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Use of lipid-lowering drugs in restricted health access settings: Results from the Trends in Drug Utilization During COVID-19 Pandemic in Turkey (PANDUTI-TR) study

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ABSTRACT

Background: COVID-19 restrictions prompted changes in chronic disease management and lifestyle modifications, potentially altering cardiometabolic indicators and lipid-lowering pharmacotherapy patterns. We aimed to assess lipid-lowering drug (LLD) utilization trends during COVID-19 restrictions.
Methods: We obtained nationwide outpatient drug sales and prescribing data for 01.03.2018–31.12.2022 from IQVIA™ Turkey. We evaluated average monthly LLD consumption, their costs, and quarterly prescribing levels in three periods: "before restrictions" (BfR, 01.03.2018–31.03.2020), "during restrictions" (DuR, 01.04.2020–31.03.2022), and "after restrictions" (AfR, 01.04.2022–31.12.2022). Drug utilization was measured via "defined daily dose/1000 inhabitants/day" (DID) metric.
Results: LLD utilization increased from 25.4 ± 3.1 DID in BfR to 36.2 ± 6.8 DID in DuR ($p < 0.001$), and to 42.6 ± 5.3 DID in AfR ($p < 0.001$ vs. BfR). Statin consumption significantly rose from 22.0 ± 3.0 DID in BfR to 31.6 ± 6.3 DID in DuR ($p < 0.001$), and further to 37.6 ± 4.7 DID in AfR ($p < 0.01$ vs. DuR). High-intensity statin consumption elevated by 115.9% in AfR compared to baseline ($p < 0.001$). Prescribing of LLDs decreased from 12.5 ± 0.6 DID in BfR to 7.2 ± 1.2 DID in DuR ($p < 0.001$), later reached 13.6 ± 3.8 DID in AfR ($p < 0.001$ vs. DuR), with prescribing for ongoing users following similar trend. Expenditure on LLDs increased from €8.4 m ± 0.9 m in BfR to €11.4 m ± 2.0 m in DuR ($p < 0.001$) and to €12.8 m ± 1.9 m in AfR ($p < 0.001$ vs. BfR).
Conclusions: This study revealed a surge in consumption of LLDs in Turkey following the onset of the COVID-19 pandemic. This rise might be related to practices facilitating drug access, in addition to potentially greater adherence, or the necessity for more intense pharmacotherapy due to elevated cardiovascular risk.

1. Introduction

The COVID-19 pandemic has resulted in shifts in priorities and expectations among individuals and other stakeholders within the healthcare system. Throughout this period, concerns about the availability and accessibility of essential medicines have increased, necessitating more flexible and adaptable healthcare systems [1]. Various health authorities, including those in Turkey, France, and Spain, have introduced measures to address this need, such as extending the validity of chronic drug prescriptions or prescription-free dispensing of chronic medicines (PDCM), i.e. enabling the procurement of the drugs for documented chronic conditions without requiring a physician's consultation, aiming to facilitate access to medication [2–4].

Given its association with unwanted cardiovascular outcomes, difficulties in the management of ongoing patients, and the rise in incident cases, dyslipidemia could be regarded as a particularly crucial chronic condition [5]. Moreover, the restrictions implemented during the pandemic might have contributed to the deterioration of the disease course and abnormal levels of blood lipids through changes in physical activity and dietary habits [6,7]. Disruptions in healthcare services due to the restrictions created additional risks by limiting individuals' access to routine visits and medications [8]. Thus, patients with dyslipidemia possibly encountered extraordinary modifications not limited to escalated disease burden and issues related to diagnosis, as well as variations

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in the prescribing, accessibility, and adherence to lipid-lowering drugs (LLDs). Moreover, whether implementations to facilitate drug access result in their wastage due to the elimination of the obligation of clinical supervision remains to be ascertained. While research on dyslipidemia during the pandemic has largely centered on cholesterol levels and medication adherence [9–11], studies thoroughly evaluating the alterations in pharmacotherapy patterns during this timeframe are needed. In this context, we aimed to investigate the alterations in utilization and expenditure of LLDs throughout the COVID-19 pandemic-associated restriction periods.

2. Methods

In this study, we evaluated the trends in consumption, prescribing and costs of LLDs throughout Turkey during COVID-19 pandemic-associated restriction periods. We also analyzed whether the trends in LLD utilization showed any regional differences. The study was the dyslipidemia pharmacotherapy-related part of the comprehensive "Trends in Drug Utilization During COVID-19 Pandemic in Turkey" (PANDUTI-TR) project, which included retrospective evaluation of drug consumption and prescribing data for various metabolic and psychiatric indications. The study commenced following the approval of Marmara University School of Medicine Ethics Committee for Clinical Studies (approval number: 09.2022.825).

The study data were obtained from the Turkey Office of IQVIA™, the local branch of the company that provides pharmaceutical market data on a national scale in various countries [12]. The data regarding the nationwide quantity of drug units distributed to retail pharmacies at the wholesale level were used to analyze drug consumption and expenditure. The number and the cost of LLDs sold from March 1st, 2018 to December 31st, 2022, along with the prescribing data corresponding to this timeframe, comprised the study data for analysis.

Drugs used for pharmacotherapy of dyslipidemia according to the Anatomical Therapeutic Chemical (ATC) classification established by the World Health Organization (WHO) were included in the study [13] (Fig. 1). Average monthly consumption levels of these medications in the periods defined as "before restrictions" (BfR, from March 1st, 2018 to March 31st, 2020), "during restrictions" (DuR, from April 1st, 2020 to March 31st, 2022), and "after restrictions" (AfR, from April 1st, 2022 to December 31st, 2022) were calculated and compared. These three periods were determined based on the dates of implementation and lifting of the COVID-19 pandemic-associated restrictions in Turkey. The restrictions were firstly implemented on March 12th, 2020 and most of them were lifted on March 3rd, 2022 [14–16]. As the data pertained to wholesale from drug warehouses, the potential delay in the impact of the restrictions on the drug consumption at the retail level was also taken into consideration. Drug consumption was expressed in units (i.e., number of packs) and DID (defined daily dose/1000 inhabitants/day) metric, where appropriate. DID, a metric of drug consumption by a population within a region, is impacted by the defined daily dose (DDD) of a drug, i.e. the assumed average maintenance dose per day for its main indication in adults, in each drug pack and the units sold [13,17]. For LLDs in fixed-dose combinations, each active ingredient was calculated separately.

For the analyses regarding drug expenditure, average monthly costs of LLDs in three time periods were calculated and compared. The costs of drugs were obtained in Turkish liras and then converted to euro by using the euro/Turkish lira currency exchange rate, which was periodically declared by the Turkish Ministry of Health and utilized for the national drug pricing [18].

The analysis of prescribing trends of LLDs was conducted using projected nationwide prescribing data provided by IQVIA™. This dataset was reportedly created by collecting prescriptions, which included diagnoses and treatment for outpatients from 1000 physicians nationwide over a span of 7 days. Subsequently, the Global Office of the company projected the data to estimate the number of drug units prescribed for each quarter of the year across Turkey. The number of units and DID values for LLDs prescribed for dyslipidemia (ICD-10 code: E78) across the BfR, DuR, and AfR periods were calculated and compared, both overall and stratified by prescription type, distinguishing between new users—individuals prescribed LLDs for the first time upon diagnosis—and ongoing users—those already receiving LLD treatment for dyslipidemia.

In lipid-lowering pharmacotherapy-related guidelines, statins were classified based on their LDL-cholesterol reducing potential as "low-intensity", "medium-intensity", and "high-intensity" [19]. The statins included in this study were analyzed in terms of consumption, prescribing (stratified by new and ongoing use), and expenditure within intensity categories and compared across BfR, DuR, and AfR.

LLDs were also analyzed for regional variations in consumption levels throughout the pandemic-associated restriction periods. To this end, the Socio-Economic Development Index-2017 (SEDI-2017) scores of 81 provinces of Turkey were used. SEDI-2017, the most recent provincial index, assesses the socioeconomic development of the provinces of Turkey through 52 indicators across eight main domains: demography, employment, education, health, competitive and innovative capacity, finance, accessibility, and quality of life [20]. The association between the SEDI scores of each province, based on these parameters, and the drug consumption levels in BfR, DuR, and AfR was explored.

Statistical analyses were conducted using IBM SPSS 29.0 and GraphPad Prism 10.1 software. Descriptive data were presented as numbers and percentages, while the mean drug consumption in each

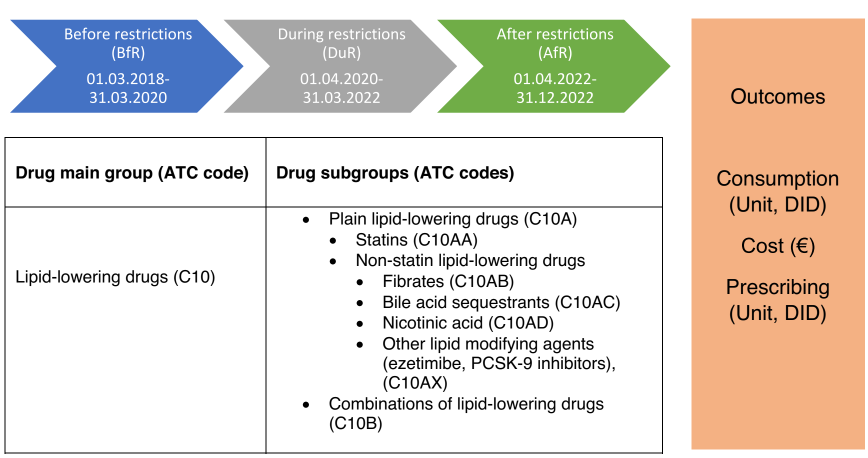


Fig. 1. The lipid-lowering drug groups evaluated along with the restriction-associated time periods and the outcomes determined in the study. *ATC, Anatomical Therapeutic Chemical; DID, defined daily dose/1000 inhabitants/day.*

period were reported as mean ± standard deviation. Normality of the continuous variables was assessed by Shapiro-Wilk test. Normally distributed data were compared via one-way analysis of variance (ANOVA) test with Tukey's post-hoc test, whereas Kruskal-Wallis test with Dunn's post-hoc test was conducted when normal distribution was not applicable. The association of provincial drug consumption levels and SEDI scores was analyzed via Spearman correlation test, and the correlation coefficients for the three periods were compared with each other [21]. A type 1 error value below 5% was considered statistically significant.

3. Results

The total number of LLD units and their cost were 133.8 million units and €599.1 million, respectively. Statins constituted 88.2% of the consumed LLDs. Projection data from prescriptions for dyslipidemia issued over the study period showed a total of 44.7 million units of prescribed LLDs, 84.9% of which were statins.

Average monthly consumption of LLDs increased from 25.4 ± 3.1 DID in BfR to 36.2 ± 6.8 DID in DuR ($p < 0.001$), and further escalated to 42.6 ± 5.3 DID in AfR ($p < 0.001$ vs. BfR). Compared to BfR (€8.4 m ± 0.9 m), the mean monthly cost of these drugs also rose in DuR and AfR, reaching €11.4 m ± 2.0 m and €12.8 m ± 1.9 m, respectively ($p < 0.001$ vs. BfR for both). Mean prescribed LLD levels per quarter decreased from 12.5 ± 0.6 DID in BfR to 7.2 ± 1.2 DID in DuR ($p < 0.001$), only to rebound to 13.6 ± 3.8 DID in AfR ($p < 0.001$ vs. DuR), (Table 1, Fig. 2).

Statins showed a steady increase across subsequent periods, rising from 22.0 ± 3.0 DID in BfR to 31.6 ± 6.3 DID in DuR ($p < 0.001$), and further to 37.6 ± 4.7 DID in AfR ($p < 0.001$ vs. BfR, $p < 0.01$ vs. DuR), (Table 1, Fig. 3a). Non-statin LLDs, predominantly comprised of fibrates (90.3% of total), exhibited a trend similar to that of LLDs overall (Table S1, Fig. S1). Compared to BfR (€6.0 m ± 0.8 m), expenditure for statins were higher in DuR (€8.1 m ± 1.6 m, $p < 0.001$) and AfR (€9.3 m ± 1.4 m, $p < 0.001$ vs. BfR), (Table 1, Fig. 3b). The prescribing of these LLDs decreased in DuR compared to BfR but returned to initial levels in AfR ($p < 0.001$ vs. DuR), (Table 1, Fig. 3c).

The average quarterly prescribing of LLDs for ongoing users decreased significantly from BfR (10.9 ± 0.5 DID) to DuR (5.7 ± 0.9 DID, $p < 0.001$) before returning to baseline levels in AfR (11.8 ± 3.9 DID, $p < 0.001$ vs DuR). Prescribing levels of LLDs for new users remained consistent across the three periods (1.6 ± 0.2, 1.5 ± 0.4, and 1.8 ± 0.1 DID, respectively, $p > 0.05$), (Fig. S2).

The most consumed statins were atorvastatin and rosuvastatin, with both escalating in the following periods compared to BfR ($p < 0.001$ for both in DuR and AfR), (Fig. S3). Moderate- and high-intensity statins showed significantly increased consumption in DuR (29.1% and 71.0%, respectively, $p < 0.001$ for each) and AfR (38.1% and 117.2%, respectively, $p < 0.01$ for each) than that in BfR, more pronounced in the latter. Compared to BfR, prescribing rates in AfR was similar in moderate-intensity statins but significantly increased for high-intensity statins. For ongoing users, prescribing of both moderate- and high-intensity statins decreased in DuR ($p < 0.01$ for both) and increased in AfR thereafter, while prescribing for new users demonstrated a stable pattern in both intensity categories ($p > 0.05$), (Fig. 4).

Modified-release formulations constituted a very small portion of LLDs (0.02% of total). While immediate-release LLDs showed a regular increase in pandemic-associated periods, this increase was not observed in modified-release forms (Table S2).

A moderate correlation between provincial consumption levels and SEDI values was detected in each of BfR, DuR and AfR. The correlation coefficients between SEDI and LLD consumption were similar across the time periods ($p > 0.05$, Table S3).

4. Discussion

This study demonstrated that over a nearly five-year period encompassing the critical periods before and after the COVID-19 pandemic—an event that could be argued to act as a naturally occurring, unexpected intervention—the average monthly consumption and costs of LLDs increased in the subsequent periods compared to pre-pandemic setting. Statins, the leading subgroup of LLDs in consumption, played a significant role in this change by showing a substantial rise throughout the successive periods. We observed that LLDs were prescribed less frequently during the pandemic, when access to healthcare services was negatively affected, whereas the prescribing of these drugs reached pre-pandemic levels with the lifting of most restrictions. This trend appears to be due to prescribing for ongoing users, as incident prescriptions did not exhibit significant changes throughout the study time intervals.

Despite the variability in pharmaceutical market trends in different countries during the COVID-19 pandemic, consumption patterns were reported to return to levels similar to those in pre-pandemic era. The fluctuations during the pandemic were revealed to be more prominent in medications for acute illnesses, while drugs for chronic diseases followed a more stable course in this regard [22]. The total consumption levels of LLDs in 30 OECD member countries were reported to rise by 12.3% in the years 2020 and 2021, which correspond to the pandemic, compared to the previous two years [23]. Our study demonstrates the advancement of mean monthly LLD consumption by more than two-

Table 1
Distribution and comparison of average values of monthly consumption and cost and quarterly prescribing of lipid-lowering drugs across COVID-19 restriction-associated periods.

	Drug groups	BfR (Mean ± SD)	DuR (Mean ± SD)	AfR (Mean ± SD)	*P*-value
Monthly consumption (units)	Statins	1,653,299.8 ± 280,772.2	2,253,268.1 ± 514,154.3*	2,502,541.7 ± 385,547.3*	<0.001
	Non-statin LLDs	226,173.4 ± 25,457.5	304,291.9 ± 58.307,6*	319.763,0 ± 49.646,5*	<0.001
	Total	1,879,473.2 ± 285,434.1	2,557,560.0 ± 541,942.0*	2,822,304.7 ± 421,099.3*	<0.001
Monthly consumption (DID)	Statins	22.0 ± 3.0	31.6 ± 6.3*	37.6 ± 4.7*‡	<0.001
	Non-statin LLDs	3.4 ± 0.4	4.6 ± 0.9*	5.0 ± 0.7*	<0.001
	Total	25.4 ± 3.1	36.2 ± 6.8*	42.6 ± 5.3*	<0.001
Monthly cost (euros)	Statins	6,025,656.0 ± 767,652.3	8,126,312.1 ± 1,591,442.3*	9,346,399.3 ± 1,402,230.7*	<0.001
	Non-statin LLDs	2,360,142.0 ± 285,195.9	3,297,086.5 ± 660,850.4*	3,460,590.5 ± 614,762.9*	<0.001
	Total	8,385,798.0 ± 866,756.1	11,423,398.7 ± 2,035,819.4*	12,806,989.9 ± 1,945,515.7*	<0.001
Quarterly prescribing (units)	Statins	2,267,710.6 ± 52,746.0	1,284,552.0 ± 214,936.6*	2,411,926.9 ± 639,892.7†	<0.001
	Non-statin LLDs	401,190.4 ± 33,682.8	245,945.6 ± 36,991.4*	385,338.3 ± 86,893.6†	<0.001
	Total	2,668,901.1 ± 79,028.0	1,530,497.6 ± 247,564.2*	2,797,265.2 ± 726,785.9†	<0.001
Quarterly prescribing (DID)	Statins	10.3 ± 0.4	5.9 ± 1.0*	11.6 ± 3.3†	<0.001
	Non-statin LLDs	2.2 ± 0.2	1.3 ± 0.2#	2.0 ± 0.5	<0.001
	Total	12.5 ± 0.6	7.2 ± 1.2*	13.6 ± 3.8†	<0.001

LLD, lipid-lowering drug. BfR, before restrictions; DuR, during restrictions; AfR, after restrictions. *, $p < 0.001$ vs. BfR; #, $p < 0.01$ vs. BfR; †, $p < 0.001$ vs. DuR; ‡, $p < 0.01$ vs. DuR.

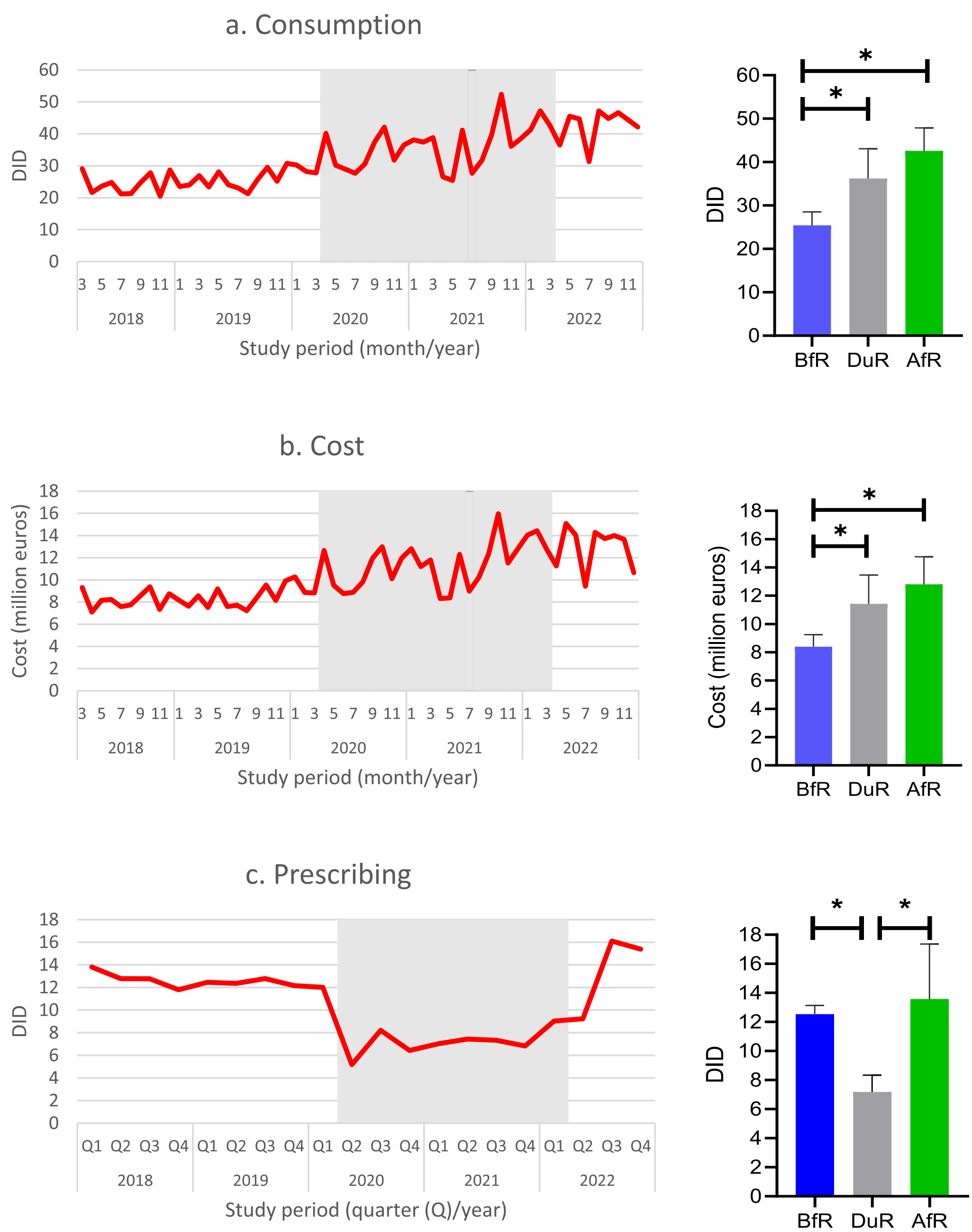


Fig. 2. Trends and comparisons of average monthly (a) consumption, (b) cost, and quarterly (c) prescribing of lipid-lowering drugs across COVID-19 restriction-associated periods. *BfR, before restrictions; DuR, during restrictions; AfR, after restrictions.* *, $p < 0.001$.

fifths in DuR and two-thirds in AfR compared to BfR, suggesting that the consumption of these drugs in Turkey during the respective periods surged beyond the global market trend, distinctly diverging from the patterns observed in various other countries. The OECD data source mentioned above supported our results, reporting the increase in consumption in Turkey being the sharpest, reaching 39.4% [23]. At first glance, regional variations in consumption trends might be expected. Indeed, a study from China reported that lifestyle practices contributing to the risk of dyslipidemia were more commonly observed in regions with lower socioeconomic development [24]. However, the association of provincial SEDI levels with the consumption of LLDs remains consistent across BfR, DuR, and AfR, implying a uniform pattern of consumption nationwide. It is also noteworthy that the prescribing of LLDs in DuR dropped to about three-fifths compared to BfR, deviating from the consumption trend, just before rising in AfR to match the baseline levels. One of the factors playing a role in this discordance might be the implementation of PDCM, as a measure to expedite drug access, with the onset of the pandemic in Turkey.

In various countries around the world, pharmacies were authorized to directly dispense medications to patients in order to mitigate disruptions in treating chronic conditions due to restricted access to healthcare services during the pandemic [25]. In conjunction with the need to minimize social contact, patients reportedly exhibited medication stockpiling behavior [26]. Moreover, enabling medication access without supervision of a physician might raise concerns in patients acquiring drugs beyond their needs, potentially resulting in medication waste. In this context, while the levels of LLDs prescribed were similar in BfR and AfR, the fact that the consumption of these drugs in AfR

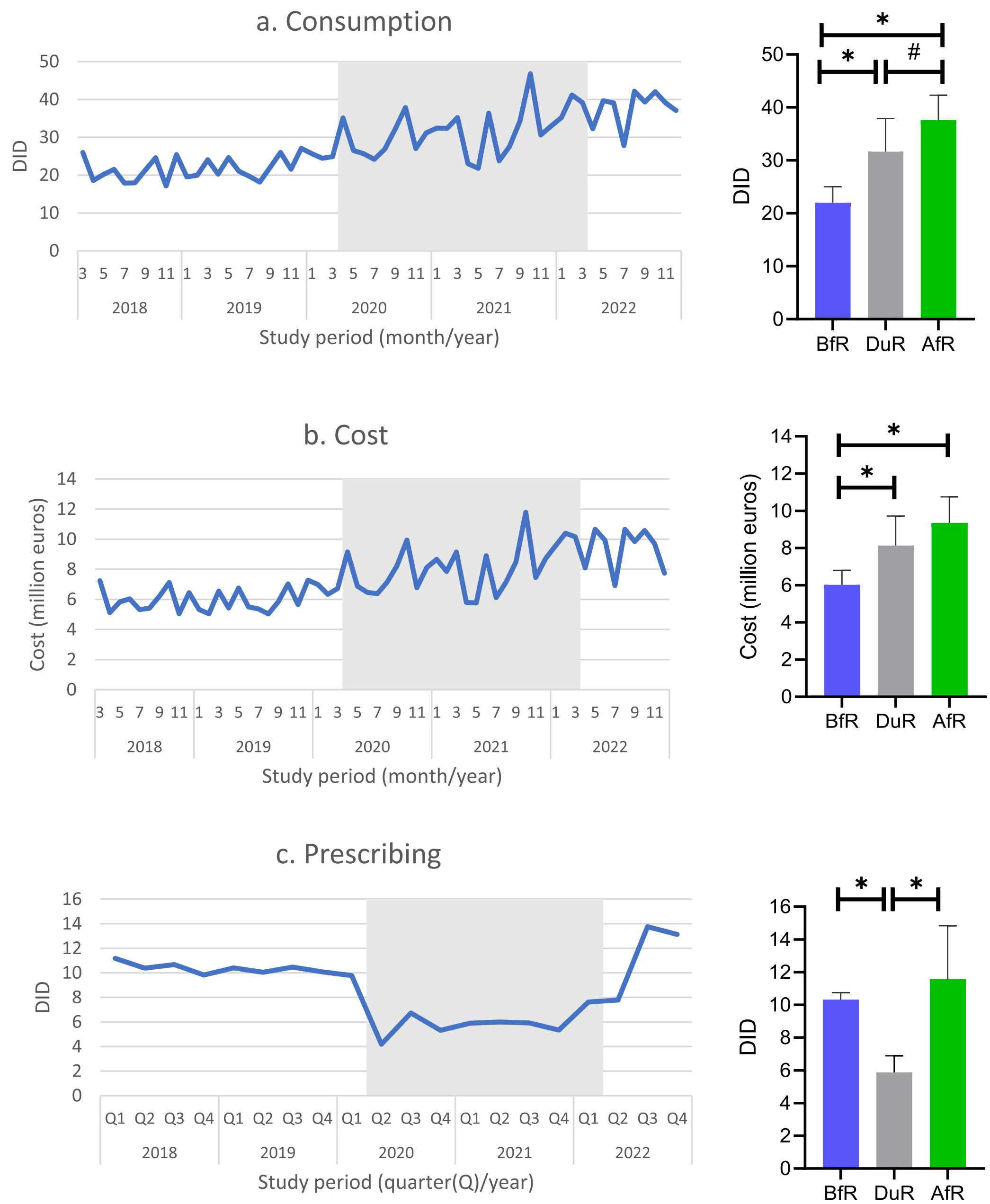
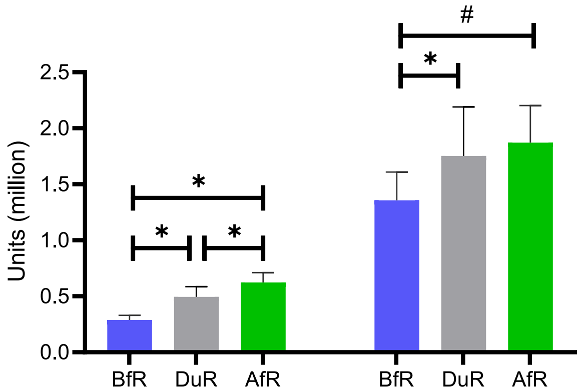


Fig. 3. Trends and comparisons of average monthly (a) consumption, (b) cost, and quarterly (c) prescribing of statins across COVID-19 restriction-associated periods. *BfR, before restrictions; DuR, during restrictions; AfR, after restrictions.* *, $p < 0.001$; #, $p < 0.01$.

exceeding the initial levels might be associated with patients obtaining medications in excess of their actual needs. Additionally, it should not be overlooked that this situation could impose an additional burden on both the reimbursement system and the community in terms of drug costs, which represent a substantial portion of healthcare expenditures. The observed surge in medication costs parallel to the consumption for both statins and non-statin LLDs suggests that the potential drug waste issues associated with the implementation of PDCM might also be reflected on expenditure. Beyond the benefits of this measure improving medication access during health crises, its potential to promote stockpiling and overconsumption should also be factored in while managing pharmacotherapy for chronic diseases under extraordinary circumstances. Issues related to adherence, such as forgetting or opting not to take drugs during that timeframe, could also be regarded among the factors contributing to increased medication waste and the associated financial burden [11].

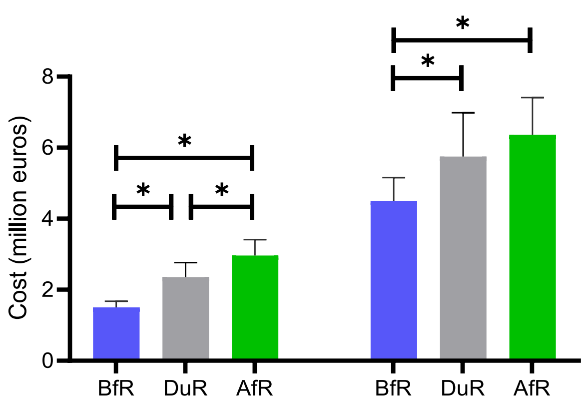
While LLD prescribing to ongoing users was noted to be reduced by nearly half in DuR and increased thereafter, no significant change was detected in new prescriptions between three periods. In studies from the United Kingdom and France, prescribing of LLDs to new patients either reportedly decreased or maintained a stable trend while the restrictions were in place [4,27]. This may be linked to a documented decline in healthcare services utilization, attributed to interruptions in these services and concerns over infection risk [28]. In Turkey, reports indicate that during 2020 and 2021, which align roughly with DuR, there was a one-fifth reduction in the number of physician visits compared to the two preceding years [29]. Nevertheless, our results showing no potential negative trend in consumption could be associated with the implementation of PDCM, particularly for managing a chronic condition such as dyslipidemia.

a. Average monthly consumption of statins



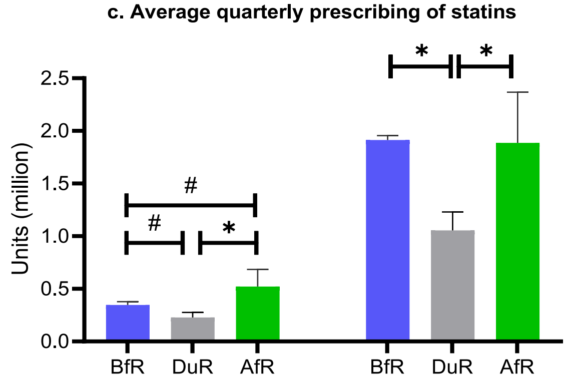
	High-intensity statins	Moderate-intensity statins
BfR	289,358.6±41,050.3	1,357,066.6±253,183.9
DuR	494,379.0±92,524.1	1,752,292.0±437,538.0
AfR	624,829.2±85,693.2	1,872,129.2±330,158.2

b. Average monthly cost of statins



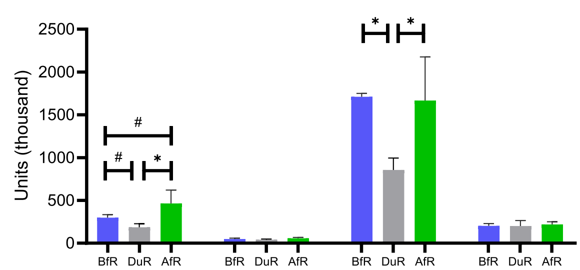
	High-intensity statins	Moderate-intensity statins
BfR	1,506,111.9±169,131.3	4,500,345.4±659,162.2
DuR	2,358,068.1±405,109.0	5,750,069.6±1,235,820.3
AfR	2,965,584.2±443,664.2	6,365,326.1±1,042,624.3

c. Average quarterly prescribing of statins



	High-intensity statins	Moderate-intensity statins
BfR	347,307.0±29,931.8	1,913,542.6±41,826.4
DuR	228,118.2±46,938.8	1,054,958.5±176,242.5
AfR	522,310.7±162,861.3	1,886,025.9±481,607.9

d. Average quarterly prescribing of statins to ongoing and new users



	High-intensity statins		Moderate-intensity statins	
	Ongoing users	New users	Ongoing users	New users
BfR	298,842.0±34,026.2	48,465.0±10,162.1	1,710,120.9±41,041.9	203,421.7±25,569.9
DuR	186,785.1±41,471.1	41,333.1±6,788.3	855,251.5±140,777.6	199,707.0±64,936.5
AfR	465,206.6±156,462.4	57,104.1±11,043.5	1,666,814.5±508,730.9	219,211.5±30,789.8

Fig. 4. Distribution and comparison of average monthly (a) consumption, (b) cost, quarterly (c) overall prescribing, and (d) prescribing stratified by ongoing and new users of statins by intensity across COVID-19 restriction-associated periods. *Low-intensity statins, which constituted only 0.3% of consumed statins, were not included in the figure. BfR, before restrictions; DuR, during restrictions; AfR, after restrictions.* *, $p < 0.001$; #, $p < 0.01$.

The increase in statin consumption, which exhibits a consistent upward trend in each period and surged by as much as 70% in AfR compared to baseline, indicates a potential rise in demand for these drugs. This rise was particularly attributed to high-intensity statins, which exceeded twice the baseline levels in AfR compared to moderate-intensity ones showing a more modest increase at the same timeframe, as much as three-eighths. The fact that statins with the highest potential to lower LDL cholesterol levels (≥50%) reached their peak prescribing levels after easing of the restrictions might point out that the need for these agents in pharmacotherapy may have increased over time. These medications are recommended in guidelines either for the primary prevention in individuals with a high ten-year cardiovascular risk (≥20%) or for the secondary prevention in those diagnosed with clinical atherosclerotic cardiovascular disease (ASCVD) [19]. Rather than the first-time users, the changes in prescribing for high- and moderate-intensity statins were more applicable to ongoing users, which might imply that the dyslipidemia-related disease burden in this group might have risen during the pandemic, in terms of either cardiovascular risk or previous events. Alterations in the blood lipid levels are cited along with rises in blood pressure levels and smoking rates among the escalating cardiovascular risk factors during COVID-19 restrictions [10,30]. The shift towards a more sedentary lifestyle along with the presumed changes in dietary habits in this period might have unwantedly affected the blood lipid profiles of the patients [6,7]. Indeed, a study in Spain reportedly compared metabolic parameters before and after the onset of the pandemic to find out they were adversely affected throughout this period [10]. In terms of secondary prevention, although the direct relationship between COVID-19 infection and ASCVD (atherosclerotic cardiovascular disease) remains controversial, existing research revealed that cardiovascular complications were more commonly encountered in certain specific groups, such as younger individuals [31,32]. The restrictions implemented to control the spread of the infection, such as curfews and alterations in healthcare services leading to disruptions, were also mentioned as factors that could indirectly affect the frequency of cardiovascular diseases [33]. By contrast, it has been reported that the rate of serious cardiovascular adverse events did not increase when restrictions were in place [34]. In this context, our findings might be associated with an increase in consumption with the aim of improving primary prevention, rather than secondary prevention, due to the potential increases in cardiovascular risks.

Dyslipidemia is among the indications with relatively low treatment adherence, mainly due to unwanted effects generally emerging through long-term complications [35]. While patient adherence was not evaluated in this study, it should be kept in mind among the reasons for the disproportionate increase in LLD consumption compared to prescribing levels. The potential concerns of patients with cardiovascular risk about the severity and complications of COVID-19 infection might have improved their overall health awareness and medication adherence, which in turn could have been reflected in the upward trending use of LLDs. Overcoming the mistrust to dyslipidemia pharmacotherapy (particularly to statins) in this era, which was formed by some irrational expert opinions and spread publicly in Turkey before the pandemic, could also have contributed to this situation [36]. Nevertheless, studies conducted in countries such as Italy, the United States, and Australia have not reported an improvement in adherence to dyslipidemia treatment during the COVID-19 restrictions [9,11,37]. It could be suggested that the potential increase in adherence may also have been influenced by better implementation of guideline recommendations for lowering LDL-cholesterol targets, particularly with high-intensity statins. Furthermore, the stricter therapeutic targets established by the 2019 guidelines from the European Society of Cardiology and European Atherosclerosis Society might have also contributed to the rise in the use of high doses of statins [19]. A study from Latvia reported a more rapid increase in the utilization of high-intensity statins following the publication of the guideline [38]. Meanwhile, a study from Turkey reported that the success rate in achieving the recommended LDL-cholesterol treatment targets could be approximately as low as one in four [39]. Further investigations are warranted for conclusively establishing the potential increase in treatment adherence associated with the observed rise in LLD consumption in our study, involving studies that evaluate the real-world experiences of stakeholders engaged in the pharmacotherapy process.

The results of the study should be interpreted with consideration of the limitations presented below. While the drug consumption data used in the study represents the entire country, it being based on product dispatch from pharmaceutical warehouses to retail pharmacies might not precisely reveal the actual amount of the drugs consumed by patients. The absence of direct patient data prevented the evaluation of the difference in LLD consumption and prescribing trends by demographic characteristics. The prescribing data was generated through projection, thus, the potential margin of error related to this process should be taken into account. The costs of LLDs were calculated using the euro exchange rate used by the health authority for drug pricing, however this rate may not fully reflect short-term fluctuations in the real-world exchange rate as it is updated yearly or every few months. The strength of the drug, which is among the parameters determining the DID value, may directly influence the classification of statins by intensity for the same active substance. Therefore, the results of the analyses based on intensity categories was expressed in units instead of DID. Moreover, AfR period in this retrospective study was determined as relatively shorter than both BfR and DuR. The large-scale earthquake occurred in February 2023 in Turkey, shortly after the completion of the study period, affected 11 of the 81 provinces of the country. The disaster caused a death toll of over 50,000, along with extensive and severe destruction, including damage to healthcare facilities such as hospitals and pharmacies. This event led to significant changes in daily life routines and healthcare service practices for an important timeframe [40]. Due to the potential impact of the earthquake on diminished access to healthcare and consequently on drug utilization, this period was not included in AfR.

In conclusion, this study demonstrated that the consumption of LLDs surged during the period of COVID-19 pandemic restrictions, supposedly driven by medical and administrative factors, and this increase continued with the easing of restrictions. The observed rise in consumption of LLDs despite reduced prescribing due to limited access to healthcare services might be associated with expedited access to chronic medications through prescription-free dispensing, potentially triggering drug waste. Increased consumption during the pandemic might also imply either a greater reliance on pharmacotherapy due to elevated cardiovascular risks associated with lifestyle changes, or an improvement in treatment adherence. The insights from the study are anticipated to shed light on the rational management and implementation of pharmacotherapy policies by health and reimbursement authorities in future health crises of a similar scope.

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CRediT authorship contribution statement

Caner Vizdiklar: Writing – review & editing, Writing – original draft, Visualization, Resources, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization. **Volkan Aydin:** Writing – review & editing, Validation, Supervision, Project administration, Methodology, Investigation, Funding acquisition, Data curation, Conceptualization. **Gokhan Tazegul:** Writing – review & editing, Validation, Investigation, Funding acquisition, Conceptualization. **Mert Kaskal:** Writing – original draft, Visualization, Validation, Formal analysis. **Ahmet Akici:** Writing – review & editing, Supervision, Resources, Project administration, Methodology, Funding acquisition, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data will be made available on request.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.vph.2024.107382.

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