

Supplementary material for

Comparison of Drug Prescribing Before and During the COVID-19 Pandemic – A Cross-national European Study

Pharmacoepidemiology and Drug Safety

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This supplement contains details on data sources, calculation of therapeutic quantities in packs, dispensed DDD per 1000 inhabitants per day (DDD/TID), and their relative changes in the periods before and during the COVID-19 pandemic. It also contains details of the ARIMA time series models.

Table S1: Data sources

Region	Source for dispensed volumes of medicines	Population size in years 2017 to 2020				Source for population size
		2017	2018	2019	2020	
Catalonia	Receptes facturades al Servei Català de la Salut. Health Department. Generalitat de Catalunya.	7 488 302	7 518 913	7 570 452	7 653 845	Registre central de població acreditada del Servei Català de la Salut (RCA). Health Department. Generalitat de Catalunya
Czechia	State Institute for Drug Control – DIS-13 Reporting supplies of distributed human medicinal products	10 589 526	10 626 430	10 669 324	10 701 777	Czech Statistical Office (https://www.czso.cz/)
Germany	GAmSi database at AOK Research Institute (WiDO)	72 258 037	72 802 100	73 009 237	73 357 862	Bundesministerium für Gesundheit (https://www.bundesgesundheitsministerium.de/themen/krankenversicherung/zahlen-und-fakten-zur-krankenversicherung/mitglieder-und-versicherte.html)
Lithuania	State Medicines Control Agency	2 824 030	2 801 501	2 792 209	2 796 025	Statistics Lithuania (https://www.stat.gov.lt/#)
Romagna	Prescribing Information System for Approved Drugs by the National Health Service”	1 117 581	1 118 683	1 120 905	1 120 074	ISTAT (http://dati.istat.it/)
Scotland	NHS Scotland Prescribing Information System (PIS)	5 424 800	5 438 100	5 463 300	5 465 000	National Records of Scotland (https://nrscotland.gov.uk)
Slovenia	Database at Health Insurance Institute of Slovenia	2 066 161	2 070 050	2 089 310	2 100 126	Statistical Office of Republic of Slovenia (https://www.stat.si/StatWeb/en)
Sweden	Prescription dispensing data from the Swedish E-health Agency	9 995 153	10 120 242	10 230 185	10 327 589	Swedish population Statistics (https://www.scb.se)

Note: Population sizes were determined to 1st July of the respective years with the following exceptions: Catalonia – 31st December, Czechia – 30th June, Romagna and Sweden – 1st January. Population sizes used for calculations in each period are those for the year in which the period started.

Figure S1: Selection procedure for the ten therapeutic subgroups with the highest volume across countries/regions

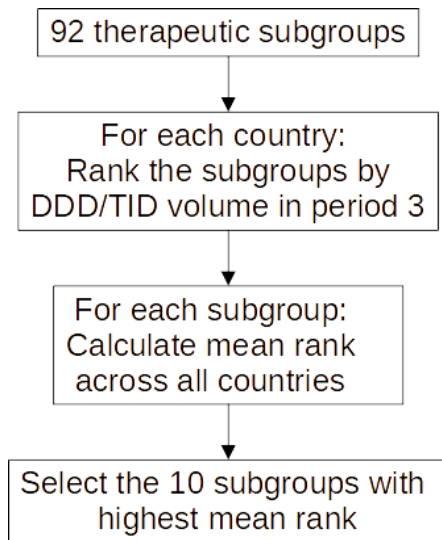
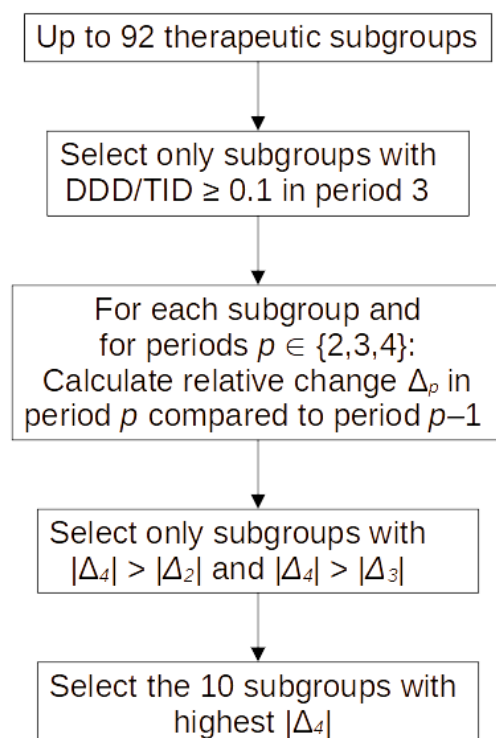


Figure S2: Selection procedure for the ten therapeutic subgroups with the largest changes per country

For each country separately:



Changes in therapeutic quantity per pack

Changes in the average therapeutic quantity per pack (DDD per pack) are influenced both by changes in the number of units or the dosage strength of the units in dispensed packs and by structural changes in the market.

Let us divide the whole market into the therapeutic subgroups indexed by i . Let d_i^0 be the DDD volume of therapeutic subgroup i in the base period and d_i^1 the DDD volume in the period of interest and similarly for the number of packs p_i^0 and p_i^1 . Then $u_i^0 = \frac{d_i^0}{p_i^0}$ and $u_i^1 = \frac{d_i^1}{p_i^1}$ are the average number of DDDs per pack in therapeutic subgroup i in the two periods. The corresponding values for the whole market will be denoted without the subscript (d^0 , d^1 and so forth).

We define the relative change in overall DDD volume in the whole market as Δd , the relative overall change in number of packs as Δp , and the relative overall change in average number of DDDs per pack as Δu .

$$\Delta d = \frac{\sum_i d_i^1}{\sum_i d_i^0} = \frac{d^1}{d^0}$$

$$\Delta p = \frac{\sum_i p_i^1}{\sum_i p_i^0} = \frac{p^1}{p^0}$$

$$\Delta u = \frac{\Delta d}{\Delta p}$$

By substituting for d_i^0 and d_i^1 and expanding the ratio by $\frac{\sum_i u_i^1 p_i^0}{\sum_i u_i^1 p_i^0}$ we get

$$\Delta d = \frac{\sum_i u_i^1 p_i^1}{\sum_i u_i^0 p_i^0} = \frac{\sum_i u_i^1 p_i^0}{\sum_i u_i^0 p_i^0} \cdot \frac{\sum_i u_i^1 p_i^1}{\sum_i u_i^1 p_i^0}$$

The first factor on the right side of the equation corresponds to the relative change of overall DDD volume under the assumption that therapeutic quantities per pack changed as they did in reality, but the number of packs had stayed fixed at the base period level. Thus this term expresses the effect of changes in the average number of DDDs per pack prescribed, cleaned of any changes in the numbers of packs, as introduced in the first paragraph of this section. We refer to this term as Δv .

Conversely, the second factor on the right side of the equation represents the relative change of overall DDD volume not attributable to changes in numbers of DDDs per pack (keeping DDDs per pack constant), but to changes in the numbers of packs. We will denote this factor with Δq .

Thus we get:

$$\Delta v = \frac{\sum_i u_i^1 p_i^0}{\sum_i u_i^0 p_i^0}$$

$$\Delta q = \frac{\sum_i u_i^1 p_i^1}{\sum_i u_i^1 p_i^0}$$

$$\Delta d = \Delta v \cdot \Delta q$$

We analyze Δq further by expanding it with p^1/p^0 and regrouping:

$$\Delta q = \frac{\sum_i u_i^1 p_i^1}{\sum_i u_i^1 p_i^0} = \frac{p^1}{p^0} \cdot \frac{(\sum_i u_i^1 p_i^1) \cdot p^0}{(\sum_i u_i^1 p_i^1) \cdot p^1} = \frac{p^1}{p^0} \cdot \frac{\sum_i u_i^1 p_i^1}{\sum_i u_i^1 p_i^1 \frac{p^1}{p^0}} = \Delta p \cdot \frac{\sum_i u_i^1 \frac{p_i^1}{p^1}}{\sum_i u_i^1 \frac{p_i^0}{p^0}}$$

The ratios p_i^0/p^0 and p_i^1/p^1 represent the market share of therapeutic subgroup i in the total market measured by number of packs.

Hence, the factor $\frac{\sum_i u_i^1 \frac{p_i^1}{p^1}}{\sum_i u_i^1 \frac{p_i^0}{p^0}}$ is clean of changes in the overall number of packs. It corresponds to

the structural shifts within the market while keeping pack sizes fixed. Thus it expresses the effect that changing market shares for each therapeutic subgroup have on Δq . We will denote this factor as Δs .

From $\Delta q = \Delta p \cdot \Delta s$ we have

$$\Delta d = \Delta p \cdot \Delta v \cdot \Delta s$$

and finally

$$\Delta u = \frac{\Delta d}{\Delta p} = \Delta v \cdot \Delta s$$

We can thus explain the change in average therapeutic quantity per pack Δu as a combined effect of changes in the dispensed therapeutic quantities per pack within the individual therapeutic subgroups (Δv) and of structural shifts in the market shares of those subgroups (Δs).

Table S2: Age and sex distribution of populations covered

Country	CATALONIA		CZECHIA		GERMANY	
Age (years)	%	% female	%	% female	%	% female
0-9	9.1	48.6	10.5	48.8	8.8	48.7
10-19	11.0	48.2	10.1	48.7	8.9	48.5
20-29	11.0	48.4	10.3	48.5	11.6	48.1
30-39	12.6	50.2	13.8	48.4	13.5	49.1
40-49	16.6	49.5	16.6	48.6	12.2	50.9
50-59	14.5	50.1	12.7	49.4	15.9	51.8
60-69	11.2	52.5	12.1	52.4	12.6	53.6
70-79	8.3	55.2	9.7	57.2	8.8	56.6
80-89	4.5	60.9	3.6	64.7	6.5	61.3
90+	1.2	71.5	0.6	73.5	1.2	73.3
Population covered	100.0	50.9	100.0	50.7	88.2	51.8

Country	LITHUANIA		ROMAGNA		SCOTLAND	
Age (years)	%	% female	%	% female	%	% female
0-9	10.4	48.7	8.1	48.2	10.3	48.6
10-19	9.4	48.8	9.2	48.3	10.6	49.0
20-29	12.2	47.8	9.2	48.1	13.2	49.6
30-39	12.9	47.4	10.8	50.5	13.4	50.7
40-49	13.2	50.3	15.6	50.4	12.3	51.2
50-59	15.0	53.1	16.0	50.6	14.5	51.7
60-69	12.6	57.9	12.3	52.5	11.9	51.7
70-79	8.5	65.5	10.3	53.9	8.9	53.5
80-89	5.9†	73.1†	6.8	58.9	4.2	59.4
90+			1.6	70.8	0.8	68.8
Population covered	100.0	53.3	100.0	51.4	100.0	51.2

Country	SLOVENIA		SWEDEN	
Age (years)	%	% female	%	% female
0-9	9.8	48.4	11.7	48.5
10-19	9.7	48.5	11.6	48.4
20-29	10.2	45.9	12.5	47.8
30-39	13.4	46.5	13.5	48.7
40-49	14.9	47.1	12.5	49.1
50-59	14.3	49.2	12.6	49.3
60-69	13.4	50.7	10.7	50.2
70-79	8.8	55.0	9.7	51.6
80-89	4.7	64.0	4.3	57.1
90+	0.9	76.6	1.0	69.6
Population covered	99.0	49.7	100.0	49.7

Note: Age (years) – age distribution of covered population; † percentage for age group 80+

Table S3: Changes between the COVID period and the immediately preceding period in the ten therapeutic subgroups (ATC level 2) of prescription drugs with the highest dispensed volumes (measured by DDD per 1000 inhabitants per day (DDD/TID)) across eight European countries/regions

Therapeutic subgroups shown:

A02	Drugs for acid related disorders	C08	Calcium channel blockers
A10	Drugs used in diabetes	C09	Agents acting on the renin-angiotensin system
B01	Antithrombotic agents	C10	Lipid modifying agents
B03	Antianemic preparations	N06	Psychoanaleptics
C07	Beta blocking agents	R03	Drugs for obstructive airway diseases

Country	ATC	Dispensed volume (DDD/TID)				Change in period 4 relative to period 3 (%)
		Period 1 (Mar 2017– Feb 2018)	Period 2 (Mar 2018– Feb 2019)	Period 3 (pre-COVID period, Mar 2019– Feb 2020)	Period 4 (COVID period, Mar 2020– Feb 2021)	
Catalonia	A02	102.3	100.2	99.6	96.3	-3.3
	A10	69.3	69.1	70.1	69.7	-0.6
	B01	64.3	63.1	68.3	67.7	-0.8
	B03	75.2	77.4	79.5	76.9	-3.1
	C07	23.9	23.2	23.1	22.6	-1.8
	C08	41.7	41.8	42.7	42.4	-0.6
	C09	204.4	203.4	204.5	201.1	-1.7
	C10	99.4	104.5	104.2	106.5	2.2
	N06	88.4	89.8	92.7	93.3	0.7
	R03	49.9	49.9	48.3	44.3	-8.2
Czechia	A02	72.4	74.2	76.9	76.3	-0.7
	A10	89.9	90.3	92.7	93.0	0.4
	B01	94.2	94.4	95.7	96.2	0.5
	B03	107.4	107.4	109.6	111.7	1.9
	C07	66.6	64.1	62.9	61.0	-3.2
	C08	63.5	59.7	59.2	56.2	-5.0
	C09	253.9	250.9	253.5	250.1	-1.3
	C10	135.3	143.3	154.5	166.5	7.8
	N06	65.1	66.8	70.2	70.4	0.3
	R03	52.6	52.5	52.9	53.1	0.3
Germany	A02	146.2	138.8	134.5	133.1	-1.0
	A10	87.2	85.3	86.1	87.8	2.0
	B01	68.6	68.2	69.4	70.3	1.3
	B03	12.8	12.7	12.5	12.1	-3.1
	C07	85.7	80.8	78.6	76.9	-2.1
	C08	87.2	85.7	89.2	91.6	2.8
	C09	356.0	352.4	363.2	368.5	1.5
	C10	91.6	94.1	100.8	109.0	8.2
	N06	66.4	65.4	66.1	67.1	1.5
	R03	52.9	50.8	50.4	49.9	-1.0

(continued)

Table S3: Changes between the COVID period and the immediately preceding period in the ten therapeutic subgroups (ATC level 2) of prescription drugs with the highest dispensed volumes (measured by DDD per 1000 inhabitants per day (DDD/TID)) across eight European countries/regions (continued)

Country	ATC	Dispensed volume (DDD/TID)				Change in period 4 relative to period 3 (%)
		Period 1 (Mar 2017– Feb 2018)	Period 2 (Mar 2018– Feb 2019)	Period 3 (pre-COVID period, Mar 2019– Feb 2020)	Period 4 (COVID period, Mar 2020– Feb 2021)	
Lithuania	A02	34.8	33.9	34.9	38.2	9.3
	A10	51.8	54.7	58.0	59.8	3.1
	B01	22.8	26.3	29.5	30.7	3.9
	B03	3.3	3.2	3.7	3.3	-9.2
	C07	79.0	80.9	83.1	84.7	1.9
	C08	28.5	28.3	28.6	26.7	-6.7
	C09	217.8	222.3	229.2	227.4	-0.8
	C10	39.9	47.8	64.0	75.9	18.7
	N06	52.8	54.1	58.1	59.9	3.2
	R03	33.6	33.2	34.7	34.2	-1.6
Romagna	A02	58.9	59.3	57.5	55.7	-3.2
	A10	62.5	63.1	64.1	61.5	-4.1
	B01	108.2	110.2	112.1	105.6	-5.7
	B03	12.7	11.9	17.8	26.4	48.5
	C07	57.4	57.6	57.9	57.3	-1.0
	C08	56.6	56.5	57.2	57.2	-0.1
	C09	237.0	236.4	235.6	231.6	-1.7
	C10	98.8	101.4	104.8	106.0	1.1
	N06	49.7	51.0	51.3	50.8	-0.9
	R03	35.3	35.1	34.8	29.9	-14.1
Scotland	A02	144.3	145.8	149.1	148.5	-0.4
	A10	63.7	65.2	66.6	67.6	1.5
	B01	81.5	81.1	80.8	81.2	0.6
	B03	207.6	215.2	228.0	221.7	-2.8
	C07	38.2	37.8	37.4	36.9	-1.3
	C08	83.2	84.7	86.8	87.6	0.9
	C09	208.1	208.3	209.1	207.2	-0.9
	C10	156.1	160.6	166.1	170.6	2.7
	N06	145.3	153.8	163.2	170.4	4.4
	R03	81.2	79.7	77.3	79.2	2.5

(continued)

Table S3: Changes between the COVID period and the immediately preceding period in the ten therapeutic subgroups (ATC level 2) of prescription drugs with the highest dispensed volumes (measured by DDD per 1000 inhabitants per day (DDD/TID)) across eight European countries/regions (continued)

Country	ATC	Dispensed volume (DDD/TID)				Change in period 4 relative to period 3 (%)
		Period 1 (Mar 2017– Feb 2018)	Period 2 (Mar 2018– Feb 2019)	Period 3 (pre-COVID period, Mar 2019– Feb 2020)	Period 4 (COVID period, Mar 2020– Feb 2021)	
Slovenia	A02	68.8	70.9	73.5	73.9	0.5
	A10	81.2	82.7	83.7	84.4	0.9
	B01	97.1	98.3	98.9	98.9	0.0
	B03	6.7	6.3	6.0	5.0	-16.6
	C07	44.6	44.9	44.8	44.2	-1.3
	C08	57.2	55.8	54.7	53.2	-2.8
	C09	250.7	247.3	243.4	236.1	-3.0
	C10	133.9	138.6	148.6	155.7	4.8
	N06	67.8	70.5	72.6	71.7	-1.2
	R03	42.0	43.1	43.9	42.2	-3.9
Sweden	A02	65.2	64.3	65.5	64.9	-0.8
	A10	62.5	64.9	67.8	69.3	2.2
	B01	85.2	85.2	85.7	85.0	-0.8
	B03	148.7	133.0	127.8	122.5	-4.1
	C07	48.1	47.1	46.6	45.5	-2.3
	C08	85.3	87.2	91.3	94.5	3.5
	C09	180.1	183.3	189.6	193.0	1.8
	C10	116.3	125.3	135.4	144.1	6.4
	N06	115.3	118.7	123.8	126.8	2.5
	R03	54.8	55.4	57.3	60.2	5.0

Tables S4 – S11 show for each of eight European countries/regions the ten therapeutic subgroups of prescription drugs with the greatest relative change in DDD per 1000 inhabitants per day (DDD/TID) in the COVID period (March 2020 – February 2021) compared to the same months one year before (period 3). The tables also show the main contributing chemical subgroups (ATC level 4) which together cover at least 2/3 of their respective therapeutic subgroup (ATC level 2) DDD volume.

Table S4: Catalonia

ATC level 2	ATC level 4	Change between COVID period and pre-COVID period (%)	Chemical subgroup
G01	G01AF	-15.7	Imidazole derivatives
H02	H02AB	-23.4	Glucocorticoids
J01	J01CA	-53.4	Penicillins with extended spectrum
J01	J01CR	-28.8	Combinations of penicillins, incl. beta-lactamase inhibitors
J01	J01MA	-29.1	Fluoroquinolones
J02	J02AC	-28.4	Triazole derivatives
J04	J04AC	-29.3	Hydrazides
J04	J04AM	-10.8	Combinations of drugs for treatment of tuberculosis
J06	J06BA	95.0	Immunoglobulins, normal human
M01	M01AE	-26.9	Propionic acid derivatives
M03	M03BX	-21.2	Other centrally acting agents
P03	P03AC	31.2	Pyrethrines, incl. synthetic compounds
R01	R01AD	-18.6	Corticosteroids

Table S5: Czechia

ATC level 2	ATC level 4	Change between COVID period and pre-COVID period (%)	Chemical subgroup
A11	A11CC	18.6	Vitamin D and analogues
B02	B02AA	-61.0	Amino acids
B02	B02BA	-1.0	Vitamin K
C04	C04AD	-17.8	Purine derivatives
C04	C04AX	-5.5	Other peripheral vasodilators
D01	D01BA	-24.4	Antifungals for systemic use
J01	J01AA	-21.0	Tetracyclines
J01	J01CE	-57.9	Beta-lactamase sensitive penicillins
J01	J01CR	-33.2	Combinations of penicillins, incl. beta-lactamase inhibitors
J01	J01DC	-46.8	Second-generation cephalosporins
J01	J01FA	-42.3	Macrolides
J04	J04AB	-18.2	Antibiotics
J04	J04AC	-26.1	Hydrazides
J05	J05AB	-0.1	Nucleosides and nucleotides excl. reverse transcriptase inhibitors
J05	J05AF	2.0	Nucleoside and nucleotide reverse transcriptase inhibitors
J05	J05AR	-0.3	Antivirals for treatment of HIV infections, combinations
P01	P01BA	-9.9	Aminoquinolines
R01	R01AD	-17.7	Corticosteroids
R05	R05CB	-24.9	Mucolytics

Table S6: Germany

ATC level 2	ATC level 4	Change between COVID period and pre-COVID period (%)	Chemical subgroup
C04	C04AD	6.9	Purine derivatives
C04	C04AX	-78.5	Other peripheral vasodilators
D04	D04AB	-40.3	Anesthetics for topical use
D04	D04AX	-30.1	Other antipruritics
D08	D08AE	32.1	Phenol and derivatives
J01	J01AA	-12.8	Tetracyclines
J01	J01CA	-36.4	Penicillins with extended spectrum
J01	J01CR	-15.9	Combinations of penicillins, incl. beta-lactamase inhibitors
J01	J01DC	-42.1	Second-generation cephalosporins
J01	J01FA	-52.5	Macrolides
M02	M02AA	-17.7	Antiinflammatory preparations, non-steroids for topical use
M02	M02AX	-22.6	Other topical products for joint and muscular pain
P03	P03AC	-20.7	Pyrethrines, incl. synthetic compounds
P03	P03AX	-49.6	Other ectoparasiticides, incl. scabicides
R01	R01AA	-50.4	Sympathomimetics, plain
R01	R01AD	-6.0	Corticosteroids
R02*	R02AB	-46.9	Antibiotics
R05	R05CA	-50.8	Expectorants
R05	R05CB	-29.0	Mucolytics
S02	S02AA	-25.4	Antiinfectives
S02	S02CA	-11.1	Corticosteroids and antiinfectives in combination

* R02AB covers only 29% of R02 DDD volume, other ATC level 4 subgroups are Germany-specific groups not listed in the WHO ATC classification.

Table S7: Lithuania

ATC level 2	ATC level 4	Change between COVID period and pre-COVID period (%)	Chemical subgroup
A02	A02BC	17.6	Proton pump inhibitors
D01	D01BA	-19.5	Antifungals for systemic use
G02	G02BB	-9.8	Intravaginal contraceptives
J01	J01AA	0.9	Tetracyclines
J01	J01CA	-40.6	Penicillins with extended spectrum
J01	J01CE	-77.0	Beta-lactamase sensitive penicillins
J01	J01CR	-33.3	Combinations of penicillins, incl. beta-lactamase inhibitors
J01	J01EE	-52.3	Combinations of sulfonamides and trimethoprim, incl. derivatives
J01	J01FA	-41.2	Macrolides
J02	J02AC	-13.6	Triazole derivatives
N02	N02AB	2.7	Phenylpiperidine derivatives
N02	N02CC	20.6	Selective serotonin (5HT1) agonists
P01	P01BA	20.5	Aminoquinolines
P02	P02CA	-22.6	Benzimidazole derivatives
R01	R01AD	-34.4	Corticosteroids
R06	R06AX	-9.9	Other antihistamines for systemic use

Table S8: Romagna

ATC level 2	ATC level 4	Change between COVID period and pre-COVID period (%)	Chemical subgroup
A12	A12AA	-49.9	Calcium
A12	A12AX	-26.1	Calcium, combinations with vitamin D and/or other drugs
D01	D01BA	-21.8	Antifungals for systemic use
D07	D07AC	6.7	Corticosteroids, potent (group III)
D07	D07AD	44.3	Corticosteroids, very potent (group IV)
D10	D10BA	16.0	Retinoids for treatment of acne
J01	J01CA	-50.5	Penicillins with extended spectrum
J01	J01CR	-41.4	Combinations of penicillins, incl. beta-lactamase inhibitors
J01	J01FA	-47.0	Macrolides
J02	J02AC	-16.4	Triazole derivatives
J04	J04AB	-21.8	Antibiotics
J04	J04AC	-24.1	Hydrazides
L02	L02AE	-10.2	Gonadotropin releasing hormone analogues
L02	L02BG	-14.5	Aromatase inhibitors
P02	P02CA	-26.8	Benzimidazole derivatives
R03	R03AK	-0.1	Adrenergics in combination with corticosteroids or other drugs, excl. anticholinergics
R03	R03BA	-51.8	Glucocorticoids
R03	R03BB	-10.5	Anticholinergics

Table S9: Scotland

ATC level 2	ATC level 4	Change between COVID period and pre-COVID period (%)	Chemical subgroup
A01	A01AB	-16.0	Antiinfectives and antiseptics for local oral treatment
A08	A08AB	-26.9	Peripherally acting antiobesity products
A12	A12AA	8.4	Calcium
D01	D01BA	-38.9	Antifungals for systemic use
G03	G03AC	-44.3	Progestogens
G03	G03CA	1.9	Natural and semisynthetic estrogens, plain
H01	H01BA	-11.3	Vasopressin and analogues
H02	H02AB	-14.5	Glucocorticoids
J01	J01AA	-12.0	Tetracyclines
J01	J01CA	-29.1	Penicillins with extended spectrum
J01	J01FA	-20.2	Macrolides
J02	J02AC	-12.9	Triazole derivatives
R01	R01AD	-8.0	Corticosteroids

Table S10: Slovenia

ATC level 2	ATC level 4	Change between COVID period and pre-COVID period (%)	Chemical subgroup
A11	A11CC	45.7	Vitamin D and analogues
B02	B02AA	9.9	Amino acids
B02	B02BX	11.8	Other systemic hemostatics
B03	B03AA	-15.0	Iron bivalent, oral preparations
B03	B03AB	-25.3	Iron trivalent, oral preparations
D01	D01BA	-33.8	Antifungals for systemic use
D10	D10BA	-12.2	Retinoids for treatment of acne
G01	G01AF	-10.3	Imidazole derivatives
J01	J01CA	-51.9	Penicillins with extended spectrum
J01	J01CE	-59.8	Beta-lactamase sensitive penicillins
J01	J01CR	-21.1	Combinations of penicillins, incl. beta-lactamase inhibitors
J01	J01FA	-36.5	Macrolides
J02	J02AC	-15.5	Triazole derivatives
P02	P02CA	-18.6	Benzimidazole derivatives
R01	R01AD	-16.9	Corticosteroids

Table S11: Sweden

ATC level 2	ATC level 4	Change between COVID period and pre-COVID period (%)	Chemical subgroup
A01	A01AA	-25.3	Caries prophylactic agents
A03	A03AX	-3.5	Other drugs for functional gastrointestinal disorders
A03	A03FA	-1.7	Propulsives
A11	A11CC	14.3	Vitamin D and analogues
C02	C02CA	13.1	Alpha-adrenoreceptor antagonists
D01	D01BA	-15.1	Antifungals for systemic use
D05	D05BB	-6.6	Retinoids for treatment of psoriasis
D11	D11AX	17.1	Other dermatologicals
J01	J01AA	-13.7	Tetracyclines
J01	J01CA	-17.2	Penicillins with extended spectrum
J01	J01CE	-34.8	Beta-lactamase sensitive penicillins
J01	J01CF	-9.6	Beta-lactamase resistant penicillins
R01	R01AD	-4.8	Corticosteroids
R03	R03AC	1.7	Selective beta-2-adrenoreceptor agonists
R03	R03AK	8.6	Adrenergics in combination with corticosteroids or other drugs, excl. anticholinergics
R03	R03BA	5.5	Glucocorticoids

Figures S3 and S4 show relative changes in the top ten therapeutic subgroups with highest dispensed volume (in the pre-COVID period) across eight European countries/regions split in half-years.

Legend for Figures S3 and S4:

Country codes:

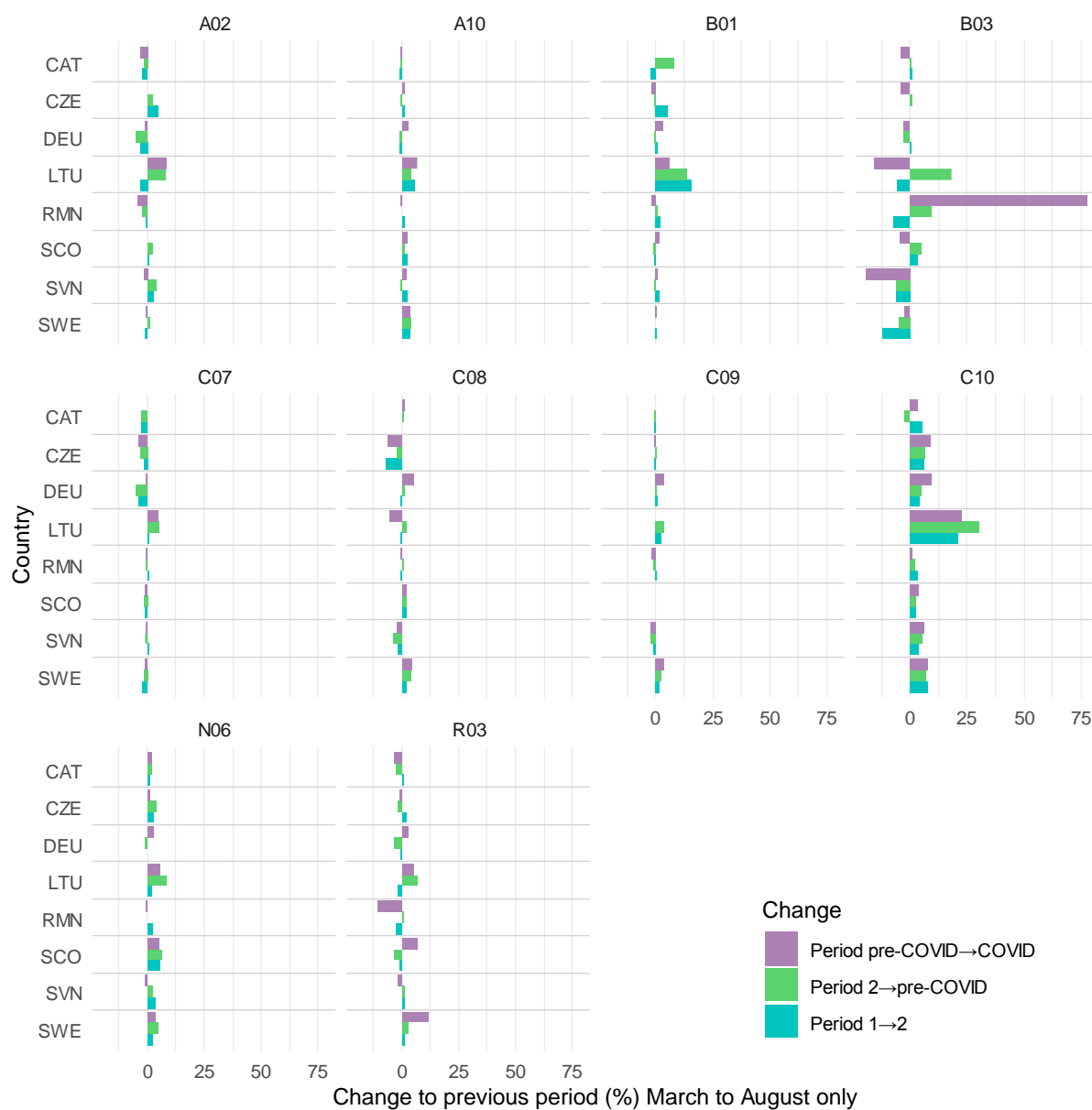
CAT	Catalonia	CZE	Czechia	DEU	Germany	LTU	Lithuania
RMN	Romagna	SCO	Scotland	SVN	Slovenia	SWE	Sweden

Therapeutic subgroups:

A02	Drugs for acid related disorders	C08	Calcium channel blockers
A10	Drugs used in diabetes	C09	Agents acting on the renin-angiotensin system
B01	Antithrombotic agents	C10	Lipid modifying agents
B03	Antianemic preparations	N06	Psychoanaleptics
C07	Beta blocking agents	R03	Drugs for obstructive airway diseases

Note: B03 - change of reimbursement rules in Romagna: since September 2019 the package of folic acid (B03BB01) 5mg with 120 tablets has been included in the list of reimbursed medicines whereas before only smaller packages were reimbursed.

Figure S3: Top ten therapeutic subgroups with highest dispensed volume (in the pre-COVID period) across eight European countries/regions: relative change of DDD/TID between four 6-month periods March to August in 2017 to 2020



Legend for Figure S3:

Periods:

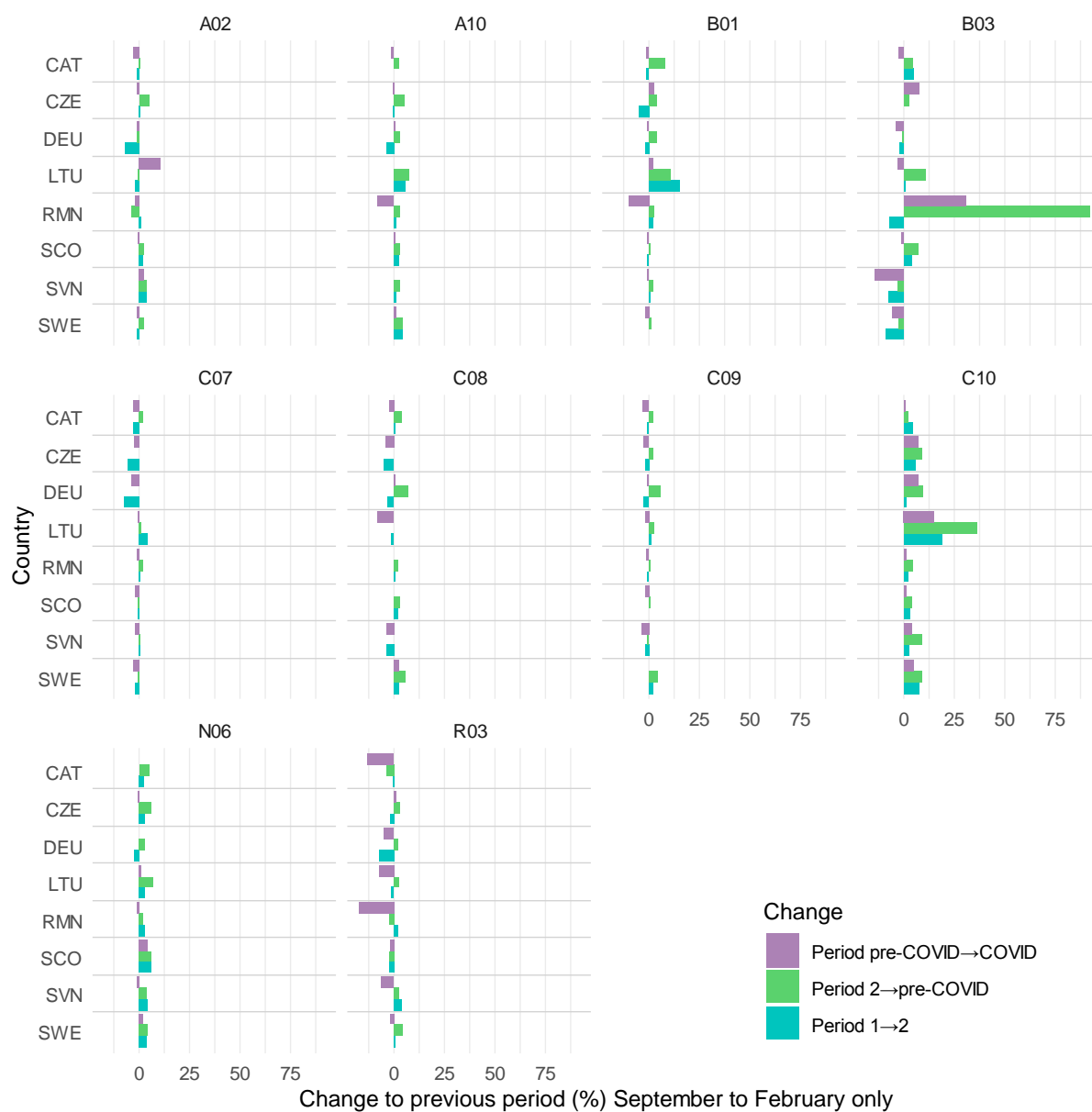
Period 1: March 2017 – August 2017

Period 2: March 2018 – August 2018

Pre-COVID period: March 2019 – August 2019

COVID period: March 2020 – August 2020

Figure S4: Top ten therapeutic subgroups with highest dispensed volume (in the pre-COVID period) across eight European countries/regions: relative change of DDD/TID between four 6-month periods September to February in 2017 to 2021



Legend for Figure S4:

Periods:

Period 1: September 2017 – February 2018

Period 2: September 2018 – February 2019

Pre-COVID period: September 2019 – February 2020

COVID period: September 2020 – February 2021

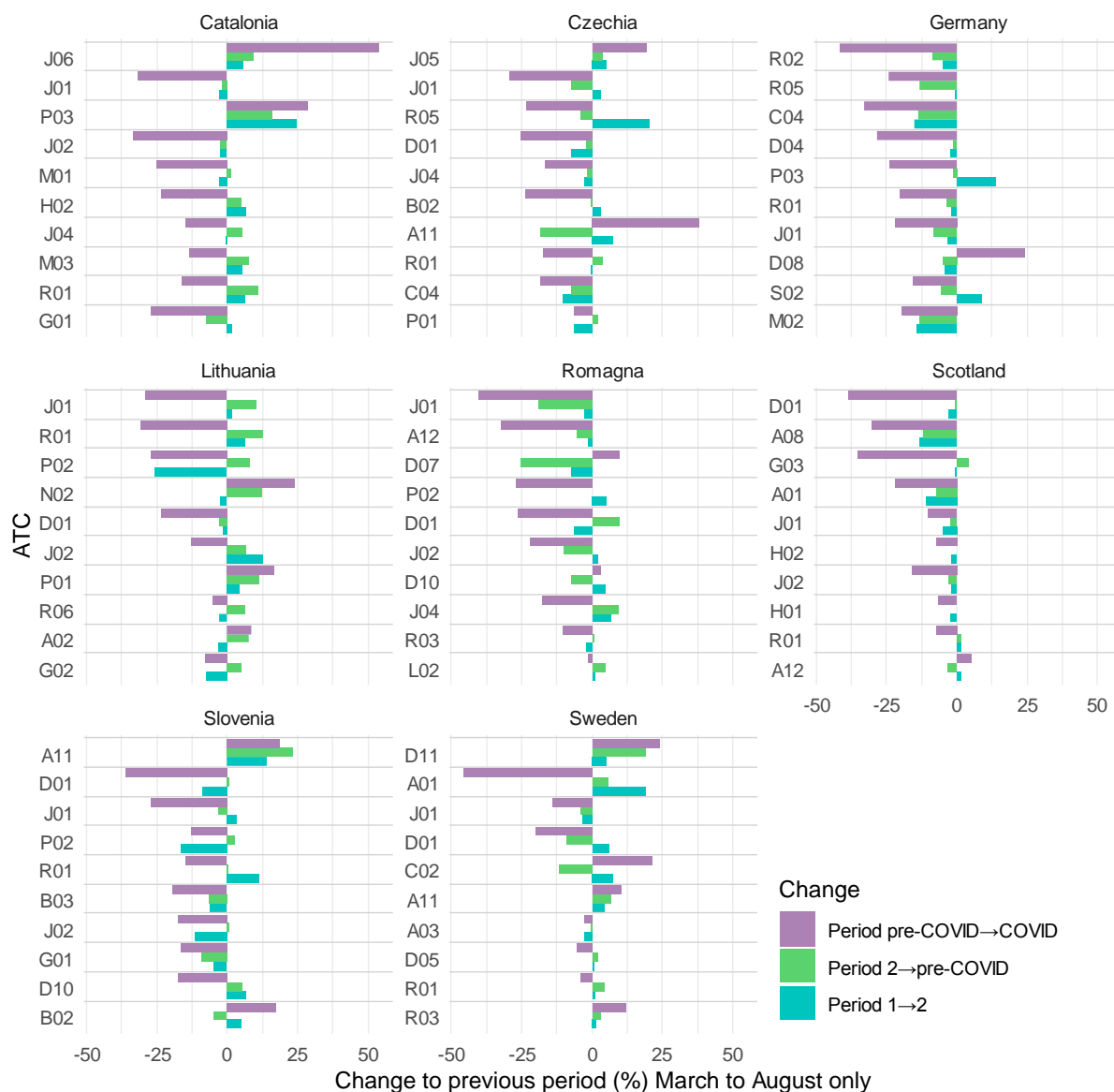
Figures S5 and S6 show relative changes in the top ten therapeutic subgroups with most marked relative change in DDD/TID volume (in the COVID period relative to the pre-COVID period) across eight European countries/regions split in half-years.

Legend for Figures S5 and S6:

Therapeutic subgroups

A01	Stomatological preparations	H02	Corticosteroids for systemic use
A02	Drugs for acid related disorders	J01	Antibacterials for systemic use
A03	Drugs for functional gastrointestinal disorders	J02	Antimycotics for systemic use
A08	Antiobesity preparations, excl. diet products	J04	Antimycobacterials
A11	Vitamins	J05	Antivirals for systemic use
A12	Mineral supplements	J06	Immune sera and immunoglobulins
B02	Antihemorrhagics	L02	Endocrine therapy
B03	Antianemic preparations	M01	Antiinflammatory and antirheumatic products
C02	Antihypertensives	M02	Topical products for joint and muscular pain
C04	Peripheral vasodilators	M03	Muscle relaxants
D01	Antifungals for dermatological use	N02	Analgesics
D04	Antipruritics, incl. antihistamines, anesthetics, etc.	P01	Antiprotozoals
D05	Antipsoriatics	P02	Anthelmintics
D07	Corticosteroids, dermatological preparations	P03	Ectoparasiticides, incl. scabicides, insecticides and repellents
D08	Antiseptics and disinfectants	R01	Nasal preparations
D10	Anti-acne preparations	R02	Throat preparations
D11	Other dermatological preparations	R03	Drugs for obstructive airway diseases
G01	Gynecological antiinfectives and antiseptics	R05	Cough and cold preparations
G02	Other gynecologicals	R06	Antihistamines for systemic use
G03	Sex hormones and modulators of the genital system	S02	Otologicals
H01	Pituitary and hypothalamic hormones and analogues		

Figure S5: Top ten therapeutic subgroups with most marked relative change in DDD/TID volume (in the COVID period relative to pre-COVID period) across eight European countries/regions: relative change of DDD/TID between four 6-month periods March to August in 2017 to 2020



Legend for Figure S5:

Periods:

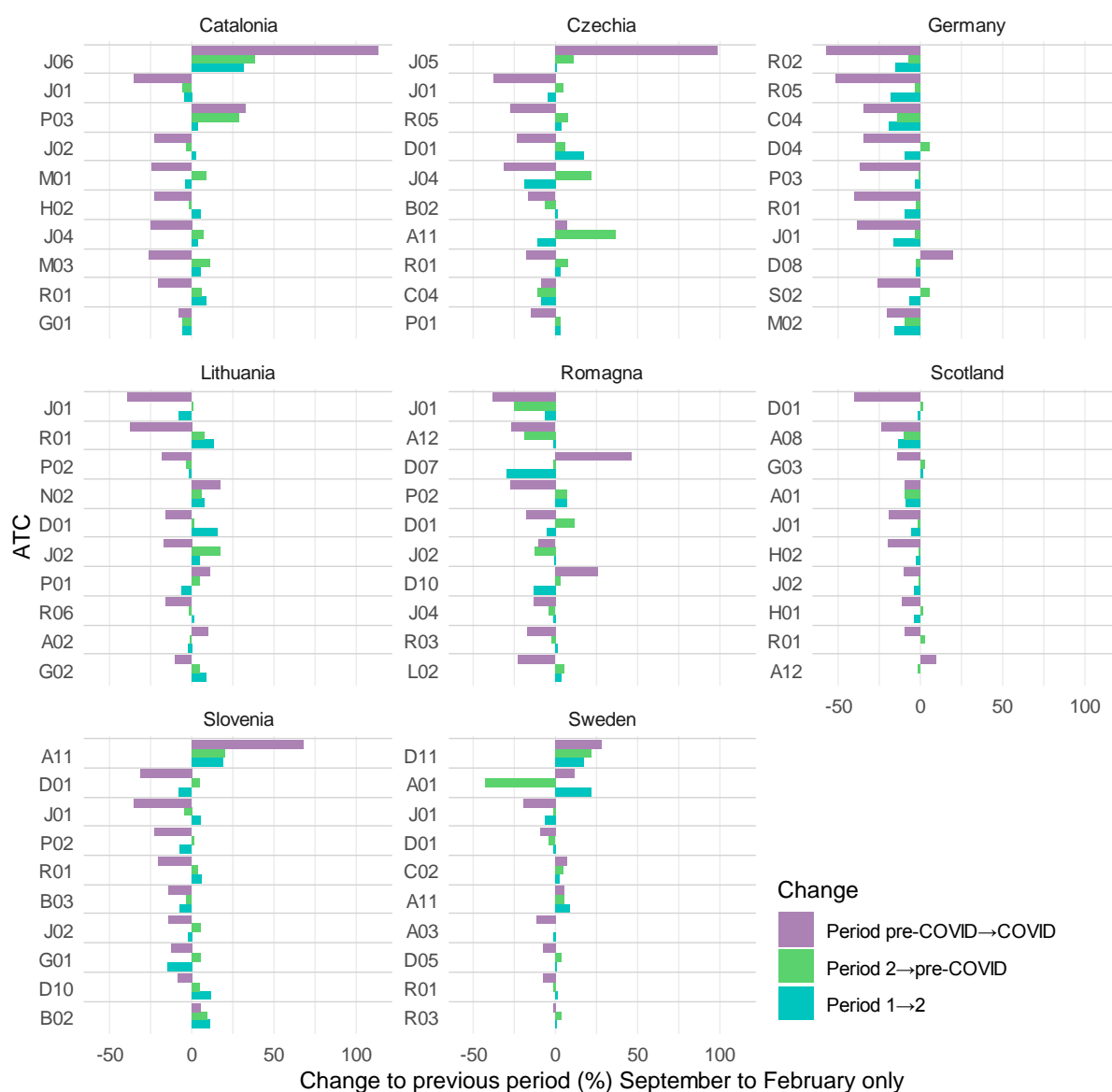
Period 1: March 2017 – August 2017

Period 2: March 2018 – August 2018

Pre-COVID period: March 2019 – August 2019

COVID period: March 2020 – August 2020

Figure S6: Top ten therapeutic subgroups with most marked relative change in DDD/TID volume (in the COVID period relative to pre-COVID period) across eight European countries/regions: relative change of DDD/TID between four 6-month periods September to February in 2017 to 2021



Legend for Figure S6:

Periods:

Period 1: September 2017 – February 2018

Period 2: September 2018 – February 2019

Pre-COVID period: September 2019 – February 2020

COVID period: September 2020 – February 2021

Time series analysis

Figures S7 and S8 show ARIMA models of total market development (in DDD/TID) in eight European countries/regions. Details of the models with the pandemic impact assessment are in Table S12.

Legend for Figures S7 and S8:

Black line – time series (actual values)

Red vertical line – onset of the pandemic

Grey line – ARIMA model (accounting for long-term effect of the COVID-19 pandemic and its short-term stockpiling effect in the first three months of pandemic)

Blue line – prediction on the base of the ARIMA model for data before the onset of the pandemic

Violet strips – confidence intervals (CI) of predictions (on the base of the ARIMA model for data before the onset of the pandemic). Darker violet: 80% CI, lighter violet: 95% CI.

Figure S7:

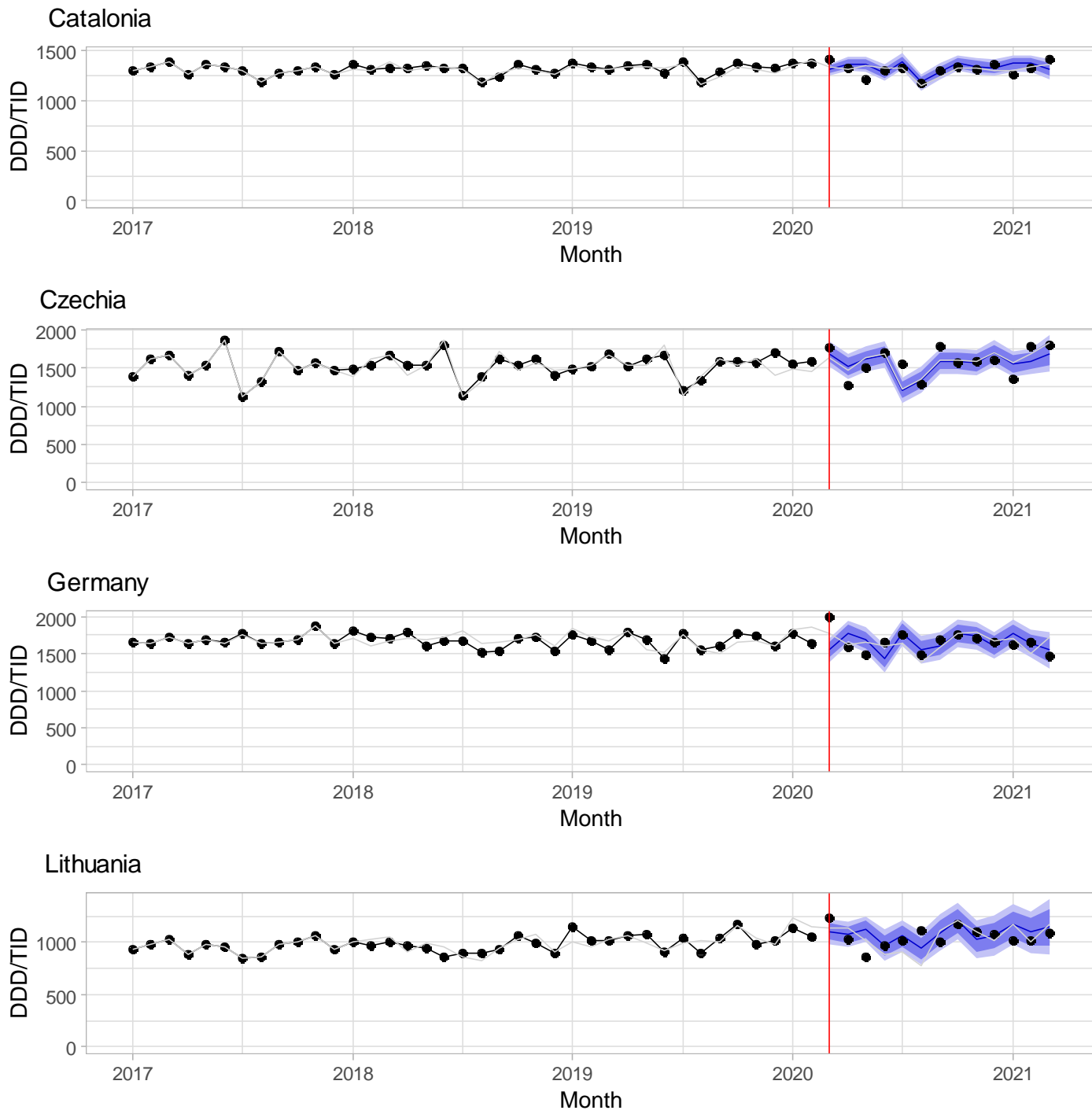


Figure S8:

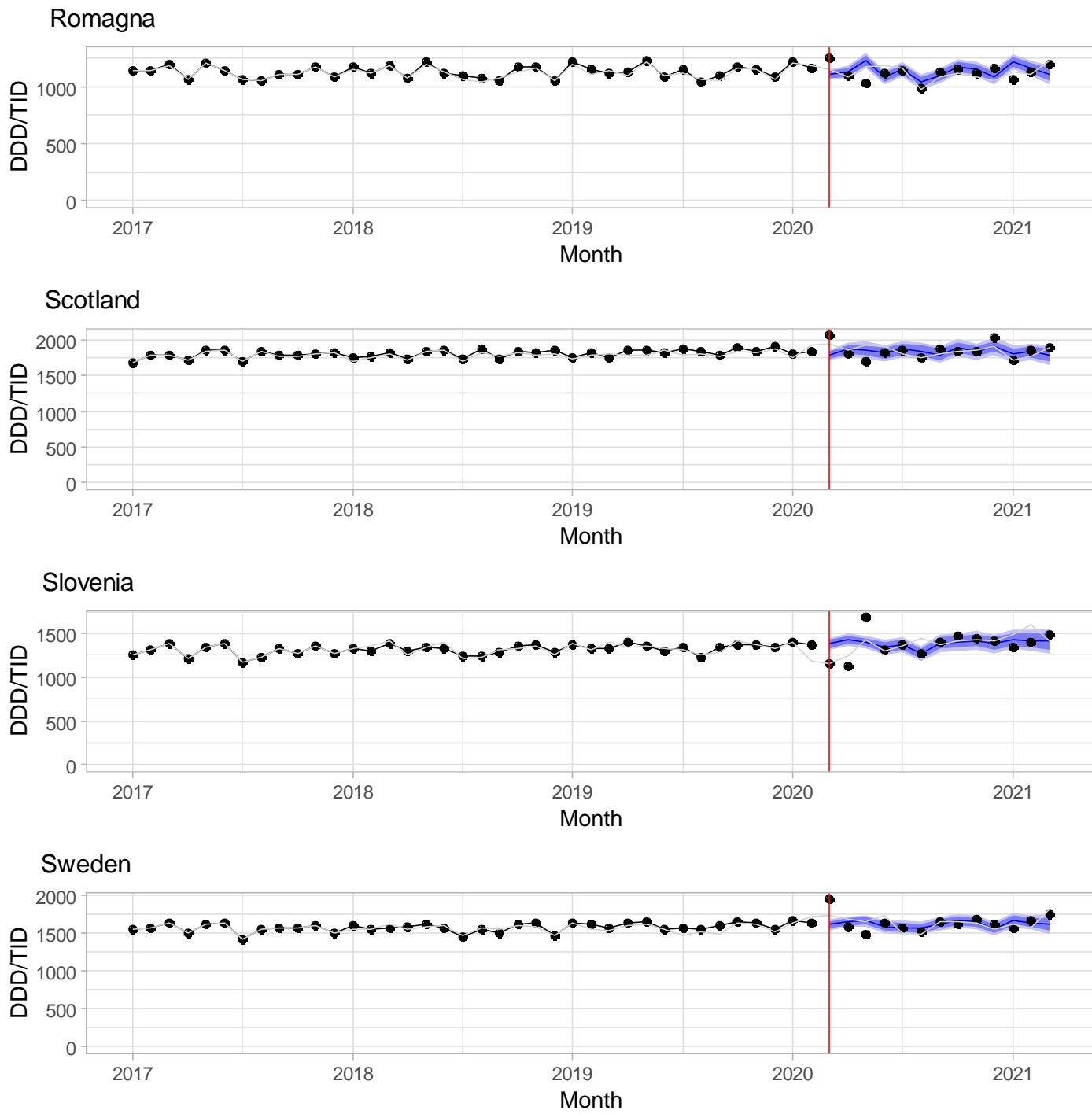


Table S12: Details on the ARIMA models used for impact assessment of the pandemic on global dispensed volume of prescription drugs

Country/region	Model	Parameter	Estimated value	Standard error	P-value [†]
Catalonia	ARIMA(0,0,2)(0,1,0) ₁₂	ma1	-0.538	0.159	<0.001
		ma2	0.333	0.212	0.118
		long-term	-31.811	9.449	<0.001
		short-term	43.383	14.874	<0.001
Czechia	ARIMA(0,0,0)(0,1,0) ₁₂	long-term	16.109	32.430	0.619
		short-term	-70.985	50.240	0.158
Germany	ARIMA(0,0,3)(0,1,0) ₁₂	ma1	-0.645	0.172	<0.001
		ma2	0.384	0.215	0.074
		ma3	0.526	0.170	0.002
		long-term	-33.974	31.589	0.282
		short-term	117.292	24.906	<0.001
Lithuania	ARIMA(2,1,0)(0,1,0) ₁₂	ar1	-0.803	0.144	<0.001
		ar2	-0.560	0.136	<0.001
		long-term	-38.237	62.662	0.542
		short-term	109.461	44.051	<0.001
Romagna	ARIMA(2,0,0)(0,1,0) ₁₂	ar1	-0.620	0.140	<0.001
		ar2	-0.466	0.137	<0.001
		long-term	-29.078	6.190	<0.001
		short-term	47.029	11.958	<0.001
Scotland	ARIMA(0,0,2)(0,1,0) ₁₂	ma1	-0.547	0.160	<0.001
		ma2	0.471	0.148	0.001
		long-term	-13.899	16.794	0.408
		short-term	116.710	25.047	<0.001
Slovenia	ARIMA(2,1,0)(0,1,0) ₁₂	ar1	-0.893	0.131	<0.001
		ar2	-0.637	0.133	<0.001
		long-term	-74.580	52.878	0.158
		short-term	-168.937	35.744	<0.001
Sweden	ARIMA(3,0,0)(0,1,0) ₁₂	ar1	-0.359	0.147	0.014
		ar2	-0.105	0.161	0.514
		ar3	0.383	0.153	0.012
		long-term	2.222	17.613	0.900
		short-term	113.902	25.272	<0.001

Note: [†]z-test

Parameters: ma1 – first order moving average, ma2 – second order moving average, ma3 – third order moving average, ar1 – first order autoregression, ar2 – second order autoregression, long-term – lasting effect of the pandemic, short-term – short duration effect of the onset of the pandemic.

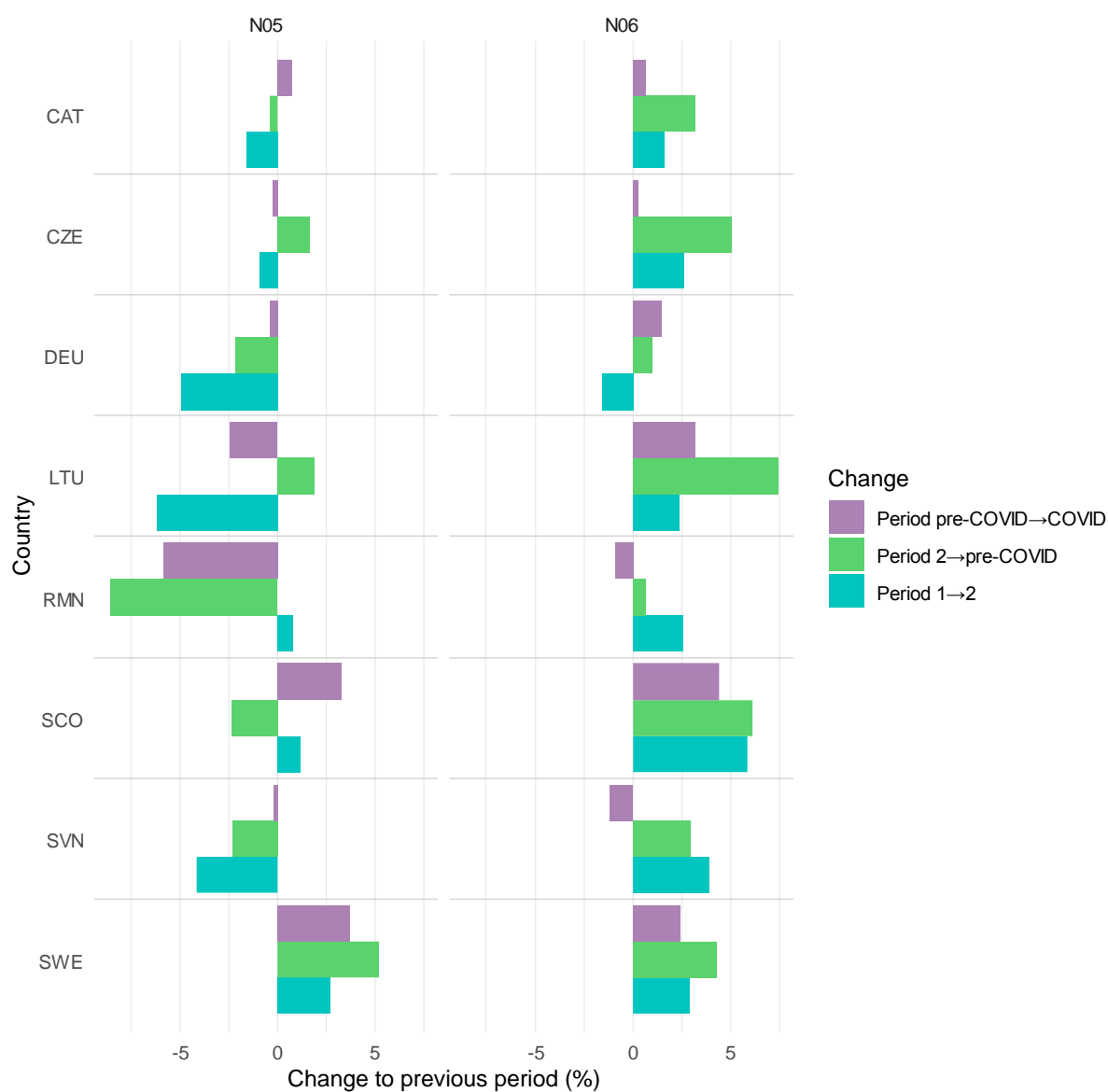
For Czechia, the used final model had a significant Ljung-Box test, which means that residuals were not completely free of autocorrelation, however, we did not manage to find a better parsimonious model.

Table S13: Change (%) in average therapeutic quantity per pack (Δu) broken down to changes of average therapeutic quantity per pack within chemical subgroups (Δv) and change of market shares of the chemical subgroups (Δs) for eight European countries/regions, September to February in the years 2017 to 2021; chemical subgroups at ATC level 4

Baseline:	9/2017 to 2/2018			9/2018 to 2/2019			9/2019 to 2/2020		
Outcome period:	9/2018 to 2/2019			9/2019 to 2/2020			9/2020 to 2/2021		
Country	Δv	Δs	Δu	Δv	Δs	Δu	Δv	Δs	Δu
Catalonia	1.013	1.001	1.014	1.004	1.000	1.004	1.011	1.013	1.024
Czechia	1.018	0.994	1.011	1.024	1.003	1.027	1.038	1.019	1.058
Germany	1.002	1.014	1.016	1.001	1.012	1.014	1.011	1.048	1.059
Lithuania	1.006	1.004	1.010	1.014	0.997	1.011	0.986	1.014	1.000
Romagna	1.001	1.003	1.005	1.026	1.016	1.043	1.027	1.019	1.047
Scotland	1.003	1.010	1.013	0.997	1.007	1.004	1.009	1.013	1.022
Slovenia	1.025	0.993	1.018	1.029	1.002	1.031	1.068	1.009	1.077
Sweden	0.995	1.011	1.006	1.008	1.005	1.012	1.004	1.013	1.017

Note: For the sake of better legibility we show the values $\delta v = \Delta v - 1$, $\delta s = \Delta s - 1$, and $\delta u = \Delta u - 1$.

Figure S9: Psycholeptics and psychoanaleptics: relative change of DDD/TID between four periods across eight European countries/regions



Legend for Figure S9:

Periods:

Period 1: March 2017 – February 2018

Period 2: March 2018 – February 2019

Pre-COVID period: March 2019 – February 2020

COVID period: March 2020 – February 2021

Country codes:

CAT	Catalonia	CZE	Czechia	DEU	Germany	LTU	Lithuania
RMN	Romagna	SCO	Scotland	SVN	Slovenia	SWE	Sweden

Therapeutic subgroups:

N05 Psycholeptics N06 Psychoanaleptics