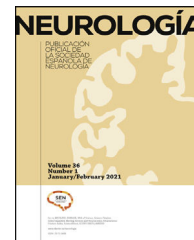




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## REVIEW ARTICLE

# Incidence of Bell's palsy after coronavirus disease (COVID-19) vaccination: a systematic review and meta-analysis

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### KEYWORDS

Bell palsy;  
Incidence;  
COVID-19 vaccines

### Resumen

**Objetivo:** Estimar la incidencia agrupada de la parálisis de Bell después de la vacunación contra el COVID-19.

**Métodos:** Realizamos búsquedas sistemáticas (dos investigadores independientes) en PubMed, Scopus, EMBASE, Web of Science y Google Scholar. También se realizaron búsquedas en la literatura gris, incluidas las referencias de las referencias y los resúmenes de congresos. Extrajimos datos sobre el número total de participantes, el primer autor, el año de publicación, el país de origen, femenino/masculino, el tipo de vacunas y el número de pacientes que desarrollaron parálisis de Bell después de la vacunación contra el COVID-19.

**Resultados:** La búsqueda bibliográfica reveló 370 artículos, eliminando posteriormente los duplicados que quedaban 227. Después de una cuidadosa evaluación de los textos completos, quedaron veinte artículos para el metanálisis. Las vacunas más comúnmente administradas fueron Pfizer seguida de Moderna.

En total, 4,54e+07 personas recibieron vacunas contra la COVID-19 y 1739 casos desarrollaron parálisis de Bell. En nueve estudios, se inscribieron controles (individuos sin vacunación). El número total de controles fue de 1809069, de los cuales 203 desarrollaron parálisis de Bell. La incidencia de la parálisis de Bell después de las vacunas COVID-19 fue ignorable. La probabilidad de desarrollar parálisis de Bell después de las vacunas contra la COVID-19 fue de 1,02 (IC 95 %: 0,79-1,32) (I<sup>2</sup> = 74,8 %, p < 0,001).

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## PALABRAS CLAVE

Parálisis de Bell;  
Incidencia;  
Vacunas COVID-19

**Conclusión:** los resultados de esta revisión sistemática y metanálisis muestran que la incidencia de parálisis facial periférica después de la vacunación contra el COVID-19 es despreciable y que la vacunación no aumenta el riesgo de desarrollar parálisis de Bell. Tal vez, la parálisis de Bell es un síntoma de presentación de una forma más grave de COVID-19, por lo que los médicos deben ser conscientes de esto.

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## Incidencia de la parálisis de Bell después de la vacunación contra la COVID-19: una revisión sistemática y un metanálisis

### Abstract

**Objective:** To estimate the pooled incidence of Bell's palsy after COVID-19 vaccination.

**Methods:** PubMed, Scopus, EMBASE, Web of Science, and Google Scholar were searched by 2 independent researchers. We also searched the grey literature including references of the references and conference abstracts. We extracted data regarding the total number of participants, first author, publication year, the country of origin, sex, type of vaccines, and the number of patients who developed Bell's palsy after COVID-19 vaccination.

**Results:** The literature search revealed 370 articles, subsequently deleting duplicates 227 remained. After careful evaluation of the full texts, 20 articles remained for meta-analysis. The most commonly administered vaccines were Pfizer followed by Moderna.

In total, 4.54e+07 individuals received vaccines against COVID-19, and 1739 cases developed Bell's palsy. In nine studies, controls (individuals without vaccination) were enrolled. The total number of controls was 1 809 069, of whom 203 developed Bell's palsy. The incidence of Bell's palsy after COVID-19 vaccines was ignorable. The odds of developing Bell's palsy after COVID-19 vaccines was 1.02 (95% CI: 0.79-1.32) ( $I^2 = 74.8\%$ ,  $P < .001$ ).

**Conclusion:** The results of this systematic review and meta-analysis show that the incidence of peripheral facial palsy after COVID-19 vaccination is ignorable and vaccination does not increase the risk of developing Bell's palsy. Maybe, Bell's palsy is a presenting symptom of a more severe form of COVID-19, so clinicians must be aware of this.

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## Introduction

In December 2019, a new coronavirus was detected in Wuhan, China which spread rapidly all over the world.<sup>1</sup> It is in the pandemic stage and different vaccines have been developed to stop the pandemic.<sup>2</sup> The European Medicines Agency, the US Food and Drug Administration, and the UK Medicines and Healthcare products Regulatory Agency have approved various types of vaccines since December 2020.<sup>2</sup> Each vaccine has its safety and efficacy profiles which raises the necessity for careful evaluation. The side effects have a wide range from injection site pain (swelling) to extreme reactions such as anaphylaxis.<sup>3,4</sup> Neurological complications have been reported after COVID-19 vaccination including Guillain-Barré syndrome (GBS), neuromyelitis optica spectrum disorders (NMOSD), transverse myelitis, multiple sclerosis (MS), thrombosis with thrombocytopenia syndrome, and Bell's palsy.<sup>5-10</sup>

Bell's palsy is acute peripheral facial nerve with unknown aetiology and sudden onset of unilateral peripheral facial paralysis.<sup>10</sup> It is transient and more than half of the affected patients recover within 6 months without treatment.<sup>11</sup> The

relationship between vaccination and incidence of Bell's palsy is unclear while mimicry of host molecules by the vaccinal antigen could be the possible explanation.<sup>12</sup> Up to now, different studies reported various incidence rates of Bell's palsy after vaccination with different vaccines.<sup>13-16</sup> So, we designed this systematic review and meta-analysis to estimate the pooled incidence of Bell's palsy after COVID-19 vaccination.

## Methods

PubMed, Scopus, EMBASE, Web of Science, and Google Scholar were searched by 2 independent researchers. We also searched the grey literature including references of the references and conference abstracts by 10th February 2022.

After deleting duplicates, we screened the titles and abstracts of the potential studies and in the case of discrepancy, they asked the third one to solve the disagreement.

Then the full texts of the remained studies were assessed and the data were extracted. The extracted data were

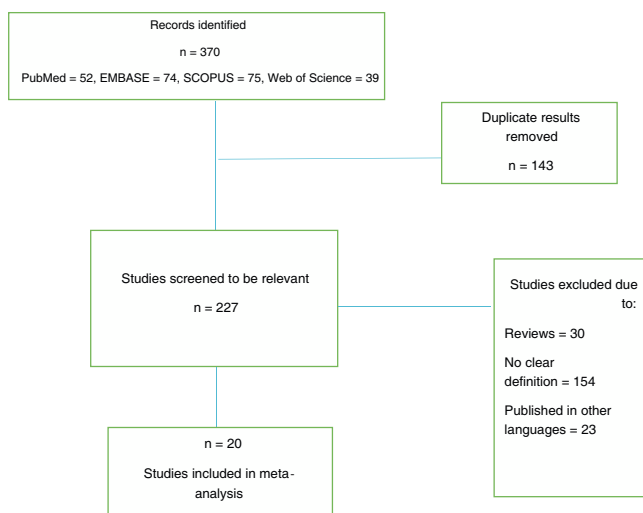


Figure 1 Flow diagram of including studies.

entered in a datasheet and the third one checked the data of two sources.

We extracted data regarding the total number of participants, first author, publication year, the country of origin, sex, type of vaccines, and the number of patients who developed Bell's palsy after COVID-19 vaccination.

The MeSH terms which were used for searching in the PubMed are attached in a supplementary file.

Inclusion criteria were: retrospective/prospective cohort studies which reported incidence of facial palsy after vaccination, articles published in English.

Exclusion criteria were: Letters to the editor, case-control, case reports, and cross-sectional studies which had no clear data.

Risk of bias assessment: Newcastle-Ottawa Scale (NOS) (adapted for cohort studies).<sup>17</sup>

## Statistical analysis

All statistical analyses were performed using STATA (Version 14.0; Stata Corp LP, College Station, TX, USA).

To determine heterogeneity, inconsistency ( $I^2$ ) was calculated.

We used random-effects model for meta-analysis as the heterogeneity between study results ( $I^2$ ) was more than 50%.

## Results

The literature search revealed 370 articles, subsequently after deleting duplicates 227 remained. After careful evaluation of the full texts, 20 articles remained for meta-analysis (Fig. 1).

The most commonly administered vaccines were Pfizer (in 16 studies [80%]) followed by Moderna (4 [25%]).

In total,  $4.54e+07$  individuals received vaccines against COVID-19, and 1739 cases developed Bell's palsy

Totally  $1.79e+07$  patients received Pfizer vaccines and 429 cases developed Bell's palsy. In 12 studies, it was determined the dose of the vaccines (first or second). In 9 studies,

controls (individuals without vaccination) were enrolled. The total number of controls was 1 809 069, of whom 203 developed Bell's palsy. The quality assessment scores of included studies ranged between 6 and 8 (Table 1).

The incidence of Bell's palsy after COVID-19 vaccines was ignorable (Fig. 2).

The odds of developing Bell's palsy after COVID-19 vaccines was 1.02 (95% CI: 0.79-1.32) ( $I^2 = 74.8\%$ ,  $P < 0.001$ ) (Fig. 3) (only 9 studies had controls).

**Table 1** Basic characteristics of included studies.

Author/ year/ country	All vac	Male/ female/ unknown All vac	Vac type/ dose	Bell's palsy vac	Male/female Bell's palsy	Vac type/ dose Bell's palsy	All controls	Controls Bell's palsy	NOS score
Barbara H. Bardenheier/2021/ USA <sup>18</sup>	8275	Unknown	Pf = 5842  Mod = 2433	1	1/0	Pf : 1  1st = 1 2nd = 0 Mod = 0	11 072	0	8
Joshua TC Tan/2021/ Singapore <sup>15</sup>	64 661	59 574/4929/ 158	Pf : 37 367  1st = 37 367 2nd = 37 162 Mod : 27 294 1st = 27 294 2nd = 25 258	1	1/0	Pf : 1  1st = 1 2nd = 0 Mod : 0			7
Rana Shibli/2021/ Israel <sup>19</sup>	2 594 990	1 256 958/1 338 032	Pf  1st = 2 594 990 2nd = 2 434 674	284	153/131	Pf  1st = 132 2nd = 152			7
Filippos Filippatos/2021/ Greece <sup>20</sup>	502	393/109	Pf  2nd	1	1/0	Pf  1st = 0 2nd = 1			6
Eric Yuk Fai Wan/2022/ Hong Kong <sup>10</sup>	989 144	Unknown	Pf : 537 205  1st = 537 205 2nd = 247 957 CoronaVac : 451 939 1nd = 451 939 2nd = 324 632	44	29/15	Pf : 16  1st = 8 2nd = 8 CoronaVac : 28 1st = 19 2nd = 9			7
G. Gómez de Terreros Caro/ 2021/Spain <sup>21</sup>	877	Unknown	Pf  2nd	1	1/0	Pf  1st = 1 2nd = 0			6
H.M. El Sahly/2021/USA <sup>22</sup>	15 180	7917/7263	Mod	8		Mod  1st = 0	15 166	3	8

Table 1 (Continued)

Author/ year/ country	All vac	Male/ female/ unknown All vac	Vac type/ dose	Bell's palsy vac	Male/female Bell's palsy	Vac type/ dose Bell's palsy	All controls	Controls Bell's palsy	NOS score
Jasmine Shimin Koh/ 2021/Singapore <sup>14</sup>	1 398 074	761 950/636 124	Pf : 1 212 130  Mod : 185 944 1st = 1 398 074 2nd = 915 344	11	5/6	2nd = 8 Pf = 11  Mod = 0 1st = 6 2nd = 5 Pf			7
Nagla A El- Shitany/2021/Saudi Arabia <sup>23</sup>	455	163/292	Pf  1st = 203 2nd = 252	3		Pf  1st = 3 2nd = 0			7
Francisco Tsz Tsun Lai/2022/ Hong Kong <sup>24</sup>	335 620	161 467/174 153	Pf : 153 178  CoronaVac : 182 442 1st	13		Pf : 4  1st = 4 2nd = 0 CoronaVac: 9 1st = 9 2nd = 0 Pf : 250	547 796	24	8
Martina Patone/2021/UK <sup>25</sup>	32 552 534	14 219 053/16 759 298/1 574 183	Pf : 12 134 782  AZD : 20 417 752 1st	685	319/366	Pf : 250  1st = 250 2nd = 0 AZD : 435 1st = 435 2nd = 0 Pf : 22			7
Reid McMurry/2021/ USA <sup>26</sup>	68 266	28 408/39 857/1	Pf : 51 795  1st = 51 795 2nd = 39 058 Mod : 16 471 1st = 16 471 2nd = 11 851	26		Pf : 22  1st = 14 2nd = 8 Mod : 4 1st = 2 2nd = 2 Pf	68 266	75	8
David Shasha/2022/ Israel <sup>27</sup>	231 159	114 634/118 525	Pf	31		Pf	233 159	36	8

Table 1 (Continued)

Author/ year/ country	All vac	Male/ female/ unknown All vac	Vac type/ dose	Bell's palsy vac	Male/female Bell's palsy	Vac type/ dose Bell's palsy	All controls	Controls Bell's palsy	NOS score
Youn Young Choi/2021/Korea <sup>28</sup>	638	283/355	1st = 233 159 2nd = 131 033 Pf	1	1/0	1st = 23 2nd = 8 Pf			6
Noam Barda/2021/Israel <sup>29</sup>	884 828	461 590/423 238	Pf	81		1st = 1 2nd = 0 Pf	884 828	59	8
Nicola P. Klein/2021/USA <sup>30</sup>	6 175 813	2 830 791/33 45 022	Pf : 3 539 611	535		mRNA(Pf/Mod)			7
Merryn Voysey/2021/ Multicentre <sup>16</sup>	12 021	Unknown.	1st = 3 539 611 2nd = 3 214 737 Mod : 2 636 202 1st = 2 636 202 2nd = 2 454 578 AZD	3			11 724	3	8
J. Sadoff/2021/ Multicentre	21 895	12 071/9820/4	J&J	3		J&J	21 888	2	8
Fernando P. Polack/ 2020/Multicentre <sup>3</sup>	18 860	9639/9221	Single dose Pf	4		Pf			7
L.R. Baden/2021/USA <sup>13</sup>	15 181	7923/7258	1st = 18 860 2nd = 18 556 Mod 1st = 15 181 2nd = 14 711	3		Mod	15 170	1	8

Pf = Pfizer, Mod = Moderna, AZD = AstraZeneca.

UK: United Kingdom.

The incidence of Bell's palsy after COVID-19 vaccines was ignorable (Fig. 2).

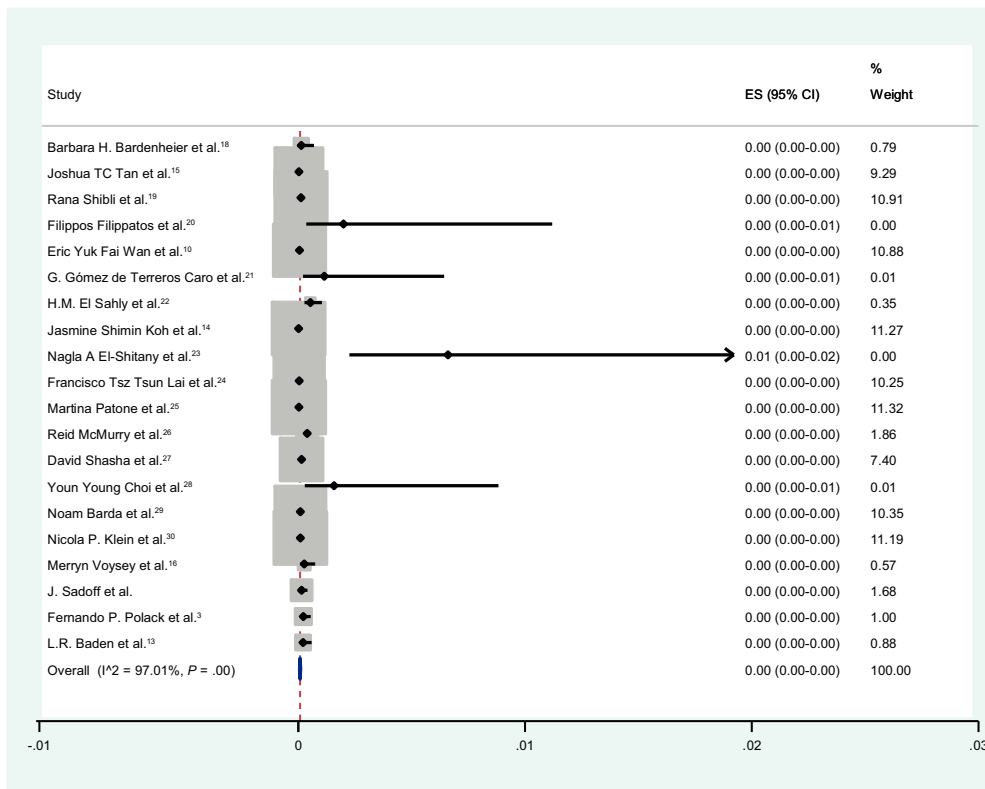


Figure 2 The incidence of Bell's palsy after COVID-19 vaccines.

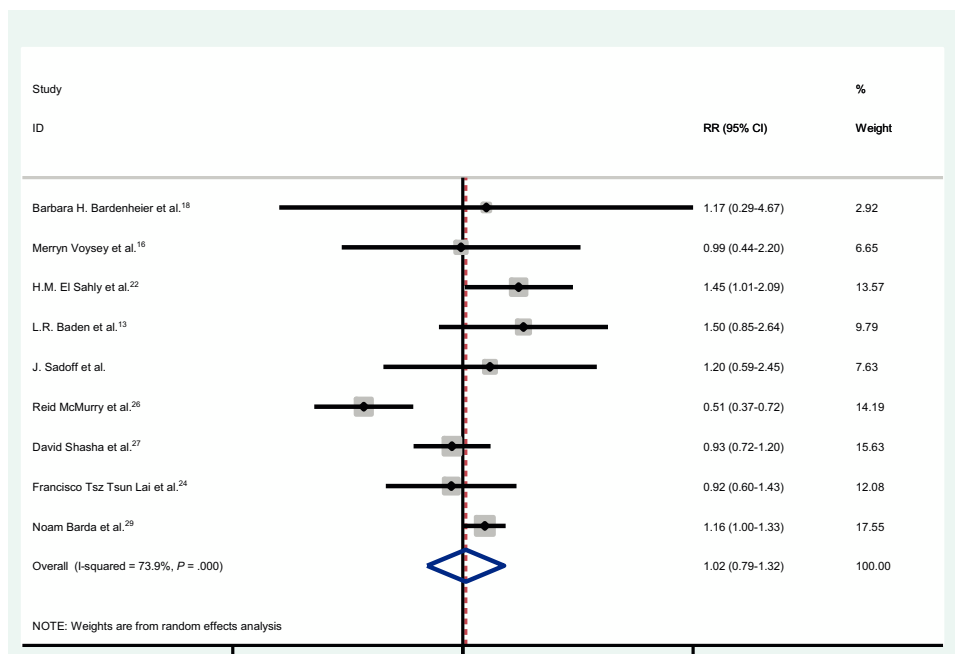


Figure 3 The odds of developing Bell's palsy after COVID-19 vaccines.

## Discussion

To our knowledge, this is the first systematic review and meta-analysis estimating the pooled incidence of Bell's palsy after COVID-19 vaccines. The results show that the pooled incidence is ignorable and administration of the COVID-19 vaccines does not increase the risk of developing Bell's palsy.

In a multi-centric study in the USA which was conducted by Baden et al.,<sup>13</sup> 15 181 individuals who received Moderna vaccine and 15 170 controls were evaluated. Their results show that 3 individuals in the vaccinated group and one in the control group developed Bell's palsy.<sup>13</sup> The odds of developing Bell's palsy in their study was 1.5, which was not significant (95% CI: 0.85-2.6).

McMurry et al.<sup>26</sup> enrolled 68 266 vaccinated individuals and 68 266 controls. In their study, the incidence of Bell's palsy was higher among controls which suggested that administration of COVID-19 vaccines decreases the risk of Bell's palsy (OR = 0.51, 95% CI: 0.37-0.72).<sup>26</sup>

In another large study which was conducted in Israel, Barda et al.<sup>29</sup> recruited 884 828 vaccinated and the same number of controls. The incidence of Bell's palsy was higher in the vaccinated group while there was no significant association between Bell's palsy and COVID-19 vaccination.<sup>29</sup>

Association between vaccination and Bell's palsy occurrence had been reported previously. Strong associations were reported between the intranasal inactivated influenza vaccine and also influenza H1N1 monovalent vaccine.<sup>31,32</sup> The aetiology of Bell's palsy after vaccination is not fully understood while there are some hypotheses that re-activation of a herpes virus infection, mimicry of host molecules, or activation of dormant auto-reactive T cells play a role.<sup>12</sup> As the results of this systematic review show, there is no association between COVID-19 vaccination and Bell's palsy.

A new study shows that the incidence of neurological adverse effects after COVID-19 infection is higher than rates of neurological complications after vaccination, besides serious neurological adverse effects are rare.<sup>33</sup>

In all included studies in this systematic review, Pfizer, Moderna, and AstraZeneca vaccines were used. Pfizer and Moderna are mRNA vaccines while the Oxford-AstraZeneca vaccine is an adenoviral (ChAdOx1) vector-based COVID-19 vaccine with a wide range of complications including thrombosis with thrombocytopenia syndrome, transverse myelitis, Guillain-Barré syndrome, etc.<sup>34-36</sup> In only two included studies AstraZeneca was administered which showed no significant association between vaccination and Bell's palsy.

This study had some strengths. First, it is the first systematic review and meta-analysis in this field. Second, we estimated the odds of developing Bell's palsy after vaccination.

## Conclusion

The results of this systematic review and meta-analysis show that the incidence of peripheral facial palsy after COVID-19 vaccination is ignorable and vaccination does not increase

the risk of developing Bell's palsy. Maybe, Bell's palsy is a presenting symptom of a more severe form of COVID-19, so clinicians must be aware of this.

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