A Comparison of Factors Influencing Patient Knowledge: Results Across Selected REMS Surveys

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ABSTRACT

Background: Draft FDA guidance requires Risk Evaluation and Mitigation Strategies (REMS) that include a medication guide (MG) to be assessed through a survey of patients' understanding of the serious risks of the drug. With more REMS comes significant diversity in the products, disease areas, and patient populations represented. Experience suggests that many factors can influence REMS survey results, including patient characteristics, type of treatment (e.g., chronic vs. acute), severity of the disease and potential risks, and REMS program elements (MG only vs. programs with other elements).

Objective: To compare results across multiple REMS surveys to explore how patient knowledge of the key risk messages varies by certain factors.

Methods: Anonymized pooled data were examined from six REMS assessment surveys ranging in size from 200 to 9,000 respondents. Awareness of primary risk was stratified by MG receipt and review, type of REMS, disease type, and other patient characteristics, and compared across surveys to identify patterns.

Results: The six patient surveys covered drugs in five disease areas: two for acute conditions, one for an intermittent condition, and three for chronic conditions. Awareness of the primary risk associated with each product ranged from 24% to 98% and was lowest for acute conditions. In all studies, awareness was higher in patients reporting having received and read the MG. For each survey, over half of participants reported receiving the MG (range, 64% to 99%), and 47% to 97% of respondents indicated they had read the MG. Awareness was higher for the drug that included elements to assure safe use. Awareness also was higher in patients who were new users, reported being counseled by a health care provider, and were in subgroups specifically identified as being at higher risk.

Conclusions: Results from REMS assessment surveys vary significantly across programs and can be influenced by many factors. Reviewing results across surveys provides an opportunity to evaluate the potential factors associated with knowledge of information communicated in the MG, as well as provides critical information that can help to improve design for future REMS programs.

BACKGROUND

- Risk Evaluation and Mitigation Strategies (REMS) that include a medication guide (MG) must be assessed through a survey of patients' understanding of the serious risks of the drug.[1]
- Since the initiation of REMS, many products have been required to conduct REMS assessments, resulting in significant diversity in the products, disease areas, and patient populations represented.
- Many factors may influence REMS survey results (e.g., patient characteristics, severity of the disease, and potential risks) and REMS program elements (MG-only vs. programs with other elements).

OBJECTIVE

- To compare results across multiple REMS surveys and to explore how patient knowledge of the key risk information varies by certain patient-specific factors or REMS-specific factors (characteristics of the drug or REMS program).

METHODS

- Anonymized pooled data were examined from six REMS surveys that were administered between 2003 and 2010.
- Eligible patients who had filled a prescription for one of the medications were recruited through different strategies (e.g., pharmacy network, clinic). Surveys were administered by phone, paper, Web, or tablet computer.
- In addition to the descriptive analysis mentioned in the abstract, bivariate and multivariable analyses are also presented in this poster to further support the objective.
- Figure 1 lists factors that were common to six REMS surveys.

Figure 1. Factors Used in Statistical Analyses

Patient-Specific Factors Assessed

- **Read MG** (yes [includes those who read at least some of the MG] or no [includes those that did not receive or did not read the MG])
- **Age, years** (< 40, 40-60, ≥ 61)
- **Sex** (male or female)
- **Race** (white or nonwhite)
- **Education level** (high school diploma or less, or some education beyond high school)

REMS-Specific Factors Assessed

- **Type of REMS** (MG-only versus MG-plus [e.g., MG plus a communication plan and/or elements to assure safe use])
- **Condition type** (acute, intermittent, or chronic conditions based on medication indication)
- **Potential side effects associated with treatment** (classified as more or less severe based on their potential to cause death)

Univariate Analysis

- A univariate analysis examined patient- and REMS-specific factors for all six REMS surveys:
  - REMS-specific factors are described for each survey.
  - Number of patients and percentages are provided for all patient-specific factors.

Outcome: Knowledge of Primary Key Risk Information

- For this analysis, one question from each REMS survey was selected to serve as the primary outcome to assess knowledge of key risk information.

- Study 6 was excluded from the bivariate and multivariable analyses due to concern that this large survey with elements to assure safe use would bias the results.

Bivariate Analysis

- A bivariate analysis using pooled data was conducted to examine the association of patient- and REMS-specific factors (listed in Figure 1) with level of knowledge of the primary key risk.
  - The percentage of knowledge of the key risk information was explored for each factor.

Logistic Regression

- A logistic regression using pooled data was conducted to evaluate the relationship between knowledge of the key risk information and patient- and REMS-specific factors:
  - The generalized estimating equations method was used to account for data clustering within the REMS survey.
  - All patient-specific factors listed in Figure 1 were included in the model; however, the only REMS-specific factor included was a combined variable,* chronic/more severe and nonchronic/less severe.

    *The REMS for chronic conditions were also the REMS in which the potential side effects were more severe, likewise the REMS for non-chronic conditions were those in which the side effects were less severe. Because we could not distinguish separate effects of condition and side effect severity, we adopted a combined measure to indicate both variables.
  - The interaction between Read MG and condition type was also included in the model.

RESULTS

Univariate Analysis

- Table 1 displays the distribution of respondent characteristics for each REMS survey (N = 5,984).
- Knowledge of the primary risk within each REMS survey ranged from 26% to 95%.

Table 1. REMS-Specific and Patient-Specific Factors by Individual REMS Survey

REMS-Specific Factor	Study 1	Study 2	Study 3	Study 4	Study 5	Study 6
Condition type	Chronic	Acute	Acute	Intermittent	Chronic	Chronic
Type of REMS	MG-only	MG-only	MG-only	MG-only	MG-plus	MG-plus
Potential side effects associated with treatment	More severe	Less severe	Less severe	Less severe	More severe	More severe
Patient-Specific Factor	**(n = 298) n (%)**	**(n = 196) n (%)**	**(n = 210) n (%)**	**(n = 208) n (%)**	**(n = 205) n (%)**	**(n = 4,867) n (%)**
Age, years*						
< 40	36 (12)	37 (19)	49 (23)	33 (16)	0	1,010 (21)
40-60	220 (74)	63 (33)	101 (48)	101 (49)	65 (32)	2,328 (48)
≥ 61	41 (14)	92 (48)	59 (28)	74 (36)	140 (68)	1,485 (31)
Sex						
Male	233 (79)	54 (28)	68 (33)	130 (63)	21 (10)	397 (8)
Female	63 (21)	138 (72)	141 (68)	78 (38)	184 (90)	4,321 (92)
Race						
White	165 (56)	166 (86)	178 (85)	132 (64)	190 (93)	4,636 (95)
Nonwhite	132 (44)	28 (14)	31 (15)	76 (37)	15 (7)	231 (5)
Education level						
High school diploma or less	37 (12)	50 (26)	53 (26)	80 (39)	61 (30)	1,325 (27)
Some education beyond high school	261 (88)	142 (74)	155 (75)	128 (62)	143 (70)	3,509 (73)
Read MG						
Yes	212 (71)	92 (47)	104 (50)	110 (53)	180 (93)	4,638 (97)
No	86 (29)	102 (53)	105 (50)	98 (47)	14 (7)	151 (3)
Outcome						
Knowledge of key risk information	144 (48)	50 (26)	61 (29)	86 (41)	103 (50)	4,622 (95)

* If age category did not align exactly, patients were placed in the closest category.

Bivariate Analysis

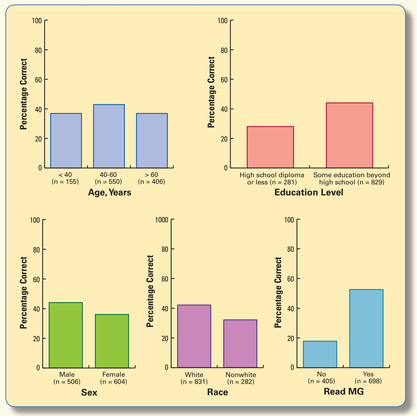
- Table 2 displays the percentage of respondents who correctly answered the key risk knowledge question by REMS-specific characteristics for the pooled data set, which included Studies 1 through 5 (n = 1,117).
- The highest percentage of correct responses were found in surveys in which the medication was used to treat chronic conditions, had more severe side effects, or had an MG-plus REMS.
- During an initial exploration of the data, risk knowledge was higher among certain patient categories (e.g., new users of a medication, those being counseled by a health care provider) in surveys that included this information. Because not all studies included this information, data are not presented.

Table 2. Knowledge of Key Risk Information by REMS-Specific Factors

Variable Name	Percentage Correct
Condition type	
Acute (n = 406)	27
Intermittent (n = 208)	41
Chronic (n = 503)	49
Type of REMS	
MG-only (n = 912)	37
MG-plus (n = 205)	50
Potential side effects associated with treatment	
More severe (n = 503)	49
Less severe (n = 614)	32

- Figure 2 compares the percentage of respondents aware of the key risks by patient-specific factors.

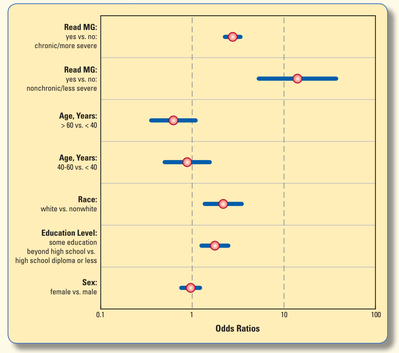
Figure 2. Knowledge of Key Risk Information by Patient-Specific Factors



Multivariable Logistic Regression

- Figure 3 displays the odds ratios obtained from the multivariable logistic regression (n = 1,093):
  - Respondents from chronic/more severe REMS who read at least some of the MG were 2.7 times more likely (95% confidence interval [CI]: 2.2, 3.4) to be aware of the risk than respondents who did not read the MG.
  - Respondents from nonchronic/less severe REMS who read at least some of the MG were 13.9 times more likely (95% confidence interval [CI]: 5.1, 37.8) to be aware of the risk than respondents who did not read the MG.
  - White respondents were 2.2 times more likely (95% CI: 1.3, 3.6) to be aware of the risk than nonwhite respondents.
  - Respondents with more than a high school diploma were 1.8 times more likely (95% CI: 1.2, 2.6) to be aware of the risk than respondents with a high school diploma or less.

Figure 3. ORs and 95% CIs of Correctly Answering Risk Question: Results From Multivariable Logistic Model With REMS Surveys 1-5 (n = 1,093)



LIMITATIONS

- For this analysis, only one question was used as a surrogate to assess patient knowledge of the primary key risk information, although some surveys included multiple questions about the primary risk or had more than one key safety risk.
- Only factors that were common among all REMS surveys were analyzed. Other factors not measured in these surveys could contribute to higher levels of knowledge, but could not be evaluated (e.g., relevance of risk to specific subgroups within the sampled population).
- Because a combined variable was used for condition type and severity of side effects, it was not possible to assess the effect of these factors independently on knowledge of key risks.
- As with any voluntary survey, selection bias may influence results.

CONCLUSIONS

- Patients with chronic conditions taking medication with more severe side effects who read the MG were three times more likely to correctly answer the primary risk question than patients who did not read the MG.
- In contrast, patients with nonchronic conditions taking medication with less severe side effects who read the MG were 14 times more likely to correctly answer the primary risk question than patients who did not read the MG.
- Knowedge of key risk information was higher in whites and those with greater than high school education, and did not vary by sex or age.
- Reviewing results across surveys provides an opportunity to evaluate the potential factors associated with knowledge of key risk information that may be used to help tailor communication about key risks to specific patient subgroups.

REFERENCE

1 Food and Drug Administration (FDA). Guidance for Industry: Format and Content of Proposed Risk Evaluation and Mitigation Strategies (REMS), REMS Assessments, and Proposed REMS Modifications. Draft Guidance. September 2009. Available at: http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM184128.pdf. Accessed July 21, 2011.

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