

## ANALYZING MEDICINES INFORMATION OF OVER-THE-COUNTER MEDICINES LEAFLETS IN SLOVENIA

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**Abstract:** Appropriate information on over-the-counter (OTC) medicines is provided by pharmacies in the form of written medicines information and by pharmacist's advice. In Slovenia, prescription medicines and OTC medicines patient information leaflets (PILs) and summaries of product characteristics (SmPCs) are regulated by the Agency of the Republic of Slovenia for Medicinal Products and Medical Devices. Promotional leaflets must include two obligatory sentences required by Slovene legislation. But we consider these legislative requirements on medicine information insufficient and establish a need for adequate balance of information regarding benefits and risks. Therefore benefit and risk claims within OTC medicine leaflets related to three therapeutic groups – infectious diseases, allergies, and osteoporosis treatment – were targeted. We aimed to determine their ratio, and one- or two-sidedness of the messages. Two-sided messages are considered to be more advantageous. Fair, balanced promotion and advertising and rational medicine use is suggested by the World Health Organization (WHO). The Food and Drug Administration requires a fair balance between information relating to side effects and contraindications, and information relating to effectiveness of the medicine, in terms of scope, depth, and detail. Risks and benefits should be properly presented within the medicine information. Medicine information should have a positive impact on the public health. 30 leaflets with OTC medicines were analyzed, 10 for each selected therapeutic group. The collected leaflets were obtained from the representative sample derived from Slovene pharmacies. At selecting a sample of leaflets we considered regional equivalency. Therapeutic groups for treatment of viral diseases, allergies, and osteoporosis were chosen. The texts were coded by two researchers. Besides determining frequencies, a t-test and a chi-squared test were used as statistical methods. A majority of the analyzed leaflets seem to be two-sided, with a smaller share of two-sided leaflets

in the osteoporosis treatment group. However, generally there is an imbalance between the benefits and the risks observed. Only in one leaflet do risk claims exceed benefit claims in terms of scope, depth, and detail. There are 353 benefit claims and 79 risk claims in the OTC medicine leaflets related to infectious diseases and 77 benefit claims and 18 risk claims in the OTC medicine leaflets related to allergies. The messages are mainly two-sided, with benefit and risk claims included. There are 265 benefit claims and 22 risk claims in OTC medicine leaflets related to osteoporosis; six leaflets include two sided-messages. A fair-balance criterion is not confirmed. We concluded that benefit claims exceed risk claims in the analyzed leaflets not only in scope but also in depth and detail. Only one company is estimated to be socially responsible and to respect treatment safety. Two-sided messages do not always exist, thereby establishing a need for educating manufacturers and patients. The companies' strategies include a larger share of two-sided messages. An association between a preventive OTC treatment and a prevalence of benefits is shown in our research study. Stricter legislation regarding the scope, depth, and detail of both the benefits and risks contained in medicine information packs and leaflets is needed. Also educating the leaflets' creators and patients should take place.

**Keywords:** one-sided, two-sided messages, OTC medicines, fair-balance, unbalanced

## **ANALIZA INFORMACIJ O ZDRAVILIH BREZ RECEPTA NA PROMOCIJSKIH PROSPEKTIH V SLOVENIJI**

**Povzetek:** Ustrezne informacije o zdravilih brez recepta lekarne omogočajo v obliki pisnih informacij o zdravilih in nasveta farmacevta. V Sloveniji navodila za uporabo zdravil in povzetke glavnih značilnosti zdravil na recept in brez recepta ureja Javna agencija Republike Slovenije za zdravila in medicinske pripomočke. Promocijski prospekti morajo vključevati dva obvezna stavka, ki ju zahteva slovenska zakonodaja. Vendar menimo, da so te zakonodajne zahteve nezadostne in da obstaja potreba po ustreznem ravnotežju informacij glede koristnosti in tveganj. Zatorej smo se osredotočili na trditve o koristnostih in tveganjih v prospektih z informacijami o zdravilih brez recepta, povezanih s tremi terapevtskimi skupinami – zdravljenje infekcijskih bolezni, alergij in osteoporoze. Naš cilj je bil določitev njihovega razmerja ter eno- ali dvostranskost sporočil. Dvostranska sporočila se štejejo za naprednejša. Ustrezno, uravnoteženo promocijo in

oglaševanje ter racionalno uporabo zdravil predlaga Svetovna zdravstvena organizacija. Ameriška agencija za hrano in zdravila Food and Drug Administration zahteva ustrezno ravnotežje med informacijami o neželenih učinkih in kontraindikacijah in informacijami o učinkovitosti zdravila, in sicer glede obsega, globine in podrobnosti. Tveganja in koristnosti bi morali biti v informacijah o zdravilih primerno predstavljeni. Informacije o zdravilih bi morale pozitivno vplivati na javno zdravje. Analizirali smo 30 prospektov za zdravila brez recepta, po 10 iz vsake izbrane terapevtske skupine. Zbrane prospekte smo dobili iz reprezentativnega vzorca slovenskih lekarn. Pri izboru vzorca prospektov smo upoštevali enakomerno regionalno porazdelitev. Izbrali smo terapevtske skupine za zdravljenje virusnih bolezni, alergij in osteoporoze. Besedila sta kodirala dva raziskovalca. Poleg določitve frekvenc smo kot statistično metodo uporabili t-test in test hi-kvadrat. Večina analiziranih prospektov je dvostranskih, z manjšim deležem prospektov z dvostranskimi sporočili v skupini zdravljenja osteoporoze. Vendar smo, na splošno gledano, opazili neravnotežje med koristnostmi in tveganji. Le v enem prospektu trditve o tveganjih presegajo trditve o koristnostih, glede obsega, globine in podrobnosti. Določili smo 353 trditve o koristnostih in 79 trditve o tveganjih v prospektih za zdravila brez recepta, povezanih z infekcijskimi boleznimi, ter 77 trditve o koristnostih in 18 trditve o tveganjih v prospektih za zdravila brez recepta, povezanih z alergijami. Sporočila so večinoma dvostranska, z vključenimi trditvami o koristnostih in tveganjih. 265 trditve o koristnostih in 22 trditve o tveganjih smo določili v prospektih za zdravila brez recepta, povezanih z osteoporozo; šest prospektov vključuje dvostranska sporočila. Merilo ustreznega ravnotežja ni potrjeno. Zaključili smo, da trditve o koristnostih presegajo trditve o tveganjih v analiziranih prospektih ne le v obsegu, ampak v globini in podrobnostih. Le za eno podjetje smo ocenili, da je družbeno odgovorno in upošteva varnost zdravljenja. Dvostranska sporočila niso vedno prisotna, zato je treba izobraževati proizvajalce in paciente. Strategije podjetij vključujejo večji delež dvostranskih sporočil. V svoji raziskavi kažemo povezavo med preventivnim zdravljenjem z zdravili brez recepta in prevalenco trditve o koristnostih. Potrebna je strožja zakonodaja glede obsega, globine in podrobnosti obojih, torej trditve o koristnostih in tveganjih, ki jih vsebujejo navodila z informacijami o zdravilih in prospekti. Uveljaviti se mora tudi izobraževanje ustvarjalcev prospektov in pacientov.

**Ključne besede:** enostranska, dvostranska sporočila, zdravila brez recepta, ustrezno ravnotežje, neravnotežje

## 1. INTRODUCTION

Patient information leaflets are leaflets that accompany medicines, most prominently providing information regarding medical conditions, doses, and side effects. In Slovenia, it is documented that necessary instructions and information regarding prescription medicines will be provided by relevant healthcare professionals, including pharmacists and physicians. Over-the-counter medicines (OTC) differ in this regard, in that, when an OTC medicine is purchased, the pharmacy alone is the provider of medicine information and advice. Most often, appropriate information on OTC medicines is provided by pharmacies in the form of patient information leaflets (Kasesnik & Kline, 2011). In Slovenia, promotional leaflets must meet standards of professional public need and official requirements and must include two obligatory sentences required by Slovene legislation. However, we find these minor requirements do not ensure an adequate balance of information regarding benefits and risks. Research regarding the readability of some patient information leaflets, summary of product characteristics, and promotional materials related to some prescription and OTC medicines market in Slovenia has also been conducted in Slovenia (Kasesnik & Kline, 2011).

Benefits and risks of medicines should be presented in the manner so that a patient receives reliable, complex medicine information, regardless of whether medicines are prescription or over-the-counter. However, medicine information has not always been balanced. Some negative effects of Direct-to-Consumer-Advertising (DTCA) of prescription medicines have been described and therefore opponents disagree with DTCA on the basis of its negative effects. According to one published study (Belch, 1981), the claims in these advertisements are emphasizing the benefits, not the risks, and the claims are aimed to increase prescribing for, instead of educating the patients. On the other hand, promoting the treatment of under-treated diseases is stated as the goal of DTCA. The authors conclude that it is important to follow medicine advertising and to report when it is not in accordance with public health goals.

In Slovenia, prescription medicines patient information leaflets and summaries of product characteristics are regulated by the Agency of the Republic of Slovenia for Medicinal Products and Medical Devices. Although many regulative procedures follow a common EU course, there are still some steps performed at a national level. Also patient information leaflets of OTC medi-

cines are checked by the Agency of the Republic of Slovenia for Medicinal Products and Medical Devices. Legislative control of nutritional supplements in Slovenia has not been so strict so far. Promotion and advertising of medicines are determined by the Drug and Medical Devices Advertising Rules (Drug and medical devices advertising rules, 2001). However, we estimate the legislation concerning promotion and advertising of prescription and OTC medicines should be upgraded. It has also been noted by the health authorities that OTC promotional materials are not supervised enough. An important part of the OTC promotional materials are also leaflets displayed at pharmacies and intended for the visitors to take and read them; these leaflets are a subject of this study. Leaflets are of promotional nature and are allowed for OTC medicines, but not for prescription medicines. Promotion of prescription medicines is only allowed to be directed to health professionals. According to the Drug and Medical Devices Advertising Rules two obligatory sentences concerning carefully reading the patient information leaflet before taking the medicine and consulting the experts regarding risk and adverse events are required (see also Statistical Analysis).

After reviewing the published literature we found out that the papers describing claims in promotional materials were lacking, especially research results with OTC medicines promotional items. In Slovenia, a previous study (Kasesnik, 2009) included an overview of promotional materials on an extensive sample from Slovene pharmacies, but with less detail and fewer analyses. The present study also includes a different methodological approach, considering specific Slovene regulative criteria, besides the FDA criteria, and therefore the study can be valuable for the Slovene as well as the global environment.

Therefore promotion of OTC medicines leaflets has not been adequately managed. Promotional claims should follow the regulative rules, and also communications science findings should be considered in order to ensure an adequate comprehension of claims by the general public. However, creators of many promotional leaflets have not seemed to focus on the claims, although their comprehension may affect taking and handling the medicines. Fair balance provision has been explored in this study, despite the fact that it is required only in USA. Namely, it reflects the ratio that should be achieved when appropriate informing takes place. Regardless of the regulation rules within individual countries, enabling information fair balance is essential and thus study findings can be broadly applicable.

### 1.1. 'FAIR BALANCE' OF BENEFITS AND RISKS IN MEDICINE LEAFLETS

WHO suggests that effective medicines regulation promotes and protects public health by ensuring that, among other measures, promotion and advertising is fair, balanced, and aimed at rational medicine use (Medicines regulatory support, 2015). It is required by FDA that a fair balance is presented between information relating to side effects and contraindications, and information relating to effectiveness of the medicine, in terms of scope, depth, and detail (FDA Code of Federal Regulations, 2015). The scope means a benefit to risk ratio concerning a number of claims, the depth was interpreted within this study as extensive, profound, well-balanced information and the detail was interpreted as particularized, comprehensive information, thorough in the treatment of details. Advertisements should not convey a deceptive impression of risks and benefits in the overall presentation of information. Therefore, achieving a mechanistic balance between risks and benefits, in terms of scope, is not the only factor (Before the Department of Health and Human Services Food and Drug Administration, 2003); persuasive strength of claims, although not determined by this study, also affects the balance. PhRMA Guiding Principles Direct to Consumer Advertisements About Prescription Medicines are available, with an aim to benefit the public health by increasing awareness about diseases, educating and motivating patients to discuss with their physicians and finally to get appropriate health care and to comply with prescription drug treatment regimens (Direct to Consumer Pharmaceutical Advertising, 2015).

Well-balanced information facilitates understanding of the advertised medicine's potential risks and benefits. Failure to provide consumers with balanced information of the benefits and risks may lead to misleading consumers. An imbalance between the benefits and the risks within OTC medicine leaflets and publications has been shown (Kasesnik, 2009). In 92% of the studied leaflets and publications, an imbalance between benefits and risks was found. The imbalance has been defined as the situation whereby risk claims represent less than 50% of the sum of benefits and risk claims. Findings of another study (Davis & Meader, 2009) suggest that content analysis combined with an assessment of consumer reactions and attitudes after viewing a DTC advertisement lead to a better determining of fair balance. The desired ratio is defined as the equal share of benefits and risks, although it has been rarely observed in medicine promotional leaflets. In Slovenia, OTC medicine promotion

is regulated by the Drug and Medical Devices Advertising Rules (Drug and medical devices advertising rules, 2001; hereinafter: Rules). According to the Rules, promotion of prescription medicines to the general public is not allowed. For OTC medicines, the elements of advertising are set by the Rules, including a presentation of risks. Advertisements must not be misleading regarding the content of medicine or effects and possible adverse events, and it is not allowed to convince patients that a visit of the physician is not needed. Information at promotion of prescription medicines to the scientific public must be accurate, unambiguous, authenticatable, and complete, to ensure an assessment of efficacy and therapeutic value of the promoted medicine. Also qualifications of sales representatives and the obligations of the license holder towards the Agency of the Republic of Slovenia for Medicinal Products and Medical Devices and competent inspection organization are determined.

Two-sided messages include benefits and risks. They are perceived as not only having shortcomings but also advantages in comparison with one-sided messages (Lang et al., 1999). Increases in perceived source credibility and trustworthiness of the advertisement as advantages of two-sided messages suggest that content analysis combined with an assessment of consumer reactions and attitudes after viewing a DTC advertisement lead to a better determining of fair balance messages, while a decreased purchase intention is a recognized shortcoming of two-sided messages, although results are conflicting (Belch, 1981; Etgar & Goodwin, 1982; Golden & Alpert, 1987; Sawyer, 1973; Swanson, 1987). Perception of two-sided messages (Qi et al., 2010) depends also on the level of need for cognition (NFC), the tendency to engage in enjoy thinking. The need for cognition is a feature of an individual to apply the central or systematic route. Persuasiveness of the messages can be presumed, although it can be firmly determined only by testing of perception and behaviour. The Elaboration Likelihood Model (Qi et al., 2010) describes persuasion as the result of the central route, when thoughtful consideration takes place, and the peripheral route, when expertise or attractiveness are used to form attitude. One study utilizing meta-analyses (O'Keefe & Jensen, to appear) compared the persuasiveness of gain versus loss messages. According to this study, a message's contents can be framed in a positive ('gain') frame that emphasizes the advantages of compliance, or a negative ('loss') frame that emphasizes the disadvantages of noncompliance. The authors predicted a higher persuasive strength of negative information. In another study (Edwards et al., 2002), the authors

state that problems in communicating risks result from the effects of different information frames, such as advising patients on the basis of different data.

## 2. RESEARCH PROBLEM AND HYPOTHESES

### 2.1. RESEARCH PROBLEM

The Agency of the Republic of Slovenia for Medicinal Products and Medical Devices regulates the content of patient information leaflets of prescription medicines as well as OTC medicines and summaries of product characteristics. Although many legislation procedures follow a common EU course, there are still some steps performed at a national level. Promotion and advertising of medicines are regulated by the Drug and Medical Devices Advertising Rules (Drug and medical devices advertising rules, 2001), although a supervision is not sufficient. Leaflets are displayed on the shelves of pharmacies; they are brought by the representatives of the pharmaceutical companies, usually on the basis of pharmacy managers' permission. Minimal requirements are needed for a content of the leaflets to comply with the legislative requirements. Ethical approaches of individual pharmaceutical companies, as well as a level of knowledge of the creators, largely affect the content of a promotional message.

Despite the fact that a fair balance provision is not obligatory for the Slovene area and OTC medicines are targeted, as opposed to prescription medicines of DTCA, it is important for the safety of patients and for their treatment that this criterion is fulfilled. In Slovene legislation (Drug and medical devices advertising rules, 2001) two obligatory sentences have to be included and this ratio is required. The first sentence states that patient information leaflets (PILs) should be carefully read before taking the medicine. The second sentence states that a physician or a pharmacist should be consulted regarding risk and adverse events. OTC medicine leaflets do not seem to be widely researched, especially concerning the benefit to risk ratio. Besides the suggested practical incentives for pharmaceutical companies and regulatory institutions, an advancement in medication information science is expected. Apart from filling a literature gap in the area of OTC medicine leaflets, the results of the study are expected to influence the safety of the treatment, if they are considered in the content of leaflets.

### 2.2. HYPOTHESES

*Hypothesis 1 (H1): Benefit claims exceed risk claims in OTC medicine leaflets, in terms of scope, irrespective of the therapeutic group.*

Benefits are expected to be pronounced in order to promote an OTC medicine, hence the motives are predicted to be commercial. Although it would be responsible to consider information balance and treatment safety, it is not expected to be widely used.

Benefits are expected to include also more depth and detail (FDA Code of Federal Regulations, 2015). It is assumed that many companies do not recognize the advantages of fair-balanced information, whereby these companies may tend to pronounce benefits to increase sales, and create leaflets with unbalanced information. The claims are described to emphasize the benefits, not the problems, with the aim of increasing prescribing rather than educating the consumer (Belch, 1981).

*Hypothesis 2 (H2): Leaflets include two-sided messages, more so in acute cases of infectious diseases and allergies rather than in prophylactic, osteoporosis treatment.*

The treatment of infectious diseases and allergies is an acute therapy, with apparent symptomatic relief; thus, a presentation of benefits and risks of OTC medicines should be more common than in osteoporosis treatment. A one-sided strategy may intentionally be selected for asymptomatic individuals to purchase a medicine, or even to mislead potential patients. Selecting one-sided messages may illustrate insufficient knowledge regarding their advantages (Lang et al., 1999) and/or a non-compliance with the Slovene national legislative requirements (Drug and medical devices advertising rules, 2001).

*Hypothesis 3 (H3): Benefit claims exceed risk claims, in terms of scope, more in prophylactic, osteoporosis treatment than in acute treatment, the latter being treatment of infectious diseases and allergies.*

Osteoporosis is a progressive disease, with severe symptoms appearing only in the later stages of the disease. Selling medicines to asymptomatic patients may be a harder task for the pharmaceutical companies, therefore predominance of benefits claims is expected.

A relationship between both claims may affect the persuasiveness of these leaflets. However, the persuasiveness of the aforementioned leaflets has not been a subject of the present study

and further research is needed to confirm or reject that assumption. The published hypothesis (O'Keefe & Jensen, to appear) states a persuasive power of loss-framed messages, whereas gain-framed messages are more persuasive in the prevention area.

### 3. METHODS

A larger sample of leaflets and publications was collected from a representative sample of Slovenian pharmacies, as part of the previous studies (Kasesnik, 2009; Kasesnik & Omerzu, 2009). These leaflets are available to inform pharmacy visitors. Leaflets and publications numbering 1,474 were obtained through visiting 19 public and seven private pharmacies from different Slovene regions. Leaflets and publications were collected from March to May 2009. No additional research has been conducted, Slovenian legislation regarding these leaflets and publications and their composition remains the same. Besides, there was a sample of leaflets taken from the pharmacies in a systematic manner. They were divided into 10 groups: leaflets describing self-medication medicines, publications with articles and advertisements, leaflets encompassing nutritional supplements, leaflets with cosmetic products, leaflets with medical devices, leaflets for creating disease awareness, educational leaflets, leaflets with social marketing messages, and 'other' leaflets.

Slovenia is a EU country with 2 million inhabitants and a GDP of 37.2 billion EUR in 2014, according to the Statistical Office of the Republic of Slovenia (Statistical Office of the Republic of Slovenia, 2015). The Slovene territory is divided into 12 statistical regions, with different rates of economic development. Because great health inequalities between the east and west regions of the country were observed, some measures were introduced to diminish these disparities. To achieve this goal, the WHO concept of 'investment in health and development' was used to motivate local and regional stakeholders (European Portal for Action on Health Inequalities. Slovenia, 2015). However, we chose a criterion of an approximate equal share of the selected pharmacies within every Slovene statistical region. Printed leaflets from Slovene pharmacies were selected, because these materials are a very important and widespread source of OTC information in Slovenia. There are some other routes of OTC promotion directed at the general public, e.g. lectures. Some TV commercials with a large reach also take part, but are observed to be fewer, probably due to the price.

Within the selected pharmacies we took one item of every different leaflet to reach 1,474. At selecting a sample of 30 items, the shares of the leaflets were still approximately the same within specific Slovene statistical regions. For conducting the present study, a smaller sample was used, consisting of 119 leaflets with OTC medicines for treating infectious (viral) diseases, 46 leaflets with OTC medicines for treating allergies, and 48 leaflets with OTC medicines for treating osteoporosis. Leaflets with OTC medicines are those for the symptomatic treatment of viral diseases. 30 leaflets from these three therapeutic groups were selected for further analysis, 10 for each therapeutic group, differing in content and by region. One basic criterion for choosing 30 leaflets out of a larger sample related to each of the three therapeutic groups was therefore content variability; e.g. the leaflets should have as mutually different content and claims as possible, very similar content was avoided. The other criterion was the regional principle, hence equal shares of collected leaflets from each Slovene region were aimed. Therapeutic groups were mainly chosen on the basis of large consumption and a difference in their indication area. A large prevalence of respective diseases was presumed to be related to a comparatively larger number of different promotional leaflets. Also a presumed large number and a variability of appeals in promotional leaflets are the criteria for selecting these therapeutic groups. Treating osteoporosis by OTC medicines was selected because of its preventive nature; also, treating the ageing population has been growing in scope, and it presents some challenges related to efficient communication with the older generation.

Although the leaflets were obtained from Slovene pharmacies, they were mainly issued by globally operating pharmaceutical companies. Therefore, some similarities are presumed with international markets and results are applicable in a wider context. However, two obligatory, regulatory-based risk sentences are expected to be often included for the promotional leaflets to be in accordance with national legislation (Drug and medical devices advertising rules, 2001). On the other hand, a low presentation of other risk claims is predicted. We provide an abstract summary of both benefits and risks claims utilized for content analysis in appendix one. A summary of the OTC medicines included in this study, based on the disease group, is provided in appendix two.

#### 3.1. CODING

The texts were first coded by one researcher and then by the second researcher and again

by the first researcher. Ambiguities were solved by coordinating different opinions and a final version was presented. An inter-rater reliability of the coding was 92%. We accurately researched the scope of benefits and risks. For the benefits, we coded the claims which promoted different advantageous effects. Coding of risks was related to the claims of adverse events, contraindications, warnings, interactions, or similar OTC medicine related, undesired effects associated with patient treatment. We counted a number of benefit and risk claims within every leaflet, and we coded benefit and risk claims according to the description in the previous two sentences. Also depth and detail of two types of claims were estimated. As described above, the depth means extensive, profound, well-balanced information and the detail relates to particularized, comprehensive information, thorough in the treatment of details. We broadly defined social responsibility as a commitment to health and an improvement to the quality of life and at an operational level as the desired benefit to risk ratio in the OTC medicine leaflets, leading to potentially beneficial health outcomes.

### 3.2. STATISTICAL ANALYSIS

Frequencies of claims in the leaflets within targeted therapeutic groups are determined. By a t-test appropriate for small samples, statistical (non)significance is established. Calculations of the test values are presented (Table 2).

We tested the required balance as set by legislation provisions (Drug and medical devices advertising rules, 2001), with a 80:20 ratio between benefit and risk claims. We set that ratio on the basis of a predicted occurrence of benefit and risk claims, the latter including also two obligatory sentences, as set by legislation provisions. A chi-squared test was performed in order to test the statistical difference between benefits and risks, in the total sample and within researched therapeutic groups (Table 3). Statistical calculations, a t-test, and a chi-squared test were performed using SPSS.

Therefore, the statistical analyses in this study rely on the 'required' (80:20) ratio, which are more realistic for the researched Slovene promotional materials in this study and can fulfil the Slovene regulative requirements. The 'desired' ratio of claims (50:50) exceeds the national regulative requirements; it is a stricter criterion and is a part of quality information; however, it is not expected to be common in the analyzed leaflets.

## 4. RESULTS

The results of testing H1 are shown in Table 1, Table 2, and Table 3, and the results relating to H2 are presented in Table 1. All three tables include the testing of H3.

Benefit and risk claims in 30 OTC medicine leaflets related to the three therapeutic groups were determined. Besides frequencies of benefit and risk claims, their ratios in percentages were also set (Table 1). The difference in the depth and detail of benefit and risk claims was estimated. The results of the t-test are shown in Table 2 and the results of the chi-squared test are indicated in Table 3.

Table 1 shows the determined frequencies of claims and the ratio between benefits and risks, expressed in percentages.

### 4.1. BENEFITS VERSUS RISKS IN LEAFLETS WITH INFECTIOUS DISEASES TREATING OTC MEDICINES

There are 353 benefit claims (13 to 119) and 79 risk claims (0 to 50) in the OTC medicine leaflets related to infectious diseases (Table 1). In nine leaflets, the messages are two-sided, with benefit and risk claims included. Benefits mainly prevail over risks in terms of scope, with no risks included in one leaflet. Risk claims numerically exceed benefit claims in one leaflet, being the only one where the depth and detail of risks exceed the depth and detail of benefits. The t-test shows a non-significant difference of benefit and risk claims (Table 2). Benefit claims exceed risk claims in the leaflets related to the treatment of infectious diseases, in terms of scope; H1 is therefore confirmed, benefit claims exceed risk claims in OTC medicine leaflets, in terms of scope, when the infectious therapeutic group is considered.

The claims related to the benefits of infectious diseases treating OTC medicines described an effectiveness, a treatment success, and an innovativeness (preventing (a disease), efficacious, efficient working of the medicine, comparatively better therapy, high quality products, innovative, new medicine, a medicine of choice, managing certain symptoms), advising, supporting patients, their quality of life and appearance (advising by experts, presentations of possible treatment options, increasing of well-being), and a convenience, a compliance, economic advantages and safety related to the medicine usage (natural, just a few, or an absence of adverse events, an easy to use medicine, available in convenient phar-

**Table 1:** Benefit and risk claims: frequencies of claims; testing of H1, H2, and H3

Leaflet No.	Freq. of Claims – Benefits			Freq. of Claims – Risks			Benefits / Risks (%)		
	Inf	Aller	Osteo	Inf	Aller	Osteo	Inf	Aller	Osteo
1	39	8	19	7	2	0	84.8/15.2	80.0/20.0	100.0/0.0
2	45	12	5	2	2	2	95.7/4.3	85.7/14.3	71.4/28.6
3	22	10	38	6	2	4	78.6/21.4	83.3/16.7	90.5/9.5
4	119	14	12	2	2	0	98.3/1.7	87.5/12.5	100.0/0.0
5	24	8	31	2	3	0	92.3/7.7	72.7/27.3	100.0/0.0
6	18	4	29	2	2	0	90.0/10.0	66.7/33.3	100.0/0.0
7	21	9	33	6	2	4	77.8/22.2	81.8/18.2	89.2/10.8
8	23	7	33	2	2	4	92.0/8.0	77.8/22.2	89.2/10.8
9	29	1	34	0	0	4	100.0/0.0	100.0/0.0	89.5/10.5
10	13	4	31	50	1	4	20.6/79.4	80.0/20.0	88.6/11.4
<b>Total</b>	<b>353</b>	<b>77</b>	<b>265</b>	<b>79</b>	<b>18</b>	<b>22</b>	<b>81.7/18.3</b>	<b>81.1/18.9</b>	<b>92.3/7.7</b>

**Legend**

Inf = Infectious diseases treatment therapeutic group

Aller = Allergies treatment therapeutic group

Osteo = Osteoporosis treatment therapeutic group

Freq. = Frequencies

maceutical forms, appropriate for certain patients' groups, a good compliance, a fast onset of action, safe). The claims related to the risk of infectious diseases treatment were safety issues, including possible adverse events, interactions, precautions, and a need for consultation (interactions, different possible adverse events, precautions related to the medicine usage, a need to consult in the event of a concomitant treatment).

**4.2. BENEFITS VERSUS RISKS IN LEAFLETS WITH ALLERGIES TREATING OTC MEDICINES**

Benefit claims (77) exceed risk claims (18) in OTC medicine leaflets related to allergies in terms of scope. Benefit claims range between 1 and 14, whereas risk claims range between 0 and 3 (Table 1). Nine leaflets contain two-sided messages and the remaining leaflet with a one-sided message includes only one benefit claim. A statistically significant difference, determined by the t-test, is attributed to benefit and risk claims, related to allergies treating OTC medicines (Table 2). H1 is confirmed, with benefit claims exceeding risk claims in terms of scope.

The claims related to the benefits of allergies treating OTC medicines described an effectiveness, a treatment success, and an innovativeness (efficacious, efficient working of the medi-

cine, comparatively better therapy, high quality products, innovative, new medicine, a medicine of choice, managing certain symptoms), advising, supporting patients, their quality of life and appearance (advising by experts, presentations of possible treatment options), and a convenience, a compliance, economic advantages and safety, related to the medicine usage (once-daily dosing, non-sedative, enables an activity, an easy to use medicine, available in convenient pharmaceutical forms, appropriate for certain patients' groups, a good compliance, a fast onset of action, safe). The claims related to the risk of allergies treatment were safety issues, including possible adverse events, precautions, and a need for consultation (different possible adverse events, precautions related to the medicine usage, a need to consult in the event of a concomitant treatment).

**4.3. BENEFITS VERSUS RISKS IN LEAFLETS WITH OSTEOPOROSIS TREATING OTC MEDICINES**

Benefit claims considerably prevail over risk claims (265 vs. 22) in the osteoporosis treatment group (Table 1) in terms of scope. There are six leaflets with two-sided messages. Benefits numerically exceed risks, while in four leaflets there are no risks. A non-significant difference



**Table 2:** Benefit and risk claims: testing of H1, H3 by the t-test.

On the basis of the calculated test values, shown in the last two lines, the t-test for benefits and for risks was performed, within the infection diseases, allergies, and osteoporosis therapeutic groups.

Ther. group	Benefits			Risks		
	Mean of benefit claims	t-value, (absolute); Standard deviation (DS); Mean difference (d);	Significance (two-tailed) (p = 0.01)	Mean of risk claims	t-value, (absolute); Standard deviation (DS); Mean difference (d);	Significance (two-tailed) (p = 0.01)
Inf	35.300	t = 1.389 ; DS = 30.930 d = 13.590	0.198 NS	7.900	t = 0.522 ; DS = 14.970 d = 2.470	0.614 NS
Aller	7.700	t = 11.310 ; DS = 3.917 d = -14.010	0.000 S	1.800	t = 14.552 ; DS = 0.789 d = -3.630	0.000 S
Osteo	26.500	t = 1.403 ; DS = 10.792 d = 4.790	0.194 NS	2.200	t = 5.136 ; DS = 1.989 d = -3.230	0.001 S
	<b>Test value* for benefits/ther. group/leaflet</b>	695 = benefit 119 = risk claims	814 = all claims	814/3 = 271.33 claims per ther. group	80% of claims per therapeutic group = 217.06	217.06/10 = <b>21.71</b> = test value/benefits/ther. group/leaflet
	<b>Test value** for risks/ther. group/leaflet</b>	695 = benefit 119 = risk claims	814 = all claims	814/3 = 271.33 claims per ther. group	20% of claims per therapeutic group = 54.27	54.27/10 = <b>5.43</b> = test value/risks/ther. group/leaflet

**Legend**

- Ther. group = Therapeutic group
- Inf = Infectious diseases treatment therapeutic group
- Aller = Allergies treatment therapeutic group
- Osteo = Osteoporosis treatment therapeutic group

is observed in benefits and a significant difference in risks (Table 2). These results confirm H1, i.e. benefit claims exceed risk claims, in terms of scope, in all of the researched therapeutic group. H2 is also confirmed; two-sided messages are included in the analyzed leaflets, more in the infectious diseases and allergies than in the osteoporosis treatment group. H3 is confirmed; benefit claims exceed risk claims more in the prophylactic, osteoporosis group than in the acute treatment groups.

The claims related to the benefits of osteoporosis treating OTC medicines described an effectiveness, a treatment success, and an innovativeness (a convenient, long effect, strong, the strongest, efficacious, efficient working of the medicine, comparatively better therapy, high quality products, innovative, new medicine, a medicine of choice, managing certain symptoms), advising,

supporting patients, their quality of life and appearance (enabling better well-being, increasing of the quality of life, an attractiveness, an appearance, advising by experts, presentations of possible treatment options), and a convenience, a compliance, economic advantages and safety related to the medicine usage (a convenient price, naturally working, non-addictive, well-tolerated medicine, an easy to use medicine, available in convenient pharmaceutical forms, appropriate for certain patients' groups, a good compliance, a fast onset of action, safe). The claims related to the risk of osteoporosis treatment mostly focused on a possible need for consultation.

**4.4. Relation between benefits and risks, determined by the Pearson chi-squared test**

Results of the Pearson chi-squared test show that there is no statistically significant difference

**Table 3:** Benefit and risk claims: the chi-squared test; testing of H1, H3

Therapeutic group	Chi-squared test			Symmetric measure
	Pearson Chi-squared; Significance (two-sided)	Likelihood Ratio; Significance (two-sided)	Linear-by-Linear Association; Significance (two-sided)	Cramer's V; Approx. Significance (two-sided)
Total sample	6.000 0.199 NS	6.592 0.159 NS	1.226 0.268 NS	1.000 0.199 NS
Inf	40.000 0.297 NS	27.185 0.855 NS	0.685 0.408 NS	1.000 0.297 NS
Aller	18.571 0.613 NS	13.264 0.899 NS	3.523 0.061 NS	0.787 0.613 NS
Osteo	17.750 0.218 NS	16.094 0.308 NS	2.558 0.110 NS	0.942 0.218 NS

**Legend**

Inf = Infectious diseases treatment therapeutic group

Aller = Allergies treatment therapeutic group

Osteo = Osteoporosis treatment therapeutic group

between benefit claims and risk claims, nor in the total sample, nor within individual therapeutic groups; we can therefore say that there is not a significant relationship between benefit and risk claims. For detailed information see Table 3. We therefore conclude that H1 and H3 are confirmed; benefit claims exceed risk claims in analyzed OTC medicine leaflets, more in prophylactic, osteoporosis treatment than in acute treatment.

**5. DISCUSSION**

H1 is confirmed, as benefit claims exceed risk claims in OTC medicine leaflets, in terms of scope, in all analyzed therapeutic groups. Therefore, it can be concluded that benefit and risk claims do not balance. The 'fair balance' requirement, as defined by FDA (FDA Code of Federal Regulations, 2015) cannot be confirmed by our study results, although it would be desired in the analyzed leaflets, in terms of scope, depth, and detail. Not even the required ratio, with an inclusion of two obligatory phrases (Drug and medical devices advertising rules, 2001), is included in every researched leaflet. In only one leaflet do risk claims exceed benefit claims in terms of scope (50:13). The presence of only risk claim(s) is not determined.

Some authors (Kaphingst et al., 2004) question the educational potential of the advertisements, which have also failed to comply with the 'fair balance' requirement. Most of the advertise-

ments present risk information in one continuous segment, with only positive or neutral visual images accompanying them. The educational content of the DTC fulfillment materials was not evaluated as sufficient, because the readability grade level did not comply with the recommendations (Chao, 2005).

According to our study results, the second hypothesis is also confirmed. H2 states that the leaflets include two-sided messages, more in acute (being infectious diseases and allergies) than in prophylactic, osteoporosis treatment. Our results show a majority of the leaflets including two-sided messages, with the differences among therapeutic groups. Nine leaflets related to infectious diseases and allergies treatment, and six leaflets related to osteoporosis treatment, are found to include two-sided messages. Some risk information is included in two-sided leaflets; however, legislation requirements may have contributed to the inclusion of obligatory statements. The advantages of two-sided messages are the perception of source credibility toward the advertisements and brand, and also purchase intention in consumers with a high NFC (Qi et al., 2010).

The third hypothesis is also confirmed, since benefits over risks predominance is more prevalent in the osteoporosis treatment group. However, benefit claims exceed risk claims in all researched therapeutic groups in terms of scope. Although no final conclusions concerning persuasiveness can be made on the basis of

our study findings, we make some assumptions related to already published studies. The findings of the meta-analysis (O'Keefe & Jensen, to appear) indicate a persuasive power of loss-framed messages, though gain-framed messages are more persuasive for prevention behavior. Our results concur to some extent, since we have not shown a dominance of risk claims in any of the analyzed therapeutic groups related to OTC medicine leaflets. However, a final conclusion regarding the persuasive power of the messages cannot be made from this study alone.

A lack of risk claims is especially pronounced in the allergies and the osteoporosis treatment groups, with a statistically significant difference shown by the t-test. In presenting the mean difference, being a difference between the sample mean and the test value, a large mean difference is established for benefits in the infectious diseases treatment group, showing a disproportionately high occurrence of benefit claims. The results of the Pearson chi-squared test also show no statistically significant difference between benefit and risk claims within individual therapeutic groups.

In only one leaflet (related to infectious diseases) the number of risk claims exceeds the number of benefit claims (50:13). This leaflet is numbered as the tenth and has a shortened patient information leaflet included. Also, in only this leaflet are the risks presented in more depth and detail than the benefits, and the relevant pharmaceutical company is believed to be socially responsible. This company is a generic medicines producing company and is a part of a large global pharmaceutical company (O nas, 2015). The local generic company is oriented to discovering, developing, and marketing innovative products to prevent and cure diseases (Our mission, 2015). The company describes an importance of social responsibility, based on patients, business management, people and society, and environmental care (Družbena odgovornost, 2015). This company's balance between benefits and risks in the OTC medicine leaflets confirms the social responsibility statements, at least in terms of researched written materials. Risk claims are taken from the patient information leaflet and correctly inform patients about possible negative effects related to taking the OTC medicine. The intentions of the company seem to be more responsible towards patients' health than commercially orientated. At the beginning of 2012, a generic division of this company created 10% higher revenue and 8% higher profit in comparison with its 2011 data (Sandoz lani z 10-odstotno rastjo prodaje, Lek uspešno, 2015). This company is

also estimated as the most admired in the pharmaceutical branch worldwide. Among nine key attributes an especially high score is ascribed to social responsibility (World's most admired companies, 2015).

Where a 'fair balance' is observed, a motivating and persuasive potential may also be comparatively higher. However, pharmaceutical companies often seem to disregard scientific findings. They use persuasive techniques to present medicines' effects to professionals (Edwards et al., 2002). Conveying information in an improper way is reported, for example, by presenting relative risks. Although this approach is noticed in public health and may sometimes be justifiable in achieving the greatest public health gain, it is not consistent with truly informed decision making. Using information about relative risk in isolation of base rates is regarded as manipulation and should be avoided (Edwards et al., 2002). It is suggested that both absolute and relative risk formats are used.

### 5.1. STUDY LIMITATIONS

Due to a lack of funding, a representative sample of promotional materials related to three therapeutic groups has been used, although promotional materials available in pharmacies include information belonging to a wide range of therapeutic groups. Larger samples and other therapeutic groups related to OTC medicine leaflets could be analyzed in the future. We have focused on the benefits and risks claims in terms of scope, partly also depth and detail, however, other aspects of information (e.g. importance, potential influence) have not been considered. Because the analyzed leaflets were collected some years ago, results deriving from newer leaflets could differ from the results presented in this study. Printed leaflets have been analyzed; however, internet sources have been increasingly important and could be researched in the future.

### 5.2. IMPLICATIONS FOR FUTURE RESEARCH

The present study contributes to researching OTC medicine leaflets and the results may provide incentives to pharmaceutical companies for including balanced information in their promotional leaflets. These measures should improve the safety of treatment with OTC medicines.

Future research efforts should be directed towards other therapeutic areas, apart from the three considered in this study. The present study was performed by a small team of researchers and therefore a relatively small leaflet sample was used. For future research a larger sample

is suggested. Research could be upgraded by determining a persuasive strength of claims.

## 6. CONCLUSIONS

A fair balance of information is not established. Benefit claims exceed risk claims in the analyzed leaflets not only in scope but in depth and detail. Only one company surpasses legislative requirements while few others utilize mild risk statements, included as part of patient information leaflet warnings, contraindications and adverse events. Only to that company could social responsibility be attributed, leading to potentially beneficial health outcomes. A large share of two-sided OTC medicine leaflets is determined. However, not all companies are aware of the advantages of two-sided messages, that is, not only potentially safer usage of promoted medicines, but also higher corporate reputation and higher purchase intentions of some customers. When an approach of companies is more courageous, their strategies include a larger share of two-sided messages. Our results also show an association between a preventive OTC treatment and a prevalence of benefits. It is apparent that a need for stricter legislation addressing the scope, depth and detail of both the benefits and risks contained in medicine information packs and leaflets is required. Educating the leaflets' creators and patients may lead to an improvement in the understanding of the texts, and to safer medicine usage.

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## APPENDICES

### Appendix One: Abstract of benefits/risks utilised for content analysis

#### BENEFITS

Sub-categories of appeals	Appeals
Effectiveness, a success of treatment, innovativeness	Efficacious, increased efficaciousness. The medicine works, takes care for, supports. A high quality of products, comparatively better than another therapy. Enabling treating of the disease. Innovative, modern; the medicine of choice; the only medicine of this type; new. Managing (diminishing) certain symptoms. Preventing. A convenient effect still a certain period after stopping taking the medicine. Strong, the strongest.
Advising, supporting patients, their quality of life, appearance	A possibility of advising by experts, possible treatment options. Enabling, increasing of well-being. Enabling better well-being. Increasing of the quality of life. Increases attractiveness, better appearance.
Convenience, compliance, economic advantages; safety	Easy to use. Available in a convenient pharmaceutical form. The medicine is appropriate for the patients of a certain age range, gender and medical status. Good compliance (kind, mild medicine, a nice taste); a fast onset of action. Safe. Natural. Just few (or an absence of) adverse events. Can be dosed once daily. The medicine does not sedate. It enables an activity. A convenient price. The medicine is working naturally. Non-addictive. Well tolerated.

#### RISKS

Sub-categories of appeals	Appeals
Safety issues, including possible adverse events, interactions, precautions, etc.	Various possible adverse events. Precautions. Interactions.
Safety issues, including a need for consultation	A need to consult in the event of a concomitant other treatment.

**Appendix Two: Included OTC Medicines (Active substances) based upon disease group**

Leaflet No.	Active substances (OTC medicines for treating infectious diseases)	Active substances (OTC medicines for treating allergies)	Generic name (OTC medicines for treating osteoporosis)
1	Acetylsalicylic acid	Loratadine	Minerals / Vitamins
2	Paracetamol	Pseudoephedrine / Loratadine	Glucosamine sulfate
3	Paracetamol / Pseudoephedrine chloride / Ascorbic acid	Pseudoephedrine / Loratadine	Glucosamine sulfate
4	Benzalconium chloride	Loratadine	Minerals (Calcium, Magnesium) / Vitamins (Vitamin D3, etc.)
5	Paracetamol / Ascorbic acid Paracetamol / Pseudoephedrine chloride / Dextromethorphan bromide	Oxymetazoline	Calcium, Magnesium, Vitamin D3
6	Acetylsalicylic acid	Tetrahydrozoline	Magnesium
7	Benzylamine chloride	Dimetindene maleate	Minerals (Calcium, Magnesium, Zincum, Iron) / Vitamins (Vitamins B, Folic acid, Vitamin D, Vitamin E, Coenzyme Q10, etc.)
8	Chlorhexidine / Lidocain	Dimetindene maleate	Minerals (Calcium, Magnesium, Zincum, Iron) / Vitamins (Vitamins B, Folic acid, Vitamin D, Vitamin E, Coenzyme Q10, etc.)
9	7 Amino acids / Vitamins (Vitamins A, B2, B6, B12, Folic acid, C) / Minerals (Zincum, Selenium, Magnesium, etc.)	Dimetindene maleate	Minerals (Calcium, Magnesium, Zincum, Iron) / Vitamins (Vitamins B, Folic acid, Vitamin D, Vitamin E, Coenzyme Q10, etc.)
10	Paracetamol	Oxymetazoline	Minerals (Calcium, Magnesium, Zincum, Iron) / Vitamins (Vitamins B, Folic acid, Vitamin D, Vitamin E, Coenzyme Q10, etc.)