analysis decision. **Study concept and design:** Feldman-Billard, Massin, and Meas. **Acquisition of data:** Massin and Guillausseau. **Analysis and interpretation of data:** Feldman-Billard and Héron. **Drafting of the manuscript:** Feldman-Billard, Meas, and Héron. **Critical revision of the manuscript for important intellectual content:** Massin and Guillausseau. **Obtained funding:** Massin. **Study supervision:** Feldman-Billard, Guillausseau, and Héron.

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**Figure 2.** Individual systolic blood pressure (A) and heart rate (B) values of the 12 patients with diabetes who showed hypoglycemic events (before [T0] and after [T1] the event). Full lines indicate the values from the 6 patients who were taking chrontrope/dromotrope-negative agents (β-blockers in 5 cases), whereas broken lines are dedicated to patients free of these drugs. One of the latter patients (full circles at broken line extremities) had only 2 glucose readings of 59 mg/dl (to convert to millimoles per liter, multiply by 0.0555) over a 10-minute period (ie, borderline normal values), and he was the only one who showed neither blood pressure nor heart rate modification between T0 and T1.

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**HEALTH CARE REFORM**

**Coverage of FDA Medication Boxed Warnings in Commonly Used Drug Information Resources**

A boxed (or “black box”) warning is the strongest medication-related safety warning that the Food and Drug Administration (FDA) can issue for a prescription drug. These warnings, which appear in the prescribing information, highlights of the prescribing information, and promotional materials for a given drug, are surrounded by a box that contains the word “WARNING” followed by a description of the safety risk.

The application of boxed warnings to commonly prescribed drugs in the past 5 years has captured the atten-
tion of clinicians, administrators, regulatory agencies, and the public. In California, acute care hospitals must implement safe medication processes specific to the use of drugs with boxed warnings or face administrative penalties and substantial fines.2

Surprisingly, an official list of drugs with FDA boxed warnings does not exist.3-5 MedWatch notifications concerning boxed warnings are available online from 1996 onward, but are archived by date of release and not quickly searchable by drug name. Fortunately, many drug information resources provide convenient access to boxed-warning information; however, the comprehensiveness of these resources with respect to these warnings is unknown. The purpose of our study was to create a list of currently marketed prescription drugs with boxed warnings and examine the ability of 8 drug information resources to detect these drugs as boxed-warning agents.

Methods. Our first step was to create a reference standard of boxed-warning drugs. We did this by compiling boxed-warning information from multiple sources (Figure). Dosage forms and salts of the same active ingredient were recorded as a single entry if they carried the same boxed warning. Combination products were listed only if their warning drug.

Results. We found 416 marketed prescription drugs with a boxed warning in the current prescribing information, 135 (32%) of which were covered in all 8 resources evaluated. While the resources’ sensitivity for identifying a boxed-warning drug ranged widely (42%-98%), the likelihood that a boxed warning was correct (positive predictive value) was consistently high (95%-100%) across sources (Table). Furthermore, all resources contained monographs without a boxed warning where one should have existed.

Comment. The boxed warning alerts health care providers of a greater-than-usual risk for an adverse effect that could lead to significant patient harm or death from use of a drug. The FDA’s decision to impose a boxed warning follows a review of events from adverse drug reaction reports, published literature, reports to foreign regulatory agencies, claims databases, and ongoing clinical trials.16 Knowing whether a drug carries a boxed warning may influence if and how a prescriber uses a given drug, particularly when an alternative—one without a boxed warning—may exist.

While our findings are limited to data gathered from select resources in June 2009, our work shows that iden-
tification of a drug with a boxed warning from a drug information resource is likely to be correct, though coverage of such warnings may be incomplete. Online repositories of current manufacturer’s prescribing information, the definitive indicator of boxed-warning status, are also imperfect. As a result, the absence of a boxed warning for a drug in any given resource may not reliably indicate that a drug does not carry such a warning. Until an official boxed-warning registry is established, clinicians should be aware that resources for boxed warnings exist, though cross-referencing the information may be necessary to ensure that a boxed-warning for a drug is duly recognized. Subscribing to MedWatch safety alerts, RSS (really simple syndication) feeds, or text messaging can also help clinicians keep abreast of new medication-related safety information, including boxed warnings, as they are announced.

Christine M. Cheng, PharmD
B. Joseph Guglielmo, PharmD
Judy Maselli, MSPH
Andrew D. Auerbach, MD, MPH

Author Affiliations: Department of Clinical Pharmacy (Drs Cheng and Guglielmo) and Divisions of General Internal Medicine (Ms Maselli) and Hospital Medicine (Dr Auerbach), University of California, San Francisco.

Correspondence: Dr Cheng, UCSF Department of Clinical Pharmacy, 521 Parnassus Ave, C-152, Box 0622, San Francisco, CA 94143-0622 (chengc@pharmacy.ucsf.edu).

Author Contributions: Study concept and design: Cheng, Guglielmo, and Auerbach. Acquisition of data: Cheng and Auerbach. Analysis and interpretation of data: Cheng, Guglielmo, Maselli, and Auerbach. Drafting of the manuscript: Cheng, Guglielmo, and Auerbach. Critical revision of the manuscript for important intellectual content: Cheng, Guglielmo, Maselli, and Auerbach. Statistical analysis: Maselli and Auerbach. Administrative, technical, and material support: Cheng, Guglielmo, and Auerbach. Study supervision: Guglielmo and Auerbach.

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COMMENTS AND OPINIONS

Avoiding Upper Respiratory Tract Infections by Not Touching the Face

Because of the current fears of influenza, the media have emphasized hand washing, which is an effective way to prevent the spread of viral illness.1 However, another technique—not touching the facial mucosa—has hardly been mentioned.2 Yet, in some individuals, it can dramatically reduce illness.

Table. Detection of Boxed Warnings in 8 Resources

<table>
<thead>
<tr>
<th>Resources for Boxed-Warning Summaries</th>
<th>Resources for Manufacturers’ Prescribing Information</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lexi-Drugs²</td>
<td>FormWeb⁶</td>
</tr>
<tr>
<td>No. of true warningsᵃ</td>
<td>407</td>
</tr>
<tr>
<td>No. of false warningsᵇ</td>
<td>3</td>
</tr>
<tr>
<td>Positive predictive value, %ᶜ</td>
<td>99.3</td>
</tr>
<tr>
<td>Sensitivity, %ᵈ</td>
<td>98</td>
</tr>
<tr>
<td>No. of drugs with information present, boxed warning missing</td>
<td>7</td>
</tr>
<tr>
<td>No. of boxed warning drugs with no information present (drug absent from resource)</td>
<td>2</td>
</tr>
</tbody>
</table>

ᵃTrue warning is defined as a boxed warning contained in both the resource and the current prescribing information.
ᵇFalse warning is defined as a boxed warning contained in the resource but not in the current prescribing information.
ᶜPositive predictive value is defined by the number of correct boxed warnings in a resource divided by the total number of boxed warnings in a resource.
ᵈSensitivity is defined by the proportion of true warnings in a resource divided by the overall total number of boxed warnings (n=416).