Informing Patients About Drugs

Summary Report on Alternative Designs for Prescription Drug Leaflets

David E. Kanouse, Sandra H. Berry, Barbara Hayes-Roth, William H. Rogers, and John D. Winkler
This project was funded at least in part with Federal funds from the Food and Drug Administration, U.S. Department of Health, Education, and Welfare under Contract No. 223-78-3009.

The Rand Publication Series: The Report is the principal publication documenting and transmitting Rand's major research findings and final research results. The Rand Note reports other outputs of sponsored research for general distribution. Publications of The Rand Corporation do not necessarily reflect the opinions or policies of the sponsors of Rand research.

Published by The Rand Corporation
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August 1981

Prepared for
The Food and Drug Administration

Rand
SANTA MONICA, CA. 90406
PREFACE

The Food and Drug Administration (FDA), which is responsible for labeling prescription drugs, has promulgated regulations requiring drug information leaflets (patient package inserts or PPIs) for several major classes of prescription drugs. These leaflets, which accompany the prescription as it is dispensed to the patient, are designed to inform patients about a drug’s actions, indications, and proper use, and to alert them about risks, necessary precautions, and possible side effects.

To determine how PPIs might most effectively be designed to communicate drug information, Rand has analyzed the effects of various types of leaflets through a series of studies conducted with the cooperation of selected pharmacies in Los Angeles County. This report summarizes the major analytic findings and discusses their implications for public policy. The report should be of interest to government policymakers and to members of the research and professional health care community. More broadly, it should interest all who are concerned with the use of empirical methods to address some of the controversial issues surrounding the regulation of drug information for patients.

More detailed descriptions of the work summarized in this report may be found in the following Rand publications:


ACKNOWLEDGMENTS

A project of this kind requires the talents of many individuals who must carry out the numerous tasks involved in design, sampling, preparation of survey materials, contacts with pharmacies, interviewing, data preparation, and analysis. We wish to thank the several dozen Rand colleagues who contributed to this effort.

This summary report has benefited from the comments of Bradford Gray of the Institute of Medicine; Evelyn W. Gordon, Steven R. Moore, and Louis A. Morris of the Food and Drug Administration; and Robert L. Kane and Albert P. Williams of Rand. All offered helpful suggestions on presentation and interpretation; none is responsible for remaining shortcomings. We are grateful to Diane Alexander for skillful preparation of the various drafts and to Helen B. Turin for her able editorial assistance.

Finally, we owe a special debt of thanks to the pharmacists, community groups, and survey respondents who cooperated with us by providing the data. Without their help, the study would have been impossible.
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I. INTRODUCTION AND SUMMARY

In 1980, the Food and Drug Administration (FDA) promulgated regulations requiring drug manufacturers to provide, and pharmacists to dispense, informational leaflets to patients filling prescriptions for a wide variety of drugs. These leaflets, which have come to be known as patient package inserts (PPIs), are designed to inform patients about a drug's actions, indications, and proper use, and to provide warning information about risks, necessary precautions, and side effects.

Written materials have been provided to consumers of nonprescription drugs for many years, but such materials have not been required for prescription drugs until fairly recently. The first prescription labeling requirement was introduced in 1968 to warn patients that improper use of isoproterenol inhalation products could cause serious breathing difficulty. Since then, prescription drug labeling has been required for several other drugs, most notably oral contraceptives and other estrogenic products.

In addition to imposing PPI requirements for a few selected drugs, the FDA has long been studying the possibility of requiring PPIs for a wide variety of drugs. Formal discussions with health professionals and consumer and industry groups began in 1974. The following year, several consumer groups filed a petition with FDA to require more adequate patient labeling of prescription drugs.

In response to this petition, and at the urging of its National Advisory Committee, FDA established a "Patient Prescription Drug Labeling Project" to explore the prospects and problems entailed in a general PPI requirement. A research program was launched, and in 1976 FDA initiated and co-sponsored a national symposium on PPIs. More recently, it sponsored a national conference on PPI content and format.

As a result of this program of study and research, FDA recently issued final regulations establishing procedures and requirements for preparation and distribution of PPIs for prescription drugs. Initially,
the regulations would apply to ten classes of prescription drugs, with the possibility of later extensions, revisions, modifications, or curtailment based on the results of the early program. After the final regulations were issued, the new administration stayed their effective date, consistent with President Reagan’s executive order. At this writing, the FDA Commissioner is conducting a full review of the patient prescription drug labeling program, to determine whether the benefits of PPIs outweigh their costs, and to assess the relative advantages of alternative means for delivering drug information to patients.

The research reported here is the most thorough investigation conducted thus far on the effects of PPIs; it represents a prospective study of the effects of various prototype PPIs on actual drug users. Begun in 1978, the study was undertaken to address an issue that has long concerned policymakers; namely, how PPIs might best be designed so as to communicate important drug information to the patient.

Drug information documents vary radically in format, length, content, and style. Some written documents consist of simple checklists of precautions and warnings (Fox, 1969), while others contain a detailed discussion of the disease with little mention or the drug itself (Sackett et al., 1975). To determine what type of document works best, it is desirable to conduct controlled experiments that systematically vary such factors as the content, style, and format of the document while controlling or randomizing other factors.

The research described in this report applied just such a strategy to study alternative leaflets for three drugs: erythromycin, a commonly prescribed antibiotic used mainly to treat upper respiratory tract infections; conjugated estrogens, female hormones used primarily to treat vasomotor symptoms of the menopause, or to replace natural estrogens following surgical removal of the ovaries; and flurazepam hydrochloride (Dalmane), a hypnotic drug used to treat sleeping disorders. For each drug, we conducted three studies investigating the effects of six different structural variables: specificity of instructions, amount of explanation, writing style, risk emphasis, format, and reduced content (length). The results are based on data from a sample of 1,821 men and women filling prescriptions for one of the study drugs at any of 69 pharmacies in Los Angeles County during the fall of 1979 and winter and spring of 1980. Pharmacists recruited subjects into the study when they filled their prescriptions. Each subject was randomly assigned to receive one of several different versions of a PPI especially prepared for

---

8The ten drugs and classes of drugs are: ampicillin, benzodiazepines, cimetidine, clofibrate, digoxin, methoxsalen, phenytoin, propanolol, thiazides, and bendecotin.
this study; some subjects were assigned to a control group that received no PPI or (for conjugated estrogens) a PPI prepared and distributed by the manufacturer. Outcomes were assessed by means of a telephone interview conducted an average of two to three weeks after the date of the prescription, and by means of a subsequent mail questionnaire.

Our principal findings are summarized below.

1. **PPIs are likely to be widely read.** In our study, about 70 percent of those who received PPIs reported having read them. Among those using the drug for the first time, readership was still higher. For two of the three drugs, older people were more likely than younger people to report having read the PPI. We found no evidence that PPIs are read only by an information-seeking elite; the less educated were just as likely to read them as anyone else.

2. **Many patients use PPIs as reference documents.** Between 45 and 56 percent of those who received a PPI reported having kept it, and between 22 and 32 percent reported having read it more than once. The fact that PPIs receive such use suggests a potential advantage over other methods of providing drug information that do not place the information in the hands of the patient.

3. **PPIs lead to reliable gains in drug knowledge.** Erythromycin patients who received PPIs were better able to answer questions about how the drug works and how to use it, and more likely to know that the drug is contraindicated for patients with a history of liver problems. Dalmane patients who received PPIs were more aware of possible drug interactions and of the potential dangers of taking the drug during pregnancy or lactation. PPIs appear to be an effective vehicle for getting more information to more people.

4. **PPIs seem to have little effect on how patients use a drug.** We found no evidence that patients who received a PPI were any more or less likely to comply with the prescribed regimen or (if the amount to be taken was left up to them) to alter their patterns of drug use. Our results also provide no evidence that patients' initial decisions regarding drug therapy are much affected by receiving a PPI. Most respondents elected to take the drug once they had purchased it; only a tiny fraction seem to have changed their decision as a result of the information they received.

5. **The costs of returned prescriptions are likely to be quite low.** Previous estimates of the annual cost of returned prescriptions that will result from FDA's proposed labeling program have been as high as $87.75 million—a figure based on the assumption that for every 60 new prescriptions, PPIs will cause one additional prescription to be returned. Our results indicate that this estimate is several orders of magnitude too high. During the course of the study, only three prescriptions were returned to pharmacies for cash refunds, out of more than
2000 prescriptions dispensed with PPIs. Even if pharmacies were to pass on the full costs of returned prescriptions to the consumer, the resulting increases in drug prices would be extremely small.

6. **PPIs do not, in general, lead patients to report more side effects.** PPI critics have contended that warning patients about side effects will cause them to experience those effects through suggestion. However, we found no difference in the number of side effects reported by respondents who received leaflets and those who did not, indicating that the provision of side effect information does not, by itself, cause patients to "imagine every symptom in the leaflet." We did find evidence of increased side effect reporting for certain kinds of leaflets, however.

7. **PPIs are unlikely to change the frequency with which patients contact their physicians.** Some critics have claimed that PPIs will substantially increase the number of times patients call physicians to seek further information or reassurance, thereby increasing the costs of health care. Others have claimed that PPIs will encourage patients to bypass their physicians in favor of self-diagnosis, self-monitoring, and self-care. We found no evidence that PPIs had any effect whatsoever on the number of times patients contacted their physicians. For one of the three study drugs (erythromycin) we found some evidence that PPIs may have altered the *content* of physician-patient interactions. Patients who received PPIs were more likely to report having discussed drug safety and side effects with their physicians.

8. **Patients find written drug information helpful.** For all three of our study drugs, most respondents who received PPIs reported that they found PPIs helpful in understanding the drug and its effects. In addition, most respondents who were taking Dalmane or erythromycin also said that the PPI contained new information, helped them to follow their doctor's orders, and helped them to know when to take the drug. For all three drugs, evaluations tended to be most favorable among the groups that are ordinarily least responsive to consumer-oriented information—e.g., less educated respondents and minorities. These results indicate that the appeal of PPIs is not limited to the more sophisticated patients who make up the "carriage trade."

9. **The amount of explanation provided in a PPI makes very little difference in how much information patients understand or remember.** Some of our results suggest, however, that PPIs that run heavily toward explanation may convey a slightly different impression about the drug. All in all, there seems to be no advantage in writing PPIs that contain large amounts of explanation.

10. **PPIs that contain numerous specific instructions can lead to increased reporting of side effects and other adverse outcomes.** Although we cannot be certain why these effects occur, we suspect that many patients find a barrage of specific behavioral recommendations unset-
tling and begin to monitor their physical states more closely, which may lead them to notice (or imagine) more side effects and to feel that they have experienced less improvement in their symptoms. Because all of the leaflets we studied included at least some behavioral recommendations, our results do not lead us to conclude that all such recommendations will have deleterious effects. Such effects seem to occur only when the PPI contains a large number of fairly detailed instructions.

11. There is little advantage to be gained by highlighting information about a drug’s risks. Patients who received leaflets in which risk information was emphasized through order of presentation and typographical devices displayed no greater knowledge of risks than other patients. We did find evidence, however, that risk emphasis sometimes affected patients’ attitudes. The most striking effects were on estrogen users, who became more positive in their beliefs about estrogen’s effectiveness, possibly to justify the risks they were assuming by their continued use of the drug.

12. The simplicity with which a PPI is written has surprisingly little effect. Some of the leaflets we studied would be considered fairly difficult by most objective yardsticks, yet patients judged these leaflets—like other leaflets that had undergone systematic attempts to simplify them—to be “fairly easy” to read. The leaflets’ complexity had no effect on how much respondents learned from them and very little effect on other outcomes. Within the range of complexity we examined, these results imply that heroic efforts to simplify the language in a PPI are probably unnecessary. We suspect that patients expect a certain amount of complexity in medical information and are willing to put some effort into meeting the message halfway.

13. PPIs in outline format may reach a larger audience but with a different message. For two of the three study drugs, we found evidence that PPIs having an outline format were more widely read than those in a text format. PPIs in outline format did not, however, convey any more (or less) information, and our results indicate that patients found them more alarming. For both estrogen and erythromycin, significantly fewer patients who received outline PPIs expressed willingness to take the drug again. Erythromycin users who received these PPIs also reported significantly more side effects and other health problems. Thus, the outline versions appeared to induce some of the negative outcomes often predicted for PPIs in general—outcomes that we did not find for most other PPIs that we studied.

14. Shorter leaflets convey less information than longer leaflets, but do so no better. Some of the leaflets we studied were shortened quite drastically by reducing their informational content. As one would expect, patients who received these shorter leaflets demonstrated less
knowledge of the facts that were omitted in them, but included in full-length versions. They did not, however, display any greater knowledge of the facts covered in all versions. There is apparently little advantage to be gained in a strategy of selectively presenting drug information in the hope that the reduced message will reach more people who will understand it better. Most patients can readily handle PPIs of 1000 words or more without suffering information overload.
II. DATA AND METHODOLOGY

Our data derive from telephone interviews and mail followup questionnaires administered to a sample of 1821 men and women, each of whom had earlier filled a prescription for one of the study drugs at one of the sample pharmacies. We interviewed participants by telephone an average of two to three weeks after they had filled their prescriptions. The interview took an average of 45 minutes to complete and covered participants’ knowledge and experience with the drug and reactions to the PPI. It also included a group of standard demographic items and a test of the respondent’s familiarity with medical terms. At the end of the telephone interview, the interviewer asked whether the respondent would be willing to fill out a followup questionnaire. If the respondent agreed, the questionnaire was sent by mail along with a check for $2.50 as payment for study participation.

DESCRIPTION OF THE SAMPLE AND PROCEDURE

Subjects were recruited with the cooperation of 69 pharmacies in Los Angeles County, systematically chosen so that a broad range of pharmacy and customer characteristics would be represented.\footnote{Details of the pharmacy sample selection procedure are provided in Berry, Kanouse, and Rogers (1981).} Eligibility was limited to adults (age 18 or over) who were picking up their own prescriptions and were able to speak English. There were also certain other drug-specific eligibility requirements, mostly designed to limit the sample to people who would find the PPI applicable (see Table 1).

Pharmacists approached eligible customers when they presented or picked up their prescriptions and told them the pharmacists were cooperating with The Rand Corporation in a study of “the information people have about prescription drugs.” The pharmacist handed the customer a brochure entitled, “Questions and Answers About the Prescription Drug Information Study,” which the customer could read while waiting for the prescription to be filled. This brochure briefly explained the study’s purpose and what would be asked of participants. Customers who agreed to participate were then asked to read and sign an authorization form, giving the pharmacist permission to release information about the prescription to Rand. The form explained that
Table 1

ELIGIBILITY REQUIREMENTS FOR STUDY PARTICIPANTS

<table>
<thead>
<tr>
<th>Eligibility Requirement</th>
<th>Reason for Requirement</th>
</tr>
</thead>
<tbody>
<tr>
<td>All drugs</td>
<td></td>
</tr>
<tr>
<td>Over 18 years old</td>
<td>Must give informed consent</td>
</tr>
<tr>
<td>Picking up own prescription</td>
<td>Informed consent obtained at pharmacy</td>
</tr>
<tr>
<td>Able to speak English</td>
<td>PPIs written only in English</td>
</tr>
<tr>
<td>Erythromycin</td>
<td></td>
</tr>
<tr>
<td>Tablet form of drug (no injections, liquids, suppositories)</td>
<td>PPI written for tablet form</td>
</tr>
<tr>
<td>Estrogens</td>
<td></td>
</tr>
<tr>
<td>Women only</td>
<td>PPI written for women</td>
</tr>
<tr>
<td>Tablet form of drug (no injections or creams)</td>
<td>PPI written for tablet form</td>
</tr>
</tbody>
</table>

the study was voluntary, outlined the procedure that would be used to contact the customer for an interview, and emphasized the confidentiality of the data and the customer's freedom to withdraw from the study at any time. Data provided by sample pharmacies indicate that about 56 percent of all customers who were asked to participate agreed to do so.

We picked up signed authorization forms from each pharmacy once a week, along with information concerning enrollees' prescriptions including the brand name of the drug, dosage and regimen, and number of tablets or capsules dispensed. We checked this information against eligibility criteria before we called respondents for an interview. Across the three study drugs, 93 percent of all those who signed up were found to be eligible.

Eligible respondents were called for a telephone interview no soon-
er than three days following the date they had picked up their prescriptions. The first call was made at a day and time the respondent had specified as convenient. We attempted to complete the interview on the first call whenever possible but called back a minimum of six times if the respondent was difficult to reach. We successfully completed telephone interviews for 87 percent of all eligible participants; 8 percent could not be reached and 6 percent refused the interview or broke off before it was completed.

Most of the results we report are based on the sample of 1821 subjects who completed interviews. Supplementary information is available for 1491 of these respondents (82 percent) who subsequently returned mail questionnaires.

Table 2 provides summary information on the demographic characteristics of the sample of users for each drug. Most of the erythromycin users we interviewed were young (under the age of 45), whereas most Dalmane users were older (age 56 or over), and most estrogen users were middle-aged (between 45 and 65). These differences reflect age specificity in the prevalence of the symptoms that the study drugs are prescribed to treat. The groups also differed in average educational level. Erythromycin and estrogen respondents were considerably better educated than Dalmane respondents, partly because the latter were older and partly because insomnia is more prevalent among the less educated (Bixler et al., 1979).

Our sample of estrogen users was limited to women; the samples of Dalmane and erythromycin users were not. Nevertheless, more than two-thirds of our respondents for these latter drugs were women. The greater representation of women partly reflects their more frequent use of these drugs, and partly their somewhat greater willingness to participate in the study.

Users of the three drugs also differed considerably in the amount of experience they had with the drug. Fifty-nine percent of our erythromycin respondents said that they had never taken the drug before; in contrast, only 33 percent of Dalmane respondents and 5 percent of estrogen respondents were first-time users. Indeed, half of the estrogen respondents had been taking the drug for seven years or more.

\[9^a\]For erythromycin, we waited a minimum of three days before attempting the first call, in order to give respondents a chance to gain some experience with the drug. For Dalmane and estrogens, we waited a minimum of ten days.

\[9^b\]Obivously, menopausal symptoms are more common among middle-aged women. Perhaps less obviously, insomnia is more prevalent among older people (Bixler et al., 1979).
<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Erythromycin</th>
<th>Dainane</th>
<th>Estrogen</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>32.0</td>
<td>30.1</td>
<td>--</td>
</tr>
<tr>
<td>Female</td>
<td>68.0</td>
<td>69.9</td>
<td>100.0</td>
</tr>
<tr>
<td>Total</td>
<td>100.0</td>
<td>100.0</td>
<td>100.0</td>
</tr>
<tr>
<td>Age (years)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>18-35</td>
<td>43.3</td>
<td>16.3</td>
<td>6.1</td>
</tr>
<tr>
<td>36-45</td>
<td>15.6</td>
<td>9.8</td>
<td>15.4</td>
</tr>
<tr>
<td>46-55</td>
<td>15.9</td>
<td>20.9</td>
<td>39.0</td>
</tr>
<tr>
<td>56-65</td>
<td>16.1</td>
<td>24.5</td>
<td>30.0</td>
</tr>
<tr>
<td>66 or older</td>
<td>9.1</td>
<td>28.5</td>
<td>9.5</td>
</tr>
<tr>
<td>Total</td>
<td>100.0</td>
<td>100.0</td>
<td>100.0</td>
</tr>
<tr>
<td>Race/ethnicity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>77.4</td>
<td>76.6</td>
<td>84.9</td>
</tr>
<tr>
<td>Black</td>
<td>10.2</td>
<td>13.5</td>
<td>5.6</td>
</tr>
<tr>
<td>Hispanic</td>
<td>4.0</td>
<td>3.0</td>
<td>2.1</td>
</tr>
<tr>
<td>American Indian or Alaska Native</td>
<td>2.8</td>
<td>1.6</td>
<td>1.8</td>
</tr>
<tr>
<td>Asian or Pacific Islander</td>
<td>1.2</td>
<td>0.5</td>
<td>1.2</td>
</tr>
<tr>
<td>Othera</td>
<td>4.4</td>
<td>4.7</td>
<td>4.4</td>
</tr>
<tr>
<td>Total</td>
<td>100.0</td>
<td>100.0</td>
<td>100.0</td>
</tr>
<tr>
<td>Education (years)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0-8</td>
<td>3.6</td>
<td>13.4</td>
<td>3.4</td>
</tr>
<tr>
<td>9-11</td>
<td>10.6</td>
<td>14.2</td>
<td>8.8</td>
</tr>
<tr>
<td>12</td>
<td>31.8</td>
<td>33.0</td>
<td>37.3</td>
</tr>
<tr>
<td>13-15</td>
<td>32.2</td>
<td>23.4</td>
<td>34.8</td>
</tr>
<tr>
<td>16</td>
<td>13.1</td>
<td>9.5</td>
<td>8.1</td>
</tr>
<tr>
<td>17 or more</td>
<td>8.7</td>
<td>6.5</td>
<td>7.6</td>
</tr>
<tr>
<td>Total</td>
<td>100.0</td>
<td>100.0</td>
<td>100.0</td>
</tr>
<tr>
<td>Number of respondents</td>
<td>880</td>
<td>369</td>
<td>572</td>
</tr>
</tbody>
</table>

*a Unclassifiable or more than one classification.
THE CONSUMER SURVEY

To obtain additional information on responses to the study PPIs, we conducted a supplementary survey of a convenience sample of 960 men and women. Subjects for this "consumer survey" were volunteers from various community organizations—church groups, civic groups, charitable organizations, and the like. As much as possible, they were chosen to be demographically similar to our sample of actual drug users.

Consumer subjects were surveyed in groups of 3 to 55; the average group size was 21. Each subject was randomly assigned to receive one of the study PPIs and read it carefully. Subjects were then given a questionnaire containing items that measured comprehension of the material in the PPI and soliciting their subjective reactions to it by asking them to rate it on several scales. These subjective reactions, obtained immediately after subjects had read the PPI, provide useful information on how the PPI was perceived—information that is not available in the telephone survey.

Consumer subjects did not receive individual compensation for their study participation. However, each cooperating group received a payment of $1.00 for each study participant it supplied. The survey sessions, which took about an hour to complete, were usually conducted during or immediately after a regularly scheduled group meeting.

DESIGN AND STUDY VARIABLES

The project comprised three separate studies sharing a common experimental design—a $3 \times 2 \times 2$ factorial with three levels of drug (a nonrandom factor), and two structural variables, each with two levels. The particular pair of variables that were combined factorially changed from study to study. In addition, each study had three control groups (one for each drug). A schematic representation of the design is shown in Table 3. Control groups for Dalmane and erythromycin were not given a PPI. The estrogen control group received the PPI distributed by the manufacturer (as required by FDA regulation).

Each of the three studies examined the effects of two different structural features of PPIs. In the first study, for example, the PPIs differed systematically in the specificity of their instructions and the amount of explanation they provided. In the second study, they varied in the simplicity of their writing style and their emphasis on risk information; and in the third study, they varied in length and format. Altogether, then, the studies examined six different structural features. Each feature was studied in combination with one other feature, which permits us to examine interactions between pairs of features that
Table 3

SUMMARY OF EXPERIMENTAL DESIGN

<table>
<thead>
<tr>
<th>Drug</th>
<th>$A_1$</th>
<th>$A_2$</th>
<th>No PPI Control</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$B_1$</td>
<td>$B_2$</td>
<td></td>
</tr>
<tr>
<td>Erythromycin (R)</td>
<td>$R_{11}$</td>
<td>$R_{12}$</td>
<td>$R_{21}$</td>
</tr>
<tr>
<td>Dalmane (D)</td>
<td>$D_{11}$</td>
<td>$D_{12}$</td>
<td>$D_{21}$</td>
</tr>
<tr>
<td>Estrogens (S)</td>
<td>$S_{11}$</td>
<td>$S_{12}$</td>
<td>$S_{21}$</td>
</tr>
</tbody>
</table>

$a$ Varies from study to study. For a description of the features varied in each study, see Table 4.

$b$ Control subjects for estrogens received the manufacturer's drug labeling rather than no information at all.

were combined within studies. Finally, for two of the drugs, each study included a group of subjects that received no PPI. Thus, the design permits an assessment of the effects of receiving any of the study PPIs compared with receiving none at all. Such an assessment can be made by pooling results for experimental groups and control groups across studies.

Table 4 lists the structural features that were included in each study and provides a brief definition of each. The features are listed according to the study in which they were manipulated. For example,
the first study orthogonally combined specificity of instructions with amount of explanation. Details on the background and rationale for selecting study variables and on the methods used to manipulate them may be found in Kanouse et al. (1981a).

STATISTICAL METHODOLOGY

Our general objective was to assess how PPIs with different structural features affect patients' knowledge, attitudes, and behavior. To do this, we compared the effects of the various leaflets in each study for each drug and examined the effects of receiving any of the experimental leaflets with the effects of receiving none at all (or in the case of conjugated estrogens, receiving the leaflet provided by the manufacturer). We analyzed results separately by drug. Within drugs, however, analyses of results for the three studies and for the overall comparison between experimental groups and controls were carried out simultaneously by means of analysis of covariance. The model we used regressed each outcome measure against a set of predictor variables, some of which were dummy variables representing the experimental treatment conditions; others represented background variables (covariates) that we expected would influence outcomes independent of the effects of the experimental treatments. The covariates used in our model varied somewhat from drug to drug; they included demographic variables such as the respondent’s age, sex, race, and education, as well as variables measuring the respondent’s previous experience with the drug.4 In the sections that follow, we summarize the results of these analyses.

4Detailed specifications of the variables used in our covariance model for each drug may be found in the following publications: Conjugated estrogens: Kanouse et al. (1981b); Erythromycin: Winkler et al. (1981); Dalmane: Berry et al. (1981).
Table 4

INDEPENDENT VARIABLES: STRUCTURAL FEATURES OF PPIs

<table>
<thead>
<tr>
<th>Study</th>
<th>Variables</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Specificity of instructions</td>
<td>(Two levels) Extent to which &quot;core facts&quot; are elaborated with behaviorally oriented instructions on how and when to take the drug, what to do about adverse reactions, etc.</td>
</tr>
<tr>
<td>1</td>
<td>Amount of explanation</td>
<td>(Two levels) Extent to which &quot;core facts&quot; about the drug are elaborated with explanations about why it works as it does, why certain people should not take it, why certain side effects may occur, etc.</td>
</tr>
<tr>
<td>2</td>
<td>Risk emphasis</td>
<td>(Two levels) &quot;Risk emphasis&quot; version highlights information about risks, precautions, dangers and side effects; &quot;no risk emphasis&quot; version presents the same information without special emphasis.</td>
</tr>
<tr>
<td>2</td>
<td>Writing style</td>
<td>(Two levels) Simplified versus complex; simplified version contains fewer technical words, shorter sentences, uses active voice more frequently, and follows other roles designed to minimize reading difficulty.</td>
</tr>
<tr>
<td>3</td>
<td>Format</td>
<td>(Two levels) Text versus outline; text version presents information in full sentences and paragraphs. Outline version presents key words and phrases organized under major headings.</td>
</tr>
<tr>
<td>3</td>
<td>Length</td>
<td>(Two levels) Full content versus reduced content version; reduced content version presents fewer facts (e.g., does not list as many side effects).</td>
</tr>
</tbody>
</table>
III. EFFECTS OF RECEIVING A LEAFLET

The study design permits two kinds of analytic assessment. First, we can estimate the effects of receiving any of the study leaflets by comparing outcomes for subjects who received a leaflet with outcomes for subjects who did not. (This comparison is possible, of course, only for erythromycin and Dalmane, because all estrogen subjects received a leaflet). Second, we can compare the effects of receiving one kind of leaflet rather than another by examining how outcomes vary as a function of the study variables. Our findings on the effects of leaflet variations are summarized in Sec. IV. Here we report our findings on the effects of receiving any of the study leaflets as opposed to no leaflet at all.

BEHAVIORAL RESPONSES TO THE LEAFLETS

During the course of our planning for the study, purveyors of professional folk wisdom repeatedly warned us that "no one reads PPIs." Our results suggest otherwise. The entries in the top row of Table 5 show the percentage of respondents who report having read the leaflet that they received. The results, which are remarkably consistent across drugs, show that more than two-thirds of all subjects who received a leaflet report having read it. Over half say that they read it before they started taking the medication from their current prescription, and over 20 percent report having read it more than once.

These percentages are probably inflated somewhat by the fact that all of our respondents knew that they were in a study, so that their attention to the leaflet was somewhat greater than it might otherwise have been. But even after allowing for this possibility, we believe the results indicate that PPIs are likely to reach a wide audience.

This conclusion is bolstered by additional findings on the association between readership and patient background variables. It would not have surprised us to find that PPIs reach a fairly specialized audience—for example, one that is disproportionately well educated or medically sophisticated. This was not the case, however. We found that the less educated were just as likely to report having read the leaflet as anyone else. In fact, only one variable consistently predicted readership for all three drugs: Respondents who were taking the drug for the first time were more likely to read the leaflet. In addition, for two of the three
Table 5

**Behavioral Responses to Study Leaflets**

(Percent of Respondents)

<table>
<thead>
<tr>
<th>Behavioral Response</th>
<th>Erythromycin</th>
<th>Dalmane</th>
<th>Estrogens</th>
</tr>
</thead>
<tbody>
<tr>
<td>Read leaflet</td>
<td>73.8</td>
<td>69.0</td>
<td>70.4</td>
</tr>
<tr>
<td>Read before starting Rx</td>
<td>62.0</td>
<td>56.7</td>
<td>55.5</td>
</tr>
<tr>
<td>Read more than once</td>
<td>31.7</td>
<td>21.7</td>
<td>28.9</td>
</tr>
<tr>
<td>Kept leaflet</td>
<td>54.2</td>
<td>56.5</td>
<td>45.0</td>
</tr>
<tr>
<td>Showed to someone else</td>
<td>24.3</td>
<td>16.7</td>
<td>14.3</td>
</tr>
<tr>
<td>Number of respondents</td>
<td>793</td>
<td>337</td>
<td>572</td>
</tr>
</tbody>
</table>

*Based on responses of all subjects who received a leaflet, regardless of which one they received. For estrogen, percentages include control subjects who received the leaflet distributed by the pharmaceutical company.

Study drugs (estrogens and erythromycin), we found that older respondents were more likely to read the leaflet. In general, our results indicate that prescription drug leaflets reach a surprisingly diverse population of drug users, suggesting that the market for this kind of information is fairly unsegmented.

Furthermore, many patients treat the leaflet as a reference document, to be kept on hand for possible future consultation. Several previous studies have also indicated that PPIs receive this kind of use (Dwyer and Hammel, 1978; Hladik and White, 1976; Kanouse and Morris, 1978; Romankiewicz, Gotz, and Carlin, 1978; Weibert, 1977). The fact that PPIs seem to be used in this way suggests a possible
advantage over other methods for distributing drug information (e.g., in a binder in the pharmacy), because most of these methods are designed to provide patients with access to information without actually giving it to them.

PATIENTS' KNOWLEDGE ABOUT THE DRUGS

For each of the two study drugs for which we were able to make comparisons, we found small but statistically reliable gains in respondents' knowledge about the drug as a result of receiving a PPI. Erythromycin patients who received a study leaflet were better able to answer questions about how erythromycin works and how to use it (e.g., that tablets should be taken on an empty stomach); they were also significantly more likely to know that erythromycin is contraindicated for patients with a history of liver problems. Dalmane patients who received a leaflet demonstrated significantly greater awareness of possible drug interactions, including a specific interaction with anticonvulsants. They were also more aware of the dangers of taking the drug while pregnant or nursing.

Leaflets for both drugs conveyed at least some additional information about drug side effects. We found, however, that patients tended to know very little about side effects regardless of whether they received a leaflet. Indeed, for Dalmane patients, our results suggest that the leaflet succeeded not so much in conveying specific information about such effects as a general impression that they occur: Respondents in the leaflet conditions tended to name more side effects that were not listed in the leaflet, as well as ones that were. For erythromycin patients, however, knowledge gains were more specific, possibly because the side effects themselves were thematically more consistent, hence more easily remembered.

DRUG-TAKING BEHAVIOR

How PPIs will affect patients' drug-taking behavior is a matter of great concern to critics and proponents of PPIs alike. Proponents have argued that well-designed leaflets may facilitate patients' compliance with medical regimens, by improving patients' understanding of the regimen and (perhaps) by motivating them to follow it. Critics have expressed concern that written warnings about dangers and side effects may frighten patients into noncompliance (Dorsey, 1977) and that providing instructions about the appropriate use of the drug may encour-
age inappropriate self-diagnosis and self-medication (see Institute of Medicine, 1979, for a concise review of the various positive and negative scenarios).

Our results indicate that PPIs are unlikely to have any of these effects. We found respondents’ drug-taking behavior to be largely unaffected by whether they received a PPI. We examined this behavior in a number of ways. During the telephone interview we asked respondents to count the number of tablets or capsules remaining in their prescription containers and compared this amount with the number dispensed (based on pharmacy records) to determine the number taken. In addition, we asked erythromycin patients to estimate the number of doses they had missed or taken late; we asked Dalmane patients to estimate the number of doses they had taken that were probably not necessary and the number that they had not taken that were probably needed. Respondents for both drugs were asked about their intended future use of the drug (willingness to take again for erythromycin patients, intention to seek a refill or new prescription for Dalmane patients). Respondents who received leaflets did not differ significantly on any of these measures from those who did not.

Previous research had suggested that written drug information may improve compliance with short-term therapy (Lima et al., 1976; Linkewich, Catalano, and Flack, 1974; Mattar, Markello, and Yaffe, 1975; Sharpe and Mikeal, 1974) but is likely to be less successful for long-term therapy (Hecht, 1974; Kanouse and Morris, 1978; Ley, Jain and Skilbeck, 1976; McKenney et al., 1973; Sackett et al., 1975). However, we did not find any evidence of improved compliance for erythromycin, the short-term drug included in our study. Compliance was high (79 to 89 percent) in all conditions.

Critics contend that PPIs are likely to affect the patient’s initial decision of whether to undergo drug therapy. Our results are especially striking on this point. For all three drugs, the vast majority of patients reported taking at least some of the tablets or capsules from their prescription (98 percent of erythromycin respondents, 97 percent of the estrogen respondents, and 88 percent of Dalmane respondents). Moreover, for the latter two drugs, the principal reason cited by those who had not begun taking doses from their current prescription was that they had not used up all the doses in a previous prescription. Across the three study drugs, only seven respondents specifically mentioned the PPI as the main reason they had not taken the drug (one erythromycin respondent, two estrogen respondents, and four Dalmane respondents). Of course, the reasons cited by other respondents (e.g., “found out about bad side effects,” “discovered I shouldn’t take them,” or “didn’t need them”) leave open the possibility that the PPI influenced their decision. But even if these respondents are counted as possible influences, our
results indicate that PPIs are unlikely to dissuade large numbers of patients from taking the drug.

RETURNED PRESCRIPTIONS

Pharmacists have expressed concern that PPIs will induce many patients who have purchased a drug to return it unused to the pharmacy, demanding a refund. Because the drug cannot be resold, the pharmacy must bear the cost of the refund (or loss of goodwill if it refuses to make the refund) and ultimately pass it along to the consumer. Assumptions about the frequency of returned prescriptions play a key role in estimates of the total costs of FDA's patient drug labeling program and are therefore a matter of critical concern in public policy assessments of the program's costs and benefits.

To shed light on this issue, we asked the pharmacists who participated in our study to report all cases in which study participants returned a prescription for a refund. Field personnel were instructed to record this information on forms used to monitor weekly field operations in each pharmacy. Field personnel also regularly reminded pharmacists of our desire to monitor such cases quite closely, and we included written reminders in study newsletters sent to participating pharmacies.

During the course of the study we received reports of only two returned prescriptions (both for Dalmane) out of more than 2000 prescriptions for which study enrollees received PPIs. In addition, we received one report from a telephone survey respondent of a returned prescription for erythromycin.

The extremely low incidence of returned prescriptions for these three drugs clearly suggests that the costs associated with such returns are likely to be quite small. Even if pharmacists were to pass on the full costs to the consumer, on the basis of these figures prescription prices would probably increase no more than a small fraction of 1 percent.²

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¹Although state laws prohibit returned prescriptions, many pharmacists accept them for full cash refunds in order to maintain customer goodwill.

²A contrasting estimate by the American Pharmaceutical Association (Apple, 1981) places the annual cost of returned prescriptions at $87.75 million. This estimate assumes that for every 60 new prescriptions, PPIs will cause one additional prescription to be returned, over and above the existing number (which is unknown). Because 753.2 million new prescriptions are filled annually, APhA's estimate places the number of additional returned prescriptions at 12.56 million. Although it would take a much larger study than ours to determine the true rate with any precision, our data clearly indicate that APhA's estimate is extravagantly wide of the mark.
CLINICAL COURSE

As might be expected from our finding that PPIs do not affect patients' drug-taking behavior, we found no evidence that PPIs, in and of themselves, affect patients' perceptions of the extent to which their symptoms have improved, or their ratings of their overall health. We did find, however, that certain types of leaflets do affect these outcomes. Most important, leaflets containing specific instructions had significant negative effects on self-reported improvement for both erythromycin and Dalmane patients; for estrogen patients, leaflets in outline format had a similar negative effect. These findings, discussed more fully in Sec. IV, indicate that the way PPIs are structured can influence patients' assessments of their own clinical progress. However, providing patients with drug information does not by itself have any discernible effect.

REPORTING OF SIDE EFFECTS

It is frequently contended that warning patients about possible side effects will produce those effects through suggestion (Blechman, 1980; Carlova, 1974; Loftus and Fries, 1979). Although previous research indicates that suggestion-induced side effects may not occur very often (Kanouse and Morris, 1978; Myers and Calvert, 1973, 1976, 1978; Paulson et al., 1976; Weibert, 1977), the possibility that they will is of great concern to federal officials contemplating a policy that would distribute written warnings about side effects to millions of patients.

In our study, we addressed this issue by asking respondents to indicate whether they had experienced any of several minor medical problems between the time they picked up their prescription and the time they were interviewed. Some of these problems were mentioned in the leaflets as possible drug side effects; others were similar problems that were not listed as side effects. For each problem that the respondent had experienced, we asked whether the respondent thought the problem was related to the drug.

We found no difference between those who received leaflets and control subjects in the number of side effects and other health problems they reported. Thus, the data provide no support for the contention that warning patients about possible side effects will lead them to "imagine they have every symptom in the leaflet." However, we did find evidence of such effects for certain kinds of leaflets. For erythromycin patients, the leaflets in outline format led to significantly increased reporting of
health problems—both those in the leaflet and those not listed. For Dalmane patients, leaflets containing either specific instructions or additional explanation (but not both) led to similar increases in reporting. These findings, discussed more fully in Sec. IV, indicate that the effects of PPIs on these outcomes depend on how the information is structured, not whether it is presented.

Although PPIs do not generally seem to increase the frequency with which patients report experiencing side effects, they may make patients more likely to attribute any problems that they do experience to the drug (Kanouse and Morris, 1978). We found a trend toward more frequent drug attributions in our data for erythromycin, but it was not statistically significant. Among Dalmane users, there was no evidence whatsoever for such a labeling-attribution effect. Instead, we found that most respondents, regardless of whether they had received a PPI, were disinclined to blame the drug for any problems that they experienced. As a group, Dalmane respondents were willing to label only 20 percent of the PPI-listed problems that they experienced as possibly drug related. The corresponding figure for erythromycin respondents (36 percent) indicates that they were somewhat more likely than Dalmane respondents to make a drug-related attribution. Our data, in conjunction with those reported by Kanouse and Morris (1978), suggest that PPIs are apt to influence patients' attributions for side effects only for some drugs. One plausible hypothesis that could be tested in future research is that PPIs increase drug attributions for possible side effects only when the patient has little reason to avoid making such attributions. For elective drugs such as Dalmane and estrogens, patients probably have a somewhat greater stake in believing that their use of the drug is not causing them any problems.

CONTACTS WITH PHYSICIANS

Members of the medical community have expressed concern that PPIs might affect the amount of contact between patients and providers of health care services. Two contrasting fears have been voiced. The first is that PPIs will decrease the number of contacts with physicians, interfering with the provision of physician services (Gross, 1978), possibly encouraging patients to engage in ill-advised attempts at self-diagnosis, self-monitoring, and self-care (Carlova, 1974; Demkovitch, 1975).

A similar trend appeared in our data for Dalmane; however, the Study 3 sample size was small, and the trend is not statistically reliable.

Estrogen users attributed 23 percent of the PPI-listed problems they had experienced to the drug.
1979; Vincent, 1977). The contrasting fear is that PPIs will increase patients' demands for providers' time (thereby increasing the costs of health care) because patients will need and seek more reassurance (Carlova, 1974).

Previous research offers little evidence on whether either of these effects occurs. The only relevant data, based on estimates by users of oral contraceptives of how they were affected by the PPI they received, suggest that the PPI probably had very little effect on the number of physician contacts (Morris, Mazis, and Gordon, 1977). Our own data suggest a similar conclusion. Respondents who received PPIs reported neither more nor less frequent contacts with their physicians from the time they picked up their prescriptions until the time of the interview. However, erythromycin respondents who received PPIs were more likely to report having discussed drug safety and side effects with their physicians, suggesting that for some drugs PPIs may affect the content, if not the frequency, of physician-patient interactions.

PATIENT ATTITUDES

Prescription drug labeling may have effects that are not readily apparent from the categories of patient behavior discussed above. For example, PPIs may affect how patients feel about the drug they are taking or the care they are receiving, without such effects showing up in their patterns of health care utilization or their drug-taking behavior. To examine some of these possible effects, we included a variety of attitudinal measures in our survey instruments. We were concerned with measuring patients' attitudes toward the drug they were taking and toward physicians, particularly with respect to information-giving.

A number of attitudinal effects of specific PPIs are discussed in Sec. IV. In general, however, the provision of drug information per se had little or no effect on patients' attitudes, with two notable exceptions. First, Dalmane users who received PPIs expressed more negative attitudes toward physicians. They were less likely to agree with such statements as "Most doctors carefully explain what will happen to their patients" and "Doctors are very careful to check everything when examining their patients" and more likely to agree with oppositely worded statements. Second, erythromycin respondents who received PPIs were more likely to endorse statements indicating that doctors do not always agree about how to treat illness and that doctors sometimes expose their patients to unnecessary risks.

Taken together, these findings suggest that PPIs may induce somewhat more skeptical attitudes toward physicians and the quality of care
they provide. We found no evidence, however, that patients who received PPIs were any less satisfied with the amount of drug information their own physician had provided.

**PATIENT EVALUATIONS OF THE LEAFLET**

Respondents who received a leaflet and reported having read it were asked whether the leaflet said anything that they didn't know before or whether it mostly contained information they already had; whether the leaflet helped them to understand more about the drug, understand the drug's effects, follow the doctor's orders, or know when to take the drug; and whether any part of the leaflet worried them. They were also asked to indicate how hard or easy to read the leaflet would be for most people and to estimate how many years of schooling most people would need to be able to read and understand the leaflet.

Table 6 summarizes responses to these questions. It compares responses for the three study drugs, pooled across all versions of the leaflets studied for each drug. As the table shows, most respondents said that they found the leaflet helpful, especially in providing information about the drug and its effects. A majority of erythromycin and Dalmane respondents also said that the leaflet contained new information, helped them to follow doctor's orders, and helped them to know when to take the drug. Estrogen respondents were less likely to say these things, probably because many had already read a similar leaflet provided by the manufacturer.

About a fifth to a quarter of all respondents who read the leaflet said that some of the information it contained worried them. Among erythromycin respondents, first-time drug users were especially likely to say that the leaflet worried them.

On the whole, respondents found the study leaflets to be "fairly easy" or "very easy" to read; they judged that most people would need only a ninth or tenth grade education to read and understand the leaflets. Although the estrogen leaflets were judged more difficult than those for the other drugs, the differences were slight.

The generally positive evaluations that patients accorded the study leaflets are consistent with findings from a large body of previous research showing that patients respond favorably to this kind of written drug information. However, our data indicate that this favorable reaction applies even to patients who would not ordinarily be

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5See Dwyer and Hammel (1978); Fleckenstein et al. (1976); Hladik and White (1976); Kanouse and Morris (1978); Mazis, Morris, and Gordon (1977); Romankiewicz, Getz, and Carlin (1978); Udow et al. (1979); Weibert (1977).
Table 6

RESPONDENT EVALUATIONS OF STUDY LEAFLETS

(Percent)

<table>
<thead>
<tr>
<th>Description of Measure</th>
<th>Erythromycin</th>
<th>Dalmane</th>
<th>Estrogens</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leaflet contained new information</td>
<td>74.5</td>
<td>57.9</td>
<td>26.5</td>
</tr>
<tr>
<td>Leaflet helped respondent understand more about drug</td>
<td>92.9</td>
<td>89.9</td>
<td>78.5</td>
</tr>
<tr>
<td>Leaflet helped respondent follow the doctor's orders</td>
<td>75.2</td>
<td>69.9</td>
<td>48.2</td>
</tr>
<tr>
<td>Leaflet helped respondent understand effects of drug</td>
<td>89.0</td>
<td>88.6</td>
<td>83.8</td>
</tr>
<tr>
<td>Leaflet helped respondent know when to take drug</td>
<td>75.0</td>
<td>68.9</td>
<td>39.7</td>
</tr>
<tr>
<td>Leaflet made respondent worry</td>
<td>20.1</td>
<td>24.3</td>
<td>27.1</td>
</tr>
<tr>
<td>How hard leaflet was to read</td>
<td>1.54</td>
<td>1.52</td>
<td>1.65</td>
</tr>
<tr>
<td>Years of education required to read leaflet</td>
<td>9.25</td>
<td>9.07</td>
<td>9.70</td>
</tr>
<tr>
<td>Number of respondents</td>
<td>585</td>
<td>232</td>
<td>400</td>
</tr>
</tbody>
</table>

Based on the responses of all subjects who received a leaflet and reported having read it, regardless of which one they received. For estrogen, percentages include control subjects who received the leaflet distributed by the pharmaceutical company. Means for "how hard to read" measure are on a four-point scale, with 1 = very easy, 4 = very hard.
considered prime candidates for consumer-oriented information. The conventional wisdom is that less educated, lower income, or minority consumers are much less likely to be "information seekers," and are generally less responsive to consumer-oriented information (Claxton, Fry, and Portis, 1974; Green, 1966; Ray, 1977). Yet we find no evidence that PPIs appeal only to better educated, middle class patients. Education and race were largely unrelated to respondents' propensity to read the PPI. And among those who did read it, less educated respondents and minorities more often reported that they found it useful. Thus, our results indicate that this kind of information appeals to many kinds of patients and not just those who make up "the carriage trade."
IV. EFFECTS OF STRUCTURAL AND STYLISTIC VARIATIONS

In addition to providing information on how patients are affected by receiving PPIs, the study provides important evidence on how these effects are likely to vary as a function of the design features included in the PPI. Indeed, that was our principal reason for conducting the study. In this section, we review our findings regarding the six structural and stylistic variables we studied and discuss the implications of these findings for the design of patient drug labeling documents.

EFFECTS OF EXPLANATION AND SPECIFIC INSTRUCTIONS

In the first of three studies, we investigated the effects of including additional explanatory or instructional material in the basic PPI for each of the three study drugs. This additional material did not introduce any categorically novel information; rather, it elaborated on information already presented either by offering further explanation about why certain facts were true (why the drug works as it does, why certain people should not take it, etc.) or by providing further elaboration on recommended actions (how to take the drug, what to do if side effects occur, etc.).

There were a priori reasons to believe that providing additional information might enhance—or detract from—a PPI's effectiveness in communicating drug information. Elaboration might help the reader place the information in a conceptual framework, facilitating memory for the information. However, it could detract from the communication's effectiveness by loading too much information on the reader, interfering with the ability to sort out the important facts and remember them.¹

We found no evidence that the additional information provided in our Study 1 leaflets did either of these things. Instead, the two elaboration variables—especially instructions—affected the overall "tone" of the PPI, with resulting differences in respondents' attitudes and behavior. These effects varied by drug. They were most marked for Dalmane,

¹See Kanouse and Hayes-Roth (1980) and Kanouse et al. (1981a) for more detailed discussions.
less marked for erythromycin, and totally absent for estrogens, where the Study 1 variables made little difference.

The specific instruction leaflets for Dalmane contained a number of specific recommendations about how to minimize problems that could result from taking the drug. These leaflets urged respondents: (1) to try to fall asleep naturally before taking Dalmane; (2) to try omitting a dose whenever the drug had been taken for several nights in a row; (3) to be careful, while taking Dalmane, when using household appliances, making repairs, and climbing ladders; and (4) to store the drug away from the bed in order to avoid taking an overdose. These exhortations on how to use the drug and how to carry out everyday activities while using it may account for respondents’ comparative reluctance to share these leaflets with someone else or to discuss their use of the drug with other people. (Presumably, other household members would be in a position to observe and comment on compliance with these instructions.) In addition, respondents who received these leaflets reported less improvement in their sleeping problems and expressed less positive attitudes toward sleeping pills and tranquilizers. The inclusion of additional explanation did not by itself have much effect on outcomes; however, explanation and instructions together interacted to affect several outcomes, including the number of side effects and other health problems that respondents reported and their ratings of how much the leaflet helped them to understand the drug. The leaflets containing either specific instructions or explanation (but not both) may have tended to be out of balance; they confronted respondents with a barrage of unsettling recommendations that were not thoroughly explained, or with detailed explanations of drug effects that were not accompanied by action recommendations. Respondents found these leaflets to be less informative and (judging from the increased number of symptoms they reported) sufficiently disquieting to prompt them to monitor their symptoms more closely.

Specific instructions also had negative effects on the attitudes of erythromycin users. Respondents who received leaflets containing specific instructions reported less improvement in the symptoms for which the drug had been prescribed, were less satisfied with the drug’s benefits, and were less willing to take the drug again in the future. These respondents’ actual use of the drug was no different from that of other respondents. These results therefore suggest that explicit instructions may have caused these respondents to monitor their symptoms more closely, alert for signs of trouble, and that as a result their attitudes about the course of treatment and their progress became more negative.

The inclusion of additional explanation had very little effect on erythromycin patients. Respondents who received leaflets containing such explanation were somewhat more likely to report taking some
doses late; we suspect, however, that the additional emphasis these leaflets placed on the reasons for correct spacing and timing of doses correctly simply made respondents more aware of the times they departed from ideal practice and did not affect their actual drug-taking behavior.

Among erythromycin patients, leaflets containing both explanation and instructions led to more negative attitudes toward prescription drugs in general. Although we are not sure of the reason for this, one possible explanation has to do with the sheer amount of information provided; the fact that there is so much to say about a commonly prescribed antibiotic may have given respondents the impression that prescription drugs are not always helpful and not always safe.

Although our analysis of the effects of explanation and instructions for estrogen leaflets revealed few noteworthy effects, we did find a significant effect that we attribute to one specific aspect of our explanation manipulation for that drug. Respondents who received explanation leaflets were significantly more likely to mention cancer as a long-term risk of estrogen therapy. We think this is because the explanation versions were the only ones to provide quantitative information on the increased risks faced by estrogen users. For many respondents, this information may have dramatized these risks or lent additional credence to the statement that they exist.

We see no evidence in our data that explanation does anything to enhance patients’ comprehension or retention of the most important drug information. At the same time, our data suggest that systematic attempts to explain a good deal of the information in a PPI can alter the overall impression it conveys—possibly in ways that are not intended. Thus, we judge that there is little to be gained and (perhaps) much to be lost by drafting PPIs that run heavily to explanation. Of course, this does not mean that we would advise against the judicious use of explanations where they seem really needed. It simply means that, in our view, the findings we have reported argue against a strategy that uses the rule “when in doubt, explain.”

On the question of providing specific behavioral instructions, we believe our findings support a similar conclusion, only more strongly. We found no evidence that such instructions aid communication or have any other beneficial effects and a good deal of evidence that they can have negative effects on therapeutic outcomes, including self-rated clinical course and reporting of side effects. Although we cannot say for certain why these effects occur, we suspect that some patients find these specific recommendations unsettling enough that they begin monitoring their physical states more actively and with a greater bias toward finding signs of trouble. It is also possible that the inclusion of numerous specific instructions in the leaflets gives them an imperious
tone that makes respondents more defensive about their use of the drug.

Again, we must emphasize that our results do not lead us to argue against including behavioral recommendations in drug information leaflets. All of the study leaflets contained such recommendations; we found negative outcomes only when those recommendations were especially numerous and detailed.

EFFECTS OF RISK EMPHASIS AND WRITING STYLE

The second of our three studies investigated the effects of variations designed to highlight information about a drug’s risks (dangers, precautions, and side effects) and to simplify the style in which information is presented. Each of these variables addresses important policy concerns. First, there is widespread disagreement as to whether PPIs should be designed primarily to serve a “right to know” function or an “improved compliance” function (Dwyer and Ross, 1980; Institute of Medicine, 1979; Jonsen, 1978; Morris, 1978). Although risk information plays a role in PPIs serving both functions, its relative importance is probably somewhat greater when the document’s primary purpose is to facilitate informed decisionmaking. Second, research suggests that consumers also disagree about the importance of risk information; some argue that such information should receive special emphasis while others argue that many patients might find such an emphasis unduly alarming (Morris et al., 1979). Our study approaches this question empirically by comparing leaflets that use structural and formatting conventions (order of presentation, boldface type) to highlight risk information with leaflets that present the same information without special emphasis.

The PPIs currently in use for estrogens and oral contraceptives have been criticized for their level of reading difficulty (Liguori, 1978). Yet it is by no means clear whether attempts to simplify the language in a PPI will lead to improvements in patients’ comprehension of the information, or if they will do so without affecting the way the information is perceived—e.g., the extent to which the leaflet is seen as patronizing (Morris, Myers, and Thilman, 1980). To address this issue, we compared leaflets that varied in stylistic complexity. The variations were generated by systematic application of a set of rules that previous research on text comprehension had identified as important. Kanouse et al. (1981a) provide a detailed description of this variable and its manipulation.

Our results offer some surprises. We found that risk emphasis had
no effect on the amount of risk information that respondents were able
to remember, suggesting that a strategy of emphasizing such risks does
little to increase patients' understanding of them. At the same time,
such a strategy may have important—and occasionally paradoxical—
effects on patient attitudes. Estrogen users who received leaflets em-
phasizing risk information were significantly more likely to say that
estrogen is helpful in treating vaginal discomfort, perhaps the most
distressing menopausal symptom for many women. Risk emphasis may
have led some of these women to alter their beliefs about the drug's
benefits to compensate for the perceived risks. Respondents who re-
ceived these leaflets also reported having experienced significantly
fewer side effects. Special emphasis on the drug's more serious long-
term risks may have altered women's thresholds for noticing or re-
porting minor side effects. It is also possible that this result reflects
some defensive denial of any untoward effects. Certainly there was
ample motivation for such denial. Most of the estrogen users in our
sample had been taking the drug for a long time, felt extremely positive
about it, and intended to continue taking it. Most also evaluated the
risks as fairly small.

Risk emphasis also affected the attitudes of erythromycin and Dal-
mane users, but the effects were quite limited. Among Dalmane respond-
ents who received leaflets, those given the risk emphasis versions
were less likely to report that the leaflet helped them understand when
to take the drug and were also less likely to report having showed the
leaflet to someone else. The risk emphasis leaflets did not, however,
have any differential effects on their behavior. Among erythromycin
respondents who received leaflets, those who received the risk empha-
sis versions were less likely to report that the leaflet helped them
understand more about the drug; they said that side effects and other
health problems would bother them significantly more and reported
significantly less improvement in their overall health.

These results indicate that the use of structural or stylistic devices
to highlight information about a drug's risks are not likely to be benefi-
cial. We suspect that most patients—especially those taking a drug for
the first time—bring to their reading of the PPI a natural concern about
what might happen to them as a result of taking the drug. If so, it is
probably not necessary to highlight the information. If it is there, they
will find it.

We found no evidence that a simplified writing style led to any
improvements in patients' understanding of the material covered by
the leaflets or that it had any other major effects on patient outcomes.
Consumer subjects who read the erythromycin leaflets thought that the
more technical (nonsimplified) versions were more likely to serve the
purpose of improving the quality of health care, suggesting that writing
style created subtle differences in the PPI's tone. However, we did not
detect any differences in how erythromycin patients themselves re-
sponded to the leaflets.

Consumers who read the estrogen leaflets thought that the simpli-
fied versions were in fact somewhat simpler, and estrogen patients
were more likely to say that they contained "new information." Again,
however, writing style did not have any discernible effects on patients' 
knowledge, attitudes, or behavior.

Dalmane patients seemed to respond more positively to the more 
complex leaflets than to the simplified versions. They were more likely
to say that the complex leaflets contained "new information" and
helped them to understand more about the drug. These differences may
be attributable to the impersonality of the complex leaflet and that it
contained fewer imperatives ("Check with your doctor if..." "Be espe-
cially careful..."). As with the drugs, however, writing style had no 
measurable effects on patients' knowledge or behavior and only one
effect on attitudes. (Patients who received the more complex leaflets
expressed slightly less positive attitudes toward physicians.)

Despite the general absence of any differences associated with writ-
ing style by itself, we found some evidence that the variable interacted
with risk emphasis in affecting certain outcomes. These results were
both complex and drug-specific and are not reviewed here.

Our general conclusion is that the level of writing complexity in a
PPI matters considerably less than is commonly supposed. We must
enter a caveat, however. Our manipulation of writing complexity was
not intended to cover the full range of complexity along which PPIs
could in theory range, but rather a probable range of variation, given
reasonable variations in the amount of effort devoted to simplifying
these documents. We are reasonably confident that an extreme
manipulation would have yielded significant differences in patients'
responses, but it is doubtful that such differences would do much to
inform policy. No one contemplates Dick and Jane leaflets on the one
hand or medical treatises on the other. Our results pertain to leaflets
varying within a middle range; they suggest that within that range,
simplification has surprisingly little effect.

Our more complex leaflets would, by most yardsticks of "readabili-
ty," be considered fairly difficult (Kanouse et al., 1981a), yet most
patients said they considered them "fairly easy." This suggests that
professional judgments about a leaflet do not necessarily predict what
patients themselves will think. We suspect that patient expectations
regarding the complexity of medical information have a good deal to do
with this. Most patients have learned that medical information is not
always easily understood.
EFFECTS OF LENGTH AND FORMAT

Our third study investigated the effects of radically reducing the amount of information presented in a PPI and of presenting the information in an outline rather than a text format. Each of these variations represents a potentially attractive way of making the information more accessible to the reader. Examination of the effects of using an outline format is especially important, because this approach has not yet been represented in PPIs developed or approved by FDA, although it has been used extensively by others (e.g., Long, 1977).

Our evidence concerning the effects of these variables derives from only two of the study drugs (erythromycin and estrogens); a small study sample size limited our ability to detect treatment differences for Dalmane.

Our results clearly show that leaflets in outline format are considered simpler and easier to read than those in text format. Moreover, more people read the estrogen leaflets in outline format than in text format; this was not true for erythromycin, however. Use of an outline format may increase PPI readership somewhat, but only for some drugs. Unfortunately, we are not able to say which ones.2

Differences in readership did not translate into differences in knowledge. Respondents who received leaflets in outline format displayed no more—but no less—knowledge about the drug. Thus, we cannot conclude that PPIs in outline format stand any better chance of conveying more information to more people than a text format PPI.

Results for both drugs suggest that the outline versions were more alarming. Estrogen users who received these versions rated the health risks of using estrogen as significantly greater and were significantly less willing to say that they would continue taking the drug. They also reported less improvement in their overall health. Among erythromycin users who received leaflets, respondents who received outline versions reported having experienced significantly more side effects and other health problems since they began taking the drug, rated the drug as less effective in treating infection, and expressed less willingness to take it again.

These results contain several elements of the negative effects that have been predicted for PPIs in general. Although the “frightened patient” scenario does not apply to PPIs in general, it may have some validity for PPIs in outline format. We surmise that risk information

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2The greater readership accorded the outline versions of the estrogen leaflets may reflect the fact that these versions looked quite different from the ones patients were used to receiving. However, we suspect that the finding may generalize to other drugs as well. Our limited data for Dalmane indicate that the outline versions for this drug were more widely read as well.
takes on a special prominence—and seems especially alarming—when displayed in the context of an outline. The alarming effects of this format do not, however, seem to result from increased patient understanding of the drug’s risks. For that reason, we believe the results raise serious questions about the desirability of using this format.³

Consumers considered shorter PPIs to be simpler; consumers who read the estrogen leaflets also seemed to like these versions somewhat more. We found little evidence that actual drug users responded to them any differently. As one would expect, respondents who received these leaflets were less knowledgeable about facts omitted in the shorter versions but included in the longer ones. When we compared knowledge of the content common to all versions, however, there were no differences.

The shorter PPIs had almost no effect on other outcomes. Erythromycin users who received these leaflets rated them as somewhat less helpful in understanding the effects of the drug and felt less positive about the drug itself. In addition, they reported having received less information from their doctor about how erythromycin works and what its side effects are. The shorter leaflets did in fact present less information on both these topics. They may have presented just enough information to make respondents feel that there was more to know. Perhaps because respondents who received shorter leaflets felt that they had been given inadequate information, they were more likely to say that they would not follow a doctor’s orders without understanding them.

We see little reason to recommend that those who design PPIs should place high priority on minimizing their length. Patients seem able to handle PPIs containing 1000 words or more without suffering from information overload. A good rule of thumb might be to put in all the facts considered important—and only those facts.

As in the first two studies, we found a number of interactions. The most interesting of these appeared in our results for estrogens. Respondents who received full-length text versions or short outline versions were more likely to report that they had discussed drug safety and side effects with their doctor since picking up their prescription and that their physician had told them there might be side effects. These results may be attributable to the physical layout of the leaflets in these two

³Our judgment assumes that a change in behavior is not an objective of PPIs unless that change is based on improved knowledge. We recognize that some might disagree. Feeling that many medications are overused, they might argue that PPIs should be designed to reduce the use of such medications by whatever means. Our own position is that whatever else they might do, PPIs should attempt to do it by providing patients with the information they need to make their own decisions. Emotionally based appeals are inconsistent with this goal, even though they may accomplish the "same" behavior change as a well-designed, strictly informational appeal.
conditions, which seemed to enhance the visual prominence of side
effect information by presenting it in a somewhat different format from
the rest of the information covered in the leaflets. If so, then inconsist-
tencies in format within a PPI may call special attention to certain
kinds of information.
BIBLIOGRAPHY

Apple, W. S., Letter to Vice President George Bush, April 30, 1981.
Carlova, J., "Drug Package Inserts for Patients: Good Idea or Bad?" *Medical Economics*, October 14, 1974, pp. 140-149.
Fleckenstein, L., P. Joubert, R. Lawrence, B. Patsner, J. M. Mazullo, and L. Lasagna, "Oral Contraceptive Patient Information: A


