



Take-Wait-Stop: A Patient-Centered Strategy for Writing PRN Medication Instructions

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Recent studies have linked patient misunderstanding of label instructions for as needed (PRN) medications to dosing errors. This study conducted a preliminary field test of patient-centered PRN label instructions. Patients participated in a hypothetical dosing experiment and were randomized to a patient-centered label (referred to as “Take-Wait-Stop”) or standard label. Participants were asked to demonstrate dosing the medicine over 24 hours. Three types of independent dosing errors were measured: (a) taking more than two pills at one time, (b) exceeding the maximum daily dose, and (c) waiting fewer than 4 hours between doses. Generalized linear models were used to assess the association between label type, health literacy, and sociodemographic characteristics. Participants’ mean age was 39.8 years, 62.1% were female, 43.7% were White, and 72.4% had adequate literacy. Of participants, 31.8% who were shown the standard label demonstrated taking in excess of 6 pills in 24 hours compared with only 14.0% of participants who were shown the Take-Wait-Stop label ($p = .05$). Overall, only 1 person demonstrated he would take more than 2 pills in a single dose. Of the standard label group, 20.5% demonstrated dosing intervals of fewer than 4 hours compared with 23.3% of the Take-Wait-Stop label group ($p = .75$). In a multivariate model, participants who were exposed to the standard label were 2.5 times more likely to exceed the recommended maximum daily dose (95% CI [1.05, 7.70], $p = .03$). The Take-Wait-Stop label was beneficial in preventing participants from exceeding the maximum dose in 24 hours, although it did not significantly reduce other dosing errors.

Recent studies have demonstrated a high prevalence of patient confusion and unintentional misuse with current labeling standards for *as needed* (i.e., *PRN*, which is abbreviation for the Latin “pro re nata,” meaning “as the circumstance arises”) medications (Shone, King, Doane, Wilson, & Wolf, 2011; Simon, 1999; Wolf et al., 2012). Dosing errors and adverse drug events have been documented for both prescription and over-the-counter PRN medications (Shone et al., 2011; Simon, 1999). These studies show that patients frequently misinterpret the complex instructions associated with a PRN medication, resulting in wrong doses or incorrect frequencies (number of times per day). In the settings of adult acetaminophen use as well as pediatric cold medications such unintended dosing errors have even resulted in liver failure and deaths (Bower, Johns, Margolis, Williams, & Bell, 2007; Dart et al., 2009).

The majority (77%) of prescription instructions for chronic medications describe fixed dosing intervals (i.e., two times daily; Institute of Medicine, 2008). Although

the public health goal for chronic medications is to promote routine use, the objective for PRN medications is to prevent routine use and overuse. PRN instructions require patients to actively participate in interpreting label instructions because the medication intended use is meant to be limited based on symptoms. This added complexity of PRN medication instructions intuitively makes the task of appropriately taking the prescribed drug more prone to errors resulting from misinterpretation; previous studies have demonstrated (in the chronic medication setting) that patients' comprehension is improved with more explicit, deconstructed instructions (Davis et al., 2009; Wolf, Davis, et al., 2011).

As part of ongoing research efforts to promote more patient-centered drug labeling across prescription medicines, we conducted a preliminary field test of a labeling strategy referred to as the "Take-Wait-Stop" method. This method is a patient-centered, PRN-specific set of label instructions developed by our team. Key components of patient-centered prescription label design have been previously described in the literature (National Council for Prescription Drug Programs, 2013; Sahm et al., 2012; Shrank et al., 2010; Wolf, Davis, et al., 2011). In accordance with these design tenets, we deconstructed the core components of PRN instructions and more explicitly conveyed (a) dose (number of pills per use), (b) interval (mandatory time between doses), and (c) maximum daily dose that is not to be exceeded. The emphasis on action terms ("Take-Wait-Stop") was chosen to help frame each behavioral step and to serve as a mnemonic device supporting individuals' ability to quickly understand and recall proper use of a PRN medicine. We hypothesized that patients viewing the Take-Wait-Stop label would be less likely to make dosing errors.

Method

Participants

This study was part of a larger investigation of patients' medication use after receiving a new prescription for an acetaminophen-containing analgesic medication. Between April and October 2011, patients receiving a prescription for an acetaminophen-containing analgesic medicine were consecutively recruited from an emergency department in a teaching hospital in Chicago, Illinois. This was a convenience sample, and patients were recruited during daytime hours on weekdays on the basis of the research assistant's availability. Patients were deemed eligible to participate if they (a) spoke English, (b) were 18 to 80 years of age, and (c) did not have psychological impairment or intoxication (as judged by a trained research staff member). Patients were prescribed a pain medication containing acetaminophen. Patients were excluded if they were admitted to the hospital or were receiving a refill of an acetaminophen-containing pain medication that they used chronically at home. After completion of the study, patients were compensated US\$50. The Institutional Review Board at Northwestern University approved this study.

Procedure

Patients who gave consent were instructed to return 4 to 7 days after initial recruitment to complete an in-person interview about their use of the new acetaminophen-containing medication (results reported separately). The interview also included questions pertaining to basic demographic information (age, sex, race/ethnicity), socioeconomic information (education, household income), health status

(self-reported overall health, number of prescription medications, number of over-the-counter medications), and a literacy assessment. We used the Rapid Estimate of Adult Literacy in Medicine, a widely used and validated instrument for measuring health literacy (Davis et al., 1991).

The investigators chose to conduct the pilot test of the patient-centered PRN label in this population in part because all of the patients had recent exposure to taking a PRN medication and their recollection of their recent (or ongoing) pain episode increased the fidelity of the pilot test. After they completed the demographic assessment, participants were randomized to receive either the standard PRN label (Figure 1A) or the patient-centered, Take-Wait-Stop label for a PRN medicine (Figure 1B) to test the efficacy of the Take-Wait-Stop label in improving accurate medication dosing. The Take-Wait-Stop label design was based on previous research and included the explicit, deconstructed instructions along with simplified text, numeric characters instead of words (e.g., “1 tab” instead of “one tab”) and “carriage returns” to place

City Pharmacy
3254 MAPLE STREET
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Caution: Federal Law Prohibits the Transfer of this drug to any other person than for whom it was prescribed

55555-000 04/13/2011 Dr. R. Parker

JOHN DOE

TAKE 1-2 PILLS BY MOUTH EVERY 4 HOURS AS NEEDED FOR PAIN. DO NOT EXCEED 6 PILLS IN 24 HOURS.

HYDROCODONE/APAP 5MG/500MG TABS
QTY 20 MFG DRUGCO

1 REFILL BEFORE 06/31/2010
USE BEFORE 12/31/10

Mtg:CLA RPh:PAUL JOHNSONS

(A)

City Pharmacy
3254 MAPLE STREET
CLEVELAND, OHIO, 28129 (555)321-4567

Caution: Federal Law Prohibits the Transfer of this drug to any other person than for whom it was prescribed

55555-000 04/13/2011 Dr. R. Parker

JOHN DOE

TAKE: 1 OR 2 PILLS
WAIT: 4 HOURS BEFORE TAKING AGAIN
STOP: DO NOT TAKE MORE THAN 6 PILLS IN 24 HOURS.

HYDROCODONE/APAP 5MG/500MG TABS
QTY 20 MFG DRUGCO

1 REFILL BEFORE 06/31/2010
USE BEFORE 12/31/10

Mtg:CLA RPh:PAUL JOHNSONS

(B)

Figure 1. (A) Standard label; (B) patient-centered label (Take-Wait-Stop).

each part of the instructions on separate lines (Wolf, Davis, et al., 2011). In addition, to convey the maximum daily dosage to patients in plain language, the new label used the word *Stop* to replace the typical wording *Do not exceed*. This wording was chosen on the basis of previous qualitative research that found patients—particularly those with limited literacy skills—preferred this wording and felt that the word *stop* was easier to understand and pronounce than the word *exceed* (King et al., 2011). The core components of the instructions were deconstructed so that each action or intended behavior was separate and would potentially allow patients to be more cognizant of each step to be taken. This deconstruction is supported by previous research that more explicit medication instructions (in non-PRN medications) improve patient understanding and is a health literacy best practice (Davis et al., 2009; Wolf, Davis, et al., 2011).

To assess medication dosing, participants were presented with a dosing tray that contained 24 slots representing each hour of a day. Participants were given the hypothetical prescription bottle and instructed to place plastic pills into the slots to demonstrate how much and when they would take doses of the medication throughout the day. Our team has repeatedly used this approach to guide—and not lead—patients in documenting medication use (Wolf, Curtis, et al., 2011).

Given that the medicines assessed in this activity were PRN, research assistants used the following standard script to ensure that patients would feel free to continue to redose for the full 24 hours rather than stopping at one dose so that the risk of misuse by either too narrow intervals between doses or exceeding the maximum dose could be fully assessed:

Please imagine that you have been prescribed this medicine for your pain.

Using this container, I would like you to show me how you might take this medicine on a day you were having pain.

So imagine that it is 8am and you are having pain.

Please show me how many pills of this medicine you would take at 8am by placing the beads into the box.

If you were still in pain after taking this dose of medicine, when could you take this medicine again?

Show me at what time and how many pills of this medicine you would take for your next dose.

The final two prompts were repeated until reaching 24 hours or until the patient said that he or she would not take any additional pills.

Outcomes

The outcome of interest was incorrect dosing of the medication; this was measured in three ways. First, patients could incorrectly dose their medication by placing more than two pills into a single dose in the tray (*dose error*). Second patients could exceed the maximum daily dose if they placed more than the recommended six pills into the dosing tray (*max dose error*). Third, patients could incorrectly dose the PRN medicine by not waiting a sufficient amount of time between intervals (fewer than 4 hours; *timing error*). Each of these outcomes was independent, given that an individual could take too much medication in a single dose, but then not take any additional pills throughout that day and therefore not exceed the maximum daily dose.

Analysis Plan

Descriptive statistics (percentage, mean and standard deviation) were calculated for demographic variables. Bivariate analyses were performed for each of the three outcomes to assess whether patients' performance differed on the task depending on the label to which they were exposed (standard vs. Take-Wait-Stop). Generalized linear models with a Poisson distribution and log link function with robust variance estimates were used for outcomes found to be statistically significant in the bivariate analysis to estimate prevalence ratios with 95% confidence intervals. We chose this approach as an odds ratio from logistic regression could overestimate associations due to the high percentage of responses falling in one category (Barros & Hirakata, 2003; Zou, 2004). Final models controlled for age, race (White, Black, other), and literacy level (adequate, limited). Results are reported as adjusted relative risk (RR). All statistical analyses were performed using STATA software version 12.1 (StataCorp, College Station, TX).

Results

We enrolled 87 participants in this field test. The majority of the sample was female (62.1%) and had adequate literacy (72.4%). In addition, the majority of the sample had been recently prescribed and had taken an acetaminophen-hydrocodone combination drug at home (93.1%). The other acetaminophen combination drugs recently prescribed to the sample included: acetaminophen-caffeine-butalbital and acetaminophen-codeine. There were no statistically significant differences between the baseline characteristics of patients in the standard label group and the Take-Wait-Stop label group (Table 1).

The outcomes of the dosing activity by label type are shown in Table 2. Of the sample, 23% exceeded the maximum daily dose noted on the bottle and for this error type, there were statistically significant differences by study arm (standard label error rate = 31.8% vs. Take-Wait-Stop label error rate = 14%, $p = .05$). The mean number of tablets that patients exceeded the recommended dose by was 3.45 tabs (range = 1–13). The rate of errors related to medication timing (interval of fewer than 4 hours) was also high at 21.8%, but there were no differences in performance on the basis of label type. On average, patients who took the dose at an unsafe time interval were taking the dose 1.8 hours before the next safe dose was due. Only one person made the error of taking more than two pills per dose.

After controlling for age, race, and literacy level, the relationship between label type and dosing errors remained statistically significant. Those exposed to the standard label were 2.5 times more likely to exceed the recommended maximum daily dose (95% CI [1.05, 7.70], $p = .03$). Black participants were also more likely to make maximum daily dose errors (RR 3.15, 95% CI [1.11, 8.93], $p = .03$), as well as participants whose race/ethnicity was categorized as *other* (RR 4.88, 95% CI [1.57, 15.19], $p = .006$). Neither age nor literacy skills were found to be independent predictors of dosing errors.

Discussion

In our sample, nearly a quarter of participants demonstrated they would exceed the maximum daily dose of a prescribed PRN medication, and one in five dosed out the drug at too frequent time intervals. As an initial field test of a more patient-centered, explicitly worded labeling strategy for as-needed medicines, our findings suggest this approach could be a promising direction for improved labeling. Individuals who

Table 1. Demographics of sample completing the hypothetical dosing activity

Variable	Total (<i>N</i> = 87)	Label type		<i>p</i>
		Standard (<i>n</i> = 44)	Take-Wait-Stop (<i>n</i> = 43)	
Age, <i>M</i> (<i>SD</i>)	39.8 (12.9)	40.1 (13.1)	39.4 (12.8)	.79
Gender				.31
Male	37.9	43.2	32.6	
Female	62.1	56.8	67.4	
Race				.82
White	43.7	45.5	41.9	
Black	40.2	40.9	39.5	
Other	16.1	13.6	18.6	
Education				.55
High school or less	25.3	29.6	20.9	
Some college	33.3	34.1	32.6	
College graduate	41.4	36.4	46.5	
Literacy				.68
Adequate	72.4	70.5	74.4	
Inadequate	27.6	29.6	25.6	
Income				.08
Less than \$20,000	26.4	22.7	30.2	
\$20,000–50,000	29.9	40.9	18.6	
More than \$50,000	43.7	36.4	51.2	

received the Take-Wait-Stop label were significantly less likely to exceed the maximum daily dose. However, problems with waiting the appropriate amount of time between doses were not reconciled with this more explicit set of instructions, but they were also not worse than a current standard.

The Take-Wait-Stop label worked best on untangling one common aspect of instructions—the maximum daily dose message—that may more likely be omitted or underemphasized in current labeling practices. Thus, the greatest benefit was found in reduced errors around exceeding the maximum daily dose. Given that only one patient

Table 2. Outcomes of dosing activity, by label type

Outcome	Total (<i>N</i> = 87)		Label type				<i>p</i>
			Standard (<i>n</i> = 44)		Take-Wait-Stop (<i>n</i> = 43)		
	<i>n</i>	%	<i>n</i>	%	<i>n</i>	%	
Exceeded maximum dose	20	23.0	14	31.8	6	14.0	.05
More than two pills per dose	1	1.2	1	2.3	0	0.0	.47
Interval of fewer than 4 hr	19	21.8	9	20.5	10	23.3	.75

exceeded correct number of pills for a single dose, it is clear that this is not a primary source of confusion with label instructions, and it is understandable why our more explicit strategy did not affect this type of error.

In addition, the Take-Wait-Stop approach did not significantly improve problems with errors related to spacing of doses as demonstration of intervals which were too narrow did not differ by label type. There are several possible reasons for this. The instructions for calculating dosing interval and maximum daily dose require some proficiency with basic math skills. Yet, patients with limited literacy, who would also disproportionately struggle with numeracy tasks, were not more likely to make these errors. As a seemingly simple behavior, it could be that without specific times of day stated, the more explicit Take-Wait-Stop instruction for dosing interval did not notably reduce the complexity of the task. In addition while this was a hypothetical scenario, the framing around persistent pain could have elicited a need for a more immediate response. Perhaps this is the most difficult challenge with PRN medicines—that safety information such as maximum daily dose can be conveyed to the patient, but how the medicine is used is ultimately in the hands of the patient experiencing symptoms. When patients experience symptoms and attempt to self-titrate the amount of medicine, their need for pain relief may overtake their recall of instructions or concerns about safety.

It is interesting that patients' literacy level did not affect their performance on the task. As a field test, this study was not specifically powered to detect such differences and the lack of a difference may be because the patient sample to a large extent had adequate literacy. It is important to note that non-White race/ethnicity was associated with a greater risk of exceeding maximum daily dose. This could be related to language proficiency or cultural factors such as beliefs associated with medication risks (Bailey, Agarwal, Sleath, Gumusoglu, & Wolf, 2011; Bailey et al., 2009). It is unfortunate that our data limit our ability to truly understand the root cause of this finding. Other study limitations include the hypothetical nature of our outcome of demonstrated dosing errors and type; participants' performance may not accurately represent their actual behavior at home. However, all patients enrolled had been taking an acetaminophen-based PRN analgesic before participating in the study and therefore had recent experience at home. Although in this context this is a strength, it is also a potential weakness because patients may have been prescribed a different analgesic and therefore may have been performing the task based on the instructions for their home medication.

On closer review of the actual medications patients were taking to determine their potential influence on the results, we found that none of the prescriptions had dosing intervals of more than 4 hours and none recommended taking more than two pills per dose. Further, only one bottle had a warning about maximum daily dose on the primary label, and less than half (44%) had auxiliary warning labels on the bottle stating a maximum daily dose in milligrams. Therefore, the presence of a maximum daily dose warning, and providing this information in number of pills (vs. milligrams), was new to patients. Thus, it is unlikely that actual medication use negatively influenced performance on these hypothetical tasks.

Overall, we found that patients taking PRN prescription medications frequently make dosing errors, and the use of the Take-Wait-Stop strategy significantly reduced those associated with maximum daily dose. Future directions should (a) improve how a Take-Wait-Stop approach can better communicate all aspects of proper dosing and (b) conduct a larger trial of this approach in actual use.

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