficacy compared to placebo.	No additional trials.	Same as 2006: Risperidone **is at least as efficacious as pimozide or clonidine** for Tourette's syndrome.
Anxiety	Moderate	Not covered.	Three placebo-controlled trials of quetiapine as monotherapy for Generalized Anxiety Disorder (GAD) could be pooled; relative risk of responding on HAM-A favored the quetiapine group. One head to head trial showed no difference between risperidone and paroxetine on HAM-A score improvement. One trial each found quetiapine equally effective as paroxetine and escitalopram.	Quetiapine **has efficacy** as treatment for Generalized Anxiety Disorder

Table B. Summary update: efficacy of atypical antipsychotics for off-label use (continued)				
Usage	**Strength of Evidence**	**2006 Findings**	**2011 Findings**	**2011 Conclusions**
Attention deficit/ hyperactivity disorder – no co-occurring disorders	Low	Not covered.	One trial showed risperidone superior to placebo in reducing scores on the Children's Aggression Scale – Parent version (CAS-P).	Risperidone may be **efficacious** in treating children with ADHD with no serious co-occurring disorders.
Attention deficit/ hyperactivity disorder–mentall y retarded children	Low	Not covered.	One trial showed risperidone led to greater reduction in SNAP-IV (Swanson, Nolan, and Pelham teacher & parent rating scale) scores than methylphenidate.	Risperidone **may be superior to methylphenidate** in treating ADHD symptoms in mentally retarded children.
Attention deficit/ hyperactivity disorder – bipolar children	Low	Not covered.	Two trials of aripiprazole showed no effect on SNAP-IV (Swanson, Nolan, and Pelham teacher & parent rating scale) scores than placebo.	Aripiprazole is **inefficacious** in reducing ADHD symptoms in children with bipolar disorder.
Eating disorders	Moderate – olanzapine Low - quetiapine	Not covered.	Five trials of olanzapine were found; three reporting Body Mass Index (BMI) could be pooled. There was no difference in change in BMI at either one or three months compared to placebo. One trial of quetiapine reported no statistical difference from placebo in BMI increase at three months.	Olanzapine and quetiapine **have no efficacy** in increasing body mass in eating disorder patients.
Insomnia	Very low.	Not covered.	In one small trial (N=13) of quetiapine, sleep outcomes were not statistically different from placebo.	Quetiapine may be **inefficacious** in treating insomnia.
Substance abuse – alcohol	Moderate – aripiprazole Low – quetiapine	Not covered. Not covered.	Two trials of aripiprazole and one of quetiapine reported % of patients completely abstinent during follow-up. In our pooled analysis, the effect versus placebo was insignificant.	Aripiprazole is **inefficacious** in treating alcohol abuse /dependence. Quetiapine may also be **inefficacious**.

Table B. Summary update: efficacy of atypical antipsychotics for off-label use (continued)				
Usage	**Strength of Evidence**	**2006 Findings**	**2011 Findings**	**2011 Conclusions**
Substance abuse – cocaine	Low	Not covered.	Two trials of olanzapine and one of risperidone reported there was no difference in efficacy versus placebo as measured by the Addiction Severity Index (ASI).	Olanzapine is **inefficacious** in treating cocaine abuse/ dependence. Risperidone may also be **inefficacious**.
Substance abuse – meth-amphetamine	Low	Not covered.	One trial found aripiprazole inefficacious in reducing use of intravenous amphetamine, as measured by urinalysis. Another trial found aripiprazole inefficacious in reducing craving for methamphetamine.	Aripiprazole is **inefficacious** in treating methamphetamine abuse/dependence.
Substance abuse – methadone clients	Low	Not covered.	One trial of methadone clients found no difference between risperidone and placebo in reduction of cocaine or heroin use.	Risperidone is an inefficacious adjunct to methadone maintenance.

ADHD = attention-deficit hyperactivity disorder; BEHAVE-AD = Behavioral Pathology in Alzheimer's Disease Scale; BPRS = Brief Psychiatric Rating Scale; CGI-BPD = Clinical Global Impression Scale for Borderline Personality Disorder; CGI-I = Clinical Global Impression Improvement; CGI-S = Clinical Global Impression-Severity; CMAI = Cohen-Mansfield Agitation Inventory; HAM-A = Hamilton Anxiety Scale; HAM-D = Hamilton Depression Rating Scale; MADRS = Montgomery-Asberg Depression Rating Scale; MDD = major depressive disorder; NPI = Neuropsychiatric Inventory; OCD = obsessive-compulsive disorder; PANSS = Positive and Negative Syndrome Scale; PCT = placebo-controlled trial; PTSD = post-traumatic stress disorder; SSRI = selective serotonin reuptake inhibitor; SNRI = serotonin-norepinephrine reuptake inhibitors; ZAN-BPD = Zanarini Rating Scale for Borderline Personality Disorder

Table C. Summary update: safety of atypical antipsychotics for off-label use			
Adverse Event	**Head-to-Head Comparisons**	**Active Comparisons**	**Placebo Comparisons**
Weight gain– Elderly patients	In one large trial (CATIE-AD) patients who were treated with olanzapine, quetiapine, or risperidone averaged a monthly gain of 1.0, 0.7, and 0.4 lbs respectively, compared with a monthly weight loss of 0.9 lbs for placebo patients.	More common in patients taking olanzapine than risperidone or conventional antipsychotics, particularly if their BMI was less than 25 at baseline, according to a large cohort study.	More common in patients taking olanzapine and risperidone than placebo according to our meta-analysis.
Weight gain– Adults 18–64	More common in olanzapine patients than ziprasidone patients in one trial.	More common among patients taking olanzapine than patients taking conventional antipsychotics in three trials. More common in patients taking aripiprazole than patients taking conventional antipsychotics in one trial. More common among patients taking olanzapine than patients taking mood stabilizers in two trials.	More common in patients taking aripiprazole, olanzapine, quetiapine, and risperidone than placebo according to our meta-analysis.
Weight gain– Children & adolescents	No head-to-head studies.	No difference between clonidine and risperidone in one trial.	More common in patients taking risperidone in two PCTs. No difference in one small PCT of ziprasidone.
Mortality– Elderly patients	No difference between olanzapine and risperidone according to a meta-analysis of six trials of olanzapine published in 2006.	Six large cohort studies compared mortality in elderly patients taking atypical and conventional antipsychotics. Four of these studies found a significantly higher rate of death with conventional antipsychotics, while two found no statistical difference in mortality between the drug classes.	The difference in risk for death was small but statistically significant for atypicals, according to a 2006 meta-analysis which remains the best available estimate. Sensitivity analyses found no difference between drugs in the class. Patients taking atypicals had higher odds of mortality than those taking no antipsychotics in the two cohort studies that made that comparison. There are no trials or large observational studies of ziprasidone in this population; therefore, we cannot make conclusions regarding safety here.

Table C. Summary update: safety of atypical antipsychotics for off-label use (continued)			
Adverse Event	**Head-to-Head Comparisons**	**Active Comparisons**	**Placebo Comparisons**
Endocrine/ diabetes – Elderly patients	No evidence reported.	No evidence reported.	No difference in endocrine events in risperidone patients in one PCT. Regarding diabetes, risk was elevated but not statistically significant in one industry-sponsored cohort study of olanzapine patients.
Endocrine/ diabetes – Adults 18–64	Diabetes more common in patients taking olanzapine than patients taking risperidone in one trial.	No evidence reported.	Endocrine events more common in patients taking quetiapine, risperidone, and ziprasidone in one PCT each. More common in olanzapine in two pooled PCTs. Diabetes more common in patients taking quetiapine in six pooled PCTs; however, the pooled odds ratio was elevated at 1.47 but not statistically significant. More common in olanzapine patients in one PCT; the odds ratio of 5.14 was not statistically significant, with very wide confidence intervals (0.6 to 244). Lower odds of diabetes in risperidone patients in one large observational study

Table C. Summary update: safety of atypical antipsychotics for off-label use (continued)			
Adverse Event	**Head-to-Head Comparisons**	**Active Comparisons**	**Placebo Comparisons**
CVA – Elderly patients	No evidence reported.	Hospitalization for CVA was increased in the first week after initiation of conventional antipsychotics, but not for initiation of atypicals in a large cohort study.	More common in risperidone patients than placebo according to four PCTs pooled by the manufacturer. In our new meta-analysis of PCTs, risperidone was the only drug associated with an increase. More common in olanzapine than placebo according to five PCTs pooled by the manufacturer.
EPS –	More common in patients taking aripiprazole and risperidone patients than patients taking quetiapine in one large trial (CATIE-AD).	No evidence reported.	More common in patients taking risperidone, according to our meta-analysis. Quetiapine and aripiprazole were not associated with an increase. More common in olanzapine in one PCT.
EPS – Adults 18–64	No evidence reported.	Less likely in patients taking quetiapine than mood stabilizers in one small trial. Less likely in patients taking olanzapine or aripiprazole than patients taking conventional antipsychotics in one trial each.	More common in patients taking aripiprazole, quetiapine, and ziprasidone than placebo according to our meta-analysis.
Sedation – Elderly patients	More common in elderly patients taking olanzapine or quetiapine than risperidone according to our analysis, but not quite statistically significant.	No difference in one trial of olanzapine versus benzodiazepines. No difference in three trials of olanzapine and three of risperidone versus conventional antipsychotics.	More common in patients taking aripiprazole, olanzapine, quetiapine, and risperidone than placebo according to our meta-analysis.
Sedation – Children and adolescents	No head-to-head trials.	No difference in one small trial of clonidine versus risperidone. More patients on haloperidol than risperidone reported sleep problems in one trial.	Less common in aripiprazole patients than placebo patients in one PCT. No difference from placebo in one small PCT of ziprasidone.

Table C. Summary update: safety of atypical antipsychotics for off-label use (continued)			
Adverse Event	**Head-to-Head Comparisons**	**Active Comparisons**	**Placebo Comparisons**
Sedation – Adults 18–64	More common in patients taking quetiapine than risperidone in two trials.	Olanzapine patients had higher odds than mood stabilizer patients in two trials. No difference in one trial of risperidone versus olanzapine. More common in olanzapine and quetiapine patients than SSRIs patients in three and two trials respectively. Olanzapine patients had lower odds than patients taking conventional antipsychotics in our pooled analysis of three trials.	More common in patients taking aripiprazole, olanzapine, quetiapine, risperidone, and ziprasidone than placebo in our meta-analysis.

BMI = body mass index; CATIE-AD = Clinical Antipsychotic Trials of Intervention Effectiveness-Alzheimer's Disease; CVA = cerebrovascular accident; EPS = extrapyramidal symptoms; PCT = placebo-controlled trial; SSRI = serotonin selective reuptake inhibitor

Key Question 5: What is the effective dose and time limit for off-label indications?

There are too few studies comparing doses of atypical antipsychotic medications to draw a conclusion about a minimum dose needed. Most trials used flexible dosing, resulting in patients taking a wide range of doses. According to a meta-analysis we were able to conduct using the percentage of remitters and responders according to the MADRS as outcome, 150 mg quetiapine daily augmentation has equal efficacy as augmentation with 300 mg for patients with MDD who respond inadequately to SSRIs. More trials examining different doses of other atypicals for MDD would help guide clinicians in treating this population. In addition, more dosage trials for treating conditions such as OCD, PTSD, and anxiety disorder would allow for pooling and comparison of results.

Though there is some trial data regarding duration of treatment in PTSD, eating disorders, and borderline personality disorder, the outcome of treatment appears to be the same regardless of reported followup time.

Remaining Issues

The overarching finding of this review is that although atypical antipsychotic medications are used for a large number of off-label indications, there is moderate to strong evidence of efficacy for only a few of the drugs and for only a few of the off-label indications. Most of the evidence is for the drugs risperidone, olanzapine, and quetiapine, for the off-label indications of dementia, depression, and OCD. For the newly approved atypicals (asenapine, iloperidone, and paliperidone), we found no clinical trials assessing their use for any off-label condition, and for some off-label uses, we found no or only a small number of trials. Head-to-head comparisons of atypical antipsychotic drugs for off-label uses are few, and evidence from placebo-controlled trials for off-label use suggests that efficacy differs between drugs, meaning that the assumption of a "class effect" for atypical antipsychotics may be unwarranted. This means that each drug requires its own evaluation of efficacy for each off-label indication, which is a large task; drugs demonstrated to be efficacious will need to be compared in head-to-head in trials.

There is almost no evidence about how treatment efficacy may vary within populations, including variations due to gender, race, ethnicity, or medical comorbidities. In addition, existing evidence about the role of baseline severity of disease is too heterogeneous to allow us to draw conclusions. In future research, standardized measures of disease severity might allow for greater knowledge of the patient populations who would benefit from treatment with atypical agents.

Regarding adverse effects of the atypical antipsychotics, existing evidence varies by drug and by description of the adverse event. It would facilitate assessments of comparative effectiveness if future studies contained a standardized list of assessed side effects. As many trials report only those side effects observed, we are unable to compare between trials for many of the side effects.

Another area where clinical guidance is needed is in the dosages required to achieve effects in off-label indications. The dosages used in off-label indications varied from those used in on-label indications. There were few trials that compared effects by dose. Most studies used "flexible" dosing, where a patients dosage can be adjusted during the trial. Thus, a dosage comparison across trials was generally not possible. More research, examining differing dosages within the same population, is required in order to guide clinicians in the appropriate doses to prescribe. A similar issue is that of treatment length. More research reporting responses at various time points would be helpful in determining how long treatment is required. Given the risk of side effects when using these agents, clinicians need to know when a result is expected to prevent continuing an inefficacious agent, unnecessarily.

Newer agents, such as asenapine, iloperidone, and paliperidone, cannot be assumed to have efficacy and harms similar to the older atypical antipsychotics, since the evidence to date does not support that there is a general "class effect" in terms of either efficacy or harm for most off-label indications. Trials assessing the newer agents' efficacy and safety are necessary if they are to be used off-label for any of the above treatment areas.

Full Report

This executive summary is part of the following document: Maglione M, Ruelaz Maher A, Hu J, Wang Z, Shanman R, Shekelle PG, Roth B, Hilton L, Suttorp MJ, Ewing BA, Motala A, Perry T. Off-Label Use of Atypical Antipsychotics: An Update. Comparative Effectiveness Review No. 43. (Prepared by the Southern California/RAND Evidence-based Practice Center under Contract No. HHSA290-2007-10062-1.) AHRQ Publication No. 11-EHC087-EF. Rockville, MD: Agency for Healthcare Research and Quality. September 2011. www.effectivehealthcare.ahrq.gov/reports/final.cfm.

For More Copies

For more copies of Off-Label Use of Atypical Antipsychotics: An Update: Executive Summary No. 43 (AHRQ Pub. No 11-EHC087-1), please call the AHRQ Clearinghouse at 1–800–358–9295 or email ahrqpubs@ahrq.gov.

AHRQ Pub. No. 11-EHC087-1
September 2011

CMS Initiative to Improve Behavioral Health and Reduce the Use of Antipsychotic Medications in Nursing Home Residents

RESOURCES

Updated 6/4/2012

CMS Launches Initiative to Improve Behavioral Health and Reduce the Use of Antipsychotic Medications in Nursing Homes Residents

On March 29, via a video streaming event, CMS launched a new initiative aimed at improving behavioral health and safeguarding nursing home residents from unnecessary antipsychotic drug use. As part of the initiative, CMS is developing a national action plan that will use a multidimensional approach including public reporting, raising public awareness, regulatory oversight, technical assistance/training and research. The action plan will be targeted at enhancing person-centered care for nursing home residents, particularly those with dementia-related behaviors. Watch the CMS video.

CMS' National Initiative to Improve Behavioral Health & Reduce the Use of Antipsychotic Medications for Nursing Home Residents:

Clive Ballard's Presentation on Management of Behavioral and Psychological Symptoms in People with Dementia Living in Care Homes: A UK Perspective

From Dr. Peter Rabins:
Assessment Form for Residents with Dementia

Additional Resources from Advancing Excellence Partners

Alzheimer's Association

http://www.alz.org/professionals_and_researchers_dementia_care_practice_recommendations.asp

Contact:
Cyndy Cordell
cyndy.cordell@alz.org

The American Geriatrics Society (AGS)

http://www.americangeriatrics.org

American Health Care Association (AHCA)

http://www.ahcancal.org/QUALITY_IMPROVEMENT/QUALITYINITIATIVE/Pages/default.aspx

Contact:
Sandy Fitzler
sfitzler@AHCA.org
202-898-6307

American Medical Directors Association (AMDA)

Psychopharmacologic Interdisciplinary Medication Review

Sample Psychotropic Medication Policy

Contact:
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585-784-6405

AMDA's Clinical Practice Guidelines
Dedicated to Long Term Care Medicine: Excerpt from AMDA Dementia Clinical Practice Guideline

http://www.amda.com/advocacy/brucbs.cfm

American Society of Consultant Pharmacists

http://www.ascp.com/antipsychotic

Contact:
Arnold Clayman
aclayman@ascp.com
703-739-1300

California Advocates for Nursing Home Reform (CANHR)

http://www.canhr.org/stop-drugging

Contact:
Michael Conners
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Contact:
Anthony Chicotel
tony@canhr.org

The Consumer Voice

Long Term Care Ombudsmen Resource Center Issue Overview

http://www.theconsumervoice.org/advocate/antipsychotic-drugs

Fact Sheet including guidance to residents and advocates regarding individualized assessment where an individual has behavioral symptoms

http://www.theconsumervoice.org/sites/default/files/advocate/advocacy-groups/INDIVIDUALIZED_ASSESSMENT_with_Behavior_Symptoms.pdf

Contact:
Janet Wells
jwells@theconsumervoice.org

Person-centered Care Planning

http://www.theconsumervoice.org/sites/default/files/resident/nursing-home/assessment-and-care-planning.pdf

Department of Veterans Affairs

http://www.ncbi.nlm.nih.gov/books/NBK54971

The Eden Alternative

The Eden Alternative has created a webpage that summarizes new groundbreaking educational offerings designed to introduce providers to fundamental and advanced techniques in person-directed care proven to reduce the off-label use of antipsychotic drugs.

http://www.edenalt.org/how-we-serve/reduce-the-use-of-antipsychotic-medications-in-people-living-in-long-term-care-settings

Contact:
Meredith Burrus
Education Coordinator
The Eden Alternative
(615) 785-1600
(585) 461-3951
mailto:education@edenalt.org

LeadingAge

http://www.leadingage.org/Newsletter.aspx?id=4694&pv=t

Contact:
Cheryl Phillips, M.D.
cphillips@leadingage.org

National Gerontological Nursing Association (NGNA)

http://www.ngna.org

The National Long-Term Care Ombudsman Resource Center

Person-centered Care Planning

http://www.ltcombudsman.org/ombudsman-support/training#Training_Programs_and_In-services

Toxic Medicine

What You **Should Know** to Fight the Misuse of Psychoactive Drugs in California Nursing Homes

CANHR
Long Term Care Justice and Advocacy

"...you have probably got 15,000 elderly people in nursing homes dying each year from the off-label use of antipsychotic medications for an indication that the FDA knows the drug doesn't work...With every pill that gets dispensed in a nursing home, the drug company is laughing all the way to the bank... We have got so many clinical trials that show these drugs don't work, that it is like malpractice to be using it."

— Testimony of Dr. David Graham, a prominent FDA drug safety expert, at a February 13, 2007 hearing of the House Committee on Energy and Commerce, Subcommittee on Oversight and Investigations: The Adequacy of FDA Efforts to Assure the Safety of the Nation's Drug Supply.

About CANHR's Stop Drugging Campaign

This guide is part of CANHR's Campaign to Stop Chemical Restraints in nursing homes and other long-term care facilities. Ending the misuse of psychoactive drugs is one of CANHR's top priorities because over-drugging is a leading cause of misery, neglect and death for residents who suffer from dementia. The Campaign features a one-of its-kind website where you can join the Campaign, examine drugging rates for each California nursing home, view CANHR's 3-part video series on chemical restraints, learn about better methods of care, read and participate in CANHR's Stop Drugging Our Elders Blog, and much more.

Please join the Campaign today and help us improve residents' lives and end this form of elder abuse.

www.canhr.org/stop-drugging

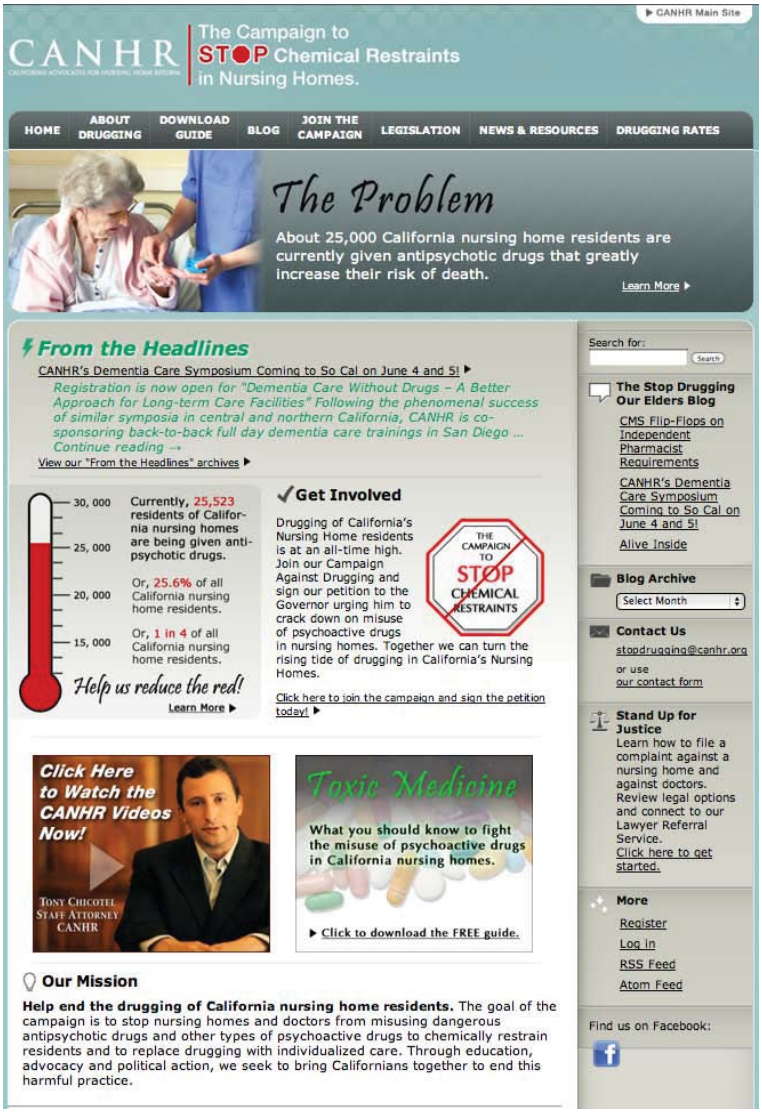


Table of Contents

Introduction

Nursing homes often conjure images of elderly people lying in bed or slumped in wheelchairs completely detached from the world around them. Many visitors and even staff members believe that unresponsive residents are the sad evidence of unavoidable mental declines brought about by dementia or simple old age. However, the poor quality of life for many nursing home residents is often caused not by the symptoms of their disease but by the side effects of their medications.

There is rampant misuse of psychoactive drugs in California nursing homes. Nearly 60% of all California nursing home residents are given psychoactive drugs, a 30% increase since 2000. Many psychoactive medications have dangerous side effects, especially antipsychotic drugs.

Tens of thousands of nursing home residents with dementia receive powerful antipsychotic drugs that are not intended or approved for their medical conditions. Rather, the drugs are often used to sedate and control them, a terrible substitute for the individualized care they need and deserve. The U.S. Food and Drug Administration (FDA) has issued its most dire warning – known as a black box warning – that antipsychotic drugs cause elders with dementia to die.

Antipsychotic drugs don't just hasten death, they often turn residents into people their own families barely recognize by dulling their memories, sapping their personalities and crushing their spirits. When families win battles to take residents off these drugs, they sometimes find that the person they've always known is still there. As one resident's daughter told us, "I got my dad back."

The increased use of psychoactive drugs in nursing homes has been accompanied by an epidemic disregard for the rights of residents to give or withhold their informed consent. Despite legal requirements, the informed consent of residents or their representatives is often ignored.

It is possible to stop a loved one from being drugged by a nursing home. This Guide gives you important facts about psychoactive drugs and advice on how to stop their inappropriate use.

What are Psychoactive Drugs?

Psychoactive drugs – sometimes called psychotropics or psychotherapeutics – contain powerful chemicals that act on the brain to change a person's mood, personality, behavior, and/or level of consciousness.

Types of Psychoactive Drugs

THERE ARE 4 MAJOR CLASSES OF PSYCHOACTIVE DRUGS:

- antipsychotics such as Zyprexa and Haldol;
- anti-anxiety drugs such as Ativan and Valium;
- anti-depressants such as Prozac and Zoloft; and
- sedative/hypnotics such as Halcion and Restoril.

Psychoactive drugs have positive uses. However, many nursing homes routinely use psychoactive drugs as a substitute for needed care and as a form of chemical restraint.

Antipsychotics are the drug of choice in California nursing homes. These extraordinarily dangerous drugs are designed to treat schizophrenia and psychosis, but nursing homes often use them instead to drug residents with dementia into submission. One of every four California nursing home residents is given these drugs on a daily basis. Risperdal, Seroquel, Zyprexa, and Haldol are the most commonly used antipsychotic drugs. Page 17 lists the brand and generic names of antipsychotic drugs.

Antianxiety drugs, such as Ativan and Valium, are also often used to sedate or restrain residents. Like antipsychotic drugs, they are often prescribed for unapproved uses and can cause serious side effects.

Antidepressant drugs are sometimes prescribed in nursing homes without attempting any non-drug interventions even though antidepressants have important downsides, such as increasing a resident's fall risk.

Psychoactive drugs are not the only type of drugs used to sedate or subdue residents with dementia. For example, antiseizure drugs (such as Depakote and Neurontin) are sometimes misused for this purpose.

Risks Galore, Including Death

Psychoactive drugs have numerous, potentially fatal side effects. Some of the most common include tremors, over-sedation, toxicity, anxiety, confusion, delirium and insomnia.

Perversely, psychoactive drugs often cause the agitation and anxiety they are prescribed to treat, leading to even more drugs or higher doses. Elderly nursing home residents are especially at risk of harmful drug interactions because most take many other medications and are in poor health. The use of psychoactive drugs puts them at greatly increased risk of falls and serious injuries that lead to immobility and often death.

The U.S. Food and Drug Administration (FDA) issued an advisory in June 2008 to healthcare professionals that states:

- Elderly patients with dementia-related psychosis treated with conventional or atypical antipsychotic drugs are at an increased risk of death.
- Antipsychotic drugs are not approved for the treatment of dementia-related psychosis. Furthermore, there is no approved drug for the treatment of dementia-related psychosis. Healthcare professionals should consider other management options.

The risk of death from antipsychotic drugs cannot be overstated. The California Attorney General characterized them as "deadly weapons" in

criminal charges against Kern County nursing home officials who are accused of causing the deaths of three residents through misuse of antipsychotic drugs.

The FDA has also issued its most dire warning – known as a black box warning – that antipsychotic drugs cause elders with dementia to die.

Sample FDA Black Box Warning for Risperdal. This warning applies to all antipsychotic drugs:

WARNING:
Increased Mortality in Elderly Patients with Dementia Related Psychosis

Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death. Analyses of 17 placebo-controlled trials (modal duration of 10 weeks), largely in patients taking atypical antipsychotic drugs, revealed a risk of death in drug-treated patients of between 1.6 to 1.7 times the risk of death in placebo-treated patients. Over the course of a typical 10-week controlled trial, the rate of death in drug-treated patients was about 4.5%, compared to a rate of about 2.6% in the placebo group. Although the causes of death were varied, most of the deaths appeared to be either cardiovascular (e.g., heart failure, sudden death) or infectious (e.g., pneumonia) in nature. Observational studies suggest that, similar to atypical antipsychotic drugs, treatment with conventional antipsychotic drugs may increase mortality. The extent to which the findings of increased mortality in observational studies may be attributed to the antipsychotic drug as opposed to some characteristic(s) of the patients is not clear. RISPERDAL (risperidone) is not approved for the treatment of patients with dementia-related psychosis.

Antipsychotic Drug Use Varies Widely

Why are so many residents given antipsychotics if these drugs are so dangerous?

In many cases, nursing homes use them to sedate and control residents and as a substitute for needed care. Caregivers may be poorly trained and facilities understaffed. Drug companies heavily promote misuse of antipsychotic drugs through illegal marketing campaigns directed at doctors and nursing homes. Absentee doctors often rubber-stamp drug orders requested by nursing home staff. Resident or family consent is rarely sought and almost never truly informed. State licensing officials do little to enforce the laws against drugging.

Yet some nursing homes rarely use antipsychotic drugs, showing that it is possible to avoid their use. At the other extreme, there are California nursing homes that give antipsychotics to all, or nearly all of their residents. It is primarily the culture of the nursing home, not your medical needs, which determines whether you (or your relative) will be subjected to these drugs.

Advocacy Tip

See how your nursing home compares with others by reviewing its antipsychotic drugging rate on CANHR's stop-drugging website (www.canhr.org/stop-drugging). Obtained from the federal government, the ratings show the percentage of residents taking antipsychotics and other types of psychoactive drugs at each nursing home. This is useful information if you are trying to prevent use of these drugs or if you are trying to find a facility that doesn't have a drugging problem.

Psychoactive Drugs Cannot Be Used Without Informed Consent

Informed consent is a legal right that requires doctors to respect the decisions of their patients. As the term suggests, the concept has two components: information and consent.

The information part of informed consent requires doctors to explain any proposed treatment to their patients and, if applicable, to their patients' legal representatives.

The consent part of informed consent simply requires that patients or their representatives agree to any form of health care treatment before it is undertaken. Failure to obtain consent before administering treatment is battery against the patient.

California nursing home regulations require doctors to disclose the following information when seeking consent from residents or their representatives for the use of psychoactive drugs:

1. the reason for the particular psychoactive drug;
2. the medical condition for which the drug is needed;
3. how long and how often the drug will be used;
4. how the resident's medical condition will be affected;
5. the nature, degree, duration and probability of known side effects;
6. the reasonable alternative treatments; and
7. the resident's right to accept or refuse the psychoactive drug and, if he or she consents, the right to revoke consent for any reason at any time.

The key informed consent regulations are found at sections 72528 and 72527(a)(4) &(5) of Title 22 of the California Code of Regulations. See the Laws and Regulations section on page 18 for a complete listing of pertinent laws and regulations.

Nursing homes are required to verify that consent has been given for psychoactive drugs, even when the drug was prescribed before the resident's admission. Consent is not required in an emergency.

Informed consent requirements are often completely or partially ignored by doctors and nursing homes. However, there are steps you can take to protect your relative from being drugged.

Questions to Ask Doctors and Nursing Homes When Psychoactive Drugs are Proposed

- What specific, documented behaviors or symptoms prompted the need for a psychoactive drug? (e.g., are there delusions or is the resident simply agitated?)
- Have all possible medical or environmental causes been ruled out? (e.g., pain, dehydration, infection, sleep disruptions)
- Has the doctor recently physically examined the resident to determine the need for the drug?
- What alternative treatments have been tried? Are other options still available?
- What are the risks and side effects of the drug?
- Has the FDA issued black box warnings for this drug?
- Has the FDA approved the use of this drug for this purpose?
- How will side effects be monitored? Who will do it?
- Will the proposed drug interact with any of the resident's other medications?
- Is the proposed drug duplicating other current medications?
- Will the resident start on the lowest possible dose of medication?
- When and how often will the need for the drug be reassessed? (the law requires a reassessment at least every three months)

Advocacy Tips When Psychoactive Drugs are Proposed

- You do not have to accept a doctor's recommendation to use psychoactive drugs.
- Do not give consent if the doctor has not directly examined the resident to determine the need for the drug.
- Antipsychotic drugs can be deadly. Don't consent to their use unless you are certain that all other care and treatment options have been exhausted.
- Insist that the doctor or nursing home provide written information on adverse consequences of the proposed drugs, including black box warnings.
- Carefully review and consider the written information before making a decision.
- Consider seeking a second opinion from a trusted physician or advocate if you have doubts about giving consent.

Periodically request a complete list of current medications from the nursing home and/or review the resident's medication administration records kept by the facility, especially if unauthorized drugging is suspected. If you discover that psychoactive drugs are being used without consent, file a formal complaint with the Department of Public Health, notify the local ombudsman program, and consult with CANHR about other actions you can take. See page 14 for more information on remedies.

Ask for a care plan meeting to discuss the need for proposed psychoactive drugs. The nursing home should hold a care plan meeting because the need for psychoactive drugs signals a significant change in the resident's condition. You have a right to attend and participate in this meeting. Use the care plan meeting to determine if the drug is really needed and whether the home has carefully considered all alternatives. Before the meeting, review CANHR's fact sheet, *Making Care Plans Work*, to learn about care plan rights and effective meeting strategies.

Your Right to Review Medical Records:

Nursing home residents and their legal representatives have the right to review their records within 24 hours of a request. Copies of records must be provided within two business days of a request. Requests for copies should be done in writing. If the nursing home refuses to honor a request to review records or for copies, see page 14 for possible remedies.

Important Note: Before instructing a nursing home to stop administering an unwanted psychoactive drug, seek information on withdrawal symptoms. Sudden termination of many psychoactive drugs, especially antipsychotic drugs, can cause serious withdrawal symptoms. If such a drug is being stopped, the doctor should write an order to gradually discontinue it.

Who Can Exercise a Resident's Rights?

If the resident is capable of granting or withholding consent, only the resident may do so. If the resident lacks capacity to make a decision, then the resident's representative may grant or refuse consent. A resident and legal representative can withdraw consent to use a psychoactive drug at any time.

Under California law, persons who may act as your representative include a conservator, an agent designated under a valid advance health care directive or power of attorney for health care, your next of kin, or someone appointed by a court for this purpose.

Right to Refuse

Even if a nursing home resident has problems making health care decisions, she may refuse psychoactive drugs at any time. The right to refuse treatment is a basic constitutional right that may not be violated without a court order. A doctor's declaration that a resident does not have capacity is not enough to override the resident's right to refuse treatment. A nursing home may not retaliate or try to evict a resident who exercises her right to refuse psychoactive drugs.

Chemical Restraints and Unnecessary Drugs are Illegal

Even if a nursing home resident or representative has given informed consent to the use of a psychoactive drug, the drug's use may violate state and federal laws prohibiting chemical restraints and unnecessary drugs.

A chemical restraint is any drug imposed for purposes of discipline or convenience and not required to treat a resident's medical symptoms.

An unnecessary drug is any drug when used in excessive dose, for excessive duration, without adequate monitoring, without adequate indications for its use, or in the presence of adverse consequences that indicate the dose should be discontinued or reduced.

The federal government has even tougher standards on antipsychotic drugs. Nursing homes must not give these drugs to residents who have not used them unless they are necessary to treat a specific condition that has been diagnosed and documented in the resident's record. Federal guidelines state that antipsychotic drugs should not be used if the only symptoms are:

wandering	unsociability
poor self-care	inattention or indifference to surroundings
restlessness	fidgeting
impaired memory	nervousness
mild anxiety	uncooperativeness
insomnia	behavior that does not represent a danger to others

Measured by these standards, most antipsychotic and antianxiety drugs used by nursing homes to treat residents with dementia are both unnecessary and a form of chemical restraint.

Gradual Dose Reduction

Whenever a nursing home resident agrees to take an antipsychotic drug, the nursing home must nevertheless attempt to reduce or eliminate the drug use whenever possible. The use of antipsychotic drugs for each resident should be reviewed at least once every three months. Nursing home regulations require the drugs be reduced unless a doctor has determined that a dose reduction would be unsafe.

Nursing home residents or their representatives who have agreed to psychoactive drugs should closely monitor their administration and insist that they be discontinued whenever possible.

Behavior Problem or Unmet Need?

Behavior problem. Combative. Agitated. Difficult. These are just a few of the ways used to describe the distress so commonly shown by people with dementia. The key to preventing the distress, it turns out, is to use the behaviors and other information as a means to identify and resolve the root causes of the anguish.

Behavior is communication, not a disease. Dementia diminishes a person's ability to communicate verbally, so people with this condition often compensate by communicating behaviorally. Rather than drugging residents to suppress the behaviors, nursing home caregivers must try to figure out what the behaviors mean and respond appropriately.

Some nursing homes are showing that drugs are not needed to prevent or treat challenging behaviors. Their caregivers know the residents, their needs and preferences well enough that they can prevent or diminish distress before it becomes a big problem. These facilities show that behaviors aren't so challenging when residents are comfortable, live in a pleasant environment, get timely medical care and are supported by well-trained caregivers who care about them.

Least Medicating Approach

Psychoactive drugs should always be the last resort for treating symptoms of dementia, not the first option. Nursing homes should look first to treating underlying medical problems, relieving pain, improving the environment, personalizing care, engaging the resident in pleasurable activities, and doing everything possible to make residents feel comfortable and at peace. This "least medicating" approach is the key to better dementia care.

Advocacy Tip

The best step most nursing homes can take to stop unnecessary drugging is to improve staff training on how to respond to symptoms of dementia. The quality of staff training is not necessarily outside your control. Ask the facility if it has arranged for the local Alzheimer's Association chapter to conduct trainings for its staff. If not, urge it to do so.

Ask the doctor to assess possible medical causes of behavioral concerns. Agitation and confusion may be caused by untreated infections, dehydration, malnutrition, adverse medication reactions, pain, and other medical problems. If the doctor won't conduct a thorough medical examination, explore options for replacing the physician or consulting with a geriatrician.

Individualized care and more attention are the best substitutes for drugs. Insist that your loved one's care be customized by adapting personal care, sleep schedules, meals, bathing methods and other services to his or her preferences. Urge the facility to consistently assign caregivers who work well with your relative.

Adequate staffing is needed to respond quickly to physical needs such as help with toileting, getting in and out of bed, bathing, hunger and thirst. If staffing is not adequate, encourage the administrator to improve it.

Improving and simplifying the environment can relieve resident anxiety. Nursing homes must offer a homelike environment. Insist that it do so. For example, distracting noises (such as intercoms and buzzer systems) should

be eliminated. Temperatures should be comfortable. So should seating. No one wants to sit in a wheelchair all day. Hallways should be uncluttered. Lighting should be pleasant. Decorate and furnish your loved one's room to make it comfortable.

What is Comfort Care?

Life in a nursing home can be a difficult adjustment, especially for someone who is forgetful or easily confused due to dementia. Surrounded by new faces and new routines, institutional care can be disorienting and isolating.

To help prevent the distress that often triggers psychoactive drug use in nursing homes, enlightened care providers are increasingly turning to "comfort care" to enhance residents' quality of life. As its name suggests, comfort care strives to keep residents comfortable through a nurturing, individualized approach that focuses on their emotional, social, and spiritual needs, as well as their medical and personal care needs. The goal of comfort care is to keep each resident comfortable and avoid unnecessary drugs by:

- anticipating their needs;
- knowing them so well that basic needs never become major problems;
- embracing a philosophy of individualized care;
- adjusting the pace, approach and communications with them to suit the needs of people with dementia;
- recognizing and treating pain aggressively; and
- treating family and friends as partners in care.

To learn more, read Encouraging Comfort Care: A Guide for Families of People with Dementia Living in Care Facilities, available free from the Illinois Chapter of the Alzheimer's Association: http://www.alzheimers-illinois.org/pti/comfort_care_guide.asp

Help the facility staff plan to engage your relative in pleasurable activities throughout the day with whatever he or she likes, such as walks, music, exercise, reading, visits from pets, group activities, and singing.

Roommate problems may trigger conflict. If this is a problem, ask the facility to find a compatible roommate or, if available, offer a private room.

Encourage patience and understanding. Common symptoms of dementia such as restlessness, pacing, and repeated questions should be expected and accepted.

Meet with the staff to plan care approaches at regular or specially requested care plan meetings. Learn about care plan rights and how to make care plan meetings effective in CANHR's fact sheet, *Making Care Plans Work*.

To learn more about the least medicating approach, visit CANHR's stop-drugging website to see the "Alternatives to Drugs" in the News and Resources section at http://www.canhr.org/stop-drugging/archives/188.

Remedies to Illegal Drugging

If a California nursing home is using or threatening to use psychoactive drugs without consent, call CANHR at 1-800-474-1116 to discuss actions you can take to protect your rights.

There are a variety of actions you can take, including using the suggestions in this guide to seek change from the facility and the physician. Other options include:

Seeking help from local advocacy organizations: The local long term care ombudsman office (http://www.aging.ca.go/Programs/LTCOP/Contacts/) may be helpful. The ombudsman program helps residents resolve concerns about care and rights. However, the ombudsman does not have any powers or direct authority over the nursing home. Local legal service programs may also be able to offer advocacy assistance. Contact CANHR for information.

Filing formal complaints: The California Department of Public Health (CDPH) licenses and inspects nursing homes and enforces state and federal standards. Read CANHR's fact sheet, *How to File a Nursing Home Complaint*, for instructions on how to file a complaint with CDPH. The fact sheet also explains how to file a complaint with the Bureau of Medi-Cal Fraud and Elder Abuse within the California Attorney General's Office. You can file a complaint against the doctor who prescribed the drugs through the Medical Board of California (http://www.medbd.ca.gov/consumer/complaint_info.html).

Suing the facility and doctor: Legal actions can help enforce your rights and seek damages if you or a family member has been harmed. Call CANHR to discuss referral to a qualified elder abuse attorney.

Alerting state legislators: CANHR is working to strengthen California laws against the drugging of nursing home residents. You can help by informing your assembly member and state senator about the inappropriate use of psychoactive drugs. Find your legislators at http://www.leginfo.ca.gov/yourleg.html.

Alerting the media: Nothing gets a nursing home's attention faster than the local media. If other options fail, consider asking the media to help expose dangerous drugging practices.

Resources

CANHR's Stop-Drugging Website at www.canhr.org/stop-drugging

Related CANHR Fact Sheets available at www.canhr.org/factsheets:

- *Making Care Plans Work*
- *How to File a Complaint*
- *Nursing Home Care Standards*
- *Restraint Free Care*
- *Outline of Nursing Home Residents' Rights*

For more suggestions on caring for older adults with dementia without relying on psychoactive drugs:

- Encouraging Comfort Care: A Guide for Families of People with Dementia Living in Care Facilities, free from the Alzheimer's Association at www.alzheimers-illinois.org/pti/comfort_care_guide.asp
- Dementia Beyond Drugs: Changing the Culture of Care, by G. Allen Power, MD
- Visit www.bathingwithoutabattle.unc.edu

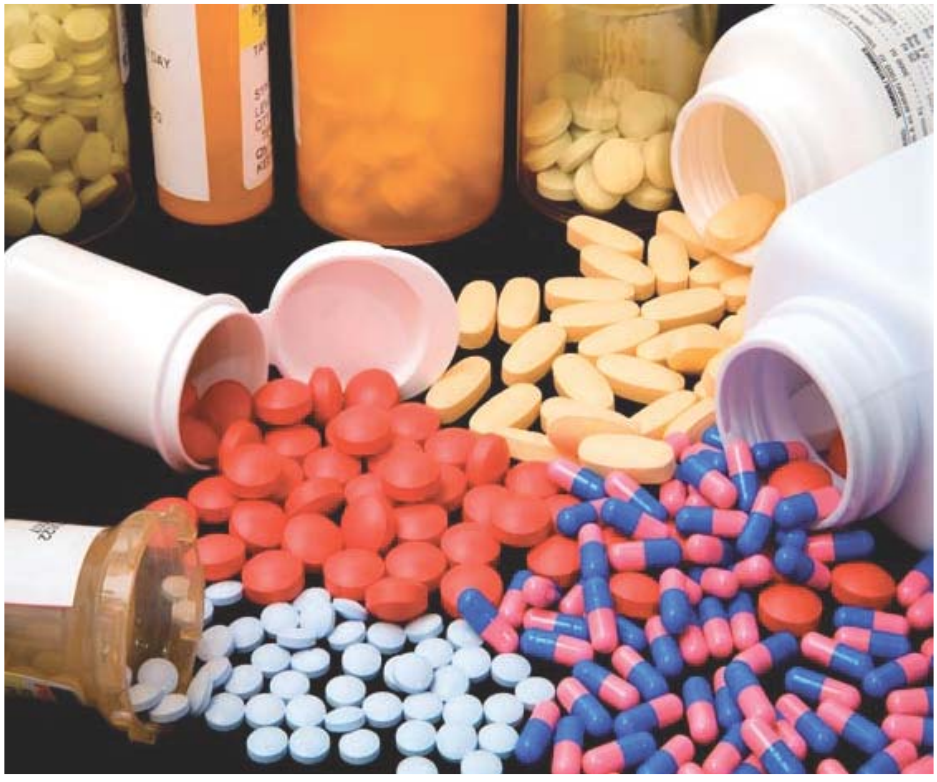
Antipsychotic Drugs

Conventional Antipsychotic Drugs

Compazine (prochlorperazine)
Haldol (haloperidol)
Loxitane (loxapine)
Mellaril (thioridazine)
Moban (molindone)
Navane (thiothixene)
Orap (pimozide)
Prolixin (fluphenazine)
Stelazine (trifluoperazine)
Thorazine (chlorpromazine)
Trilafon (perphenazine)

Atypical Antipsychotic Drugs

Abilify (aripiprazole)
Clozaril (clozapine)
FazaClo (clozapine)
Geodon (ziprasidone)
Invega (paliperidone)
Risperdal (risperidone)
Seroquel (quetiapine)
Zyprexa (olanzapine)
Symbyax (olanzapine and fluoxetine)



Laws and Regulations

Visit CANHR's stop-drugging website to read the content of the following laws and regulations.

Laws on informed consent:
California Code of Regulations (CCR), Title 22, §§ 72527(a)(3), (4) & (5), 72527(e) & 72528; California Health and Safety (H&S) Code §§ 1418.8 & 1418.9; United States Code (USC), Title 42, §§ 1395i-3(c)(1)(A)(i) & 1396r(c)(1)(A)(i); Code of Federal Regulations (CFR), Title 42, §§ 483.10(d)(2) & 483.10(b)(3)

Laws on the right to refuse care and treatment:
22 CCR §§72527(a)(4) & 72528(a)(6), H&S Code §1599.72; 42 CFR §483.10(b)(4)

Laws authorizing representatives to exercise rights:
22 CCR §72527(d), H&S Code §§1599.3 & 1418.8(c), 42 CFR §483.10(a)(3) & (4)

Laws on the right to review and obtain medical records:
42 USC §§1395i-3(c)(1)(A)(iv) and 1396r(c)(1)(A)(iv); 42 CFR §483.10(b)(2); H&S Code §§123100-123149.5

Laws prohibiting chemical restraint:
22 CCR §72527 (a)(23) & 72319; H&S Code 1180.4(k); 42 CFR §483.13(a); 42 USC §§ 1395i-3(c)(1)(A)(ii) & 1396r(c)(1)(A)(ii)

Laws on unnecessary drugs and gradual dose reduction
42 CFR §483.25(l); 42 USC §1396r(c)(1)(D)

Laws requiring care and services for mental or psychosocial adjustment difficulties:
42 CFR §483.25(f); 42 USC §§ 1395i-3(b)(2) & (4) and 1396r(b)(2) & (4) and 1396r(b)(2) & (4)

"The misuse of antipsychotic drugs as chemical restraints is one of the most common and longstanding, but preventable, practices causing serious harm to nursing home residents today."

— Testimony of Toby S. Edelman, Senior Policy Attorney for the Center for Medicare Advocacy at a November 30, 2011 hearing of the U.S. Senate Special Committee on Aging titled: *Overprescribed: The Human and Taxpayers' Costs of Antipsychotics in Nursing Homes*. Experts testified that antipsychotics are dangerous and expensive for "treating" dementia and are typically surpassed by simple nonpharmacologic options.

WARNING

Antipsychotic drugs nearly double the risk of death for older persons with dementia. These drugs are not approved for the treatment of dementia. In addition to death, antipsychotic drug side effects may include stroke, heart attack, increased risk of pneumonia, excessive sedation, lethargy, dizziness, falls, agitation, confusion, restlessness, delirium, hallucinations, tremors, involuntary body movements, muscle weakness, seizures, parkinsonism, cognitive decline, neuroleptic malignant syndrome, headache, dry mouth, constipation, weight gain, weight loss, urinary retention, and blurred vision.

California Advocates for Nursing Home Reform (CANHR)
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(800) 474-1116 (Consumers only) • (415) 974-5171 • **www.canhr.org**