60.5% of African American providers advised their African American patients to consume less salt ($P<.001$). Thirty-one percent of primary health care providers reported the biggest barrier to counseling their prehypertensive and hypertensive patients about sodium intake was that "patients are unlikely to comply"; 22% cited "lack of time"; and 11% reported "patients have other immediate health issues."

Comment. The majority of primary health care providers agree that their patients should reduce sodium intake; report providing specific advice in line with recommended strategies; and counsel patients with prehypertension, hypertension, or chronic kidney disease to consume less salt. In contrast to 2010 dietary guidelines,[6] a minority of health care providers report counseling patients with diabetes or older patients to consume less salt. Also, a minority of providers of race/ethnicity groups other than African American report counseling African American patients to consume less salt.

The most frequent types of advice provided to patients were in line with current recommended strategies to reduce sodium intake.[7] Interestingly, the majority of health care providers also indicated they advise patients to remove the salt shaker or add less salt during cooking, despite current knowledge that for most people these behaviors are unlikely to result in major salt reduction.[7]

The results should be interpreted in the context of some potential selection and reporting biases. The survey was not a nationally representative sample of physicians or nurse practitioners, and health care providers who are more concerned about patient care may be more likely to respond and respondents may overstate their counseling behaviors. However, physicians were selected to be representative of the age, sex, and race/ethnicity of the American Medical Association master file.

Our results suggest that more effort is required to inform health care providers about the need for all patients to reduce sodium intake and their ability to make a difference in their patient's behavior.[8] Specifically, the primary care physicians and nurse practitioners' knowledge, attitudes, and practices regarding dietary salt intake will play an important role in the effort to reduce sodium intake for Americans, especially for those who seek care for hypertension and other cardiovascular diseases.

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Online-Only Material: The eTable is available at http://www.archinternmed.com.

1. Meneton P, Jeunemaitre X, de Wardener HE, MacGregor GA. Links between dietary salt intake, renal salt handling, blood pressure, and cardiovascular diseases. *Physiol Rev*. 2005;85(2):679-715.
2. United States Department of Agriculture. What we eat in America, NHANES 2007-2008, individuals 2 years and over (excluding breastfeeding children), day 1 dietary intake data, weighted. Revised August 2010. http://www.ars.usda.gov/SP2UserFiles/Place/12355000/pdf/0708/Table_3_NIN_INC_07.pdf. Accessed August 29, 2011.
3. Viera AJ, Cohen LW, Mitchell CM, Sloane PD. High blood pressure knowledge among primary care patients with known hypertension: a North Carolina Family Medicine Research Network (NC-FM-RN) study. *J Am Board Fam Med*. 2008;21(4):300-308.
4. Kreuter MW, Chheda SG, Bull FC. How does physician advice influence patient behavior? evidence for a priming effect. *Arch Fam Med*. 2000;9(5):426-433.
5. Ayala C, Tong X, Valderrama AL, Ivy A, Keenan N. Actions taken to reduce sodium intake among adults with self-reported hypertension: HealthStyles survey, 2005 and 2008. *J Clin Hypertens (Greenwich)*. 2010;12(10):793-799.
6. US Department of Health and Human Services and US Department of Agriculture. *Dietary Guidelines for Americans, 2010*. 7th ed. Washington DC: US Government Printing Office; 2011.
7. IOM (Institute of Medicine). *Strategies to Reduce Sodium Intake in the United States*. Washington, DC: National Academies Press; 2010.
8. Havas S, Dickinson BD, Wilson M. The urgent need to reduce sodium consumption. *JAMA*. 2007;298(12):1439-1441.

The FDA and New Safety Warnings

In response to postmarket drug safety surveillance and research data, the US Food and Drug Administration (FDA) and drug manufacturer may take 1 of 2 types of action. In extreme cases the FDA may remove a drug from the market. More often the product label or package insert is revised to reflect newly discovered risks. The most clinically significant new information is added to 1 of 3 legally defined sections of the prescribing information[1]: (1) a boxed warning (information that is essential to be considered when prescribing the drug); (2) a contraindication (clinical situations when a drug's risks clearly outweigh its benefits); and (3) a warning (adverse reactions with reasonable evidence of a causal association, reactions that may require discontinuation, or reactions that interfere with a laboratory test).

We analyzed 1 calendar year of these major label changes to provide insights into this safety program. We report the number of actions, severity of events, and nature and scope of the safety information. We also describe the types of drugs affected, whether they were recently approved drugs or established treatments, and what type and level of scientific evidence was used to support of these label changes.

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Table. Boxed Warnings, Contraindications, and Warnings in 2009

FDA Action	No. (%) New (n=135)	Updated (n=43)	Downgrade (n=3)	Total (N=180)[a]
Boxed warning	25 (18.5)	12 (27.9)	0	**37**
Contraindication	19 (14.1)	3 (7.0)	1 (33.3)	**23**
Warning	90 (66.7)	28 (65.1)	2 (66.7)	**120**

Abbreviation: FDA, US Food and Drug Administration.
[a]The total does not include efalizumab (Raptiva; Genentech), which was withdrawn in April 2009.

Methods. Major safety regulatory actions during 2009 were defined as drug withdrawals for safety, new or revised boxed warnings, contraindications, or warnings for approved prescription drugs.[2] For each action we calculated the years since initial drug approval and identified the brand name or generic status. We categorized the cited evidence source (ie, clinical trial, meta-analysis, epidemiological study, adverse event report). We also evaluated whether the scientific evidence was derived directly from studies of the target drug or inferred from studies of other drugs either with similar chemical structure and mechanism of action or that were indicated for use in the same patient population. A complete description of the study methods is available in the eAppendix (http://www.archinternmed.com).

Results. In 2009, the FDA approved 181 major safety regulatory actions, including 1 drug safety withdrawal, 25 new boxed warnings, 19 new contraindications, 90 new warnings, and 46 revisions of previous actions (**Table**). Among the newly identified adverse effects were suicidal behavior, life-threatening viral infections, renal failure, and increased cancer risk in children. Adverse event reports from drug manufacturers or through the MedWatch program were the predominant source of scientific information and formed the basis of 77 of 135 new regulatory actions (57%) and 19 of 25 new boxed warnings (76%). Clinical studies were cited as the evidence source for 26 of 135 actions (19%) but only 2 were derived from statistically significant differences and 1 was based on a single study case. A large FDA meta-analysis of suicidal behavior and antiepileptic drugs generated warnings for 19 drugs.[3] In 23 of 135 new actions (17%), the scientific evidence was derived from other drugs, with 15 based on similar chemical structure and mechanism, and 8 based on the same indication and/or patient population. The safety actions occurred a median of 11 years after initial approval and included 61 drugs marketed for 15 years or more; only 36 actions involved drugs within first 5 years after approval.

Comment. These major safety regulatory actions disclose clinically significant risks of widely used drugs, typically many years after approval. Scientific evidence cited to alert physicians about new risks for marketed drugs used notably less rigorous methods than the well-controlled, blinded, and randomized clinical trials used to document benefit prior to approval. When reported adverse events supported the warning, little or no detail was provided about the number and type of reports relied on or any systematic analysis performed.

Some of the most extensive changes involved class warnings applied to a group of drugs without distinguishing between them. All drugs indicated for epilepsy treatment got the same suicidal behavior warning, even those not included in the meta-analysis and drugs with markedly different mechanisms of action. The class warning was extended to 1 benzodiazepine—clonazepam (Klonopin; F. Hoffmann-La Roche Ltd) with an indication in epilepsy treatment—but not to other benzodiazepines. In another case the FDA announced and put similar suicidal behavior and violence warnings on 2 smoking cessation treatments—varenicline (Chantix; Pfizer Inc) and bupropion hydrochloride (Zyban; GlaxoSmithKline)—even though the FDA's unpublished but publicly available studies revealed that varenicline accounted for 10 times as many reports as bupropion and had higher risks.[4,5]

The 11-year median time since approval for actions in this 1-year study was markedly higher than the 7 years reported in a 2002 study of boxed warnings or withdrawals since 1975.[6] Improving postmarket drug safety requires timelier ascertainment of drug risks together with higher quality and better documented scientific evidence.

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Downloaded From: http://jamanetwork.com/ on 06/20/2013

1. US Food and Drug Administration. *Guidance for Industry:* US Food and Drug Administration. *Warnings and Precautions, Contraindications, and Boxed Warning Sections of Labeling for Human Prescription Drugs and Biological Products—Content and Format (Draft Guidance)*. Silver Spring, MD: US Food and Drug Administration; 2006.
2. Drug Safety Labeling Changes. US Food and Drug Administration Web site. http://www.fda.gov/Safety/MedWatch/SafetyInformation/Safety-RelatedDrugLabelingChanges/default.htm. Accessed July 24, 2011.
3. Safety Alerts for Human Medical Products > Antiepileptic Drugs. US Food and Drug Administration Web site. 2009. http://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm074939.htm. Accessed October 13, 2011.
4. Pollock M, Mosholder A. *Suicidality: Varenicline; Bupropion; Nicotine Transdermal Patch*. Silver Spring, MD: US Food and Drug Administration, Center for Drug Evaluation and Research; 2008.
5. Pollock M. *AERS Crude Counts of Psychiatric Adverse Events, Accidental Injuries, Angioedema, and Serious Skin Reactions: Varenicline; NDA 21928; Pfizer Inc Bupropion (Zyban); NDA 20711; GlaxoSmithKline*. Silver Spring, MD: US Food and Drug Administration, Center for Drug Evaluation and Research; 2009.
6. Lasser KE, Allen PD, Woolhandler SJ, Himmelstein DU, Wolfe SM, Bor DH. Timing of new black box warnings and withdrawals for prescription medications. *JAMA*. 2002;287(17):2215-2220.

COMMENTS AND OPINIONS

Interventions to Improve Recognition of Delirium: A Sine Qua Non for Successful Transitional Care Programs

It is encouraging to see the effectiveness of the Care Transitions Intervention[1] and a transitional care program[2] reproduced in real-world settings, 2 different interventions devised to improve transition of care from acute care settings to lower levels of care. It is however important to highlight a frequently underrecognized condition, namely delirium, that is highly prevalent in hospitalized older patients and is associated with significant morbidity and mortality. Any intervention that aims to improve transition of care from an acute care setting to a lower level of care should include strategies to assess for delirium during hospitalization and at the time of discharge and to provide education to caregivers and patients on delirium.

Studies have shown that up to 50% of delirium persists months beyond discharge from acute care settings; however, delirium is reported in only 3% to 16% of documented cases at discharge.[3] Persistent delirium at the time of hospital discharge is associated with poor outcomes. Delirium that persists beyond discharge has been associated with frequent rehospitalization, prolonged institutionalization, and mortality even over a 1-year follow up-period compared with patients without delirium at the time of discharge.[4] Patients with delirium during hospitalization had 2.5-times higher average costs per day compared with patients without delirium in a study reviewing 1-year health care costs associated with delirium in elderly patients.[5]

A study by Inouye and colleagues[3] has validated 5 risk factors including dementia, visual impairment, functional impairment, high medical comorbidity, and use of physical restraints for prediction of delirium at discharge in hospitalized older patients, 4 of which are modifiable risk factors. Implementing interventions to modify the risk factors listed are essential to reduce prevalence of delirium at the time of discharge that would then reduce morbidity, mortality, and rates of rehospitalization following transition to post–acute care settings. Studies on cost-effectiveness of care transition interventions would more likely prove to be cost saving if costs due to delirium-related morbidities were included as outcome measures in future studies.

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1. Voss R, Gardner R, Baier R, Butterfield K, Lehrman S, Gravenstein S. The care transitions intervention: translating from efficacy to effectiveness. *Arch Intern Med*. 2011;171(14):1232-1237.
2. Stauffer BD, Fullerton C, Fleming N, et al. Effectiveness and cost of a transitional care program for heart failure: a prospective study with concurrent controls. *Arch Intern Med*. 2011;171(14):1238-1243.
3. Inouye SK, Zhang Y, Jones RN, Kiely DK, Yang F, Marcantonio ER. Risk factors for delirium at discharge: development and validation of a predictive model. *Arch Intern Med*. 2007;167(13):1406-1413.
4. Marcantonio ER, Kiely DK, Simon SE, et al. Outcomes of older people admitted to postacute facilities with delirium. *J Am Geriatr Soc*. 2005;53(6):963-969.
5. Leslie DL, Marcantonio ER, Zhang Y, Leo-Summers L, Inouye SK. One-year health care costs associated with delirium in the elderly population. *Arch Intern Med*. 2008;168(1):27-32.

In reply

We agree that delirium is an important and underdiagnosed condition in elderly patients who are hospitalized. Given the poor outcomes for untreated delirium and the existence of known interventions, identifying delirium prior to discharge is especially important. The Care Transitions Intervention includes educating patients and their caregivers about red flags—the signs and symptoms that should trigger outreach for follow-up care before patients' conditions require emergency department visits or hospital readmission—and delirium can be incorporated into this portion of the Care Transitions Intervention. As Alici points out, delirium must first be recognized and documented before any interventions can occur, including hospital-based measures as well as delirium-specific coaching and red flags. A delirium screen such as the Confusion Assessment Method can be performed by less-skilled individuals and could therefore be feasible for hospital staff to incorporate into their standard patient assessments for at-risk patients, such as elderly patients. We believe that the routine adoption of a delirium screening tool, such as the Confusion Assessment Method, would increase the medical recognition and management of delirium during and following patients' hospitalizations.

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