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Incidence rates of adverse events of special interest: Guillain-Barré syndrome and Bell's palsy

Report for IMRD UK database (United Kingdom)

Details	
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Executive summary	To support the assessment of suspected adverse reactions following vaccination for COVID-19, there is a need to identify background incidence rates for events of interest. To test the ability of inhouse datasets held at the European Medicines Agency to generate such background rates, a feasibility study was done to see if useful, accurate results could be generated within a short timeframe. As an exemplar, the IMRD-UK database was used to calculate the incidence rate of Guillain-Barré syndrome and Bell's palsy, using a methodology similar to that employed by the ACCESS consortium. For Guillain-Barré syndrome, there was an overall incidence rate of 1.54 (95% CI 1.30-1.82) per 100,000 person-years, peaking in the 60-69 years age group and higher for males than females. This result compares favourably with those reported elsewhere. For Bell's palsy, there was an overall incidence of 29.1 (95% CI 28.0-30.3) per 100,000 person-years. This increased with age, peaking at 50-59 years, and was broadly similar between sexes. Again, this result compares favourably with those reported elsewhere.
Lay summary	The roll out of vaccines for COVID-19 is being done on an unprecedented scale but with limited previous experience of their use in the general population. A key role for medicines regulators over the coming months will be to monitor and assess the safety of such vaccines. The use of "spontaneous" reporting systems, whereby healthcare professionals and patients report potentially harmful effects following the use of COVID-19 vaccines, will be a key means

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	of assessing their safety. When assessing such reports, it can be difficult to understand whether harms are caused by use of a vaccine or whether they occur coincidentally for reasons that are not related to the vaccination. To support regulators in their assessment of suspected harmful effects, there is a need to understand how often such harms occur in the generally population under normal conditions. This study describes how commonly Guillain-Barré syndrome (a rare but potentially serious inflammatory disease of the nervous system) and Bell's palsy (a more common condition that causes weakness in the muscles on one side of the face) occur in the general population. In doing so, this study will allow regulators to assess whether illnesses that are reported following the use of COVID-19 vaccines are likely to have arisen by chance or whether they need further investigation as a potentially harmful effects of the vaccine.
Acknowledgment	IQVIA Medical Research Data (IMRD) incorporates data from THIN, A Cegedim Database. Reference made to THIN is intended to be descriptive of the data asset licensed by IQVIA.

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1. Rationale and background

Background rates of adverse events of special interest (AESIs) are of importance in order to be able to determine if an event rate in patients with a certain drug exposure is higher than expected in the general, non-exposed population. Such background rates can then serve as comparative data when reports of suspected adverse reactions are reviewed, for example in the case of immune-mediated or neurologic events for COVID-19 vaccines.

This study assesses the feasibility of generating background rates of events of interest in the IMRD UK (formerly known as THIN) database, using two AESIs as a case study: Guillain-Barré syndrome (GBS) and Bell's palsy. The present study has obtained event rates for Guillain-Barré syndrome and Bell's paresis using similar methods as in the ACCESS protocol [1-3]. Results from this study are compared to results from ACCESS and from the ADVANCE project [4, 5], which published incidence rates of autoimmune diseases in European healthcare databases [5] between 2003 and 2014. This study also serves as a pilot to define a process for rapid generation of background rates should data be promptly required to address potential safety concerns emerging from the COVId-19 vaccination campaigns.

2. Research question and objectives

This study has addressed the following objectives:

1. To obtain yearly incidence rates for Guillain-Barré syndrome and Bell's palsy between 2017 and 2019 as pre-COVID-19 event rates in the UK;
2. To stratify the incidence rates for Guillain-Barré syndrome and Bell's palsy between 2017 and 2019 in the UK by year, gender and age group.

3. Research Methods

3.1. Study Design

A cohort of patients registered with GP practices with a minimum observation time of 365 days was established. For each year of the study, patient time denominators were then established. For this feasibility assessment, patients were required to have a minimum observation time of 365 days prior to the start of each yearly period in order to establish whether events were incident (first-ever) cases. For both Guillain-Barré syndrome and Bell's palsy, patients were excluded from the analysis if they had any prior history of the condition (or related conditions) on the database. In this cohort, patient follow-up time within each yearly time period was established with a minimum of one and a maximum of 365 follow-up days. The numerator consisted of patients with no history of the event that experienced the event during the yearly time period. The first recorded event date during the yearly time period was captured in these patients. Patient follow-up time was truncated at the occurrence of the first event. For each endpoint, a "narrow" and "broad" case definition was defined, to reflect the uncertainly of diagnostic coding.

3.2. Study period

The study period was between 2017 and 2019.

3.3. Setting

The study population consisted of patients registered with GPs in the UK who contributed to the IMRD UK databases from 2017 to 2019, who had at least 365 days of observation prior to start of the yearly period and were observable during at least one of day of 2017, 2018 or 2019.

3.4. Variables

Results are stratified by year, quarter (Q1: 01Jan-31Mar; Q2: 01Apr-30Jun; Q3: 01Jul-30Sep; Q4: 01Oct-31Dec), sex and age group (0-19 years, 20-29 years, 30-39 years, 40-49 years, 50-59 years, 60-69 years, 70-79 years & ≥80 years).

3.4.1. Outcomes

- Bell's palsy, narrow definition:

Read codes used for endpoint definition	Read codes use for establishing baseline history
F310.00 Bell's (facial) palsy	1476.00 H/O: Bell's palsy 2BR6.00 O/E -cranial nerve 7-palsy-LMN 2BR7.00 O/E -cranial 7 -paralysis -LMN F31..00 Facial nerve disorders F310.00 Bell's (facial) palsy F31y.00 Other facial nerve disorders F31yz00 Other facial nerve disorder NOS

- Bell's palsy, broad definition:

Read codes used for endpoint definition	Read codes use for establishing baseline history
2BR6.00 O/E -cranial nerve 7-palsy-LMN 2BR7.00 O/E -cranial 7 -paralysis -LMN F31..00 Facial nerve disorders F310.00 Bell's (facial) palsy F31y.00 Other facial nerve disorders F31yz00 Other facial nerve disorder NOS	1476.00 H/O: Bell's palsy 2BR6.00 O/E -cranial nerve 7-palsy-LMN 2BR7.00 O/E -cranial 7 -paralysis -LMN F31..00 Facial nerve disorders F310.00 Bell's (facial) palsy F31y.00 Other facial nerve disorders F31yz00 Other facial nerve disorder NOS

- Guillain-Barré syndrome, narrow definition:

Read codes used for endpoint definition	Read codes use for establishing baseline history
F370000 Guillain-Barré syndrome F370200 Miller-Fisher syndrome	F370.00 Acute infective polyneuritis F370000 Guillain-Barré syndrome F370100 Postinfectious polyneuritis F370200 Miller-Fisher syndrome F370z00 Acute infective polyneuritis NOS

- Guillain-Barré syndrome, broad definition:

Read codes used for endpoint definition	Read codes use for establishing baseline history
F370.00 Acute infective polyneuritis	F370.00 Acute infective polyneuritis
F370000 Guillain-Barré syndrome	F370000 Guillain-Barré syndrome
F370100 Postinfectious polyneuritis	F370100 Postinfectious polyneuritis
F370200 Miller-Fisher syndrome	F370200 Miller-Fisher syndrome
F370z00 Acute infective polyneuritis NOS	F370z00 Acute infective polyneuritis NOS

3.4.2. Denominators

The population eligible for the study consisted of all patients registered with an IMRD-UK GP for a duration of one-year or more. Patients were followed from the latest of date of registration, Acceptable Mortality Reporting (AMR) date or date of practice computerisation, and followed until the earliest of transfer out date, date of death or date of last data collection (January 2020). Patient with a history of Bell's Palsy or Guillain-Barré syndrome (or with closely related diagnoses) at baseline were excluded (see section 3.4.1. for details of codes used).

3.5. Database

This study used IMRD UK version January 2020 (formally known as THIN). In the United Kingdom, GPs play a gatekeeper role in the healthcare system, as they are responsible for delivering primary health care and specialist referrals. Over 98% of the UK-resident population is registered with a GP, so that GP patient records are broadly representative of the UK population in general. Patients are affiliated to a practice, which centralizes the medical information from GPs, specialist referrals, hospitalizations, and tests. IMRD-UK contains longitudinal electronic patient records extracted from the VISION practice management software, which has been contributed to by > 790 general practices across the United Kingdom covering up to 6% of the UK population. Data are largely representative of the UK population in terms of age, sex, deprivation status, and geographic distribution. It contains GP prescriptions with medicinal products identified through a bespoke system of drug codes linked to generic drug names (substance names) or a substitute thereof in a drug and device dictionary. Diagnostic codes are recorded using the Read code system of clinical terms. Records are available from 1986 onwards.

3.6. Analysis

3.6.1. Incidence rate calculation

In patients without an outcome event during the time period the follow-up time in years was calculated with the following formula:

$$follow\ up\ time = \frac{(\text{End date for the period} - \text{start date for the period} + 1)}{365}$$

The incidence rate is the calculated as the number of events divided by the total follow up time.

$$incidence\ rate = \frac{\text{number of new onset events}}{\text{total follow up time}}$$

In patients with an outcome event during the time period, the date of the outcome was used instead of the end date for the period. The incidence rate was calculated as the number of patients with an outcome event per 100,000 person-years.

Incidence rates were also calculated for the entire population as well as stratified by gender and age group. Analyses of yearly incidence rates were performed using SAS. Confidence intervals around incidence rates were calculated using exact method [6].

3.7. Results

3.7.1. Bell's Palsy, narrow definition

The incidence rates of Bell's Palsy using the narrow definition stratified by year of event, age and sex is shown in Table 1. The overall incidence was 29.2 (95% CI 28.2-30.4) per 100,000 person-years for the narrow definition. It increased with age, peaking at 50-59 years, and was broadly similar across the three years of the study and between sexes.

Table 1 Incidence rate of Bell's Palsy per 100,000 person-years (narrow definition)

strata	***events***	***follow-up time (person years)***	***Rate per 100,000*** *(95% CI)*
overall	2739	9,366,832	29.24 (28.16-30.36)
2017	990	3,345,006	29.60 (27.78-31.50)
2018	893	3,116,911	28.65 (26.80-30.59)
2019	856	2,904,915	29.47 (27.53-31.51)
under 20 years	275	2,041,481	13.47 (11.93-15.16)
20-29 years	307	1,102,176	27.85 (24.83-31.15)
30-39 years	409	1,280,728	31.93 (28.91-35.19)
40-49 years	451	1,298,932	34.72 (31.59-38.08)
50-59 years	527	1,363,938	38.64 (35.41-42.08)
60-69 years	360	1,056,061	34.09 (30.66-37.80)
70-79 years	260	782,429	33.23 (29.31-37.52)
80 years & over	150	441,086	34.01 (28.78-39.91)
Male	1379	4,666,934	29.55 (28.01-31.15)
Female	1360	4,699,899	28.94 (27.42-30.52)
Q1 - Winter	748	2,383,745	31.38 (29.17-33.71)
Q2 - Spring	684	2,378,694	28.76 (26.64-30.99)
Q3 - Summer	645	2,337,221	27.60 (25.51-29.81)
Q4 - Autumn	662	2,267,172	29.20 (27.02-31.51)

inclusion Read codes: 'F310.00'
exclusion Read codes: '1476.00' '2BR6.00' '2BR7.00' 'F31..00' 'F310.00' 'F31y.00' 'F31yz00'
27,780 of 4,270,640 subjects excluded at baseline with history of event
4,242,860 subjects contribute follow-up time to the analysis

3.7.2. Bell's Palsy, broad definition

The incidence rates of Bell's Palsy using the broad definition stratified by year of event, age and sex is shown in Table 2. The overall incidence was marginally higher than for the narrow definition 30.4 (95% CI 29.3-31.6) per 100,000 person-years.

Table 2 Incidence rate of Bell's Palsy per 100,000 person-years (broad definition)

strata	***events***	***follow-up time (person years)***	***Rate per 100,000*** *(95% CI)*
overall	2,850	9,366,818	30.43 (29.32-31.56)
2017	1,033	3,345,001	30.88 (29.03-32.82)
2018	930	3,116,906	29.84 (27.95-31.82)
2019	887	2,904,910	30.53 (28.56-32.61)
under 20 years	293	2,041,479	14.35 (12.76-16.09)
20-29 years	317	1,102,175	28.76 (25.68-32.11)
30-39 years	417	1,280,727	32.56 (29.51-35.84)
40-49 years	468	1,298,930	36.03 (32.84-39.45)
50-59 years	542	1,363,936	39.74 (36.46-43.23)
60-69 years	376	1,056,059	35.60 (32.10-39.39)
70-79 years	283	782,427	36.17 (32.08-40.64)
80 years & over	154	441,086	34.91 (29.62-40.88)
Male	1,426	4,666,927	30.56 (28.99-32.18)
Female	1,424	4,699,891	30.30 (28.75-31.91)
Q1 - Winter	783	2,383,740	32.85 (30.59-35.23)
Q2 - Spring	715	2,378,691	30.06 (27.90-32.34)
Q3 - Summer	662	2,337,219	28.32 (26.21-30.57)
Q4 - Autumn	690	2,267,168	30.43 (28.21-32.79)

inclusion Read codes: '1476.00' '2BR6.00' '2BR7.00' 'F31..00' 'F310.00' 'F31y.00' 'F31yz00'
exclusion Read codes: '1476.00' '2BR6.00' '2BR7.00' 'F31..00' 'F310.00' 'F31y.00' 'F31yz00'
27,780 of 4,270,640 subjects excluded at baseline with history of event
4,242,860 subjects contribute follow-up time to the analysis

3.7.3. Guillain-Barré syndrome, narrow definition

The incidence rates of Guillain-Barré syndrome using the narrow definition stratified by year of event, age and sex is shown in Table 3. The overall incidence rate was 1.58 (1.34-1.85). The incidence increased with age, peaking in the 60-69 years age group, was higher for males than females, but was broadly similar across the three years of the study.

Table 3 Incidence rate of Guillain-Barré per 100,000 person-years (narrow definition)

strata	***events***	***follow-up time (person years)***	***Rate per 100,000*** *(95% CI)*
overall	149	9,431,061	1.58 (1.34-1.85)
2017	55	3,367,515	1.63 (1.23-2.13)
2018	50	3,138,278	1.59 (1.18-2.10)
2019	44	2,925,268	1.50 (1.09-2.02)
under 20 years	14	2,043,554	0.69 (0.37-1.15)
20-29 years	12	1,106,725	1.08 (0.56-1.89)
30-39 years	20	1,288,934	1.55 (0.95-2.40)
40-49 years	16	1,309,395	1.22 (0.70-1.98)
50-59 years	33	1,376,893	2.40 (1.65-3.37)
60-69 years	30	1,067,625	2.81 (1.90-4.01)
70-79 years	14	791,729	1.77 (0.97-2.97)
80 years & over	10	446,207	2.24 (1.07-4.12)
Male	90	4,697,427	1.92 (1.54-2.36)
Female	59	4,733,634	1.25 (0.95-1.61)
Q1 - Winter	45	2,399,973	1.88 (1.37-2.51)
Q2 - Spring	37	2,394,957	1.54 (1.09-2.13)
Q3 - Summer	28	2,353,300	1.19 (0.79-1.72)
Q4 - Autumn	39	2,282,832	1.71 (1.21-2.34)

inclusion Read codes: 'F370000' 'F370200'
exclusion Read codes: 'F370.00' 'F370000' 'F370100' 'F370200' 'F370z00'
1,544 of 4,270,640 subjects excluded at baseline with history of event
4,269,096 subjects contribute follow-up time to the analysis

3.7.4. Guillain-Barré syndrome, broad definition

The incidence rates of Guillain-Barré syndrome using the broad definition were identical to those from the narrow definition. This indicates the alternative codes used for identifying potential case of Guillain-Barré syndrome (F370.00 - Acute infective polyneuritis; F370100 - Postinfectious polyneuritis; F370z00 - Acute infective polyneuritis NOS) were not used in IMRD-UK from 2017 to 2019.

4. Interpretation of the results and discussion

4.1. Bell's Palsy

4.1.1. Published incidence rates of Bell's palsy

Bell's palsy is expected to have an annual incidence rate of 15-30 per 100,000 population [5, 7-10], but in a Korean population the annual incidence rate was 57 per 100,000 population [11] and in the Swiss population the annual incidence rate was also around 50 per 100,000 population [12]. A published review of the literature stated that although most incidence estimates varied between 11 and 40 cases per 100,000 population per year, figures as low as 8 and as high as 240 cases per 100,000 population per year were found in the literature [13]. Bell's palsy is considered to be most common between ages 15 to 40 [14]. The incidence may be higher in the winter compared to summer months [15, 16]. In Italy, a higher occurrence of facial palsy was observed during the COVID-19 outbreak compared to the year before [17].

4.1.2. Incidence rates of Bell's palsy from the ADVANCE study

Results from the ADVANCE study showed an overall incidence rate per 100,000 person-years of Bell's palsy of 23.84 (95% confidence interval 23.64-24.05). The ADVANCE study, where based on ICD 10 codes, used the narrow definition of facial paresis. Results by database showed the following incidence rates (95% confidence intervals) per 100,000 person-years:

- THIN UK: 32.1 (31.65–32.58)
- ARS Italy: 6.7 (6.47–6.97)
- BIFAP Spain: 42.4 (41.62–43.10)
- Denmark: 27.5 (26.49–28.46)

The results found in IMRD-UK (29.1; 95% CI 28.0-30.3) compare favourably with those given above. Differences could be attributed to the different time period used in both studies.

4.1.3. Limitations of estimating incidence rates of Bell's palsy in IMRD-UK

Bell's Palsy is a clinical diagnosis that would be expected to be made in general practice. We have not found evidence of it having been validated in any UK general-practice databases, so it is possible that there is some misdiagnosis or misclassification on the database. Read codes exist for related conditions exist (e.g. "O/E -cranial nerve 7-palsy-LMN", "O/E -cranial 7 -paralysis -LMN", "Facial nerve disorders", "Other facial nerve disorders" and "Other facial nerve disorder NOS") and it is not clear why the description of a clinical symptom or a more generic clinical term might be used in preference to a diagnosis of Bell's palsy, but it could relate to diagnostic uncertainty. The narrow definition used above could therefore be considered preferable.

This study considered only incident cases. Incidence was based on not having had a prior history of event for a minimum of one-year prior to the start of follow up. The "one year minimum" classification will likely lead to some misclassification of events. However, both Bell's Palsy and Guillain-Barré syndrome are sufficiently rare conditions so the extend of such misclassification is expected to be limited. Recurrent cases were not explicitly considered as it is hard to ascertain whether the repeated use of the same diagnostic code relate to new events or the same initial event which is the subject of repeated consultations.

The denominator used for the calculation of incidence rates is based on the patients registered with GP practices. For some groups – the young adult population in particular – this may differ from the actual population at risk, as some patients with minimal healthcare requirements might be slow to register with a new family doctor when moving to a new location.

4.2. Guillain-Barré syndrome

4.2.1. Published incidence rates of Guillain-Barré syndrome

In a meta-analysis of published studies [18] crude incidences per 100,000 were stated to range from 0.81 to 1.89. The incidence rate increased with increasing age (from 0.62 to 2.66) [18]. The variation between incidence estimates in different studies was larger in older compared to younger patients [18]. The incidence rates were higher in male compared to female patients [18]. Similar incidence rates were reported in another review of the published literature with incidence rates per 100,000 between 0.84 and 1.91 [19]. Guillain-Barré syndrome is believed to be an autoimmune reaction following certain bacterial and viral infections [18], and has for example been reported following influenza vaccination [20, 21]. It has also been reported in patients following COVID-19 [22]. A study from Italy showed a variation in annual incidence rates per 100,000 from 0.9 to 5.37 with a mean of 3 [21].

4.2.2. Incidence rates of Guillain-Barré syndrome from the ADVANCE study

Results from the ADVANCE study showed an overall incidence rate per 100,000 person-years of Guillain-Barré syndrome of 2.06 (95% confidence interval 2.00-2.12). The ADVANCE study, where based on ICD 10 codes, used the same definition of Guillain-Barré syndrome. Results by database showed the following incidence rates (95% confidence intervals) per 100,000 person-years:

- THIN UK: 1.8 (1.67–1.89)
- ARS Italy: 2.6 (2.49–2.80)
- BIFAP Spain: 1.1 (0.97–1.21)
- Denmark: 2.4 (2.27–2.49)

4.2.3. Incidence rates of Guillain-Barré syndrome from the ACCESS study

The only results available from ACCESS at the time of writing are incidence rates for Guillain-Barré syndrome from between 2017 and 2020 in Italy. Reported yearly incidence rates per 100,000 person-years (95% confidence intervals) are the following:

- 2017: 3.8 (3.15-4.48)
- 2018: 3.8 (3.19-4.52)
- 2019: 4.0 (3.39-4.75)
- 2020: 3.7 (2.83-4.87)

The results found for IMRD-UK (taken from a different epoch to those for THIN given above) are broadly in line with those described in the literature and in the ADVANCE study, although are perhaps lower that the early findings from the ACCESS study group.

4.2.4. Limitations of estimating incidence rates of Guillain-Barré Syndrome in IMRD-UK

A diagnosis of Guillain-Barré syndrome is one which would be expected to be made – at least in part – in secondary care, with the diagnostic process perhaps including electromyography, nerve conduction studies and/or lumbar puncture. As such it could be that primary care recording of this diagnosis is incomplete. However, given the potential seriousness of the condition and the GPs' role as gatekeepers to secondary care, even if a diagnosis was confirmed in hospital, accurate recording of the diagnosis on the GP practice system would be expected. We are not aware of any studies that have validated Read code diagnoses of Guillain-Barré in UK primary care databases.

As for Bell's palsy above, this study considered only incident cases. Incidence was based on not having had a prior history of event for a minimum of one-year prior to the start of follow up. The "one year minimum" classification will likely lead to some misclassification of events. However, both Bell's Palsy and Guillain-Barré syndrome are sufficiently rare conditions so the extend of such misclassification is expected to be limited. Recurrent cases were not explicitly considered as it is hard to ascertain whether the repeated use of the same diagnostic code relate to new events or the same initial event which is the subject of repeated consultations.

Finally, as for Bell's palsy, the denominator used for the calculation of incidence rates is based on the patients registered with GP practices. For some groups – the young adult population in particular – this may differ from the actual population at risk, as some patients with minimal healthcare requirements might be slow to register with a new family doctor when moving to a new location.

5. Reference list

1. Sturkenboom, M. *ACCESS programme for large scale COVID-19 vaccine monitoring*. Regulatory Science 2020; Available from: https://www.regulatoryscience.nl/editions/2020/11/miriam-sturkenboom-access-program-for-large-scale-covid-19-vaccine-monitoring.
2. ACCESS Consortium. *Event Definition form: 1. Guillain Barré Syndrome. Version 0.2.* 2020; Available from: https://drive.google.com/drive/folders/1Y_3cuGRN1g-jBv2ec1fC0aYcpxEjtrY9.
3. ACCESS Consortium. *Background rates of Adverse Events of Special Interest for monitoring COVID-19 vaccines [EUPAS37273]*. 2020; Available from: http://www.encepp.eu/encepp/viewResource.htm?id=37274.
4. Kurz, X., et al., *The ADVANCE Code of Conduct for collaborative vaccine studies.* Vaccine, 2017. **35**(15): p. 1844-1855.
5. Willame, C., et al., *Incidence Rates of Autoimmune Diseases in European Healthcare Databases: A Contribution of the ADVANCE Project.* Drug Saf, 2021.
6. Ulm, K., *A simple method to calculate the confidence interval of a standardized mortality ratio (SMR).* Am J Epidemiol, 1990. **131**(2): p. 373-5.
7. Mustafa, A.H.K. and A.M. Suleiman, *Bell's Palsy: A Prospective Study.* Int J Dent, 2020. **2020**: p. 2160256.
8. Yanagihara, N., *Incidence of Bell's palsy.* Ann Otol Rhinol Laryngol Suppl, 1988. **137**: p. 3-4.
9. Rowlands, S., et al., *The epidemiology and treatment of Bell's palsy in the UK.* Eur J Neurol, 2002. **9**(1): p. 63-7.
10. Morris, A.M., et al., *Annualized incidence and spectrum of illness from an outbreak investigation of Bell's palsy.* Neuroepidemiology, 2002. **21**(5): p. 255-61.
11. Choi, H.G., et al., *High Incidence of Bell's Palsy After Mastoidectomy: A Longitudinal Follow-up Study.* Otol Neurotol, 2017. **38**(10): p. 1517-1522.
12. Alvarez, V., P. Dussoix, and J.M. Gaspoz, *[Facial palsy: diagnosis and management by primary care physicians].* Rev Med Suisse, 2009. **5**(188): p. 258-62.
13. De Diego-Sastre, J.I., M.P. Prim-Espada, and F. Fernández-García, *[The epidemiology of Bell's palsy].* Rev Neurol, 2005. **41**(5): p. 287-90.
14. Holland, J. and J. Bernstein, *Bell's palsy.* BMJ Clin Evid, 2011. **2011**.
15. Erdur, H., et al., *Evidence for Seasonal Variation of Bell's Palsy in Germany.* Neuroepidemiology, 2018. **51**(3-4): p. 128-130.
16. Wijnans, L., et al., *Bell's palsy and influenza(H1N1)pdm09 containing vaccines: A self-controlled case series.* PLOS ONE, 2017. **12**(5): p. e0175539.
17. Codeluppi, L., et al., *Facial palsy during the COVID-19 pandemic.* Brain Behav, 2020: p. e01939.
18. Sejvar, J.J., et al., *Population incidence of Guillain-Barré syndrome: a systematic review and meta-analysis.* Neuroepidemiology, 2011. **36**(2): p. 123-33.
19. McGrogan, A., et al., *The epidemiology of Guillain-Barré syndrome worldwide. A systematic literature review.* Neuroepidemiology, 2009. **32**(2): p. 150-63.
20. Vellozzi, C., S. Iqbal, and K. Broder, *Guillain-Barre syndrome, influenza, and influenza vaccination: the epidemiologic evidence.* Clin Infect Dis, 2014. **58**(8): p. 1149-55.
21. Martín Arias, L.H., et al., *Guillain-Barré syndrome and influenza vaccines: A meta-analysis.* Vaccine, 2015. **33**(31): p. 3773-8.
22. Caress, J.B., et al., *COVID-19-associated Guillain-Barré syndrome: The early pandemic experience.* Muscle Nerve, 2020. **62**(4): p. 485-491.