

compared with controls, but not after day 8.⁴ Moreover, even in the contemporary era, in a trial of 45 852 patients with acute MI, neither a composite outcome of death, reinfarction, or cardiac arrest nor death was significantly reduced by metoprolol compared with placebo.⁵ More recent trials suggest that long-term β -blocker use is not a necessity for patients without heart failure.⁶

While it is true that many patients were excluded from the propensity score–matched analysis, the online supplement included a regression adjustment to a propensity score, in which all patients were included and the results were similar to the main analysis. Moreover, the analysis with β -blocker use as a time-dependent covariate showed results that were similar to the main analysis.

Drs Costagliola and Hernán state that our article illustrates several ways an observational study may differ from an RCT. As outlined in our response above, the results of our observational study are not very different from RCTs in patients without heart failure. While the concerns about enrolling patients with prevalent β -blocker use and immortal time bias are valid and are limitations of the study, it should be noted that the results of our study are not vastly different from those of RCTs. Despite this, we agree and stated in the article that observational studies have inherent limitations, including inability to correct for unmeasured confounders.

The results of our study are hypothesis generating and should be confirmed in future RCTs. Until that time, physicians should base recommendations for β -blocker use on RCTs. However, in patients without heart failure, this evidence for the prevention of long-term clinical outcomes is nonexistent.

Sripal Bangalore, MD, MHA
P. Gabriel Steg, MD
Deepak L. Bhatt, MD, MPH

Author Affiliations: New York University School of Medicine, New York, New York (Dr Bangalore; sripalbangalore@gmail.com); Université Paris Diderot, Paris, France (Dr Steg); and VA Boston Healthcare System, Boston, Massachusetts (Dr Bhatt).
Conflict of Interest Disclosures: The authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Dr Steg reported receiving research grants (to INSERM U-698) from the New York University School of Medicine, sanofi, and Servier; serving as a consultant to Ablynx, Amarin, Amgen, Astellas, AstraZeneca, Bayer, Boehringer Ingelheim, Bristol-Myers Squibb, Daiichi/Sankyo, Eisai, GlaxoSmithKline, Lilly, Medtronic, Merck Sharp & Dohme, Novartis, Otsuka, Pfizer, Roche, sanofi, Servier, and The Medicines Company; holding stock in Aterovax; and receiving reimbursement for travel expenses from Merck Sharp & Dohme. Dr Bhatt reported serving on the advisory board for Medscape Cardiology and the board of directors for the Boston VA Research Institute, Society of Chest Pain Centers; being the chair of the American Heart Association Get With The Guidelines Science Subcommittee; receiving honoraria from the American College of Cardiology (editor, Clinical Trials, Cardiosource), Duke Clinical Research Institute (clinical trial steering committees), Slack Publications (chief medical editor, Cardiology Today Intervention), and WebMD (continuing medical education steering committees); serving as senior associate editor for the *Journal of Invasive Cardiology*; receiving research grants from Amarin, AstraZeneca, Bristol-Myers Squibb, Eisai, Ethicon, Medtronic, sanofi-aventis, and The Medicines Company; and performing unfunded research for FlowCo, PLx Pharma, and Takeda. Dr Bangalore did not report any disclosures.

1. Drug Topics website. Top 200 generic drugs by retail dollars. <http://drugtopics.modernmedicine.com/drugtopics/data/articlestandard//drugtopics/252011/727239/article.pdf>. Accessed March 23, 2012.

2. Jonsson G, Abdelnoor M, Müller C, Kjeldsen SE, Os I, Westheim A. A com-

parison of the two beta-blockers carvedilol and atenolol on left ventricular ejection fraction and clinical endpoints after myocardial infarction: a single-centre, randomized study of 232 patients. *Cardiology*. 2005;103(3):148-155.

3. Shu F, Dong BR, Lin XF, Wu TX, Liu GJ. Long-term beta blockers for stable angina: systematic review and meta-analysis. *Eur J Prev Cardiol*. 2012;19(3):330-341.

4. First International Study of Infarct Survival Collaborative Group. Randomised trial of intravenous atenolol among 16 027 cases of suspected acute myocardial infarction: ISIS-1. *Lancet*. 1986;2(8498):57-66.

5. Chen ZM, Pan HC, Chen YP, et al; COMMIT (CLOpidogrel and Metoprolol in Myocardial Infarction Trial) collaborative group. Early intravenous then oral metoprolol in 45,852 patients with acute myocardial infarction: randomised placebo-controlled trial. *Lancet*. 2005;366(9497):1622-1632.

6. Bangalore S, Messerli FH, Cohen JD, et al; INVEST Investigators. Verapamil-sustained release-based treatment strategy is equivalent to atenolol-based treatment strategy at reducing cardiovascular events in patients with prior myocardial infarction: an International Verapamil SR-Trandolapril (INVEST) substudy. *Am Heart J*. 2008;156(2):241-247.

RESEARCH LETTER

Antipsychotic Use Among Nursing Home Residents

To the Editor: The prescribing of antipsychotic medications persists at high levels in US nursing homes (NHs) despite extensive data demonstrating marginal clinical benefits and serious adverse effects, including death.^{1,2} However, imprecise and outdated data have limited the understanding of the current state of antipsychotic medication prescribing in NHs.³ We analyzed recent and detailed NH prescription data to address: (1) What is the current level of antipsychotic use? (2) Does antipsychotic use in NHs display geographic variation? and (3) Which antipsychotics are most commonly prescribed?

Methods. We used September 2009 through August 2010 prescription dispensing data from a large, long-term care pharmacy (Omnicare Inc) that serves 48 states and half of all NH residents in the United States. Pharmacy claims data are complete and accurate due to the connection to reimbursement documentation. Data elements include state location, patients' sex, age, and enrollment dates, and national drug codes for all drugs dispensed regardless of payer (eg, Medicare Part D, private insurance, and out of pocket).

Overall and state-level annual prevalence of antipsychotic use was calculated as the percentage of NH residents receiving at least 1 antipsychotic drug. We arrayed the states into distributions of lowest to highest quintiles of antipsychotic use, calculated means and 95% confidence intervals, generated a map to illustrate geographic variation, and tested for differences using a robust regression model with quintile indicators. We identified the name and type of antipsychotic (atypical or conventional) and estimated the median and interquartile range (IQR) of the number of prescriptions and duration of use calculated as days receiving therapy during the first 90 days observed. All analyses were calculated using SAS software version 9.2 (SAS Institute Inc) and 2-sided tests; statistical significance was set at $P < .05$. The study was approved by the institu-

tional review board of the University of Massachusetts Medical School.

Results. We identified 1 402 039 unique NH residents and a subset of residents observed continuously for at least 90 days (n=561 681 residents and n=5038 NHs). Approximately 39.4% of study NHs had more than 100 residents, 76.2% were for profit, and 59.7% had multiple owners.

Of the overall sample of 1 402 039 NH residents, 308 449 (22.0%; 95% CI, 21.9%-22.1%) received 1 or more prescriptions of antipsychotics. Prevalence of antipsychotic drug prescribing in NHs varied significantly (quintile 1 vs quintiles 2-5, $P < .001$) with the highest quintile states (28.1%; 95% CI, 27.0%-29.1%) located in the central south and the lowest quintile states (17.2%; 95% CI, 16.3%-18.1%) located mostly in the west (FIGURE). Of 4 338 723 antipsychotic prescriptions in NHs, the majority (68.6%; 95% CI, 68.5-68.7) were for the atypical agents quetiapine fumarate, risperidone, and olanzapine (n=2 988 573) (TABLE). Among the 186 076 residents receiving antipsychotics and observed for 90 days, 13 956 (7.5%; 95% CI, 7.3%-7.6%) received only 1 prescription for antipsychotics while the median number was 10 (IQR, 5-14) prescriptions. The median duration of antipsychotic therapy during the 90-day observation period ranged from 30 (IQR, 8-74) days to 77 (IQR, 67-85) days.

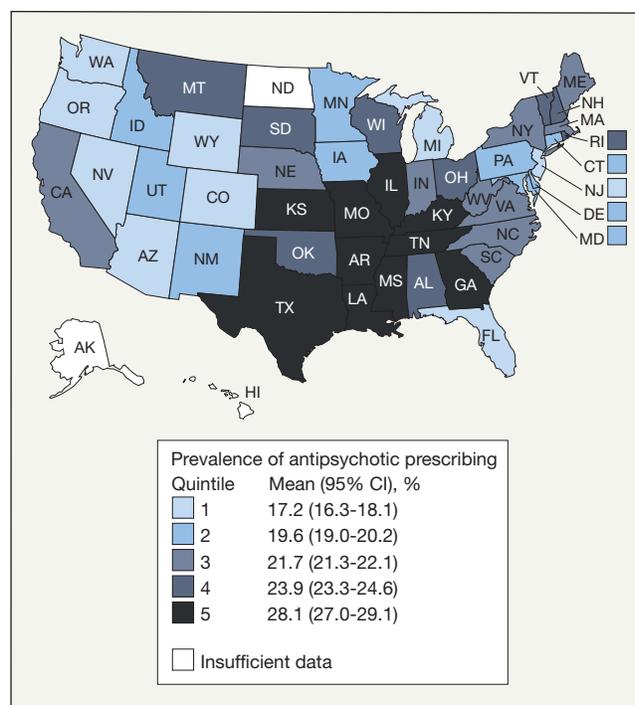
Comment. Our finding that 22.0% of NH residents received antipsychotics in 2009-2010 is within the lower range of rates that were documented 25 years earlier before the passage of the Omnibus Budget Reconciliation Act of 1987, which instituted regulations on the appropriate use of antipsychotics in NHs.^{4,5}

The reasons for our findings are unclear. Geographic variation suggests the absence of an evidence-based approach to the use of these medications in NHs. The most common antipsychotics prescribed are often used

for off-label indications related to dementia, and the extended durations of use raise concerns about the care of frail elders residing in NHs.

While our study included data from only 1 long-term care pharmacy, a comparison of our sample with data from NHs in the 2010 Online Survey, Certification and Reporting showed substantial overlap (61.9% vs 66.4% female, respec-

Figure. State-Level Prevalence of Antipsychotic Prescribing in Nursing Homes



State-level samples ranged from 767 to 104 460 residents.

Table. Most Commonly Prescribed Antipsychotic Medications in Nursing Homes (NHs)

Generic Drug Name	No. of Residents Prescribed Drug	% of Total Prescriptions	Type of Antipsychotic	Duration of Use During 90-Day Stay in NH, Median (IQR), d ^a
Quetiapine fumarate	1 356 223	31.1	Atypical	72 (67-85)
Risperidone	1 061 897	24.4	Atypical	70 (50-83)
Olanzapine	570 453	13.1	Atypical	70 (48-83)
Haloperidol	402 077	9.2	Conventional	30 (7-70)
Aripiprazole	347 900	8.0	Atypical	69 (50-82)
Clozapine	232 125	5.3	Atypical	77 (67-85)
Ziprasidone	138 881	3.2	Atypical	66 (30-82)
Chlorpromazine	65 159	1.5	Conventional	30 (8-74)
Fluphenazine	54 867	1.3	Conventional	54 (26-76)
All others ^b	109 141	2.9	Atypical and conventional	70 (52-83)

Abbreviation: IQR, interquartile range.

^a Calculated among 186 076 residents of NHs receiving at least 1 antipsychotic and observed for at least 90 days.

^b Includes paliperidone, perphenazine, thiothixene, loxapine, trifluoperazine, combination of olanzapine and fluoxetine, asenapine, lloperidone, molindone, pimozine, trilafton, loxitan, and mesoridazine.

tively; 66.4% vs 71.4% aged ≥ 75 ; and 54.5% vs 66.0% eligible for Medicaid). We were unable to assess appropriate vs inappropriate prescribing.

Becky A. Briesacher, PhD

Jennifer Tjia, MD, MSCE

Terry Field, DSc

Daniel Peterson, MS

Jerry H. Gurwitz, MD

Author Affiliations: Meyers Primary Care Institute and University of Massachusetts Medical School, Worcester.

Corresponding Author: Becky A. Briesacher, PhD, University of Massachusetts Medical School, 377 Plantation St, Biotech 4, Ste 315, Worcester, MA 01605 (becky.briesacher@umassmed.edu).

Author Contributions: Dr Briesacher had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Briesacher, Tjia, Gurwitz.

Acquisition of data: Briesacher.

Analysis and interpretation of data: Briesacher, Tjia, Field, Peterson, Gurwitz.

Drafting of the manuscript: Briesacher.

Critical revision of the manuscript for important intellectual content: Briesacher, Tjia, Field, Peterson, Gurwitz.

Statistical analysis: Briesacher, Tjia, Field, Peterson.

Obtained funding: Briesacher, Tjia, Gurwitz.

Administrative, technical, or material support: Briesacher.

Study supervision: Briesacher.

Conflict of Interest Disclosures: The authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Dr Briesacher reported receiving research support and consulting fees from Novartis. Dr Tjia reported serving as a consultant to Qualidigm. No other disclosures were reported.

Funding/Support: This study was supported by the Agency for Healthcare Research and Quality grant R18HS019351-01. Dr Briesacher was also supported by research scientist award K01AG031836 from the National Institute on Aging.

Role of the Sponsor: The funding organizations had no role in the design and conduct of the study; in the collection, analysis, and interpretation of the data; or in the preparation, review, or approval of the manuscript.

Additional Contributions: We thank Kathy M. Mazor, EdD, Leslie R. Harrold, MD, MPH, and Celeste A. Lemay, MPH (Meyers Primary Care Institute and University of Massachusetts Medical School, Worcester), and Jennifer L. Donovan, PharmD, RPh, Abir O. Kanaan, PharmD (Massachusetts College of Pharmacy and Health Sciences, Worcester), for collaborating on the study. We also thank Sarah Foy and

Sruthi Valluri (Meyers Primary Care Institute, Worcester, Massachusetts) for administrative assistance in preparing the manuscript. No compensation was received by any of the persons listed.

1. Briesacher BA, Limcangco MR, Simoni-Wastila L, et al. The quality of antipsychotic drug prescribing in nursing homes. *Arch Intern Med*. 2005;165(11):1280-1285.
2. Maher AR, Maglione M, Bagley S, et al. Efficacy and comparative effectiveness of atypical antipsychotic medications for off-label uses in adults: a systematic review and meta-analysis. *JAMA*. 2011;306(12):1359-1369.
3. Chen Y, Briesacher BA, Field TS, Tjia J, Lau DT, Gurwitz JH. Unexplained variation across US nursing homes in antipsychotic prescribing rates. *Arch Intern Med*. 2010;170(1):89-95.
4. Shorr RI, Fought RL, Ray WA. Changes in antipsychotic drug use in nursing homes during implementation of the OBRA-87 regulations. *JAMA*. 1994;271(5):358-362.
5. Rovner BW, Edelman BA, Cox MP, Shmueli Y. The impact of antipsychotic drug regulations on psychotropic prescribing practices in nursing homes. *Am J Psychiatry*. 1992;149(10):1390-1392.

CORRECTIONS

Incorrect Body Mass Index Range: In the Editorial entitled "Does Body Mass Index Adequately Convey a Patient's Mortality Risk?" published in the January 2, 2013, issue of *JAMA* (2013;309[1]:87-88), in the third to last paragraph of the Editorial, the last sentence of the paragraph should have stated "The average resulting from combining persons in the lowest mortality category (BMI of 22-25) with those who have greater mortality (BMI of 18.5-22) might explain why the NHLBI category of normal weight has an observed mortality similar to class 1 obesity (BMI of 30-<35)." This article has been corrected online.

Incorrect Title: In the Book Review of *Malignant: Medical Ethicists Confront Cancer*, published in the October 10, 2012, issue of *JAMA* (2012;308[14]:1483-1484), the title of the book under review was incorrectly reported as *Malignant: Medical Ethics Confront Cancer*. This article has been corrected online.

Error in Wording: In the JAMA Patient Page entitled "Energy Drinks" published in the January 16, 2013, issue of *JAMA* (2013;309[3]:297), a wording error occurred in the last paragraph. The first sentence should have read, "Energy drinks are regulated by the US Food and Drug Administration." The article has been corrected online.