

Early Detection of Hearing Impairment Signals Post-mRNA COVID-19 Vaccination: A Disproportionality Analysis Study on French Pharmacovigilance Database

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Supplementary Information

Supplementary table 1: Other vaccines group

ATC class	Commercial name	Vaccine indication
J07AG01	ACT-HIB®	<i>Haemophilus influenzae</i> type b
J07AH09	BEXSERO®	<i>Neisseria meningitidis</i> group B
J07AE01	DUKORAL®	<i>Vibrio cholerae</i> group O1
J07AH07	MENJUGATE®	<i>Neisseria meningitidis</i> group C
J07AH08	MENQUADFI®	<i>Neisseria meningitidis</i> group A, C, W and Y
J07AH08	MENVEO®	<i>Neisseria meningitidis</i> group A, C, W and Y
J07AH07	NEISVAC®	<i>Neisseria meningitidis</i> group C
J07AH08	NIMENRIX®	<i>Neisseria meningitidis</i> group A, C, W and Y
J07AL01	PNEUMOVAX®	<i>Pneumococcus</i> 23 seotypes
J07AL02	PREVENAR®	<i>Pneumococcus</i> 13 seotypes
J07AX	SPIROLEPT®	Leptospirosis
J07AH09	TRUMENBA®	<i>Neisseria meningitidis</i> group B
J07AP03	TYPHERIX®	<i>Salmonella typhi</i>
J07AP03	TYPHIM Vi®	<i>Salmonella typhi</i>
L03AX03	VACCIN BCG®	<i>Mycobacterium tuberculosis</i>
J07AJ52	BOOSTRIX®	Diphtheria, tetanus, pertussis
J07CA02	BOOSTRIX TETRA®	Diphtheria, tetanus, pertussis and poliomyelitis
J07CA09	HEXYON®	Diphtheria, tetanus, pertussis, poliomyelitis, <i>Haemophilus influenzae</i> and hepatitis B
J07CA02	INFANRIX TETRA®	Diphtheria, tetanus, pertussis and poliomyelitis
J07CA06	INFANRIX QUNITA®	Diphtheria, tetanus, pertussis, poliomyelitis and <i>Haemophilus influenzae</i>
J07CA09	INFANRIX HEXA®	Diphtheria, tetanus, pertussis, poliomyelitis, <i>Haemophilus influenzae</i> and hepatitis B
J07CA06	PENTAVAC®	Diphtheria, tetanus, pertussis, poliomyelitis and <i>Haemophilus influenzae</i>
J07CA02	REPEVAX®	Diphtheria, tetanus, pertussis and poliomyelitis
J07CA01	REVAXIS®	Diphtheria, tetanus, pertussis
J07CA02	TETRAVAC-ACELLULAIRE®	Diphtheria, tetanus, pertussis and poliomyelitis
J07CA10	TYAVAX®	<i>Salmonella typhi</i> and hepatitis A
J07CA09	VAXELIS®	Diphtheria, tetanus, pertussis, poliomyelitis, <i>Haemophilus influenzae</i> and hepatitis B
J07BC02	AVAXIM®	Hepatitis A
J07BM02	CERVARIX®	Human papillomavirus type 16 and 18
J07BX	DENG VAXIA®	Dengue fever virus

J07BB02	EFLUELDA®	Influenza
J07BA01	ENCEPUR®	Tick-borne encephalitis
J07BC01	ENGERIX B®	Hepatitis B
J07BB01	FLUARIX®	Influenza
J07BB03	FLUENZ TETRA®	Influenza
J07BM03	GARDASIL®	Human papillomavirus type 6, 11, 16 and 18
J07BC02	HAVRIX®	Hepatitis A
J07BC01	HBVAXPRO®	Hepatitis B
J07BB02	IMMUGRIP®	Influenza
J07BF03	IMOVAX POLIO®	Poliomyelitis
J07BX	IMVANEX®	Smallpox
J07BB02	INFLUSPLIT TETRA®	Influenza
J07BB02	INFLUVAC TETRA®	Influenza
J07BA02	IXIARO®	Japanese encephalitis
J07BD52	M-M-RVAXPRO®	Measles, mumps and rubella
J07BD52	PRIORIX®	Measles, mumps and rubella
J07BG01	RABIPUR®	Rabies
J07BH01	ROTARIX®	Rotavirus
J07BH02	ROTATEQ®	Rotavirus
J07BL01	STAMARIL®	Yellow fever
J07BA01	TICOVAC®	Tick-borne encephalitis
J07BC20	TWINRIX®	Hepatitis A and B
J07BG01	VACCIN RABIQUE PASTEUR®	Rabies
J07BC02	VAQTA®	Hepatitis A
J07BK01	VARILRIX®	Chicken pox
J07BK01	VARIVAX®	Chicken pox
J07BB02	VAXIGRIPTETRA®	Influenza

[Supplementary table 2: PTs of the narrow SMQ "hearing impairment", excluding "tinnitus"](#)

PT code	Preferred term
10000526	Acoustic stimulation tests abnormal
10075083	Altered pitch perception
10003761	Audiogram abnormal
10003778	Auditory disorder
10003789	Auditory recruitment
10048827	Autophony
10004129	Barotitis media
10070723	Bone anchored hearing aid implantation
10009830	Cochlea implant
10010280	Conductive deafness
10011878	Deafness
10052556	Deafness bilateral
10011891	Deafness neurosensory
10011893	Deafness occupational

10011894	Deafness permanent
10011900	Deafness transitory
10048812	Deafness unilateral
10013032	Diplacusis
10049712	Dysacusis
10014399	Electrocochleogram abnormal
10061462	Eustachian tube disorder
10015543	Eustachian tube dysfunction
10015544	Eustachian tube obstruction
10063013	Haematotympanum
10075385	Hearing aid therapy
10020559	Hyperacusis
10048865	Hypoacusis
10027582	Middle ear adhesions
10062545	Middle ear effusion
10065838	Middle ear inflammation
10079388	Misophonia
10027757	Mixed deafness
10061302	Myringitis
10080897	Neonatal deafness
10080902	Neonatal hypoacusis
10067587	Neurosensory hypoacusis
10078830	Noninfective myringitis
10061327	Ossicle disorder
10063643	Otoacoustic emissions test abnormal
10033102	Otosalpingitis
10033103	Otosclerosis
10033109	Ototoxicity
10085733	Paracusis
10036626	Presbycusis
10039191	Rinne tuning fork test abnormal
10061373	Sudden hearing loss
10084652	Tinnitus retraining therapy
10045208	Tympanic membrane atrophic
10062218	Tympanic membrane disorder
10045210	Tympanic membrane perforation
10063604	Tympanic membrane scarring
10045215	Tympanometry abnormal
10045218	Tympanosclerosis
10047878	Weber tuning fork test abnormal

[Supplementary table 3: Ototoxic drugs used to adjust the disproportionality analysis](#)

Code ATC	INN
J01GB06	amikacin
J01GB07	netilmicin

J01GB01	tobramycin
J01FA10	azithromycin
J01FA09	clarithromycin
J01FA01	erythromycin
J01XA02	teicoplanin
A07AA09, J01XA01	vancomycin
S01AA15	streptomycin
A01AB04, A07AA07, G01AA03, J02AA01	amphotericin
P01BC02	mefloquine
P01BC01	quinine
L01CB01	etoposide
L01CA01	vinblastine
L01CA02	vincristine
L01CA03	vindesine
L01CA04	vinorelbine
L01XA02	carboplatin
L01XA01	cisplatin
L01XA03	oxaliplatin
QJ01GB03	gentamicin
QA07AA01	neomycin

[Supplementary table 4: PTs reported in more than 5% of mRNA vaccines notifications](#)

PT code	Preferred term
10022004	Influenza-like illness
10003549	Asthenia
10019211	Headache
10068879	Vaccination site pain
10025197	Lymphadenopathy

[Supplementary table 5: PTs reported in more than 2.5% of mRNA vaccines notifications](#)

PT code	Preferred term
10022004	Influenza-like illness
10003549	Asthenia
10019211	Headache
10068879	Vaccination site pain
10025197	Lymphadenopathy
10003239	Arthralgia
10012735	Diarrhoea
10033425	Pain in extremity
10037660	Pyrexia
10028411	Myalgia
10028813	Nausea
10033775	Paraesthesia
10021432	Immunisation reaction
10027327	Menstrual disorder
10019974	Herpes zoster

[Supplementary table 6: Selection of PTs from the SMQ "hearing impairment"](#)

PT code	Preferred term
10000526	Acoustic stimulation tests abnormal
10003761	Audiogram abnormal
10003778	Auditory disorder
10078794	Auditory nerve disorder
10010280	Conductive deafness
10011878	Deafness
10052556	Deafness bilateral
10011891	Deafness neurosensory
10011894	Deafness permanent
10011900	Deafness transitory
10048812	Deafness unilateral
10013032	Diplacusis
10049712	Dysacusis
10014399	Electrocochleogram abnormal
10015544	Eustachian tube obstruction
10063013	Haematotympanum
10048865	Hypoacusis
10061290	Middle ear disorder
10062545	Middle ear effusion
10065838	Middle ear inflammation
10027757	Mixed deafness
10067587	Neurosensory hypoacusis
10078830	Noninfective myringitis
10033109	Ototoxicity
10085733	Paracusis
10036626	Presbycusis
10039191	Rinne tuning fork test abnormal
10061373	Sudden hearing loss
10062218	Tympanic membrane disorder
10062177	VIIIth nerve lesion
10047878	Weber tuning fork test abnormal

[Supplementary table 7: Modified Siegel's criteria for hearing loss \(HL\) grades](#)

Level of HL	HL range (dB)
Grade 1	≤25
Grade 2	26-40
Grade 3	41-70
Grade 4	71-90
Grade 5	>90

Supplementary table 8: ROR for hearing impairment performed monthly during 2021, at the end of each month

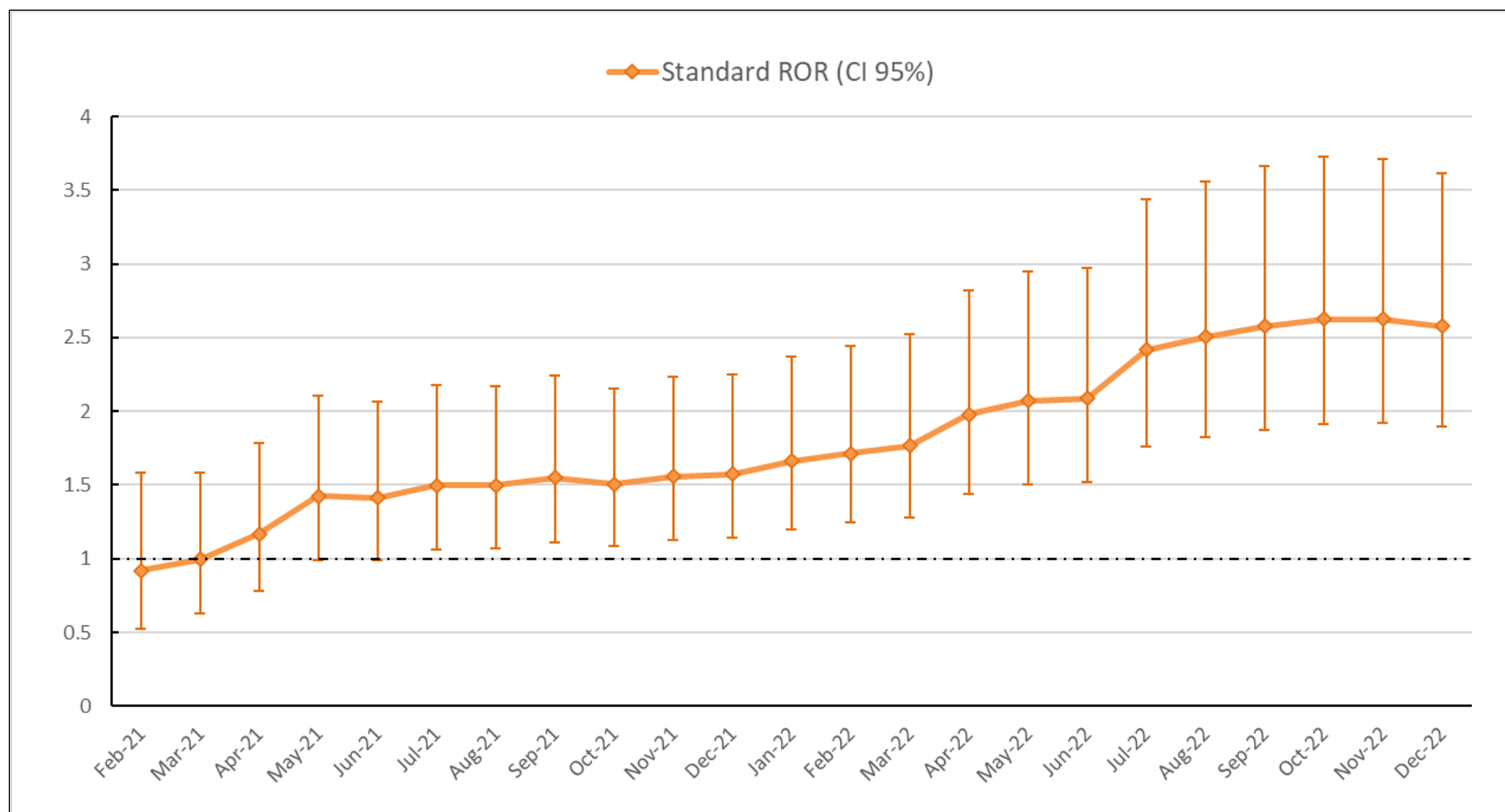
	ROR (IC 95%)										
	Feb-21	Mar-21	Apr-21	May-21	Jun-21	Jul-21	Aug-21	Sep-21	Oct-21	Nov-21	Dec-21
Standard method	0.92 (0.52 - 1.58)	1.00 (0.63 - 1.58)	1.17 (0.78 - 1.79)	1.42 (0.99 - 2.11)	1.41 (0.99 - 2.07)	1.50 (1.06 - 2.18)	1.50 (1.07 - 2.17)	1.55 (1.11 - 2.24)	1.50 (1.08 - 2.16)	1.56 (1.12 - 2.23)	1.58 (1.14 - 2.25)
Adjusted *	1.32 (0.63 - 2.89)	1.70 (0.88 - 3.45)	1.70 (0.94 - 3.23)	1.83 (1.09 - 3.23)	2.06 (1.26 - 3.56)	2.26 (1.41 - 3.80)	2.28 (1.45 - 3.78)	2.55 (1.63 - 4.22)	2.44 (1.58 - 3.99)	2.46 (1.60 - 0.86)	2.48 (1.62 - 4.02)
Exclusion of RRPT5	1.40 (0.79 - 2.41)	1.47 (0.93 - 2.33)	1.61 (1.07 - 2.47)	1.88 (1.30 - 2.79)	1.84 (1.29 - 2.69)	1.93 (1.37 - 2.81)	1.89 (1.35 - 2.74)	1.94 (1.39 - 2.80)	1.84 (1.32 - 2.64)	1.88 (1.36 - 2.69)	1.88 (1.35 - 2.68)
Adjusted * and exclusion of RRPT5	2.03 (0.96 - 4.52)	2.67 (1.36 - 5.56)	2.54 (1.38 - 4.92)	2.54 (1.50 - 4.52)	2.74 (1.67 - 4.74)	2.95 (1.84 - 4.97)	2.83 (1.80 - 4.69)	3.11 (1.99 - 5.14)	2.91 (1.89 - 4.74)	2.89 (1.88 - 4.69)	2.88 (1.88 - 4.66)
Exclusion of RRPT2.5	1.71 (0.97 - 2.95)	1.74 (1.10 - 2.76)	1.83 (1.22 - 2.80)	2.10 (1.46 - 3.11)	2.02 (1.42 - 2.96)	2.10 (1.49 - 3.06)	2.04 (1.45 - 2.95)	2.06 (1.48 - 2.98)	1.92 (1.39 - 2.76)	1.99 (1.43 - 2.84)	2.00 (1.45 - 2.87)
Exclusion of RRPT10	1.06 (0.60 - 1.83)	1.18 (0.75 - 1.87)	1.37 (0.91 - 2.09)	1.66 (1.15 - 2.46)	1.64 (1.15 - 2.40)	1.74 (1.23 - 2.53)	1.72 (1.23 - 2.50)	1.78 (1.27 - 2.57)	1.71 (1.23 - 2.45)	1.76 (1.27 - 2.51)	1.76 (1.27 - 2.52)
Standard method excluding missing values	0.91 (0.52 - 1.57)	0.99 (0.63 - 1.57)	1.16 (0.77 - 1.77)	1.41 (0.98 - 2.09)	1.40 (0.98 - 2.05)	1.48 (1.05 - 2.16)	1.48 (1.06 - 2.15)	1.54 (1.10 - 2.22)	1.49 (1.07 - 2.14)	1.54 (1.11 - 2.21)	1.56 (1.13 - 2.23)

* Adjusted for age sex and concomitant ototoxic drugs

Supplementary table 9: Number of cases and non-cases considered for each disproportionality analysis.

		Feb-21	Mar-21	Apr-21	May-21	Jun-21	Jul-21	Aug-21	Sep-21	Oct-21	Nov-21	Dec-21
Standard and adjusted* method	IR cases	20	39	63	116	162	215	267	319	352	391	432
	RR cases	8 537	15 061	20 835	31 689	44 946	56 660	70 660	81 971	91 196	98 777	109 008
	IR non-cases	34	35	35	35	35	35	35	35	36	36	36
	RR non-cases	13 351	13 469	13 537	13 622	13 719	13 818	13 883	13 953	14 035	14 173	14 314
Exclusion of RRPT10	IR cases	20	39	63	116	162	215	267	319	352	391	432
	RR cases	7 245	12 514	17 466	26 703	37 980	47 897	60 271	70 182	78 778	85 902	95 497
	IR non-cases	34	35	35	35	35	35	35	35	36	36	36
	RR non-cases	13 117	13 232	13 297	13 375	13 466	13 560	13 623	13 687	13 763	13 887	14 018
Exclusion of RRPT5	IR cases	20	39	63	116	162	215	267	319	352	391	432
	RR cases	4 708	8 584	12 685	20 147	29 033	36 854	47 041	55 130	62 656	68 816	76 948
	IR non-cases	34	35	35	35	35	35	35	35	36	36	36
	RR non-cases	11 211	11 313	11 373	11 442	11 524	11 608	11 668	11 725	11 795	11 909	12 024
Exclusion of RRPT2.5	IR cases	20	39	63	116	162	215	267	319	352	391	432
	RR cases	2 817	5 287	8 184	13 203	19 334	24 837	31 991	37 916	43 876	47 678	52 695
	IR non-cases	34	35	35	35	35	35	35	35	36	36	36
	RR non-cases	8 196	8 269	8 320	8 376	8 438	8 497	8 542	8 585	8 638	8 719	8 798

* Adjusted for age sex and concomitant ototoxic drugs, IR = index reports, RR = reference reports.



[Supplementary Figure 1: Trends in the standard ROR for hearing impairment performed monthly from February 2021 to December 2022](#)

ROR = Reported Odd Ratio, CI 95% = 95% confidence interval.