effects (Figure, C).[4] Pulse methylprednisolone therapy was tried, but she subsequently died 4 days later.

*Case 2.* An 83-year-old man with history of hypertension and diabetes mellitus presented with new-onset AF. He was treated initially with 6 days of intravenous and then 4 days of oral amiodarone (a total of 4.6 g), which was subsequently switched to oral dronedarone for 4 days. He was transferred to our hospital for management of AF. On admission, dronedarone therapy was stopped, but he developed progressive dyspnea 2 days later. Chest radiography and thoracic computed tomography revealed diffuse ground glass opacities over both lungs, compatible with BOOP (Figure, D and E). Treatment with broad-spectrum antibiotics failed, and he developed respiratory failure necessitating mechanical ventilation. All the microbiological investigation findings were negative. His condition improved with pulse methylprednisolone therapy, and he was successfully weaned off from the ventilator.

**Comment.** Although it is arguable that both patients were treated with amiodarone before switching to dronedarone, the temporal sequence of their onset of respiratory symptoms as well as similar radiological features would suggest that dronedarone may in fact play an important role in the pathogenesis. Furthermore, the lung toxic effects appear to occur both after the short- and long-term exposure to dronedarone. Our observations suggest that serial monitoring of chest radiography is needed in patients receiving dronedarone, especially in those with prior exposure to amiodarone.

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1. Zimetbaum PJ. Dronedarone for atrial fibrillation—an odyssey. *N Engl J Med*. 2009;360(18):1811-1813.
2. Hohnloser SH, Crijns HJ, van Eickels M, et al; ATHENA Investigators. Effect of dronedarone on cardiovascular events in atrial fibrillation. *N Engl J Med*. 2009;360(7):668-678.
3. Quaglino D, Ha HR, Duner E, et al. Effects of metabolites and analogs of amiodarone on alveolar macrophages: structure-activity relationship. *Am J Physiol Lung Cell Mol Physiol*. 2004;287(2):L438-L447.
4. Malhotra A, Muse VV, Mark EJ. Case records of the Massachusetts General Hospital: weekly clinicopathological exercises. Case 12-2003. An 82-year-old man with dyspnea and pulmonary abnormalities. *N Engl J Med*. 2003; 348(16):1574-1585.

## EDITOR'S NOTE

### Dronedarone Use and Fatal Lung Toxic Effects?

Siu et al have observed a rare potential adverse effect of dronedarone in patients who have had previous exposure to amiodarone. Dronedarone is an antiarrhythmic agent that can be useful in some patients with nonpermanent atrial fibrillation who have not had recent heart failure. Many clinicians, including cardiologists, are currently using this drug in specific patient populations, including young individuals, at least initially, in preference to long-term oral therapy with amiodarone, a more highly toxic agent. Nonetheless, it is clinical observations like these, and not randomized controlled studies, which can (and often do) serve the purpose of alerting us to new and important consequences of our therapies. The implied warning provided by this report in these 2 patients who have had prior exposure to amiodarone should be taken seriously, and newly described adverse effects should be actively sought and reported by physicians using newly developed approved drugs of all types.

*Nora Goldschlager, MD*

## RESEARCH LETTERS

### Bridging the Chasm: Effect of Health Information Exchange on Volume of Laboratory Testing

Sharing of patient information between health care providers, including through health information exchanges (HIEs), has been proposed as one of the essential changes to improve the quality and efficiency of the health care system in the United States.[1] It has been estimated that HIEs could decrease health care costs across the country by approximately $78 billion annually.[2] Despite numerous potential advantages of HIEs, there are few studies documenting their benefits.[3] This lack of objective information might have slowed down their acceptance.[4] Studies that demonstrate tangible evidence of benefits provided by HIEs are urgently needed. Provider surveys show that reduction in duplicate testing is one of the most commonly expected benefits.[5,6] We therefore investigated whether the introduction of an HIE between 2 academic medical centers was associated with a reduction in volume of laboratory testing.

**Methods.** We conducted a retrospective study to investigate whether the availability of laboratory test results



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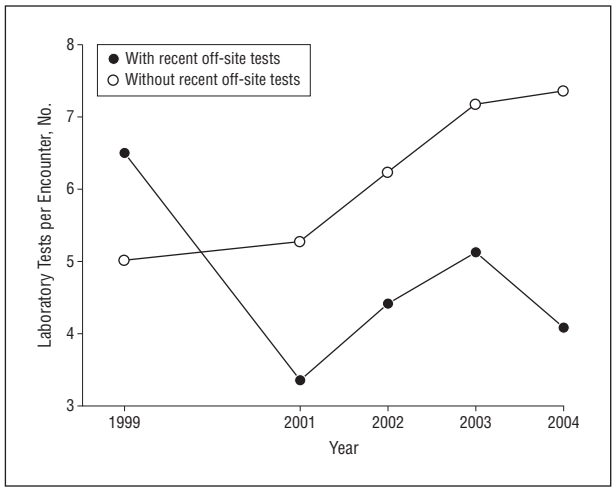


**Figure.** Number of laboratory tests per encounter. Compared are the encounters with recent off-site tests with those without, before and after the implementation of the health information exchange.

from a nonencounter hospital reduced the number of subsequent laboratory tests at the encounter hospital. The institutional review board at Partners HealthCare approved the study.

All new outpatient consultations at 2 affiliated academic hospitals between January 1, 1999, and December 31, 2004, were studied. Encounters during the year 2000 when an internal HIE was being rolled out were excluded. We also excluded patients hospitalized for 10 days or fewer after the index encounter and patients with tests in both hospitals prior to the encounter.

A single new consultation encounter—the index encounter—served as a unit of analysis. The number of laboratory tests performed until the end of the day of the index encounter at the same institution as the encounter (postencounter on-site tests) served as the primary outcome variable. Presence of laboratory tests performed at either of the institutions during the 7 days prior to the index encounter and whether the encounter took place before (1999) or after (2001-2004) the HIE rollout served as the primary predictor variables.

A multivariable Poisson regression model was used to evaluate the effect of the recent preencounter tests on the number of postencounter on-site laboratory tests while covariates were adjusted for.

**Results.** We identified 122 771 patients between January 1, 1999, and December 31, 2004. We excluded 5146 patients who were admitted to the hospital 10 days or fewer after the index encounter and 19 patients who had tests in both institutions during the week prior to the encounter. The remaining 117 606 patients were included in the study.

Of the 346 study encounters with recent off-site tests, 44 took place prior to HIE rollout. Among the 117 260 encounters without preceding off-site tests, 21 968 took place prior to HIE rollout. Patients with recent off-site tests had a mean (SD) of 22.07 (30.13) tests prior to the index encounter. Patients without recent off-site tests had a mean (SD) of 1.62 (10.61) tests prior to the index encounter. Most of the encounters without off-site tests (110 110 or 93.9%) did not have any tests in the preceding week.

In univariate analysis, the number of laboratory tests performed after encounters that had recent off-site laboratory tests decreased by 49% after introduction of the HIE (**Figure**). In multivariable analysis using a Poisson regression model adjusted for the patient demographics, Charlson Comorbidity Index, site of the encounter, season, encounter year, and the number of prior tests at the encounter and nonencounter institutions, the number of tests after the encounters with prior off-site tests decreased by 52.6% (95% CI, 16.6%-73.1%) after the electronic medical record integration ($P=.01$).

The number of postencounter tests increased by 2.5% for each point increase in the Charlson Comorbidity Index ($P<.001$), and it rose up to 51.7% with every subsequent year ($P<.001$). The number of tests decreased by 0.84% for every $10 000 increase in the patient's median household income ($P<.001$). It was also 9.06% lower for the patients on Medicaid ($P<.001$) compared with patients with private health insurance.

**Comment.** In this large retrospective study we have demonstrated that the introduction of an internal HIE was associated with a significant decrease in the number of laboratory tests ordered for patients new to the provider when recent laboratory results were available from another institution. Importantly, our results indicate that the reduction in laboratory tests may be as high as 50%. This could potentially translate into significant savings in settings where patients frequently receive care at multiple institutions.

Our research therefore confirms the hypothesis that having access to the patients' laboratory test results influences the decision process in regard to ordering further tests, which supports the predictions of financial savings made in the HIE cost-benefit models.[2] Further studies are required to evaluate the impact and direct financial savings associated with sharing other health information, including imaging studies, physician notes, and discharge summaries.

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1. National Alliance for Health Information Technology. Report to the Office of the National Coordinator for Health Information Technology on defining key health information technology terms [registration required]. http://healthit.hhs.gov/portal/server.pt/gateway/PTARGS_0_10741_848133_0_0_18/10_2_hit_terms.pdf. Accessed September 24, 2011.
2. Walker J, Pan E, Johnston D, Adler-Milstein J, Bates DW, Middleton B. The value of health care information exchange and interoperability. *Health Aff (Millwood)*. 2005(suppl Web exclusives):W5-10-W5-18.
3. Frisse ME, Johnson KB, Nian H, et al. The financial impact of health information exchange on emergency department care [published online November 4, 2011]. *J Am Med Inform Assoc*. doi:10.1136/amiajnl-2011-000394.
4. Adler-Milstein J, Bates DW, Jha AK. A survey of health information exchange organizations in the United States: implications for meaningful use. *Ann Intern Med*. 2011;154(10):666-671.
5. Hincapie AL, Warholak TL, Murcko AC, Slack M, Malone DC. Physicians' opinions of a health information exchange. *J Am Med Inform Assoc*. 2011;18(1):60-65.
6. Wright A, Soran C, Jenter CA, Volk LA, Bates DW, Simon SR. Physician attitudes toward health information exchange: results of a statewide survey. *J Am Med Inform Assoc*. 2010;17(1):66-70.

## Association Between More Frequent Chocolate Consumption and Lower Body Mass Index

Chocolate has shown favorable metabolic associations with blood pressure (BP),[1-3] insulin sensitivity,[1] and cholesterol level.[3] Chocolate is rich in antioxidant phytonutrients like catechins that could contribute to favorable relationships of chocolate consumption to insulin sensitivity and BP. However, because chocolate is often consumed as a sweet and bears calories, there are concerns related to its intake.

Body mass index (BMI) is part of the metabolic syndrome (MetS) picture, and other MetS elements relate favorably to moderate chocolate consumption. Therefore, we hypothesized that the benefits of modest frequent chocolate intake might extend to reduced fat deposition, potentially offsetting the added calories. To evaluate this, we examined the cross-sectional relationship of chocolate consumption frequency to BMI.

**Methods.** *Subjects.* A total of 1018 men and women aged 20 to 85 years from San Diego, California, without known cardiovascular disease, diabetes, or extremes of low-density lipoprotein cholesterol (LDL-C) levels (115-190 mg/dL inclusive [to convert to millimoles per liter, multiply by 0.0259]), were screenees for participation in a broadly sampling clinical study examining noncardiac effects of statins.[4,5] The study protocol was approved by the University of California, San Diego Human Research Protections Program; all participants gave written informed consent.

*Measures.* To measure chocolate consumption frequency, 1017 subjects responded to the question "How many times a week do you consume chocolate?" Body mass index (calculated as weight in kilograms divided by height in meters squared) was determined for 972 subjects (95.6%), who had both weight and height recorded at the screening visit.

Of the subjects, 975 (95.8%) completed the validated Fred Hutchinson Food Frequency Questionnaire (FFQ). Calories (determined via FFQ) could mediate associations of chocolate with BMI (contravening calorie adjustment): analyses were performed with and without calorie adjustment. Fruit and vegetable intake and saturated fat (satfat) intake were assessed for relevance. Fruits and vegetables (linked to lower BMI) bore no relationship to chocolate consumption frequency ($\beta = 0.004$ [SE = 0.007]; $P = .55$), excluding this as a candidate confounder, but satfats (which, however, accompany chocolate via stearic acid) were significantly related both to chocolate intake ($\beta = 0.035$ [SE = 0.005]; $P < .001$) and higher BMI. Analyses were performed with and without satfat adjustment. Amount of chocolate consumed (vs frequency with which it was

**Table. Chocolate Consumption Frequency Predicts Lower BMI: Regression Results[a]**

| | Chocolate Consumption Frequency, Association With BMI | |
|---|---|---|
| **Adjustment Model** | **β (SE)** | ***P* Value** |
| Unadjusted | –0.142 (0.053) | .008 |
| Age and sex adjusted | –0.126 (0.053) | .02 |
| Age, sex, and activity adjusted | –0.130 (0.052) | .01 |
| Age, sex, activity, and calorie adjusted | –0.146 (0.059) | .01 |
| Age, sex, activity, and satfat adjusted | –0.190 (0.059) | .001 |
| Age, sex, activity, satfat, and CES-D adjusted | –0.191 (0.059) | .001 |
| Age, sex, activity, satfat, fruit and vegetable, and CES-D adjusted | –0.201 (0.060) | .001 |
| Age, sex, activity, satfat, fruit and vegetable, CES-D, and calories adjusted | –0.208 (0.060) | .001 |

Abbreviations: BMI, body mass index; CES-D, Center for Epidemiological Studies Depression scale; satfat, saturated fat.

[a]A model containing calories (and activity, as well as age and sex) was included, since calories and activity are usual predictors of BMI. However, calories were otherwise not in adjustment models because chocolate inherently contains calories and adjustment could justly be deemed inappropriate—overstating the benefits of chocolate to BMI. Closely similar results were obtained using an alternate activity measure. Significance was identical for all except the third and fourth models, where significance was stronger ($P = .006$ and $P = .007$, vs $P = .01$ and $P = .01$).



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