Frequency and attitudes of patients purchasing medications online: Hungarian cross-sectional study - Can we profile consumers turning to the Internet pharmacy market?

KEYWORDS:
survey, Internet pharmacy, online medications, Hungary, attitude

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ABSTRACT

Background:

During the past two decades Internet has become an accepted way to purchase products and services. Apparently, buying medications online is no exception. Beside its benefits several patient safety risks are linked to the purchase of medicines outside the traditional supply chain. Although ten thousands of Internet pharmacies are accessible on the web, the actual size of the market is unknown. Further, limited data is available on the use of Internet pharmacies, the number and attitude of people obtaining medications and other health products from the Internet.

Objectives: The authors aimed to gather information on the frequency and attitudes of patients purchasing medications online in a nationally representative sample of outpatients. Attitudes towards main supply chain channels, perceived benefits and disadvantages influencing online medication purchase are evaluated.

Methods: A cross sectional explorative study using a personally administered survey was conducted in a representative sample of Hungarian outpatients in 2018.

Results: A total of 1055 outpatients completed the survey (response rate 77.2%). Mean age was 45 years and 43.2% reported to have chronic health conditions. Majority (82.7%) of the respondents were aware of that medications can be obtained online, but only 4.17% (n=44) used the Internet for medication purchase previously. Attitudes towards the different pharmaceutical supply chain retail channels showed significant differences (p<0,01), respondents accepted retail pharmacy units as the most appropriate source of medications while rejected Internet pharmacies. Respondents were asked to evaluate nine statements regarding the potential benefits and disadvantages about the online medicine purchase, and based on the computed relative attitude rate there is a weak still significant tendency toward rejection (p<0,01). Correspondence of demographic factors, internet usage behavior and prospective online drug purchase attitude was evaluated. Respondents who use the internet more and purchase goods online will more likely to buy medications online. Further, younger age and higher educational level will determine the medication purchase behavior.

Conclusions:
Reasonable number of patients will purchase medications on the Internet in the near future. As illegitimate actors dominate the global online pharmacy market, there is an increased risk of patients buying products from illegal actors. Consequently, improved patient-provider communication and promotion campaigns are needed to inform the public on the safe use of Internet pharmacies, as these initiatives can directly prevent patient safety threats.
Introduction
The Internet market of pharmaceuticals
The Internet has revolutionized and changed our lives, communication and procurement practices and strategies [1]. As the access to the Internet is increasing, the use of Internet to seek health information is also expending. Regarding to estimations worldwide approximately 4.5% of all Internet searches are linked to health-related question or information [2]. Population based surveys found in the U.S. that 72% of the online population, while in Europe 71% of Internet users searched for health information at least once in the previous 12 months [3] [4] [5]. These tendencies are further prospered by mobile devices [6]. However, consumers turn to the Internet today for not only just retrieving health information but to self-diagnose and obtain various health services or products [7] [8].

According to an early definition by Fung et al, an online pharmacy is an internet-based vendor (legal or illegal) that sells medicines and may operate as an independent Internet-only site, online branch of “brick-and-mortar” pharmacy, or sites representing partnership among pharmacies [9]. Briefly, an online pharmacy is a website that offers to deliver, distribute, or dispense medications on the Internet direct to consumers [10] [11]. The growing market of online pharmacies is facilitated by the rapid expansion of the Internet, the growing ubiquity of digital health, the shift towards self-diagnosing from the direct doctor-patient relations, consumer experience in online purchases, and the ease of mail order trade and distance selling [12] [13].

Internet supply of pharmaceuticals has developed in numerous ways and according to different models in each part of the world due to diverse regulatory, economic and cultural environments. In the United States the Internet pharmacy market is mainly prescription based, while in Europe this segment is forming according to a non-prescription based model [14]. As Internet pharmacies can be accessed globally, thus the legislative and economic perspectives should be considered in every country worldwide. Therefore, online pharmacies generate regulatory confusion as pharmaceuticals and health services "move" between jurisdictional boundaries and both the country of operation and the country of delivery must be evaluated [15]. While the country of operation determines the licensing requirements and the quality assurance standards for the practice of Internet selling of medications, mail order must be performed in accordance to the latter. However, as many illegitimate websites are
unwilling to indicate their real-world location, one cannot be sure of the regulatory framework under which the Internet pharmacy is operating [15]. It is further complicated by the fact that national authorities are typically powerless outside their own borders [16] [17]. There are several patient safety risks linked to the online purchase of medicines outside the traditional supply chain including counterfeit medications. The proportion of counterfeit medicines is estimated to be 10% worldwide [18] ranging from less than 1% in the developed countries [19] to over 30% in developing countries such as Africa, Asia, India and Latin America [20] [21].

According to the survey of the National Association of Boards of Pharmacy (NABP) in 2017, the 95.7% of 11 749 online pharmacies were noncompliant with the U.S. legislation and standards (in 2013. it was 97%) [22] [23]. These sites are listed as Not Recommended in the “Initiatives” section of the NABP website, www.nabp.pharmacy. Of the websites identified as Not Recommended, the majority were found to be dispensing prescription drugs without a valid prescription [22]. In 2016, based on industry data (LegitScript), there were 30 000 to 35 000 illicit online pharmacies on the web and most of them (approximately 92%) offered drugs without prescription. 82% operated in English, 9% in Japanese, 3% in Chinese and 2.4% in Russian, and it is notable that roughly 10-15% of the internet pharmacies changed their language based on the visitor’s geolocation. The risk of obtaining illegitimate medications online is increasing on a daily basis as it is estimated that about 20 illicit online pharmacies are created each day [24]. Also it is worrying that 9-10% of the vendors were selling controlled substances without any regulatory overview and prescription requirement. Notably these numbers reflect website numbers and not sellers, as actors operate multiple websites and approximately the number of the primary actors varies between 2000 and 3500 [24].

Illegal actors primarily focus on the uncontrolled sale of prescription drugs outside the regulated drug supply system [25]. Their marketing strategy include emphasizing the most commonly referred benefits of online pharmacies (convenience, speed, discounts, privacy, not visiting the physician, bulk orders and discounts, bonus medicines as gift, etc.) and holding back information regarding adverse-effects, contraindications and drug interactions [21]. Pricing strategies include extra price for prescription only medicines without
prescription, decreased unit cost with larger quantities ordered, promotion of unknown cheaper generics/brands from developing countries [25] [26] [27].

It can be said that almost every therapeutic category of drugs is available through the Internet. Not only the performance and image-enhancing and “lifestyle drugs” [28] [29] such as PDE-5 inhibitors [30] [31] [32] or anti-baldness products [33], but life-saving medicines (e.g. from the WHO Essential Medicines List), analgesics (NSAID, opioids) [34] [35], psychiatric- [36], obesity- [37] [38], and cardiologic drugs [18] can be freely purchased over the Internet. Further patient safety and public health concerns are raised by the online marketing of infectology and oncology drugs arising from the threat of trans border spread of infectious diseases, growing antimicrobial resistance and possible safety issues (e.g.: cytotoxic drug contamination) [39] [38] [40] [41] [42]. Offered drug categories include original, generic, illegal generic and biological or biosimilar pharmaceuticals (such as vaccines, heparin, bevacizumab [18] [40] [43] [44], etc.). And not just approved products, but candidates awaiting marketing authorization [12] [13] and even medications recalled from the market [45] can be purchased by patients. Shortage drugs (biologics and non-biologicals) are also available for patients or health professionals on the Internet and advertised as over-the-counter preparations [42] [12] [46]. The illegal Internet marketing and counterfeiting of health products is even more complicated when further product categories such as herbal products and dietary supplements are taken into consideration. Beside the lack of evidence regarding efficacy, their quality and safety can be compromised originating from batch-to-batch variability, contamination or adulteration [47]. The number of herbal remedies and dietary supplements adulterated with active pharmaceutical ingredients is increasing [33] [48].

The main characteristics of this illegal market segment consist of trading of seemingly identical products in an uncontrolled environment with no restrictions on the consumers (e.g.: no pricing and advertisement practice, people under 18 can also purchase medications via the Internet) or on products (larger quantities can be purchased) from a large amount of virtual supply [21] [49] [18] [50].

**Consumers purchasing medicines online**

During the past two decades Internet has become an accepted way to purchase medications due to its convenience, the potential to save money and privacy. Early reports on the use of
the Internet for purchasing drugs indicate that the practical reality of obtaining prescriptions or purchasing prescription drugs online is very small [51]. However, by the end of the 2010s reports show that the use of Internet pharmacies and the number of people obtaining medications and other health products online is constantly increasing [52]. According to several surveys the percentage of people purchasing medicines online varies as-published data differs due to type of product, sample population, education and income or substance abuse status [12] [10]. Thus, the authors aimed to summarize previously published data and key findings on patients procuring medications and health products on the Web and perceptions on Internet pharmacies.

In **Table 1** the authors summarize recent scientific on online medication purchasing of the general population published between 2012-2017. Accordingly, it does not contain data presented previously in a systematic review by Orizio G [10]. In addition, of surveys focusing solely on online/mail order pharmacy users, prescription drugs’ customers and patients participating in prescription refill programs. Questionnaires from small sample size or specific patient groups (e.g. drug abusers, people buying illegal drugs, men obtaining phosphodiesterase-5 inhibitors, etc.) are excluded. Further, non-peer reviewed publications and estimates are not indicated either to eliminate bias. Studies not representing the current web used by the general population (e.g. early reports and studies focusing on the dark web) are also not summarized. It must be noted, that differentiation of actual product categories purchased online is rather difficult, as approved medicines, medicinal products and dietary supplements are often measured as a single category in articles evaluating consumers buying from online pharmacies.
Table 1. Summary of selected recent studies on the prevalence of purchasing drugs and dietary supplements online

<table>
<thead>
<tr>
<th>First author (year of publication)</th>
<th>Location (year of data collection)</th>
<th>Number of respondents</th>
<th>Sample population</th>
<th>Survey method</th>
<th>Percentage of respondents purchasing health products (drugs and/or supplements) online</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abanmy N. (2017) [53]</td>
<td>Saudi Arabia (2013/14)</td>
<td>633</td>
<td>Random sample of Internet users</td>
<td>Online</td>
<td>2.7%</td>
</tr>
<tr>
<td>Desai K. (2015) [52]</td>
<td>USA (2007)</td>
<td>5074</td>
<td>Internet users</td>
<td>Data from HINTS national dataset</td>
<td>14.5%</td>
</tr>
<tr>
<td>Brown J. (2014) [56]</td>
<td>USA (2002/2010)</td>
<td>88 240</td>
<td>Noninstitutionalized individuals</td>
<td>Data from MEPS national dataset</td>
<td>0.5% prescription medication</td>
</tr>
<tr>
<td>Fittler A. (2013) [57]</td>
<td>Hungary (2010/2011)</td>
<td>422</td>
<td>Hospital patients</td>
<td>Personally administered</td>
<td>8.4%</td>
</tr>
<tr>
<td>Mazer M. (2012) [58]</td>
<td>USA (2007)</td>
<td>1657</td>
<td>Emergency department patients</td>
<td>Personally administered</td>
<td>5.4% medication</td>
</tr>
</tbody>
</table>
The number, attitude and characteristics of online pharmacy users have been studied by several authors. Despite the fact that Internet pharmacies are in business for nearly two decades, only limited scientific evidence has been published on the prevalence of online pharmacy use by the general population [54]. It must be noted, that in countries where the Internet pharmacy market is dominated by retail pharmacy chains selling prescription only medications and offering refill programs (e.g. US, UK, Germany), patient characteristics are different form nations where only non-prescription products can be marketed (e.g. central EU) through the Internet. As noted by numerous authors who have reviewed published data, it is most difficult to measure the number of online pharmacies and their customers – especially illegitimate ones [10]. Existing research only provides some estimates of the scale of online medicine purchasing [59].

A US survey in a cohort of 443 online pharmacy users representing an average of 1.5 million individuals per year, have found that compared with nonusers, online users were older, more likely to have private insurance, had more prescriptions, higher family income and education levels [56]. Atkinson found that age and marital status was associated with online buying [60]. Desai and colleagues have documented that about 14.5% of the US population used the internet to obtain medications or vitamins in 2007, individuals who buy medicines online are more often married, white, 50–64 years old with some college education and an income of $75,000 or more [52]. It should be noted that mail-order pharmacies are required by certain health plans in the United States which may result in higher number of patients using mail online pharmacies for maintenance medications [61] compared to other countries. A Hungarian survey among hospital patients has showed that 8.4% of the respondents ordered drugs or dietary supplements online and 3.7% of the respondents are considering this option in the future. Gender, age and educational profile did not significantly affected the experience in ordering health related products from the Internet [57]. An Italian study in involving more than 100 adult subjects investigated the use of the Internet for searching for information on medicines, dietary supplements and disease. Although 68.5% of the respondents were aware of the possibility to purchase medicines on the Internet only 9.2% of had a positive opinion about it. Interestingly, the number of participants with actual online medication purchase experience was not measured [62]. Mazer M. et al has found that among emergency department patients 57% reported awareness of online pharmacies and
5.4% used the Internet to order medications. Multiple medications and prescription plan significantly influenced online pharmacy use, while no difference in age or student status was observed between users and non-users [58]. A survey among Saudi citizens showed that the online purchase of medicines is not yet popular as 23.1% of the respondents were aware of the existence of Internet pharmacies and only 2.7% had bought medicines online. However, satisfaction level was high among those who had such experience, and a good number of respondents (42.7%) indicated that they are willing to try an online pharmacy in the future [53]. Similar results were reported by Alfaahad NF. in the kingdom, as clear majority of the Saudi respondents have not heard about online pharmacies (82.6%) and very few (1.4%) have purchased medicinal product online, however about two third (66.4%) were enthusiastic to utilize the online options of purchasing medicines [54]. On the other hand, a Romanian survey found that only minority (3.2%) of the respondents have not heard of the possibility of purchasing medicines online, 8.3% already purchased, moreover 7.1% intended to do so in the near future [55].

A systematic review by Orizio G. et al investigated available evidence on online pharmacies and summarized 15 articles published between 2003-2010. The authors summarized population surveys on consumers and their perceptions and attitudes, but could not find coherent information on the number of consumers and their characteristics [10]. According to another review by Orsolini L. a range of variables must be taken into account in profiling online pharmacy customers. Most online customers were reported to be young, Caucasian, people without any health insurance, however there are variations in gender and age depending on the type of medication purchased. Women and people with higher levels of education were associated with online search of health-related information, conversely subjects with low literacy level are prone to make purchase from illegal websites [63].

The above studies provide important clues into what types of patients or consumers may be more likely to buy products from online pharmacies. At the same time, we must admit that it is rather difficult to profile a “typical online pharmacy customer” as users are just as diverse as the medications they are looking for [12]. The authors of the current study have identified a knowledge deficit and lack of scientific evidence regarding studies on patients’ attitudes towards Internet pharmacies. Further, we believe that such scientific evidence is necessary to
plan, implement and evaluate prevention campaigns aiming to facilitate the safety of the online pharmaceutical market.

**Aims**
Our work aims to describe online medication purchasing behaviors, attitudes and demographics predicting willingness to buy medications for personal use in a nationally representative sample of outpatients in the Southern Transdanubian region of Hungary. Motivations for using Internet pharmacies and factors associated with buying healthcare products online are also evaluated. A complex methodology called *Risk Based Safety Mapping of Online Pharmaceutical Market* has been developed earlier by our research group and published in 2017 [27] to evaluate patient safety threats. The aim of our current study is to evaluate actual patient safety risk in outpatient setting and integrate this data into our methodology. Furthermore, we aimed to estimate patient safety risks in the drug supply- and healthcare system.

**Methods**
In our cross sectional explorative study a personally administered survey was used. The characteristics and background of the respondents were measured through the following independent variables: gender, age, education level, place of residency, average income, internet usage, online purchase habits in general, self-reported health status.

A Hungarian language questionnaire was developed by the authors (FA, VRGy pharmacists and KM psychologist) for this study based on previous research [57] and a preceding pilot study. In the online pilot study open questions were used, covering the topics of the study questionnaire to map the general attitudes of the prospective sample. In the main study data were collected directly from Hungarian citizens from Southern Transdanubian region who have used outpatient health service for chronic or acute conditions between January and March 2018. Participants were considered eligible if they were of age 16 years or older, while were excluded if they were unwilling to participate in the survey.

Trained research associates administered the 28 item questionnaire compromising of an introductory paragraph on the aims of the survey, information on confidentiality and anonymity followed by five main sections: Evaluation of channels available for procuring
medications; Online medicine purchase experiences and attitude; Internet use; Health status and medication use; Demographics. The study protocol was approved by the institutional review board (approval number: 6835). 5-point Likert-type scales, multiple-response and multiple-choice option questions were used. The English translated version of questionnaire (Multimedia Appendix 1) and original Hungarian version (Multimedia Appendix 2) are provided as supplementary material. Statistical analyses were conducted using SPSS version 22. Descriptive statistics was used to describe respondent characteristics.

Results
Respondent characteristics
A total of 1366 patients were approached by our trained research associates and 1055 surveys were completed (response rate 77.2%). See patient characteristics in Table 2. The distribution of female and male respondents was nearly equal. Our sample consisted of people obtaining outpatient health service for chronic or acute conditions, thus it represents patients rather than the general population regarding age and number of medications used. Mean age was 45 years, standard deviation ± 17.36 years. Nearly half (43.2%) of the respondents reported to have chronic health conditions and majority took at least one medication regularly.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of respondents</td>
<td>1055</td>
</tr>
<tr>
<td>Age (years)</td>
<td>mean ±SD 45.08 ± 17.36</td>
</tr>
<tr>
<td></td>
<td>min. – max. 16 - 89</td>
</tr>
<tr>
<td></td>
<td>median 45</td>
</tr>
<tr>
<td>Gender</td>
<td>516 male, 539 female</td>
</tr>
<tr>
<td>Education</td>
<td>primary school completed 68 (6.4%)</td>
</tr>
<tr>
<td></td>
<td>high school graduation 656 (62.2%)</td>
</tr>
<tr>
<td></td>
<td>college or University graduation 329 (31.2)</td>
</tr>
<tr>
<td></td>
<td>college+ (PhD, DLA) 2 (0.2%)</td>
</tr>
<tr>
<td>Patients with chronic conditions</td>
<td>456 (43.2%)</td>
</tr>
<tr>
<td>Number of regular medications per patient</td>
<td>mean ± SD 1.55 ± 2.63</td>
</tr>
<tr>
<td></td>
<td>min – max 0 - 25</td>
</tr>
<tr>
<td>Frequency of Internet use</td>
<td></td>
</tr>
</tbody>
</table>
Our survey sample represents the Hungarian society regarding level of education [64]. According to recent statistics 72% of individuals in the EU-28 accessed the internet on a daily basis, while 57% of Europeans (aged 16 to 74 in) ordered or bought goods or services over the Internet for private use. Accordingly, our sample represents European population for Internet use and online purchases [65].

**Evaluation of supply chain retail channels, previous and prospective purchases**

Attitudes towards the three main supply chain retail participants (conventional community pharmacy units, non-pharmacy units and internet pharmacies) of medications were evaluated. The respondents were asked to rate pharmacies, non-pharmacy units (e.g. petrol stations) and Internet sources on a 5-points Likert scale. They had to express, that according to their opinion how appropriate, are these sources for medication purchase. 1 stood for "not appropriate at all" and 5 for "totally appropriate". A Repeated Measures ANOVA was conducted on the sample, and significant differences were found. The respondents accepted retail pharmacy units as the most appropriate source of medications while showed neutral attitudes toward non-pharmacy units and rejected Internet pharmacies (F(1.951,2056.656)=1776.775 p<0.01)

**Table 3. Attitudes towards the three main supply chain retail channels on a 5-points Likert scale (1 not appropriate at all, 5 totally appropriate)**

<table>
<thead>
<tr>
<th></th>
<th>Mean</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pharmacy</td>
<td>4.79</td>
<td>0.53</td>
</tr>
<tr>
<td>Non-Pharmacy Units</td>
<td>2.94</td>
<td>1.38</td>
</tr>
<tr>
<td>Internet</td>
<td>2.25</td>
<td>1.42</td>
</tr>
</tbody>
</table>

According to our results 82.7% of the respondents (n=872) were aware that medications can be obtained online, while only 4.17% (n=44) used the Internet for medication purchase at least once. However, this number is likely to increase in the future as numerous patients
were open to prospective online purchases, 9.5% (n=100) stated they were very likely and further 13.8% (n=146) noted they are likely to buy medications online in the future.

**Perceived benefits and disadvantages**
To measure the factors influencing the attitudes toward online medication purchase, nine statements regarding the potential benefits and disadvantages were measured respectively based on the results of the pilot study. The respondents were asked to evaluate each statement (Table 4) on potential benefits and disadvantages regarding their own attitudes on a 5-points Likert scale. 1 stood for “I don't agree” and 5 for “I agree”.
Table 4. Comparative evaluation of potential benefits and disadvantages of online drug shopping.

<table>
<thead>
<tr>
<th>Potential Benefits</th>
<th>Mean Evaluation</th>
<th>SD</th>
<th>Potential Disadvantages</th>
<th>Mean Evaluation</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Convenient</td>
<td>4.29</td>
<td>1.07</td>
<td>It is easier to abuse preparations</td>
<td>4.24</td>
<td>1.13</td>
</tr>
<tr>
<td>People who can't get to a pharmacy can also purchase</td>
<td>4.18</td>
<td>1.11</td>
<td>There is no control, so I can get products that I don't need or worsen my condition</td>
<td>4.22</td>
<td>1.06</td>
</tr>
<tr>
<td>People who can't get to a pharmacy can also purchase</td>
<td>4.1</td>
<td>1.19</td>
<td>I do not get proper information regarding the use of the products</td>
<td>3.86</td>
<td>1.06</td>
</tr>
<tr>
<td>People who can't get to a pharmacy can also purchase</td>
<td>3.34</td>
<td>1.43</td>
<td>Because of the delivery time, I'm getting the drug later compared to a pharmacy</td>
<td>3.80</td>
<td>1.15</td>
</tr>
<tr>
<td>Fast</td>
<td>3.71</td>
<td>1.29</td>
<td>The source of the product is not reliable</td>
<td>3.78</td>
<td>1.27</td>
</tr>
<tr>
<td>Products can be compared faster and more easily</td>
<td>3.15</td>
<td>1.34</td>
<td>It is hard for me to choose between the great numbers of products</td>
<td>3.70</td>
<td>1.25</td>
</tr>
<tr>
<td>Products can be compared faster and more easily</td>
<td>2.87</td>
<td>1.21</td>
<td>I don't get the right product</td>
<td>3.65</td>
<td>1.31</td>
</tr>
<tr>
<td>Products can be compared faster and more easily</td>
<td>2.85</td>
<td>1.43</td>
<td>I get counterfeit medicine</td>
<td>3.61</td>
<td>1.25</td>
</tr>
<tr>
<td>Products can be compared faster and more easily</td>
<td>2.23</td>
<td>1.19</td>
<td>The quality of the product is lower compared than in local pharmacies</td>
<td>3.20</td>
<td>1.29</td>
</tr>
</tbody>
</table>

The attitude reactions about the online medicine purchase was weighted and a relative attitude rate was computed (Mean= -0.37 SD=1.2). There is a weak still significant tendency toward rejection (t(1054)=9.642 p<0.01). Our results showed that even there are several factors that are positively influencing the respondents' attitude toward online medication purchase they still tend to reject this source of drug acquisition. Linear regression analysis was conducted to measure the predictive power of the reported attitudes on willingness to purchase medication online. Our results showed that the attitudes have significant predictive power (F(2,1054)=224.87 p<0.01 $R^2=0.299$).
Attitudes towards prospective online purchases

Our study could not prove clear association with buying medications online due to the small ratio of respondents with previous purchasing experience. However, we could evaluate willingness to buy medications on the Internet. The correspondence of demographic factors, internet usage behavior and prospective online drug purchase attitude was examined. Correlation analysis was conducted. Significant correlation was found between age, average time spent on Internet, Internet purchase in general, settlement size, and education level.

Table 5. Correspondence of demographic factors, internet usage behavior and prospective online drug purchase attitude

<table>
<thead>
<tr>
<th>Age</th>
<th>Average time spent on the Internet</th>
<th>Internet purchase frequency in general</th>
<th>Settlement size</th>
<th>Educational level</th>
<th>Average income</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prospective online medication purchase attitude</td>
<td>-0.278</td>
<td>0.308</td>
<td>0.374</td>
<td>0.066</td>
<td>0.195</td>
</tr>
</tbody>
</table>

Linear regression analysis was conducted with stepwise method to measure the effect of correlating factors on willingness to purchase medications online. According to our results the factor of Internet purchase in general, education level and age together will predict the attitude toward online medications purchase ($F(3,1053)=65.83 \ p<0.01 \ R^2=0.158$). Further Linear Regression Analysis was conducted to determine the predicting factors of online purchase behavior in general. Our results showed that general online purchase is determined by the time spent on the Internet, age and educational level ($F(3,1053)=292.35 \ p<0.01 \ R^2=0.455$), and time spent on the Internet is highly determined by age and education level ($F(2,1053)=445.13 \ p<0.01 \ R^2=0.459$). Based on our results an explanation model was developed. According to our results attitude toward online medication purchase can be explained by the factor of general online purchase behavior, which is determined by the time spent on the Internet, which has a strong correspondence to age. The educational level will predict all the other factors and through this have a general impact on online medication purchase attitude.
As our current paper focuses on patient attitudes towards the online pharmacy market and willingness to buy medications from the Internet, results regarding the online purchase of dietary supplements, patient health status and self-medication will be discussed in a succeeding publication.

**Discussion**

**Principal Results**

Patients’ attitude towards online pharmacies and purchasing health products on the Internet is a key element of maintaining the integrity of the medication supply chain and protecting patients from digital iatrogenesis [66]. Policy makers and authorities must be aware that medications are different from most items purchased on the Internet as they directly have an impact on one’s health [52].

Users of online pharmacies, whether legitimate sites or not, are purchasing medications used for both acute and chronic conditions, as well as common medications of abuse. Without appropriate advice and the supervision of the medical doctor or the pharmacist, all drugs (prescription only and over the counter) and even dietary-supplements can cause harm. Main concerns are insufficient or incorrect information about patient’s health status and medications, inappropriate self-diagnosis or incomplete management of drug related issues such as polypharmacy, therapeutic duplications, adverse events and drug-drug or drug-herbal interactions [58]. It is obvious that illegitimate online pharmacies pose a clear danger by marketing counterfeit medications or substandard products. However, even legitimate actors may have issues associated with their use [52].

Given the variable quality of Internet pharmacies it is critical to identify vulnerable patients and develop targeted campaigns to inform them. Our results may support the development of patient centered interventions by identifying consumer characteristics associated with willingness to buy medications online.

Majority (82.7%) of the respondents were aware that medications can be obtained online. In our study sample 4.17% of the respondents have used the Internet for purchasing medications previously, and this number is likely to increase in the future as numerous patients were likely to buy medications online in the future (23.3%). Attitudes towards the three main supply chain retail channels showed that respondents accepted community pharmacy units as the most appropriate source of medications while showed neutral
attitudes toward non-pharmacy units and rejected Internet pharmacies. The comparative evaluation of potential benefits and disadvantages of online drug shopping showed that even there are several factors that are positively influencing the respondents’ attitude toward online medication purchase (e.g. convenience, people who can’t get to a pharmacy can also purchase products, purchase medicines after opening hours) they still tend to reject this source of drug acquisition. Seemingly Hungarian patients are not yet open towards online medication purchase, but based on our findings attitudes will likely change in the near future as more people gain experience in buying products or services online.

Based on our results the main factors influencing the willingness toward online medication purchase was determined. We found that Internet usage and online purchase behavior in general will predict the attitude toward online medication purchase. It means that the respondents who use the Internet more and purchase goods online will more likely to buy medications online. These two factors are highly influenced by the age, meaning that the younger generation is much more involved in the online market. Beside these results, educational level and attitude will determine the medication purchase behavior. People holding higher level degrees and having more positive attitude about online medication purchase are more likely to do so. The attitude ratings are also related to age mostly in aspects of benefits (r=0.23). Based on these data we think that online medication purchase is not an isolated phenomenon but highly integrated in the behavioral tendency that people try to manage more and more things online. Being this a general tendency in the society, we think that efforts against online medication purchase in general is worthless, but it would be highly important to develop stronger control over online pharmacies and provide education about the responsible Internet purchase behavior.

As previous authors have noted, we must further emphasize the opportunity for health providers (general practitioners, pharmacists, nurses) to help patients navigate Internet purchase to prevent medication incidents caused by the use of unapproved and illegitimate online pharmacies [52] [57].

Strengths and Limitations

In our study the potential misunderstanding of the survey questionnaire was eliminated by the personally administered survey and the trained research associates. Compared to numerous previous studies our method made it possible to identify the two seemingly
similar, however actually different product categories (medications and dietary supplements) separately as in the beginning of the survey the special attributes of medications were measured and discussed for future reference. In our sample we gathered results from a balanced respondent population, representing the patient population regarding age and the general population regarding gender and education level. Previously published survey results of online consumers may not reflect the prevalence and the attitude of the general population as Internet use is strongly related to several demographic variables. Accordingly, by using personally administered questionnaires our study eliminates such bias.

The authors are aware that the study has limitations. Online pharmacy use was self-reported and therefore subject to recall bias and untruthful reporting by the individual that may underestimate actual prevalence. Legitimate and illegitimate actors are not differentiated in our study, particularly because customers may be misled by online sellers or not be able to differentiate them objectively [12] [67]. Our study was performed in hospitals, general practitioners’ offices and community pharmacies in Southern Hungary, consequently it represents the national patient population, not all the Hungarian population. However, this can be considered as a potential strength, as patients are more likely to buy medications and they are also vulnerable to the potential dangers associated with Internet pharmacies. Prevalence and attitudes of inpatients were measured and published previously by the Authors [57].
Conclusions

Our results support our previous hypothesis that the use of the Internet to purchase medications is present and national results are in correlation with international data. Despite a weak, still significant tendency toward rejection toward online pharmacies were identified, reasonable number of patients were planning to purchase medications on the Internet in the near future.

We aimed to identify drivers to online medication purchasing in order to develop targeted campaigns informing vulnerable patients. Based on the literature review and our study results it must be noted that it is rather difficult to profile consumers turning to the Internet pharmacy market as users are probably just as diverse as the treatments they are looking for. However, following the evaluation of prospective online drug purchase attitude we came to the conclusion that respondents who use the Internet more and purchase goods online will more likely to buy medications online. Further, younger age and higher educational level will also determine the medication purchase behavior. Our results can support educational interventions promoting safe online medication procuring practices and provide valuable data on patients’ attitudes.

More national and international surveys are required to document online pharmacy penetration and the types of online pharmacies used. Furthermore, there is a need to better understand consumers that purchase medications from the web. It is highly recommended for the participants of the healthcare system - both in institutional and outpatient setting - to start documenting procurement information during the medical anamnesis of patients. This way more robust and informative data will be available on the penetration of this relatively novel distribution channel of the drug supply system.

Further research should also focus on exploring adverse effects resulting from medications purchased online. New emerging technologies, such as machine learning algorithms applied to Big Data is the basis for a new research area known as “digital” surveillance or “infoveillance” [68]. Accordingly, actual patient safety risk in outpatient can be identified (a) within the healthcare system by collecting data obtained during medical anamnesis or by the evaluation of patient records; or (b) online by novel data-science methods. Authors aim to integrate these pharmacovigilance and infoveillance techniques into their complex methodology called Risk Based Safety Mapping of Online Pharmaceutical Market [27].
Consumers use search engines to find health related information. And although they were not necessarily looking to purchase medications, they are offered prescription drugs, exposed to advertisements, and given links to online sellers of medications [67] [59]. As illegitimate actors dominate the global online pharmacy market, there is an increased risk of patients buying products from illegal actors and consuming dietary supplements or potentially counterfeit medications. The Internet has created new opportunities for the management of potentially deviant behavior and made it easy for consumers to ignore medicine legislation and bypass risk concerns. However, it is not the individual consumer who is the problem as the threat appears intrinsic to the Web itself [59].

Improved patient-provider communication, promotion and education campaigns are needed to inform the public on the safe use of Internet pharmacies, as these initiatives can prevent threats to patient safety. Targeted interventions by pharmacists (medication review or reconciliation, advice on how to evaluate online distributors and differentiate legal and illegal medication suppliers) are potential prevention strategies that must be emphasized more and implemented in everyday practice.

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Conflicts of Interest
None declared

Multimedia Appendix 1
English translated version of the questionnaire used in our study.
Multimedia Appendix 2
Original Hungarian version of the questionnaire used in our study.
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