Variability in Pharmacy Interpretations of Physician Prescriptions

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Abstract

Background: The clarity of prescription drug instructions is a health literacy and medication safety concern.

Objective: To assess the variability of pharmacy interpretations of physician prescriptions.

Design: Identically written prescriptions for 4 common medications (atorvastatin, alendronate, trimethoprim/sulfamethoxazole, ibuprofen) were filled in 6 pharmacies (2 largest chains, 2 grocery stores, 2 independents) in 4 cities (Boston, Chicago, Los Angeles, Austin).

Measurement: Components of the instruction were coded as dose, frequency, administration route, timing, indication, and auxiliary instructions.

Results: In all, 85 labels were evaluated. Dose frequency was omitted on 6% of instructions (“take 1 tablet for cholesterol”). Timing was explicitly stated on 2% of instructions (“in the morning”). All prescriptions included indications; pharmacies transcribed these onto 38% of labels. The prescription for alendronate stated not to lie down for at least 30 minutes after taking; this was transcribed with 50% of instructions. Reading difficulty was above recommended levels for 46% of instructions; with 14% greater than a high school level.

Conclusions: Efforts are needed to ensure patients receive clear, consistent information supporting safe medication use.

Keywords

pharmacy; physician; prescription; sig; instruction; medication; variability; health literacy

According to the Institute of Medicine 2006 Report, Preventing Medication Error, more than one-third of the 1.5 million adverse drug events that occur in the United States each year happen in outpatient settings.1 The report cited poor patient understanding and unintentional misuse of prescription (Rx) drugs, and specifically poor understanding of drug labeling, as a root cause of a large proportion of medication errors. Recent studies and the Institute of Medicine 2008
Report, *Standardizing Medication Labels*, have also directed greater attention to the clarity of label instructions for prescribed drug regimens.\(^2\)-\(^6\) Estimates cited in this report suggest nearly half of adults may misunderstand common dosage instructions and warnings encountered on medication labels.\(^5\),\(^6\) Patients with limited literacy and those managing multiple medication regimens are at greater risk for misunderstanding how to self-administer prescription drugs.

The value of drug label dosage instructions, also known as “sig” messages (short for signatura), is particularly significant because physicians and pharmacists frequently miss opportunities to adequately counsel patients on how to safely take new medicines.\(^3\) Leaflets accompanying prescription drugs are often too complex for most patients to comprehend and are consequently ignored.\(^4\),\(^5\) As a result, the sig message on the prescription drug container label becomes an important, and sometimes the only resource for patients to learn how to use medications. However, these instructions, as initially written by the physician, are intended to be read by the pharmacist and not the patient. They usually include Latin abbreviations that require translation by the pharmacy before being placed onto the drug container label.\(^1\),\(^7\) Despite their brevity, these seemingly simple sig messages detailing dose, administration, and timing for prescribed medicines are not clear to patients.\(^5\),\(^8\) Several practices have been found to decrease patients’ functional understanding of sig messages and use of medications.\(^5\) Instructions with vague dosage frequencies and text words for stating dosage (ie, “twice” vs. “2 times”) have all been cited as common causes of patient misinterpretations.

Minimal standards have been widely adopted in medicine for the writing of sig instructions, although the translation of physician prescriptions has long been a component within pharmacy education.\(^9\)-\(^11\) However, the concordance and consistency of pharmacy translations of sig instructions, to our knowledge, has not been extensively evaluated in practice. A prior study by this research team examined drug label variability with regards to content and layout, and use of warning label stickers.\(^12\) Pharmacies widely varied in their use of auxiliary warnings, but also in the way they detailed information on the label for patients, more often emphasizing provider versus patient content. We hypothesized a similar degree of variability might exist with regard to the process used by pharmacies when interpreting and transcribing physician sig messages for prescriptions. In this study, we extend our previous research to assess variability in pharmacy translations of typical sig instructions, and the frequency that certain evidence-based practices are followed. Evidence of variability would raise concerns about medication therapy management, especially among patients with poor health literacy, and could lead to medication safety problems.\(^1\),\(^2\),\(^11\)

**Methods**

The methods have been described in detail in an earlier study evaluating the variability in drug label content and format (ie, font size, typographic cues, and use of warning label stickers).\(^12\) Briefly, sig messages transcribed on prescription container labels were gathered and compared from identically written physician prescriptions that were filled for commonly prescribed drugs in multiple pharmacies across the United States.

**Study Pharmacies**

Pharmacies in 4 US cities representing geographically diverse metropolitan areas (Los Angeles, CA; Boston, MA; Austin, TX; and Chicago, IL) were identified. In each city, we located 6 different pharmacies, including the 2 largest chain pharmacies in each area, 2 grocery store pharmacies, and 2 independent pharmacies.
Study Prescriptions

Four commonly-prescribed medications were chosen to be used in our study sample: (1) atorvastatin (Lipitor), the top selling medication in the United States, (2) alendronate (Fosamax), a medication with very specific administration directions (patients must take with 6–8 oz. of water and avoid reclining for 30 minutes), (3) trimethoprim-sulfamethoxazole (Bactrim), an antibiotic for acute use, and (4) ibuprofen, a nonsteroidal anti-inflammatory and analgesic agent. See Table 1 for the exact content of the written prescription dosage instructions. Collaborating physicians in each city wrote identically-worded prescriptions for each of the above drugs for female patients.

Prescription Attributes

The verbatim dosage instruction on the container label was transcribed into a Microsoft Excel file for further review by the lead author (M.S.W.). The relevant components of the instruction were then coded for analysis purposes following standards set for the codification of physician sig messages. This included administration timing [specific time of day identified (yes or no); eg, “morning” or “bedtime,”] indication for use [included as part of dosage instruction (yes or no)], and auxiliary messages [added or included (yes or no)].

Readability Analysis

Although dosage instructions are typically brief, a prior study by Davis et al found reading difficulty to be a significant independent predictor of patient comprehension of prescription label auxiliary warning instructions. Specifically, instructions that had a reading difficulty of seventh grade and above were greater than 4 times more likely to be misinterpreted by patients compared with instructions written at the most basic reading level.

The presumed reading difficulty of the pharmacy-interpreted dosage instructions was assessed using 2 common readability formulas; the Gunning Fog Index and Lexile analysis. The Gunning Fog Index is a common measure that determines the reading grade level of text passages using a simple algorithm based on sentence length and frequency of multisyllable words. The index score directly translates to the number of formal years of education necessary to easily understand the passage. Lexile analysis is a computer program that calculates a score based on sentence length and word frequency in popular literature. The range of the Lexile values starts below zero (beginning reading level) and runs up to 2000. A Lexile value of 300 corresponds to a second-grade level of reading difficulty, 400 to third grade, and 1300 being equivalent to a high school graduate level.

Analysis Plan

The data were evaluated descriptively using STATA version 9 (College Station, TX). Differences in dosage instruction content by pharmacy type was examined using a χ² test, with significance set at α < 0.05. For reading difficulty, an average grade level was calculated from the 2 measures (Gunning Fog Index, Lexile) and differences by pharmacy type were examined using analysis of variance. This study received an exemption from the West Los Angeles Veterans Affairs Institutional Review Board.

Results

A total of 96 prescriptions were filled, 24 each for ibuprofen, alendronate, trimethoprim-sulfamethoxazole, and atorvastatin. Eleven pharmacies substituted over-the-counter ibuprofen for the prescription written and did not create a patient-specific pharmacy label, leaving 85 sig messages for evaluation.
The content and presentation of the dosage instructions by pharmacy varied widely; representative examples of transcribed instructions are shown in the provided Table 1. For 6% of instructions, dose frequency was omitted entirely (eg, “take 1 tablet for cholesterol”). The precise timing of administration was specified only 2% of the time (eg, “in the morning”). All of the prescriptions were written with an indication for use (high cholesterol, osteoporosis prevention, urinary tract infection, pain), and pharmacies transcribed these onto only 38% of the labels. Seven of the 24 labels (29%) for trimethoprim-sulfamethoxazole included its indication for a urinary tract infection; only 3 of these labels wrote out the indication instead of transcribing the abbreviation “UTI” from the prescription. Half of the pharmacy label dosage instructions for alendronate included the directions specified on the physician prescription to not lie down for at least 30 minutes after taking. Chain drug store pharmacies were significantly more likely to include the indication for use with the dosage instruction compared with grocery store and independent pharmacies (56%, 20%, and 28%, respectively; \( P < 0.05 \)).

The mean Lexile score was 753 (SD = 205); equivalent to a sixth- to seventh-grade level of reading difficulty, while the mean Gunning Fog Index was 5.8 (SD = 3.2). The 2 readability scores were very strongly correlated (\( r = 0.92 \)). Using an average reading difficulty level from the 2 measures, approximately half (54%) of the dosage instructions were found to be at a recommended level of sixth grade or below; 32% were written at the seventh- to eighth-grade level, and 14% were at a high school level or above. The reading difficulty of instructions varied by drug and pharmacy type. Instructions for ibuprofen were the most difficult, whereas instructions for atorvastatin were the most simple [mean grade level: 7.9 (SD = 1.0) vs. 5.1 (SD = 2.3), \( P < 0.04 \)]. Prescriptions that were filled at independent pharmacies had instructions with significantly lower reading difficulty scores followed by grocery stores, while chain drug stores were found to have the highest reading difficulty [mean grade level: 4.8 (SD = 1.5), 5.3 (SD = 2.1), and 7.0 (SD = 2.2), respectively, \( P < 0.001 \)].

**Discussion**

This is the first study to our knowledge to document variability in pharmacy practice for translating common physician sig messages for widely used prescription drugs. Although much of the noted variation between pharmacies was subtle, interpretations of physician dosage instructions reflect suboptimal health literacy practices that could lead to inadequate patient understanding and unintentional misuse.\(^2,8,12\) Nearly half of the translated sig messages on container labels were written with a reading difficulty (>sixth grade) that was previously found to increase the likelihood of instruction misinterpretation.\(^9\) In addition, instructions rarely were written with explicit timing of administration requiring patients to make inferences about administration, which can be a challenging cognitive task for the elderly.\(^16\) Because a majority of physician prescriptions identify administration timing with default Latin abbreviations, pharmacists must translate this for the patient.\(^1,6\) When an optimal dosage timing is known, such as for atorvastatin to be taken at bedtime, it would likely benefit patients to have this instruction. Yet unless this specific administration timing is detailed by the physician at the point of prescribing, it does not seem likely that pharmacists will include this guidance to patients in their translation.

The finding that important auxiliary instructions guiding the safe use of alendronate, included in the physician’s prescription, often were left off the primary drug label raises serious concern. Pharmacies have traditionally identified warnings and precautions using secondary labeling (ie, stickers), but prior studies have found these warning stickers to be rarely attended to by patients and more often than not are misinterpreted.\(^5,7\) Thus, the use of these auxiliary stickers has been discouraged.\(^17\) Although a less common occurrence, some of the drug label sig messages completely omitted administration timing altogether. This overall variability and
presentation of instructions may impede a patient's ability to recognize and become familiar
with drug instructions, and appropriately self-administer medications.

Our sample of pharmacies from 4 diverse cities was too small for us to further examine
variability, either within pharmacy type (chain, grocery store, or independent) or by
prescription drug. Our finding that chain drug stores had a 2-fold greater likelihood of including
indication for use compared with grocery store or independent pharmacies is interesting.
Although the reason for this is not entirely clear, it is possible that this information is part of
a standard dispensing protocol or linked to pharmacy software more widely used among bigger
chains. Further research should be directed at comparing in detail the prescription drug
dispensing process across different types of pharmacies.

A patient's ability to understand dosage instructions is critical for preventing medication errors.
1 Variability between pharmacies in how physician prescriptions are interpreted may be a cause
for concern. Standardization in the manner in which sig messages are written and presented
may simplify medication-taking for patients, and facilitate better adherence to prescribed
regimens, as well as safe and appropriate medication use. Health information technology, such
as the electronic medical record, could be used at the point of prescribing to ensure physicians
incorporate patient-friendly sig messages that are clear, concise, and consistent.18 This may
also limit the noted variability in pharmacy translations and improve the quality of container
label dosage instructions. Further training and research is needed to better guide both physicians
and pharmacists on “best practices” for detailing dosage instructions so they are best
understood by patients. Regulatory guidance to develop pharmacy labeling standards might
also be considered.

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**REFERENCES**

1. Institute of Medicine. Preventing Medication Errors. Aspden, P.; Wolcott, J.; Bootman, L., et al.,
[PubMed: 17351847]
8. Wolf MS, Davis TC, Shrank WH, et al. To err is human: patient misinterpretations of prescription drug
readability, understanding, and medication use: a systematic review. Ann Pharmacother 2007;41:783–
801. [PubMed: 17426075]

*Med Care. Author manuscript; available in PMC 2009 May 11.*
18. Wolf, M. Promoting Health Literacy for Newly Prescribed Medications via the EMR. National Cancer Institute; Apr 10. 2007 R21 CA132771-01
## Table 1
Physician-Written Prescriptions and Pharmacy Interpretations

<table>
<thead>
<tr>
<th>Prescription</th>
<th>Examples of Pharmacy “Sig” Interpretations</th>
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<tr>
<td>Lipitor 10 mg tabs  &lt;br&gt; Take 1 tab QD  &lt;br&gt; Dispense 30  &lt;br&gt; Indication: for high cholesterol  &lt;br&gt; No refills</td>
<td>“Take 1 tablet daily.”  &lt;br&gt; “Take 1 tablet by mouth for high cholesterol.”  &lt;br&gt; “Take one (1) tablet(s) by mouth once a day.”  &lt;br&gt; “Take 1 tablet by mouth every day for high cholesterol.”  &lt;br&gt; “Take 1 tablet by mouth daily.”  &lt;br&gt; “Take one tablet by mouth every day for osteoporosis prevention. Do not lie down for at least 30 minutes after taking.”  &lt;br&gt; “Take 1 tablet every day. 30 minutes before breakfast with a glass of water. Do not lie down.”  &lt;br&gt; “Take 1 tablet every day.”  &lt;br&gt; “Take 1 tablet by mouth twice daily for UTI.”  &lt;br&gt; “Take 1 tablet by mouth twice daily for urinary tract infection.”  &lt;br&gt; “Take 1 tablet by mouth 2 times a day.”  &lt;br&gt; “Take 1 tablet twice daily for 3 days.”  &lt;br&gt; “Take 1 to 2 tablets by mouth as needed for pain.”  &lt;br&gt; “Take 1 to 2 tablets by mouth 3 times daily as needed for pain.”  &lt;br&gt; “Take 1 to 2 tablets by mouth as needed for pain ** Not to exceed 4 times a day.”  &lt;br&gt; “Take 1 to 2 tablets 3 times a day as needed for pain.”</td>
</tr>
<tr>
<td>Fosamax 5 mg tabs  &lt;br&gt; Take 1 tab QD  &lt;br&gt; Dispense 30  &lt;br&gt; Indication: osteoporosis prevention  &lt;br&gt; Do not lie down for at least 30 min</td>
<td>“Take 1 tablet daily.”  &lt;br&gt; “Take 1 tablet by mouth daily.”  &lt;br&gt; “Take one tablet by mouth every day for osteoporosis prevention. Do not lie down for at least 30 minutes after taking.”  &lt;br&gt; “Take 1 tablet every day, 30 minutes before breakfast with a glass of water. Do not lie down.”  &lt;br&gt; “Take 1 tablet every day.”  &lt;br&gt; “Take 1 tablet by mouth twice daily for UTI.”  &lt;br&gt; “Take 1 tablet by mouth twice daily for urinary tract infection.”  &lt;br&gt; “Take 1 tablet by mouth 2 times a day.”  &lt;br&gt; “Take 1 tablet twice daily for 3 days.”  &lt;br&gt; “Take 1 to 2 tablets by mouth as needed for pain.”  &lt;br&gt; “Take 1 to 2 tablets by mouth 3 times daily as needed for pain.”  &lt;br&gt; “Take 1 to 2 tablets by mouth as needed for pain ** Not to exceed 4 times a day.”  &lt;br&gt; “Take 1 to 2 tablets 3 times a day as needed for pain.”</td>
</tr>
<tr>
<td>Bactrim DS tabs  &lt;br&gt; Take 1 tab BID  &lt;br&gt; Dispense 6  &lt;br&gt; Indication: UTI  &lt;br&gt; No refills</td>
<td>“Take 1 tablet daily.”  &lt;br&gt; “Take 1 tablet by mouth twice daily for UTI.”  &lt;br&gt; “Take 1 tablet by mouth twice daily for urinary tract infection.”  &lt;br&gt; “Take 1 tablet by mouth 2 times a day.”  &lt;br&gt; “Take 1 tablet twice daily for 3 days.”  &lt;br&gt; “Take 1 to 2 tablets by mouth as needed for pain.”  &lt;br&gt; “Take 1 to 2 tablets by mouth 3 times daily as needed for pain.”  &lt;br&gt; “Take 1 to 2 tablets by mouth as needed for pain ** Not to exceed 4 times a day.”  &lt;br&gt; “Take 1 to 2 tablets 3 times a day as needed for pain.”</td>
</tr>
<tr>
<td>Ibuprofen 200 mg tabs  &lt;br&gt; Take 1–2 tabs TID PRN pain  &lt;br&gt; Dispense 30  &lt;br&gt; No refills</td>
<td>“Take 1 tablet daily.”  &lt;br&gt; “Take 1 tablet by mouth daily.”  &lt;br&gt; “Take one tablet by mouth every day for osteoporosis prevention. Do not lie down for at least 30 minutes after taking.”  &lt;br&gt; “Take 1 tablet every day, 30 minutes before breakfast with a glass of water. Do not lie down.”  &lt;br&gt; “Take 1 tablet every day.”  &lt;br&gt; “Take 1 tablet by mouth twice daily for UTI.”  &lt;br&gt; “Take 1 tablet by mouth twice daily for urinary tract infection.”  &lt;br&gt; “Take 1 tablet by mouth 2 times a day.”  &lt;br&gt; “Take 1 tablet twice daily for 3 days.”  &lt;br&gt; “Take 1 to 2 tablets by mouth as needed for pain.”  &lt;br&gt; “Take 1 to 2 tablets by mouth 3 times daily as needed for pain.”  &lt;br&gt; “Take 1 to 2 tablets by mouth as needed for pain ** Not to exceed 4 times a day.”  &lt;br&gt; “Take 1 to 2 tablets 3 times a day as needed for pain.”</td>
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Tabs indicates tablets; QD, once daily; BID, twice daily; UTI, urinary tract infection; TID, 3 times daily; PRN, as needed.