

Supplemental Material S1.

- Section A – Overview of the studies assessing the effect of medication on speech patterns in schizophrenia
- Section B – MedDRA Query developed for the retrieval of communicative atypicalities reports
- Section C – Population Investigated
- Section D – Disproportionality and Robustness Analyses

Section A – Overview of the studies assessing the effect of medication on speech patterns in schizophrenia

The literature to date evaluating the role of medication on speech patterns in schizophrenia is very sparse. A very limited number of studies ($n = 5$) explicitly took into account the role of antipsychotic medications in influencing speech patterns:

- Puschel et al. (1998) compared acoustic patterns between patients with schizophrenia and control subjects and examined the effect of medication on vocal features. The authors found an association between medication effect, i.e., "neurological side effects of treatment," and the speech parameters "total recording time," "total length of pauses," and "mean pause duration per second"; however, the effects were in an unexpected direction (higher symptoms associated with longer pauses), whereas the other medication effects were not associated with the acoustic parameters. The authors therefore concluded that "Acute medication effects did not explain these findings".
- Cannizaro et al. (2005) studied 13 patients with schizophrenia who participated in a pharmaceutical clinical trial and were treated with a clinically effective dose of risperidone for 14 days. The authors compared acoustic features using two speech tasks of varying complexity (free speech vs. constrained task, i.e., reading) to determine distinct and overlapping features of speech pauses. The authors found that participants with schizophrenia in the free speech condition used greater total pause and a higher percentage of pauses, as well as longer pauses and greater variation in pauses in both the constrained- speech task and the free speech task.
- Cohen et al. (2017) examined the speech patterns of patients with schizophrenia who participated in a six-week randomized controlled trial in which galantamine or oxytocin was administered. The assessment was conducted at baseline and repeated six weeks later. The authors did not find significant change in voice or facial expressions as a result of either galantamine or oxytocin treatments.
- de Boer et al. (2020) compared patients with schizophrenia who received antipsychotic medications divided into two categories based on their mechanism of action, i.e., high and low dopamine occupancy of the D2 receptor (D2R), respectively. Overall, they found more severe negative speech disorders (i.e., slower articulation rate, increased pauses, and shorter utterances) in patients taking antipsychotics with high D2R occupancy, whereas patients with low D2R occupancy had less pronounced disorders, suggesting that speech disorders may be exacerbated by antipsychotics with high D2R occupancy.
- Parola et al. (2022) sought to assess the generalizability of de Boer et al.'s (2021) findings in a cross-linguistic sample of 231 patients with schizophrenia and 238 matched controls in four languages (Danish, German, Mandarin, and Japanese). The authors found that medication type (high or low D2 receptor occupancy) was related

to voice patterns, but inconsistently across languages. The most prevalent patterns were that patients taking medication with high D2R occupation had lower pitch variability, higher number of pauses, longer turn duration, and higher speech rate compared to patients taking medication with low D2R occupation. Higher medication dosage (CPZ equivalents) was associated with lower median pitch, lower speech rate, longer pause and utterance duration, and lower total number of words.

Overall, the few studies available, the small sample sizes, the limited information on the characteristics of drug treatment, and the large differences between studies do not allow conclusions to be drawn about the effects of medication on speech patterns in schizophrenia. The only potentially reliable effect indicated by the studies to date which need to be further explored in future studies is the difference found in the studies by de Boer et al. (2020) and Parola et al. (2022) between high and low D2R medications.

References

Püschel, J., Stassen, H. H., Bomben, G., Scharfetter, C., & Hell, D. (1998). Speaking behavior and speech sound characteristics in acute schizophrenia. *Journal of psychiatric research*, 32(2), 89-97.

Cannizzaro, M. S., Cohen, H., Rappard, F., & Snyder, P. J. (2005). Bradyphrenia and bradykinesia both contribute to altered speech in schizophrenia: a quantitative acoustic study. *Cognitive and behavioral neurology*, 18(4), 206-210.

Cohen, A. S., Mitchell, K. R., Strauss, G. P., Blanchard, J. J., Buchanan, R. W., Kelly, D. L., ... & Carpenter, W. T. (2017). The effects of oxytocin and galantamine on objectively-defined vocal and facial expression: Data from the CIDAR study. *Schizophrenia research*, 188, 141.

De Boer, J. N., Voppel, A. E., Brederoo, S. G., Wijnen, F. N. K., & Sommer, I. E. C. (2020). Language disturbances in schizophrenia: the relation with antipsychotic medication. *NPJ schizophrenia*, 6(1), 1-9.

Section B – MedDRA Query developed for the retrieval of communicative atypicalities reports

Table S1 – MedDRA Query for the retrieval of communicative atypicalities reports. We identified multiple sub-queries including semantically overlapping MedDRA Preferred Terms. The clusters were obtained on the basis of semantic overlapping, and therefore on the possibility that the reporters may have used interchangeably different terms, rather than with a reference to existing speech and language pathologies.

Cluster	MedDRA Preferred Terms		
Cluster 1 (dysphonia-related)	Dysphonia Dysphonia psychogenic Muscle tension dysphonia	Spasmodic dysphonia Aphonia Aphonia psychogenic	Phonastenia Stridor
Cluster 2 (speech motor control-related)	Dysarthria Dyslalia	Dysphemia	
Cluster 3 (prosody-related)	Aprosody Dysprosody		
Cluster 4 (aphasia-related)	Aphasia Primary progressive aphasia		
Cluster 5 (tachyphrenia-related)	Logorrhea Pressure of speech	Flight of ideas Tachyphrenia	
Cluster 6 (bradyphrenia-related)	Poverty of speech Bradyphrenia	Lack of spontaneous speech Poverty of thought content	Taciturnity Thought blocking
Cluster 7 (abnormal reasoning-related)	Ideas of reference Illogical thinking	Impaired reasoning Magical thinking	Paralogism
Cluster 8 (stereotypy-related)	Coprolalia Echolalia	Perseveration Repetitive speech	Verbigeration
Cluster 9 (incoherence-related)	Disorganized speech Incoherent Clang associations	Derailment Loose associations Tangentiality	Thinking abnormal
Other terms excluded from clusters	Pedantic speech Intellectualization Morbid thoughts Pathological doubt Intrusive thoughts Circumstantiality	Speech disorder developmental Mutism Speech disorder Cognitive linguistic disorder	Social communication disorder Language disorder Speech sound disorder Slow speech Confabulation

Section C – Population investigated

Using the query shown in the Table S1, we extracted from the deduplicated FAERS the cases of interest (any communication impairment), separated by underlying condition (psychotic, affective, and non-neuropsychiatric reports –i.e., reports without neurologic drugs; **Figure S1**).

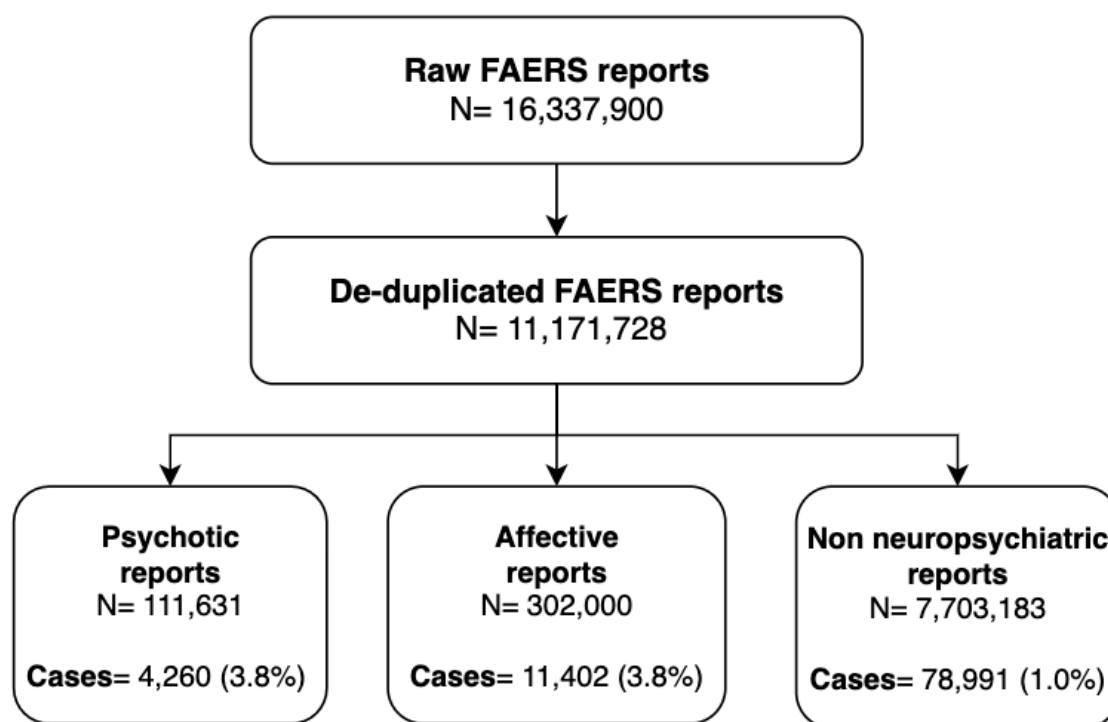


Figure S1 – Case retrieval flowchart. Cases (i.e., any communication-impairment) and non-cases in the three populations as retrieved from the FAERS. Note that some reports can be included in more than one population. 12,319 reports (599 cases, 11,720 non-cases) were included in both the psychotic and the affective populations.

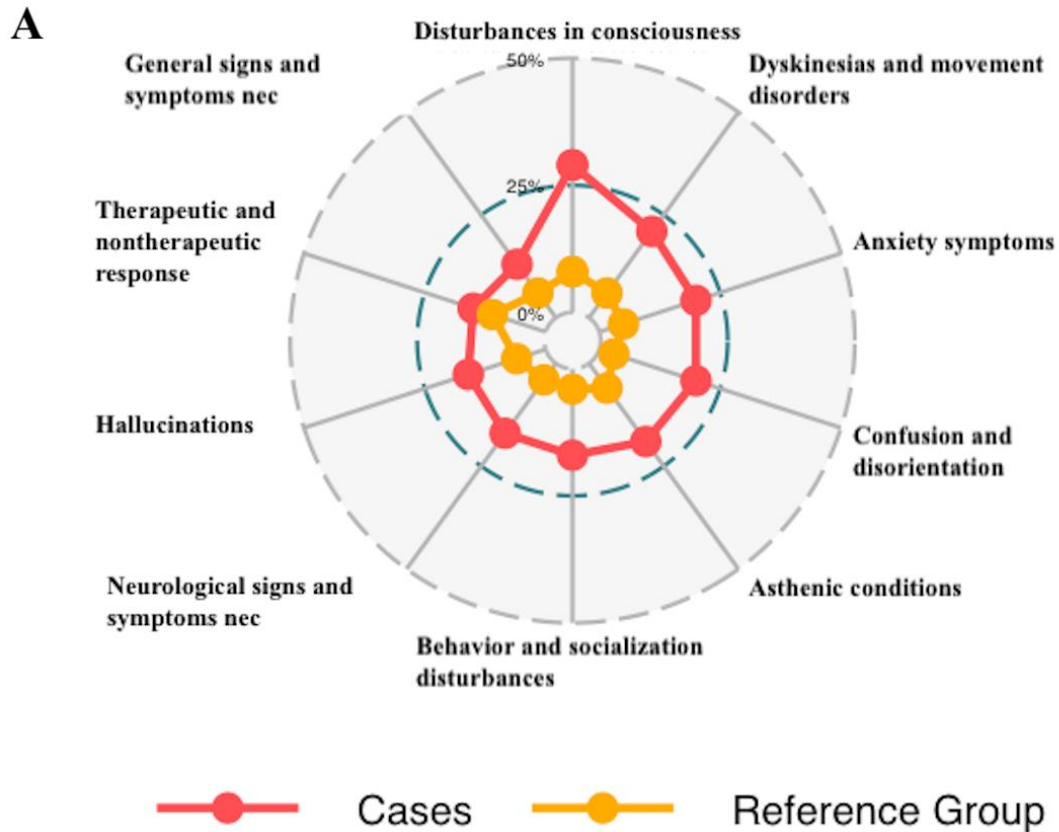
To identify potential risk factors or biases, we compared demographic and reporting information between cases and non-cases in each population (Table S2).

Most of the reports (>80%) were submitted from North America and Europe. Consumers submitted more communicative-impairment reports within psychotic and non-neuropsychiatric reports. The numbers of co-reported comorbidities and concomitant drugs were similar between cases and non-cases. However, the presence of communicative impairments was associated, across the three populations, with a higher number of co-occurrent adverse events (i.e., more symptoms are recorded in each report), disability, and hospitalization rate.

Table S2 – Demographic characterization of the reports. For each population, we compared frequency of reports (absolute number and valid percentage –i.e., not including missing values), sex and age, continent of reporting, role of the reporter, outcome, and number of co-occurrent symptoms.

Psychotic disorders					Affective disorders				Non-neuropsychiatric			
	Cases		Non-cases		Cases		Non-cases		Cases		Non-cases	
	N	%	N	%	N	%	N	%	N	%	N	%
Reports	4,260	3.8	107,371	96.2	11,402	3.8	290,598	96.2	78,991	1.0	7,624,192	99.0
Sex												
Female	1,659	41.0	41,698	41.0	7,421	68.0	185,864	67.0	48,706	64.7	4,267,049	61.6
Male	2,415	59.0	59,321	59.0	3,509	32.0	89,666	33.0	26,567	35.3	2,658,172	38.4
Missing	186	-	6,352	-	472	-	15,068	-	3,718	-	698,971	-
Age category												
<18	95	2.9	2,660	3.4	383	4.2	10,920	5.0	2,618	4.7	295,418	5.9
18-29	634	19.0	13,727	17.6	906	10.0	23,537	11.0	2,750	5.0	383,547	7.7
30-49	1,225	37.0	30,010	38.4	3,008	33.0	71,307	32.0	11,298	20.5	1,048,614	21.0
50-64	751	23.0	18,590	23.8	2,818	31.0	67,206	31.0	16,808	30.4	1,515,597	30.3
65-74	316	9.5	7,115	9.1	1,139	13.0	27,117	12.0	11,501	20.8	875,729	19.5
75-84	220	6.6	4,690	6.0	605	6.7	14,674	6.7	7,903	14.3	601,304	12.0
>84	70	2.1	1,365	1.7	175	1.9	5,002	2.3	2,335	4.2	183,242	3.6
Missing	949	-	29,214	-	2,368	-	70,835	-	23,778	-	2,620,741	-
Reporter												
Consumer	1,474	36.0	25,546	25.0	5,245	51.0	132,509	50.0	42,718	57.5	3,512,207	48.4
Physician	1,239	31.0	39,039	38.0	2,290	22.0	66,128	25.0	14,820	20.0	1,716,345	23.7
Pharmacist	265	6.5	9,501	9.3	452	4.4	11,834	4.5	10,052	13.5	1,102,747	15.2
Lawyer, healthcare practitioner or other	1,078	26.5	28,334	27.7	2,199	22.6	55,101	20.5	6,683	9.0	918,824	12.7
Missing	204	-	4,951	-	1,216	-	25,026	-	4,718	-	374,069	-
Continent												
North america	1,965	48.0	49,878	49.0	7,243	68.0	192,321	70.0	57,201	48.0	48,878	48.5
Europe	1,543	38.0	37,129	36.0	2,479	23.0	60,169	22.0	11,192	37.7	37,129	36.1
Asia	304	7.4	9,112	8.9	437	4.1	12,207	4.4	4,183	7.4	9,112	8.9
Other	282	6.6	6,631	6.1	491	4.9	9,713	3.6	3,828	6.9	6,631	6.5
Missing	166	-	4,621	-	752	-	16,188	-	2,587	-	4,621	-
Outcome												
Death or life-threat	492	11.5	18,758	17.5	1,146	10.1	27,729	9.5	6,742	8.5	280,865	3.7
Disability or congenital anomaly	180	4.2	2,201	2.0	764	6.7	12,636	4.3	3,397	4.3	129,814	1.7
Hospitalization or intervention required	1,722	40.4	34,241	31.9	3,605	31.6	70,739	24.3	19,966	25.3	1,466,799	19.2
Other serious	1,109	26.0	30,305	28.2	3,314	29.1	81,271	28.0	20,186	25.6	1,929,892	25.3
Non specified outcome	757	17.8	21,886	20.4	2,573	22.6	98,223	33.8	28,700	36.3	3,256,211	42.7
Co-occurrent events												
50% (25%-75%)	7 (5-11)		3 (1-5)		8 (5-14)		3 (2-5)		5 (3-9)		2 (1-4)	
Concomitant drugs												
50% (25%-75%)	4 (2-8)		3 (1-6)		5 (2-9)		4 (2-9)		2 (1-4)		2 (1-3)	
Comorbidities												
50% (25%-75%)	3 (1-5)		2 (1-4)		3 (1-6)		3 (1-6)		1 (1-2)		1 (1-2)	

There were differences in the adverse events co-reported with cases, relative to non-cases, in the three populations (Figure S2-S5), with anxiety symptoms, consciousness disturbances, dyskinesias and confusion being more frequent in psychotic and affective cases, while multiple respiratory conditions, pain, headache, nausea, and vomit were more common in non-neuropsychiatric reports. Indications and concomitant drugs overlapped between cases and non-cases in affective and psychotic reports, but non-neuropsychiatric ones had a higher proportion of cases with, as indication, multiple sclerosis acute and progressive (12% vs 0%), bronchospasm and obstruction (8% vs 1%) and rheumatoid arthropathies (5% vs 0%), and, as drugs, immunosuppressant agents and selective beta-2 adrenoceptors.



B

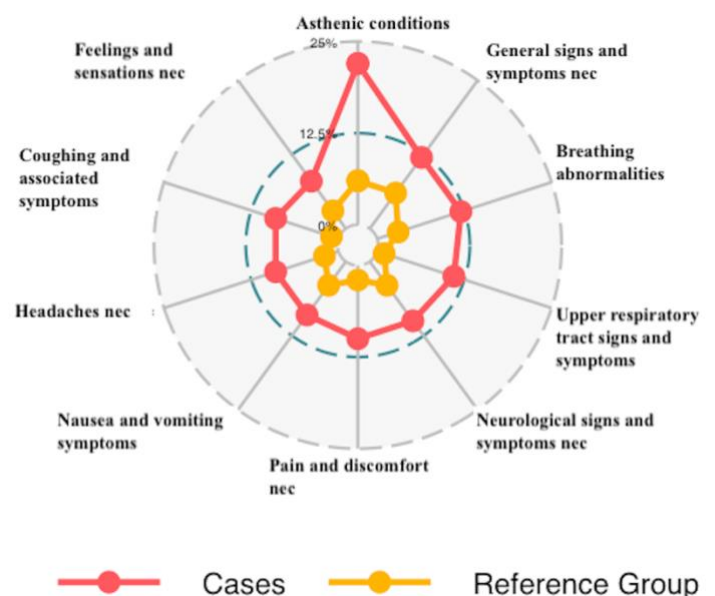
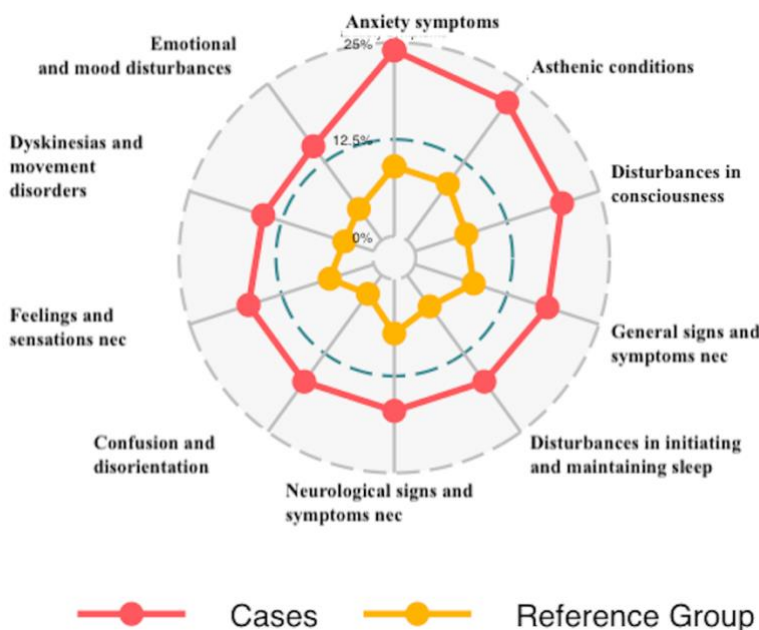
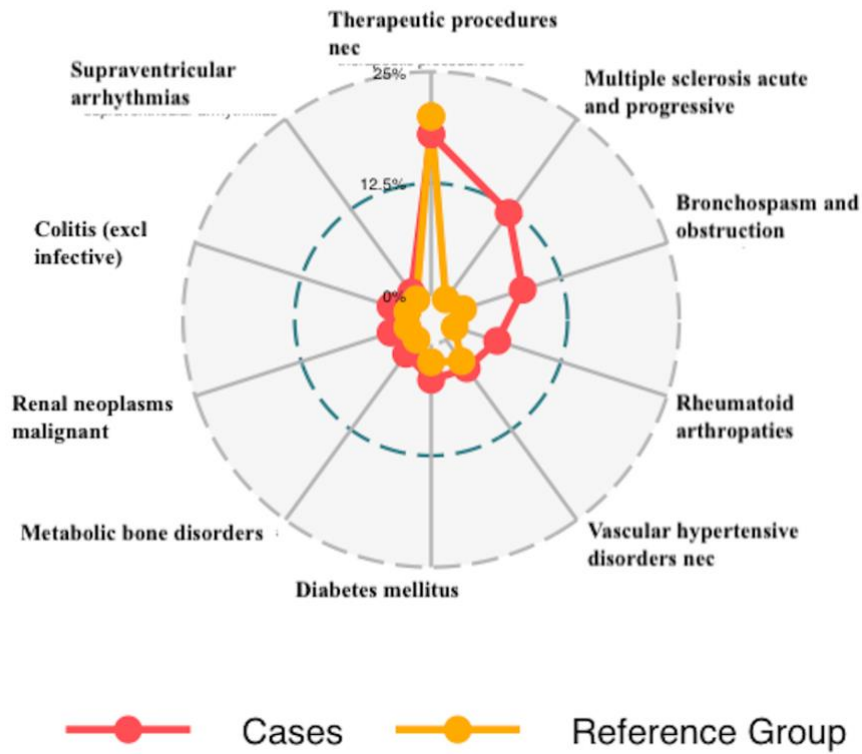


Figure S2 – Radar-plot of adverse events co-reported with communication ones.

For each population (A: psychotic, B: affective and C: non-neuropsychiatric reports), we identified the 10 most commonly co-reported adverse events (5 for cases and 5 for non-cases) and displayed in a clockwise order starting from the top. In red, we report the relative incidence of each co-reported adverse event in reports mentioning communication-related adverse events. In yellow we report the non-cases (reference group). To facilitate interpretation, we represent two reference levels (circles): 12.5% and 25% of co-occurrences. Note that, for clarity, panel A has a different scale (25% and 50%) than the other panels.

A



B

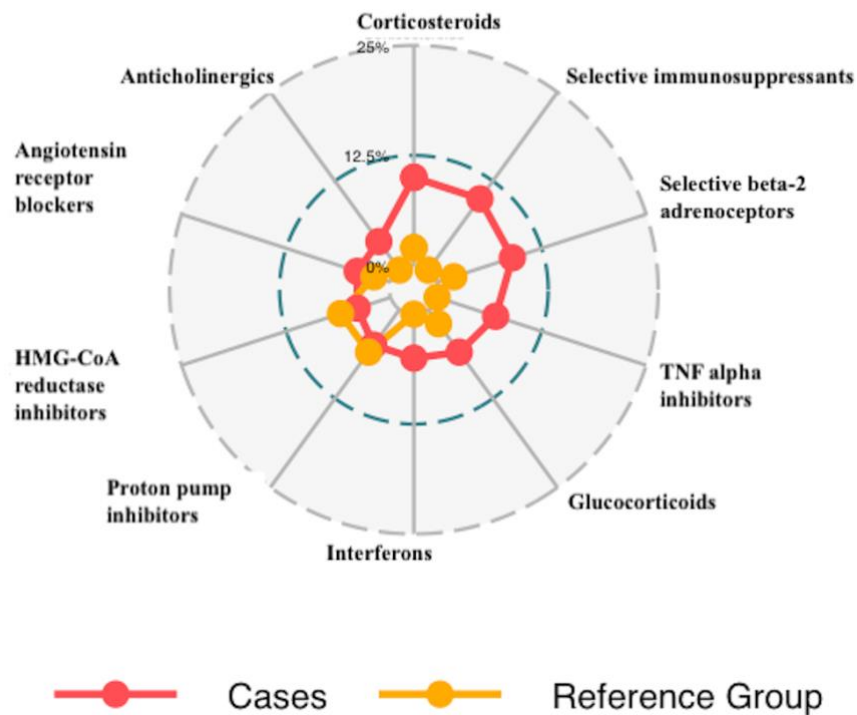


Figure S3 – Radar-plot of comorbidities and concomitants in non-neuropsychiatric reports

For non-neuropsychiatric reports, we displayed the 10 most commonly co-reported indications (A) and drugs (B): 5 for cases and 5 for non-cases. We displayed them in a clockwise order starting from the top. In red, we report the relative incidence in reports mentioning communication-related adverse events. In yellow we report the non-cases (reference group). To facilitate interpretation, we represent two reference levels (circles): 12.5% and 25% of co-occurrences.

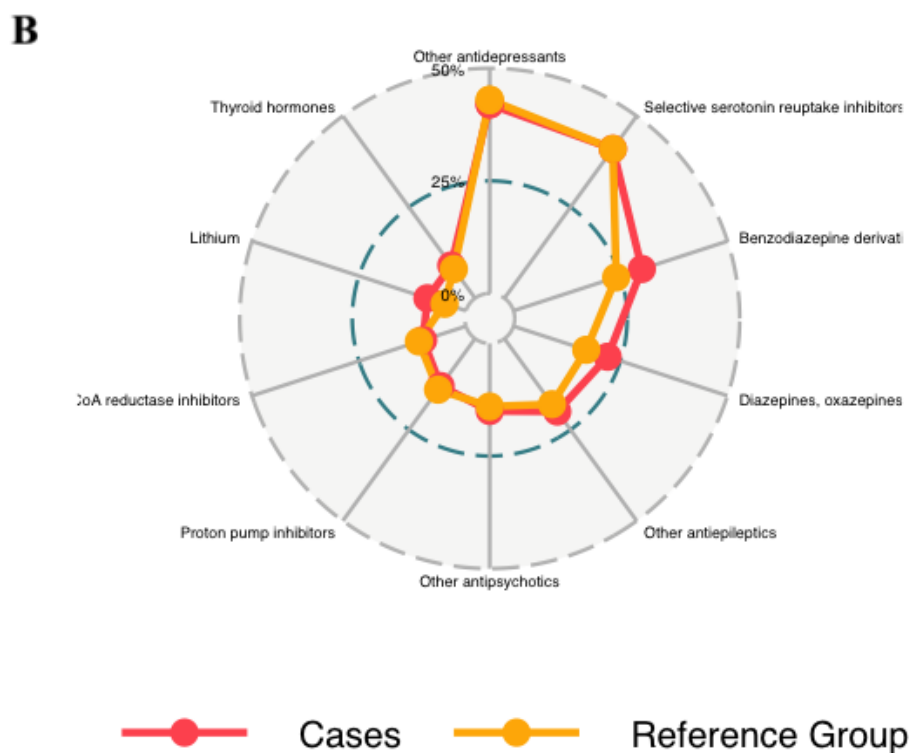
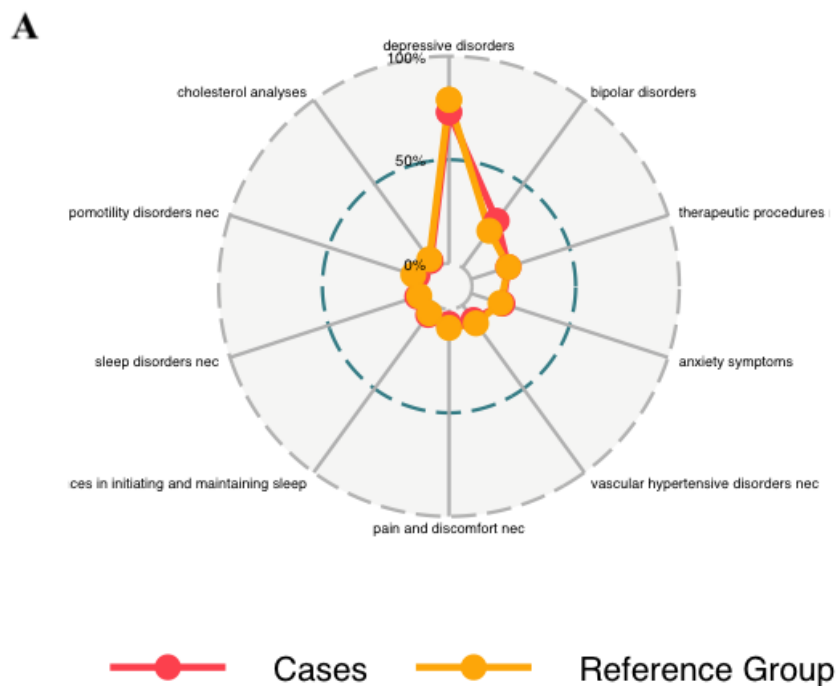


Figure S4 – Radar-plot of comorbidities and concomitants in affective reports

For affective reports, we displayed the 10 most commonly co-reported indications (A) and drugs (B): 5 for cases and 5 for non-cases. We displayed them in a clockwise order starting from the top. In red we report the relative incidence in reports mentioning communication-related adverse events. In yellow we report the non-cases (reference group). To facilitate interpretation, we represent two reference levels (circles): 50% and 100% of co-occurrences for A, 25% and 50% of co-occurrences for B.

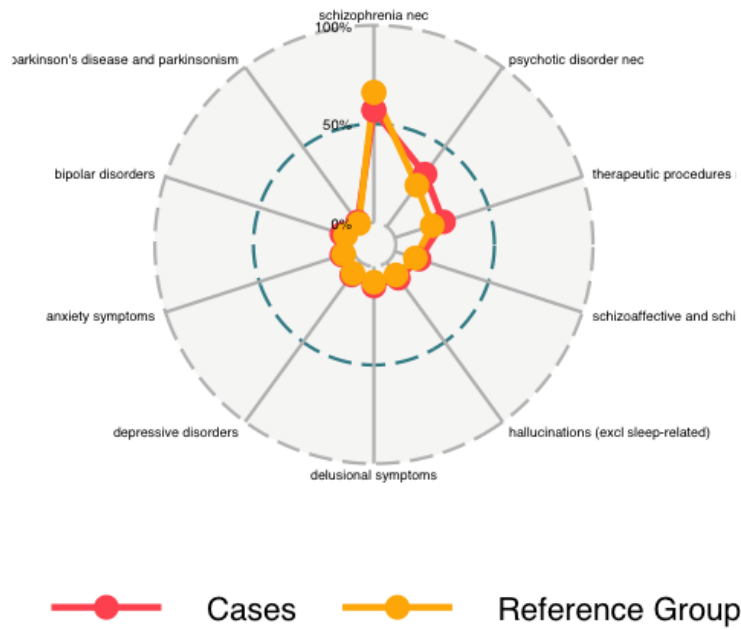
A**B**

Figure S5 – Radar-plot of comorbidities and concomitants in psychotic reports

For psychotic reports, we displayed the 10 most commonly co-reported indications (A) and drugs (B): 5 for cases and 5 for non-cases. We displayed them in a clockwise order starting from the top. In red we report the relative incidence in reports mentioning communication-related adverse events. In yellow we report the non-cases (reference group). To facilitate interpretation, we represent two reference levels (circles): 50% and 100% of co-occurrences.

Section D – Disproportionality and Robustness Analyses

We performed a disproportionality analysis evaluating associations between drugs (from the ATC 2022 classification, excluding mineral supplements and drugs included in the ‘Various’ class) and communication-related adverse events (sub-clusters of overlapping terms as identified in Table S1). The estimated reporting odds ratios (ROR) were shown in Supplementary Materials 2.

For each sub-query, we report a potential association when the adverse event is included in the package insert of the drug (SIDER) or is more likely to be reported together with the drug of interest than with any other drug but the one analyzed (FAERS).

Unexpected drugs, i.e., drugs associated with the sub-queries investigated but not included in the SIDER, were stratified according to expected biases (Figure 2 – Step 4) through clinical reasoning and according to the causal inference framework discussed in the introduction (paragraphs 1.3 and 1.4). In particular, we scanned the unexpected association for potential reverse causality (DAG B), potential confounding by indication (DAG C), and by concomitant (DAG D), and therefore identified by exclusion the uncontroversial ones (plausible adverse reactions, DAG A, for which no specific confounder was expected).

Finally, we performed robustness analyses to partly account for these biases:

- we excluded reports with the specific communicative impairment among indications, or restricted the investigation to a specific indication, to account for reverse causality bias (DAG B; Robustness Analysis 1).
- we excluded reports with pathologies that may be responsible for indication bias (DAG C; Robustness Analysis 2), at least for drugs that are approved for multiple indications (otherwise, the bias was considered non-fixable).
- we excluded reports with the drug responsible for the ambiguity to account for the concomitant bias (DAG D; Robustness Analysis 3).

Here we present the results of the disproportionality and the robustness analyzes for the different sub-queries.

Table S3– Drug-related dysphonia. Expected signals from the SIDER and unexpected signals from the FAERS were integrated in the following table, together with robustness considerations. Drugs were aggregated based on the ATC classification, Class 1 and Class3. In the FAERS column, robust new signals were reported in **bold**, while non-robust new signals were reported in *italic*.

ATC level 1	ATC level 3	SIDER	FAERS	DAGs & Robustness
Nervous	Antidepressants	clomipramine, fluoxetine, citalopram, paroxetine, sertraline, fluvoxamine, escitalopram		
	Antipsychotics	fluphenazine, olanzapine, risperidone, aripiprazole, paliperidone		
	Dopaminergic	ropinirole, pramipexole		
	Anti-Dementia	rivastigmine		
	Parasympathomimetics	pilocarpine, cevimeline		
	Drugs for addictive disorders	nicotine, varenicline, naltrexone		
	Antiepileptics	clonazepam, oxcarbazepine, eslicarbazepine, vigabatrin, topiramate, gabapentin		
	Opioids	nalbuphine		
	Other analgesics	paracetamol		
	Antimigraine	dihydroergotamine, sumatriptan, rizatriptan		
	Anesthetics, general	sevoflurane, fentanyl, remifentanyl		
	Anesthetics, local	lidocaine		
	Anxiolytics	alprazolam, buspirone		
	Hypnotics and sedatives	midazolam		
	Other nervous	riluzole		
Cardiovascular	Potassium sparing agents		triamterene	D: ACEI
	ACE-Inhibitors	enalapril, perindopril, cilazapril, fosinopril		
	Selective calcium channel blockers, vascular	nifedipine, lercanidipine		
	Beta blockers	bisoprolol		
	Antiarrhythmics I and III	flecainide		
	Selective calcium channel blockers, cardiac		diltiazem	D: ACEI
	Lipid modifying agents		evolocumab	D: ACEI
Alimentary and Metabolism	Belladonna	atropine, hyoscyamine		
	Propulsives	metoclopramide		
	Anabolic steroids	nandrolone		
	Drugs for peptic ulcer and reflux	lansoprazole	<i>omeprazole, esomeprazole</i>	B-C: reflux laryngitis, non fixable
	Insulins	insulin detemir		
	Antiemetics and antinauseants	ondansetron	<i>palonosetron</i>	C: emesis-related laryngitis non fixable
Blood	Antithrombotic	dipyridamole		
	Irrigating solutions	sorbitol		
Hormones	Anti-parathyroid agents	calcitonin		
	Anterior pituitary hormones		corticotropin	

	Hypothalamic hormones		octreotide	
Antiinfectives	Quinolone	ofloxacin, ciprofloxacin, lomefloxacin, levofloxacin, trovafloxacin		
	Other Beta-lactam	ertapenem		
	Macrolides	clindamycin		
	Aminoglycoside	tobramycin	amikacin	B: infective laryngitis; plausibly not completely fixed because of reports with specified agent but not site of infection
	Drugs for tuberculosis	rifapentine		
	Antimycotics, systemic	amphotericin b, itraconazole, posaconazole, caspofungin		
	Direct acting antivirals	foscarnet, zidovudine, zalcitabine, lamivudine, raltegravir, ribavirin, boceprevir		
Respiratory	Decongestans, topical	ipratropium, beclometasone, flunisolide, budesonide, fluticasone, mometasone, ciclesonide, nedocromil, cromoglicic acid		
	Other drugs for obstructive diseases, inhalant	tiotropium, aclidinium	umeclidinium	
	Antihistamines, systemic	cetirizine, levocetirizine	rupatadine, fexofenadine	B: allergic respiratory conditions (restricted to urticaria)
	Adrenergics, inhalant	salbutamol, pirbuterol, salmeterol, formoterol	procaterol, indacaterol, olodaterol	
	Other drugs for obstructive diseases		<i>theophylline, bamifylline, zafirlukast, omalizumab, mepolizumab, benralizumab</i>	D: inhalants (and C: obstructive conditions)
	Expectorants	acetylcysteine, mannitol	<i>guaifenesin, dornase alfa</i>	B: cough non fixable
Immunomodulating	Hormone antagonists	exemestane		
	Hormones	medroxyprogesterone		
	Protein kinase inhibitors	axitinib, sorafenib, pazopanib, regorafenib, cabozantinib, nilotinib, ponatinib	lenvatinib, nintedanib, everolimus	
	Monoclonal antibodies		bevacizumab, pembrolizumab	
	Antimetabolites	capecitabine		
	Plant alkaloids	vinflunine, paclitaxel		
	Cytotoxic antibiotics	doxorubicin, epirubicin, ixabepilone		
	Other antineoplastic	oxaliplatin, procarbazine, estramustine, bortezomib, celecoxib	niraparib	
	Immunosuppressants	lenalidomide	adalimumab	
	Immunostimulants	interferon alfa-2b		
Musculo-skeletal	Drugs affecting bone	ibandronic acid		
	Muscle relaxants, peripherally		botulinum toxin	B: spasmodic dysphonia
	Antiinflammatory, non steroids	ibuprofen		
	Muscle relaxants, directly	dantrolene		
Sensory	Antiinfectives	interferon		
	Antiglaucoma	travoprost		

Dermatologicals	Antipsoriatic, systemic	acitretin
	Anti-acne, topical	isotretinoin
Genitourinary	Urologicals	oxybutynin, solifenacin, tiroprium, sildenafil
	Other gynecologicals	fenoterol
	Androgens	testosterone
	Other sex hormones	danazol
Various	All other therapeutics	protamine, flumazenil
	Other diagnostics	edrophonium
	X-ray contrast media, iodinated	iopromide
	Magnetic resonance imaging contrast media	gadoversetamide

Table S4– Drug-related speech motor control disorder. Expected signals from the SIDER and unexpected signals from the FAERS were integrated in the following table, together with robustness considerations. Drugs were aggregated based on the ATC classification, Class 1 and Class3. In the FAERS column, robust new signals were reported in **bold**, while non-robust new signals were reported in *italic*.

ATC level 1	ATC level 3	SIDER	FAERS	DAGs & Robustness
Nervous	Antipsychotics	perphenazine, ziprasidone, lurasidone, loxapine, clozapine, olanzapine, quetiapine, asenapine, risperidone, aripiprazole, paliperidone, lithium	haloperidol	
	Anxiolytics	diazepam, oxazepam, lorazepam, clobazam, alprazolam, meprobamate, buspirone		
	Hypnotics and sedatives	flurazepam, nitrazepam, flunitrazepam, triazolam, temazepam, midazolam, zolpidem, zaleplon		
	Antiepileptics	phenytoin, mephenytoin, fosphenytoin, clonazepam, carbamazepine, eslicarbazepine, valproic acid, vigabatrin, tiagabine, lamotrigine, felbamate, topiramate, gabapentin, zonisamide, pregabalin, lacosamide, retigabine, perampanel		
	Anesthetics, general	fentanyl		
	Anesthetics, local	bupivacaine, lidocaine, prilocaine, ropivacaine		
	Opioids	morphine, hydromorphone, buprenorphine, butorphanol, tramadol, tapentadol		
	Antidepressants	amitriptyline, maprotiline, fluoxetine, citalopram, paroxetine, fluvoxamine, escitalopram, moclobemide, trazodone, nefazodone, mirtazapine, bupropion, duloxetine		
	Dopaminergic	amantadine, pramipexole, rasagiline		
	Anticholinergic		<i>benzatropine</i>	B: parkinsonism non fixable
	Other analgesics	ziconotide		
	Antimigraine	sumatriptan, rizatriptan		
Cardiovascular	Beta blockers	nadolol	bisoprolol	
	Thiazides		hydrochlorothiazide	
	Selective calcium channel blockers, vascular		amlodipine, manidipine, benidipine	
	ACE-Inhibitors		ramipril	
	Propulsives		metoclopramide	

Alimentary and Metabolism	Belladonna	atropine, hyoscyamine		
Blood	Antithrombotic		clopidogrel, ticlopidine, cilostazol, alteplase	B: ischaemic stroke-related aphasia
Hormones	Corticosteroids, systemic		dexamethasone, methylprednisolone	
Antiinfectives	Quinolone	ofloxacin, norfloxacin, levofloxacin	ciprofloxacin	
	Other antibacterials	metronidazole		
	Direct acting antivirals	aciclovir, valaciclovir, saquinavir	vidarabine, cidofovir	
Respiratory	Antihistamines, systemic		diphenhydramine	
Immunomodulating	Alkylating agents	ifosfamide, lomustine	cyclophosphamide	
	Antimetabolites	methotrexate, nelarabine, fluorouracil, capecitabine	mercaptopurine, tioguanine, cytarabine	
	Plant alkaloids	irinotecan	vincristine	
	Cytotoxic antibiotics	doxorubicin, epirubicin		
	Other antineoplastic	cisplatin, oxaliplatin, procarbazine, bortezomib, pentostatin, mitotane, anagrelide	asparaginase, pegaspargase	
	Monoclonal antibodies		blinatumomab	
	Immunosuppressants	tacrolimus, lenalidomide	<i>natalizumab, eculizumab, fingolimod</i>	C: natalizumab and fingolimod are used in multiple sclerosis, non fixable
	Immunostimulants		<i>interferon beta-1a</i>	C: multiple sclerosis non fixable
Musculo-skeletal	Muscle relaxants, centrally	baclofen, cyclobenzaprine	<i>tizanidine</i>	C: multiple sclerosis non fixable
	Antiinflammatory, non steroids	indometacin, ibuprofen	rofecoxib	
Genitourinary	Estrogens	estradiol		
	Progestogens	progesterone		

Table S5– Drug-related aphasia. Expected signals from the SIDER and unexpected signals from the FAERS were integrated in the following table, together with robustness considerations. Drugs were aggregated based on the ATC classification, Class 1 and Class3. In the FAERS column, robust new signals were reported in **bold**, while non-robust new signals were reported in *italic*.

ATC level 1	ATC level 3	SIDER	FAERS	DAGs & Robustness
Nervous	Antipsychotics	clozapine, quetiapine, risperidone, aripiprazole	lithium	
	Anti-Dementia	donepezil, rivastigmine, galantamine, memantine		
	Dopaminergic	ropinirole, pramipexole, selegiline, rasagiline		
	Anticholinergic		<i>procyclidine</i>	C: Parkinson, non fixable
	Antimigraine	sumatriptan, naratriptan, eletriptan		
	Hypnotics and sedatives	zolpidem		
	Anxiolytics		diazepam, lorazepam	
	Antiepileptics	lamotrigine, topiramate, gabapentin, pregabalin, retigabine, oxcarbazepine, eslicarbazepine, phenytoin, fosphenytoin	clonazepam	

	Antidepressants	clomipramine, citalopram, paroxetine, sertraline, escitalopram, trazodone, mirtazapine, bupropion, venlafaxine, reboxetine	amitriptyline	
	Anesthetics, general	fentanyl		
	Other analgesics	ziconotide		
	Parasympathomimetics	pilocarpine, cevimeline		
	Drugs for addictive disorders	nicotine		
	Opioids		tramadol	
Cardiovascular	Antiarrhythmics I and III	quinidine		
	Beta blockers	bisoprolol	labetalol	
	Selective calcium channel blockers, vascular		nitrendipine	
	Lipid modifying agents		atorvastatin	
Alimentary and Metabolism	Propulsives		domperidone	
	Blood glucose lowering drugs	gliclazide, glimepiride		
	Drugs for peptic ulcer and reflux		omeprazole	
	Antiemetics and antinauseants		ondansetron	
Blood	Antithrombotic		phenprocoumon, ticlopidine, alteplase	B: ischaemic stroke-related aphasia
Hormones	Corticosteroids, systemic		methylprednisolone	
	Thyroid preparations		levothyroxine	
Antiinfectives	Quinolone	ofloxacin, ciprofloxacin, norfloxacin, lomefloxacin, sparfloxacin, levofloxacin, moxifloxacin, gemifloxacin		
	Antimycotics, systemic	posaconazole		
	Drugs for tuberculosis	rifabutin		
	Direct acting antivirals	ganciclovir, foscarnet, ritonavir, zalcitabine		
	Other Beta-lactam		cefepime	
Immunomodulating	Immunosuppressants	lenalidomide, tacrolimus	<i> fingolimod, natalizumab</i>	C: mulitple sclerosis, non fixable
	Immunostimulants	glatiramer, interferon alfa-2b	<i> interferon beta-1a, peginterferon beta-1a</i>	C: mulitple sclerosis, non fixable
	Alkylating agents	carmustine, temozolomide	cyclophosphamide, ifosfamide	C: brain tumor
	Antimetabolites	methotrexate, nelarabine, capecitabine	fludarabine, cytarabine, fluorouracil	C: brain tumor
	Other antineoplastic	oxaliplatin	pegaspargase, axicabtagene ciloleucel, tisagenlecleucel-t	C: brain tumor
	Plant alkaloids		vincristine, etoposide, irinotecan	C: brain tumor
	Cytotoxic antibiotics		daunorubicin, mitoxantrone	C: brain tumor
	Protein kinase inhibitors		erlotinib, dabrafenib, trametinib, avapritinib	C: brain tumor
	Monoclonal antibodies		bevacizumab, blinatumomab	C: brain tumor
Musculo-skeletal	Antiinflammatory, non steroids	diclofenac		
Sensory	Diagnostic agents	fluorescein		

	Antiglaucoma		diclofenamide
Dermatologicals	Anti-acne, topical	isotretinoin	
Genitourinary	Estrogens	estradiol	
	Antiandrogens	cypoterone	
	Hormonal contraceptives		drospirenone
Various	X-ray contrast media, iodinated	iopamidol, iopromide, ioversol	
	Magnetic resonance imaging contrast media	gadobutrol	
	All other therapeutics	deferoxamine	
Antiparasitic	Antimalarials	quinine	mefloquine
	Antinematodals		ivermectin

Table S6– Drug-related stereotypes. Expected signals from the SIDER and unexpected signals from the FAERS were integrated in the following table, together with robustness considerations. Drugs were aggregated based on the ATC classification, Class 1 and Class3. In the FAERS column, robust new signals were reported in **bold**, while non-robust new signals were reported in *italic*.

ATC level 1	ATC level 3	SIDER	FAERS	DAGs & Robustness
Nervous	Antiepileptics	topiramate		
	Antidepressants	phenelzine, bupropion		
Immunomodulating	Alkylating agents	ifosfamide		
Various	X-ray contrast media, iodinated	iopamidol		

Table S7– Drug-related tachyphrenia. Expected signals from the SIDER and unexpected signals from the FAERS were integrated in the following table, together with robustness considerations. Drugs were aggregated based on the ATC classification, Class 1 and Class3. In the FAERS column, robust new signals were reported in **bold**, while non-robust new signals were reported in *italic*.

ATC level 1	ATC level 3	SIDER	FAERS	DAGs & Robustness
Nervous	Antiepileptics	carbamazepine	valproic acid, lamotrigine	
	Dopaminergic	pramipexole		
	Antipsychotics	aripiprazole	lurasidone, quetiapine, lithium	
	Anxiolytics	alprazolam		
	Hypnotics and sedatives	flurazepam		
	Antidepressants	duloxetine		
	Psychostimulants	methylphenidate, dexamethylphenidate, lisdexamfetamine		
Hormones	Thyroid preparations		levothyroxine	
Immunomodulating	Alkylating agents	ifosfamide		
	Other antineoplastic		niraparib	
Musculo-skeletal	Antiinflammatory, non steroids		ibuprofen	
Antiparasitic	Antinematodals		ivermectin	

Table S8– Drug-related bradyphrenia. Expected signals from the SIDER and unexpected signals from the FAERS were integrated in the following table, together with robustness considerations. Drugs

were aggregated based on the ATC classification, Class 1 and Class3. In the FAERS column, robust new signals were reported in **bold**, while non-robust new signals were reported in *italic*.

ATC level 1	ATC level 3	SIDER	FAERS	DAGs & Robustness
Nervous	Other analgesics	ziconotide		
	Antimigraine	clonidine		
	Antiepileptics	topiramate, zonisamide, pregabalin	clonazepam, valproic acid	
	Dopaminergic	pramipexole		
	Antipsychotics	ziprasidone, aripiprazole	olanzapine, lithium	
	Anxiolytics	alprazolam		
	Hypnotics and sedatives		lormetazepam	
Alimentary and Metabolism	Antiobesity		lorcaserin	
Immunomodulating	Alkylating agents	ifosfamide		
Genitourinary	Estrogens	estradiol		

Table S9– Drug-related incoherence. Expected signals from the SIDER and unexpected signals from the FAERS were integrated in the following table, together with robustness considerations. Drugs were aggregated based on the ATC classification, Class 1 and Class3. In the FAERS column, robust new signals were reported in **bold**, while non-robust new signals were reported in *italic*.

ATC level 1	ATC level 3	SIDER	FAERS	DAGs & Robustness
Nervous	Anxiolytics	diazepam, lorazepam, buspirone		
	Hypnotics and sedatives	amobarbital, secobarbital, flurazepam, nitrazepam, estazolam, triazolam, quazepam, zopiclone, zolpidem, zaleplon, eszopiclone, ramelteon, suvorexant		
	Antidepressants	clomipramine, doxepin, fluoxetine, citalopram, paroxetine, sertraline, fluvoxamine, escitalopram, nefazodone, mirtazapine, bupropion, venlafaxine, reboxetine		
	Psychostimulants	methylphenidate, modafinil, dexamethylphenidate		
	Parasympathomimetics	pilocarpine, cevimeline		
	Drugs for addictive disorders	varenicline, acamprosate, naltrexone		
	Dopaminergic	pergolide, ropinirole, selegiline, tolcapone, entacapone		
	Antipsychotics	olanzapine, quetiapine, risperidone, aripiprazole		
	Antiepileptics	phenobarbital, phenytoin, fosphenytoin, carbamazepine, oxcarbazepine, valproic acid, vigabatrin, tiagabine, felbamate, topiramate, gabapentin, levetiracetam, pregabalin		
	Anesthetics, general	fentanyl, propofol, oxybate sodium		
	Opioids	morphine, oxycodone, butorphanol, tramadol, tapentadol		
	Antimigraine	zolmitriptan, eletriptan, frovatriptan		
	Anti-Dementia	memantine		
	Other nervous	riluzole		
Cardiovascular	Cardiac stimulants		droxidopa	
	Beta blockers	betaxolol, esmolol, carvedilol		
	Antiadrenergic, peripherically acting	doxazosin		
	Selective calcium channel blockers, cardiac	diltiazem		

	Selective calcium channel blockers, vascular	nisoldipine	
Alimentary and Metabolism	Drugs for peptic ulcer and reflux	pantoprazole	
	Antiemetics and antinauseants	dronabinol, nabilone	
	Antiobesity	sibutramine	
Blood	Antithrombotic	ticagrelor	
Hormones	Posterior pituitary hormones	desmopressin	
	Thyroid preparations	levothyroxine, liothyronine	
Antiinfectives	Quinolone	lomefloxacin, sparfloxacin, trovafloxacin, moxifloxacin, gatifloxacin	
	Antimycotics, systemic	amphotericin b	
	Direct acting antivirals	ganciclovir, valganciclovir, ritonavir, stavudine, efavirenz	zanamivir
Respiratory	Antihistamines, systemic	cetirizine, levocetirizine	diphenhydramine
	Decongestans, topical	azelastine	
	Adrenergics, inhalant	salbutamol	
	Expectorants	acetylcysteine	
Immunomodulating	Alkylating agents	carmustine	
	Plant alkaloids	paclitaxel	
	Cytotoxic antibiotics	doxorubicin, daunorubicin, epirubicin	
	Other antineoplastic	bexarotene, pentostatin	
	Hormones	megestrol, leuprorelin, goserelin	
	Immunostimulants	interferon alfa-2b, glatiramer	peginterferon alfa-2b
	Immunosuppressants	mycophenolic acid, tacrolimus, thalidomide	siponimod
Sensory	Mydriatics	cyclopentolate, homatropine	
Dermatologicals	Antibiotics, topical	rifaximin	
Genitourinary	Urologicals	oxybutynin, darifenacin	
Antiparasitic	Antimalarials	mefloquine	
	Antinematodals	ivermectin	

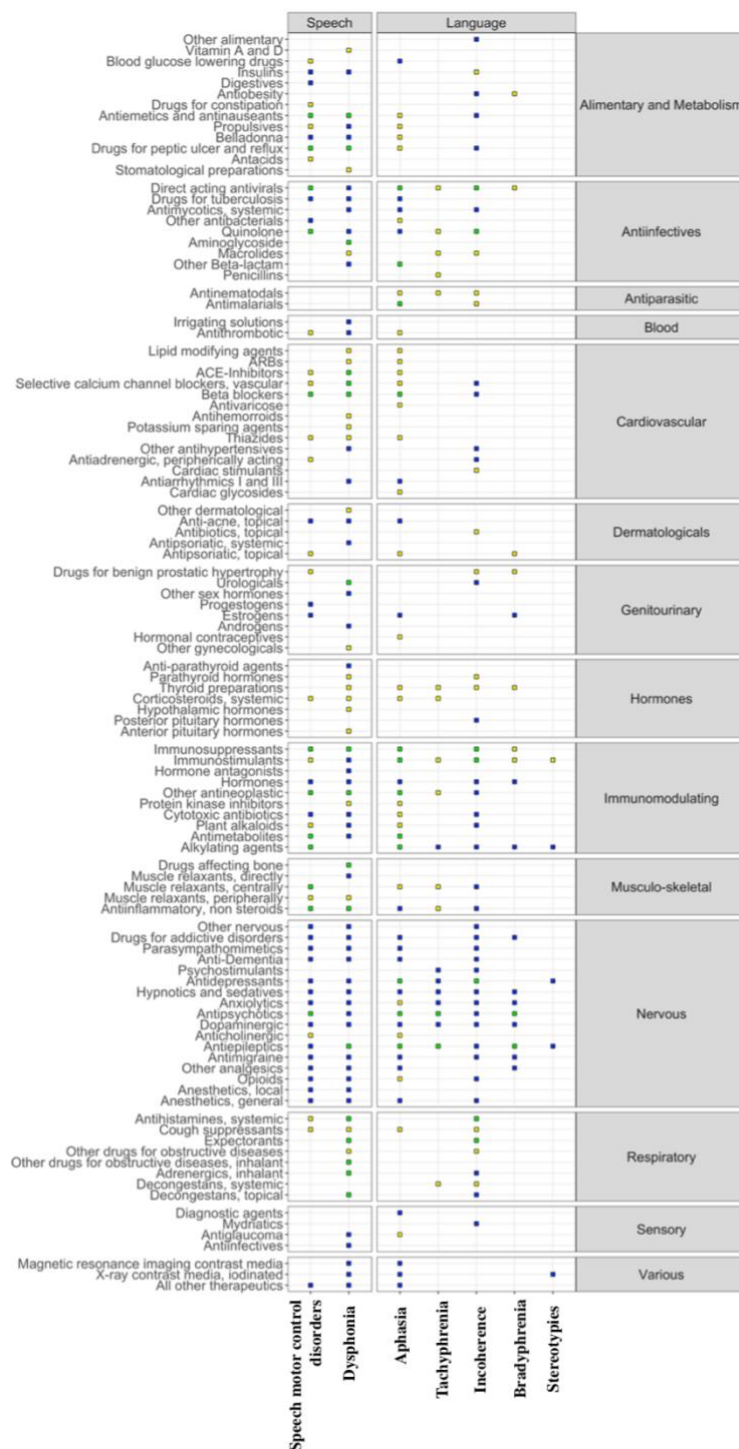


Figure S6 – Heat Map of drug-related communicative atypicalities. We showed expected and unexpected associations between drug classes at the third level of the ATC classification (y-axis – left, aggregated by the first level of the ATC classification – right) and communicative impairment sub-queries (x-axis – bottom, aggregated in Speech and Language – top). Blue squares represent expected associations based on SIDER, yellow squares unexpected associations, and green squares drug classes that included both expected and unexpected medications. Rows and columns with no significant association were not shown.

Table S10 – List of drugs associated with communicative atypicalities. Expected drugs are those already identified in SIDER. Unexpected drugs are split in 2 classes: new or integrated, for which drugs within the same class are already known to associate with the impairment. *Robust FAERS signals*.

	DYSPHONIA	SPEECH MOTOR CONTROL	APHASIA	STEREOTYPES	TACHYPHRENIA/ BRADYPHRENIA	INCOHERENCE
SUMMARY DRUG CLASS	53 expected, 10 integrated, 9 new	17 expected, 10 integrated, 10 new	19 expected, 10 integrated, 22 new	4 expected	8 expected, 3 integrated, 5 new	34 expected, 4 integrated, 6 new
SIDER	clomipramine, fluoxetine, citalopram, paroxetine, sertraline, fluvoxamine, escitalopram, fluphenazine, olanzapine, risperidone, aripiprazole, paliperidone, ropinirole, pramipexole, rivastigmine, pilocarpine, cevimeline, nicotine, varenicline, naltrexone, clonazepam, oxcarbazepine, eslicarbazepine, vigabatrin, topiramate, gabapentin, nalbuphine, paracetamol, dihydroergotamine, sumatriptan, rizatriptan, sevoflurane, fentanyl, remifentanyl, lidocaine, alprazolam, buspirone, midazolam, riluzole, enalapril, perindopril, cilazapril, fosinopril, nifedipine, lercanidipine, bisoprolol, flecainide, atropine, hyoscyamine, metoclopramide, nandrolone, lansoprazole, insulin detemir, ondansetron, dipyridamole, sorbitol, calcitonin, ofloxacin, ciprofloxacin, lomefloxacin, levofloxacin, trovafloxacin, ertapenem, clindamycin, tobramycin, rifapentine, amphotericin b, itraconazole, posaconazole, caspofungin, foscarnet, zidovudine, zalcitabine, lamivudine, raltegravir, ribavirin, boceprevir, ipratropium, beclometasone, flunisolide, budesonide, fluticasone, mometasone, ciclesonide, nedocromil, cromoglicic acid, tiotropium, acridinium, cetirizine, levocetirizine, salbutamol, pirbuterol, salmeterol, formoterol, acetylcysteine, mannitol, exemestane, medroxyprogesterone, axitinib, sorafenib, pazopanib,	perphenazine, ziprasidone, lurasidone, loxapine, clozapine, olanzapine, quetiapine, asenapine, risperidone, aripiprazole, paliperidone, lithium, diazepam, oxazepam, lorazepam, clobazam, alprazolam, meprobamate, buspirone, flurazepam, nitrazepam, flunitrazepam, triazolam, temazepam, midazolam, zolpidem, zaleplon, phenytoin, mephentyoin, fosphenytoin, clonazepam, carbamazepine, eslicarbazepine, valproic acid, vigabatrin, tiagabine, lamotrigine, felbamate, topiramate, gabapentin, zonisamide, pregabalin, lacosamide, retigabine, perampanel, fentanyl, bupivacaine, lidocaine, prilocaine, ropivacaine, morphine, hydromorphone, buprenorphine, butorphanol, tramadol, tapentadol, amitriptyline, maprotiline, fluoxetine, citalopram, paroxetine, fluvoxamine, escitalopram, moclobemide, trazodone, nefazodone, mirtazapine, bupropion, duloxetine, amantadine, pramipexole, rasagiline, ziconotide, sumatriptan, rizatriptan, nadolol	clozapine, quetiapine, risperidone, aripiprazole, donepezil, rivastigmine, galantamine, memantine, ropinirole, pramipexole, selegiline, rasagiline, sumatriptan, naratriptan, eletriptan, zolpidem, lamotrigine, topiramate, gabapentin, pregabalin, retigabine, oxcarbazepine, eslicarbazepine, phenytoin, fosphenytoin, clomipramine, citalopram, paroxetine, sertraline, escitalopram, trazodone, mirtazapine, bupropion, venlafaxine, reboxetine, fentanyl, ziconotide, pilocarpine, cevimeline, nicotine, quinidine, bisoprolol, gliclazide, glimepiride, ofloxacin, ciprofloxacin, norfloxacin, lomefloxacin, sparfloxacin, levofloxacin, moxifloxacin, gemifloxacin, posaconazole, rifabutin, ganciclovir, foscarnet, ritonavir, zalcitabine, lenalidomide, tacrolimus, glatiramer, interferon alfa-2b, carmustine, temozolomide, methotrexate, nelarabine, capecitabine, oxaliplatin, diclofenac, fluorescein, isotretinoin, estradiol, cyproterone, iopamidol, iopromide, ioversol, gadobutrol, deferoxamine, quinine	topiramate, phenelzine, bupropion, ifosfamide, iopamidol	ziconotide, clonidine, carbamazepine, topiramate, zonisamide, pregabalin, pramipexole, ziprasidone, aripiprazole, alprazolam, flurazepam, duloxetine, methylphenidate, dexamethylphenidate, lisdexamphetamine, ifosfamide, estradiol	diazepam, lorazepam, buspirone, amobarbital, secobarbital, flurazepam, nitrazepam, estazolam, triazolam, quazepam, zopiclone, zolpidem, zaleplon, eszopiclone, ramelteon, suvorexant, clomipramine, doxepin, fluoxetine, citalopram, paroxetine, sertraline, fluvoxamine, escitalopram, nefazodone, mirtazapine, bupropion, venlafaxine, reboxetine, methylphenidate, modafinil, dexamethylphenidate, pilocarpine, cevimeline, varenicline, acamprosate, naltrexone, pergolide, ropinirole, selegiline, tolcapone, entacapone, olanzapine, quetiapine, risperidone, aripiprazole, phenobarbital, phenytoin, fosphenytoin, carbamazepine, oxcarbazepine, valproic acid, vigabatrin, tiagabine, felbamate, topiramate, gabapentin, levetiracetam, pregabalin, fentanyl, propofol, oxybate sodium, morphine, oxycodone, butorphanol, tramadol, tapentadol, zolmitriptan, eletriptan, frovatriptan, memantine, riluzole, betaxolol, esmolol, carvedilol, doxazosin, diltiazem, nisoldipine, pantoprazole, dronabinol, nabilone, sibutramine, desmopressin, lomefloxacin, sparfloxacin, trovafloxacin, moxifloxacin, gatifloxacin, amphotericin b, ganciclovir, valganciclovir, ritonavir, stavudine, efavirenz, cetirizine, levocetirizine, azelastine, salbutamol, acetylcysteine, carmustine, paclitaxel, doxorubicin, daunorubicin,

	regorafenib, cabozantinib, nilotinib, ponatinib, capecitabine, vinflunine, paclitaxel, doxorubicin, epirubicin, ixabepilone, oxaliplatin, procarbazine, estramustine, bortezomib, celecoxib, lenalidomide, interferon alfa-2b, ibandronic acid, ibuprofen, dantrolene, interferon, travoprost, acitretin, isotretinoin, oxybutynin, solifenacin, tropsium, sildenafil, testosterone, danazol, protamine, flumazenil, edrophonium, iopromide, gadoversetamide					epirubicin, bexarotene, pentostatin, megestrol, leuprorelin, goserelin, interferon alfa-2b, glatiramer, mycophenolic acid, tacrolimus, thalidomide, cyclopentolate, homatropine, oxybutynin, darifenacin
FAERS	* triamterene, diltiazem, evolocumab, corticotropin, octreotide, amikacin, umecclidinium, rupatadine, procaterol, indacaterol, olodaterol, zafirlukast, omalizumab, mepolizumab, benralizumab, lenvatinib, nintedanib, everolimus, bevacizumab, pembrolizumab, niraparib, adalimumab, botulinum toxin, fenoterol * omeprazole, esomeprazole, palonosetron, fexofenadine, theophylline, bamifylline, guaifenesin, dornase alfa	* haloperidol, benzatropine, bisoprolol, hydrochlorothiazide, amlodipine, manidipine, benidipine, ramipril, metoclopramide, clopidogrel, ticlopidine, cilostazol, alteplase, dexamethasone, methylprednisolone, ciprofloxacin, vidarabine, cidofovir, diphenhydramine, cyclophosphamide, mercaptopurine, tioguanine, cytarabine, vincristine, asparaginase, pegaspargase, blinatumomab, eculizumab, rofecoxib * natalizumab, fingolimod, interferon beta-1a, tizanidine	* lithium, diazepam, lorazepam, clonazepam, amitriptyline, tramadol, labetalol, nitrendipine, atorvastatin, domperidone, omeprazole, ondansetron, phenprocoumon, ticlopidine, alteplase, methylprednisolone, levothyroxine, cefepime, cyclophosphamide, ifosfamide, fludarabine, cytarabine, fluorouracil, pegaspargase, axicabtagene ciloleucel, tisagenlecleucel-t, vincristine, etoposide, irinotecan, daunorubicin, mitoxantrone, erlotinib, dabrafenib, trametinib, avapritinib, bevacizumab, blinatumomab, diclofenamide, drospirenone, mefloquine, ivermectin * procyclidine, fingolimod, natalizumab, interferon, beta-1a, peginterferon beta-1a		* valproic acid, lamotrigine, clonazepam, lurasidone, quetiapine, olanzapine, lithium, lormetazepam, levothyroxine, niraparib, ibuprofen, ivermectin, lorcaserin *	* droxidopa, ticagrelor, levothyroxine, liothyronine, zanamivir, diphenhydramine, peginterferon alfa-2b, siponimod, rifaximin, mefloquine, ivermectin *
PROPOSED MECHANISM	Anticholinergic toxicity, Extrapyramidal dystonia, laryngeal irritation, vocal cord thickening, anti-angiogenetic action, cytotoxicity, vocal cord hemorrhages, vocal cord nodules	Extrapyramidal dystonia, sedation, neurotoxicity, stroke, dopaminergic, catecholaminergic and GABAergic pathways	Neurotoxicity, Blood brain barrier permeability, dopamine antagonism, stroke		Altered arousal	

Bibliography

1. Faham M, Ahmadi A, Silverman E, Harouni GG, Dabirmoghaddam P. Quality of Life After Botulinum Toxin Injection in Patients With Adductor Spasmodic Dysphonia; a Systematic Review and Meta-analysis. *J Voice*. 2021;35(2):271-283. doi:10.1016/j.jvoice.2019.07.025
2. Haft S, Farquhar D, Carey R, Mirza N. Anticholinergic Use Is a Major Risk Factor for Dysphonia. *Ann Otol Rhinol Laryngol*. 2015;124(10):797-802. doi:10.1177/0003489415585867
3. Schwartz SR, Cohen SM, Dailey SH, et al. Clinical Practice Guideline: Hoarseness (Dysphonia). *Otolaryngol Head Neck Surg*. 2009;141(1_suppl):1-31. doi:10.1016/j.otohns.2009.06.744
4. Galván CA, Guarderas JC. Practical Considerations for Dysphonia Caused by Inhaled Corticosteroids. *Mayo Clin Proc*. 2012;87(9):901-904. doi:10.1016/j.mayocp.2012.06.022
5. Bangalore S, Kumar S, Messerli FH. Angiotensin-converting enzyme inhibitor associated cough: deceptive information from the Physicians' Desk Reference. *Am J Med*. 2010;123(11):1016-1030. doi:10.1016/j.amjmed.2010.06.014
6. Hanna J, Bee J, Sataloff RT. Laryngeal ulceration and hemoptysis secondary to inadvertent alendronate overdose: case report and review of the literature. *Ear Nose Throat J*. 2012;91(11):484-485. doi:10.1177/014556131209101109
7. Stachler RJ, Francis DO, Schwartz SR, et al. Clinical Practice Guideline: Hoarseness (Dysphonia) (Update). *Otolaryngol Head Neck Surg*. 2018;158(1_suppl):S1-S42. doi:10.1177/0194599817751030
8. Busso CIM, Serrano RL. Hoarseness during isotretinoin therapy. *Journal of the American Academy of Dermatology*. 2005;52(1):168. doi:10.1016/j.jaad.2004.04.044
9. Kim H, Park H, Lee J, Cho B. A rare side-effect of systemic isotretinoin treatment: hoarseness. *Journal of the European Academy of Dermatology and Venereology*. 2006;20(10):1389-1390. doi:10.1111/j.1468-3083.2006.01755.x
10. Kudo M, Finn RS, Qin S, et al. Lenvatinib versus sorafenib in first-line treatment of patients with unresectable hepatocellular carcinoma: a randomised phase 3 non-inferiority trial. *Lancet*. 2018;391(10126):1163-1173. doi:10.1016/S0140-6736(18)30207-1
11. Motzer RJ, Nosov D, Eisen T, et al. Tivozanib versus sorafenib as initial targeted therapy for patients with metastatic renal cell carcinoma: results from a phase III trial. *J Clin Oncol*. 2013;31(30):3791-3799. doi:10.1200/JCO.2012.47.4940
12. Saavedra E, Hollebecque A, Soria JC, Hartl DM. Dysphonia induced by anti-angiogenic compounds. *Invest New Drugs*. 2014;32(4):774-782. doi:10.1007/s10637-013-0049-2
13. Wen PY, Drappatz J, de Groot J, et al. Phase II study of cabozantinib in patients with progressive glioblastoma: subset analysis of patients naive to antiangiogenic therapy. *Neuro Oncol*. 2018;20(2):249-258. doi:10.1093/neuonc/nox154

14. Sulibhavi A, Tharmalingam S, McCarroll L, Soliman AMS. Reversible Bevacizumab Induced Vocal Fold Necrosis. *Journal of Voice*. 2020;0(0). doi:10.1016/j.jvoice.2020.11.028
15. Melo ÉGA, Silveira P a. L, Mello CA. Transient vocal fold lesion and hoarseness associated with the use of ramucirumab: Case report. *Eur Ann Otorhinolaryngol Head Neck Dis*. 2019;136(4):317-319. doi:10.1016/j.anorl.2018.08.017
16. Zamponi V, Mazzilli R, Mazzilli F, Fantini M. Effect of sex hormones on human voice physiology: from childhood to senescence. *Hormones (Athens)*. 2021;20(4):691-696. doi:10.1007/s42000-021-00298-y
17. Chadwick KA, Simpson CB, McGarey PO, Estes CM, Nix J, Sulica L. Voice Change Following Testosterone Supplementation in Women: A Multi-Institutional Case Series. *Journal of Voice*. 2021;35(6):936.e1-936.e7. doi:10.1016/j.jvoice.2020.03.008
18. Berretta M, Taibi R, Bearz A, et al. Dysphonia as an unusual toxic event of oxaliplatin-based chemotherapy. *J Chemother*. 2004;16(6):595-598. doi:10.1179/joc.2004.16.6.595
19. Benfaremo D, Manfredi L, Luchetti MM, Gabrielli A. Musculoskeletal and Rheumatic Diseases Induced by Immune Checkpoint Inhibitors: A Review of the Literature. *Curr Drug Saf*. 2018;13(3):150-164. doi:10.2174/1574886313666180508122332
20. Bruno F, Palmiero RA, Ferrero B, et al. Pembrolizumab-Induced Isolated Cranial Neuropathy: A Rare Case Report and Review of Literature. *Frontiers in Neurology*. 2021;12:575. doi:10.3389/fneur.2021.669493
21. Gavrilă GA, Mihailă RG, Manitiu I. Differential diagnosis problems in a patient with dysphonia and chronic lymphocytic leukemia. *Pak J Med Sci*. 2015;31(1):223-225. doi:10.12669/pjms.311.6091
22. Villari CR, Courey MS. Management of Dysphonia After Radiation Therapy. *Otolaryngol Clin North Am*. 2015;48(4):601-609. doi:10.1016/j.otc.2015.04.006
23. Hamdan AL, Kurban Z, Azar ST. Prevalence of phonatory symptoms in patients with type 2 diabetes mellitus. *Acta Diabetol*. 2013;50(5):731-736. doi:10.1007/s00592-012-0392-3
24. Lechien JR, Saussez S, Harmegnies B, Finck C, Burns JA. Laryngopharyngeal Reflux and Voice Disorders: A Multifactorial Model of Etiology and Pathophysiology. *J Voice*. 2017;31(6):733-752. doi:10.1016/j.jvoice.2017.03.015
25. Ruiz R, Jeswani S, Andrews K, et al. Hoarseness and Laryngopharyngeal Reflux: A Survey of Primary Care Physician Practice Patterns. *JAMA Otolaryngology–Head & Neck Surgery*. 2014;140(3):192-196. doi:10.1001/jamaoto.2013.6533
26. Craig-McQuaide A, Akram H, Zrinzo L, Tripoliti E. A review of brain circuitries involved in stuttering. *Front Hum Neurosci*. 2014;8:884. doi:10.3389/fnhum.2014.00884
27. Ekhardt C, van Hunsel F, van Harten P, van Baarsen J, Yingying T, Bast B. Drug-Induced Stuttering: Occurrence and Possible Pathways. *Front Psychiatry*. 2021;12:692568. doi:10.3389/fpsy.2021.692568
28. Rizwan A, Mor YS, Frank AP. A Case of Steroid-Associated Expressive Aphasia. *Cureus*. 2021;13(10). doi:10.7759/cureus.18863

29. Belin C, Devic P, Ayrignac X, et al. Description of neurotoxicity in a series of patients treated with CAR T-cell therapy. *Sci Rep.* 2020;10(1):18997. doi:10.1038/s41598-020-76055-9
30. Bennett AC, Bennett CL, Witherspoon BJ, Knopf KB. An evaluation of reports of ciprofloxacin, levofloxacin, and moxifloxacin-association neuropsychiatric toxicities, long-term disability, and aortic aneurysms/dissections disseminated by the Food and Drug Administration and the European Medicines Agency. *Expert Opinion on Drug Safety.* 2019;18(11):1055-1063. doi:10.1080/14740338.2019.1665022
31. Carl D, Gröllich C, Hering S, Schabet M. Steroid responsive encephalopathy associated with autoimmune thyroiditis following ipilimumab therapy: a case report. *BMC Res Notes.* 2015;8:316. doi:10.1186/s13104-015-1283-9
32. Higa GM, Wise TC, Crowell EB. Severe, disabling neurologic toxicity following cisplatin retreatment. *Ann Pharmacother.* 1995;29(2):134-137. doi:10.1177/106002809502900206
33. Patel UH, Mir MA, Sivik JK, Raheja D, Pandey MK, Talamo G. Central Neurotoxicity of Immunomodulatory Drugs in Multiple Myeloma. *Hematol Rep.* 2015;7(1):5704. doi:10.4081/hr.2015.5704
34. Chien CF, Huang P, Hsieh SW. Reversible global aphasia as a side effect of quetiapine: a case report and literature review. *Neuropsychiatr Dis Treat.* 2017;13:2257-2260. doi:10.2147/NDT.S141273