

SUPPLEMENTARY MATERIAL

Drug utilisation patterns of alternatives to ranitidine-containing medicines in patients treated with ranitidine: a network analysis of data from six European national databases.

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Supplemental Table 1 Characteristics of databases and distribution of ranitidine users by referral period.

Database	Managing Organization	Country	Individuals	Database date range	Total number of persons during study period	Ranitidine users		
						Pre-referral period	In-referral period	Post-referral period
DA Germany	IQVIA	Germany	37.3M	1992 - present	21,463,677	27,821	3,128	1,601
IPCI	Erasmus MC	Netherlands	2.8M	2006 - present	1,885,701	22,709	1,843	1,539
LPD Belgium	IQVIA	Belgium	1.1M	2005 - present	781,905	14,693	2,042	157
LPD France	IQVIA	France	18.1M	1994 - present	10,011,441	20,256	2,719	1,510
SIDIAP	IDIAP Jordi Gol	Spain	7.9M	2006 - present	6,617,777	81,284	4,776	28
UK IMRD	IQVIA	UK	15.2M	2005 - present	4,695,649	138,205	24,183	9,779
Total					45,456,150	304,968	38,691	14,614

Notes: Ranitidine users – Total number of persons using ranitidine. A person with several ranitidine exposures in a period is counted only once. Pre-referral period = September 2017 – August 2019, In-referral period = September 2019 – March 2020, post-referral period = April 2020 – March 2022

Germany has no mandatory GP system and patient have free choice of specialist. As a result, data are collected from visits to general and specialists' practices.

Supplemental Table 2 List of drug exposures of interest

ATC code	Ingredient
Histamine 2 receptor antagonists (H₂RA)	
A02BA01	Cimetidine
A02BA02	Ranitidine
	Famotidine
A02BA04	Nizatidine
A02BA05	Niperotidine
A02BA06	Roxatidine
A02BA08	Lafutidine
A02BA51	Cimetidine combinations
A02BA53	Famotidine combinations
Proton pump inhibitors (PPI)	
A02BC01	Omeprazole
A02BC02	Pantoprazole
A02BC03	Lansoprazole
A02BC04	Rabeprazole
A02BC05	Esomeprazole
A02BC06	Dexlansoprazole
A02BC07	Dextrabeprazole
A02BC08	Vonoprazan
A02BC53	Lansoprazole, combinations
Antacids	
A02AA	Magnesium compounds
A02AB	Aluminium compounds
A02AC	Calcium compounds
A02AD	Combinations and complexes of aluminium, calcium and magnesium compounds
A02AF	Antacids with anti-flatulents
A02AG	Antacids with antispasmodics
A02AH	Antacids with sodium bicarbonate
A02AX	Antacids, other combinations
Other drugs for peptic ulcer and GERD	
A02BB	Prostaglandins
A02BD	Combinations for eradication of <i>Helicobacter pylori</i>
A02ABX	Other drugs for peptic ulcer and gastroesophageal reflux disease (GORD)

Abbreviations: GERD - gastro-oesophageal reflux disease

Supplemental Table 3 Demographic characteristics of ranitidine users by database and referral period

Database			Pre-referral period		Referral period		Post-referral period	
			N	(%)	N	(%)	N	(%)
LPD Belgium	Sex	FEMALE	8,932	60.79	1,226	60.04	95	60.51
		MALE	5,761	39.21	816	39.96	62	39.49
	Age (yrs)	<18	880	5.99	98	4.80	<5	0
		18-74	11,866	80.76	1,640	80.31	117	74.52
		75+	1,947	13.25	304	14.89	37	23.57
	Duration	1-15 days	1,254	8.53	101	4.95	13	8.28
		16-30 days	4,366	29.71	545	26.69	17	10.83
		31-100 days	5,532	37.65	956	46.82	88	56.05
		over 100 days	3,541	24.10	440	21.55	39	24.84
	Dose	PDD/DDD < 1	3,047	20.74	457	22.38	63	40.13
		PDD/DDD = 1	10,428	70.97	1,409	69.00	78	49.68
		PDD/DDD > 1	1,218	8.29	176	8.62	16	10.19
	Formulation	Injectable Product	15	0.10	7	0.34	0	0
		Oral Product	14,678	99.90	2,035	99.66	157	100.00
LPD France	Sex	FEMALE	11,758	58.05	1,565	57.56	850	56.29
		MALE	8,406	41.50	1,142	42.00	652	43.18
		No matching concept	92	0.45	12	0.44	8	0.53
	Age (yrs)	<18	470	2.32	46	1.69	15	0.99
		18-74	15,839	78.19	2,084	76.65	1,122	74.30
		75+	3,947	19.49	589	21.66	373	24.70
	Duration	1-15 days	5,980	29.52	657	24.16	253	16.75
		16-30 days	10,583	52.25	1,563	57.48	952	63.05
		31-100 days	2,176	10.74	327	12.03	206	13.64
		over 100 days	1,517	7.49	172	6.33	99	6.56
	Dose	Not available	20,256	100.00	2,719	100.00	1,510	100.00
	Formulation	Injectable Product	47	0.23	<5	0	<5	0
		No matching concept	37	0.18	<5	0	<5	0

Database			Pre-referral period		Referral period		Post-referral period	
			N	(%)	N	(%)	N	(%)
DA Germany	Sex	Oral Product	20,172	99.59	2,714	99.82	1,505	99.67
		FEMALE	16,147	58.04	1,825	58.34	915	57.15
		MALE	11,613	41.74	1,292	41.30	675	42.16
	Age (yrs)	No matching concept	61	0.22	11	0.35	11	0.69
		<18	736	2.65	69	2.21	27	1.69
		18-74	21,219	76.27	2,313	73.95	1,191	74.39
		75+	5,866	21.08	746	23.85	383	23.92
	Duration	1-15 days	5,506	19.79	468	14.96	222	13.87
		16-30 days	4,910	17.65	474	15.15	220	13.74
		31-100 days	12,391	44.54	1,948	62.28	1,088	67.96
		over 100 days	5,014	18.02	238	7.61	71	4.43
	Dose	PDD/DDD < 1	5,912	21.25	722	23.08	406	25.36
		PDD/DDD = 1	21,164	76.07	2,328	74.42	1,158	72.33
		PDD/DDD > 1	745	2.68	78	2.49	37	2.31
	Formulation	Injectable Product	757	2.72	99	3.16	69	4.31
		Oral Product	27,064	97.28	3,029	96.84	1,532	95.69
UK IMRD	Sex	FEMALE	83,835	60.66	14,666	60.65	5,904	60.37
		MALE	54,370	39.34	9,517	39.35	3,875	39.63
	Age (yrs)	<18	15,751	11.40	1,983	8.20	443	4.53
		18-74	96,378	69.74	17,135	70.86	7,175	73.37
		75+	26,076	18.87	5,065	20.94	2,161	22.10
	Duration	1-15 days	4,430	3.21	768	3.18	359	3.67
		16-30 days	54,063	39.12	9,647	39.89	4,579	46.82
		31-100 days	37,704	27.28	7,914	32.73	3,464	35.42
		over 100 days	42,008	30.40	5,854	24.21	1,377	14.08
	Dose	PDD/DDD < 1	33,931	24.55	5,694	23.55	1,900	19.43
		PDD/DDD = 1	100,931	73.03	17,826	73.71	7,603	77.75
		PDD/DDD > 1	3,343	2.42	663	2.74	276	2.82

Database			Pre-referral period		Referral period		Post-referral period	
			N	(%)	N	(%)	N	(%)
IPCI	Formulation	Injectable Product	15	0.01	7	0.03	5	0.05
		No matching concept	7	0.01	<5	0	<5	0
	Sex	Oral Product	138,183	99.98	24,175	99.97	9,772	99.93
		FEMALE	13,752	60.56	1,091	59.20	936	60.82
		MALE	8,957	39.44	752	40.80	603	39.18
	Age (yrs)	<18	2,064	9.09	182	9.88	314	20.40
		18-74	17,402	76.63	1,414	76.72	1,027	66.73
		75+	3,243	14.28	247	13.40	198	12.87
	Duration	1-15 days	6,748	29.72	628	34.07	565	36.71
		16-30 days	4,589	20.21	524	28.43	507	32.94
		31-100 days	6,360	28.01	589	31.96	342	22.22
		over 100 days	5,012	22.07	102	5.53	125	8.12
	Dose	PDD/DDD < 1	5,969	26.28	526	28.54	707	45.94
		PDD/DDD = 1	15,289	67.33	1,160	62.94	789	51.27
		PDD/DDD > 1	1,451	6.39	157	8.52	43	2.79
SIDIAP	Formulation	Injectable Product	<5	0	<5	0	<5	0
		No matching concept	29	0.13	8	0.43	10	0.65
	Sex	Oral Product	22,676	99.85	1,834	99.51	1,528	99.29
		FEMALE	54,041	66.48	3,187	66.73	17	60.71
		MALE	27,243	33.52	1,589	33.27	11	39.29
	Age (yrs)	<18	1,754	2.16	89	1.86		NA
		18-74	70,383	86.59	4,141	86.70	19	67.86
		75+	9,147	11.25	546	11.43	9	32.14
	Duration	1-15 days	29,968	36.87	2,230	46.69	14	50.00
		16-30 days	18,854	23.20	1,379	28.87	<5	0
		31-100 days	14,562	17.91	910	19.05	8	28.57
		over 100 days	17,900	22.02	257	5.38	<5	0
	Dose	PDD/DDD < 1	80,262	98.74	4,702	98.45	28	100.00

Database		Pre-referral period		Referral period		Post-referral period	
		N	(%)	N	(%)	N	(%)
Formulation	PDD/DDD = 1	12	0.01	<5	0	0	0
	PDD/DDD > 1	1,010	1.24	73	1.53	0	0
	Injectable Product	38	0.05	7	0.15	25	89.29
	Oral Product	81,246	99.95	4,769	99.85	<5	0

Abbreviations: PDD – Prescribed daily dose; DDD – Defined daily dose.

Supplemental Table 4 Indication of use for ranitidine

Database	Indication	Pre-referral period		Referral period		Post-referral period	
		N	(%)	N	(%)	N	(%)
LPD Belgium	GERD	376	2.56	52	2.55	5	3.18
	Gastritis wo H pylori	1,246	8.48	178	8.72	6	3.82
	Gastritis with H pylori	96	0.65	12	0.59	<5	0
	Duodenitis wo H pylori	0	0	0	0	0	0
	Gastric and duodenal ulcer wo H pylori	90	0.61	12	0.59	0	0
	Gastric and duodenal ulcer with H pylori	24	0.16	<5	0	00	0
	Dyspepsia indigestion	68	0.46	5	0.24	<5	0
LPD France	GERD	594	2.93	48	1.77	52	3.44
	Gastritis wo H pylori	812	4.01	118	4.34	70	4.64
	Gastritis with H pylori	120	0.59	16	0.59	<5	0
	Duodenitis wo H pylori	10	0.05	<5	0	<5	0
	Duodenitis with H pylori	<5	0	0	0	0	0
	Gastric and duodenal ulcer wo H pylori	97	0.48	16	0.59	5	0.33
	Gastric and duodenal ulcer with H pylori	8	0.04	<5	0	0	0
DA Germany	Dyspepsia indigestion	112	0.55	5	0.18	<5	0
	GERD	690	2.48	67	2.14	41	2.56
	Gastritis wo H pylori	2,300	8.27	243	7.77	134	8.37
	Gastritis with H pylori	158	0.57	5	0.16	5	0.31
	Duodenitis wo H pylori	130	0.47	10	0.32	<5	0
	Duodenitis with H pylori	11	0.04	0	0	<5	0
	Gastric and duodenal ulcer wo H pylori	242	0.87	26	0.83	9	0.56
	Gastric and duodenal ulcer with H pylori	24	0.09	<5	0	0	0
	Dyspepsia indigestion	64	0.23	<5	0	<5	0

UK IMRD	GERD	2,676	1.94	356	1.47	92	0.94
	Gastritis wo H pylori	2,115	1.53	380	1.57	74	0.76
	Gastritis with H pylori	120	0.09	21	0.09	0	0
	Duodenitis wo H pylori	651	0.47	100	0.41	27	0.28
	Duodenitis with H pylori	43	0.03	9	0.04	0	0
	Gastric and duodenal ulcer wo H pylori	221	0.16	43	0.18	7	0.07
	Gastric and duodenal ulcer with H pylori	12	0.01	7	0.03	<5	0
	Dyspepsia indigestion	1,812	1.31	219	0.91	50	0.51
	Zollinger-Ellison syndrome	0	0	0	0	0	0
IPCI	GERD	978	4.31	92	4.99	141	9.16
	Gastritis wo H pylori	697	3.07	55	2.98	50	3.25
	Gastritis with H pylori	54	0.24	<5	0	<5	0
	Duodenitis wo H pylori	378	1.66	32	1.74	31	2.01
	Duodenitis with H pylori	39	0.17	0	0	<5	0
	Gastric and duodenal ulcer wo H pylori	128	0.56	12	0.65	9	0.58
	Gastric and duodenal ulcer with H pylori	45	0.20	7	0.38	<5	0
	Dyspepsia indigestion	185	0.81	16	0.87	12	0.78
SIDIAP	GERD	2,855	3.51	168	3.52	<5	0
	Gastritis wo H pylori	4,280	5.27	223	4.67	0	0
	Gastritis with H pylori	465	0.57	22	0.46	0	0

Supplemental Table 5 Incidence of other medication use by period

Ingredient	Period	Incidence per 1000 PY					
		DA Germany	IPCI	LPD Belgium	LPD France	SIDIAP	UK IMRD
Cimetidine	Pre-referral	0.02	0.05	0.03	0.11	NA	0.05
	Referral	0.15	1.07	0.00	0.19	NA	0.68
	Post-referral	0.04	0.22	0.00	0.08	NA	0.53
Famotidine	Pre-referral	0.02	0.02	NA	0.01	0.08	0.01
	Referral	0.17	1.19	NA	0.09	3.27	0.22
	Post-referral	0.14	1.33	NA	0.10	1.57	1.51
H ₂ RA Class	Pre-referral	0.80	4.55	9.05	1.17	5.92	8.25
	Referral	0.39	1.66	3.75	0.61	2.35	3.82
	Post-referral	0.22	1.67	0.10	0.26	1.53	1.59
Omeprazole	Pre-referral	4.52	28.20	17.49	20.79	55.19	35.08
	Referral	5.25	29.78	21.29	21.46	59.94	41.69
	Post-referral	4.96	23.31	17.72	19.92	49.57	37.76
Lansoprazole	Pre-referral	18.07	21.37	36.85	8.32	2.42	0.56
	Referral	22.22	25.38	47.29	9.72	2.57	0.76
	Post-referral	23.32	21.72	44.45	10.47	2.47	0.74
Pantoprazole	Pre-referral	0.07	0.08	0.61	4.24	1.42	13.35
	Referral	0.10	0.12	0.64	4.61	1.45	15.93
	Post-referral	0.09	0.08	0.67	4.57	1.43	14.32
Rabeprazole	Pre-referral	0.06	0.28	0.07	2.73	0.59	0.07
	Referral	0.09	0.34	0.05	2.78	0.58	0.10
	Post-referral	0.10	0.27	0.07	2.68	0.58	0.08
Esomeprazole	Pre-referral	1.56	2.52	8.71	19.55	2.36	1.65
	Referral	2.03	2.57	10.25	21.31	2.52	1.92
	Post-referral	2.44	2.87	9.93	23.19	2.61	1.92
Prostaglandins	Pre-referral	0.05	1.46	0.05	0.70	0.26	0.05
	Referral	0.05	0.97	0.05	0.01	0.16	0.03
	Post-referral	0.05	0.91	0.08	0.01	0.09	0.02
Combination therapy for eradication of <i>Helicobacter pylori</i>	Pre-referral	0.20	0.93	0.11	0.64	1.93	NA
	Referral	0.19	1.07	0.16	0.70	2.37	NA
	Post-referral	0.19	0.71	0.20	0.73	2.49	NA
Other drugs for peptic ulcer and GERD	Pre-referral	0.67	1.20	0.85	0.47	0.23	4.48
	Referral	0.89	1.29	1.25	0.47	0.22	4.88
	Post-referral	1.01	1.29	0.85	0.49	0.12	4.70

Pre-referral period = September 2017 – August 2019; referral period = September 2019 – March 2020; post-referral period = April 2020 – March 2022; NA – Not available, because number of incident users is below 5.

Supplemental Table 6 Incidence of medication use by calendar year

Ingredient	Database	Incidence per 1,000 PY					
		2017	2018	2019	2020	2021	2022
Ranitidine	DA Germany	0.69	0.74	0.71	0.11	0.04	0.02
	IPCI	4.60	4.40	3.64	0.61	0.26	0.04
	LPD Belgium	9.88	8.95	7.98	0.41	0.04	0.13
	LPD France	0.95	1.07	0.95	0.20	0.07	0.01
	SIDIAP	5.61	5.89	4.63	0.02	0.00	NA
	UK IMRD	8.08	8.17	7.19	1.02	0.17	0.03
Cimetidine	DA Germany	0.02	0.02	0.07	0.05	0.04	0.06
	IPCI	0.05	0.04	0.60	0.20	0.26	0.19
	LPD Belgium	0.08	0.03	NA	0.00	0.00	NA
	LPD France	0.12	0.11	0.15	0.09	0.07	0.13
	UK IMRD	0.06	0.06	0.25	0.91	0.20	0.16
	DA Germany	0.02	0.02	0.07	0.13	0.15	0.26
Famotidine	IPCI	0.02	0.01	0.53	0.87	1.58	1.64
	LPD France	0.01	0.01	0.03	0.06	0.12	0.21
	SIDIAP	0.08	0.08	1.56	1.27	1.80	1.91
	UK IMRD	0.01	0.01	0.08	0.78	1.83	1.88
	IPCI	NA	NA	0.04	0.02	NA	0.00
	LPD France	NA	0.00	0.00	0.01	0.00	0.00
Nizatidine	UK IMRD	0.01	0.01	0.15	0.42	0.24	0.16
	DA Germany	0.03	0.04	0.14	0.17	0.19	0.32
	IPCI	0.07	0.05	1.01	0.91	1.80	1.80
H2 no Ranitidine	LPD Belgium	0.08	0.03	NA	0.00	0.00	NA
	LPD France	0.13	0.13	0.18	0.15	0.18	0.33
	SIDIAP	0.08	0.08	1.56	1.27	1.80	1.91
	UK IMRD	0.07	0.07	0.46	1.64	1.98	2.10
	DA Germany	0.72	0.77	0.78	0.23	0.22	0.33
	IPCI	4.58	4.44	3.85	1.21	1.91	1.83
H2 Class							

Omeprazole	LPD Belgium	9.94	8.97	7.99	0.41	0.04	0.14
	LPD France	1.07	1.19	1.07	0.30	0.24	0.34
	SIDIAP	5.68	5.95	5.08	1.08	1.80	1.92
	UK IMRD	8.12	8.18	7.26	1.44	1.85	2.10
	DA Germany	4.52	4.57	4.82	4.76	5.13	7.08
	IPCI	29.87	28.91	29.10	25.11	23.37	22.05
Pantoprazole	LPD Belgium	18.84	17.56	18.14	18.84	17.12	26.26
	LPD France	21.27	21.57	21.23	18.59	21.14	29.96
	SIDIAP	54.96	56.42	59.82	46.88	54.58	53.75
	UK IMRD	35.67	35.62	38.04	37.81	39.45	35.83
	DA Germany	17.00	18.26	19.99	21.33	24.66	34.96
	IPCI	20.31	21.29	23.85	22.37	22.27	21.06
Lansoprazole	LPD Belgium	35.13	36.24	41.15	45.07	43.70	70.45
	LPD France	7.99	8.39	9.05	9.43	11.11	15.30
	SIDIAP	2.48	2.43	2.54	2.29	2.59	2.55
	UK IMRD	0.65	0.56	0.63	0.80	0.69	0.57
	DA Germany	0.08	0.08	0.08	0.09	0.09	0.11
	IPCI	0.09	0.07	0.09	0.09	0.07	0.07
Rabeprazole	LPD Belgium	0.72	0.58	0.62	0.70	0.65	0.88
	LPD France	4.40	4.37	4.36	4.29	4.80	6.57
	SIDIAP	1.34	1.41	1.50	1.28	1.51	1.60
	UK IMRD	13.60	13.54	14.13	14.95	14.29	12.89
	DA Germany	0.06	0.06	0.07	0.09	0.10	0.14
	IPCI	0.28	0.28	0.31	0.25	0.30	0.22
Esomeprazole	LPD Belgium	0.06	0.08	0.06	0.05	0.07	0.11
	LPD France	2.91	2.79	2.70	2.65	2.69	3.45
	SIDIAP	0.61	0.60	0.59	0.55	0.61	0.57
	UK IMRD	0.06	0.07	0.08	0.09	0.07	0.06
	DA Germany	1.42	1.51	1.82	2.04	2.64	3.87
	IPCI	2.59	2.62	2.42	2.39	3.18	3.56
	LPD Belgium	8.53	8.96	9.25	9.62	9.92	16.27

Dexlansoprazole PPI	LPD France	19.66	19.96	20.58	20.15	25.22	34.62
	SIDIAP	2.21	2.32	2.60	2.23	2.83	2.92
	UK IMRD	1.65	1.65	1.76	1.83	2.01	1.74
	DA Germany	0.00	0.00	NA	NA	0.00	NA
	DA Germany	20.90	22.26	24.45	25.83	29.75	42.25
	IPCI	45.45	45.58	47.62	42.90	41.89	40.50
	LPD Belgium	55.14	55.59	60.96	64.90	62.10	100.05
	LPD France	47.55	48.38	49.62	47.32	56.32	78.11
Antacids	SIDIAP	56.22	57.86	61.47	48.51	56.67	55.92
	UK IMRD	43.82	43.94	46.85	46.99	48.00	43.65
	DA Germany	0.31	0.33	0.42	0.50	0.53	0.78
	IPCI	12.05	12.53	12.87	11.14	11.40	11.09
	LPD Belgium	8.77	9.01	9.86	9.95	10.24	15.94
	LPD France	2.60	2.85	3.02	3.09	3.39	4.44
	SIDIAP	6.51	8.32	8.64	6.63	8.94	10.08
	UK IMRD	12.75	12.07	12.47	12.01	13.02	12.32
Prostaglandins	DA Germany	0.05	0.04	0.06	0.05	0.05	0.05
	IPCI	1.86	1.59	1.14	0.98	0.90	0.91
	LPD Belgium	0.04	0.04	0.04	0.04	0.10	0.08
	LPD France	1.20	0.94	0.01	0.00	0.01	0.01
	SIDIAP	0.26	0.28	0.21	0.11	0.08	0.08
	UK IMRD	0.08	0.04	0.05	0.02	0.02	0.02
	DA Germany	0.19	0.19	0.20	0.19	0.19	0.24
	IPCI	0.84	0.94	1.00	0.76	0.77	0.51
Combination therapy for eradication of Helicobacter pylori	LPD Belgium	0.08	0.10	0.15	0.16	0.22	0.32
	LPD France	0.58	0.63	0.69	0.63	0.81	1.06
	SIDIAP	1.08	1.83	2.41	1.84	2.92	3.28
	DA Germany	0.47	0.65	0.80	0.87	1.05	1.48
	IPCI	1.21	1.24	1.21	1.27	1.32	1.19
	LPD Belgium	0.72	0.79	1.04	1.00	0.85	1.00
	LPD France	0.50	0.45	0.47	0.44	0.51	0.74
Other drugs for peptic ulcer and GERD							

SIDIAP	0.23	0.22	0.24	0.15	0.13	0.00
UK IMRD	5.04	4.53	4.45	4.58	4.87	4.40

NA – Not available because number of incident users is below 5

Supplemental Table 7 Incidence of medication use in individuals with new indications for ranitidine or alternative medicines use – by year.

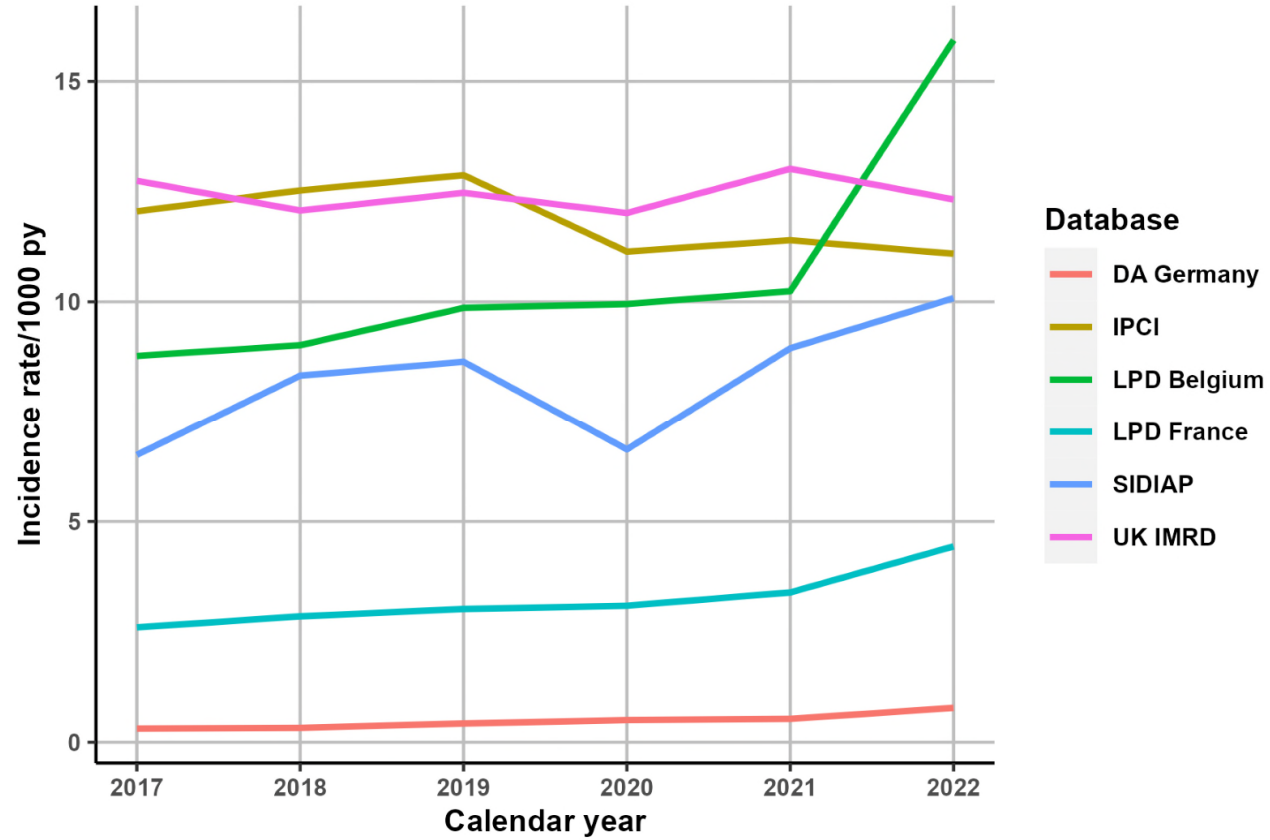
Ingredient	Database	Incidence per 1000 PY					
		2017	2018	2019	2020	2021	2022
Ranitidine	DA Germany	18.84	15.78	12.39	1.93	0.54	0.09
	IPCI	85.60	58.43	47.47	9.67	4.54	NA
	LPD Belgium	194.97	151.21	135.57	4.67	NA	NA
	LPD France	20.94	19.74	16.10	3.52	0.89	0.00
	SIDIAP	96.86	72.98	58.79	NA	0.00	0.00
	UK IMRD	145.07	115.01	104.97	20.62	3.22	NA
Cimetidine	DA Germany	0.38	0.21	1.19	0.85	0.63	0.58
	IPCI	NA	NA	5.18	3.18	4.98	1.81
	LPD Belgium	0.62	NA	0.00	0.00	0.00	0.00
	LPD France	2.31	1.81	2.10	1.39	0.92	0.74
	UK IMRD	0.74	0.42	2.00	8.84	4.63	1.52
	DA Germany	0.41	0.33	1.25	1.88	2.13	1.32
Famotidine	IPCI	NA	NA	4.15	12.85	23.14	10.19
	LPD France	0.18	0.14	0.54	0.72	1.65	1.72
	SIDIAP	1.42	1.34	24.86	24.52	32.45	22.82
	UK IMRD	NA	NA	0.56	9.41	32.99	26.07
	IPCI	0.00	0.00	0.58	NA	0.00	0.00
	LPD France	0.00	NA	NA	0.10	0.00	0.00
Nizatidine	UK IMRD	NA	NA	0.65	3.16	4.53	1.90
	DA Germany	0.78	0.54	2.39	2.47	2.72	1.86
	IPCI	NA	NA	8.64	14.70	27.54	11.55
H2 no Ranitidine	LPD Belgium	0.62	NA	0.00	0.00	0.00	0.00
	LPD France	2.49	2.00	2.67	2.03	2.57	2.33
	SIDIAP	1.42	1.34	24.86	24.52	32.45	22.82
	UK IMRD	0.99	0.50	3.02	17.17	38.12	28.17
	DA Germany	19.48	16.30	13.57	3.62	3.03	1.92
	H2 Class						

Ingredient	Database	Incidence per 1000 PY					
		2017	2018	2019	2020	2021	2022
Omeprazole	IPCI	84.72	58.85	49.77	19.73	29.15	11.55
	LPD Belgium	195.38	151.38	135.57	4.67	NA	NA
	LPD France	23.18	21.69	17.97	4.99	3.30	2.33
	SIDIAP	98.04	73.94	66.54	21.40	32.38	22.82
	UK IMRD	145.38	115.05	105.57	28.30	36.61	28.55
	DA Germany	121.45	106.54	105.39	86.91	88.69	52.03
	IPCI	239.39	171.50	193.34	199.03	174.59	68.84
Pantaprazole	LPD Belgium	287.78	226.37	244.92	217.71	235.96	159.19
	LPD France	220.88	196.03	196.30	156.14	170.68	110.14
	SIDIAP	763.96	534.60	642.85	501.57	557.17	318.31
	UK IMRD	533.20	389.22	391.02	342.94	389.68	205.54
	DA Germany	472.88	422.78	425.49	373.27	412.60	235.19
	IPCI	183.32	144.71	169.72	186.98	164.77	70.88
	LPD Belgium	538.08	476.80	565.66	515.11	583.80	365.45
Lansoprazole	LPD France	115.95	105.36	116.72	102.03	121.57	78.28
	SIDIAP	52.22	37.95	39.39	37.73	39.62	27.97
	UK IMRD	17.45	11.46	12.77	15.59	17.20	10.66
	DA Germany	1.68	1.36	1.41	1.25	1.37	0.62
	IPCI	1.05	1.05	0.81	1.59	NA	0.00
	LPD Belgium	7.60	6.41	6.22	6.55	8.00	3.23
	LPD France	59.10	52.88	52.57	47.74	50.58	30.26
Rabeprazole	SIDIAP	33.75	22.82	26.60	29.13	29.36	19.26
	UK IMRD	219.22	174.07	174.31	160.55	186.69	103.91
	DA Germany	1.85	1.41	1.36	1.78	1.88	1.03
	IPCI	2.64	3.27	3.57	3.97	4.69	1.36
	LPD Belgium	0.92	0.41	0.44	0.45	0.73	NA
	LPD France	59.91	49.25	47.60	38.08	40.60	22.85
	SIDIAP	19.66	14.50	12.49	14.83	12.77	8.97
	UK IMRD	1.79	1.39	1.49	2.16	1.81	0.95

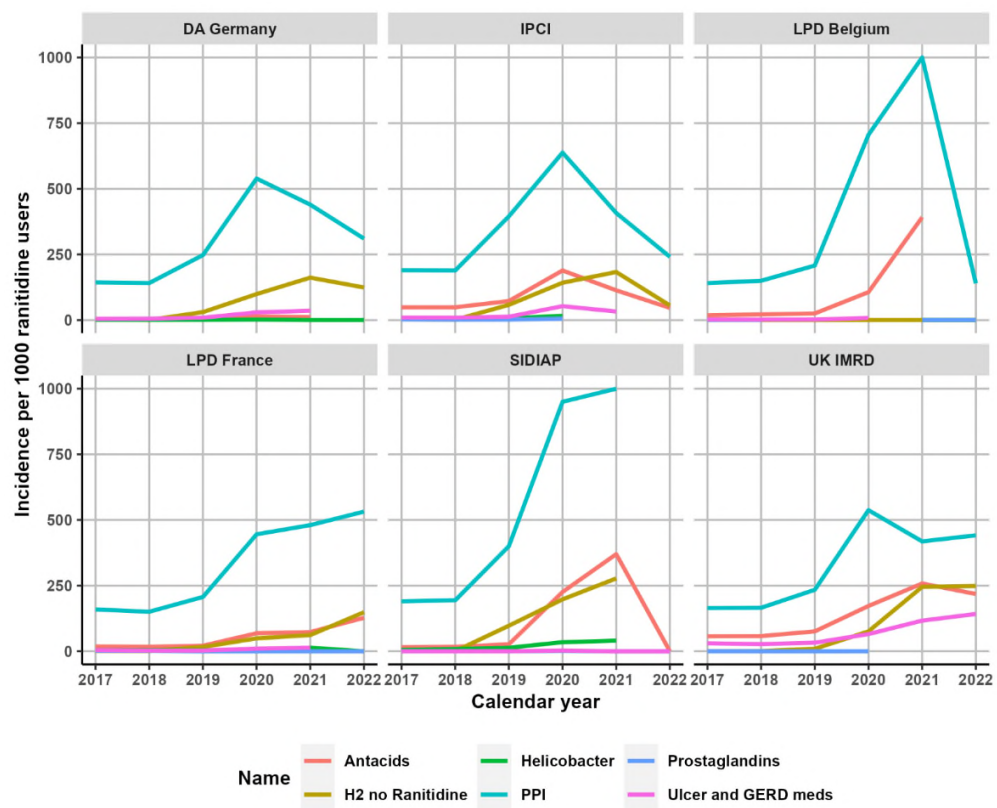
Ingredient	Database	Incidence per 1000 PY					
		2017	2018	2019	2020	2021	2022
Esomeprazole	DA Germany	41.51	36.02	40.58	39.40	44.70	28.08
	IPCI	27.77	23.94	21.32	26.48	69.42	32.84
	LPD Belgium	82.85	74.00	78.05	78.52	92.15	62.52
	LPD France	326.26	289.43	293.29	249.00	297.23	188.17
	SIDIAP	49.61	37.83	36.63	40.30	49.23	33.77
	UK IMRD	48.83	39.71	41.38	44.18	52.20	36.73
Dexlansoprazole	DA Germany	0.00	0.00	NA	NA	NA	0.00
PPI	DA Germany	574.40	521.45	527.50	451.06	503.95	285.93
	IPCI	346.25	263.26	305.56	319.54	304.35	126.13
	LPD Belgium	809.13	710.55	811.82	712.00	823.13	524.87
	LPD France	638.32	575.11	593.17	487.15	582.66	358.34
	SIDIAP	783.02	549.10	655.47	525.96	586.53	338.36
	UK IMRD	640.33	474.39	477.50	411.40	469.54	243.80
Antacids	DA Germany	8.90	6.75	7.51	7.65	6.41	4.16
	IPCI	55.72	47.99	58.88	64.49	70.74	34.19
	LPD Belgium	91.07	81.72	94.77	91.69	103.61	65.29
	LPD France	60.72	56.19	57.93	49.00	52.44	30.81
	SIDIAP	30.79	31.09	25.88	19.64	24.42	21.24
	UK IMRD	120.75	93.14	92.98	99.92	125.53	86.21
Prostaglandins	DA Germany	0.24	0.09	0.09	0.09	0.07	NA
	IPCI	1.05	1.37	1.04	1.19	0.88	NA
	LPD Belgium	NA	NA	NA	NA	0.64	NA
	LPD France	2.85	1.90	NA	0.00	0.00	0.00
	SIDIAP	NA	0.51	0.30	NA	NA	NA
	UK IMRD	NA	NA	NA	0.00	0.00	0.00
Combination therapy for eradication of <i>Helicobacter pylori</i>	DA Germany	11.91	9.07	8.76	7.44	7.01	4.31
	IPCI	52.20	38.81	44.01	40.92	38.81	12.00
	LPD Belgium	1.85	1.89	3.64	3.05	4.64	3.00
	LPD France	27.65	24.63	27.30	19.52	24.70	15.25

Ingredient	Database	Incidence per 1000 PY					
		2017	2018	2019	2020	2021	2022
Other drugs for peptic ulcer and GERD	SIDIAP	15.87	20.41	25.40	21.47	32.19	30.34
	DA Germany	15.24	15.23	18.18	17.44	18.75	12.32
	IPCI	21.79	19.09	17.63	20.39	22.12	9.74
	LPD Belgium	13.45	13.14	18.49	14.08	15.37	7.38
	LPD France	11.35	9.08	9.28	7.44	8.46	5.51
	SIDIAP	0.83	0.83	0.96	0.54	0.33	0.00
	UK IMRD	87.39	60.74	58.01	60.84	79.77	49.29

NA – Not available



*Supplemental Figure 1
Incidence of antacids use
over time*



Supplemental Figure 2 Patterns of late switching