NOT FOR PUBLICATION

COMMISSION ON HUMAN MEDICINES

VACCINE BENEFIT RISK EXPERT WORKING GROUP

Title of paper: AstraZeneca and Pfizer/BioNTech – Analysis of the nature and seriousness of adverse reactions with COVID-19 vaccines

Type of paper: For advice

Active(s) rINN	Pfizer/BioNTech COVID-19 vaccine BNT162b2 AstraZeneca COVID-19 vaccine
Product name(s)	
Marketing Authorisation Holder(s)	Pfizer/BioNTech AstraZeneca
Legal status	Prescription only medicines
Therapeutic classification (ATC code)	
Previous assessments	
Assessor(s)	Name: [redacted] (Scientific Assessor) Email: [redacted] Name: [redacted] (Scientific Assessor) Email: [redacted]

1. Background

The Pfizer/BioNTech COVID-19 vaccine was authorised for use under Regulation 174 by the MHRA on 2 December 2020. It is estimated that over 7 million doses have been administered in the UK as of 31 January 2021. The AstraZeneca COVID-19 vaccine was authorised for use under Regulation 174 by the MHRA on 30 December 2020, and over 3 million doses have been administered in the UK as of 31 January 2021.

The MHRA is aware of anecdotal reports in the UK of reactions to the COVID-19 vaccines being more severe than that expected, and this this is predominantly coming from healthcare workers, which are the younger age group being vaccinated at the current stage of the vaccination programme. There is the potential for this to impact the acceptability of the vaccine and thus affect the update of the vaccination programme, and therefore warrants investigation.

This paper presents the available data from clinical trials and post-authorisation safety data on the nature of events serious events reported with the COVID-19 vaccines and identification of any patterns within this. A comparison with UK reporting with the flu vaccine is also provided. Advice from the EWG is sought as to whether they agree with the conclusions drawn.

1. **Analysis of seriousness profile of ADR reports received**

We assessed seriousness of ADR reports according to CIOMs seriousness criteria which is used to classify the seriousness of a case. There are 6 seriousness criteria used on Yellow Card reports:

- results in death,
- is life-threatening,
- requires inpatient hospitalization or prolongation of existing hospitalization,
- results in persistent or significant disability/incapacity,
- is a congenital anomaly/birth defect, or,
- other medically significant, such as affecting everyday activities

When submitting a Yellow Card, reporters are asked whether they would define the events as serious, and if so to select one or more of these seriousness criteria which applies.

While it is acknowledged that some of the criteria can be used subjectively by reporters and are not always accurately applied, particularly with the disability/incapacitation, hospitalization and life-threatening flags, this is a useful indicator of the profile of the perceived seriousness of reports received for a vaccine or drug.

Table 1. Comparison of the proportions of reports falling under CIOMS serious categories for AstraZeneca COVID-19 vaccine and Pfizer/BioNTech COVID-19 vaccine

	AZ COVID	**Pfizer COVID**
Total reports (serious* [%])	9,683 (4658 [48%])	19,203 (6669 [35%])

By CIOMS flag (% of all cases)**		
Disability/ incapacitated	640 (6.6%)	1094 (5.6%)
life threatening	41 (0.4%)	149 (0.8%)
hospitalised	111 (1.1%)	309 (1.6%)
died	63 (0.7%)	129 (0.7%)
'other'***	3987 (41%)	5384 (28%)

*Any CIOMS flag

** Each report may contain >1 flag – total will not equal 100%

*** reporter can flag as serious for any reason they consider it serious

Overall, both vaccines follow similar patterns with regards to seriousness reporting. The percentage of reports flagged with any serious criteria does differ between the vaccines, with 48% of reports flagged as serious for the AstraZeneca vaccine and 35% for Pfizer/BioNTech. This difference is powered by selection of the "other medically significant" flag, which is the most subjective criterion but there is a difference in the proportion of reports seen here between the vaccines. The CDC has published an overview of the safety experience in the US with Pfizer/BioNTech and it was identified that in VAERS 8% of reports were of serious events[1], however, this definition of seriousness doesn't include the "other" seriousness category as with the UK data and therefore doesn't indicate a significantly different profile to the Yellow Card data for this vaccine.

For both vaccines where reports are flagged as serious, the vast majority have been marked as "other medically significant" which may represent patients feeling particularly unwell following vaccination and needing to take days off work to recover, or experiencing symptoms such as pyrexia which, for healthcare professionals, would require them to take days off work until SARS-CoV-2 infection can be ruled out. The next highest category is Disability/ incapacity, which again likely represents patients feeling incapacitated due to the reactogenicity and/or needing to take days off work. These are also the patterns that have been seen with case review during routine signal detection, which includes the large majority of these cases being reported in females, asides from the death category where the split is more even. This is something which is also reflected in the CDC data which found 76% of reports were in females[1]. It is estimated that 77% of NHS employees are female[2], and CPRD analysis of usage indicates that 64% of vaccines administered are in females, although this does not entirely account for the different in proportions of reports.

The next most selected criterion is hospitalization, followed by life threatening and fatal. The number of cases flagging these criteria is significantly less than the other 2 criteria. No cases reporting congenital anomalies have been received for AstraZeneca and only 3 for Pfizer, in two of which it was unclear why this flag had been selected and one related to spontaneous abortion, therefore this seriousness criteria is not further discussed in this paper.

[1] COVID-19 vaccine safety update, Advisory Committee on Immunization Practices (ACIP)January 27, 2021. CDC
[2] https://www.nhsemployers.org/case-studies-and-resources/2019/05/gender-in-the-nhs-infographic#:~:text=With%20a%20workforce%20that%20comprises,regular%20discussion%20within%20the%20NHS

It is important to note that while the proportion of Yellow Cards received reporting serious criteria is relatively high, this is a very small proportion of the total vaccinated population (even if factoring in potential under-reporting as 100% reporting is not expected) and a significant reporting bias is likely to be present whereby more serious or significant events are more likely to be reported through the scheme. Combined with the high-profile nature of this vaccination campaign, the data reported is likely to be biased towards the most serious and noteworthy events and those with the most immediate onset following vaccination.

2. **Most frequently reported reaction Preferred Terms (PTs) in reports flagged as serious**

We analysed the reaction PTs most frequently reported in cases reported as serious. For reports flagged with any of the serous criteria overall, those flagged for disability/incapacity and other medically significant, the most frequently reported PTs were broadly the same for both COVID vaccines, save for some alterations in order of reactions. These were consistent with reactogenicity reactions which are seen with all vaccines and are listed in the product information for the vaccines[3,4].

This analysis was extended for events which could be reported synonymously for headache and chills, namely migraine and tremors respectively, and it was identified that for Pfizer/BioNTech there have been 361 reports of migraine, of which 160 reported one or more CIOMS flag as serious, and for tremor there have been 244 reports of which 113 report a serious flag. For AstraZeneca, there have been 295 reports of migraine of which 158 reported one or more CIOMS flag as serious and for tremor there are 433 reports, of which 268 report CIOMs seriousness. While these events could be related to other effects, and particularly tremor which may be related to nervous system disorders, many of the cases identified also reported other reactogenicity events suggesting these are being reported synonymously. Additionally, a number of the tremor cases are also suggestive of being related to anxiety in response to vaccination. The reporting of migraine also provides an insight into the strength of headache which may be experienced as part of the reactogenicity profile.

Of the serious events reported under the life threatening and hospitalised flags, dyspnoea and dizziness are currently unlisted however these cases do not have a strong pattern of events and are related to a variety of factors including possible anxiety related reaction, cardiac events, COVID-19 infection and anaphylaxis and hypersensitivity reactions. Similarly, of those reporting listed events such as pyrexia, fatigue and headache, many of the events are reported in the context of other events which would be contributory, such as COVID-19 or other infections, anaphylaxis, and cardio and cerebral events. However, there are a number of cases indicating severe reactogenicity which concerned patients enough to seek medical care or feel frightened as to the seriousness, although it is not always confirmed in these cases if the patient was admitted or attended hospital. It is worth noting that many cases include more than one of these PTs, and so are not indicative of the number of individual cases for each event, and the proportion of cases reporting these kinds of reactions remains small compared to overall reporting and usage of the vaccines.

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3 https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/955899/Temporary_Authorisation_HCP_Information_BNT162_6_0_UK_editclean.pdf

4 https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/951851/uk-clean-spc-covid-19-vaccine-astrazeneca-reg174.pdf

The most frequent events reported in fatal cases is in line with recent reviews of this topic, and largely reflect COVID-19 or other infections or expected co-morbidities for the demographic groups currently being prioritized for vaccination, or provided non-specific terms.

Table 2. Summary of top 5 most reported events under each CIOMS category for AstraZeneca COVID-19 vaccine and Pfizer/BioNTech COVID-19 vaccine

	Any CIOMS flag	**disability/ incapacitated**	**life threatening**	**hospitalized**	**Died***	**'other'**
AstraZeneca						
1	Headache (n= 2037)	Pyrexia (n= 310)	Anaphylactic reaction (n= 9)	Pyrexia (n= 36)	Death (n= 41)	Headache (n= 1773)
2	Pyrexia (n= 1960)	Headache (n= 306)	Dyspnoea (n= 4)	Headache (n= 19)	Sudden death (n= 5)	Pyrexia (n= 1677)
3	Chills (n= 1251)	Fatigue (n= 176)	Pyrexia (n= 3)	Dyspnoea (n= 12)	Malaise (n= 4)	Chills (n= 1105)
4	Fatigue (n= 1088)	Nausea (n= 176)	Vomiting (n= 3)	Chest pain (n= 12)	Cerebrovascular accident (n= 4)	Fatigue (n= 946)
5	Nausea (n= 999)	Chills (n= 170)	Nausea (n= 3)	Vomiting (n= 10)	Pyrexia (n= 3)	Nausea (n= 859)
Pfizer						
1	Headache (n=1897)	Headache (n=377)	Anaphylactic reaction (n=40)	Dyspnoea (n=36)	Death (n=61)	Headache (n= 1552)
2	Fatigue (n=1451)	Pyrexia (n=307)	Dyspnoea (n=15)	Pyrexia (n=36)	COVID-19 (n=19)	Fatigue (n= 1218)
3	Pyrexia (n=1438)	Fatigue (n=268)	Fatigue (n=15)	Dizziness (n=29)	Cardiac arrest (n=11)	Pyrexia (n= 1144)
4	Nausea (n=1070)	Myalgia (n=226)	Dizziness (n=12)	Anaphylactic reaction (n=28)	Dyspnoea (n=11)	Nausea (n= 871)
5	Myalgia (n=993)	Nausea (n=208)	COVID-19 (n=10)	Headache (n=27)	Vomiting (n=9)	Myalgia (n= 784)

Note: Each report may contain >1 flag; reporter can flag as serious for any reason they consider it serious. Multiple PTs may be covered in reports *PTs are not necessarily the fatal event

For those cases reporting the top 5 events received with any serious flag for the Pfizer/BioNTech vaccine, the majority of the events were reported to be recovered or recovering at the time of reporting, with all but myalgia having recovered as the most commonly reported outcome. Similarly with AstraZeneca, the majority of events are reported as recovered or recovering.
There approximately 30-40% of cases with the outcome "not recovered" reported across the top 5 events in serious cases for Pfizer and 15-40% for AstraZeneca, although this is partly likely due to swift reporting following the onset of symptoms and lack of follow up information on the outcomes of these cases.

3. **Breakdown of seriousness profile by age**

Anecdotal reports have suggested that the younger vaccinated population, which currently consists largely of healthcare professionals, are experiencing more severe reactogenicity reactions than they were expecting. A trend for higher reporting of solicited reactogenicity events in younger recipients was also seen in clinical trials. We have therefore analysed serious reports broken down by age category and used exposure data to look at reporting trends by age group.

Table 3. Reporting rate per 100,000 vaccinees according to seriousness criteria, broken down by age for AstraZeneca.

	Reporting rate per 100,000 vaccinees*					
Age group	**Total serious**	**Disability/ incapacitated**	**Life threatening**	**Hospitalised**	**Died**	**Other**
Under 18	1404	468	0	0	0	1170
18-49	592	92	3	11	0	510
50-54	284	53	46	4	0	230
55-64	164	28	1	1	0.40	137
65-69	58	4	0	2	5.39	48
70-74	60	3	1	0	0.22	57
75-79	52	3	0	1	0.90	48
80+	43	4	2	4	4.72	33

*based on usage data up to 31 January 2021, extrapolated from CPRD data

Table 4. Reporting rate per 100,000 vaccinees according to seriousness criteria, broken down by age, for Pfizer/BioNTech.

	Reporting rate per 100,000 vaccinees*					
Age group	**Total serious**	**Disability/ incapacitated**	**Life threatening**	**Hospitalised**	**Died**	**Other**
Under 18	346	-	-	-	-	346
18-49	216	35	3	6	0.33	182

50-54	159	39	3	4	0.52	119
55-64	117	27	2	4	0.28	89
65-69	40	6	<1	2	1.40	35
70-74	29	3	1	1	0.37	25
75-79	24	1	1	1	1.39	21
80+	35	4	2	5	3.30	26

*based on usage data up to 31 January 2021, extrapolated from CPRD data for UK wide and age breakdowns

Aside from cases reporting fatal outcomes (CIOMS "died"), there is a higher reporting rate of serious events across all categories in the younger age groups, with a trend for decreasing rates as age increases. This, twinned the analysis showing most serious events are related to reactogenicity, suggests a stronger reactogenicity profile in the younger age group which is in line with a known stronger immune response in this group. This result is not unexpected; however, it does support the anecdotal evidence of a more serious side effect profile in younger recipients and this may impact the acceptability and tolerability of the side effect profile of the vaccines particularly if these events are causing concern for those experiencing them.

4. **Comparison with clinical trial data**

In the Pfizer/BioNTech COVID-19 clinical trial data on local and systemic reactogenicity were collected in a subset of patients and included analysis by age (16-55 years; >55 years). The frequency of moderate pain after any dose was increased for younger participants compared to older participants (40.4% vs 23.6%). The systemic reactogenicity results were also analysed by age and the frequency and severity of systemic events were increased in the younger group compared to the older group. There was also a trend for a higher rate of reporting of higher grade reactogenicity events for the younger group compared to the older group. These results were not unexpected considering reactogenicity is related to immune response, which tends to be stronger in younger age groups. The same pattern was seen in AstraZeneca Covid-19 clinical trials where analysis by age was split into 18-64 and 65+. While the number of participants aged over 65 was low, which limits interpretation, both local and systemic solicited reactions were reported more frequently in younger participants, as were higher grades of severity of these reactions.

Overall, for unsolicited adverse events, events were reported more frequently in the younger group than the older group, with a greater difference after BNT162b2 compared to after placebo: 28.8% vs 12.6%. This was also the case for AZD1222. Although there was a higher frequency of serious events (for both vaccines) and those of higher severity grade (for BNT162b2) in the older population, this is likely reflecting comorbidities in the older age group. While this seems contradictory to the Yellow Card data, the fact that most serious cases received by the MHRA are related to reactogenicity events, this is likely more similar to the solicited reporting in the clinical trials, and spontaneous reporting of other events will be impacted by biases such as knowledge and accessibility of reporting.

Regarding adverse events following the second dose for Pfizer/BioNTech, the frequencies of local reactions were similar after Doses 1 and 2. The frequency and severity of systemic events were increased post-Dose 2 compared to post-Dose 1. In the Yellow Card data, a total of 503 reports have been identified as reporting reactions with a second dose of the Pfizer/BioNTech vaccine, although this data is not routinely captured in the cases and so there are limitations to this analysis. Of these

203 (40%) are reported as serious, with 32 (6%) reporting disability/incapacitation, none (0%) reporting life threatening events, 8 (2%) hospitalized, 5 (1%) patients died and 172 (34%) reporting the "other" serious flag. Compared to overall reporting with either dose, this represents a slightly higher proportion of serious events reported with the second dose. This is also reflected in reactogenicity reported to v-safe, the CDCs vaccine monitoring system, which has identified a higher reporting of local and systemic reactions following the second dose of the vaccine[1]. This may indicate a stronger side effect profile with the second dose, not dissimilar to that reported in clinical trials, although spontaneous reporting on the second dose is likely to be impacted by expectation bias following the first dose.

For AstraZeneca, solicited AEs, both local and systemic, were milder and reported less frequently after the second dose compared with the first. Post-authorization usage of the AstraZeneca vaccine for 2nd doses is much lower than for the Pfizer vaccine, which is expected given the change in strategy with regards to administration of the second dose. Only 1 case refers to a second dose with AstraZeneca Covid-19 vaccine as the reported brand. Given the date that this report was received it is likely that this is either a misclassification of the brand or that the patient had a different brand for the second dose. The report is not flagged as serious.

5. **Comparison of proportionality of reporting with inactivated flu vaccine**

While it's not possible to directly compare the safety profiles of the two vaccines without head-to-head trials, we analysed ADR reporting for the previous 10 seasons of flu vaccination to compare the proportionality of the serious cases received. Flu vaccine has been used as a comparator to the COVID-19 vaccines due to its widespread use and similar usage profile targeting healthcare workers and elderly.

The proportion of cases being reported with any serious criteria (42%) was slightly lower to that reported for AstraZeneca (48%) and higher than that of Pfizer/BioNTech (35%) (Table 5). Of the individual seriousness criteria, all of these had a higher proportion of events identified in these, compared to overall reporting, compared to the two COVID-19 vaccines. The proportion reported as hospitalized is more similar to those reporting disability/incapacity currently seen with the COVID-19 vaccines. The nature of events reported in the serious cases was also similar to the COVID-19 vaccines in that it largely reflects the reactogenicity profile of the vaccine (Table 7).

A similar trend to the Covid-19 vaccines is seen with the inactivated flu vaccine in that younger recipients (apart from those under 18) make up the largest proportion of those reporting any seriousness criteria and the largest proportion reporting each type of serious criteria, apart from death (Table 6). Overall seriousness is mainly powered by reports flagged as "other medically significant". Similarities between proportions reporting disability/incapacity and hospitalization are representative of younger recipients being hospitalized although the differences are small and we cannot account for varying exposure per age group. However, this is a crude analysis and does not take into account usage as the COVID-19 vaccines did by using reporting rates and only uses proportions of reports received, and the higher rates in the younger groups for the flu vaccine is likely skewed by the uneven age brackets which have been used for comparison with the COVID-19 data based on usage statistics available for that. Therefore, when taking this into account there is not such a strong trend by age with the flu data.

There was also a higher proportion of serious events reported in female compared to males similar to that seen with the COVID-19 vaccines, although usage data is not known to provide context for this with the flu vaccine.

Table 5. The proportions of reports falling under CIOMS serious categories for the inactivated flu vaccine

	Flu (2011-2020)
Total reports (serious* [%])	7621 (3963 [42%])
By CIOMS flag (% of all cases)**	
Disability/ incapacitated	677 (9%)
life threatening	244 (3%)
hospitalised	597 (8%)
died	63 (0.8%)
'other'***	3094 (41%)

*Any CIOMS flag

** Each report may contain >1 flag – total will not equal 100%

*** reporter can flag as serious for any reason they consider it serious

Table 6. Proportion of reporting according to seriousness criteria, broken down by age, for the inactivated influenza vaccine

	Number reports (% of total reports)					
Age group	Total serious	Disability/ incapacitated	life threatening	hospitalised	died	Other
Under 18	138 (1.8%)	16 (0.2%)	5 (0.07%)	24 (0.3%)	7 (0.09%)	94 (1.2%)
18-49	1209 (16%)	176 (2.3%)	93 (1.2%)	187 (2.5%)	4 (0.05%)	960 (12.6%)
50-54	325 (4%)	50 (0.7%)	22 (0.3%)	31 (0.4%)	5 (0.07%)	267 (3.5%)
55-64	632 (8%)	113 (1.5%)	28 (0.4%)	69 (0.9%)	3 (0.04%)	513 (6.7%)
65-69	567 (7%)	110 (1.4%)	26 (0.3%)	77 (1.0%)	6 (0.08%)	455 (6.0%)
70-74	417 (5%)	98 (1.3%)	25 (0.3%)	77 (1.0%)	6 (0.08%)	312 (4.1%)
75-79	209 (3%)	48 (0.6%)	14 (0.2%)	43 (0.6%)	5 (0.07%)	150 (2.0%)
80+	229 (3%)	45 (0.6%)	19 (0.2%)	45 (0.6%)	16 (0.2%)	154 (2.0%)

Table 7. Summary of top 5 most reported events under each CIOMS category for the inactivated influenza vaccine

	Any CIOMS flag	**disability/ incapacitated**	**life threatening**	**hospitalized**	**Died***	**'other'**

1	Headache (n=578)	Arthralgia (n=19)	Anaphylactic reaction (n=67)	Malaise (n=76)	Death (n=13)	Headache (n= 511)
2	Fatigue (n=457)	Pain in extremity (n=112)	Guillain-Barre syndrome (n=25)	Pyrexia (n=62)	Stillbirth (n=7)	Fatigue (n=407)
3	Malaise (n=447)	Headache (n=86)	Dyspnoea (n= 23)	Guillain-Barre syndrome (n=49)	Pneumonia (n=6)	Pyrexia (n=373)
4	Pyrexia (n=442)	Myalgia (n=83)	Malaise (n=14)	Dyspnoea (n= 45)	Guillain-Barre Syndrome, Respiratory failure and malaise all report n=5	Malaise (n=355)
5	Pain in extremity (n=398)	Fatigue (n=78)	Pyrexia (n=13)	Headache (n=43)		Pain in extremity (n= 321)

6. **Discussion**

Of the overall reporting of serious events, there was a higher proportion reported for AstraZeneca compared to Pfizer/BioNTech, which is suggestive of a more reactogenic side effect profile, however, in the breakdown of different seriousness criteria, the reporting pattern was similar and did not suggest any dramatic differences between the two vaccines aside from the “other” seriousness criteria which was higher for AstraZeneca (41%) vs Pfizer/BioNTech (28%) and in this category is likely related to more moderate reactogenicity events. When the proportion of seriousness was compared to the inactivated flu vaccine too, there was a higher proportion of serious reports with the flu vaccine compared to the two COVID-19 vaccines, and this was similar across the different serious reporting criteria too.

The types of reactions most often reported in the serious cases was similar across both vaccines and across the different seriousness categories, and the majority of these related to reactogenicity events listed in the product information for the vaccines. This was also not dissimilar to the flu vaccine profile, and suggests that overall, the nature of reactogenicity with the COVID-19 vaccines is similar to that expected with other vaccines. Limited analysis was able to be carried out on the duration of the reactions reported due to the lack of follow up information on outcomes in many cases, however on the whole, for the top 5 reported events in the serious criteria for both vaccines, a large proportion of events had recovered which does not suggest an overly long duration at present.

The profile reported with Pfizer/BioNTech COVID-19 vaccine for the proportion of serious events reported (excluding the “other” serious criteria) was similar to that recently reported by the CDC, as were the nature of events reported overall, which also provides reassurance of a consistent side effect profile for this vaccine. No international comparison with AstraZeneca is currently available.

The most striking pattern with the reactogenicity analysis is the difference in reporting rates by age group for both the AstraZeneca and Pfizer/BioNTech vaccines. For overall seriousness, disability/incapacitation, and other there is a much higher reporting rate of serious events in the younger age groups. This is reflected in the clinical trial data for both AstraZeneca and

Pfizer/BioNTech there was a higher frequency and severity of systemic reactogenicity in the younger age group after any dose, along with moderate pain, and overall reporting of adverse events was higher in the younger age group. This is expected due to a stronger immune response typically being seen in younger patients, however, comparison with the spontaneous flu vaccine data by age does not show a similar pattern. While this comparison with flu is crude as it has not taken into account usage and only related to proportion of reporting, when taking into account the unbalanced age banding, there is not the increase in serious reports in the younger group in the flu data which suggests this experience may be specific to the current COVID-19 vaccine experience. However, this may be subject to reporting bias considering the high update of the COVID-19 vaccines in the healthcare worker population, who are more likely to be aware of the Yellow Card scheme and also be more likely to have access to reporting methods than older recipients.

There also remains an imbalance in the proportion of serious events reported for women (with the exception of fatal events), and this is not fully accounted for by the higher vaccination in females which is estimated to be 64% of vaccines given, and a similar experience is reported in the US. The reason for this imbalance is not currently clear, nor whether any reporting bias may be influencing this.

Analysis on the potential for increased severity following the second dose is limited. For AstraZeneca there was a lower frequency of higher severity events for the second dose compared to the first. particularly as there is only a small amount of second dose exposure for AstraZeneca. However, for Pfizer/BioNTech the clinical trial data reported increased systemic reactogenicity with the second dose compared to the first, and this has been reflected in VAERs data reported by the CDC. From UK spontaneous reporting data with Pfizer/BioNTech, where second or first dose is only sporadically reported, there appears to be a higher proportion of serious events reported (40%) compared to those reporting any dose. There is insufficient Yellow Card data on second doses with the AstraZeneca vaccine for analysis.

7. Conclusions

Overall, the nature of the events reported in serious cases is within the expected side effect profile of the COVID-19 vaccines and reflects the reactogenicity typical of other vaccines such as the flu vaccine. There is a pattern of higher reporting rates of serious events in younger vaccine recipients compared to older age groups, and this is driven by reporting of reactogenicity events. This is something which was also seen in the clinical trials for both vaccines and reflects the stronger immune response in younger recipients. When this pattern is compared to the flu vaccine there likely is a higher proportion of these events reported for the COVID-19 vaccines. However, this may be the result of reporting bias due to the younger age groups targeted for vaccination, with a higher than usual uptake, having better knowledge of, and access to, reporting systems.

8. Advice sought from the EWG

The EWG is asked if it agrees with the above conclusions.