

# The Effect of Drug Information Leaflets on Patient Behavior

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## Abstract

**Background:** The patient package insert, an information leaflet included by law in the packaging of prescription drugs, contains information for the user on the specific medication.

**Objectives:** To explore how patient information leaflets influence patient anxiety and adherence.

**Methods:** A prospective cohort study was conducted in the practices of 15 family physicians. All patients receiving a new prescription for antibiotics, analgesics or antihypertensives were included. Physicians completed a questionnaire containing demographic data, assessment of the patient's anxiety, a prediction regarding adherence to the treatment, and response to the information leaflet. Patients were contacted by telephone for a follow-up structured interview. Patients' reactions to the information leaflet, adherence to treatment, and use of other sources of information on medication were assessed.

**Results:** The study group comprised 200 patients. The patient information leaflet was read by 103 of them (51.5%). A higher educational level and a chronic medication were associated with reading the leaflet ( $P=0.02$  and  $0.01$  respectively). In 36 (34.9%), an increase in anxiety was reported after reading the leaflet. Among those who read the leaflet, 9.7% had decreased adherence. Patients who stated that reading the leaflet caused anxiety were more likely to reduce their use of the medication – 7/36 (19.5%) vs. 3/67 (4.5%),  $P=0.01$ .

**Conclusions:** The proportion of patients reading the drug information leaflet is about 50%, lower than that found in previous studies. Reading the leaflet did not greatly affect adherence but aroused anxiety and decreased adherence in some patients.

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The patient package insert, an information leaflet included by law in the packaging of prescription drugs, contains information for the user on the specific medication or class of drugs prescribed. It is the most readily available form of written information on drugs for patients. The leaflet is meant to be clear and understandable to the general population [1]. In Israel, patient package inserts are written in Hebrew, Arabic and English.

Effects of the patient package insert on patient knowledge and behavior have been studied previously but the results are not conclusive [1-6]. The utility of the leaflet depends first on the extent to which it is read, and second, on the degree to which patients understand it. Rates of reading the package insert vary from 83 to 97% [2-5], and comprehension of the content of the leaflet is variable [2,6-9].

The benefits of reading the leaflet include increased knowledge of the correct method of taking the drug and the possible

side effects. Studies have shown increased patient satisfaction when an information leaflet is provided [5]. Other studies have compared the effect of information given in writing to patients to that given orally. The most effective strategy appears to be a mix of oral and written instructions [1]. Written information has been found to be more effective when given for short-term antibiotic medication compared to long-term therapy of chronic illness [1]. The results of providing information on adverse effects to patients, on patient anxiety and on the appearance of adverse effects are inconclusive. Gibbs et al. [3] found no increase in adverse effects of drugs when information was provided.

This study investigated the extent of patient use of the leaflets, and how the patient information leaflet included in drug packages influences patient anxiety and adherence to drug treatment prescribed by family physicians in Israel.

## Patients and Methods

The study was conducted in 15 urban family medicine practices in central Israel. All patients receiving a new prescription for a selected number of drugs from a predetermined list of medications were eligible for inclusion in the study. The drugs selected for the treatment of acute conditions included three antibiotics for acute infection (penicillin, amoxicillin, sulfa-trimethoprim) and all non-steroidal anti-inflammatory drugs. The drugs for chronic conditions included three antihypertensive agents (angiotensin-converting enzyme inhibitors, beta-blockers and calcium channel blockers). Patients were enrolled in the study by their family physician after the study was explained to them and their informed consent to participate was obtained. This research adhered to the tenets of the Declaration of Helsinki.

## Study practices

Fifteen board-certified specialists in family medicine from the Department of Family Medicine at Tel Aviv University participated in the study. In a pilot study conducted prior to the present research it was observed that the physicians in this group see an average of 30 patients per working day and write two to three new prescriptions for the study drugs each working day.

## Questionnaire

At the initial visit physicians completed a questionnaire including demographic data on the patient, an assessment of the patient's level of anxiety (rating the patients' anxiety on a scale of 1 to

5, with 1 being the lowest and 5 the highest), a prediction of the patient's adherence to treatment, and a prediction of his/her response to the information leaflet.

Anxiety was evaluated using the Hamilton Anxiety Scale [10]. A score above 30 was defined as severe anxiety, above 25 as moderate anxiety, and above 18 as mild anxiety.

#### Data collection

Patients were contacted by telephone by the investigator 3 to 5 days after the office visit for a follow-up interview. They were asked how they reacted to the information leaflet, whether they adhered to the treatment, and what other sources they used for information on the medication. The investigator also completed the Hamilton Anxiety Questionnaire based on their answers.

#### Statistical analysis

Frequency distributions were computed for all variables. Associations between categorical variables were assessed using the chi-square statistic, means of continuous variables were compared with Student's *t*-test, and the effect of the leaflet and patient demographics on adherence were tested.

### Results

During the study period 217 patients were eligible for inclusion in the study. Of these, 2 patients did not have their prescription filled, 10 patients refused to participate in the telephone survey at follow-up, and 5 patients were not located for follow-up. In total, complete data from office visits and follow-up interviews are available for 200 of the 217 patients (93%). Characteristics of the study population are shown in Table 1.

#### Drugs prescribed

Twenty-five patients received new antihypertensive drugs and 175 received drugs for acute problems. Of the acute prescriptions, 74 were for antibiotics and 101 for an NSAID.

#### Doctors' perception of the office visit

During the office visit, the doctors gave a score of 4 or 5 (high or very high) for anxiety to 21% of the patients. When asked to predict adherence to treatment, the doctors predicted that 95% of the patients would adhere to the treatment plan recommended.

With regard to reading the information leaflet, the doctors predicted that 41.5% of their patients would read the leaflet, and that in 22% the leaflet would cause the patients to become more anxious. They felt that the leaflet would be reassuring to only 1.5% of patients.

#### Adherence to treatment and further consultation

On telephone follow-up 3–5 days after the office visit, 90% of the patients claimed to have taken the medication as prescribed, 55% of patients said they received an explanation about the drug from their doctor during the office visit, and 29 patients (14%) reported that they consulted with another person after the visit before tak-

NSAID = non-steroidal anti-inflammatory drug

**Table 1.** Characteristics of the 200 study participants

Age (yrs) (mean ± SD) (range)	15.6 ± 55 (18–87)
Female (%)	59%
Country of birth	
Israel	43%
Africa/Asia	34%
Russia/Eastern Europe	20%
Western countries	3%
Year of immigration to Israel (mean ± SD) (range)	1955 ± 11.9 (1931–1996)
Years of education (mean ± SD) (range)	12 ± 3.2 (4–22)

ing the new drug. Ten consulted with another physician, 9 with their spouse and the remainder with a nurse, pharmacist or other person. In most cases (24/29, 82%) the additional information was reassuring to the patient.

#### Patients' perception of the visit and anxiety

Regarding anxiety levels during the office visit, 64% of patients reported that they were relaxed, 25% expressed some worry, and 10% said they were stressed. The Hamilton Anxiety Scale revealed one patient with severe anxiety (score > 30) and 10 patients with mild anxiety (score > 18) at the time of the follow-up interview.

#### Factors influencing reading of the leaflet

Altogether, 103 patients (51.5%) reported reading the information leaflet in the drug package. Patient age, gender and country of origin were not associated with reading the leaflet, but higher educational level was. Among patients with up to 8 years of formal education it was read by 30%, among those with 8–12 years of education by 54%, and among those with more than 12 years of education by 58% ( $P = 0.02$ ). Increased rates of reading the leaflet were found among those given chronic medication compared to drugs for acute illness ( $P = 0.01$ ) [Table 2].

#### Effects of reading the information leaflet

For 6 of the 103 patients (5.8%) the information was reassuring, for 61 (59.2%) the information had no effect, while for 36 (34.9%) the information increased the patient's level of anxiety. One patient reported stopping the medication completely and nine patients reporting decreasing their use of the medication – as a result of reading the leaflet. Among patients who read the leaflet, adherence with treatment was decreased in 9.7% (10/103). Patients who stated that reading the leaflet caused anxiety were

**Table 2.** Association between type of drug and reading leaflet\*

Drug	No. of patients	No. (%) reading the leaflet
NSAIDs	101	48 (47%)
Antibiotics	74	35 (47%)
Chronic medications	25	20 (80%)
Total	200	103 (51.5%)

\*  $P = 0.01$  (chi-square test)

**Table 3.** Association between doctor's prediction that patients will read the leaflet and patients' report of reading the leaflet\*

Doctor's prediction	No. reading the leaflet	No. not reading the leaflet	Total
Patient will read leaflet	51	32	83
Patient will not read leaflet	52	65	117
Total	103	97	200

\* P = 0.02 (chi-square test)

Positive predictive value 61.4% (95% confidence interval = 50–73)

Negative predictive value 55.5% (95% CI = 46–64)

Sensitivity 49.5% (95% CI = 39–66)

Specificity 67.0% (95% CI = 56–76)

Likelihood ratio positive 1.5 (95% CI = 1.06–2.11).

more likely to decrease their use of the medication – 7/36 (19.5%) vs. 3/67 (4.5%), P = 0.01.

#### Doctors' predictions of adherence

The doctors were unable to predict adherence to therapy in this sample. However, they were able to predict to some extent which patients would read the leaflet [Table 3]. Their predictions on reading the leaflet had 49% sensitivity and 67% specificity. There was no association between the doctors' assessment of patient anxiety at the office visit and reading the leaflet. No correlation was found between their prediction of the effect of reading the leaflet and its effect reported by the patient.

#### Discussion

This study examined the habits of patients regarding the reading of drug information leaflets, and the effect of reading the leaflet on adherence to treatment. We found a reading rate of about 50%, which is lower than the rates reported in other countries [2–5]. We also found that increased anxiety from reading the leaflet caused a decrease in adherence to treatment in almost 10% of patients. In this sample the doctors were able to predict to some extent who would read the leaflet but were unable to accurately predict the effect on adherence.

There are several possible explanations for the difference in reading rates between this study and other published studies. Some studies used specially prepared leaflets while we used the standard Ministry of Health-approved form included in drug packages in Israel. In some studies the doctor or pharmacist handed this form to the patient, whereas our form was prepackaged with the medication. Differences may also be due to the results obtained when the doctor conducted the follow-up on his or her own patients compared to results obtained by an independent observer as in our study.

We found that educational level was the only demographic variable associated with reading the leaflet. In one study, patients of a lower socioeconomic status requested more verbal information on their treatment [11]. A study comparing the effect of verbal and written information on patients with mild mental retardation found that the written information was less useful and even confusing to some patients [8].

We also noted that reading the leaflet was associated with the type of medicine prescribed. Patients tended to read the leaflets for chronic medications more than those for acute therapy. This may be due to the perceived risk of long-term therapy and the need for more information on the drugs prescribed and their possible adverse effects. This effect does not appear to have been well studied previously.

We found that many patients chose to seek other sources of information after reading the leaflet and this generally had a reassuring effect. This is supported by another study that observed a beneficial effect of getting a "second opinion" on prescribed drug treatment [11].

The findings of our study do not support the hypothesis that reading the leaflet generally increases patient anxiety. However, in the minority of patients in which this occurs, increased anxiety is associated with decreased adherence.

The doctors were able to predict to some extent which patients would read the leaflet but were unable to predict the effect of reading the leaflet on patient anxiety. Tailoring of appropriate drug information to meet patient needs, promote adherence and decrease anxiety would appear to be the ideal course of action but given our findings may not be practical.

Koo et al. [12], investigating patients' use of written medicine information in Australia, found that the level of patient health literacy, health locus of control, occupation, patient coping style and the nature of the health problem were all associated with patient interest in written materials. Physicians' assessment of these patient-related factors may help them to better understand their patients' need for information.

Since overall adherence in the study was high, we were unable to detect the effect of anxiety on adherence. A study on the effect of anxiety on adherence will require a larger patient sample.

In conclusion, reading the patient information leaflet is associated with higher education level and the prescription of chronic medication. Reading the leaflet is not necessarily associated with an increase in patient anxiety, but when this occurs it may decrease adherence.

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## Capsule

### A bacterial anti-complement

The complement system generates a finely regulated yet potent antimicrobial response, making it an attractive target for bacterial virulence factors. Most commonly, endogenous regulatory proteins of the complement system are usurped to switch off complement activation, but the widespread human pathogen *Staphylococcus aureus* can inactivate the complement cascade by a more direct means. Previous work has shown that the extracellular fibrinogen-binding protein (Efb-C) generated by *S. aureus* blocks the complement pathway by binding to the thioester-containing domain of the complement C3b protein; indeed, *S. aureus* strains that lack Efb-C display reduced virulence. Hammel et al. resolved the crystal structures for the C3-binding domain of Efb-C in its unbound state and in

complex with the C3d domain of C3. Structure-based functional studies suggest that native C3 is bound by Efb-C in a way that alters its conformation. As a consequence, conversion to C3b is prevented, and participation in the subsequent activation of the complement cascade is also blocked. As well as binding native C3, Efb-C also had high affinity for C3b, again appearing to induce conformational changes, this time in the already activated form of the complement component. Effective targeting of the interface between Efb-C and the C3d domain by a small molecule could be useful in the treatment of *S. aureus* infection.

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Eitan Israeli

## Capsule

### Genetic risk factor for smoking-linked head and neck cancer

A simple blood test may be able to identify those most at risk for developing head and neck cancer as a result of smoking. Livneh, head of the Weizmann Institute's Biological Chemistry department, studied repair mechanisms for DNA, the material of genes. Cells maintain sophisticated repair systems to prevent the accumulation of mutations that might lead to cancer. In these systems, molecular detectors scan the DNA for injury. A sort of local operation is then performed to excise and dispose of the damaged segment and replace it with a new one. In their study, that appeared in *Cancer Research*, Livneh and team investigated whether a reduced individual ability (non-inherited) to repair DNA damage increases chances of getting head and neck cancer. Smoking damages DNA and is known to be a major cause of this disease, which can affect the throat, mouth and larynx. They focused on a DNA repair enzyme called OGG1, for which they had previously developed a blood test to measure activity levels. By comparing OGG activity in healthy people

with those in head and neck cancer patients, the research team found that the test could single out those with a heightened risk of this type of cancer: weak levels were correlated with greater risk. They found that a smoker with low OGG is 70 times more likely to develop head and neck cancer than a non-smoker with normal OGG levels. These findings join a previous study by the group where OGG activity indicated elevated risk for lung cancer – a disease also caused by smoking. Together, these studies show that a combination of low OGG activity and smoking can skyrocket a person's chances of becoming ill with a smoking-related cancer. The OGG blood test might be used in the future to identify those most at risk for lung and head and neck cancers, hopefully giving added incentive to those with the risk factor to quit smoking. In addition, drugs might be developed to reduce this risk, like those prescribed to reduce the risk of heart disease.

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