

## ***Influenced and independent? Network Analysis of 39 Months of Prescription Medication Ads in Hungarian Medical Journals***

Zoltán Brys<sup>1</sup>, Gabriella Horváth<sup>2</sup>, György Tímár<sup>2</sup>, András Pluhár<sup>3</sup>

<sup>1</sup> Literatura Medica, Network Research Section

<sup>2</sup> COMFIT Ltd.

<sup>3</sup> University of Szeged, Institute of Informatics

**Prescription medications ad in medical journals are an important element of drug marketing, which is aiming to influence physician prescription behavior. Prescription medication marketing is a complex, sensitive and controversial ethical and legal question. Using quantitative and network analysis we examined the market of the prescription medication ads in Hungarian medical journals. The full dataset contained cumulated data from January, 01, 2010 to February, 28, 2013: 4413 promotional relationship between medicamentums (n=1642) and medical journals (m=99). The results of cluster analyses of the derived networks showed meaningful, real-life validated clusters. Yet regardless of the identified complex factors influencing this special market, various distributions of the dataset showed power law distribution, which suggested that regardless its auxiliary nature, media market of medical journals in Hungary acts as an independent market.**

### **BACKGROUND**

Promotion of the prescription medication in medical journals is influenced by various factors: (1) marketing lifecycle of the promoted medicamentum (Prajapati et al, 2012), (2) professional focus of the medical journal, (3) approvals and supports of medicamentums (health funds), (4) medical hierarchy, (5) publication ethics. Various legal regulations also have serious impact on this special market: (6) advertisement laws including the regulation of the medical sales representational and the prescription regulation of physicians, (7) cost-conscious legal environment. Business and organizational culture(s) also have subtle influence on this matter.

Albeit print ads are only one tool in the promotional arsenal of a certain medicine, according to Ladeira [1] the drug-related advertising still has strong effect on physicians prescribing behavior. Yet free medical samples [2], physician-salesperson relationship [3] bonuses, commissions, various incentives [2], educational materials and other tools are also seem to be effective and strongly present in the pharmaceutical marketing mix. Emergence of web-based technologies (on-line medical journals, medical databases, e-marketing and e-detailing) also directly affects the print ad market. The structural changes of healthcare (e.g. emerging practice-communities, role of heavy specialist prescribers

[4], changing role of Key/Clinical Opinion Leaders [5, 6], health-insurance policies also have a direct impact on the promotion in medical journals.

Legal issues of the pharmaceutical ads in medical journals are strongly intertwined with various debated question of medical publication ethics: (1) ghostwriting [7], (2) conflict of interest, (3) the publication of sponsored symposiums in medical journals (4) the pharmaceutical industry sponsored medical education [8]. Generally pharmaceutical ads in medical journals are part of the drug industry and physicians relationship issue [9]. Recent record hitting FDA fine [10] also called the attention on the role of medical journals and ads. Smith [11] even argues that medical journals are only an “arm” of pharmaceutical companies.

According to our null-hypotheses (1) market of the medical journal media spaces can not act as a fully independent market due to its supplementary nature, (2) in such a complex, multi-factorial and constantly changing environment, little regularity could be demonstrated. We have chosen a Hungarian dataset for analysis because of its (1) availability and (2) the scrutiny of the Hungarian legal environment (relating to Rx advertisement, specialist filtered prescribing rights, etc.) (3) changes of sick fund management and discovered medical frauds in the analyzed period [12].

### **DATASET**

COMFIT Ltd. has been following and recording certain data of the Hungarian medical journals since 2010. Using printed issues COMFIT records the name of the promoted medicamentums (mostly Rx), journal title, issue, dates of publications and various other data. COMFIT provided the following dataset: 39 months of cumulated data of pharmaceutical ad promotions. Dataset included: 99 medical journals, 1642 promoted medicamentums, 4413 promotional connection between medicamentums and journals. The medicamentum-journal connection contained the number of the ads placed in the journal [during 39 months] and also the list price of the ads. Anatomical Therapeutic Chemical Classification System (shortly ATC) codes were also added to medicamentums.

### **NETWORK ANALYSIS**

In order to prepare and clear the dataset for network analysis, we removed eleven (11) medical journals, those

who had less than 6 or more than 200 drugs promoted. Same way we removed medicamentums from the dataset promoted only in one medical journal (797 pcs) because these vertices and edges did not contain “network-wise” information. The cleaned dataset contained 843 medicamentums, 88 medical journals and 3421 promotional relationship between them.

Using the cleaned data, three graphs were derived:

- bipartite graph (shortly JM): where nodes were whether medicamentums or journals, and edges connect a medicamentum with a journal if an ad of a medicamentum was placed (at least once) in the specific medical journal.
- medicamentum-medicamentum, (shortly MM), is a non-bipartite graph, where nodes were medicamentums and an edge connects two medicamentums if their ads were commonly placed more than 5 medical journal,
- journal-journal, (or shortly JJ), is a non-bipartite graph, where nodes were journals, and edges connect two journal if they have at least 10 commonly promoted medicamentum.

Basic graph-parameters of the three networks are as shown in figure 1.

name of the graph/Network parameter	Number of nodes	Number of edges	Clustering coefficient	Diameter	Radius	Centralization	Density
JM	931	3241	0	7	4	0.179	0.007
MM	123	664	0.583	5	1	0.544	0.086
JJ	69	215	0.446	5	1	0.421	0.092

Figure 1 The basic network parameters of the derived graphs

Our zero hypotheses were that both the decision makers placing the ads of medicamentums, and the journals have their natural preferences in their selection. That is we expect more edges among same ATC first level coded medicamentums (hereafter ATC1), and also among journals that belong to the same segment. The ATC1 distribution of the drugs in the JM graph was dominated by cardiovascular system (21%), the detailed distribution is visible at figure 2. Via analyzing all of the drug-drug connection from ATC1 perspective we had found that 17% of the connections are con-

21,1% C	Cardiovascular system
12,5% A	Alimentary tract and metabolism
12,4% X*	Medical equipments*
11,5% T*	Dietary supplements, remedies*
7,8% N	Nervous system
5,8% R	Respiratory system
5,5% L	Antineoplastic and immunomodulating agents
5,2% J	Antiinfectives for systemic use
4,6% B	Blood and blood forming organs
3,5% G	Genito-urinary system and sex hormones
3,5% M	Musculo-skeletal system
2,7% null	non-specified
1,7% D	Dermatologicals
1,0% Z*	homeopathic medicine
0,6% V	Various
0,5% H	Systemic hormonal preparations, excluding sex hormones and insulins
0,1% P	Antiparasitic products, insecticides and repellents
0,0% S	Sensory organs

\*: extra codes, not part of the formal ATC

Figure 2 Distributive Percentages of the ATC1 codes of “M” nodes of JM bipartite graph)

necting similar ATC1 code drugs. In the MM graph we have also analyzed the percentage of the edges connecting similar ATC1 coded drugs and found that it is 57%. Both results support our hypothesis as both are way higher than chance. These results also indicated to run various cluster-analyses on the dataset.

The next main tool for this analysis was the exploration of the cluster structure. In that we used the clustering method described by Raghavan et al [13], which was implemented and visualized by the Sixte Network Software. We found that both MM and JJ exhibit clustering structure that might be attributed to a natural process based on shared information.

Using Sixte Network Software we identified 9 clusters and 4 components in the MM network. The biggest component mainly were composed out of C (Cardiovascular system, 46%) and A (Metabolism, 17%) ATC1 coded drugs. We detected 4 communities having more than 10 nodes and in all C ATC1 coded medicament were also dominant. Among the clusters we found one with R (Respiratory system) ATC1 coded dominant nodes (44% of total nodes), illustrated with figure 3, and also an L01 (Antineoplastic agents) ATC 2nd level dominant cluster. Markov-Chain clustering done with Cytoscape [14] on the JJ network resulted in 4 clusters, clearly separating medical journals of oncology, pediatrics, pulmonology and internal medicine.

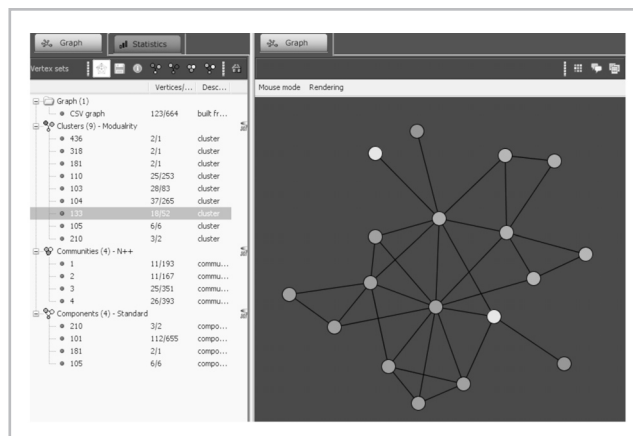


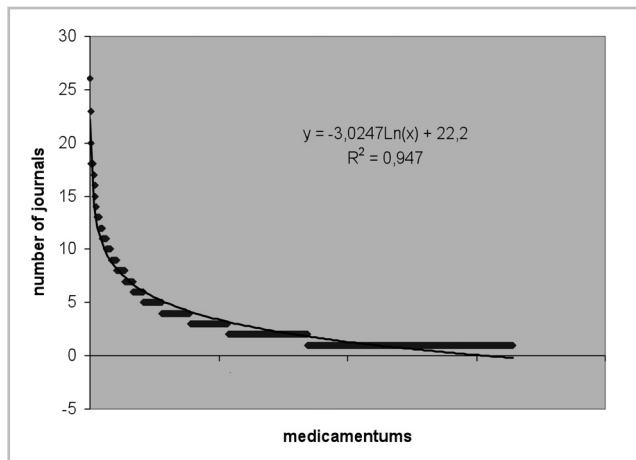
Figure 3 “R” cluster of the MM graph visualized with Sixte Network Software, each node represents a medication and an edge represents more than 5 common advertisement. Vertices (medicamentums) are colored by ATC1 code: dark Magenta = R ATC1.)

### SIMPLE DISTRIBUTION ANALYSIS

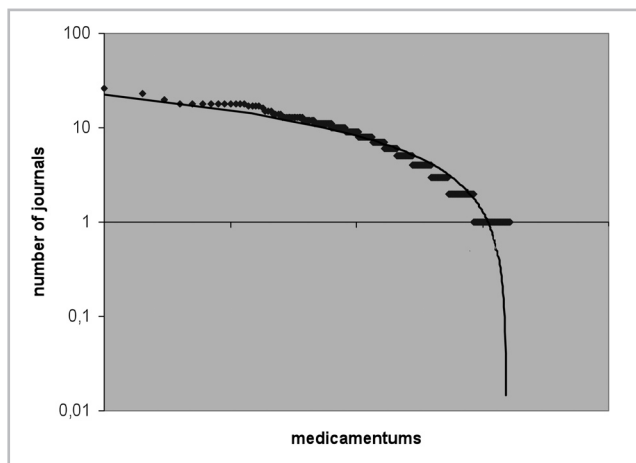
With good approximation ( $0,77 < R^2 < 0,95$ ) the following distributions can be described by a logarithmic density function:

- number of the journals (in which a medicamentum was promoted) per medicamentum  $R^2=0,947$  (figure 5 and 6)
- number of the ads per medicamentum  $R^2=0,877$

- cumulated value of list price of the ads per medicamentum  $R^2=0,812$
- number of the promoted drugs per medical journals  $R^2=0,884$
- number of the ads per medical journals  $R^2=0,822$
- cumulated value of the list price of the ads per journals  $R^2=0,773$

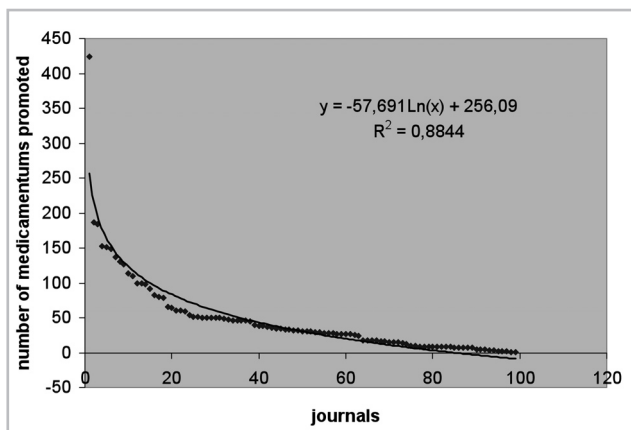


**Figure 4**  
distribution of the number of journals in which a medicamentum was promoted (per medicamentums)



**Figure 5**  
distribution of the number of journals in which a medicamentum was promoted (per medicamentums – with log axes)

The beginning of the figure 4 curve (number of journals in which a medicamentums was promoted) could be explained with the early lifecycle marketing of new medicamentums for the high prevalence somatic diseases (e.g. type 2



**Figure 6**  
Distribution of the number of promoted medicamentums per journal)

diabetes, cardiovascular diseases, etc.). The beginning of the figure 6 curve (Distribution of the number of promoted medicamentums per journals) might be interpreted or explained as a result of network effect (more frequented and influential medical journals can attract more advertiser). However neither the interest of pharmaceutical marketing, nor epidemiological factors can explain the very equable continuing parts of the exponential distributions.

## CONCLUSIONS

Based on our results we suggest that regardless the identified various and complex factors influencing media spaces market of the Hungarian medical journals, it acts as an independent market following the supply (reach of medical journals) and demand (influencing physicians behavior by pharmaceutical companies), and its structure is interpretable by network externality. However our results also propose further research on the subject, involving other data sources and specifically to analyze best-selling Rx medications and also medications with fraudulent history.

**Acknowledgement:** This work was partially supported by the European Union and the European Social Fund through project Telemedicina (Grant no.: TÁMOP-4.2.2. A-11/1/KONV-2012-0073). Authors thank to the team of Hungarian Academy of Science Research Center for Educational and Network Studies for their invitation and comments. First author also thanks to Bela Buda, whose guidance enabled deeper understanding of the subject.

## REFERENCES:

- [1] Ladeira W, Dalmar M, Maehler AE, Araujo CF, (2011) Drug prescription practices in Brazil: a structural equation model, International Journal of Pharmaceutical and Healthcare Marketing, Vol. 5 Iss: 4, pp.262 – 278
- [2] Al-Areefi MA, Hassali MA, Ibrahim MIBM (2012) A qualitative study exploring medical representatives' views on current drug promotion techniques in Yemen, Journal of Medical Marketing: Device, Diagnostic and

- Pharmaceutical Marketing August 2012 vol. 12 no. 3 143-149
- [3] Singh R (2008) Network Connectedness of Pharmaceutical Sales Rep (FLE)-Physician Dyad and Physician Prescription Behaviour: A Conceptual Model, Journal of Medical Marketing: Device, Diagnostic and Pharmaceutical Marketing, June 2008; vol. 8, 3: pp. 257-268.
- [4] FF Gönül, Carter FJ, (2012) Estimation of promotional strategies for newer vs older drugs based on physician prescribing data International Journal of Pharmaceutical and Healthcare Marketing, Vol. 6 Iss: 1, pp.39 – 54
- [5] Kroes M, Chmielarz P, Chandler L, Bergler M, Smith B(2011) Beyond KOL management: communities of practice as a new perspective on pharmaceutical market penetration, Journal of Medical Marketing: Device, Diagnostic and Pharmaceutical Marketing February 2011 vol. 11 no. 1 71-83
- [6] Borbas C, Morris N, McLaughlin B, Asinger R, Gobel F. (2000) The role of clinical opinion leaders in guideline implementation and quality improvement. Chest 2000 Aug;118(2 Suppl):24S-32S.
- [7] Tanne JH (2010) Most leading US medical schools lack rules on ghostwriting BMJ 2010;340:c799
- [8] Schneider N, Lückmann SL (2008) Pharmaceutical Industry Sponsored Medical Education, Zeitschrift für Allgemeinmedizin, 2008, vol. 84, no12, pp. 516-524
- [9] Goodle F (2009) Doctors, patients, and the drug industry, BMJ 2009;338:b463
- [10] Roehr B (2012) GlaxoSmithKline is fined record \$3bn in US. BMJ 2012;345:e4568 (Published 3 July 2012)
- [11] Smith R (2005) Medical Journals Are an Extension of the Marketing Arm of Pharmaceutical Companies. PLoS Med 2(5): e138. doi:10.1371/journal.pmed.0020138
- [12] MTI – Hungarian news agency (2012): Birságolt az OGYI a magyar orvos thaiföldi halála után (downloaded at 2012 from : <http://www.origo.hu/itthon/20110318-birsagolt-az-ogyi-a-magyar-orvos-thaifoldi-halalal-utan.html> )
- [13] Raghavan UN, Albert R, Kumara S (2007) Near linear time algorithm to detect community structures in large-scale networks, Phys Rev E 76 036106.
- [14] Smoot ME, Ono K, Ruscheinski J, Wang PL, Ideker T. (2011) Cytoscape 2.8: new features for data integration and network visualization Bioinformatics 2011 Feb 1;27(3):431-2. doi: 10.1093/bioinformatics/btq675. Epub 2010 Dec 12.
- [15] Newman MEJ (2005) Power laws, Pareto distributions and Zipf's law, Contemporary Physics, Vol. 46/5 (2005).
- [16] Prajapati, Dureja H (2012) Product lifecycle management in pharmaceuticals, Journal of Medical Marketing: Device, Diagnostic and Pharmaceutical Marketing August 2012 vol. 12 no. 3 150-158
- [17] Studdert MS, Mello MM, Brennan TA(2004) Financial Conflicts of Interest in Physicians' Relationships with the Pharmaceutical Industry — Self-Regulation in the Shadow of Federal Prosecution N Engl J Med 2004; 351:1891-1900

## A SZERZŐK BEMUTATÁSA



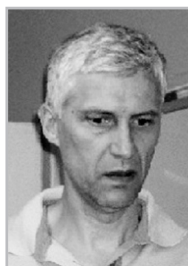
**Brys Zoltán** a Literatura Medica munkatársa, a hálózatelemzési rovat vezetője. Budapesti Műszaki és Gazdaságtudományi Egyetem Távközlési és Médiainformaticai Tanszék rendszeres vendégelőadója gráf-bányászat témakörében.



**Horváth Gabriella** 2010-ben végzett az ELTE pszichológia szakán, egészségpszichológia szakirányon. Kutatási területe a teljes gyógyszerhatás, ezen belül is a szuggesztíók és a betegtájékoztató vizsgálatok. 2014. márciusáig az orvosi médiafigyeléssel foglalkozó ComFit Kft. munkatársa volt.



**Dr. Tímár György** a Comfit Kft. ügyvezetője. Általános orvosi diplomát a Semmelweis Orvostudományi Egyetemen szerzett, dolgozott az egyetem Orvosi Biokémia Intézetében, valamint a Novartis Hungária Kft.-nél is. 2009-ben az ELTE-n Egészséggazdaságtani és egészségpolitikai diplomát szerzett.



**Pluhár András** docens a Szegedi Tudományegyetem Számítástudományi tanszékén. Kutatási területei: kombinatorika, gráfelmélet, kombinatorikus optimalizálás. Dolgozott az MTA Automataelméleti Kutató Csoportjánál, Rutgers Egyetemen és Cygron Kft.-nél.