

THE LANCET Psychiatry

Supplementary appendix

This appendix formed part of the original submission and has been peer reviewed.
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Supplementary appendix

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Table 1. EphMRA ATC of central nervous system medicines

EphMRA ATC <i>CENTRAL NERVOUS SYSTEM</i>	
N5A N5A1 N5A9	ANTIPSYCHOTICS Atypical antipsychotics Conventional antipsychotics
N5B N5B1 N5B2 N5B3 N5B4	HYPNOTICS/SEDATIVES Non-barbiturates Non-barbiturates, combinations Barbiturates, plain Barbiturates, combinations
N5C	TRANQUILLISERS
N6A N6A3 N6A4 N6A5 N6A9	ANTIDEPRESSANTS AND MOOD STABILISERS Mood stabilisers SSRI antidepressants SNRI antidepressants Antidepressants, all others

EphMRA=European Pharmaceutical Marketing Research Association; ATC= The Anatomical Classification of Pharmaceutical Products; SSRI= Selective serotonin reuptake inhibitors; SNRI= Serotonin-noradrenaline re-uptake inhibitors

Table 2. Availability and coverage of medicines consumption audit.

Country	World Bank Income level	Sector	Coverage of Total Pharma Market
Algeria	LMIC	Retail	80%
Argentina	UMIC	Retail	73%
Australia	HIC	Hospital	21%
Australia	HIC	Retail	69%
Austria	HIC	Hospital	31%
Austria	HIC	Retail	69%
Belarus	UMIC	Hospital	25%
Belarus	UMIC	Retail	75%
Belgium	HIC	Hospital	29%
Belgium	HIC	Retail	71%
Bosnia and Herzegovina	UMIC	Combined	95%
Brazil	UMIC	Not Retail	53%
Brazil	UMIC	Retail	44%
Bulgaria	UMIC	Hospital	15%
Bulgaria	UMIC	Retail	85%
Canada	HIC	Hospital	13%
Canada	HIC	Retail	87%
Chile	HIC	Retail	71%
China	UMIC	Hospital	60%
China	UMIC	Retail	12%
Colombia	UMIC	Retail	79%
Croatia	HIC	Hospital	33%
Croatia	HIC	Retail	67%
Czech Republic	HIC	Hospital	30%
Czech Republic	HIC	Retail	65%
Ecuador	UMIC	Retail	80%
Egypt	LMIC	Retail	75%
Estonia	HIC	Retail	88%
Finland	HIC	Hospital	27%
Finland	HIC	Retail	73%
France	HIC	Hospital	21%
France	HIC	Retail	79%
Germany	HIC	Hospital	14%
Germany	HIC	Retail	86%
Greece	HIC	Retail	60%
Hungary	HIC	Hospital	23%
Hungary	HIC	Retail	77%
India	LMIC	Hospital	13%

India	LMIC	Retail	81%
Ireland	HIC	Retail	80%
Italy	HIC	Hospital	55%
Italy	HIC	Retail	37%
Italy	HIC	Local Health Units	8%
Japan	HIC	Hospital	44%
Japan	HIC	Retail	56%
Jordan	UMIC	Retail	71%
Kazakhstan	UMIC	Not Retail	40%
Kazakhstan	UMIC	Retail	60%
Korea	HIC	Hospital	35%
Korea	HIC	Retail	65%
Kuwait	HIC	Retail	35%
Latvia	HIC	Hospital	8%
Latvia	HIC	Retail	92%
Lebanon	UMIC	Retail	77%
Lithuania	HIC	Hospital	8%
Lithuania	HIC	Retail	92%
Luxembourg	HIC	Retail	98%
Mexico	UMIC	Not Retail	39%
Mexico	UMIC	Retail	61%
Morocco	LMIC	Retail	88%
Netherlands	HIC	Hospital	37%
Netherlands	HIC	Retail	58%
New Zealand	HIC	Hospital	21%
Norway	HIC	Retail	78%
Pakistan	LMIC	Retail	85%
Peru	UMIC	Retail	67%
Philippines	LMIC	Hospital	11%
Philippines	LMIC	Retail	89%
Poland	HIC	Hospital	25%
Poland	HIC	Retail	75%
Portugal	HIC	Hospital	42%
Portugal	HIC	Retail	58%
Puerto Rico	HIC	Hospital	NA
Puerto Rico	HIC	Retail	NA
Romania	LMIC	Hospital	15%
Romania	LMIC	Retail	85%
Russian Fed.	UMIC	Hospital	16%
Russian Fed.	UMIC	Retail	81%
Saudi Arabia	HIC	Hospital	50%
Saudi Arabia	HIC	Retail	45%

Serbia	UMIC	Combined	100%
Slovakia	HIC	Hospital	12%
Slovakia	HIC	Retail	85%
Slovenia	HIC	Combined	97%
South Africa	UMIC	Hospital	14%
South Africa	UMIC	Retail	86%
Spain	HIC	Hospital	52%
Spain	HIC	Retail	48%
Sweden	HIC	Hospital	22%
Sweden	HIC	Retail	76%
Switzerland	HIC	Hospital	25%
Switzerland	HIC	Retail	75%
Taiwan	HIC	Hospital	83%
Taiwan	HIC	Retail	14%
Thailand	UMIC	Hospital	71%
Thailand	UMIC	Retail	22%
Tunisia	LMIC	Hospital	30%
Tunisia	LMIC	Retail	70%
Turkey	UMIC	Hospital	13%
Turkey	UMIC	Retail	87%
United Arab Emirates	HIC	Retail	45%
United Kingdom	HIC	Hospital	25%
United Kingdom	HIC	Retail	67%
United States	HIC	Hospital	34%
United States	HIC	Retail	66%
Uruguay	HIC	Retail	71%
Venezuela	UMIC	Retail	78%

NA=No detailed information; LMIC=Lower-middle-income country; UMIC=Upper-middle-income country; HIC=High-income-country. This information was provided by the IMS Health Hospital and Retail Audit Synopsis.

Table 3. Subclasses Antidepressants and DDDs

Tricyclic antidepressants	DDD/U	SSRI antidepressants	DDD/U	MAOI antidepressants	DDD/U	SNRI antidepressants	DDD/U	Other antidepressants	DDD/U
Amitriptyline	75 mg	Fluoxetine	20 mg	Isocarboxazid	15 mg	Duloxetine	60 mg	Agomelatine	25 mg
Amoxapine	0.15 g	Citalopram	20 mg	Moclobemide	0.3 g	Milnacipran	0.1 g	Bupropion	0.3 g
Butriptyline	75 mg	Paroxetine	20 mg	Phenelzine	60 mg	Venlafaxine	0.1 g	Mianserin	60 mg
Clomipramine	0.1 g	Sertraline	50 mg	Tranlycypromine	10 mg	Desvenlafaxine	50 mg	Mirtazapine	30 mg
Desipramine	0.1 g	Fluvoxamine	0.1 g					Nefazodone	0.4 g
Dibenzepin	0.3 g	Escitalopram	10 mg					Reboxetine	8 mg
Dosulepin	0.15 g							Selegiline	5 mg
Doxepin	0.1 g							Tianeptine	37.5 mg
Imipramine	0.1 g							Trazodone	0.3 g
Imipramine oxide	0.1 g							Viloxazine	0.2 g
Lofepramine	0.105 g							Vortioxetine	10 mg
Maprotiline	0.1 g								
Melitracen	75 mg								
Nortriptyline	75 mg								
Opipramol	0.15 g								
Protriptyline	30 mg								
Trimipramine	0.15 g								

SSRI= selective serotonin reuptake inhibitor; MAOI= monoamine oxidase inhibitor; SNRI= serotonin-noradrenaline re-uptake inhibitor; DDD= defined daily dose; U=Unit; mg=milligram; g=gram

Table 4. Annual consumption and percentage change of psychotropic medication use by income level, expressed as SU/Capita and DDD/TID*.

Year	All psychotropic medicine											
	HICs				UMICs				LMICs			
	SU/ Capita	% change	DDD/TID	% change	SU/ Capita	% change	DDD/TID UMIC	% change	DDD/TID	SU/ Capita	DDD/TID	% change
2008	72.02	..	108.42	..	12.23		5.81	..	4.57	..	4.97	..
2009	72.85	1.15	112.21	3.50	13.08	6.89	6.24	7.40	4.64	1.51	5.24	5.43
2010	73.20	0.48	114.57	2.10	13.54	3.56	6.79	8.81	4.77	2.84	5.43	3.63
2011	73.92	0.99	116.92	2.05	14.24	5.16	7.96	17.23	5.06	5.89	5.89	8.47
2012	72.49	-1.94	113.727	-2.73	14.40	1.15	8.78	10.30	5.07	0.19	5.83	-1.02
2013	74.02	2.12	117.11	2.97	14.63	1.54	9.28	5.69	5.17	2.12	6.03	3.43
2014	74.56	0.73	117.33	0.19	14.81	1.27	9.85	6.14	5.19	0.40	5.98	-0.83
2015	75.48	1.23	118.80	1.25	14.43	-2.54	10.55	7.11	5.25	1.13	6.25	4.52
2016	76.50	1.35	119.94	0.96	14.37	-0.48	10.94	3.70	5.37	2.30	6.53	4.48
2017	76.56	0.08	121.04	0.92	14.52	1.10	11.70	6.95	5.42	0.92	6.59	0.92
2018	76.93	0.48	121.91	0.72	14.05	-3.29	12.50	6.84	5.74	5.87	6.97	5.77
2019	77.11	0.23	123.61	1.39	14.34	2.06	13.52	8.16	5.67	-1.28	6.77	-2.87
Average % changes per year*												
	0.66% (0.51%-0.80%)		1.02% (0.80%-1.24%)		1.07% (0.25%-1.88%)		7.88% (6.99%-8.77%)		1.99% (1.67%-2.30%)		2.90% (2.40%-3.39%)	

DDD/TID=defined daily dose per 1000 inhabitants per day; SU/Capita= Standard units per person per year

LMIC=Lower-middle-income country; UMIC=Upper-middle-income country; HIC=High-income-country.

*Average % change per year calculated using linear regression

Table 5. 2008 & 2019 Consumption of psychotropic medicines according to geographic region (defined daily dose per 1000 inhabitants per day)

Country	All psychotropics 2008	All psychotropics 2019	Antidepressants 2019	Antipsychotics 2019	Sedatives /Hypnotics 2019	Tranquilisers 2019	Mood stabilisers 2019
Africa	8·94	16·98	7·12	4·98	0·62	4·22	0·02
Algeria	12·78	20·33	7·52	6·99	0·34	5·48	0·02
Egypt↓	4·46	11·28	7·17	3·04	0·09	0·96	0·01
Morocco↓	8·28	13·07	6·48	2·23	0·62	3·74	0·02
South Africa	17·82	27·93	12·86	0·81	8·91	5·33	0·04
Tunisia	10·24	23·24	7·32	7·67	1·43	6·70	0·02
Western Asia (Middle East)	20·36	29·92	21·11	4·25	1·61	2·88	0·03
Jordan↓	7·96	4·97	2·97	0·65	0·31	1·03	0·00
Kuwait↓	1·90	4·34	3·09	0·28	0·16	0·81	0·00
Lebanon	17·26	28·66	15·61	3·51	3·96	5·56	0·03
Saudi Arabia↓	4·09	6·54	5·45	0·99	0·02	0·37	0·00
Turkey	35·87	56·13	44·74	8·60	0·57	2·06	0·16
United Arab Emirates↓	2·43	3·97	3·27	0·31	0·04	0·05	0·00
Asia	4·73	5·59	2·23	0·70	0·42	2·22	0·05
China↓	1·14	4·57	1·88	1·41	0·63	0·62	0·02
India↓	4·04	4·98	2·11	0·77	0·53	1·55	0·02
Japan	87·37	82·00	16·90	10·77	44·50	9·59	0·23
Kazakhstan↓		4·84	0·92	1·67	2·10	0·15	0·00
Korea	14·15	25·42	9·26	1·31	8·37	6·45	0·03
Pakistan↓	9·37	10·85	4·24	0·92	0·64	5·04	0·01
Philippines↓	0·79	0·93	0·35	0·42	0·08	0·08	0·01
Taiwan	38·76	46·04	11·07	6·62	16·94	11·32	0·08
Thailand		20·69	8·51	6·72	0·64	4·77	0·05
Oceania	144·01	142·71	105·15	11·7	18·0	7·57	0·32
Australia	111·36	161·73	121·60	12·72	15·89	11·16	0·36
New Zealand	87·27	123·69	88·70	10·69	20·03	3·98	0·29
Northern America	142·42	167·54	120·78	13·17	14·09	19·22	0·29
Canada	131·46	168·10	123·63	14·26	18·16	11·72	0·32
United States	153·38	166·99	117·92	12·08	10·01	26·71	0·26
Latin America and the Caribbean	13·31	19·02	8·86	1·19	2·07	6·87	0·06
Argentina	48·26	57·40	20·06	3·83	3·40	30·06	0·05
Brazil	14·38	46·12	29·17	2·51	4·87	9·44	0·12
Chile	24·78	33·69	19·35	1·10	10·21	2·96	0·07
Colombia↓	3·41	4·98	2·91	0·32	1·31	0·43	0·01
Ecuador↓	4·48	8·23	3·54	0·48	3·94	0·26	0·01
Mexico↓	4·82	6·08	3·59	0·46	0·60	1·42	0·01
Peru↓	5·88	6·61	2·18	0·29	0·18	3·96	0·00
Puerto Rico	92·85	146·63	75·64	11·28	26·49	32·98	0·23
Uruguay	74·79	109·71	44·37	5·80	19·72	39·70	0·12
Venezuela↓	11·98	3·69	0·57	0·43	0·19	2·50	0·00
Europe	24·00	55·33	23·23	9·58	7·60	14·92	0·15
Austria	101·64	111·91	69·86	12·81	14·56	14·51	0·17
Belarus	8·06	20·21	4·75	2·94	11·90	0·62	0·00

Belgium	220.03	200.46	86.60	21.20	46.93	44.97	0.75
Bosnia and Herzegovina		83.51	26.21	7.01	4.92	45.34	0.02
Bulgaria	22.43	36.46	15.67	8.54	0.83	11.41	0.00
Croatia	118.64	148.89	35.25	15.92	17.39	80.26	0.07
Czech Republic	75.76	112.39	64.05	13.56	21.08	13.63	0.07
Estonia	46.54	75.13	31.72	9.02	21.01	13.32	0.05
Finland	165.64	135.89	74.82	21.09	23.88	15.86	0.25
France	152.96	138.59	53.35	13.69	29.86	41.45	0.25
Germany	72.69	86.53	56.50	13.18	11.32	5.30	0.22
Greece	113.61	160.97	87.91	26.02	9.31	37.58	0.14
Hungary	103.09	116.05	31.91	11.53	13.25	59.29	0.08
Ireland	122.15	154.75	98.72	14.12	28.26	13.37	0.27
Italy	95.16	108.64	46.66	10.06	23.95	27.78	0.19
Latvia	28.22	56.71	18.24	11.82	11.27	15.37	0.01
Lithuania	67.86	100.62	38.07	17.92	11.50	33.08	0.04
Luxembourg	157.93	140.65	55.63	7.83	45.05	31.70	0.43
Netherlands		90.43	53.47	8.73	15.08	12.77	0.37
Norway	128.59	117.58	56.54	10.19	38.93	11.89	0.04
Poland	49.99	79.63	39.83	14.51	14.29	10.93	0.08
Portugal	198.60	249.08	123.52	15.84	18.67	90.86	0.19
Romania	24.00	55.33	23.23	9.58	7.60	14.92	0.00
Russian Fed.‡	6.24	10.48	3.89	3.88	1.95	0.75	0.01
Serbia		137.31	27.46	7.09	8.26	94.50	0.00
Slovakia	68.92	99.10	43.62	13.97	15.42	26.02	0.07
Slovenia	90.77	103.84	64.44	15.83	10.48	13.03	0.06
Spain	155.44	198.48	87.48	14.81	38.80	57.13	0.25
Sweden	148.80	170.77	101.81	8.50	48.82	11.59	0.05
Switzerland	113.12	109.45	62.00	10.17	20.66	16.30	0.32
United Kingdom	88.71	151.59	123.5319	10.45	11.01	6.43	0.17

All regional estimates were calculated using a random-effect model and adjusted for income level. Please note: categories not mutually exclusive. 2008 data were not available for Serbia, the Netherlands, Bosnia and Herzegovina, Thailand and Kazakhstan.

‡Countries with the lowest 25% of DDD/TID in overall psychotropics drugs consumptions in 2019.

Table 6. Fixed-effects regression analysis of factors associated with psychotropic consumption (DDD/TID) in HICs, UMICs and LMICs: 2008–2019

Factor	Coefficient (SD)		
	HICs	UMICs	LMICs
Life expectancy	7.18 (0.70) [†]	3.73 (0.85) [†]	2.86 (0.66) [†]
Prevalence mental disorder	5.73 (3.30)	-13.25 (6.05) [‡]	-6.53 (4.51)
Health expenditure as part of GDP (%)	-1.37 (0.85)	-4.0 (1.92) [‡]	1.97 (0.95) [‡]
Observations	440	213	89
Countries	37	19	8

SD=Standard deviation; LMIC=Lower-middle-income country; UMIC=Upper-middle-income country; HIC=High-income-country.

[†]P<0.01

[‡]P<0.05

Table 7. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement checklist

	Item No	Recommendation	Page No
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	5
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	5
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	7
Objectives	3	State specific objectives, including any prespecified hypotheses	7-8
Methods			
Study design	4	Present key elements of study design early in the paper	8-9
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	8
Participants	6	(a) <i>Cohort study</i> —Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up <i>Case-control study</i> —Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls <i>Cross-sectional study</i> —Give the eligibility criteria, and the sources and methods of selection of participants	8-10
		(b) <i>Cohort study</i> —For matched studies, give matching criteria and number of exposed and unexposed <i>Case-control study</i> —For matched studies, give matching criteria and the number of controls per case	NA
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	8-9
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	8-10
Bias	9	Describe any efforts to address potential sources of bias	NA
Study size	10	Explain how the study size was arrived at	NA
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	9-10
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	9-10
		(b) Describe any methods used to examine subgroups and interactions	9-10
		(c) Explain how missing data were addressed	NA
		(d) <i>Cohort study</i> —If applicable, explain how loss to follow-up was addressed <i>Case-control study</i> —If applicable, explain how matching of cases and controls was addressed <i>Cross-sectional study</i> —If applicable, describe analytical methods taking account of sampling strategy	NA
		(e) Describe any sensitivity analyses	NA

Continued on next page

Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	NA
		(b) Give reasons for non-participation at each stage	NA
		(c) Consider use of a flow diagram	NA
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	NA
		(b) Indicate number of participants with missing data for each variable of interest	NA
		(c) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount)	NA
Outcome data	15*	<i>Cohort study</i> —Report numbers of outcome events or summary measures over time	NA
		<i>Case-control study</i> —Report numbers in each exposure category, or summary measures of exposure	NA
		<i>Cross-sectional study</i> —Report numbers of outcome events or summary measures	10
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	10-12
		(b) Report category boundaries when continuous variables were categorized	NA
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	NA
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	10-12
Discussion			
Key results	18	Summarise key results with reference to study objectives	13-17
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	18-19
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	20
Generalisability	21	Discuss the generalisability (external validity) of the study results	19
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	6, 10

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at www.strobe-statement.org.