

# Responding to the Rofecoxib Withdrawal Crisis: A New Model for Notifying Patients at Risk and Their Health Care Providers

Anil Jain, MD; Ashish Atreja, MD, MPH; C. Martin Harris, MD, MBA; Meghan Lehmann, PharmD; Jon Burns, BS; and James Young, MD

**Background:** We decided to inform our patients of the withdrawal of rofecoxib, one of the largest drug withdrawals in United States history, and instruct them to contact their providers for guidance.

**Objective:** To identify and inform patients and providers affected by the rofecoxib withdrawal.

**Design:** Descriptive observational study.

**Setting:** Tertiary care center with an electronic medical record (EMR) system.

**Patients:** Patients with an active rofecoxib prescription within the EMR.

**Intervention:** Existing information technology and traditional communication resources were used to automate the identifying and notifying of patients and providers and to deactivate rofecoxib prescriptions in the EMR.

**Measurements:** Characteristics of patients receiving rofecoxib at our institution, details of their prescription and provider, number of EMR alerts, and medication discontinuations.

**Results:** The 11 699 patients with a rofecoxib prescription in our practice were sent notifications within 24 hours of the withdrawal.

**Limitations:** We did not directly measure the effect of our notification on patients or providers.

**Conclusions:** Information technology enabled our institution to rapidly identify and notify individual patients and their providers about an important drug withdrawal. The methods modeled a feasible way for health care organizations with EMRs to participate in notification processes that may be applicable in a variety of situations.

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For author affiliations, see end of text.

On the morning of 30 September 2004, the U.S. Food and Drug Administration (FDA) issued a Public Health Advisory about the withdrawal of rofecoxib (1). This worldwide withdrawal by Merck & Co., Inc., was based on data from the Adenomatous Polyp Prevention on Vioxx (APPROVe) trial that suggested an increased risk for cardiovascular events in patients receiving rofecoxib, particularly those who had been taking the drug for longer than 18 months (1, 2). At the time of the withdrawal, approximately 2 million people were receiving rofecoxib nationwide, making it the largest prescription drug withdrawal in U.S. history (3). The withdrawal occurred at the pharmacy level, meaning that pharmacists were required to cease dispensing this agent and remove remaining stock from inventories (4). As in previous drug withdrawals from the market, both the manufacturer and the FDA undertook major initiatives to educate the general public as well as health care providers (1, 5).

No federal laws govern the process of drug withdrawal (6, 7). Furthermore, the manner and timeliness of transmitting drug withdrawal information to pharmacists, providers, and patients vary (8–10). Reports have described persistent use of medications even after their withdrawal from the market (11, 12). Consequently, in addition to the drug manufacturer, the FDA, and the dispensing pharmacies, drug withdrawal notification may also become a responsibility of the institution providing the patient's care (6, 13, 14; Morrison CM, McMains MB. Legal necessity

for early nationwide notification of pharmacies after drug recalls. Presented at the 143rd Annual Meeting of the American Pharmaceutical Association, 11 March 1996, Nashville, Tennessee).

Fortunately, health information technology has now made it feasible for health care institutions to successfully identify and inform distinct patients affected by a drug withdrawal (9, 15). We decided to use the electronic medical record (EMR), variably referred to as a computerized patient record (CPR), electronic patient record (EPR), or electronic health record (EHR), to identify patients with an active rofecoxib prescription, notify them of the withdrawal, and notify their providers (16, 17). The Cleveland Clinic Foundation Institutional Review Board deemed the study protocol exempt from review.

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## METHODS

### Technology

At the Cleveland Clinic Foundation, nearly all health care providers use a commercial EMR (Epic Systems Corp., Madison, Wisconsin) for clinical documentation, order entry, and prescriptions (18, 19). We queried our EMR clinical data warehouse (Oracle Database server, Oracle Corp., Redwood Shores, California) to identify patients with an active rofecoxib prescription. We extracted demographic characteristics, e-mail address, diagnosis history, primary and prescribing provider, and prescription dosage and duration for each patient into a data file.

### Communication to the Patients

Our institution prepared a letter template that outlined the specifics of the withdrawal and instructed patients to stop rofecoxib and contact their health care providers for guidance. We also generated a mail-merge file of patient names and addresses consistent with our institutional privacy policy and the Health Insurance Portability and Accountability Act (HIPAA) (20). After the letters were generated, mailroom personnel used an automated system to stuff and stamp envelopes before delivery to the U.S. Postal Service for mailing via regular post. We also sent our Internet-based shared EMR users an e-mail similar to the letter and placed a warning and link of the FDA withdrawal on their Web site login page (21).

### Communication to the Health Care Providers

We sent an e-mail (Microsoft Outlook, Microsoft Corp., Redmond, Washington) to our institution's health care providers that outlined the steps being taken by the Cleveland Clinic Foundation to notify patients about the rofecoxib withdrawal. We also informed the providers that they would shortly receive a list of their own patients who may be affected by the withdrawal. We also deactivated rofecoxib within our EMR medication formulary and created an automated computer alert triggered when a provider "opened" the electronic chart of a patient with an active rofecoxib prescription. Finally, we placed a warning and a link of the FDA withdrawal on our institutional Web site.

### Clinical Data and Analysis

To identify comorbid conditions, we used International Classification of Diseases, 9th Revision, diagnosis codes entered by physicians during patient encounters: peptic ulcer disease (531–534.9), bleeding peptic ulcer (531.0/2/4/6, 532.0/2/4/6, 533.0/2/4/6, 534.0/2/4/6), ischemic heart disease (410–414.99), stroke (433.xx–437.xx, excluding 435.9), transient ischemic attack (435.9), hypertension (401.xx), and congestive heart failure (428.xx). To identify the subset of patients at a potentially higher relative risk for developing cardiovascular events from rofecoxib, we categorized patients as either "aspirin indicated" or "aspirin not indicated" on the basis of the criteria for secondary cardiovascular prophylaxis used in the Vioxx

**Table 1. Patient and Health Care Provider Characteristics**

Characteristics	Patients
<b>Demographic</b>	
Patients, <i>n</i>	11 699
Mean age ± SD, <i>y</i>	58.54 ± 15.57
Women, %	64.1
Race/ethnicity, %	
African American	8.3
Hispanic	0.9
Asian	0.4
White	84.5
Other	2.0
<b>Primary care provider, %</b>	
Main campus	6.6
Family health centers	36.1
None or outside the institution	57.3
<b>Rofecoxib prescription strength, %</b>	
12.5-mg tablet	5.5
12.5-mg/5-mL suspension	0.2
25-mg tablet	88.2
25-mg/5-mL suspension	0.1
50-mg tablet	6.0
<b>Duration of prescription, % (<i>n</i> = 11 613)*</b>	
<18 mo	54.8
18 mo–3 y	35.8
>3 y	9.1
<b>Prescribing department, %</b>	
Primary care	43.6
Orthopedics	11.6
Rheumatology	6.7
Pain management	5.1
Neurology	4.8
Cardiology	4.0
Gastroenterology	1.8
Others	16.5
<b>History of comorbid conditions, %</b>	
Hypertension	29.2
Peptic ulcer disease	2.5
History of bleeding peptic ulcer	0.1
Ischemic heart disease	7.4
Previous stroke	3.5
Previous transient ischemic attack	0.8
Congestive heart failure	2.3

\* 86 patients did not have a documented start date for rofecoxib prescription.

Gastrointestinal Outcomes Research (VIGOR) trial (that is, history of myocardial infarction, angina, cerebrovascular accident, transient ischemic attack, angioplasty, or coronary bypass grafting) (22). We also queried the EMR data warehouse to determine the number of triggered clinical alerts and the number of rofecoxib prescriptions discontinued since the withdrawal.

## RESULTS

### Patient Characteristics

Table 1 shows characteristics of the identified patients. Of the 11 699 patients with an active prescription for rofecoxib, most were receiving 25 mg (*n* = 10 318), the strength used in the APPROVe trial. Duration data were available for 11 613 patients; of these, 5203 (45%) had had pre-

**Table 2. Timeline of Cleveland Clinic Foundation's Response to Rofecoxib Withdrawal\***

Thursday, 30 September 2004		
9:00 a.m.		Merck & Co., Inc., issues a press release
9:15 a.m.	15 min	U.S. Food and Drug Administration issues Public Health Advisory
9:30 a.m.	30 min	Cleveland Clinic Foundation's Drug Information Center receives notification
9:45 a.m.	45 min	Rofecoxib pulled from hospital medication stock
10:08 a.m.	68 min	Information conveyed to pertinent personnel
10:30 a.m.	90 min	Clinical data repository queried
2:00 p.m.	5 h	Automated computer alert activated
4:00 p.m.	7 h	Medication prescription deactivated within EMR
4:00 p.m.	7 h	Patients using shared EMR notified via e-mail
4:00 p.m.	7 h	E-mail notification sent to all providers
Friday, 1 October 2004		
7:00 a.m.	22 h	Letters mailed to all 11 699 patients
10:00 a.m.	25 h	All providers dispatched a list of their patients with an active rofecoxib prescription

\* EMR = electronic medical record.

scriptions for more than 18 months and 1051 (9%) had a prescription dating back more than 3 years. Of note, 297 (2.5%) patients had a history of peptic ulcer disease and 867 (7.4%) patients had a documented history of ischemic heart disease. In addition, 1207 (10.3%) patients were deemed "aspirin indicated" according to criteria for secondary cardiovascular prophylaxis. This finding suggests that these patients were at higher risk for a cardiovascular event due to rofecoxib.

### Provider Characteristics

We identified 842 providers at our institution who had prescribed rofecoxib to the identified patient population. The most frequent prescribing providers were primary care providers (internists, family practitioners, and general pediatricians) (Table 1). The number of patients identified per prescribing provider varied from 1 to 122 (average, 14). The most common diagnoses that providers linked to their prescription were osteoarthritis, joint pain, and rheumatoid arthritis.

### Notification Timings

Table 2 chronicles our response to the rofecoxib withdrawal. Approximately 1 hour after the withdrawal was announced, the Cleveland Clinic Foundation's Drug Information Center informed the various department heads, including the Chief Pharmacy Officer and the Chief Information Officer, via e-mail. A multidisciplinary ad hoc team of clinicians, pharmacists, administrators, and informaticians devised an action plan for identifying and notifying patients and providers affected by the withdrawal. Within 7 hours, we deactivated rofecoxib from our EMR medication formulary and created the automated computer alert. By 7 a.m. the next morning, we sent letters to our patients via regular post. Finally, hardcopy letters identifying a provider's list of patients with an active rofecoxib prescription were sent on 1 October via interoffice mail.

### Impact

As of 18 November 2004, clinical alerts triggered warnings for 4511 (38.6%) distinct patients during office, telephone, and refill encounters. Of these patients, 3717 (82.4%) had their prescription discontinued by the provider during that encounter. Eight letters were returned unopened and 2 were returned with replies indicating that the patient had died.

### DISCUSSION

With the health care environment becoming more complex and specialized, the utility of EMR technology to facilitate communication about important health care issues is critical. This report describes an immediate response to a major drug withdrawal using EMR patient data in combination with readily available, automated communication tools. We identified and notified 11 699 patients receiving rofecoxib who were actively managed in our EMR. We also identified 842 prescribing providers within a short time after the FDA Public Health Advisory and provided them a list of their patients.

Our response should not be viewed as a limited answer to a rare problem but rather as a generalizable model. The rofecoxib withdrawal is not an isolated crisis; it reflects an ever-growing problem in modern health care (23). For example, between 1997 and 1998, drug withdrawals affected nearly 20 million people (24, 25). With more and more drugs entering the market, there is a concern that this trend may increase (23). Historically, it appears that the FDA and the drug manufacturers shoulder the burden of managing a drug withdrawal. However, because EMR technology makes identification of patients possible, society and patients may ask that the responsibility extend to include health care providers and their institutions. This responsibility, if not acted upon, may increase the potential for legal action against the health care providers and institutions (6).

Most of the current literature has focused on using EMR technology for routine clinical care and addressing patient safety and medication errors (26, 27). Little emphasis has been given to actually demonstrating the advantages that the EMR, along with the shared EMR, has over traditional paper-based charts in rapidly identifying and communicating with a select group of patients and providers. As EMR adoption and Internet use among the general public increase, we expect a dramatic rise in the proportion of patients using the Internet for health information and the Internet-based shared EMR (21, 28, 29).

While it can be argued that notifying patients and providers within 24 hours of this particular withdrawal was not critical, we may not be so fortunate in future drug withdrawals. Many of us are aware of the 1960s' epidemic of congenital malformations (phocomelia and other organ defects) due to thalidomide (30). This effect occurs with a very low single dose and at a time during gestation when many women are not aware of pregnancy. In such situations, the

institution's ability to uniquely identify and promptly notify patients and their providers may make a tangible difference.

Thus, although we demonstrate the value of this model by using the rofecoxib drug withdrawal, the true value of the model is that it extends beyond the occasional drug withdrawal crisis and can be applied to a variety of patient care emergencies. For example, institutions may wish to notify high-risk patients to present themselves to an influenza vaccine station during an influenza vaccine shortage or an influenza outbreak. The EMR technology should be designed to enable institutions to quickly and easily identify a patient population on the basis of a diagnosis, medication, or laboratory result (that is, the EMR query process should not be the rate-limiting step in the management of a patient care emergency).

Our study has some important limitations. Patients may have discontinued rofecoxib therapy before documentation within our EMR or received drug samples that may not have been documented. We did not measure the clinical or psychological impact of our notification on our patients, who may also have been notified by their pharmacy or the mass media. Hence, it is difficult to measure the true effect of our notification without knowing the exact number of patients who exclusively received information from our intervention. Although we did not objectively measure the impact of the notification on the volume or nature of telephone calls to the provider or on provider satisfaction, we did not receive any complaints from the providers. Moreover, we did not study why some providers did not discontinue the prescription in response to the clinical alert. Nevertheless, a future survey of patients and providers would address many of these issues. Finally, we chose to mail letters via regular post; however, we could have used registered mail, automated call technology, and encrypted e-mail (16, 31).

In conclusion, our study shows the capability of modern informatics tools to efficiently identify and notify patients and their health care providers who met specific criteria during a drug withdrawal. Because many of these processes were automated, notices were dispatched to patients and providers within 24 hours of the drug withdrawal. Our methods can serve as a model for other EMR-equipped health care organizations that wish to participate in the notification process during similar patient care crises.

From The Cleveland Clinic Foundation, Cleveland, Ohio.

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**Requests for Single Reprints:** Anil Jain, MD, Cleveland Clinic Foundation, A91, 9500 Euclid Avenue, Cleveland, OH 44195.

Current author addresses are available at [www.annals.org](http://www.annals.org).

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**Current Author Addresses:** Drs. Jain and Atreja: Cleveland Clinic Foundation, A91, 9500 Euclid Avenue, Cleveland, OH 44195.  
Dr. Lehmann: Department of Pharmacy/Hb03, Cleveland Clinic Foundation, 9500 Euclid Avenue, Cleveland, OH 44195.  
Dr. Young: Cleveland Clinic Foundation, T13, 9500 Euclid Avenue, Cleveland, OH 44195.

Mr. Burns: Cleveland Clinic Foundation, CL30, 9500 Euclid Avenue, Cleveland, OH 44195.

Dr. Harris: Cleveland Clinic Foundation, H18, 9500 Euclid Avenue, Cleveland, OH 44195.