BioMed

MDPI

Article

Availability of Cardiodiabetological Drugs in Poland during the First Year of COVID-19 Pandemic: Retrospective Study

Bartosz M. Nowak [1], Mikołaj Kamiński [1,*], Bartłomiej Owczarek [2], Monika Szulińska [1] and Paweł Bogdański [1]

[1] Department of the Treatment of Obesity and Metabolic Disorders, and of Clinical Dietetics, Poznan University of Medical Sciences, 60-569 Poznan, Poland; poz.bartosznowak@gmail.com (B.M.N.); monikaszulinska@ump.edu.pl (M.S.); pawelbogdanski@ump.edu.pl (P.B.)
[2] GdziePoLek Sp. zoo, 00-008 Warsaw, Poland; bartlomiej.owczarek@gdziepolek.pl
* Correspondence: mikolaj.w.kaminski@gmail.com; Tel.: +48-516268563

Abstract: There were worries that the COVID-19 pandemic could result in a shortage of supplies of some drugs. We aimed to analyze if the COVID-19 pandemic resulted in the availability drop of different cardiodiabetological medicaments. Special attention was put to combined therapies and to investigate the general availability of these drugs. Data were obtained from the Polish startup company GdziePoLek regarding the availability of 121 cardiodiabetolocigal drugs divided into 23 separate categories in Polish pharmacies. The period of the analysis was limited from 1 January 2019 to 31 December 2020. The threshold of a 20% decrease of median availability was set to found drugs with the most severe drop in availability during the COVID-19 pandemic. We also identified medicaments with a median availability of less than 50%. We identified two drugs with the most severe drop in availability level during COVID-19 pandemics: acenocoumarol (decrease by 52.0%) and nitrendipine (decrease by 98.3%). In 2019 and 2020, 27 of 121 drugs had a median availability lower than 50%. The limited availability concerned the most novel agents and polypills, mostly non-insulin antidiabetic drugs. The decrease in drug availability in Poland was not as severe as expected. Accessibility to some novel non-refunded medicaments is limited.

Keywords: COVID-19; drug stocks; cardiovascular; diabetes; combination drugs; polypill

Citation: Nowak, B.M.; Kamiński, M.; Owczarek, B.; Szulińska, M.; Bogdański, P. Availability of Cardiodiabetological Drugs in Poland during the First Year of COVID-19 Pandemic: Retrospective Study. *BioMed* **2022**, *2*, 117–126. https://doi.org/10.3390/biomed2010013

Academic Editor: Konstantinos Dimas

Received: 9 February 2022
Accepted: 7 March 2022
Published: 9 March 2022

1. Introduction

Cardiovascular diseases are the leading cause of preterm morbidity and mortality in Poland [1]. Cardiodiabetological drugs are one of the critical interventions in the primary and secondary prevention of cardiovascular events [2]. For this reason, we assume that a shortage of cardiodiabetological drug stocks due to a national emergency may lead to the worsening control of cardiovascular diseases.

The severity of restrictions endorsed by the governments on the COVID-19 pandemic differs all around the world. The hindrance in international shipping, industry, and workforce mobility raises concerns about the availability of essential medical products. Poland's pharmacy industry relies on regular supplies of essential ingredients produced in Mainland China [3]. Therefore, the strict lockdown in China could have affected the availability of drugs. Moreover, the sanitary restrictions in healthcare facilities and fear of the novel coronavirus may have encouraged patients to overbuy drug stocks and treat themselves at home [4]. The fear of novel viruses could have led to a decrease in the number of visits in emergency departments and decreased the availability of drugs in pharmacies [5]. When angiotensin-converting enzyme 2 (ACE2) was detected as a receptor to novel coronavirus, concerns were raised on the safety of using angiotensin-converting enzyme inhibitors (ACEI) and angiotensin II receptor blockers (ARB) during the pandemic [6]. Hopefully, the use of ACEI/ARB was not associated with a worse outcome of COVID-19 [7], and discontinuation of the treatment could have led to the clinical deterioration [8]. To our best knowledge, there is no study on cardiodiabetological drug availability in Poland during the

COVID-19 pandemic. We aimed to retrospectively assess whether the pandemic affected the availability of the cardiodiabetological therapeutics and identify those that have limited availability in pharmacies.

In this paper, we aimed to (1) investigate the availability of drugs in pharmacies in Poland during the first year of the COVID-19 pandemic and (2) the general availability of cardiodiabetological drugs.

2. Materials and Methods

2.1. Data Collection

Data concerning the availability of n = 121 drugs in Polish pharmacies was obtained from startup company GdziePoLek [9]. GdziePoLek (translated "Where I Get My Meds") is a platform providing patients with near real-time information about medicines' on-shelf availability in brick and mortar pharmacies. Launched in mid-2015, as of 15 June 2021 GdziePoLek is connected to systems of 1890 pharmacies across Poland which dispatch automatic updates every 10 min. Patients access the service through progressive web front-end (PWA), available at gdziepolek.pl, which obviates the necessity to install applications in order to obtain the information. As a by-product of its patients-facing service, GdziePoLek has access to timelines of availability for each product sold through pharmacies. Statistics are available to the public and researchers as a web view accompanying each product, as well as are used to produce country's only independent bi-monthly reports about medicine deficits. GdziePoLek is controlled by the founding team and has not used government-connected capital in its development, enabling reporting on sometimes politically sensitive topics of deficits without external influence.

Medicaments were chosen to represent the most commonly used in the treatment of cardiovascular diseases and diabetes. To do so, we analyzed data provided by NFZ (Polish: Narodowy Fundusz Zdrowia, English: National Health Fund) concerning the number of refunded prescriptions in Poland [10]. Drugs were divided into 23 categories according to their mechanism of action: (1) antihypertensives: ACEI, ARB, alpha-blockers, calcium channels blockers (ant-Ca), beta-blockers, diuretics, (2) lipid-lowering drugs: statins, fibrates, (3) anticoagulants: heparins, novel oral anticoagulants (NOAC), Vitamin K antagonists (VKA) (4) antidiabetic drugs: insulins, non-insulin antidiabetic drugs (NAD), (5) others: antiarrhythmic, antiplatelets, L-thyroxine, nitrates, sacubitril/valsartan, (6) combined drugs, antihypertensive + lipid-lowering, combined antihypertensive, combined NAD, statins + ezetimibe. Full list of drugs with their respective category is available in Supplementary information (Table S1).

2.2. Data Analysis

Data manipulation, calculations, and visualization were performed using the R (version 4.0.3) programming language (R Foundation, Vienna, Austria). We limited the time span of our analysis to include data from 1 January 2019 to 31 December 2020 (24 months).

At first, we specified drugs that had lower availability during COVID-19 pandemics. We started our analysis with the date 4 March 2020, which was the day of the first confirmed case of COVID-19 in Poland [11]. There is no one widely used definition of drug shortages. One of them provided by the American Society of Hospital Pharmacists (ASHP) defines those shortages as supply problems which influence patient care when prescribers must use an alternate agent [12]. However, there is no strict value below whom we define a problem with drug availability. To see suspected medicament shortages, we set the threshold to a 20% decrease of median availability during the pandemic (from 4 March 2020 to 31 December 2020) compared to the time before the pandemic (1 January 2019 to 3 March 2020). For example, if the drug had a median availability at a level of 96%, it means that the decrease had to reach the level of $0.96 \times 0.20 = 0.192$ (19.2%). We believe that such a threshold would show us the drugs with the biggest availability problem. The decrease was measured through each drug's maximum and minimum availability during the proper

timeline. Please note that some of the other drugs may have more than a 20% decrease of availability, but not during the pandemic, excluding them from further analysis.

We also specified which drugs and drug categories have lower median availability during the COVID-19 pandemic. Firstly, we counted the basic statistical factors for each drug, such as mean, median, and amplitude. Then each drug with a median below 50% was further analyzed. Then we counted the moving average with the time span of 7 days for each medicament. Using a moving average gives us a better opportunity to see availability during the long period of our analysis.

3. Results

General Characteristics

Overall, we identified n = 2 drugs with an availability decrease of more than 20% (Figure 1): acenocoumarol (decrease by 51.99%) which is a vitamin K antagonist (VKA), and nitrendipine (decrease by 98.27%), which is ant–Ca. Drugs with an availability decrease between 5 and 20% are shown in the Supplementary information (Figure S1). The basic characteristics of availability for each of the two drugs are shown in Table 1. Nitrendipine reached the nadir of nearly complete inaccessibility in the sample of pharmacies across Poland, while acenocoumarol was still available in nearly 48% of pharmacies. After a significant period of decreased availability, the supplies of acenocoumarol stabilized and reached the level, which could be found before COVID-19 pandemics. The situation with nitrendipine availability looks much more different. After the decrease in availability, the level of nitrendipine supplies stays much lower than before novel pandemics.

Table 1. Drugs with decreases of availability by 20% during the COVID-19 pandemic in Poland (**a**) prepandemic and (**b**) during COVID-19 pandemic.

(a)							
Prepandemic 1 January 2019–4 March 2020							
	Drug	**Category**	**Median [%]**	**Mean [%]**	**Min [%]**	**Max [%]**	**Amplitude [%]**
1	Acenocoumarol	VKA	98.565	96.39	51.40	99.53	48.13
2	Nitrendipine	Ant-Ca	97.36	97.44	96.56	98.34	1.78
(b)							
COVID-19 Pandemic 4 April 2020–31 December 2020							
	Drug	**Category**	**Median [%]**	**Mean [%]**	**Min [%]**	**Max [%]**	**Amplitude [%]**
1	Acenocoumarol	VKA	96.42	88.65	47.54	98.89	51.35
2	Nitrendipine	Ant-Ca	30.84	40.69	0.07	97.37	97.30

Ant-Ca—Calcium channels blockers, VKA—Vitamin K antagonists.

We also identified 27 drugs with a median availability of less than 50% (Figure 2). From these drugs, the highest median belongs to combined medicament metformin and sitagliptin (47.05%), and lowest to bemiparin, which belongs to heparins (0.08%). From n = 27 drugs, n= 9 belongs to oral NAD, n = 5 to combined NADs, n = 3 to combined antihypertensive drugs, n = 3 to combined statins, n = 2 to ARB, n = 2 to heparins, and n = 1 to antiplatelets, the fibrates groups, and sacubitril/valsartan. The basic statistical characteristics for each of the drugs are shown in Table 2. Heparins have the lowest availability in pharmacies across Poland (median, n = 0.1%), and combined antihypertensive drugs have the highest level of availability (median, n = 32.06%). It is worth noticing that drugs prescribed to patients diagnosed with type 2 diabetes comprise n = 51.85% of all drugs with median availability below 50%. Additionally, combined drugs made n = 44.40% of all drugs in the analyzed group. Medicaments with median availability above 50% are shown in the Supplementary information (Figure S2).

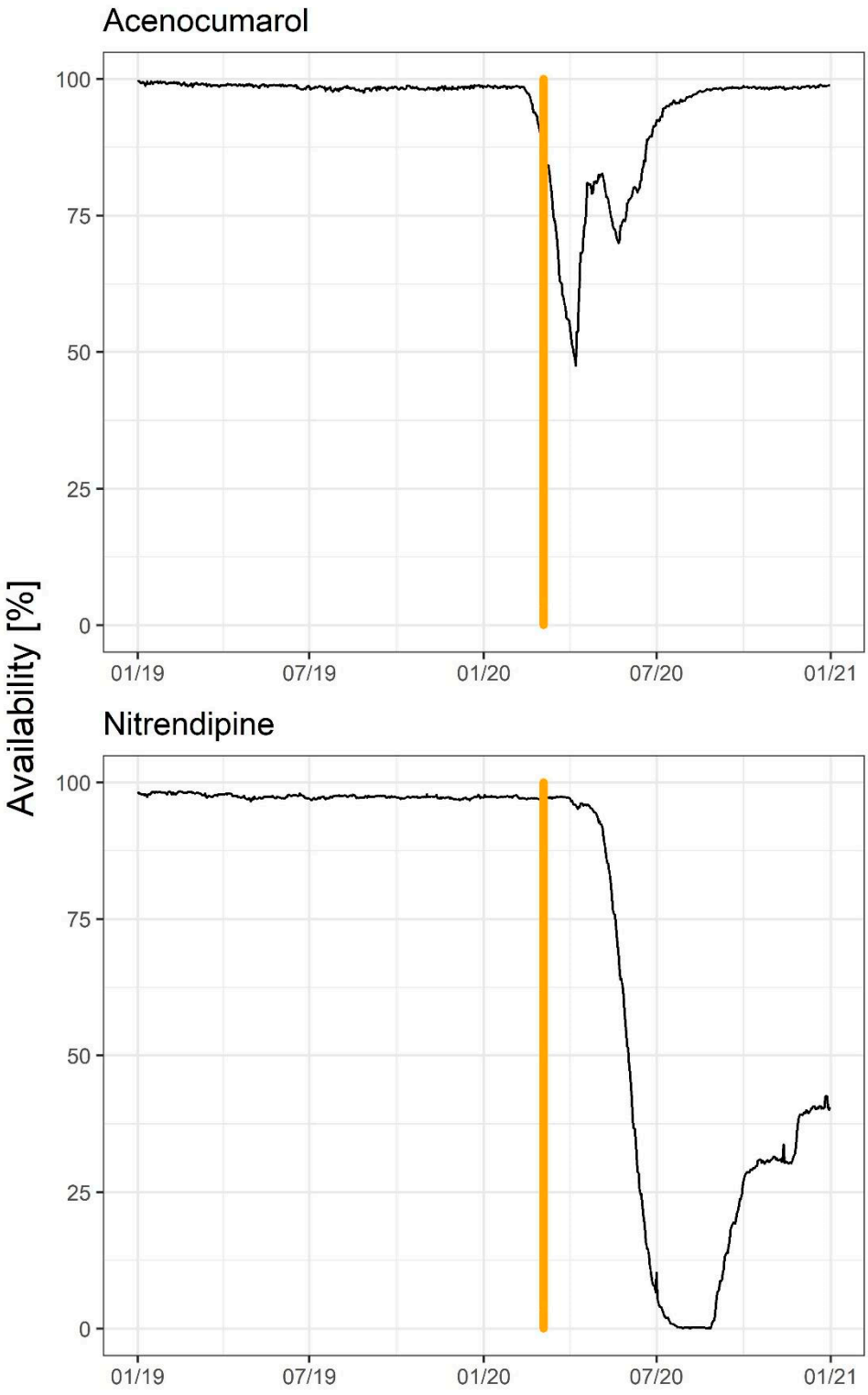
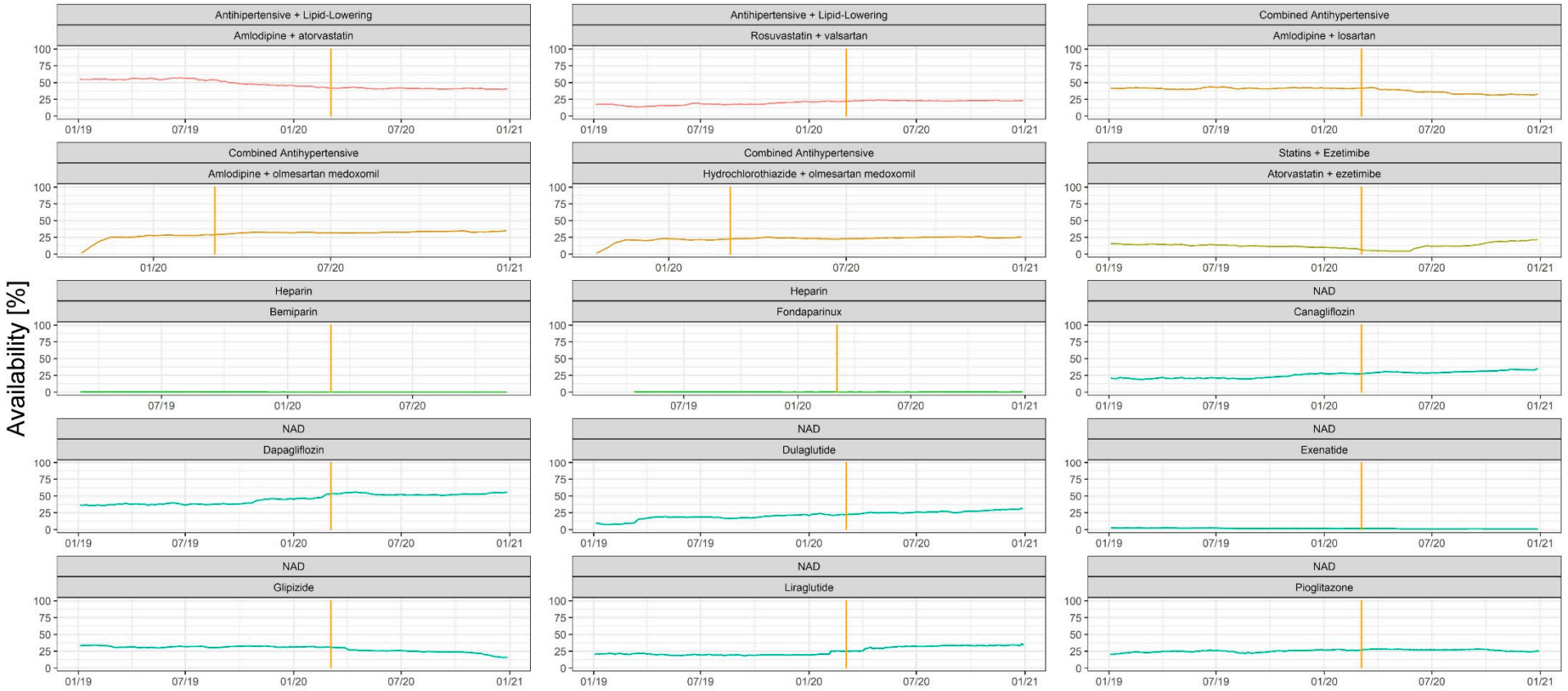
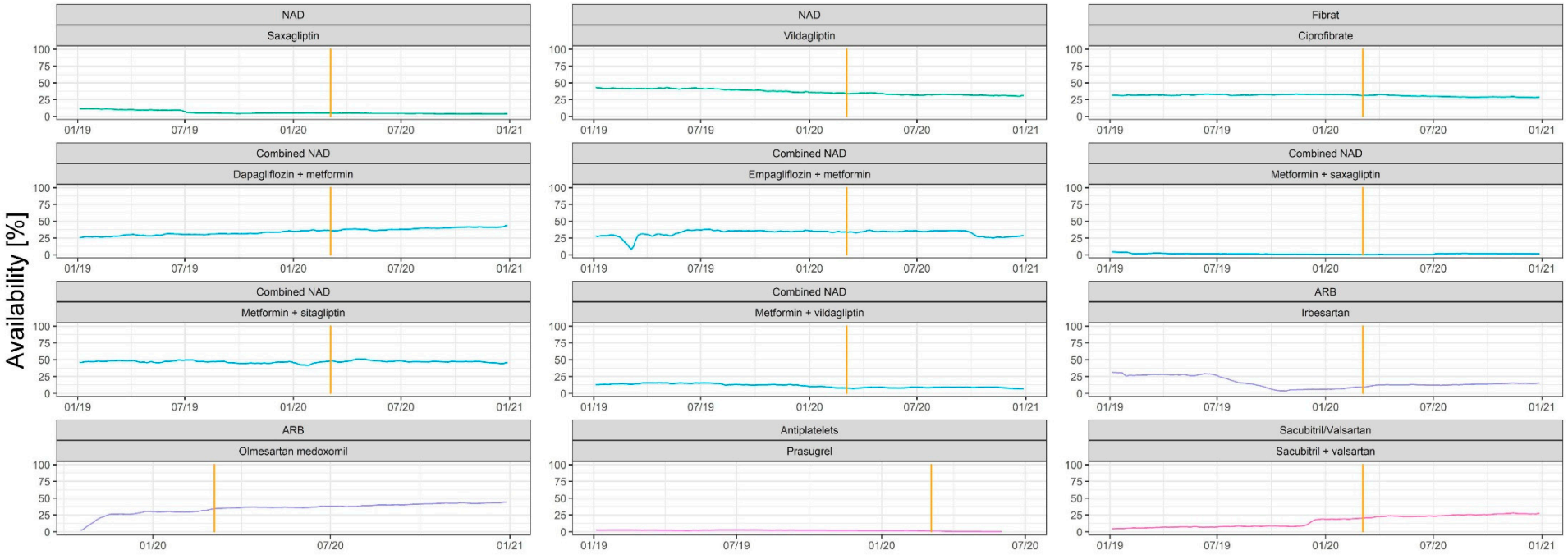


Figure 1. Availability of drugs with availability decrease by more than 20% during the COVID-19 pandemics. Orange vertical lines indicate the date 4 March 2020, the first confirmed case of COVID-19 in Poland.



(**a**)

Figure 2. *Cont.*



(**b**)

Figure 2. Drugs with median availability below 50%. The 7-days moving average was used. Orange lines indicate the date 4 March 2020, the first confirmed case of COVID-19 in Poland. The figure is divide into two parts (**a**) and (**b**) for the sake of readability.

Table 2. Drugs with median availability below 50% in the years 2019–2020 in Poland.

Drug	Category	Median [%]	Mean [%]	Min [%]	Max [%]	Amplitude [%]
Amlodipine + atorvastatin	Antihy pertensive + Lipid-Lowering	45.35	47.12	39.82	58.89	19.07
Amlodipine + losartan	Combined antihypertensive	40.87	38.91	30.93	44.59	13.66
Amlodipine + olmesartan medoxomil	Combined antihypertensive	31.83	29.82	0.18	37.64	37.46
Atorvastatin + ezetimibe	Statin + ezetimibe	12.20	12.28	4.14	22.31	18.17
Bemiparin	Heparin	0.08	0.10	0.06	0.23	0.17
Canagliflozin	NAD	27.34	26.00	18.64	36.89	18.25
Ciprofibrate	Fibrat	31.57	31.14	27.79	33.73	5.94
Dapagliflozin	NAD	45.88	45.55	35.19	57.99	22.80
Dapagliflozin + metformin	Combined NAD	35.36	34.53	25.47	45.36	19.89
Dulaglutide	NAD	21.71	21.26	6.84	33.21	26.37
Empagliflozin + metformin	Combined NAD	34.80	32.72	5.90	38.47	32.57
Exenatide	NAD	1.50	1.53	0.70	2.72	2.02
Fondaparinux	Heparin	0.11	0.12	0.06	0.27	0.21
Glipizide	NAD	30.65	28.61	15.05	34.27	19.22
Hydrochlorothiazide + olmesartan medoxomil	Combined antihypertensive	23.48	22.62	0.18	27.86	27.68
Irbesartan	ARB	13.34	15.69	3.57	31.87	28.3
Liraglutide	NAD	21.41	25.11	18.04	36.81	18.77
Metformin + saxagliptin	Combined NAD	1.46	1.42	0.34	4.54	4.20
Metformin + sitagliptin	Combined NAD	47.05	46.94	41.16	52.48	11.32
Metformin + vildagliptin	Combined NAD	10.53	11.18	6.15	17.46	11.31
Olmesartan medoxomil	ARB	36.51	34.81	0.18	46.15	45.97
Pioglitazone	NAD	25.96	25.65	20.03	29.04	9.01
Prasugrel	Antiplatelets	2.04	1.84	0.07	2.96	2.89
Rosuvastatin + valsartan	Antihy pertensive + Lipid-Lowering	21.26	20.08	13.53	25.54	12.01
Sacubitril + valsartan	Sacubitril/valsartan	18.4	15.80	4.07	30.40	26.33
Saxagliptin	NAD	4.80	5.90	3.53	12.48	8.95
Vildagliptin	NAD	35.63	36.47	29.63	45.17	15.54

4. Discussion

We analyzed cardiodiabetological drug availability in the 2019–2020 years. We found that the availability of only a few drugs decreases during the first year of the COVID-19 pandemic. Moreover, we identified many cardiodiabetological drugs, mostly novel and combined therapeutics, that have limited availability among pharmacies monitored by GdziePoLek.

4.1. Principal Results

We identified two drugs with limited availability during the COVID-19 pandemic. We observed that acenocoumarol, an anticoagulant in treating some chronic cardiovascular diseases such as atrial fibrillation, had a drop in availability, which started just several weeks before the first confirmed case of COVID-19 in Poland [11] and continued until the beginning of April. GdziePoLek wasn't able to identify the specific problem connected with this drug availability shortage. By the end of July, the availability of acenocoumarol was back to its pre-pandemic levels. This situation could indicate that patients taking acenocoumarol to keep their INR level in proper span may have started making supplies of this particular drug. In the first months of 2020 there were only limited reports about the novel virus, and the Internet was full of different information regarding COVID-19 clinical outcomes [13]. A study conducted in Portugal (which had its first confirmed case of COVID-19 on 2 March 2020) showed that drug sales had increased in the time of the first case, reaching their peak and then stabilizing. Additionally, researchers identified several drugs with an availability shortage, such as formoterol or dapagliflozin, plus metformin,

used to treat chronic diseases [14]. Possible shortages of VKA supplies and problems regarding routine INR checkups forced some medical specialists to change VKA to NOAC or low molecular weight heparins to treat their patients' chronic diseases [15,16]. It is also worth noticing that currently, acenocoumarol, in most cases, is believed to be the worst anticoagulant (yet still effective) for patients with atrial fibrillation [17,18].

Nitrendipine was the second drug identified with a severe drop in availability during the COVID-19 pandemic in Poland. It is an antihypertensive drug used mostly in emergencies. Compared to acenocoumarol, with an availability shortage at the beginning of the pandemics, the level of nitrendipine remained steady until the first day of May. Then the supply level had dropped so low that there was nearly complete inaccessibility of this drug in Polish pharmacies. The situation continued until the end of August when the supply level had slowly risen. Polish authorities released the note that the shortage of nitrendipine supplies was due to the manufacturer's inability to produce the proper quantity of drugs [19]. Shortages of generic drugs such as nitrendipine is very likely to occur because of a multiplicity of manufacturers distributed worldwide due to lower manufacturing costs [20,21]. Other sources of generic drug shortages in pharmacies might be the misallocation of certain medicaments inside the country when hospital pharmacies are preferred over the community and a higher demand than expected by the drug manufacturer [22].

The overall number of drugs with significantly decreased availability was less severe than expected. Drug production and distribution was, especially in the first months of the pandemic, a real-world challenge that had tested the resources and supply chains of drug manufacturers. Most of them were capable of securing the supply of their drugs. Additionally, many generic drugs are produced in Poland by local companies. However, they were still depending on ingredients imported from China in some percent.

We identified a significant number of drugs with a relatively low median availability during the timespan of our study. Interestingly, the median level of many combined drug supplies is relatively low. Combined drugs are becoming more and more critical in the proper management of chronic diseases and are vigorously implemented in the newest guidelines regarding the treatment of hypertension as the first treatment option for most patients [23]. Additionally, the combination of statin and ezetimibe should be proposed for patients who did not reach the LDL cholesterol target level on statin [24]. There is also a possibility of using combined oral antidiabetic drugs to better glycemic control among patients with type 2 diabetes [25,26]. Combined drugs are more effective in the treatment and very convenient in usage, especially in the older population. Combining two or more drugs in a single pill reduces the risk of accidental omission of the proper dosage and is considered to be more cost-effective [27,28]. We also have to indicate that more than half of drugs with a lower median availability belong to either NAD or combined NAD. There is a pattern that less available drugs are those more expensive and more innovative. A study conducted several years ago indicated that most Polish type 2 diabetes patients did not meet the guidelines criteria for maintenance of glycemia level [29]. It was also pointed out that most of the patients' NAD comprised metformin alone or in combination also because of restricted access to other drugs [29]. Moreover, most drugs with a limited availability are not refunded or have narrow refundation criteria (e.g., GLP-1 analogs or SGLT-2 inhibitors).

4.2. Strengths and Practical Implications

We show the importance of platforms such as GdziePoLek. Thanks to that kind of service, patients could easily find the drug of their interest in their closest neighborhood. Our study showed that during the COVID-19 pandemics, most of the essential cardiodiabetological drugs were available in most of the monitored pharmacies. There is a possibility that thanks to the option of checking the drugs' availability online, people didn't overbuy their drugs in panic. We also indicate that access to several drugs in Poland, especially novel non-refunded agents and polypills is not as good as it should be.

4.3. Limitations

Our study has some limitations. We could not have combined the data about drug availability with its corresponding sales report. While having this information, we could assess the demand for several drugs with a low median availability and those with the most severe drop of accessibility during the COVID-19 pandemics. We were also not able to conclude the specific reason for certain drugs' availability level drop. There were no reports produced by drug manufacturers regarding their availability and so we could only hypothesize on the exact reason for some medicaments' severe drop in availability. The data comprise several hundreds of pharmacies across Poland, but not all of them. There-fore, there is a possibility that some of the analyzed drugs have a different availability in some areas of Poland, and thus our analysis might not be representative for all regions. We also have to take under consideration the fact that common practice among many pharmacies is to order drugs, especially the expensive ones, upon request by the patient.

5. Conclusions

The decrease in drug availability during the COVID-19 pandemic was not as severe as expected. The availability of only two cardiodiabetological agents decreased significantly. In the years 2019–2020, novel agents and polypills had limited availability in a sample of Polish pharmacies.

Supplementary Materials: The following supporting information can be downloaded at: https://www.mdpi.com/article/10.3390/biomed2010013/s1, Table S1: List of drugs used in availability analysis. Figure S1: Availability of drugs with availability decrease by more than 5% and less than 20% during the COVID-19 pandemic. Figure S2: Drugs with median availability above 50%.

Author Contributions: Conceptualization—M.K.; Data Curation—B.O.; Methodology—M.K., M.S.; Formal analysis—B.M.N.; Investigation—B.M.N.; Methodology—B.M.N.; Software—B.M.N.; Visualization—B.M.N.; Supervision—P.B.; Writing—original draft—B.M.N., M.K., B.O.; Writing—review & editing—B.M.N., M.K., B.O., M.S., P.B. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Institutional Review Board Statement: No ethical review was required.

Informed Consent Statement: Not applicable.

Data Availability Statement: The data presented in this study are available in Supplementary Materials.

Conflicts of Interest: B.O. works for GdziePoLek company. B.O. provided the data from GdziePolek, and helped in the writing of the chapter about data collection. Authors from Poznan University of Medical Sciences didn't receive any money from GdziePoLek company and do not declare any financial or personal relationship with GdziePoLek.

References

1. OECD. Poland: Country Health Profile 2017, State of Health in the EU. *Eur. J. Public Health* **2018**, *28*, 203. [CrossRef]
2. Visseren, F.L.J.; Mach, F.; Smulders, Y.M.; Carballo, D.; Koskinas, K.C.; Bäck, M.; Benetos, A.; Biffi, A.; Boavida, J.M.; Capodanno, D.; et al. 2021 ESC Guidelines on cardiovascular disease prevention in clinical practice. *Eur. Heart J.* **2021**, *42*, 3227–3337. [CrossRef] [PubMed]
3. European Commission. Dependency of the EU Pharmaceutical Industry on Active Pharmaceutical Ingredients and Chemical Raw Materials Imported from Third Countries. 2020. Available online: https://ec.europa.eu/health/sites/default/files/files/committee/ev_20200312_795_en.pdf (accessed on 29 July 2021).
4. Coelho, C.M.; Suttiwan, P.; Arato, N.; Zsido, A.N. On the nature of fear and anxiety triggered by COVID-19. *Front. Psychol.* **2020**, *11*, 581314. [CrossRef] [PubMed]
5. Wong, L.E.; Hawkins, J.E.; Langness, S.; Murrell, K.L.; Iris, P.; Sammann, A. Where are all the patients? Addressing COVID-19 fear to encourage sick patients to seek emergency care. *NEJM Catal. Innov. Care Deliv.* **2020**, *12*, 583742242. [CrossRef]
6. Zhang, H.; Penninger, J.M.; Li, Y.; Zhong, N.; Slutsky, A.S. Angiotensin-converting enzyme 2 (ACE2) as a SARS-CoV-2 receptor: Molecular mechanisms and potential therapeutic target. *Intensive Care Med.* **2020**, *46*, 586–590. [CrossRef] [PubMed]

7. Fosbøl, E.L.; Butt, J.H.; Østergaard, L.; Andersson, C.; Selmer, C.; Kragholm, K.; Schou, M.; Phelps, M.D.; Gislason, G.H.; Gerds, T.A.; et al. Association of angiotensin-converting enzyme inhibitor or angiotensin receptor blocker use with COVID-19 diagnosis and mortality. *JAMA* **2020**, *324*, 168–177. [CrossRef]
8. Cannata, F.; Chiarito, M.; Reimers, B.; Azzolini, E.; Ferrante, G.; My, I.; Viggiani, G.; Panico, C.; Regazzoli, D.; Ciccarelli, M.; et al. Continuation versus discontinuation of ACE inhibitors or angiotensin II receptor blockers in COVID-19, Effects on blood pressure control and mortality. *Eur. Hear J.-Cardiovasc. Pharmacother.* **2020**, *6*, 412–414. [CrossRef]
9. GdziePoLek. Available online: https://www.gdziepolek.pl/ (accessed on 29 July 2021).
10. NFZ. Pharmacy Refund in Poland. Available online: https://statystyki.nfz.gov.pl/PharmacyRefund/ (accessed on 31 January 2022).
11. Gujski, M.; Raciborski, F.; Jankowski, M.; Nowicka, P.M.; Rakocy, K.; Pinkas, J. Epidemiological analysis of the first 1389 cases of COVID-19 in Poland: A preliminary report. *Med. Sci. Monit.* **2020**, *26*, e924702-1–e924702-8. [CrossRef]
12. Shukar, S.; Zahoor, F.; Hayat, K.; Saeed, A.; Gillani, A.H.; Omer, S.; Hu, S.; Babar, Z.-U.; Fang, Y.; Yang, C. Drug shortage: Causes, impact, and mitigation strategies. *Front. Pharmacol.* **2021**, *12*, 693426. [CrossRef]
13. Sousa-Pinto, B.; Anto, A.; Czarlewski, W.; Anto, J.M.; Fonseca, J.A.; Bousquet, J. Assessment of the impact of media coverage on COVID-19-Related google trends data: Infodemiology study. *J. Med. Internet Res.* **2020**, *22*, e19611. [CrossRef]
14. Romano, S.; Galante, H.; Figueira, D.; Mendes, Z.; Rodrigues, A.T. Time-trend analysis of medicine sales and shortages during COVID-19 outbreak: Data from community pharmacies. *Res. Soc. Adm. Pharm.* **2020**, *17*, 1876–1881. [CrossRef] [PubMed]
15. Patel, R.; Czuprynska, J.; Roberts, L.N.; Vadher, B.; Rea, C.; Patel, R.; Gee, E.; Saul, G.; Coles, E.; Brown, A.; et al. Switching warfarin patients to a direct oral anticoagulant during the Coronavirus Disease-19 pandemic. *Thromb. Res.* **2021**, *197*, 192–194. [CrossRef] [PubMed]
16. Kow, C.S.; Sunter, W.; Bain, A.; Zaidi, S.T.R.; Hasan, S.S. Management of outpatient warfarin therapy amid COVID-19 pandemic: A practical guide. *Am. J. Cardiovasc. Drugs* **2020**, *20*, 301–309. [CrossRef] [PubMed]
17. Hindricks, G.; Potpara, T.; Dagres, N.; Arbelo, E.; Bax, J.J.; Blomström-Lundqvist, C.; Boriani, G.; Castella, M.; Dan, G.-A.; Dilaveris, P.E.; et al. 2020 ESC Guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association for Cardio-Thoracic Surgery (EACTS). *Eur. Heart J.* **2021**, *42*, 373–498. [CrossRef]
18. Grimaldi, G.; Ancona, D.; Tricarico, D.; Stella, P.; Procacci, C.; Germinario, A.; Bavaro, V.; Montanaro, V.; Donne, A.D. Analysis of the introduction in clinical practice of new oral anticoagulants in local health agency bt: Translation of the clinical trial data to a local health care area. *Pharmaceutics* **2021**, *13*, 252. [CrossRef]
19. Ministerstwo Zdrowia. Komunikat Ministra Zdrowia w Sprawie Dostępności do Produktów Leczniczych: Nitrendypina Egis, Pregnyl, Alvesco, Dilzem, Oxycardil. 2020. Available online: https://rx.edu.pl/wp-content/uploads/2020/08/Komunikat_Ministra_Zdrowia_w_sprawie_doste%CC%A8pnos%CC%81ci_do_produkto%CC%81w_leczniczych-1-1.pdf (accessed on 29 July 2021).
20. Choo, E.K.; Rajkumar, S.V. Medication shortages during the COVID-19 crisis: What we must do. *Mayo Clin. Proc.* **2020**, *95*, 1112–1115. [CrossRef]
21. Lješkovic, N.J.; Galović, A.J.; Stojkov, S.; Jojić, N.; Gigov, S. Medicine shortages in Serbia: Pharmacists' standpoint and potential solutions for a non-eu country. *Pharmaceutics* **2021**, *13*, 448. [CrossRef]
22. Kuo, S.; Ou, H.T.; Wang, C.J. Managing medication supply chains: Lessons learned from Taiwan during the COVID-19 pandemic and preparedness planning for the future. *J. Am. Pharm. Assoc.* **2021**, *61*, e12–e15. [CrossRef]
23. Williams, B.; Mancia, G.; Spiering, W.; Rosei, E.A.; Azizi, M.; Burnier, M.; Clement, D.; Coca, A.; De Simone, G.; Dominiczak, A.; et al. 2018 practice guidelines for the management of arterial hypertension of the European society of cardiology and the European society of hypertension ESC/ESH task force for the management of arterial hypertension. *J. Hypertens.* **2018**, *36*, 2284–2309. [CrossRef]
24. Mach, F.; Baigent, C.; Catapano, A.L.; Koskinas, K.C.; Casula, M.; Badimon, L.; Chapman, M.J.; De Backer, G.G.; Delgado, V.; Ference, B.A.; et al. 2019 ESC/EAS Guidelines for the management of dyslipidaemias: Lipid modification to reduce cardiovascular risk. *Eur. Heart J.* **2020**, *41*, 111–188. [CrossRef]
25. Davies, M.J.; Alessio, D.A.D.; Fradkin, J.; Kernan, W.N.; Mathieu, C. ADA EASD consensus management of T2DM. *Diabetologia* **2018**, *61*, 2461–2498. [CrossRef] [PubMed]
26. Vieira, R.; Souto, S.B.; Sánchez-López, E.; López Machado, A.; Severino, P.; Jose, S.; Santini, A.; Fortuna, A.; García, M.L.; Silva, A.M.; et al. Sugar-lowering drugs for type 2 diabetes mellitus and metabolic syndrome—Review of classical and new compounds: Part-I. *Pharmaceuticals* **2019**, *12*, 152. [CrossRef] [PubMed]
27. Rochlani, Y.; Khan, M.H.; Banach, M.; Aronow, W.S. Are two drugs better than one? A review of combination therapies for hypertension. *Expert Opin. Pharmacother.* **2017**, *18*, 377–386. [CrossRef] [PubMed]
28. Baumgartner, A.; Drame, K.; Geutjens, S.; Airaksinen, M. Does the polypill improve patient adherence compared to its individual formulations? A systematic review. *Pharmaceutics* **2020**, *12*, 190. [CrossRef]
29. Bała, M.; Płaczkiewicz-Jankowska, E.; Leśniak, W.; Topór-Mądry, R.; Michałejko, M.; Jankowski, M.; Strzeszyński, Ł.; Sieradzki, J.; Czupryniak, L.; Małecki, M.; et al. Management and treatment goals in Polish patients with type 2 diabetes of more than ten years' duration—Results of ARETAEUS2-grupa study. *Pol. Arch. Intern. Med.* **2014**, *65*, 158–168. [CrossRef]