PRIMARY NON-ADHERENCE TO PHARMACOTHERAPY AMONG PATIENTS WITH CHRONIC DISEASES: A RETROSPECTIVE STUDY OF SLOVAKIA

Primárna non-adherencia k farmakoterapii u pacientov s chronickými ochoreniami: retrospektívna štúdia zo Slovenska

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Abstract
Background. ePrescription enables to investigate primary non-adherence (PNA) to pharmacotherapy by studying the percentage of prescriptions which have been issued (a prescription record present) but not dispensed in a pharmacy (a dispensation record missing) out of a total number of registered prescriptions. Identification of non-adherence enables to analyze its causes and target them efficiently.
Methods. This retrospective epidemiological study investigates the PNA for prescriptions for the treatment of hypertension, diabetes mellitus and hypercholesterolemia (N=108 391) in 2018. Influence on two groups of variables on PNA: prescription-related (physicians specialities, therapeutic class of drug, number of packages and doses per prescription, co-payments and medication costs) and patient-related (geographic location, age, sex, cumulative co-payments and payment support scheme) was described using a multivariable logistic regression model.
Results. The PNA for ePrescriptions issued to patients with the above-mentioned chronic diseases reached 4.0%. PNA differs between payers (3.5%) and defaulters (41.1%) on health insurance. PNA also varies between GPs (3.7%) and other specialists (5.1 – 7.4%). Higher age and multiple chronic diseases, especially in the presence of hypertension, were associated with higher adherence (PNA under 4%). Co-payment per prescription was the most important predictor among the selected prescription-related variables. Prescriptions with a small co-payment (0.01 – 0.99€) had 53% higher odds of being claimed than prescriptions free of charge. Co-payments between 1 – 2.99€ had the same effect as no co-payment.
Conclusions. Patients with chronic diseases in Slovakia display a low rate of PNA. Higher age, presence of hypertension and access to reimbursement were associated with higher adherence. A small co-payment leads to increased odds of the drug to be claimed (Tab. 4, Ref. 20). *Text in PDF www.lekarsky.herba.sk.*
KEY WORDS: adherence, ePrescription, diabetes mellitus, initial medication adherence, hypercholesterolemia, hypertension, pharmacotherapy
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Abstrakt
Úvod do problematiky. Elektronický recept umožňuje skúmať primárnu non-adherenciu (PNA) k farmakoterapii skúmaním percenta receptov, ktoré boli vystavené (prítomný záznam o recepte), ale neboli vydané v lekárni (chýba záznam o výdaji) z celkového počtu registrovaných receptov. Identifikácia non-adherencie umožňuje analyzovať jej príčiny a účinne sa na ne zamerať.
Metódy. V tejto retrospektívnej epidemiologickej štúdii sa skúma miera PNA v prípade receptov vydaných pacientom na liečbu hypertenzie, diabetes mellitus a hypercholesterolémie (N = 108 391) v roku 2018. PNA bola skúmaná v súvislosti s dvoma skupinami premenných: premenné späté s predpisom (odbornosť lekára, terapeutická skupina lieku, počet balení a dávok na predpise, doplatok a cena lieku) a premenné späté s pacientom (bydlisko, vek, pohlavie, kumulatívne ročné doplatky, úhrada lieku z verejného zdravotného poistenia).
Výsledky. Miera PNA pri elektronických receptoch vystavených pacientom s uvedenými chronickými ochoreniami dosiahla 4,0 %. Výrazný rozdiel bol medzi PNA u platcov poistného (3,5 %) oproti neplatičom (41,1 %). Rozdiely v PNA boli pozorované aj medzi predpismi praktických lekárov (3,5 %) a špecialistov (5,1 – 7,4 %). Vek a výskyt viacerých chronických ochorení (najmä hypertenzie) bol spätý s vyššou adherenciou (PNA pod 4 %). Doplatok na recepte bol najdôležitejším prediktorom výberu receptu. Predpisy s malým doplatkom (0,01 – 0,99 €) mali o 53 % vyššiu šancu výberu ako predpisy bez doplatku. Predpisy s doplatkom 1 – 2,99 € mali rovnakú šancu výberu ako predpisy bez doplatku.
Závery. Pacienti s chronickými ochoreniami na Slovensku vykazujú nízku mieru PNA. Vyšší vek, hypertenzia a prístup k úhrade liekov z verejného zdravotného poistenia boli späté s vyššou adherenciou. Malý doplatok zvyšoval šance na výber konkrétneho lieku (tab. 4, lit. 20). *Text v PDF www.lekarsky.herba.sk.*
KĽÚČOVÉ SLOVÁ: adherencia, diabetes mellitus, elektronická preskripcia, , farmakoterapia, hypercholesterolémia, hypertenzia.
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Background

Per the World Health Organization (WHO), in developed nations, the adherence rate to long-term therapeutic regimens for chronic ailments is approximately 50% (1). Notably, a robust correlation exists between medication adherence and the mitigation of complication risks (2). Conversely, non-adherence augments the economic burden of healthcare for chronic conditions. The financial reprieve derived from diminished overall pharmacotherapy expenditure is often surpassed by incremental costs, which emanate from the complications consequential to lapses in chronic disease management (3, 4).

Primary Non-Adherence (PNA) is characterized as the inability to initiate a prescribed medication regimen due to non-collection of the medication. An analytical comparison of physicians' prescription archives with pharmacy dispensation records offers insights into the prevalence of PNA. Such an approach can explain variables like patient demographics, physician specialty, diagnostic patterns, medication types, financial considerations, and geographical determinants. Proactive detection of PNA fosters precision-targeted patient communication, and facilitates the clarification of underlying causative factors, thus enabling their correction (5).

The Medication Event Monitoring System (MEMS) is upheld as the benchmark methodology for ascertaining medication adherence (6). MEMS are instrumental devices that chronicle the temporal instances of medication container access. A prospective investigative endeavor in Spain evidenced that the ePrescription dispensation mechanism serves as an efficacious metric for gauging pharmacotherapy adherence, specifically within the hypertension spectrum (7). The referenced study undertook a comparative analysis of adherence metrics between ePrescriptions and MEMS over intervals of 6, 12, 18, and 24 months. The findings clarified a negligible variance between the adherence measurements ascertained via the two methodologies.

A comprehensive evaluation of ePrescription data from Poland indicated that the aggregate PNA index stood at 20.8%, representing 94,913 filled ePrescriptions from an aggregate of 119,880 (8). A discernible trend was observed wherein PNA diminished with increasing patient age, culminating in its nadir for the 75+ age demographic. Notably, in Poland, this demographic enjoys the privilege of complimentary access to specific medications, leading to a PNA rate for these particular medications that was inferior by 3 percentage points. In Hungary, between 2012-2015, the PNA for medications endorsed by general practitioners registered at 35.9%. Intriguingly, PNA exhibited a lesser prevalence within the 65+ age bracket compared to the 45-64 age category (37.9%) (5). Vulnerable demographic groups, endowed with reduced co-payment obligations, demonstrated a PNA rate of 21.7%. Elevated PNA rates were concomitant with urban locales, advanced educational abilities, and vacancies within general medical practices. A meta-analysis, encompassing seven distinct studies with a cumulative patient population of 200,000, deduced an 11% escalation in the PNA index among patient cohorts subjected to medication co-payments, juxtaposed against their non-co-payment counterparts (9).

The current investigative work was aimed to determine the PNA prevalence relating to prescriptions allocated to patients diagnosed with hypertension, diabetes mellitus, and hypercholesterolemia within Slovakia. This assessment will incorporate two groups of variables: prescription-related (physicians specialities, therapeutic class of drug, number of packages and doses per prescription, co-payments and medication costs) and patient-related (geographic location, age, sex, cumulative co-payments and payment support scheme)

Health system and pharmaceutical policy in Slovakia

In Slovakia, health insurance is mandatory: economically active policyholders are obliged to pay contributions to the public health insurance, while the state pays contributions for the economically inactive population (children, the unemployed, people living below the poverty line, people on maternity/paternity leave, pensioners). Policyholders are entitled to get categorized medications reimbursed; their price, the level of reimbursement and thence the level of the co-payment are determined by a regulator. By law, policyholders who default on their health insurance premium payments are not entitled for other than acute and emergency healthcare, and they must pay the full cost of medications prescribed for the treatment of chronic diseases (10). Maximum limits for co-payments are set by law specifically for children, severely disabled people, and pensioners. If the total sum of co-payments per quarter exceeds the specific limit given for a group of people, the health insurance company will reimburse the patient the amount overpaid. As of 01st January 2018, the limit is set at 30 €/quarter for pensioners, 12 €/quarter for severely disabled people and 10€/quarter for children under 6 years of age. It is the sum of the co-payments for the cheapest generic alternatives to the prescribed medications which is considered when assessing whether the maximum limit for the co-payment was reached.

Methodology

The study was designed as retrospective epidemiological study. The dataset comprises Dôvera health insurance company's records of healthcare provided to its policyholders (1 478 854 policyholders as of 01st January 2018, 28.7% share of the public health insurance market in Slovakia). Here, we studied the ratio of pharmacy dispensation records to physicians' prescription records in a sample of 108 391 patients with chronic diseases such as hypertension, diabetes mellitus and hypercholesterolemia in relation to the pharmacotherapy of these diseases. This ratio can be used to determine the PNA as follows:

$$PNA = \left(1 - \left(\frac{\sum dispensation\ records}{\sum prescription\ records}\right)\right) \times 100\ (\%)$$

The prescription always contains a single medication, only the number of doses and packages on the prescription can vary.

Classification of chronic-disease patients during the classification period (according to the use of medications in the previous one-year period 1/2017 – 12/2017 or else according to the diagnoses reported in the previous two-year period 1/2016 – 12/2017) is in Table 1.

Table 1. Classification of chronic-disease patients based on pharmacotherapy or diagnosis.
Tabuľka 1. Klasifikácia pacientov s chronickými chorobami na základe farmakoterapie alebo diagnózy.

	Based on pharmacotherapy		or	Based on diagnosis	
	Standard drug doses	*ATC class*		*Number of records*	*ICD - 10*
Arterial hypertension (AH)	121	C02, C03, C07, C08, C09	or	2	I10 - I13
Diabetes mellitus (DM)	1	A10A, A10B	or	2	E10, E11
Hypercholesterolemia (HCL)	121	C10	or	2	E78

Patients may have had multiple chronic diagnoses at the same time.

ePrescription during the reference period

In this study, we analysed ePrescription records from a 12-month period (1/2018 – 12/2018) with dispensation till 01/2019 for patients with the above-mentioned chronic diseases. All patients, that had any paper prescription for the treatment of AH, DM or HCL were excluded. 108 391 patients using exclusively e-Prescription were analysed. Out of these, 91 792 suffered from AH, 17 266 from DM and 40 585 from HCL. The patients may have suffered from more than one of these diseases. Medications for the treatment of hypertension, diabetes mellitus and/or hypercholesterolemia (see ATC groups from Table 1) were analysed.

In addition to univariate analyses, two models were evaluated, both using multivariate logistic regression.

Model 1 was prescription-centred. The odds of a given prescription being claimed was modelled based on:

- the therapeutic class of medication,
- the speciality of prescribing physician,
- the number of packages and doses per prescription,
- co-payment,
- the medication cost.

In the patient-level analysis, the PNA of each patient was calculated. A PNA threshold less than 20% was chosen, under which we considered the patient to be adherent.

Model 2 was patient-centred. The odds of a patient being adherent was modelled based on:

- sex,
- age group (under 40, 40-59, 60-79, 80 and more years of age),
- region,
- presence of chronic diseases (AH, DM, HCL and their combinations),
- total number of prescriptions,
- cumulative co-payment during the reference period,
- payment support scheme - health insurance premium payers are subject only to the co-payment for medications while defaulters are subject to the full cost of medications.

The importance of variables in both models was evaluated by the Akaike Information Criterion (AIC). The difference in AIC of the full model and the model with a given parameter excluded (Δ-AIC) was calculated for each parameter separately. A higher Δ-AIC indicates that the given parameter brings more information to the model.

Results

Patients with AH, DM and/or HCL who were given exclusively ePrescriptions for medication to treat these diseases (n=108 391) were during the reference period prescribed 888 128 ePrescriptions; out of which 852 849 (96.0%) were claimed in pharmacies (PNA for men: 4,1% (n=52 218), women 3,9% (n=56 173)). Demographic parameters of the sample are in the Table 2.

Table 2. Demographic parameters of the studied sample.
Tabuľka 2. Demografické parametre súboru pacientov.

Demografic parameter		# of patients
Sex	Male	52 218
	Female	56 173
Age	Under 40	5 135
	40 – 59	40 617
	60 – 79	55 808
	80 and more	6 831
Region	Abroad	112
	Banská Bystrica	16 566
	Bratislava	7 777
	Košice	20 776
	Nitra	21 843
	Prešov	14 932
	Trenčín	9 666
	Trnava	9 355
	Žilina	7 364
Chronic diseases	AH	59 108
	DM	3 642
	HCL	9 906
	AH+DM	5 056
	AH+HCL	22 111
	DM+HCL	3 051
	AH+DM+HCL	5 517

PNA varies across both prescriptions-related and patient-related parameters (Tab. 3 and 4). PNA decreased with age (8,7% in the under 40 years age group compared to 2,4% in the over 80 years age group). Patients had lower PNA when they suffered from multiple chronic diseases, especially when hypertension was present, PNA was under 4% (3,7% in the AH+DM, 3,4% in the AH+HLC and 3,3% in the AH+HCL+DM group). The biggest difference was between health insurance payers and defaulters, with PNA of 3,5% and 41,1%, respectively. Considering possible simultaneous impact of several factors affecting PNA, we supplemented the one-dimensional analysis with multidimensional analysis, using multivariate logistic regression models.

In model 1, the odds of a given prescription being claimed were calculated based on multiple prescription-related parameters (see Tab. 3). Among the four studied therapeutic classes, the prescriptions for insulins had the highest odds of being claimed, while other diabetic drugs (peroral antidiabetics) and lipid lowering drugs had the lowest odds. All specialist practices were associated with lower odds compared to general practitioners. Larger packages were associated with higher odds (3% increase in odds per 100 doses). Similarly, adding 1 more package to prescriptions was associated with a 27% increase in odds of claiming.

Prescription co-payment was the strongest predictor in the model. Interestingly, having to pay a small but some co-payment (0.01 – 0.99€) was associated with a 53% higher odds of claiming. A co-payment in the range of 1 – 2.99€ had the same effect as no co-payment. With further increases (>3€), the odds of claiming declined. Except for defaulters, most patients did not encounter the full cost of their medication since they pay only co-payments. Still, increased medication costs were associated with higher odds of claiming in all groups up to 30-39.99€. The likelihood of claiming prescriptions in this group was more than twice as high compared to the reference group (under 10€).

Since patients often had multiple prescriptions over the study period (8.2 in average), the PNA for each patient can be calculated. 82% (89 278) of patients had all their prescriptions claimed, i.e. their PNA equalled 0%. 11% (11 689) of patients were still considered adherent, despite not having claimed all their prescriptions (they claimed at least 80%). Only 7% (7 424) of chronic patients were considered non-adherent, with 5% (5 171)

Table 3. Prescription-centred model that estimates the odds of a prescription being claimed.
Tabuľka 3. Model zameraný na predpisy, ktorý odhaduje šance na výber predpisu.

AIC = 290085	# prescriptions	PNA	Odds ratio	95% conf. int.
Intercept			16.78	16.02 – 17.57
Therapeutic class	Δ-AIC = 156.75			
Hypertension	686 964	3.8	Reference	
Hypercholesterolemia	117 771	4.6	0.92	0.89 – 0.96
Insulins	19 186	3.9	1.59	1.43 – 1.77
Peroral antidiabetics	64 207	5.0	0.91	0.86 – 0.97
Physicians speciality	Δ-AIC = 703.6			
General practitioner	713 220	3.6	Reference	
Cardiology	27 079	5.6	0.69	0.65 – 0.73
Diabetology	75 609	5.2	0.64	0.61 – 0.68
Internal Medicine	67 061	5.1	0.73	0.7 – 0.76
Other speciality	5 159	7.4	0.50	0.45 – 0.55
Doses per package	Δ-AIC = 7.83		1.0003	1.0001 – 1.0006
Packages per prescription	Δ-AIC = 995.9		1.27	1.25 – 1.29
Co-payment	Δ-AIC = 4430.52			
without co-payment	115 309	3.5	Reference	
0.01 – 0.99€	179 937	2.7	1.53	1.46 – 1.6
1 – 2.99€	270 804	4.0	1.02	0.98 – 1.06
3 – 5.99€	186 364	4.2	0.78	0.74 – 0.81
6 – 9.99€	79 339	5.0	0.53	0.5 – 0.55
10 – 29.99€	54 935	5.9	0.36	0.34 – 0.39
30€ and more	1 440	37.2	0.044	0.039 – 0.05
Medication cost	Δ-AIC = 943.66			
Under 10€	520 067	4.0	Reference	
10 – 19.99€	245 698	3.6	1.51	1.47 – 1.56
20 – 29.99€	65 874	4	1.88	1.78 – 1.98
30 – 39.99€	17 853	4.2	2.10	1.93 – 2.29
more than 40€	38 636	5.1	1.63	1.52 – 1.75

of patients claiming 50 – 79% of their prescriptions and 2% (2 253) claiming less than 50%.

In Model 2 (see Tab. 4), the effect of multiple patient-related parameters on the odds of a patient being adherent (claiming at least 80% of prescriptions) was calculated. Female patients were slightly less adherent, but the result was not statistically significant. A strong predictive value for patient adherence was observed with increasing age, with the odds of being adherent being 1.4 times higher in the 40 – 59 years age group, 2.53 times higher in the 60 – 79 years age group and 3.43 times higher in the over 80 years age group, compared to patients under 40 years of age. The presence of AH appears to improve patient adherence, while DM and HCL exert the opposite effect. Their effects are cumulative, with the HCL+DM group having the lowest odds of being adherent. In the Slovak health insurance system, non-payment of insurance premium and consequent classification as a defaulter has a huge detrimental effect on patient adherence, with defaulters being more than 14 times less likely to be adherent, adjusted for their higher co-payments (median cumulative co-payments of 60€ compared to 28€ in the payer group). Compared to patients opting solely for medications without co-payments, paying patients have lower, but similar odds of being adherent across price groups. Cumulative co-payments were the least significant parameter (except for sex, which was not statistically significant), indicating that patients are not strongly influenced by their overall medication expenditure.

Table 4. Patient-centred model that estimates the odds of a patient being adherent.
Tabuľka 4. Model zameraný na pacienta, ktorý odhaduje šance, že pacient je adherentný.

AIC = 39285.20	# patients	PNA	% adherent	Odds ratio	95 % conf. int.
Intercept				6.79	5.35 – 8.64
Sex	Δ-AIC = 0.77				
Male	52 218	4.1	92.83	Reference	
Female	56 173	3.9	93.45	0.96	0.91 – 1.01
Age	Δ-AIC = 664.71				
Under 40	5 135	8.7	85.22	Reference	
40 – 59	40 617	5.8	90.47	1.40	1.28 – 1.54
60 – 79	55 808	3.0	95.37	2.53	2.29 – 2.78
More than 80	6 831	2.4	96.93	3.43	2.91 – 4.04
Payer status	Δ-AIC = 2377.91				
Payer	106 627	3.5	93.98	Reference	
Defaulter	1 764	41.1	43.25	0.07	0.06 – 0.07
Region	Δ-AIC = 39.79				
Banská Bystrica	16 566	4.2	92.86	Reference	
Abroad	112	8.5	86.61	0.45	0.27 – 0.82
Bratislava	7 777	4.1	92.53	1.08	0.97 – 1.2
Košice	20 776	4.1	92.89	1.00	0.92 – 1.08
Nitra	21 843	4.0	93.51	1.14	1.04 – 1.23
Prešov	14 932	3.4	94.04	1.28	1.17 – 1.41
Trenčín	9 666	3.6	93.82	1.20	1.08 – 1.33
Trnava	9 355	4.2	92.57	1.06	0.95 – 1.17
Žilina	7 364	4.1	92.27	1.01	0.91 – 1.13
Chronic diseases	Δ-AIC = 194.02				
AH+HCL+DM	5 517	3.3	95.83	Reference	
DM	3 642	6.0	88.77	0.78	0.65 – 0.94
AH	59 108	4.4	92.91	1.27	1.1 – 1.48
AH+DM	5 056	3.7	94.36	1.03	0.85 – 1.24
AH+HCL	22 111	3.4	94.94	1.21	1.04 – 1.41
HCL	9 906	5.0	90.43	0.82	0.69 – 0.96
HCL+DM	3 051	4.1	91.94	0.75	0.62 – 0.91
Total number of prescriptions	Δ-AIC = 258.27			1.05	1.04 – 1.06
Cumulative co-payments	Δ-AIC = 14.17				
No co-payment	3 048	3.0	94.36	Reference	
<10 €	35 859	3.8	92.18	0.72	0.61 – 0.84
10 – 19.99 €	22 527	3.6	93.27	0.73	0.62 – 0.86
20 – 29.99 €	12 943	3.8	93.70	0.72	0.6 – 0.85
30 – 99.99 €	30 309	3.0	94.03	0.69	0.59 – 0.82
>100 €	3 705	5.5	91.79	0.60	0.48 – 0.75

Discussion

In our study, which is the first of its kind in Slovakia after the launch of ePresctiption on January 1st 2018, we found out that the PNA among Slovak chronic patients (4%) was similar to figures reported in the literature (5.2% in Colorado, 2.4% in Sweden) (11,12). Multiple prescription-related and patient-related parameters that influence adherence were evaluated.

The decrease in PNA with age observed in Model 2 agrees well with previous studies, e.g., from Hungary or Poland (5,8). Pensioners tend to have a lower PNA which might be linked to the scheme according to which they are eligible for getting part of their co-payments for medications reimbursed.

In model 2, AH was associated with better adherence, compared with HCL and DM, similar to other literature (13). This effect was also examined in the first model. Although insulins had a higher probability of being claimed, they represent a smaller portion of the diabetic pharmacotherapy than per-oral antidiabetic drugs (PADs), which had lower adherence. Poor commitment to PAD treatment was also observed in the literature, where 54.8% of patients had low adherence on the Morisky medication adherence scale (14). Drugs for HCL had similar adherence to PADs.

While in the literature family practices and internists had similar levels of adherence, significantly higher than other specialists, in our study, general practitioners have more adherent patients than all specialities (including internists) (15). It should be noted that during the classification period in Slovakia, after examination done by a specialist, patients did not have to visit them repeatedly to have their medication prescribed, instead, they can visit their GP and receive the same prescriptions there. This way, patients are more likely to proactively demand their medication from the GP, leading to a lower PNA. Also, visiting a specialist more often results in a newly prescribed therapy, for which lower adherence was observed in the literature (15).

In the literature, 26% increase in the likelihood of being non-adherent was observed with 10$ increase in monthly co-payments (in case of oral antidiabetics) (16). This would correspond to an annual increase in co-payments of 120$ (~100€). Meanwhile in our study, the 3048 patients, who only picked the medication without co-payments, had the highest odds of being adherent. Annual cumulative co-payments in all groups up to 100€ decreased the odds of being adherent by 27 – 31%. The significance of cumulative co-payments was lower than the significance of the other variables in model 2. In contrast, in the prescription-centred analysis, co-payment was the strongest predictor in model 1. Having to pay some, but small (less than 1€) co-payment increased the odds of the prescription being claimed. This contrast indicates that patients perceive their prescriptions individually and are not significantly affected by increased cumulative co-payment. Reasonable co-payments, in addition to higher adherence, could bring eventually additional resources to the system, allowing, for example, the higher and quicker rate of the reimbursement of innovative drugs. The observed effect of medication costs on the odds of claiming probably acts only as a proxy for other variables, such as the necessity of a given medication for the patient's survival and wellbeing. A psychological effect could also come into play, "more expensive" is perceived as "better", "more effective", and may increase the motivation of patients to claim their prescription in a pharmacy (17). A similar effect could explain why medications with a low co-payment higher odds had of being claimed than medications free of charge.

Defaulters (patients obliged to pay the full cost of the medication) had high PNA. Given the impact on adherence (a more than 14-fold decrease in the odds of being adherent), it is debatable whether it is economically efficient to deny them access to their chronic disease treatment while at the same time covering the treatment of their acute complications which stem from neglecting the treatment of their chronic disease.

Patients with chronic diseases in Slovakia seem to adhere very well to pharmacotherapy. 93% of chronic patients in our study achieved an 80% adherence rate, which is commonly used in the literature as the threshold for good adherence (18). It is also higher than the reported 88%, 87% and 79% adherence to hypertensive, antidiabetic and dyslipidaemia medication respectively (13). This may be partly explained by the methodology applied in this study. In the administrative data of health insurance companies, diseases can be identified based on healthcare provision records: thus, a chronic-disease patient can be identified based on the healthcare provided within a certain time frame. It should be noted that only chronic-disease patients undergoing medical treatment were included in the analysis; patients who were not diagnosed or did not undergo medical treatment were not considered. In this study, we analysed only dispensation of issued prescriptions regardless of whether the medication dosing was adequate throughout the reference period. In case a patient missed a doctor's appointment and as a result of that was not given another prescription, the PNA was not affected. Meta-analyses have also shown that secondary adherence for chronic medication can be much lower (49 %) (19, 20). Combining this with our findings, real world adherence could be as low as 45.6 % (49% of 93% equals 45.6%).

Conclusion

In summary, the present study has shown that PNA rates of Slovak chronic disease patients are very low. PNA was shown to decrease with age, and to be better in general practitioners and in patients with access to reimbursement. In the case of defaulters, it is questionable whether hindering patient adherence by letting them pay full cost of medication while covering their acute emergencies is economically advantageous. Patients are seemingly more sensitive to a higher individual co-payment than to their annual cumulative co-

-payments. A small co-payment (under 1€) leads to increased odds of claiming, which is important for future reimbursement policies. Further analysis of the present dataset will be needed for developing interventions aimed at improving patient adherence to medical treatments.*

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