**Signal loss by truancy, masking, and filtering, and underestimation of potential risks and suspected adverse reactions in the Disproportionality Signal Analyses of VAERS data associated with COVID-19 pro-vaccines**

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*CONTENTS*

## 1 TOP FOUR POINTS

- Large, use-normalized imbalances of 76-123 times (IQR) the number of safety signals for the Janssen COVID-19 pro-vaccine compared with the Pfizer and Moderna products generated by FDA's Empirical Bayesian Data Mining analysis, persisted for at least 18 months without clear comment or action.
- This analysis lacked an estimated 96% and 91% of Pfizer's and Moderna's safety signals, respectively. The FDA did not adjust for masking despite having the software to do so. Signals were filtered out by a high threshold. There were flaws in CDC's Proportional Reporting Ratio (PRR) analysis.
- Robust correction of bias due to truancy, masking, and threshold filtering suggests that as of April 29, 2022, 763 (range 487-1898) (86%, range 85-93%) signals were lost and/or delayed. Orthogonal analyses suggest losses as high as 6765 signals.
- Safety signals represent potential risk FDA was required to consider. The suppression of this largely uninvestigated potential risk is both a scientific and a regulatory failure. It impugns the reliability of decisions regarding authorization, approval, and vaccine injury compensation. Our findings warrant full disclosure of vaccine safety data and an investigation into inadequate signal detection and regulatory oversight.

## 2 CAPSULE

Persistent and ignored imbalances in safety signals identified by FDA's Empirical Bayesian Data Mining of VAERS COVID-19 data suggest losses of 763 (up to 6765) safety signals (to April 29, 2022) due to truancy, masking, and inappropriate filtering. These losses delayed recognition of safety signals and represent a still largely uninvestigated potential risk FDA was required to consider. Along with inconsistencies with statements made by regulators, these anomalies impugn the reliability of regulatory and compensation decisions and warrant an investigation into COVID-19 vaccine safety oversight, with the formulation of a corrective action plan.

## 3 LAY CAPSULE

Examination of FDA's Empirical Bayesian Data Mining of VAERS COVID-19 vaccine safety analysis suggests that over 91% of Pfizer's and Moderna's safety signals were missing from alerts circulated between regulators. A signal is a statistical warning sign (but not proof) that a particular adverse event may occur with a particular vaccine. FDA's analysis neglected to correct for masking, where signals for one vaccine are concealed by signals from other vaccines. Signals were filtered out by an inappropriately high detection threshold. These anomalies resulted in the loss of up to 6765 signals. Along with inconsistencies with statements made by regulators, these missing safety signals represent still largely uninvestigated potential risk FDA was required to consider, impugn the reliability of regulatory and compensation decisions, warranting an investigation into COVID-19 vaccine safety oversight and the formulation of a corrective action plan.

## 4 ABSTRACT

**Background**

Disproportionality Signal Analyses (DSA) of data from the US Vaccine Adverse Event Reporting System (VAERS) relating to COVID-19 pro-vaccines and conducted by FDA and CDC were released under the Freedom of Information Act (FOIA).

**Objective**

To explore dataset anomalies in the context of contemporary regulatory history.

**Methods**

Three sources of VAERS-derived disproportionality (DSA) signals were analyzed. 1) The "FOIA dataset" spanning January 2021 to July 2022 (US only, Empirical Bayesian Geometric Mean – EBGM, and Proportional Reporting Ratio - PRR). 2) The "VIOLIN dataset" (US only, PRR) extracted from an online NIH-supported database. 3) The "Oracle dataset" published by authors who include the developer of the Empirical Bayesian Data Mining (EBDM) method, and current and retired FDA staff (US + foreign, EBGM, PRR).

**Results**

These anomalies were identified:

1. Along with a broader diversity of event types, there were 76-123 (use-normalized, interquartile range) times the number of EBGM signals associated with the Janssen product compared with the Pfizer and Moderna products. These imbalances persisted over the period covered by the dataset, without obvious regulatory action.
2. Missing from FDA's analysis were an estimated 96% of Pfizer's and 91% of Moderna's safety signals, representing truancy factors of 26 and 11, respectively. 7/8 (87.5%) of EBDM signals detected in the Oracle dataset were missing in the FOIA dataset (p=0.02).
3. FDA did not correct for masking despite possessing the software to do so. Signals were filtered out by an inappropriately high detection threshold. FDA failed to consider foreign-originating VAERS reports in its EBDM, or to mine potential signals among borderline signals, thereby introducing "*Inquisitorial triage bias."*
4. Robust correction of bias due to truancy, masking, and filtering suggests an aggregate loss of 763 signals (range 487-1898; 86% loss, range 85-93%) to April 29, 2022. Orthogonal analysis suggests losses as high as 6765 signals.
5. The PRR portion of the FOIA dataset lacked analyses for the Janssen product and separate analyses for the Pfizer and Moderna products. The disclosed analysis for mRNA pro-vaccines combined appears to be missing 54% of its signals (N=1026).
6. There appear to be 4.8- and 8.8-fold true signal excesses associated with the Janssen over the Pfizer and Moderna products, respectively. Hematologic events accounted for 30% of the Janssen signals, but were absent from the Pfizer and Moderna signals. This anomaly should have warranted regulatory actions at least as extensive and transparent as those executed for Thrombosis with Thrombocytopenia Syndrome (TTS) associated with the Janssen product.

**Conclusion**

These anomalies are inconsistent with statements made by regulators, particularly regarding stroke, cancer, clotting issues, and myocarditis. These anomalies constrained the hypothesis-generating approach of identifying potential safety signals. They are incompatible with the "Enhanced surveillance" of Adverse Events Special Interest and belie the representation of VAERS as "*the nation's early warning system for vaccine safety."* The missing safety signals represent a still largely uninvestigated potential risk FDA was required to consider. Despite their limitations, our findings impugn the reliability of regulatory and injury compensation decisions concerning the COVID-19 pro-vaccines. They warrant full disclosure of vaccine safety data and an investigation into deficient signal detection and regulatory oversight.

## 5 LAY SUMMARY

This study examines safety analyses for COVID-19 vaccines based on adverse events reported to the US Vaccine Adverse Event Reporting System (VAERS) from January 2021 to July 2022. Released via a Freedom of Information Act request, these analyses aimed to identify potential safety signals. A signal means that there is a statistical warning sign (not proof) that a particular adverse event may be occurring with a particular vaccine.

*What Was Done? Researchers compared three datasets:*

- The "FOIA dataset" from the FDA and CDC, which calculated the Empirical Bayesian Geometric Mean (EBGM) and Proportional Reporting Ratio (PRR) to detect safety signals.
- The "VIOLIN dataset" from an NIH-funded database (PRR values).
- The "Oracle dataset" from a study analyzing EBGM and PRR signals for seven “high-profile” adverse events. Authors of this study included the originator of the EBGM method, as well as FDA staff.

*What Was Found? Key issues included:*

- Adjusting for actual use, there were 76-123 times the number of EBGM signals associated with the Janssen product compared with the Pfizer and Moderna products. These large imbalances persisted over the 18 months covered by the dataset, with no obvious regulatory action or comment at any of the 17 FDA or CDC advisory meetings held over this period.
- Missing from FDA’s analysis were an estimated 96% of Pfizer’s and 91% of Moderna’s safety signals. 7/8 (87.5%) of EBGM signals detected in the Oracle dataset were missing from the FOIA dataset.
- Despite possessing the software to do so, FDA did not correct for masking, which means that signals may be lost because of the mathematical interference of signals from other vaccines. For example, the myocarditis signal for Pfizer could have reduced the strength of the myocarditis signal for Moderna, and vice versa.
- Signals were filtered out because the detection threshold was set too high.
- These anomalies may account for a loss (to April 29, 2022) of 763 signals, which could be as high as 6765 signals.
- After corrections, there appear to be 4.8- and 8.8-times as many signals associated with the Janssen than the Pfizer and Moderna products, respectively. This anomaly should have triggered regulatory actions as extensive as those executed for Thrombosis with Thrombocytopenia Syndrome (TTS) associated with the Janssen product.
- The study found inconsistencies between statements made by the FDA or CDC and actual data regarding safety signals for stroke, cancer, clotting issues, and myocarditis.

*What Does This Mean?*

Regulators likely missed or ignored imbalanced safety signals, compromising their vaccine safety, approval, authorization, and injury compensation decisions. The missing safety signals represent a still largely uninvestigated potential risk FDA was required to consider. These anomalies belie the representation of VAERS as “the nation’s early warning system for vaccine safety.” Full data disclosure and further investigation are warranted.

## 6 INTRODUCTION

### *6.1 Background*

The United States monitors vaccine safety through programs within the Department of Defense, the Department of Veterans Affairs, the Indian Health Service, and the Centers for Medicare and Medicaid Services (CMS). The primary responsibility for monitoring vaccine safety resides within the Centers for Disease Control and Prevention (CDC) (1) and the Food and Drug Administration (FDA).(2) The main monitoring systems include:

- BEST (Biologics Effectiveness and Safety) Initiative (3)
- CMS Medical Claims Database (4)
- Vaccine Safety Datalink (VSD) (5)
- V-safe (1)
- COVID-19 Vaccine Pregnancy Registry (6)
- Clinical Immunization Safety Assessment (CISA) Project (7)
- Other claims databases (8)

The best-known and publicly accessible of these is the Vaccine Adverse Event Reporting System (VAERS), (9) established in 1990. Although anyone can submit a report, medical providers and manufacturers are required under certain conditions to do so. Limitations, including underreporting, misreporting, and stimulated reporting, are widely acknowledged by the FDA (4,10) whose own data document that mandatory reports for deaths following COVID-19 vaccination were underreported by between 9 and 36 times.(11) In addition to misreporting and reporting delays, other biases are present due to missing data or data that are inadequately captured in free-text rather than specific fields.(12)

Felonious false reporting has been proposed as a contributing factor to the fallibility of VAERS. However, this is difficult to assess since the number of prosecutions for cases of fraud has not been made public. In contrast, underreporting that violates the False Claims Act is alleged in an ongoing lawsuit.(13) Nevertheless, VAERS data are frequently cited by the FDA and CDC without adjusting for fraud. FDA has been confident of the utility of VAERS, with a former director of the Center for Biologics Evaluation and Research (CBER) co-authoring an article stating, *"VAERS works and has a track record that proves it"* with *"a proven track record of successfully helping to identify safety issues."* (14) CDC describes VAERS as *"the nation's early warning system for vaccine safety."* (15-18)

Although to describe these products. others have employed the term "gene-based prodrug," (19) we employ the term "pro-vaccine" (20,21) to more accurately describe their character. Unlike conventional vaccines, the Pfizer, Moderna, and Janssen COVID-19 pro-vaccines do not contain target antigens. Rather, they contain the genetic instructions read by a patient's body to produce the target spike protein antigen. This is somewhat analogous to the activation of a pro-drug that lacks the desired pharmacologic action, but is converted by the body to an active form.(22)

The COVID-19 pro-vaccines were introduced in the USA (Pfizer-BioNTech, December 11, 2020; Moderna, December 19, 2020; Janssen - Johnson & Johnson, February 27, 2021) under Emergency Use Authorizations (EUA). (23) VAERS was subsequently deluged by adverse event reports. A VAERS query (2/20/25) revealed that more adverse events had been reported for the COVID-19 pro-vaccines (1,023,251) than for all other vaccines (873,968) in all years combined since the inception of VAERS in 1990. These events include (COVID-19 vs Other) 19,252 vs. 5,840 deaths, 90,937 vs. 42,579 hospitalizations, 15,483 vs. 10,797 life-threatening events, 18,789 vs. 14,500 permanent disabilities, and 120,007 vs. 211,912 Emergency Room visits.

Before causality and its consequences can be determined, the volume of reports for a given type or class of AE must signal sufficient concern. The identification of a "signal" after drug approval is beset by informational and statistical challenges. In a carefully monitored clinical trial, since the administration and dose of a drug and the timing of adverse events are well-defined, comparisons between the incidence of AEs in drug and placebo-treated subjects are easily made. Once the drug enters widespread distribution, the number of people taking the drug, and the dose and timing of an adverse event are poorly defined.

Disproportionality Signal Analysis (DSA) attempts to approximate the occurrence rate of an AE by using surrogate estimates for the total exposure of patients to the drug. This rate is compared with the corresponding surrogate rate obtained for a reference drug (or drugs). This comparison aims to determine if the strength of statistical

association between a particular drug and a particular AE ("a drug-AE pair") meets certain criteria and should be declared a "signal of statistical association." It is emphasized that causality is determined only after further investigation of, *inter alia*, individual case reports, exposure data, and misreporting.(24-29)

Perhaps the most often used DSA techniques (30) are the "Evans" (PRR) (31) and Empirical Bayesian Data Mining (EBDM) (32) methods.(33,34) The PRR approach (31) uses the total number of reports for a drug-AE pair as a surrogate denominator to estimate the population event frequency. Empirical Bayesian Data Mining (EBDM) (32) calculates the Empirical Bayes Geometric Mean (EBGM) using the method known as Multi-item Gamma Poisson Shrinker (MGPS). MGPS uses modeling to adjust for random noise and other confounding (35) particularly to reduce the variability and generation of false positives (33) associated with low case counts. The development of this method was supported and incorporated by FDA (36,37) in the late 1990s (discussion of O'Neill and Szarfman appended to (32)).

Although with known limitations, (38,39) DSA is an important pharmacovigilance tool. To identify safety signals for the COVID-19 pro-vaccines, responsibility was given to CDC for the PRR analysis, and to FDA for EBDM.(40)

### *6.2 Objectives*

Some details of these analyses were recently disclosed (41) under the Freedom of Information Act (the "FOIA dataset"). Preliminary examination of these analyses suggests the presence of certain anomalies. This study seeks to explore these anomalies in the context of other data and the regulatory history of the COVID-19 pro-vaccines in this period.

## 7 METHODS

The study design involved a quantitative comparison of the number of DSA signals generated in the "FOIA dataset" with those generated in two other datasets. The READUS-PV checklist (24) was completed (section 15). p values have been cited or calculated without adjustment for multiple comparisons. Microsoft® Excel® 2016 was used for our analyses.

### *7.1 DSA Datasets*

Three datasets described below were consulted.

A limitation of VAERS-derived data is that reports made concerning a COVID-19 vaccine whose manufacturer is "UNKNOWN" may generate signals that, if properly assigned, could alter some of the analyses described here. The VIOLIN and Oracle datasets do contain signals for "UNKNOWN," but the FOIA dataset does not.

#### 7.1.1 The FOIA dataset

The "FOIA dataset" (41) covering January 6, 2021, to July 29, 2022, consisted of two parts

1) Weekly PRR analyses covering an approximately 3-month period from May 6, 2022, to July 29, 2022. The analyses were provided in Microsoft Excel files containing PRR values with ancillary statistics by MedDRA term (Medical Dictionary for Regulatory Activities).

   The PRR values compare the Pfizer and Moderna nucleoside-modified messenger RNA (modRNA) pro-vaccines with each other and collectively with other vaccines. Some stratifications based on age were provided, but there are no separate comparisons for the individual modRNA pro-vaccines with other vaccines. No PRR analyses for the Janssen adenovirus vector DNA pro-vaccine were provided. The July 2022 PRR analyses were previously disclosed under another FOIA request. (42) A further disclosure was made in 2023 on March 25 and May 6, 2022.(43)

2) EBDM analyses disclosed under a FOIA request made on June 30, 2022, (44) covering January 6, 2021, to July 1, 2022. Analyses were conducted by FDA using Empirica™ software (Oracle Corporation, Austin, TX). Previously, FDA had declined to release these analyses. (43) EBDM analyses were furnished as text tables contained in a single PDF file of 153 pages. Each approximately weekly EBDM "alert" report was embedded in an email sent from the responsible FDA team to other FDA staff as well as CDC staff. Each alert report included adverse events associated separately with the three COVID-19 pro-vaccines whose cumulative frequency had exceeded a preset signal threshold (EB05>2) for any of the stratifications used (all data, Serious, Fatal, Infant, Child, Teen, Adult - three groups, Female, Male). The EB05>2 threshold

was reached when the lower 5% confidence interval of the Empirical-Bayes Geometric Mean (EBGM) exceeded two.

These tables were not uniform in layout and often of poor resolution. Initial attempts to convert these text tables into an analyzable numerical form produced numerical errors that, even after extensive checking, would impugn the reliability of any analysis, highlighting the need for the release of high-fidelity data files under FOIA. Accordingly, we limited this review to an analysis of the textual portions of this dataset. Events by name, vaccine, and report date were exported to a Microsoft Excel spreadsheet.

### 7.1.2 The VIOLIN dataset

The second dataset consulted is the Cov19VaxKB component of the Vaccine Investigation and Online Information Network (the "VIOLIN" dataset). This online database (https://violinet.org/cov19vaxkb) (45) calculates PRR values from VAERS data and was developed with partial funding by NIH-NIAID, and by developers who included those affiliated with NIH. We extracted PRR and related data from VIOLIN on September 5, 2023. To calculate the significance of PRR values, the VIOLIN dataset uses (46) the Pearson chi-squared value, but without the Yates correction specified by Evans et al. (31) or as used in the PRR portion of the FOIA dataset. We recalculated chi-squared and associated p-values using the Yates correction.

Although the VIOLIN database is periodically updated, VIOLIN's provenance statements have been inconsistently updated. We are grateful to the developers for providing this clarification. From the VAERS database (6/20/25) via CDC's WONDER interface (https://wonder.cdc.gov/vaers.html), we checked the dating of the VIOLIN datasets by obtaining case and symptom counts, recognizing that subsequent VAERS corrections may have occurred. The COVID-19 vaccine case counts published by VIOLIN's developers (46) as originating from a VAERS version of December 31, 2021, were consistent with case counts we obtained from VAERS for November and December 2021 for the United States and territories (plus unknown location) (Supplemental Table 4B). Further, case counts for COVID-19 vaccines we extracted from VIOLIN on September 5, 2023, were consistent with VAERS data through April 2022. Case counts for non-COVID-19 vaccines for all available dates for vaccines extracted from VIOLIN on 9/5/23 were also similar to those indicated by VAERS WONDER.

We note that in the PRR portion of the FOIA dataset, CDC used data for non-COVID-19 vaccines that extended only to January 1, 2009, rather than to before 1990, as is available through VAERS WONDER. With these caveats, we are assigning a nominal date of April 30, 2022, to the data we extracted from the VIOLIN dataset on September 5, 2023. Since this date is within the range covered by the FOIA dataset of January 6, 2021, to July 29, 2022, the VIOLIN dataset provides a valid source of comparison.

### 7.1.3 The Oracle dataset

The third source of data consulted (the "Oracle dataset") was the supplemental material provided by Harpaz et al., (38) which examined DSA signals for *"five largely recognized adverse events and two potentially new adverse events"* (Appendicitis, Bell's palsy, Herpes zoster, myocarditis, pericarditis, pulmonary embolism, Tinnitus). The study used data derived from 19 fortnightly VAERS reports between weeks 3 (January 22, 2021) and 39 (October 1, 2021), overlapping the first half of the period covered by the EBDM component of the FOIA dataset. The study reported "all VAERS" reports. Based on when the EUAs were issued, signals could appear for the Pfizer and Moderna products in all 19 of the reports (weeks 3 to 39, 1/22/21 to 10/1/21), and for the Janssen product in 16 of the reports (weeks 9-39, 3/5/21 to 10/1/21).

The total case counts for both COVID-19 and non-COVID-19 vaccines were consistent with those we obtained from VAERS WONDER for a period between August 31 and September 30, 2021 (Supplemental Table 4B) for all locations (USA, territories, unknown location, Foreign). Without stratification for age or gender, the Oracle dataset provided underlying data and values for Reporting Odds Ratio (ROR), EBGM, Information Component (IC), Empirical-Bayes Regression-Adjusted Arithmetic Mean (ERAM), and Relative Reporting Ratio (RRR), along with related confidence intervals. We calculated PRR confidence intervals and chi-squared values. We corrected what appeared to be a typographical error in the abcd nomenclature used to designate cells in the 2x2 contingency table used for these data.

The affiliation for six of the eight coauthors of the paper by Harpaz et al. (38) is Oracle Health Sciences (Burlington, MA). One of these authors (Dr. DuMouchel) is the originator of the EBDM method (32) and developer of Oracle's Empirica™ software used by FDA to generate the EBGM signals. Another author is retired from FDA, and another is FDA's key biostatistician (Dr. Szarfman, Center for Drug Evaluation and Research), who collaborated in the

development and adoption by FDA of the EBDM methodology. The paper disclaims, *"The findings and conclusions expressed in this report are those of the authors and do not necessarily represent the views of the US FDA or the federal government."*

We note the possibility of confusion in how Harpaz et al., ISO 8601 (47) and CDC (48) designate "week number." This may result in a shift of one week when attempting to compare data from the different datasets. For this discussion, we used the definition given by Harpaz et al. that weeks 3 and 39 correspond to January 22 and October 1, 2021, respectively.

### *7.2 Other dataset*

CDC's vaccine use dataset https://data.cdc.gov/Vaccinations/COVID-19-Vaccinations-in-the-United-States-Jurisdi/unsk-b7fc/about_data) was also accessed. This dataset provides the cumulative daily tallies of the number of doses of COVID-19 vaccines administered from December 13, 2020, to May 10, 2023, segregated by number of people completing the initial series, additional doses, second booster doses, and bivalent doses. In addition to data collection or reporting errors (8.1.3), CDC's data are subject to other confounding due to the practice of heterologous boosting introduced in the fall of 2021.

### *7.3 Institutional Approval*

This study uses aggregated, de-identified data from publicly available databases. No institutional approval is required.

## 8 RESULTS

### 8.1 Characterization of the EBGM FOIA dataset

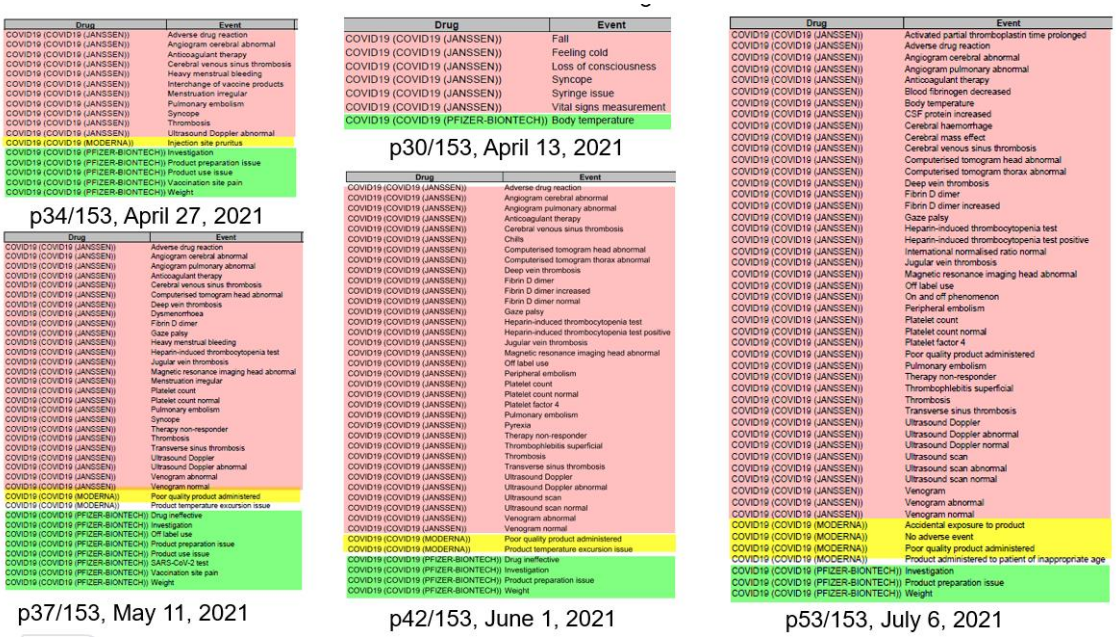
#### 8.1.1 Distribution of EBGM event signals by pro-vaccine type

For the EBDM portion of the FOIA dataset, a total of 79 weekly reports would be expected from January 6, 2021, to July 1, 2022. However, no reports were provided for 10 of these weeks. Four of the remaining 69 reports (1/10/21, 1/29/21, 2/18/21, 3/5/21) stated that there were no AEs that had met the signal threshold.

The 65 reports contained a cumulative total of 5,564 signal events, representing 189 unique signals. Some signals were reported only once, although some appeared up to 60 (median 33) times. Fifty-two of the weekly reports contained an AE signal that had not appeared previously. There were 165 (4,910), 19 (394), and 12 (260) unique event types (signal reports) for the Janssen, Pfizer, and Moderna pro-vaccines, respectively (Table 1).

A striking imbalance in the number of EBDM signal reports for the Janssen over the Pfizer and Moderna products is visually evident (Figure 1) reflecting overall numerical contributions of 89.7% (Janssen), 4.7% (Pfizer), and 5.6% (Moderna) (Figure 2).

Figure 1: Illustrative examples of data mining alerts (EB05 >2) in the FOIA dataset (highlight added)



| Drug | Event |
|---|---|
| COVID19 (COVID19 (JANSSEN)) | Adverse drug reaction |
| COVID19 (COVID19 (JANSSEN)) | Angiogram cerebral abnormal |
| COVID19 (COVID19 (JANSSEN)) | Anticoagulant therapy |
| COVID19 (COVID19 (JANSSEN)) | Cerebral venous sinus thrombosis |
| COVID19 (COVID19 (JANSSEN)) | Heavy menstrual bleeding |
| COVID19 (COVID19 (JANSSEN)) | Interchange of vaccine products |
| COVID19 (COVID19 (JANSSEN)) | Menstruation irregular |
| COVID19 (COVID19 (JANSSEN)) | Pulmonary embolism |
| COVID19 (COVID19 (JANSSEN)) | Syncope |
| COVID19 (COVID19 (JANSSEN)) | Thrombosis |
| COVID19 (COVID19 (JANSSEN)) | Ultrasound Doppler abnormal |
| COVID19 (COVID19 (MODERNA)) | Injection site pruritus |
| COVID19 (COVID19 (PFIZER-BIONTECH)) | Investigation |
| COVID19 (COVID19 (PFIZER-BIONTECH)) | Product preparation issue |
| COVID19 (COVID19 (PFIZER-BIONTECH)) | Product use issue |
| COVID19 (COVID19 (PFIZER-BIONTECH)) | Vaccination site pain |
| COVID19 (COVID19 (PFIZER-BIONTECH)) | Weight |

p34/153, April 27, 2021

| Drug | Event |
|---|---|
| COVID19 (COVID19 (JANSSEN)) | Adverse drug reaction |
| COVID19 (COVID19 (JANSSEN)) | Angiogram cerebral abnormal |
| COVID19 (COVID19 (JANSSEN)) | Angiogram pulmonary abnormal |
| COVID19 (COVID19 (JANSSEN)) | Anticoagulant therapy |
| COVID19 (COVID19 (JANSSEN)) | Cerebral venous sinus thrombosis |
| COVID19 (COVID19 (JANSSEN)) | Computerised tomogram head abnormal |
| COVID19 (COVID19 (JANSSEN)) | Deep vein thrombosis |
| COVID19 (COVID19 (JANSSEN)) | Dysmenorrhoea |
| COVID19 (COVID19 (JANSSEN)) | Fibrin D dimer |
| COVID19 (COVID19 (JANSSEN)) | Gaze palsy |
| COVID19 (COVID19 (JANSSEN)) | Heavy menstrual bleeding |
| COVID19 (COVID19 (JANSSEN)) | Heparin-induced thrombocytopenia test |
| COVID19 (COVID19 (JANSSEN)) | Jugular vein thrombosis |
| COVID19 (COVID19 (JANSSEN)) | Magnetic resonance imaging head abnormal |
| COVID19 (COVID19 (JANSSEN)) | Menstruation irregular |
| COVID19 (COVID19 (JANSSEN)) | Platelet count |
| COVID19 (COVID19 (JANSSEN)) | Platelet count normal |
| COVID19 (COVID19 (JANSSEN)) | Pulmonary embolism |
| COVID19 (COVID19 (JANSSEN)) | Syncope |
| COVID19 (COVID19 (JANSSEN)) | Therapy non-responder |
| COVID19 (COVID19 (JANSSEN)) | Thrombosis |
| COVID19 (COVID19 (JANSSEN)) | Transverse sinus thrombosis |
| COVID19 (COVID19 (JANSSEN)) | Ultrasound Doppler |
| COVID19 (COVID19 (JANSSEN)) | Ultrasound Doppler abnormal |
| COVID19 (COVID19 (JANSSEN)) | Venogram abnormal |
| COVID19 (COVID19 (JANSSEN)) | Venogram normal |
| COVID19 (COVID19 (MODERNA)) | Poor quality product administered |
| COVID19 (COVID19 (MODERNA)) | Product temperature excursion issue |
| COVID19 (COVID19 (PFIZER-BIONTECH)) | Drug ineffective |
| COVID19 (COVID19 (PFIZER-BIONTECH)) | Investigation |
| COVID19 (COVID19 (PFIZER-BIONTECH)) | Off label use |
| COVID19 (COVID19 (PFIZER-BIONTECH)) | Product preparation issue |
| COVID19 (COVID19 (PFIZER-BIONTECH)) | Product use issue |
| COVID19 (COVID19 (PFIZER-BIONTECH)) | SARS-CoV-2 test |
| COVID19 (COVID19 (PFIZER-BIONTECH)) | Vaccination site pain |
| COVID19 (COVID19 (PFIZER-BIONTECH)) | Weight |

p37/153, May 11, 2021

| Drug | Event |
|---|---|
| COVID19 (COVID19 (JANSSEN)) | Fall |
| COVID19 (COVID19 (JANSSEN)) | Feeling cold |
| COVID19 (COVID19 (JANSSEN)) | Loss of consciousness |
| COVID19 (COVID19 (JANSSEN)) | Syncope |
| COVID19 (COVID19 (JANSSEN)) | Syringe issue |
| COVID19 (COVID19 (JANSSEN)) | Vital signs measurement |
| COVID19 (COVID19 (PFIZER-BIONTECH)) | Body temperature |

p30/153, April 13, 2021

| Drug | Event |
|---|---|
| COVID19 (COVID19 (JANSSEN)) | Adverse drug reaction |
| COVID19 (COVID19 (JANSSEN)) | Angiogram cerebral abnormal |
| COVID19 (COVID19 (JANSSEN)) | Angiogram pulmonary abnormal |
| COVID19 (COVID19 (JANSSEN)) | Anticoagulant therapy |
| COVID19 (COVID19 (JANSSEN)) | Cerebral venous sinus thrombosis |
| COVID19 (COVID19 (JANSSEN)) | Chills |
| COVID19 (COVID19 (JANSSEN)) | Computerised tomogram head abnormal |
| COVID19 (COVID19 (JANSSEN)) | Computerised tomogram thorax abnormal |
| COVID19 (COVID19 (JANSSEN)) | Deep vein thrombosis |
| COVID19 (COVID19 (JANSSEN)) | Fibrin D dimer |
| COVID19 (COVID19 (JANSSEN)) | Fibrin D dimer increased |
| COVID19 (COVID19 (JANSSEN)) | Fibrin D dimer normal |
| COVID19 (COVID19 (JANSSEN)) | Gaze palsy |
| COVID19 (COVID19 (JANSSEN)) | Heparin-induced thrombocytopenia test |
| COVID19 (COVID19 (JANSSEN)) | Heparin-induced thrombocytopenia test positive |
| COVID19 (COVID19 (JANSSEN)) | Jugular vein thrombosis |
| COVID19 (COVID19 (JANSSEN)) | Magnetic resonance imaging head abnormal |
| COVID19 (COVID19 (JANSSEN)) | Off label use |
| COVID19 (COVID19 (JANSSEN)) | Peripheral embolism |
| COVID19 (COVID19 (JANSSEN)) | Platelet count |
| COVID19 (COVID19 (JANSSEN)) | Platelet count normal |
| COVID19 (COVID19 (JANSSEN)) | Platelet factor 4 |
| COVID19 (COVID19 (JANSSEN)) | Pulmonary embolism |
| COVID19 (COVID19 (JANSSEN)) | Pyrexia |
| COVID19 (COVID19 (JANSSEN)) | Therapy non-responder |
| COVID19 (COVID19 (JANSSEN)) | Thrombophlebitis superficial |
| COVID19 (COVID19 (JANSSEN)) | Thrombosis |
| COVID19 (COVID19 (JANSSEN)) | Transverse sinus thrombosis |
| COVID19 (COVID19 (JANSSEN)) | Ultrasound Doppler |
| COVID19 (COVID19 (JANSSEN)) | Ultrasound Doppler abnormal |
| COVID19 (COVID19 (JANSSEN)) | Ultrasound scan |
| COVID19 (COVID19 (JANSSEN)) | Ultrasound scan normal |
| COVID19 (COVID19 (JANSSEN)) | Venogram abnormal |
| COVID19 (COVID19 (JANSSEN)) | Venogram normal |
| COVID19 (COVID19 (MODERNA)) | Poor quality product administered |
| COVID19 (COVID19 (MODERNA)) | Product temperature excursion issue |
| COVID19 (COVID19 (PFIZER-BIONTECH)) | Drug ineffective |
| COVID19 (COVID19 (PFIZER-BIONTECH)) | Investigation |
| COVID19 (COVID19 (PFIZER-BIONTECH)) | Product preparation issue |
| COVID19 (COVID19 (PFIZER-BIONTECH)) | Weight |

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| Drug | Event |
|---|---|
| COVID19 (COVID19 (JANSSEN)) | Activated partial thromboplastin time prolonged |
| COVID19 (COVID19 (JANSSEN)) | Adverse drug reaction |
| COVID19 (COVID19 (JANSSEN)) | Angiogram cerebral abnormal |
| COVID19 (COVID19 (JANSSEN)) | Angiogram pulmonary abnormal |
| COVID19 (COVID19 (JANSSEN)) | Anticoagulant therapy |
| COVID19 (COVID19 (JANSSEN)) | Blood fibrinogen decreased |
| COVID19 (COVID19 (JANSSEN)) | Body temperature |
| COVID19 (COVID19 (JANSSEN)) | CSF protein increased |
| COVID19 (COVID19 (JANSSEN)) | Cerebral haemorrhage |
| COVID19 (COVID19 (JANSSEN)) | Cerebral mass effect |
| COVID19 (COVID19 (JANSSEN)) | Cerebral venous sinus thrombosis |
| COVID19 (COVID19 (JANSSEN)) | Computerised tomogram head abnormal |
| COVID19 (COVID19 (JANSSEN)) | Computerised tomogram thorax abnormal |
| COVID19 (COVID19 (JANSSEN)) | Deep vein thrombosis |
| COVID19 (COVID19 (JANSSEN)) | Fibrin D dimer |
| COVID19 (COVID19 (JANSSEN)) | Fibrin D dimer increased |
| COVID19 (COVID19 (JANSSEN)) | Gaze palsy |
| COVID19 (COVID19 (JANSSEN)) | Heparin-induced thrombocytopenia test |
| COVID19 (COVID19 (JANSSEN)) | Heparin-induced thrombocytopenia test positive |
| COVID19 (COVID19 (JANSSEN)) | International normalised ratio normal |
| COVID19 (COVID19 (JANSSEN)) | Jugular vein thrombosis |
| COVID19 (COVID19 (JANSSEN)) | Magnetic resonance imaging head abnormal |
| COVID19 (COVID19 (JANSSEN)) | Off label use |
| COVID19 (COVID19 (JANSSEN)) | On and off phenomenon |
| COVID19 (COVID19 (JANSSEN)) | Peripheral embolism |
| COVID19 (COVID19 (JANSSEN)) | Platelet count |
| COVID19 (COVID19 (JANSSEN)) | Platelet count normal |
| COVID19 (COVID19 (JANSSEN)) | Platelet factor 4 |
| COVID19 (COVID19 (JANSSEN)) | Poor quality product administered |
| COVID19 (COVID19 (JANSSEN)) | Pulmonary embolism |
| COVID19 (COVID19 (JANSSEN)) | Therapy non-responder |
| COVID19 (COVID19 (JANSSEN)) | Thrombophlebitis superficial |
| COVID19 (COVID19 (JANSSEN)) | Thrombosis |
| COVID19 (COVID19 (JANSSEN)) | Transverse sinus thrombosis |
| COVID19 (COVID19 (JANSSEN)) | Ultrasound Doppler |
| COVID19 (COVID19 (JANSSEN)) | Ultrasound Doppler abnormal |
| COVID19 (COVID19 (JANSSEN)) | Ultrasound Doppler normal |
| COVID19 (COVID19 (JANSSEN)) | Ultrasound scan |
| COVID19 (COVID19 (JANSSEN)) | Ultrasound scan abnormal |
| COVID19 (COVID19 (JANSSEN)) | Ultrasound scan normal |
| COVID19 (COVID19 (JANSSEN)) | Venogram |
| COVID19 (COVID19 (JANSSEN)) | Venogram abnormal |
| COVID19 (COVID19 (JANSSEN)) | Venogram normal |
| COVID19 (COVID19 (MODERNA)) | Accidental exposure to product |
| COVID19 (COVID19 (MODERNA)) | No adverse event |
| COVID19 (COVID19 (MODERNA)) | Poor quality product administered |
| COVID19 (COVID19 (MODERNA)) | Product administered to patient of inappropriate age |
| COVID19 (COVID19 (PFIZER-BIONTECH)) | Investigation |
| COVID19 (COVID19 (PFIZER-BIONTECH)) | Product preparation issue |
| COVID19 (COVID19 (PFIZER-BIONTECH)) | Weight |

p53/153, July 6, 2021

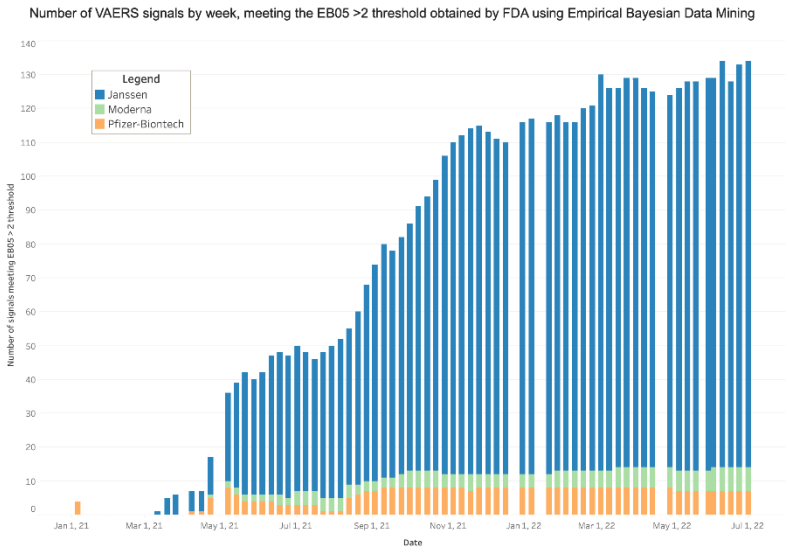
These examples were selected because their length was suitable for display on a printed page. Only the first two columns of each report are displayed here. Pink (Janssen), yellow (Moderna), and green (Pfizer) highlights have been added here. Each row represents an adverse event (Preferred Term, PT) for which an EB05>2 signal was present for at least one of the stratifications used. A typical description accompanying each alert (e.g. email dated June 1, 2021, p42/153), reads:

*"Attached please find a list of all (i.e., unvetted and regardless of notability) PTs with data mining alerts (i.e., EB05 >2) for all EUA SARS-CoV-2 vaccine VAERS reports from our weekly 'US Signals Summary Table' ('as of date' 5/28/21). Please feel free to share this hypothesis-generating output with your team/command chain, though this is not intended to be shared more broadly."*

The possibility was entertained that the tables provided in the FOIA disclosure contain only the upper portion of the table included in the spreadsheet file accompanying each email alert, whereas, in reality, the email recipients received a lengthier report. However, when comparing the four leftmost examples in Figure 1 with the rightmost example, it is evident that had there been more signals for Pfizer, there would have been sufficient room on a single page for display. Further, had there been more alerts of Moderna, the Pfizer alerts would have run off the page.

There is also the possibility that the tables provided in the FOIA disclosure did not represent the extent of the information shared in FDA's email alerts; rather, they represent incomplete disclosure under FOIA. The attorneys originating the FOIA request (44) confirmed that the disclosure contained only the 153 PDF document with no accompanying data files.

Figure 2: Number of VAERs signals for COVID-19 pro-vaccines by week, meeting the EB05>2 threshold obtained by FDA using Empirical Bayesian Data Mining.




The reports of 1/10/21, 1/29/21, 2/18/21, and 3/5/21 stated that there were no AEs that met the threshold signal. Zero values at other times indicate that no report was provided. See Supplemental Table 11 for underlying data and charts for individual pro-vaccines.

Table 1: Distribution of EBDM signals by vaccine type in the FOIA dataset, accumulated over the period reported

| Drug | # Unique AE types | Total AE signals | AEs % of total | # Unique Non-abnormal signals | Total non-abnormal AE signals | Unique abnormal AE types | Total abnormal AE signals | Abnormal AE % of Total |
|---|---|---|---|---|---|---|---|---|
| **PFIZER** | 19 | 394 | 7.1% | 6 | 187 | 13 | 207 | 4.7% |
| **MODERNA** | 12 | 260 | 4.7% | 1 | 16 | 11 | 244 | 5.6% |
| **JANSSEN** | 165 * | 4910 | 88.2% | 23 | 989 | 142* | 3921 | 89.7% |
| **UNKNOWN** | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | | | | | | | | |
| **Janssen / Pfizer SER** | | 12.46 | | | | | 18.94 | |
| **Janssen / Moderna SER** | | 18.88 | | | | | 16.07 | |

* Reflecting poor image resolution or extraction, two events appear to have duplicate designations.
"COV D-19 pneumonia" and "COVID-19 pneumonia"
"Suspected COV D-19" and "Suspected COVID-19"
Accordingly, the number of unique AE types for the Janssen pro-vaccine should be 163 and 140 in the two columns indicated.

SER Signal Excess Ratio

See Supplemental Table 9 for full signal listing by date and manufacturer.

Thirty event types (Supplemental Table 1) accounting for 1192 AE signal reports did not appear to indicate an abnormality, merely, in most cases, that a test had been performed (e.g. "Platelet count"), yielding, in some cases, a normal value (e.g. "Platelet count normal"). Subtracting these "non-abnormalities" from the total tally, there were 13 (207), 11 (244), and 142 (3921) unique event types (signal reports) for the Pfizer, Moderna, and Janssen pro-vaccines, respectively (Table 1). Only six unique signal types were shared by two of the pro-vaccines, and one event (Product administered to patient of inappropriate age) was shared by all three (Supplemental Table 10).

### 8.1.2 Distribution of EBGM signals by event type and category

Detail of the EBDM signals for the COVID-19 pro-vaccines in the FOIA dataset is shown in Table 2. Each event type was also categorized using the Common Toxicity Criteria (CTC) (49), and the numbers of event types and event signals contributing to each category were tabulated (Supplemental Table 2).

Table 2: Frequency and number of alerts for abnormal adverse event EBDM signal types for COVID-19 pro-vaccines

| **Pfizer** | | | | **Moderna** | | | | **Janssen** | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **EVENT** | **N[a]** | **First[b]** | **Cat[c]** | **EVENT** | **N[a]** | **First[b]** | **Cat[c]** | **EVENT** | **N[a]** | **First[b]** | **Cat[c]** | **Sub[c]** |
| Product preparation issue | 59 | 210423 | USE | Product administered to patient of inappropriate age | 52 | 210618 | USE | Thrombosis | 60 | 210416 | CVG | TE |
| Drug ineffective | 50 | 210507 | P | Exposure via breast milk | 42 | 210827 | REP | Ultrasound Doppler abnormal | 59 | 210423 | SYN | OTH |
| Exposure via breast milk | 44 | 210813 | REP | Product dose omission issue | 38 | 210924 | USE | Therapy non-responder | 59 | 210416 | P | |
| Disease recurrence | 33 | 210827 | P | Interchange of vaccine products | 30 | 211119 | USE | Pulmonary embolism | 59 | 210423 | CVG | TE |
| Product administered to patient of inappropriate age | 9 | 210910 | USE | Mechanical urticaria | 22 | 220128 | DER | Cerebral venous sinus thrombosis | 59 | 210423 | CVG | TE |
| Product use issue | 3 | 210423 | USE | Poor quality product administered | 17 | 210507 | USE | Angiogram cerebral abnormal | 59 | 210423 | N | |
| Vaccination site pain | 3 | 210423 | PAIN | Vaccination complication | 15 | 220318 | SYN | Adverse drug reaction | 59 | 210423 | SYN | |
| Incorrect dose administered | 1 | 211112 | USE | Product temperature excursion issue | 12 | 210507 | USE | Venogram abnormal | 58 | 210507 | CVG | TE |
| Off label use | 1 | 210507 | USE | Headache | 8 | 211001 | PAIN | Magnetic resonance imaging head abnormal | 58 | 210507 | N | |
| Paraesthesia oral | 1 | 210106 | N | Accidental exposure to product | 7 | 210702 | USE | Jugular vein thrombosis | 58 | 210507 | CVG | TE |
| Dysgeusia | 1 | 210106 | GAS | Injection site pruritus | 1 | 210423 | DER | Gaze palsy | 58 | 210507 | N | |
| Flushing | 1 | 210106 | DER | | | | | Deep vein thrombosis | 58 | 210507 | CVG | TE |
| Palpitations | 1 | 210106 | ARY | | | | | Computerised tomogram head abnormal | 58 | 210507 | N | |
| | | | | | | | | Angiogram pulmonary abnormal | 58 | 210507 | CVG | TE |
| | | | | | | | | Transverse sinus thrombosis | 57 | 210507 | CVG | TE |

Event types are listed in descending order of frequency within the FOIA dataset.
Only the top 15 events are shown for Janssen. A list of all AE signals is provided in Supplemental Table 2.

[a] Number of weekly reports that include this signal
[b] Date of first report (YYMMDD)
[c] CTC event category (see Supplemental Table 2).

An overall impression emerges:

- The cumulative number of event signals for the Janssen pro-vaccine in the FDA's EBDM analysis far exceeded that for Pfizer and Moderna by (in aggregate over the whole period) 12.46 (4910/394) and 18.88 (4910/260) times (the "signal excess ratio," SER), respectively. Excluding events that did not indicate an abnormality, these ratios were 18.94 (3921/207) and 16.07 (3921/244), respectively.
- These ratios would be greater when considering the large contribution of product use-related events (e.g. administration, dose, and quality issues or errors) for the Moderna (63.9%) and Pfizer (35.3%) compared with the Janssen (3%) pro-vaccine.
- The variety of event types where an abnormality was indicated was greater for the Janssen product, spanning 140 event types in 13 CTC categories, contrasting with 11 event types in 5 categories (Moderna) and 13 event types in 8 categories (Pfizer).
- Hematologic (thrombo-embolic, coagulation) events accounted for 30.1% of the signals for Janssen, but were absent from the Pfizer and Moderna signals.
- There were no signals for myocarditis or pericarditis in the FDA's EBDM analysis.
- There were, cumulatively, 17 event signals for death for the Janssen pro-vaccine, and none for the Pfizer of Moderna pro-vaccines.
- There were, cumulatively, 48 event signals for Guillain-Barré syndrome for the Janssen pro-vaccine, and none for the Pfizer or Moderna pro-vaccines.

### 8.1.3 Disproportion of EBGM event signals normalized for population exposure

Expressed as the Signal Excess Ratio (SER), the disproportionate fold excess of the number of EBGM signals for the Janssen COVID-19 pro-vaccines compared with the Pfizer and Moderna products must be normalized for the relative usage of the pro-vaccines. This was done using data from CDC's vaccine use dataset. Although we have assumed linearity, the number of signals generated for any vaccine will eventually plateau as a function of usage, as the number of truly associated AEs yet to be recognized dwindles. This relationship may vary by vaccine type.

The "Relative Use Ratio" (RUR) and "Use Normalized Signal Excess Ratio" (UNSER) of the Pfizer or Moderna product compared with the Janssen product were (Supplemental Tables 3A and 3B) derived from either:

- The number of people given at least one vaccine dose. Not everyone who received a first dose received subsequent doses. To the number of people completing the initial series was added the number of people receiving only one dose obtained by subtracting the various dose types from the total administered and adjusting for a two (Pfizer or Moderna) or one (Janssen) dose initial series (Supplemental Table 3A).

  For each EBDM "as of" alert date, the corresponding SER and RUR values were calculated (Supplemental Tables 3A and 3B). All "as of" dates for the FOIA dataset email alerts matched with a date available in CDC's vaccine use dataset, except two for which the closest prior date was used.

  Likely reporting delays or other inconsistencies in the CDC vaccine use dataset resulted in two minor anomalies. Firstly, for some dates, there were negative numbers of people receiving only one dose. These were removed by taking two-day backward-moving averages for each of the ratios calculated. Secondly, an anomaly for the Janssen product yielded a small (<2%) "number of people receiving only one dose" that was greater than zero after subtracting the various dose types from the total administered.

  A Use Normalized Signal Excess Ratio (UNSER) was obtained by multiplying the SER and RUR for each date. Median and range SER, RUR, and UNSER values were obtained for the span of dates represented in the EBDM FOIA dataset (Supplemental Table 3B), summarized in Table 3.

  The UNSER values for the Jansen product compared with the Pfizer and Moderna products were 112 and 104, respectively, based on the number of people who received at least one vaccine dose. This method of calculating UNSER was used hereafter, since it yields more conservative estimates than normalizing by dose.

- The total number of doses administered. The median use-normalized signal excess ratios for the Jansen product over the Pfizer and Moderna products were 206 and 213, respectively, based on the total number of doses administered.

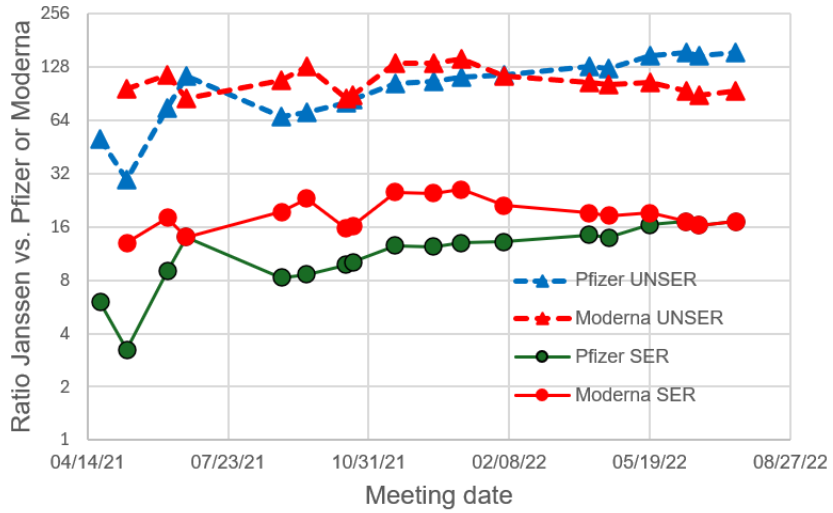
Table 3: Signal Excess, Relative Use, and Use Normalized Signal Ratios for the EBDM FOIA dataset

| | SER | | Method | RUR | | UNSER | |
|---|---|---|---|---|---|---|---|
| | **Janssen** | **Janssen** | | **Pfizer to** | **Moderna** | **Janssen** | **Janssen** |
| | **Pfizer** | **Moderna** | | **Janssen** | **Janssen** | **Pfizer** | **Moderna** |
| **All dates in FOIA dataset (1/6/21 to 7/1/22)** | | | | | | | |
| **Median** [a] | 13.0 (9-14) | 18.83 (16-22) | **N >=1 dose** | 8.60 (8.2-9) | 5.43 (5.4-5.7) | 112.3 (76-126) | 103.7 (92-123) |
| | | | **Total doses** | 16.08 (14.7-17.8) | 11.25 (10.4-11.6) | 206.2 (138-261) | 213.1 (174-234) |
| **4/29/22 (closest prior date to nominal VIOLIN date of 4/20/22)** | | | | | | | |
| **Point value** | 13.75 | 18.33 | **N >=1 dose** | 8.96 | 5.41 | 123.15 | 99.16 |
| | | | **Total doses** | 18.15 | 11.58 | 249.57 | 212.38 |

SER Signal Excess Ratio (expressed here as Janssen to Pfizer or Moderna)
RUR Relative Use Ratio
UNSER Use Normalized Signal Excess Ratio
[a] Median (interquartile range) values across all dates in FOIA dataset. Note the aggregate values based on total EBDM signal counts are (12.46 (Pfizer) and 18.88 (Moderna).
See also Supplemental Table 3B

The persistence of the large crude (SER) and Use Normalized (UNSER) excess of Janssen EBDM signals compared with Pfizer of Moderna over the period covered by the FOIA dataset is shown in Figure 3, as of the dates of ACIP or VRBPAC meetings during that time.

Figure 3: Time course of disproportionate excess (Janssen) and dearth (Pfizer, Moderna) of EBGM signals in the FOIA dataset relative to ACIP and VRBPAC meeting dates: Signal Excess (SER) and Use Normalized Signal Excess (UNSER) Ratios




The number of EBDM signals for each COVID-19 pro-vaccine in the FOIA dataset was determined (Supplemental Table 9) for each date just before the seventeen relevant ACIP or VRBPAC meetings convened between April 16, 2021, and July 1, 2022 (the date for the last report in the FOIA dataset). Signal Excess (SER, solid lines) and Use Normalized Signal Excess (UNSER, dashed lines) Ratios were calculated using data for the closest date preceding each meeting, based on the excess of Janssen over Pfizer (blue lines) or Moderna (red lines) signals, normalized for the number of people receiving at least one dose of pro-vaccine (Supplemental Table 3A). Note the logarithmic Y-axis.

### 8.1.4 Disproportion of EBGM event signals normalized for the total number of AE reports to VAERS

As a further check on the plausibility of the disproportionate number of AE signals for the Janssen product, the relative occurrence of VAERS reports derived from several sources was calculated (Supplemental Table 4A). The median fold-excesses of VAERS-reported unique patient events for Pfizer and Moderna over the Janssen products were 5.3 and 5.4, respectively. The median fold-excesses of unique symptom reports for the Pfizer and Moderna over the Janssen products were 4.8 and 4.9, respectively. Combining these figures with the median SER (Table 3) suggests that a report to VAERS involving the Janssen pro-vaccine was more likely to generate an EBGM signal than for the Pfizer and Moderna pro-vaccines by factors of about 62-69 and 90-99, respectively.

## 8.2 Disproportion of EBDM signals in the context of PRR signals derived from the VIOLIN dataset

### 8.2.1 Characterization of PRR signals derived from the VIOLIN dataset

To understand whether the disproportion of EBDM signals in the FOIA dataset was due to an inherent disproportion in signals derived from VAERS in general, or a feature of the particular analyses reported in the FOIA dataset, we examined the PRR signals generated by the VIOLIN dataset. This was necessary because the FOIA disclosure contained no Pfizer- or Moderna-specific PRR analyses, or any PRR analyses for Janssen.

What became accepted as the “canonical Evans” (38) criteria set the PRR threshold at 2, with at least three case reports and a chi-squared value of at least 4.(31) To declare a “signal,” VIOLIN modifies (the “modified” Evans criteria) the canonical criteria by adding the condition that the number of cases for a particular AE must be >0.2% (50) of the total number (Table 4). This condition is not used in the canonical criteria (31) nor in the VAERS SOP. (40) It is inconsistent with the intent of the Evans method to detect frequency changes in uncommon events. In reality, this condition does not change whether or not there is a statistical association; it merely superimposes a filtering condition to “*provide[d us] better manageability of the sets of AEs studied.”* (50)

Table 4: Summary of the three types of “Evans” criteria for assessing PRR values

| Type | PRR threshold | Number of events | Chi-squared | Citation |
|---|---|---|---|---|
| **Canonical Evans** | 2 | ≥3 | ≥ 4 with Yates’ correction | (31) |
| **Modified Evans** | 2 | ≥3<br>>0.2% of total | ≥ 4<br>VIOLIN uses Pearson's version | VIOLIN (45,46,50) |
| **Alternative Evans** | * | ≥3 | Based on the confidence interval | (31) |

***** For the present work, we use a threshold of 1

We consulted three sources of PRR signals derived from the VIOLIN database (Supplemental Table 5E) covering roughly the midpoint of our study period. Two of these were derived from publications by the database developers. (45,46) The third dataset was obtained by extracting PRR signals from the online database, from which the number of PRR signals was tallied using canonical, modified, and alternative Evans criteria.

The use of the Pearson (46) chi-squared value by the VIOLIN dataset yields 10-39% more (Supplemental Table 5E) canonical PRR signals than if the Yates version is used as specified in the original paper (31) or as used in the PRR portion of the FOIA dataset. The relative proportions of Pfizer, Moderna, and Janssen signals are approximately the same.

Focusing on signals generated using the Yates chi-squared values as of the index date of 4/30/22, the number of modified PRR signals for the Pfizer and Janssen pro-vaccines was approximately the same, but lower for the Moderna pro-vaccine, whose Moderna to Janssen ratio was 0.29 (Supplemental Table 5E).

As expected, modifying the Evans criteria reduces the number of PRR signals obtained using the canonical criteria, in fact, by up to about 90% (Supplemental Table 5E). However, using the canonical Evans criteria also yielded differences in the relative numbers (SER) of PRR signals for the three pro-vaccines. There were nearly double (1.86x, Pfizer) and two-thirds (0.61x) the number of Moderna PRR signals compared with those for Janssen. Adjusting these figures for the RUR (Pfizer 8.96, Moderna 5.41, Table 3) yields normalized PRR signal fold excesses (UNSER) for Janssen over Pfizer and Moderna of 4.82 (8.96/1.86) and 8.8 (5.41/0.61), respectively (Table 5, row J).

The observation that the signaling criteria may influence the absolute and relative behavior of the three pro-vaccines prompted further examination. The original publication describing the PRR method (31) was not rigid in

defining the criteria (> 2 case reports, PRR >2, chi-squared>4), proposing that *"*[a]*n equivalent alternative to chi-squared is to calculate a confidence interval around the PRR."*

As discussed below (10.1.2) use of a threshold of two does not change whether or not there is a statistical association; it merely superimposes a filtering condition. Accordingly, we apply here the "alternative Evans criteria" to declare a statistical association (i.e. a signal) at a threshold of PRR > 1 and p <0.05 (Table 4). The p-value was chosen as the statistical component of the signal criteria, rather than a confidence interval, since the VIOLIN dataset reported p-values for each vaccine-AE pair. Some limitations are noted (10.1.4).

Applying the "alternative Evans criteria" (p<0.05, Yates chi-squared) to the VIOLIN 4/30/22 dataset yields 48% (Pfizer), 152% (Moderna), and 51% (Janssen) more signals (Supplemental Tables 5E and 12) than using the canonical Evans criteria. These criteria also change the relative behavior of the three pro-vaccines (1.83, Pfizer vs. Janssen; 1.03, Moderna vs. Janssen). Normalizing for use yields alternative PRR signal fold excesses (UNSER) for Janssen over Pfizer and Moderna of 4.90 (8.96/1.83) and 5.25 (5.41/1.03), respectively (Table 5, row M).

Further exploration of the relationship between threshold values and signal generation, yielded plots (Supplemental Tables 5A and 5B) that indicate:

- Strong negative linear correlations ($R^2$ >0.93) between the number of signals generated and the threshold.
- Similar regression lines, both in terms of slope and intercept, for the Pfizer and Moderna pro-vaccines.
- A regression line for the Janssen pro-vaccine compared with the two modRNA products with a steeper slope and a greater intercept, reflecting the approximately 4.82 (Pfizer) to 8.8 (Moderna) -fold adjusted excess (UNSER) of PRR signals (Table 5, row J).

Table 5. Relative occurrence of EBGM (FOIA dataset) and PRR (VIOLIN dataset) signals from VAERS for COVID-19 pro-vaccines, normalized for population exposure

| Line | Ratio type (vs Janssen) | Math ** | Pfizer | Moderna | Janssen | Date | Source |
|---|---|---|---|---|---|---|---|
| **A** | Ratio, number of people given ≥1 dose RUR (based on CDC date 4/29/22) | | 8.96 | 5.41 | 1 | 4/30/22 | Supp Tab 3A |
| **B** | **Total EBGM signals** | | 394 | 260 | 4910 | 1/6/21 - 7/1/22 | Table 1 |
| **C** | Ratio, SER, aggregate (SER)<br>Median | from B | 1/12.46<br>1/13 | 1/18.88<br>1/18.83 | 1<br>1 | | Supp Tab 3B |
| **D** | Ratio, normalized to # people >-1d (UNSER)<br>(Median from paired estimation Supp Tab 3B) | Equiv to C/A | 1/112 | 1/104 | | | Table 3 |
| | | | | | | | |
| **E** | **Abnormal EBGM signals only** | | 207 | 244 | 3921` | 1/6/21 - 7/1/21 | Table 1 |
| **F** | Ratio, abnormal EBGM signals (SER) | from E | 1/18.94 | 1/16.07 | 1 | | |
| **G** | Ratio, normalized to # people (UNSER)<br>(based on median RUR for all alerts Pfizer 8.6, Moderna 5.43, Supp Tab 3B) | Equiv to F/A | 1/170 | 1/87 | 1 | | |
| | | | | | | | |
| **H** | **PRR Signals (Canonical Evans, Yates)** | | 1485 | 491 | 799 | 4/30/22 | Suppl Table 5E |
| **I** | Ratio, PRR signals SER | from H | 1.86 | 0.61 | 1 | | |
| **J** | Ratio, normalized to # people >= 1 dose UNSER | I/A | 1/ 4.82 | 1/8.8 | 1 | | |
| | | | | | | | |
| **K** | **PRR Signals (Alternative Evans, Yates, p value)** | | 2197 | 1238 | 1203 | 4/30/22 | Suppl Table 5E |
| **L** | Ratio, PRR signals SER | from K | 1.83 | 1.03 | 1 | | |
| **M** | Ratio, normalized to # people UNSER | L/A | 1/ 4.9 | 1/ 5.25 | 1 | | |

** Using the line identifier from the first column, this indicates how each ratio was derived.
SER Signal Excess Ratio (Pfizer or Moderna to Janssen)
RUR Relative Use Ratio
UNSER Use Normalized Signal Excess Ratio
All values are the median, except where noted.
The aggregate value is based on the total number of EBDM signals for the three products.

### 8.2.2 Signal truancy as a source of EBDM signal disproportion in the FOIA dataset

Implicit in CDC's statement that the disclosed PRR analyses (42) *"generally corroborated findings from Empirical Bayesian (EB) data mining,"* is the expected correlation between the numbers of PRR and EBGM signals. This was borne out (8.3) in an analysis of the Oracle dataset (Figure 5).

Using this principle, we compared the vaccine-specific UNSERs derived from near-contemporaneous data (4/29/22) in the VIOLIN and FOIA datasets (Table 6). The lack of similarity between the two sets of values suggests that EBGM signals are missing from the FOIA dataset. Dividing the FOIA UNSER by the VIOLIN UNSER yields "Truancy Factors" of 25.6 (123.2/4.82) for Pfizer and 11.3 (99.2/8.8) for Moderna (Supplemental Table 14). These truancy factors represent respective losses of 96.1% (N=204) and 91.1% (N=68) signals (individual AE types for each pro-vaccine). It is assumed that there were no signals lost for the Janssen product. (It is noted that when similarly dated data are being compared, as in the above example, the truancy factor is independent of the RUR).

Using the equivalent ratios (UNSER) of 4.9 and 5.25 derived from the alternative PRR criteria (Table 5, row M) yields, respectively, truancy factors of 25.1 (123.2/4.9, 96% signal loss) and 18.9 (99.2/5.26, 94.7% signal loss) for Pfizer and Moderna (Supplemental Table 14).

Plotting the number of canonical PRR signals from the VIOLIN dataset for each pro-vaccine against the corresponding number of EBDM signals from the FOIA dataset yields (Figure 4), contrary to expectations (e.g. Figure 5), a trendline with a negative slope and an extremely low $R^2$ value. Since these plots act as fingerprints to characterize the data, differences in the data "fingerprint" further suggest a disturbance of FOIA dataset integrity. However, adjusting the number of EBGM signals using the truancy factors yields a trendline with a strong positive slope, consistent with the expected relationship between PRR and EBGM signals found with the Oracle dataset (Figure 5).

Table 6: Correspondence of PRR and EBGM Signals in the VIOLIN and FOIA datasets

| **Signal Type** | **PRR** | **EBGM** | **EBGM** | **EBGM** | **EBGM** | **EBGM** | **EBGM** |
|---|---|---|---|---|---|---|---|
| **Database** | VIOLIN | FOIA | FOIA | FOIA | FOIA | FOIA | FOIA |
| **Date** | 4/30/22 [c] [g] | 4/29/22 [c] | Truancy adjusted [b] | N signals lost | % signals lost | 1/6/21 to 7/1/22 [d] | 1/6/21 to 7/1/22 [d] |
| **Vaccine Type** | | | | | | | |
| Pfizer | 1485 | 8 | 204 | 196 | 96.1% | 394 | |
| Moderna | 491 | 6 | 68 | 62 | 91.1% | 260 | |
| Janssen | 799 | 110 | 110 | 0 | 0.0% | 4910 | |
| | | | | | | | |
| **SER** | | | | | | | |
| Pfizer to Janssen | 1.86 | 0.07 | | | | 0.08 | |
| Moderna to Janssen | 0.61 | 0.05 | | | | 0.05 | |
| **RUR (from CDC data)** | | | | | | | |
| Pfizer to Janssen | 8.96 | | | | | 8.60 | |
| Moderna to Janssen | 5.41 | | | | | 5.43 | |
| **UNSER [e]** | | | **Truancy Factor [a]** | | | | **Truancy Factor [f]** |
| Pfizer to Janssen | 4.82 | 123.15 | 25.56 | | | 112.32 | 23.31 |
| Moderna to Janssen | 8.80 | 99.16 | 11.27 | | | 103.65 | 11.78 |

Data from Supplemental Tables 3B, 9 and 14.

SER Signal Excess Ratio: expressed here as Pfizer or Moderna to Janssen

RUR Relative Use Ratio

UNSER Use Normalized Signal Excess Ratio of Janssen to Pfizer or Moderna = RUR/SER

a Truancy factor calculated by dividing the UNSER for the FOIA dataset by the corresponding value for the VIOLIN dataset.

b EBDM (EB05>2) signals or each vaccine adjusted for truancy by multiplying the number of signals in the FOIA dataset by the truancy factor.

c Canonical VIOLIN PRR signal numbers with a nominal date of 4/30/22 are compared with near-contemporaneous EBGM signal numbers in the FOIA dataset with an alert report "as of date" of April 29, 2022.

d Total number of signals accumulated over the entire period of EBDM reports in the FOIA dataset (Table 1). Median RUR and aggregate UNSER values from 1/6/21 to 6/29/22 shown. See Supplemental Table 3B.

e UNSER obtained by dividing the RUR by the SER.

f See text for caveats

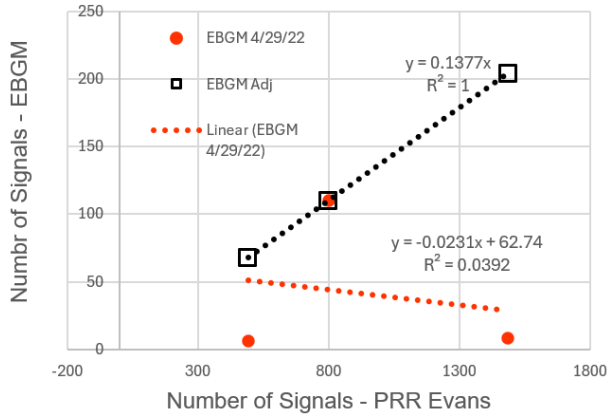
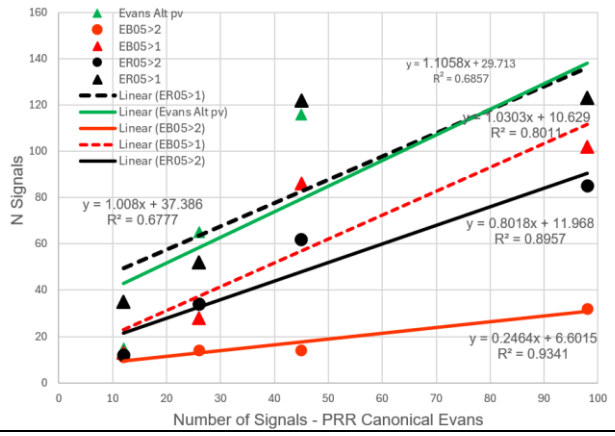
g The tally does not include 112 (77, Pfizer; 34, Moderna; 1, Janssen) signals for which the case count is >2, but with zero comparator cases (listed in Supplemental Table 22).

Ideally, truancy and signal loss could be estimated for each FOIA dataset alert and aggregated to obtain an estimate of total signal loss over the entire period covered by the FOIA dataset. This is not possible for two main reasons. Firstly, six of the ten dates for which no alert report was issued were in the first three months of 2021 (Supplemental Table 9), potentially skewing data from the initial rollout of the pro-vaccines. Secondly, we lack the equivalent PRR data from which to calculate truancy factors for each alert report.

With these caveats, it is possible to produce a *de minimis* approximation of overall truancy and signal loss in the FOIA dataset by relying on the similarity between the median RUR values across the whole period (1/6/21-7/1/22) covered by the EBDM alerts (Supplemental Table 3B) in the FOIA dataset (Pfizer 8.6, Moderna 5.43) and the RUR point values for the VIOLIN dataset of 4/30/22 (Pfizer 8.96, Moderna 5.41). This approach yields UNSER values of 112 and 104 (Table 5, row D) for the EBGM signals. Dividing this figure by the UNSER values for canonical PRR signals of 4.82 and 8.8 (Table 5, row J) yields aggregate truancy factors of 23.1 (112/4.82, range 4.1-77, 95.7% signal loss) for Pfizer and 11.8 (104/8.8, range 6.3-16.2, 91.5% signal loss) for Moderna.

Using the equivalent UNSER values for alternative PRR criteria (Pfizer 4.9, Moderna 5.26), yields, respectively, truancy factors of 22.9 (range 4-76, 95.6% loss) and 19.7 (range 10.6-27, 95% loss). (Supplemental Table 18). These values are highly consistent with those obtained from the date-specific comparison described above. Further, a plot of the cumulative number of EBGM signals in the FOIA dataset against the number of PRR signals

in the VIOLIN dataset yields a negative slope with a very small $R^2$ value, consistent with a disturbance in FOIA dataset integrity (Supplemental Table 14).

| Figure 4: Correlation between PRR (VIOLIN) and EBGM (FOIA) Signals Generated in VAERS, with truancy adjustment | Figure 5: Correlation between PRR and EBGM Signals Generated in VAERS (Oracle dataset) |
|---|---|
|  |  |
| See Table 5 for source data for PRR Evans (canonical) signals from the 4/30/22 VIOLIN dataset, using Yates' chi-squared. EBGM data are those from the 4/29/22 email alert in the FOIA dataset (see Supplemental Table 9).<br>Signals are plotted for Pfizer, Moderna, Janssen, but not "Unknown Manufacturer" as there were none in the FOIA dataset.<br>To adjust EBGM signals for truancy, RUR and UNSER values derived from CDC data of 4/29/22 were used (Supplemental Table 14)<br>See Supplemental Figures 1A and 1B for similar correlations using cumulative EBDM data from the FOIA dataset. | The number of signals is the number apparent as of 10/1/21 and plotted for Pfizer, Moderna, Janssen, and "Unknown Manufacturer."<br>See<br><br>Table 8 for source data and Supplemental Table 15 |

### *8.3 Further exploration of EBDM signals in the FOIA dataset through the lens of the Oracle dataset*

Examination of the Oracle dataset permits further exploration of anomalies in the FOIA dataset. There are advantages and limitations to Oracle's consideration of both US- and foreign-originating VAERS reports. Expanding the study population by including foreign-originating VAERS reports potentially increases the power to detect safety signals, essentially for hypothesis generation in a system represented as an "early warning for vaccine safety." (15-18) However, calculations of relative vaccine use, signal generation, and truancy are limited because of differences in the relative:

- domestic (US) and foreign use of the three COVID-19 pro-vaccines.
- pattern of domestic and foreign reporting into VAERS, despite the requirement that manufacturers report certain AEs originating outside the USA.

Although PRR or Empirical Bayesian values should be stratified by originating source, the omission of foreign-derived safety signals from FDA's EBDM analysis in the FOIA dataset is material, necessitating the following discussion.

#### 8.3.1 Oracle dataset clues about Pfizer and Moderna EBDM signal truancy in the FOIA dataset

Signals for the seven AEs studied in the Oracle dataset (Supplemental Table 13, Figure 7), differed in number and timing from their counterparts in the FOIA dataset (Table 2).

Using FDA's EB05>2 threshold, nine myocarditis-Pfizer signals were present in the Oracle dataset beginning week 21 (5/28/21) but were absent from the FOIA dataset (Table 2). Alternative PRR signals appeared in week 19, EB05>1 signals in week 17, and ER05>1 (see below) signals in week 9. No EB05>2 Moderna-myocarditis signal was present, but alternative PRR, EB05>1, and ER05>1 signals were present from week 5. There were no EB05>2 signals for pericarditis in either dataset for any pro-vaccine. There were PRR (both methods), EB05>1, and ER01>1 pericarditis signals for the Pfizer and Moderna pro-vaccines in the Oracle dataset starting week 7 (except Pfizer EB05>1, week 9).

One Bell's palsy EB05>2 signal was present in the Oracle dataset associated with the Pfizer pro-vaccine in week 9, with 19 (out of a possible 19) signals meeting the other three criteria. This signal was absent from the FOIA dataset. PRR (both methods) and Moderna-Bell's palsy EB05>1 signals were present in the Oracle dataset.

For tinnitus, no EB05>2 signals for either modRNA pro-vaccine were present in the Oracle dataset, although between 11 and 19 signals met each of the other three criteria. Three tinnitus EB05>2 signals for the Janssen pro-vaccine beginning week 15 were found, but were absent from the FOIA dataset. Between 9 and 15 signals were found for each of the other signal thresholds. Up to 403 neurologically related signals were found in the VIOLIN dataset (Supplemental Table 21), including stroke (9.1.3). A number of these were the subject of an NIH report.(51)

Considering appendicitis, 13 (Pfizer) and seven (Moderna) EB05>2 signals, both beginning in week 3, were present in the Oracle dataset but were absent from the FOIA dataset. Between 9 and 19 signals were found for each of the other threshold criteria. No appendicitis EB05>2 signals were found for Janssen, but there were 3, 10, and 1 signals for the canonical and alternative PRR, and EB05>1 criteria, respectively.

For pulmonary embolism (Figure 8), eleven EB05>2 signals were found in the Oracle dataset for the Janssen pro-vaccine, along with 13-14 signals for each of the five other threshold criteria. This is consistent with the FOIA dataset (Table 2) in which thrombo-embolic and coagulation events accounted for 30.1% of Janssen's EBGM signals (8.1.2, Table 2, Supplemental Table 2).

However, despite the FOIA dataset lacking a Pfizer or Moderna PE (or other thrombo-embolic related) signal, the Oracle dataset contained 9 (Pfizer) and 7 (Moderna) EB05>2 pulmonary embolism signals, starting week 5. Between 13 and 19 signals were present for each of the other threshold criteria for both modRNA products. The finding of Pfizer and Moderna EBGM signals for pulmonary embolism in the Oracle dataset suggests that there may have been other hematologic events associated with the modRNA pro-vaccines. This was indeed discerned from PRR signals in the VIOLIN dataset (Supplemental Table 6), where canonical PRR signals were found for 19 (Pfizer), 14 (Moderna), and 56 (Janssen) hematologic event types.

EBGM or PRR signals for Herpes zoster were absent for all the COVID-19 pro-vaccines in the Oracle dataset. However, 14 (Pfizer) and 12 (Moderna) signals were found using the ER05>1 criteria. Herpes zoster EBGM signals were absent from the FOIA dataset.

Reconciling the appearance of EB05>2 signals for these seven selected AEs in the Oracle and FOIA datasets (Table 7), there was no case of a signal present in the FOIA dataset but absent from the Oracle dataset. Signals for eight out of a possible 21 pro-vaccine-AE pairs were detected in the Oracle dataset, only one of which (Janssen, pulmonary embolism) was also detected in the FOIA dataset (Odds ratio 0.0813, 95%CI 0.0091, 0.7282, p = 0.02, Fisher's Exact test). This leaves 7/8 (87.5%) signals in the Oracle dataset that were absent in the FOIA dataset.

The failure of the FOIA dataset to detect signals was disproportionately weighted towards the Pfizer and Moderna products over the Janssen product. Of the eight signals detected in the Oracle dataset, 0/4 (Pfizer). 0/2 (Moderna) and 1 / 2 (Janssen) signals were found in the FOIA dataset. With noted limitations, this disproportion could contribute to the disproportion in the use-normalized EBGM signals for Janssen in the FOIA dataset, supporting our earlier estimation of true 4.82- and 8.8 - fold signal excesses (Table 5, Row J) in Janssen signals, and truancy factors of 25.6 and 11.3 (section 8.2.2) for Pfizer and Moderna signals, respectively.

Further corroboration of the truancy of signals in the FOIA dataset is provided by CDC's enumeration to the June 25, 2025 ACIP meeting (52) of eight statistical signals for the modRNA products obtained from the VSD. None of these signals appeared in the FOIA dataset (acute myocardial infarction, immune thrombocytopenia purpura, seizure, Bell's palsy, venous thromboembolism, ischemic stroke, Guillain-Barré syndrome, myocarditis).

Woodcock and Bartels (53) reported PRR signals related to otologic symptoms (vertigo, tinnitus, hearing loss, Bell's palsy) associated with the COVID vaccines from VAERS data to June 7, 2021.

Table 7: Reconciliation of EBGM EB05>2 Signals in the Oracle and FOIA datasets

| | Pfizer | Moderna | Janssen | All |
|---|---|---|---|---|
| **Appendicitis** | **O not F** | **O not F** | Neither O nor F | |
| **Bell's palsy** | **O not F** | Neither O nor F | Neither O nor F | |
| **Herpes zoster** | Neither O nor F | Neither O nor F | Neither O nor F | |
| **Myocarditis** | **O not F** | Neither O nor F | Neither O nor F | |
| **Pericarditis** | Neither O nor F | Neither O nor F | Neither O nor F | |
| **Pulmonary embolism** | **O not F** | **O not F** | **Both O and F** | |
| **Tinnitus** | Neither O nor F | Neither O nor F | **O not F** | |
| | | | | |
| **Number of signals / Number possible** | | | | |
| **Neither O nor F** | 3/7 | 5/7 | 5/7 | 13/21 |
| **Both O and F** | 0/7 | 0/7 | 1/7 | 1/21 |
| **Absent in O, present in F** | 0/7 | 0/7 | 0/7 | 0/21 |
| **Present in O, not F** | 4/7 | 2/7 | 1/7 | 7/21 |
| | | | | |
| **Considering only instances of signals found in the Oracle dataset** | 4 | 2 | 2 | 8 |
| **Present in O, present in F** | 0/4 | 0/2 | 1/2 | 1/8 |
| **Present in O, absent in F** | 4/4 | 2/2 | 1/2 | 7/8 |

Both O and F EB05>2 signal is present in both Oracle (O) and FOIA (F) datasets.
Neither O nor F EB05>2 signal is absent in both the Oracle (O) and FOIA (F) datasets.
O not F EB05>2 signal is present in the Oracle (O) but not in the FOIA (F) dataset.

### 8.3.2 Threshold choice and signal generation in the Oracle database.

Reducing the PRR threshold from two to one increased the number of signals by 25% to 158% in the Oracle dataset (Table 8), consistent with our estimates in the VIOLIN dataset (8.2.1) of 48% to 151%.

We enumerated EBGM signals exceeding the EB05>2 threshold defined by both the VAERS SOP (40) and the FOIA disclosure (41) that it should represent a reporting proportion at least *"twice that of other vaccines (i.e., lower bound of the 90% confidence* [credible] *interval of the* [EBGM]*)."* (40) In reporting the Oracle dataset, Harpaz et al. (38) used the EB05>1 threshold, consistent with the discussion by Evans et al. (31) that statistical association becomes evident once the PRR crosses a null of one. Applying this lower threshold (Table 8) increased the number of EB05 signals for the three pro-vaccines by two to six times. These estimates are also consistent with estimates obtained from MHRA data on non-COVID-19 vaccines (Supplemental Table 20).(54)

Table 8: Cumulative number of PRR and EBGM signals of selected AEs reported to VAERS (Oracle dataset)

| | N [a] | PRR Canonical | PRR Alt by 95%CI [c] | PRR Alt by 90%CI [d] | PRR Alt by p val [e] | EBGM [b] EB05>2 | EBGM [b] EB05>1 | ERAM [b] ER05>2 | ERAM [b] ER05>1 |
|---|---|---|---|---|---|---|---|---|---|
| **PFIZER/BIONTECH** | 133 | 98 | 104 | 104 | 123 (25%) | 32 | 102 (219%) | 85 | 123 (45%) |
| **MODERNA** | 131 | 45 | 95 | 97 | 116 (158%) | 14 | 86 (514%) | 62 | 122 (97%) |
| **JANSSEN** | 100 | 26 | 39 | 40 | 65 (67%) | 14 | 28 (100%) | 34 | 52 (53%) |
| **UNKNOWN** | 84 | 12 | 20 | 22 | 15 (25%) | 11 | 13 (18%) | 12 | 35 (192%) |
| ` | **448** | **181** | **258** | **263** | **319 (76%)** | **71** | **229 (223%)** | **193** | **332 (72%)** |

[a] Total number of reports (not signals) contained in the Oracle dataset, across the study period. Other columns report the number of signals obtained by the specified method.

[b] Number of signals in the whole study period whose lower 5% confidence interval of the Empirical-Bayes Geometric Mean (EBGM) or Empirical-Bayes Regression-adjusted Arithmetic Mean (ERAM) exceeds thresholds of one or two.(38,55) (% increase over number of signals using a threshold of 2 in parentheses)

[c] Number of signals whose lower 2.5% confidence interval of the PRR exceeds 1

[d] Number of signals whose lower 5% confidence interval of the PRR exceeds 1

[e] Number of signals whose PRR p-value (chi-squared test) is less than 0.05 (% increase over number of canonical signals in parentheses)

A PRR signal is only included if the case count is >2.
See also Supplemental Table 13.

Furthermore, in this Oracle dataset, the expected correlation between the number of PRR and EBGM signals was observed (Figure 5), in contrast to the lack of correlation between VIOLIN PRR and FOIA dataset EBGM signals (Figure 4).

### *8.4 The effect of masking in the VIOLIN and ORACLE datasets*

Masking occurs when "*signals for a vaccine of interest are hidden by the presence of other reported vaccines."* (38) For example, the number of myocarditis cases reported for Moderna will contribute to the "other vaccine" tally used in the denominator of Pfizer's myocarditis PRR, thus attenuating its signal. In the PRR portion of the FOIA dataset, the masking effect is only mitigated by combining or comparing the Pfizer and Moderna case counts. Harpaz et al., (38) note that the problem of masking is about eight times more likely in the analysis of safety signals for COVID-19 vaccines than for other vaccines.

A report from the MHRA noted that "*With the majority of the vaccine dataset now comprised of reports for COVID-19 vaccines, these have the potential to unduly influence the disproportionality statistics for other vaccines."*(54) The report, puzzlingly, concluded that *"differences in signal generation were not substantial and the differences did not have a large impact on signalling for other vaccines."*

#### 8.4.1 The effect of masking on the number of PRR signals in the VIOLIN dataset

To calculate a "demasked PRR" value for each adverse event type (Preferred Term), the total of target events for the other COVID-19 vaccines was subtracted from the number of target events for all other vaccines. A similar subtraction was made for all non-target events.

It is instructive to describe the loss of signals due to masking in terms of the fold gain in the number of signals identified after demasking of an otherwise masked dataset. Table 9 shows that demasking increases the number of PRR signals in the VIOLIN dataset by 30% (range 8 -180%, Alternative Evans criteria) and 87% (range 37-229%, Canonical Evans criteria).

Table 9: Effect of masking on the number of PRR signals in the VIOLIN dataset

| | | Masked [a] | | Demasked [b] | | Demask/ Mask [c] | |
|---|---|---|---|---|---|---|---|
| **Evans criteria** | | **Alt** | **Canon** | **Alt** | **Canon** | **Alt** | **Canon** |
| **PRR Threshold** | | **1** | **2** | **1** | **2** | **1** | **2** |
| **PFIZER** | | 2197 | 1485 | 2377 | 2039 | 1.08 | 1.37 |
| **MODERNA** | | 1238 | 491 | 1927 | 1613 | 1.56 | 3.29 |
| **JANSSEN** | | 1203 | 799 | 1626 | 1464 | 1.35 | 1.83 |
| **UNKNOWN** | | 69 | 62 | 193 | 179 | 2.80 | 2.89 |
| **Sum** | | **4707** | **2837** | **6123** | **5295** | **1.30** | **1.87** |
| **Ratio vs Janssen [d] (SER)** | | | | | | | |
| **Pfizer** | | 1.83 | 1.86 | 1.46 | 1.39 | | |
| **Moderna** | | 1.03 | 0.61 | 1.19 | 1.10 | | |
| **Ratio normalized for usage: Janssen vs [e] (UNSER)** | | | | | | | |
| **Pfizer** | 8.96 | 4.90 | 4.82 | 6.13 [f] | 6.43 | | |
| **Moderna** | 5.41 | 5.26 | 8.80 | 4.56 [f] | 4.91 | | |

The number of PRR signals in the VIOLIN dataset using the Alternative or Canonical Evans criteria, and chi-squared values with Yates' correction were calculated for:

[a] the original data, without adjustment for masking

[b] the original data, with adjustment for masking ("demasking")

[c] Ratio of the number of demasked to masked signals

[d] Signal Excess Ratio (SER) of the number of Pfizer or Moderna signals to those of Janssen.

[e] Ratio of the number of Pfizer or Moderna signals to those of Janssen, normalized for the number of people given at least one dose of vaccine (UNSER), using the normalization ratios (RUR) of 8.96 (Pfizer) and 5.41 (Moderna) (Supplemental Table 3A).

[f] These values produce truancy ratios of 20.1 (Pfizer, 123.2/6.13, 95.5% signal loss) and 21.7 (Moderna, 99.2/ 4.56, 95.8% signal loss) (Supplemental Table 3B)

See Supplemental Tables 5B, 5D, and 12. See also Supplemental Tables 5A and 5C for equivalent data generated using the Pearson chi-squared.

### 8.4.2 Masking and PRR signals in the FOIA dataset for the mRNA products combined

The PRR portion of the FOIA dataset is limited. There were no analyses for the Janssen product, and no separate analyses for the Pfizer and Moderna products. Instead, the mRNA pro-vaccines were compared with each other, and aggregated together against non-COVID vaccines. These analyses can be considered as substantively "unmasked." We enumerated the canonical PRR signals obtained from these comparisons (Table 10) for the closest available dates to the date of the VIOLIN dataset, or the last date in the FOIA EBDM dataset.

Due to the limited data provided in the PRR FOIA dataset, it is not possible to enumerate the signals from unstratified data. However, combining data in the VIOLIN dataset (4/30/22) for the Moderna and Pfizer products yields 1904 unmasked canonical PRR signals. With the above caveats, this is much greater than the 878 signals found in the PRR FOIA dataset (Table 10), representing a 2.17 truancy factor and 54% (N=1026) signal loss. Of these 878 signals, 778 are unique, with 59 signals occurring in two age classes, and 24 occurring in three age classes (a listing of signals is given in Supplemental Table 19). The nature of the data provided does not permit an assessment of the number of signals obtained using a threshold of 1.

Table 10: Number of canonical PRR signals present in CDC datasets released under FOIA

| Comparison | Date | Age | N | Source |
|---|---|---|---|---|
| Pfizer vs. Moderna | 7/8/22 | >18 | 225 | (42) |
| Moderna vs. Pfizer | 7/8/22 | >18 | 94 | (42) |
| mRNA vs non-COVID vaccines | 4/29/22 | >5 | 878 | (41,43) |
| mRNA vs non-COVID vaccines | 7/1/22 | >5 | 901 | (41,43) |

See data for all dates provided in the PRR disclosures in Supplemental Tables 16A and 16B
N Number of canonical PRR signals obtained for the comparison indicated.

### 8.4.3 The effect of masking on the number of PRR and EBDM signals in the ORACLE dataset

The subtractions needed to "demask" are easy to perform when there are, as in the case of the COVID-19 pro-vaccines, only a few potentially masking products. As Harpaz et al., (38) point out, although the same subtractions could be made in the calculation of the EBGM, in the general case involving many more product-AE pairs, this technique becomes computationally infeasible. Accordingly, DuMouchel and colleagues adapted their MGPS method used to compute EBGM values to compute the "Empirical-Bayes Regression-Adjusted Arithmetic Mean" (ERAM) using a method they term "Regression-Adjusted Gamma Poisson Shrinker" (RGPS). (38,55)

Using RGPS, Harpaz et al. identified a masking effect of smallpox vaccine on the myocarditis signals for the modRNA pro-vaccines. Harpaz et al. estimated the size of the masking effect for any AE by calculating the percent difference between the corresponding ERAM and EBGM values. In their study, (Table 6 in (38)) the masking effect ranged from 39-232%. From the Oracle dataset, we calculated the overall masking effect size for all 21 pro-vaccine-AE pairs as 123% (range -3% to 403%). Applying the same formula to PRR values in the VIOLIN dataset yielded a similar value of 120%.

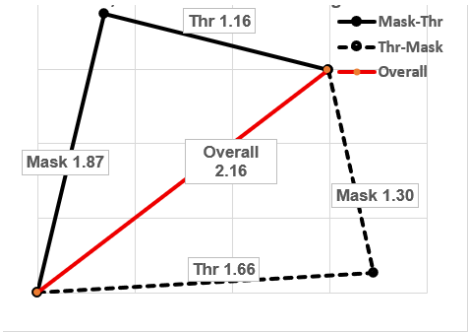
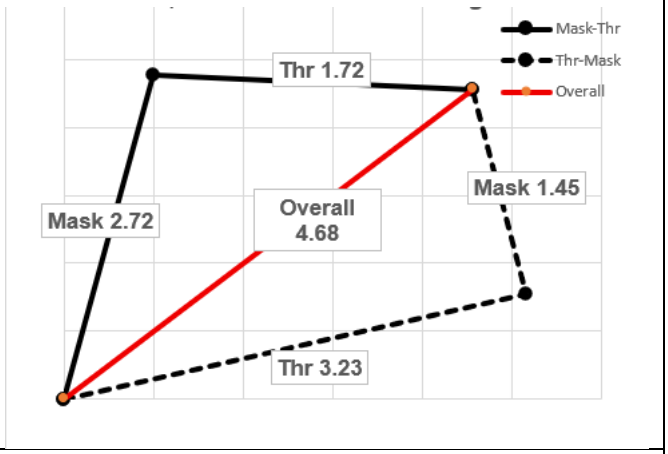
These estimates are consistent with our estimate based on the additional number of signals found after demasking in the Oracle dataset (Table 8, Supplemental Table 12) of 45% (range 21-169%, threshold 1) and 172% (range 9-343%, threshold 2), and in the VIOLIN dataset of 30% and 87%% at the two thresholds, respectively (Table 9).

## *8.5 The aggregate effect of truancy, masking, and high thresholding on DSA signal generation*

### 8.5.1 Relationship between signal losses due to masking and threshold filtering

Expressing signal loss in terms of the gain in signals identified after defiltering (lowering the threshold) and/or demasking, we find signal increases of 4.68- and 2.16-fold for the Oracle and VIOLIN datasets, respectively. These figures correspond to combined signal losses due to masking and threshold filtering of 79% and 54%, respectively. Although the aggregate effects are identical, the component effects of filtering or demasking will depend on their order of execution (Figure 6, Supplemental Figure 2). Except in the cases where the manufacturer is unknown, whichever procedure is performed first yields the greater signal gain. With some differences in the fold gains in the number of signals generated, similarities between the two databases and between the pro-vaccines are generally evident.

Figure 6: Component and aggregate effects of masking and threshold filtering on signal generation in the Oracle and VIOLIN datasets

| VIOLIN, All vaccines, overall 116% gain | ORACLE, All vaccines, overall 368% gain |
|---|---|
|  |  |
| The number of masked signals at a threshold of 2 is represented at the "start position" at the lower left of each diagram. The increase in the number of signals identified after demasking (Mask) or defiltering by reducing the threshold (Thr) is indicated by the length on a log scale of the line emanating from each point, with the fold signal increase indicated in the label near the center of each line. The increases after demasking followed by defiltering are indicated by the solid black line. The reversed order is indicated by the dashed black line, always yielding the same net result. The combined effect of demasking and defiltering by lowering the threshold is indicated by the red line, which has been aligned at the same angle for ease of comparison. Underlying data are found in Supplemental Table 12. Signal gain diagrams by individual pro-vaccine are shown in Supplemental Figure 2. | |
| (Left) In the VIOLIN dataset, demasking was accomplished by the subtractions outlined in 8.4.1. Defiltering was accomplished by lowering the threshold from two to one ("Alternative" criteria.)<br><br>Executing both procedures increases the number of PRR signals by 2.16-fold (range 1.76 – 3.92).<br>Expressed as a % loss of signals, demasking first reveals a loss of 46%, and a 13.5% loss if the threshold is then lowered. Reversing the order of execution reveals losses of 40% (defiltering) and 23% (demasking)<br>. | (Right) In the Oracle dataset, demasking was accomplished by tallying the number of signals generated using the RGPS (ERAM) rather than the MGPS (EBGM), Empirical Bayesian methods.<br><br>Executing both procedures increases the number of Empirical Bayesian signals by 4.68-fold (range 3.18 – 8.71).<br>Expressed as the % loss of signals, demasking first reveals a loss of 63%, and a 42% loss if the threshold is then lowered. Reversing the order of execution reveals losses of 69% (defiltering) and 31% (demasking). |

### 8.5.2 Effect of the type of "significance component" of the signal criteria on signal generation

For reasons the *Discussion* will elucidate, there are likely to be mismatches in the number of signals generated depending on which significance component (i.e. chi-squared value, p-value, or confidence interval) is chosen. We confirmed this using the Oracle dataset (Table 8, Supplemental Table 13). Nevertheless, the use-normalized fold excesses of Janssen signals over Pfizer or Moderna remain fairly similar between the three methods. Repeating the exercise for unmasked data in the VIOLIN dataset (Supplemental Table 5D), at a threshold of 2, yields between 3337 (lower 95% CI) and 5295 (chi-squared) signals. At a threshold of 1, between 6123 ($p<0.05$ value) and 6889 (lower 90% CI) signals were generated. However, the corresponding use-normalized excess for Janssen signals over Pfizer and Moderna remained stable (median, range) for both at Pfizer (6.43, 6.1-7.6) and Moderna (4.9, 4.5-6.2).

### 8.5.3 Evidence basis: expected VAERS DSA signal losses due to truancy, filtering, and masking

In addition to providing an evidentiary road map, Table 11 summarizes the number of DSA signals that should have been evident to regulators charged with monitoring VAERS and COVID-19 pro-vaccine safety. The table summarizes the biases in signal estimation due to truancy, threshold, and masking. The table provides the provenance of the Signal Excess Ratios (SER) and Relative Use Ratios (RUR) used to correct these biases as originating from the FOIA, VIOLIN, and Oracle datasets, and CDC vaccine use data. Table 11 is color-coded to

indicate whether calculations have been based on data from nearly-identically dated data sources, or from sources whose dates differ by several months (see 8.2.2).

Although CDC was required to *"perform PRR data mining on a weekly basis or as needed,"* (40) only limited analyses were disclosed. Without requiring adjustment, the VIOLIN dataset contains 2837 canonical PRR signals for COVID-19 pro-vaccines, as of 4/30/22. Direct interrogation of the VIOLIN dataset using a threshold of 1 and avoiding masking and filtering, yields between 6123 and 6889 PRR signals (Table 11, rows A and B). 7294 unique vaccine-adverse event pairs meet one or more of the versions of PRR criteria (Supplemental Table 17).

Using nearly-identically dated data sources to determine the effects of truancy, masking, and filtering, yields 887 Empirical Bayesian signals for all COVID-19 pro-vaccines that would have been expected in FDA's report as of April 29, 2022. Thus, 763 (86%) signals were lost (Table 11, row C).

Supporting this estimate are those obtained using combinations of data sources dated 10/1/21, 4/30/22, or 7/1/22, which suggest between 573 to 2032 Empirical Bayesian signals would have been expected in FDA's weekly reports for these dates. Thus, between 487-1898 (85-93%) signals appear lost due to truancy, masking, and high thresholding (Table 11, rows D-H).

Table 7 of Harpaz et al. (38) provides a further point of triangulation and enumerates 24971 associations in VAERS as a whole as of 10/1/21, assumed to meet the ER05>1 (demasked, defiltered) criteria. Adjusting this downwards to reflect an approximate 33% excess of foreign to US reports, yields 18803 signals (Table 11, row I). This is still much larger than the above estimates, despite their estimate of only 2.31% masked associations (i.e. the increase in associations generated at a threshold of 1).

Lastly, these primary findings are supported by a number of sensitivity analyses described throughout this work.

Table 11: Expected number of DSA signals from VAERS and aggregate effect of truancy. threshold and masking on signal loss

| Row | Dataset | Signal | Date | Truancy factor derived from | | | | Masking & filtering ratios derived from | Crude c | After adjustment for | | | Signal loss | | Note |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Type | | Target UNSER | | Comparator UNSER | | | | Truancy | Masking | Filtering | | | |
| | | | | SER a | RUR a | SER b | RUR a | | Number of signals | | | | N | % | |
| A | VIOLIN | PRR | 4/30/2022 | NA | NA | NA | NA | NA | 2837 | NA | 5295 | 6123 | 5999 | 98% | d |
| B | | | | | | | | | | | | 6889 | 6765 | 98% | |
| C | FOIA | EBDM | 4/29/2022 | FOIA 4/29/22 | CDC 4/29/22 | PRR Signals VIOLIN 4/30/22 | CDC 4/29/22 | PRR Signals VIOLIN 4/30/22 | 124 | 405 | 770 | 887 | 763 | 86% | e |
| D | FOIA | EBDM | | | | | | EBDM Signals Oracle 10/1/21 | | 405 | 1134 | 1856 | 1732 | 93% | |
| E | | | 10/1/2021 | FOIA 10/1/21 | CDC 10/1/21 | | | PRR Signals VIOLIN 4/30/22 | 86 | 258 | 498 | 573 | 487 | 85% | f |
| F | | | | | | | | EBDM Signals Oracle 10/1/21 | | 258 | 724 | 1192 | 1106 | 93% | |
| G | | | 7/1/2022 | FOIA 7/1/22 | CDC 6/29/22 | | | PRR Signals VIOLIN 4/30/22 | 134 | 443 | 842 | 971 | 837 | 86% | g |
| H | | | | | | | | EBDM Signals Oracle 10/1/21 | | 443 | 1243 | 2032 | 1898 | 93% | |
| I | VAERS | EBDM | 10/1/2021 | NA | NA | NA | NA | NA | | | | | 18717 | | h |

Notes

For source data, unless specified, see Supplemental Table 12. All data involve VAERS reports from the USA only, except as noted.

Same or near identical dating of source data is indicated by the same color. 10/1/2021 4/29/2022 7/1/2022

The tally of VIOLIN PRR signals does not include 112 (77, Pfizer; 34, Moderna; 1, Janssen) signals for which the case count is >2, but with zero comparator cases (listed in Supplemental Table 22).

a Supplemental Table 3A, Supplemental Table 3B

b Supplemental Table 5D

c Number of masked signals, at threshold of 2

d The estimate of 6889 uses the criteria of the lower 5% confidence interval of the PRR >1. See

e 405 includes an estimated 23 signals for unknown manufacturer

f 258 includes an estimated 16 signals for unknown manufacturer

g 443 includes an estimated 25 signals for unknown manufacturer

h Table 7 of Harpaz et al. lists 24971 associations in VAERS, adjusted to 18803 to account for the approximately 33% excess of foreign to US reports. Subtracting 86 yields 18717. These are assumed to be associations using the ER05>1 criteria.

SER Signal Excess Ratio (expressed here as Janssen to Pfizer or Moderna)

RUR Relative Use Ratio

UNSER Use Normalized Signal Excess Ratio

NA Not applicable

### 8.5.4 The combined effect of masking and filtering on the timing of signals generated

Demasking and defiltering may not only identify new suspected adverse reactions (such as Herpes zoster and tinnitus (38)), but may also detect signals sooner. The chronologies of PRR, EBGM, and ERAM signal generation at thresholds of 2 and 1 for myocarditis and pericarditis in the Oracle dataset are compared in Figure 7. Due to the nature of the data in the Oracle dataset, it was not possible to obtain a set of demasked PRR values. Generally, signals emerge sooner and persist longer as the threshold decreases from 2 to 1, and when ERAM / RGPS demasking is used. A similar pattern can be discerned for pulmonary embolism (Figure 8), despite signals appearing sooner.

Figure 7: Chronology of myocarditis and pericarditis signal generation by different methods in the Oracle dataset

**Myocarditis**
**(no EB05>2 signal in FOIA dataset)**

**Pfizer (3515 cases)**

| Mask | | | ON | ON | OFF | ON | ON | OFF |
|---|---|---|---|---|---|---|---|---|
| Threshold | | | 2 | 2 | 2 | 1 | 1 | 1 |
| Week | Report | Cases | PRR C | EB>2 | ER>2 | PRR A | EB>1 | ER>1 |
| 3 | 22-Jan | 3 | 0 | 0 | 0 | 0 | 0 | 0 |
| 5 | 5-Feb | 6 | 0 | 0 | 0 | 0 | 0 | 0 |
| 7 | 19-Feb | 9 | 0 | 0 | 0 | 0 | 0 | 0 |
| 9 | 5-Mar | 18 | 0 | 0 | 0 | 0 | 0 | 1 |
| 11 | 19-Mar | 21 | 0 | 0 | 0 | 0 | 0 | 1 |
| 13 | 2-Apr | 22 | 0 | 0 | 0 | 0 | 0 | 1 |
| 15 | 16-Apr | 23 | 0 | 0 | 0 | 0 | 0 | 1 |
| 17 | 30-Apr | 51 | 0 | 0 | 0 | 0 | 1 | 1 |
| 19 | 14-May | 83 | 0 | 0 | 0 | 1 | 1 | 1 |
| 21 | 28-May | 266 | 1 | 1 | 1 | 1 | 1 | 1 |
| 23 | 11-Jun | 465 | 1 | 1 | 1 | 1 | 1 | 1 |
| 25 | 25-Jun | 671 | 1 | 1 | 1 | 1 | 1 | 1 |
| 27 | 9-Jul | 897 | 1 | 1 | 1 | 1 | 1 | 1 |
| 29 | 23-Jul | 1186 | 1 | 1 | 1 | 1 | 1 | 1 |
| 31 | 6-Aug | 1651 | 1 | 1 | 1 | 1 | 1 | 1 |
| 33 | 20-Aug | 1952 | 1 | 1 | 1 | 1 | 1 | 1 |
| 35 | 3-Sep | 2053 | 1 | 1 | 1 | 1 | 1 | 1 |
| 37 | 17-Sep | 2731 | 1 | 1 | 1 | 1 | 1 | 1 |
| 39 | 1-Oct | 3515 | 1 | 0 | 1 | 1 | 1 | 1 |

**Moderna (1175 cases)**

| Mask | | ON | ON | OFF | ON | ON | OFF |
|---|---|---|---|---|---|---|---|
| Threshold | | 2 | 2 | 2 | 1 | 1 | 1 |
| Cases | PRR C | EB>2 | ER>2 | PRR A | EB>1 | ER>1 |
| 7 | 1 | 0 | 0 | 1 | 1 | 1 |
| 16 | 1 | 0 | 1 | 1 | 1 | 1 |
| 27 | 1 | 0 | 1 | 1 | 1 | 1 |
| 29 | 1 | 0 | 1 | 1 | 1 | 1 |
| 32 | 0 | 0 | 1 | 1 | 1 | 1 |
| 38 | 0 | 0 | 1 | 1 | 1 | 1 |
| 52 | 0 | 0 | 0 | 0 | 1 | 1 |
| 59 | 0 | 0 | 0 | 0 | 0 | 1 |
| 130 | 0 | 0 | 0 | 0 | 0 | 1 |
| 252 | 0 | 0 | 1 | 1 | 1 | 1 |
| 334 | 0 | 0 | 1 | 1 | 1 | 1 |
| 382 | 0 | 0 | 1 | 1 | 1 | 1 |
| 444 | 0 | 0 | 1 | 1 | 1 | 1 |
| 575 | 0 | 0 | 1 | 1 | 1 | 1 |
| 655 | 0 | 0 | 1 | 1 | 1 | 1 |
| 704 | 0 | 0 | 1 | 1 | 1 | 1 |
| 895 | 0 | 0 | 1 | 1 | 1 | 1 |
| 1175 | 0 | 0 | 1 | 1 | 1 | 1 |

**Pericarditis**
**(no EB05>2 signal in FOIA dataset)**

**Pfizer (2408 cases)**

| Mask | | ON | ON | OFF | ON | ON | OFF |
|---|---|---|---|---|---|---|---|
| Threshold | | 2 | 2 | 2 | 1 | 1 | 1 |
| Week | Cases | PRR C | EB>2 | ER>2 | PRR A | EB>1 | ER>1 |
| 3 | 4 | 0 | 0 | 0 | 0 | 0 | 0 |
| 5 | 9 | 0 | 0 | 0 | 0 | 0 | 0 |
| 7 | 18 | 1 | 0 | 0 | 1 | 0 | 1 |
| 9 | 25 | 1 | 0 | 0 | 1 | 1 | 1 |
| 11 | 34 | 1 | 0 | 0 | 1 | 1 | 1 |
| 13 | 34 | 0 | 0 | 0 | 1 | 1 | 1 |
| 15 | 39 | 0 | 0 | 0 | 1 | 0 | 1 |
| 17 | 58 | 0 | 0 | 0 | 1 | 0 | 1 |
| 19 | 84 | 0 | 0 | 0 | 1 | 1 | 1 |
| 21 | 147 | 0 | 0 | 0 | 1 | 1 | 1 |
| 23 | 261 | 1 | 0 | 1 | 1 | 1 | 1 |
| 25 | 390 | 1 | 0 | 1 | 1 | 1 | 1 |
| 27 | 533 | 1 | 0 | 1 | 1 | 1 | 1 |
| 29 | 743 | 1 | 0 | 1 | 1 | 1 | 1 |
| 31 | 1111 | 1 | 0 | 1 | 1 | 1 | 1 |
| 33 | 1345 | 1 | 0 | 1 | 1 | 1 | 1 |
| 35 | 1401 | 1 | 0 | 1 | 1 | 1 | 1 |
| 37 | 1767 | 1 | 0 | 1 | 1 | 1 | 1 |
| 39 | 2408 | 1 | 0 | 1 | 1 | 1 | 1 |

**Moderna (671 cases)**

| Mask | | ON | ON | OFF | ON | ON | OFF |
|---|---|---|---|---|---|---|---|
| Threshold | | 2 | 2 | 2 | 1 | 1 | 1 |
| Week | Cases | PRR C | EB>2 | ER>2 | PRR A | EB>1 | ER>1 |
| 3 | | | | | | | |
| 5 | 4 | 0 | 0 | 0 | 0 | 0 | 0 |
| 7 | 14 | 1 | 0 | 0 | 1 | 1 | 1 |
| 9 | 22 | 1 | 0 | 0 | 1 | 1 | 1 |
| 11 | 24 | 0 | 0 | 0 | 1 | 0 | 1 |
| 13 | 29 | 0 | 0 | 0 | 1 | 1 | 1 |
| 15 | 33 | 0 | 0 | 0 | 0 | 0 | 1 |
| 17 | 49 | 0 | 0 | 0 | 0 | 0 | 1 |
| 19 | 59 | 0 | 0 | 0 | 0 | 0 | 0 |
| 21 | 92 | 0 | 0 | 0 | 0 | 0 | 1 |
| 23 | 174 | 0 | 0 | 0 | 1 | 0 | 1 |
| 25 | 234 | 0 | 0 | 0 | 1 | 0 | 1 |
| 27 | 266 | 0 | 0 | 1 | 1 | 1 | 1 |
| 29 | 310 | 0 | 0 | 1 | 1 | 1 | 1 |
| 31 | 423 | 0 | 0 | 1 | 1 | 1 | 1 |
| 33 | 469 | 0 | 0 | 1 | 1 | 1 | 1 |
| 35 | 493 | 0 | 0 | 0 | 0 | 0 | 1 |
| 37 | 570 | 0 | 0 | 0 | 0 | 0 | 1 |
| 39 | 671 | 0 | 0 | 0 | 0 | 0 | 1 |

Each panel contains six columns representing signals generated by Canonical PRR (PRR C), EB05>2 (EB>2), ER05>2 (ER>2), Alternative PRR (PRR A, using the lower 95% confidence interval), EB05>1 (EB>1), and ER05>1 (ER>1) criteria.
The presence or absence of a signal at each report date is signified by a 1 (pink color) or 0 (green color).
The Oracle dataset is based on VAERS reports from US and foreign sources.

Figure 8: Chronology of pulmonary embolism signal generation by different methods in the Oracle dataset

Pulmonary Embolism

**Pfizer (4394 cases)**
no FOIA EB05>2 signal

| | Mask | | ON | ON | OFF | ON | ON | OFF |
|---|---|---|---|---|---|---|---|---|
| | Threshold | | 2 | 2 | 2 | 1 | 1 | 1 |
| Week | Report | Cases | PRR C | EB>2 | ER>2 | PRR A | EB>1 | ER>1 |
| 3 | 22-Jan | 10 | 1 | 0 | 1 | 1 | 1 | 1 |
| 5 | 5-Feb | 20 | 1 | 1 | 1 | 1 | 1 | 1 |
| 7 | 19-Feb | 41 | 1 | 1 | 1 | 1 | 1 | 1 |
| 9 | 5-Mar | 64 | 1 | 1 | 1 | 1 | 1 | 1 |
| 11 | 19-Mar | 81 | 1 | 1 | 1 | 1 | 1 | 1 |
| 13 | 2-Apr | 92 | 1 | 1 | 1 | 1 | 1 | 1 |
| 15 | 16-Apr | 129 | 1 | 1 | 1 | 1 | 1 | 1 |
| 17 | 30-Apr | 276 | 1 | 1 | 1 | 1 | 1 | 1 |
| 19 | 14-May | 365 | 1 | 1 | 1 | 1 | 1 | 1 |
| 21 | 28-May | 604 | 1 | 1 | 1 | 1 | 1 | 1 |
| 23 | 11-Jun | 690 | 1 | 0 | 1 | 1 | 1 | 1 |
| 25 | 25-Jun | 769 | 1 | 0 | 1 | 1 | 1 | 1 |
| 27 | 9-Jul | 1366 | 1 | 0 | 1 | 1 | 1 | 1 |
| 29 | 23-Jul | 2329 | 1 | 0 | 1 | 1 | 1 | 1 |
| 31 | 6-Aug | 3112 | 1 | 0 | 1 | 1 | 1 | 1 |
| 33 | 20-Aug | 3407 | 1 | 0 | 1 | 1 | 1 | 1 |
| 35 | 3-Sep | 3495 | 1 | 0 | 1 | 1 | 1 | 1 |
| 37 | 17-Sep | 3959 | 1 | 0 | 1 | 1 | 1 | 1 |
| 39 | 1-Oct | 4394 | 1 | 0 | 1 | 1 | 1 | 1 |

**Moderna (1475 cases)**
no FOIA EB05>2 signal

| | Mask | | ON | ON | OFF | ON | ON | OFF |
|---|---|---|---|---|---|---|---|---|
| | Threshold | | 2 | 2 | 2 | 1 | 1 | 1 |
| Week | Cases | PRR C | EB>2 | ER>2 | PRR A | EB>1 | ER>1 | |
| 3 | 6 | 1 | 0 | 1 | 1 | 1 | 1 | |
| 5 | 21 | 1 | 1 | 1 | 1 | 1 | 1 | |
| 7 | 38 | 1 | 1 | 1 | 1 | 1 | 1 | |
| 9 | 55 | 1 | 1 | 1 | 1 | 1 | 1 | |
| 11 | 85 | 1 | 1 | 1 | 1 | 1 | 1 | |
| 13 | 105 | 1 | 1 | 1 | 1 | 1 | 1 | |
| 15 | 155 | 1 | 1 | 1 | 1 | 1 | 1 | |
| 17 | 300 | 1 | 1 | 1 | 1 | 1 | 1 | |
| 19 | 363 | 1 | 0 | 1 | 1 | 1 | 1 | |
| 21 | 534 | 1 | 0 | 1 | 1 | 1 | 1 | |
| 23 | 703 | 1 | 0 | 1 | 1 | 1 | 1 | |
| 25 | 776 | 1 | 0 | 1 | 1 | 1 | 1 | |
| 27 | 850 | 1 | 0 | 1 | 1 | 1 | 1 | |
| 29 | 1027 | 0 | 0 | 1 | 1 | 1 | 1 | |
| 31 | 1159 | 0 | 0 | 1 | 1 | 1 | 1 | |
| 33 | 1227 | 0 | 0 | 1 | 1 | 1 | 1 | |
| 35 | 1266 | 0 | 0 | 1 | 1 | 1 | 1 | |
| 37 | 1373 | 0 | 0 | 1 | 1 | 1 | 1 | |
| 39 | 1475 | 0 | 0 | 1 | 1 | 1 | 1 | |

**Janssen (643 cases)**
FOIA EB05>2 signal at w17

| | Mask | | ON | ON | OFF | ON | ON | OFF |
|---|---|---|---|---|---|---|---|---|
| | Threshold | | 2 | 2 | 2 | 1 | 1 | 1 |
| Week | Cases | PRR C | EB>2 | ER>2 | PRR A | EB>1 | ER>1 | |
| 3 | | | | | | | | |
| 5 | | | | | | | | |
| 7 | | | | | | | | |
| 9 | | | | | | | | |
| 11 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | |
| 13 | 8 | 1 | 0 | 0 | 1 | 0 | 1 | |
| 15 | 49 | 1 | 1 | 1 | 1 | 1 | 1 | |
| 17 | 213 | 1 | 1 | 1 | 1 | 1 | 1 | |
| 19 | 270 | 1 | 1 | 1 | 1 | 1 | 1 | |
| 21 | 325 | 1 | 1 | 1 | 1 | 1 | 1 | |
| 23 | 349 | 1 | 1 | 1 | 1 | 1 | 1 | |
| 25 | 380 | 1 | 1 | 1 | 1 | 1 | 1 | |
| 27 | 400 | 1 | 1 | 1 | 1 | 1 | 1 | |
| 29 | 429 | 1 | 1 | 1 | 1 | 1 | 1 | |
| 31 | 482 | 1 | 1 | 1 | 1 | 1 | 1 | |
| 33 | 506 | 1 | 1 | 1 | 1 | 1 | 1 | |
| 35 | 531 | 1 | 1 | 1 | 1 | 1 | 1 | |
| 37 | 582 | 1 | 0 | 1 | 1 | 1 | 1 | |
| 39 | 643 | 1 | 0 | 1 | 1 | 1 | 1 | |

Each panel contains six columns representing signals generated by canonical PRR (PRR C), EB05>2 (EB>2), ER05>2 (ER>2), Alternative PRR (PRR A, using the lower 95% confidence interval), EB05>1 (EB>1), and ER05>1 (ER>1) criteria. The presence or absence of a signal at each report date is signified by a 1 (pink color) or 0 (green color). For Janssen, no data were included in the Oracle dataset for week 9, however, the absence of a signal is inferred in the first week after EUA issuance. The Oracle dataset is based on VAERS reports from US and foreign sources.

FDA's 2005 guidance (56) on pharmacovigilance is silent on the issue of masking. In contrast, a similar document whose authors included representatives from AstraZeneca, Pfizer, the European Medicines Agency (EMA), and MHRA (39) recommended quantification of the masking effect. The EMA guide that evolved from this work (57) refers (Chapter 11) to the use of RGPS to reduce masking. The Empirica Signal software used by FDA for the EBDM analyses in the FOIA dataset, at least in version 9.1 available in August 2020, included the ability to perform RGPS analyses.(58) This was the same software version used by Harpaz et al. (38)

## 9 REGULATORY CONTEXT OF ANOMALIES FOUND IN THE FOIA DATASET

### *9.1 Inconsistencies between the FOIA, Oracle, or VIOLIN datasets and FDA or CDC statements*

Examination of the signals in the FOIA, Oracle, and VIOLIN datasets reveals inconsistencies with statements made by FDA or CDC (Table 12).

#### 9.1.1 Misreporting of data mining alerts

A senior CDC safety expert and recipient of the weekly FOIA dataset EBDM alerts, conveyed to FDA's VRBPAC (p75/355 in (59), slide 12 of (16)) on February 26, 2021: *"there were no empirical, Bayesian data mining alerts detected for any adverse event COVID-19 vaccine pairs as of the last data mining run that the FDA performed on February 18th."* While technically true, this statement is inconsistent with the January 6, 2021 FOIA dataset report of EB05>2 signals for the Pfizer product (paraesthesia, dysgeusia, flushing, palpitations) and in the Oracle dataset for appendicitis (Moderna and Pfizer, week 3), and pulmonary embolism (Moderna and Pfizer, week 5) (Supplemental Table 13, Figure 8).

This same person co-authored, along with other FDA and CDC staff, some of whom were email recipients of the FOIA dataset EBGM alerts (41) a preprint posted in October 2021. (60) This preprint described the safety monitoring of mRNA pro-vaccines to June 14, 2021. The preprint stated: *"No adverse health outcome alerts were identified in EB data mining. However, five mRNA COVID-19 administrative error alerts (e.g. 'product temperature excursion issue') with disproportionality (EB05>2) were identified during the surveillance period."*

This statement is inconsistent with the alerts listed in Supplemental Table 2 first occurring before June 14, 2021 (paraesthesia, dysgeusia, flushing, palpitations, Injection site pruritus). The statement, or any reference to EB data mining, was absent in a peer-reviewed version of this preprint.(61)

FDA's Review Memorandum preceding the 2021 EUA for the Pfizer pro-vaccine for teenagers (62) stated (p34/43): *"Data mining query with the Empirica Signal tool was performed* […] *The data lock point was April 16, 2021. The alert score for disproportional reporting uses the* […] *EB05 >2.0. An EB05 of 2.064 was found for the PT 'Body Temperature' in adults ages 45-64.9 years of age. There were no other PTs with an EB05 >2.0."* This statement is inconsistent with the EB05>2 signals reported in the FOIA dataset (January 6, 2021) for oral paraesthesia, dysgeusia, flushing, palpitations, and in the Oracle dataset for appendicitis (starting week 3), pulmonary embolism (starting week 5), and Bell's palsy (week 9). In weeks 15 and 17 of the Oracle dataset (corresponding to the lock point date indicated in the Review memorandum), signals for pulmonary embolism and appendicitis were present (Supplemental Table 13).

### 9.1.2 CMS signals: pulmonary embolism, myocardial infarction, immune thrombocytopenia, DIC

In December 2022, based on their *"near real-time active surveillance"* of CMS (US Centers for Medicare & Medicaid Services) data through Jan 15, 2022, FDA and CMS staff reported (4) signals (with dates) from a Poisson Maximized Sequential Probability Ratio Test, for pulmonary embolism (2/27/21), acute myocardial infarction (2/27/21), disseminated intravascular coagulation (3/13/21), and immune thrombocytopenia (4/24/21) in people age 65 years and older, given the Pfizer, but not the Moderna or Janssen products. After adjusting for medical and demographic differences, only the signal for pulmonary embolism persisted. FDA announced these findings *"in the spirit of transparency*" on July 12, 2021, (63) stating:

> *"These events have not been identified as safety concerns or signals in the CDC Vaccine Safety Datalink (VSD) or the Veterans Administration (VA) Healthcare data systems screening methods. The Vaccine Adverse Event Reporting System* ***(VAERS),*** *another government monitoring system,* ***also has not identified any association between any COVID-19 vaccine and these AEI****"* [adverse events of interest] (emphasis added).

This statement is inconsistent with EB05>2 signals (Supplemental Table 13) present in the Oracle dataset for pulmonary embolism for all three COVID-19 pro-vaccines starting week 5 (Pfizer, Moderna) and week 15 (Janssen). Canonical PRR signals were also present starting week 3 (Pfizer, Moderna) and week 13 (Janssen). This inconsistency impugns FDA's decision (63) that it was "*not taking any regulatory actions based on these signal detection activities because these signals are still under investigation and require more robust study."*

### 9.1.3 Signals for stroke

At the VRBPAC meeting of January 26, 2023, CDC (64) reported a VSD signal for ischemic stroke associated with the Pfizer bivalent product. It was suggested that if this was a true signal, it was only in those over 65, and likely associated with the cotemporal injection of an influenza vaccine. A second presentation from FDA (65) stated (slide 16) that there were *"No excess reports of stroke from VAERS."* An update presentation at the April 19, 2023, ACIP meeting made similar statements, specifically (slide 23) "*No safety signals were detected for ischemic stroke for primary series or monovalent boosters for Pfizer-BioNTech or Moderna COVID-19 vaccines in U.S. and global monitoring."* (15) A May 2023 update stated: *"Other safety monitoring systems have not observed similar findings."* (66) There was no discussion of this AE at the June 2023 ACIP meeting.

As we noted previously, (67) these statements are inconsistent with canonical PRR signals for ischemic stroke associated with the modRNA vaccines (combined data) in FOIA disclosures. (41,42) Associations were found in the 4/30/22 VIOLIN dataset for all three COVID-19 pro-vaccines with PRR values of 2.35 (Pfizer), 1.6 (Moderna), and 3.34 (Janssen). Signals in VAERS for stroke were evident as early as April 10, 2021 according to Aggarwal (68) who found PRR, ROR, and IC signals for Cerebrovascular Accidents for all three pro-vaccines.

These signals were not discussed in a general update at the ACIP meeting of September 12, 2023, given by the VSD lead (69) who, a month later, coauthored a report (70) of an elevated risk for ischemic stroke in those younger than 65 years receiving the Pfizer bivalent pro-vaccine and influenza vaccine on the same day. This work was based on data accumulated between September 1, 2022, and March 31, 2023. On the same day, FDA and CMS scientists published a report (71) based on Medicare data between August 31 to November 6, 2022, of an elevated risk associated with the Pfizer bivalent product for non-hemorrhagic stroke (NHS) in those over 85 years. In those over 65 years also receiving a high-dose/adjuvanted influenza vaccine, there were elevated risks for NHS with the Pfizer bivalent product and for NHS with Transient Ischemic Attack with the Moderna bivalent product.

### 9.1.4 Signals for cancer

The director of FDA's Center for Biologics Evaluation and Research (CBER) testified before the House Select Subcommittee on the Coronavirus Pandemic on February 15, 2024, that *"we have not detected any increase in cancers with the Covid-19 vaccines."* (1 hr 55 mins in (72)) This statement is inconsistent with the 23 PRR signals in the dataset for July 29, 2022, disclosed in December 2022 (42) and recently (41) for some cancer types or codes (Supplemental Table 7). Further, in the VIOLIN dataset, we found 25 (Pfizer), 6 (Moderna), and 4 (Janssen) canonical PRR signals for cancer-related events. Demasking and defiltering yielded 32, 18, and 9, signals, respectively (Supplemental Table 8).

### 9.1.5 VSD Signals for acute myocardial infarction and venous thromboembolism

The presentation by the VSD lead at the ACIP meeting of September 12, 2023 (69) included slide 64, which suggested that, *"VSD may consider further investigating mRNA vaccine primary series signals of VTE and AMI."* Slide number 42 showed Rapid Cycle Analysis signals for Pfizer and both mRNA pro-vaccines together (but not Moderna alone) for acute myocardial infarction (AMI) and venous thromboembolism (VTE). Although the date of the analysis indicated on the slide was May 2022, the equivalent VSD presentations made to the two ACIP meetings bracketing this date (i.e. April 20, 2022 (73), and September 1, 2022 (18)), were silent about these signals. A version of a presentation made to VRBPAC on June 14, 2022 obtained pursuant to a US Senate investigation, contained a slide substantially similar to slide 42 described above. (p84 and 129/201 in document 2 of (74)) However, this slide did not appear in the version as presented on FDA's web page. Canonical PRR signals for AMI, Venous Embolism, and venous thrombosis (limb) for the modRNA products combined were present in the FOIA dataset for July 2022, as well as in data released separately (43) for April 29 and May 6, 2022.

### 9.1.6 Signals for myocarditis

On May 10, 2021, FDA lowered the age range for Pfizer's COVID-19 EUA to include children ages 12 to 15 years, with the endorsement of CDC's ACIP on May 12. On May 17, ACIP's Vaccine Safety Technical (VaST) Work Group discussed *"relatively few reports of myocarditis,"* whose rates within CDC systems had *"not differed from expected baseline rates."* (75) A week later, a signal for 16–24-year-olds was reported as present in VAERS but absent in VSD.(76) CDC issued information to the lay public on May 27.(77) This was followed by a presentation to FDA's VRBPAC on June 10 and by FDA's addition of a Warning to the Fact Sheet about myocarditis and pericarditis on June 25, 2021.(78)

Information about myocarditis would surely have been material to ACIP's determination on May 12, 2021 that *"Desirable consequences clearly outweigh undesirable consequences in most settings,"* and yet the presentations by CDC, VaST, and Pfizer to ACIP were silent on the issue. (79) Such omission must be viewed in light of a FOIA disclosure (80) documenting requests for information by Israel's Ministry of Health on February 28, 2021 (page 14/201 in Document 2 of (74)) and March 2, 2021 (p712/985 in (80)), after noticing "*a large number of reports, particularly in young people, following the administration of the Pfizer vaccine."* This request precipitated discussion between within CDC, FDA, and the Department of Defense (e.g. p985/985 in (80)), who were noted as submitting a paper for publication on the topic. It is unclear if that particular paper was published, but one report (81) describes at least 22 active-duty military personnel presenting between January and April 2021 with acute chest pain and elevated cardiac troponin levels following receipt of an mRNA COVID-19 pro-vaccine. With reports about myocarditis cases appearing in the press (82) on April 27, 2021, FDA and CDC issued statements (page 153/201 in Document 2 of (74)), cited in part (83) as:

- [the agency has not seen] *"any new safety signals for myocarditis following administration of any of the authorized COVID19 vaccines." (FDA)*
- *"at this point, there is no safety signal for myocarditis or pericarditis for COVID-19 vaccines in U.S. monitoring systems."* (CDC)

These statements were inaccurate as discussed (8.3.1, 8.5), because various signals for myocarditis or pericarditis had emerged around or before the time of the Israeli inquiry on February 28, 2021. FDA has recently (July 14, 2025) stated FDA (84) *"The history of vaccine-associated myocarditis reflects missed opportunities for safety mitigation.*

Table 12: Examples of inconsistencies between FOIA, Oracle or VIOLIN datasets and FDA or CDC statements regarding safety signals

| Date | Setting | Statement | Inconsistent with | Event / Signal | Other reference |
|---|---|---|---|---|---|
| February 26 2021 | VRBPAC | *"No alerts detected.."* (59) (16) | Oracle, FOIA datasets | paraesthesia, dysgeusia, flushing, palpitations appendicitis pulmonary embolism | Table 1 |
| April 16, 2021 | FDA Review Memo | *"no other PTs with an EB05 >2.0"* (62) | Oracle, FOIA datasets | paraesthesia, dysgeusia, flushing, palpitations appendicitis pulmonary embolism, Bell's palsy | Supplemental Table 13 |
| October 28,2021 | Preprint authored by FDA and CDC | *"No adverse health outcome alerts were identified in EB data mining. However, five mRNA COVID-19 administrative error alerts* […] *were identified during the surveillance period"* | Oracle, FOIA datasets | paraesthesia, dysgeusia, flushing, palpitations appendicitis pulmonary embolism, Bell's palsy | (60) Supplemental Table 2 |
| November 12, 2021 | Paper by FDA and CDC staff (11) | *"one signal of disproportionate reporting (EB05>2) for US VAERS death reports"* | FOIA datasets | Signal absent | |
| July 12 2021 | Paper by FDA and CMS staff (4) | *"VAERS* […] *has not identified any association between any COVID-19 vaccine and these AEI"* | Oracle | PE, AMI, DIC, ITP | |
| January 26 2023 | VRBPAC (64) | *"No excess reports of stroke from VAERS."* (65) | FOIA – PRR VIOLIN | Ischemic stroke | (15,66,67,69-71) |
| February 15 2024 | House Select Committee (72) | *"we have not detected any increase in cancers with the Covid-19 vaccines."* | PRR FOIA July 29 2022 | Cancer signals | Supp Table 7 Supp Table 8 |
| September 12 2023 | ACIP (69) | *"VSD may consider further investigating mRNA vaccine primary series signals of VTE and AMI."* | Signals present in FOIA PRR May to July 2022 (43) | VSD signals dated May 2022 not previously disclosed | |
| May 17 2021 | ACIP | Myocarditis *"not differed from expected baseline rates."* (75) | Myocarditis signal announced May 27, 2021 (77) FOIA disclosure shows awareness of signal in early March 2021 (80) | Myocarditis | |

### *9.2 The impact of signal anomalies on the robustness of the regulatory process*

In 2017 FDA outlined (23) the statutory and regulatory basis for the Emergency Use Authorizations (EUA) it later issued for the COVID-19 pro-vaccines. Rather than the requirements of a conventional approval that establishes a new drug as "safe and effective," an EUA (p12/49) requires a lower standard whereby *"based on the totality of the scientific evidence available, it is reasonable to believe that the product may be effective."* The "totality" standard allows the FDA to consider evidence of a type or procedural or statistical quality not normally considered in a conventional approval.

The safety standard for an EUA requires that "*the known and potential benefits of the product,* […] *outweigh* [its] *known and potential risks."* In the same 2017 guidance (p12/49) FDA declared that to make this safety determination, "*FDA intends to look at the totality of the scientific evidence,"* which could arise from a variety of

sources "*available for FDA consideration."* Safety signals, including statistical signals, represent "potential risks" FDA was required to consider.

Beyond the initial COVID-19 vaccine EUAs, these evidentiary standards applied to the subsequent amendments and to ongoing EUA review of emerging data. Such emerging data included the 487-1898 Empirical Bayesian signals that we estimate were lost by filtering, masking, and truancy, representing an 86% suppression of the still largely uninvestigated *"potential risks"* FDA was required to consider.

The suppression of risk is both a scientific and a regulatory failure. The dissemination of anomalous and risk-suppressed EBGM signal data by the FDA within the FDA itself and to other agencies impugns the robustness of decision-making by regulators and their advisory committees, medical professionals, scientists, and the lay public regarding vaccine safety, authorization, approval, and injury compensation.

The problem is compounded if CDC could not place the FDA's EBDM data in the context of PRR analyses it was required to conduct. (40) This possibility is realized by reports that CDC only started conducting PRR analyses in March 2022.(43)

### *9.3 Relationship to regulatory actions regarding Janssen-associated thrombotic events*

The effectiveness of how the totality of evidence regarding safety signals was integrated into regulatory decisions can be evaluated through the case of thrombosis with thrombocytopenia syndrome (TTS) associated with the Janssen vaccine.

#### 9.3.1 Basis for pausing the use of the Janssen product

Against a background of seemingly similar cases involving the Astra-Zeneca product from outside the USA, and following six US cases reported to VAERS of cerebral venous sinus thrombosis (CVST) with thrombocytopenia after the Janssen product, the CDC and FDA recommended pausing the use of the Janssen product on April 13, 2021. Convening the next day, ACIP requested more data and an early follow-up meeting, occurring on April 23. The pause was then lifted (85) along with a new warning regarding TTS.(86) A booster dose was authorized in October 2021, and a contraindication was added in December 2021 (87) with ACIP's preferential recommendation for the modRNA products. (88) FDA further restricted the use of the Janssen pro-vaccine in May 2022, (88) revoking the EUA "at the manufacturer's request" on June 1, 2023. (89)

It is noteworthy that the appropriately cautious regulatory actions of April 2021 were made without a formal statistical analysis. CDC characterized the inciting six reports (in 6.86 million Janssen doses) of CVST with thrombocytopenia as a *"reporting rate imbalance"* (1:09:40 in (90)) compared with no reports after 97.9 million Pfizer doses, and 3 questionably similar reports with 84.7 million Moderna doses. Furthermore, as Janssen stated, (32:33 in Part 1 of (91)) *"causality has not been fully established"* for what could be an important potential risk.

#### 9.3.2 Relationship to signals for other clotting disorders.

At this time, the status of other thrombotic events surfaced, albeit fleetingly. CDC's Health Alert (92) recommended that clinicians *"Maintain a high index of suspicion for symptoms that might represent serious thrombotic events."* Answering an ACIP member at the April 14 meeting, VaST stated (20:01 in Part 1 of (91)) that they had not focused on more general clotting disturbances. CDC indicated that it would study other thrombosis-related events.(2:30:40 in Part 1 of (91)) Before the April 14 meeting, regulators discussed by email broadening the definition of a "case of interest" (p45/201 in Document 3 of (74)). They were also shown VSD analyses (p146/202 in Document 8 of (74)) indicating borderline rate ratios for DIC (1.29) and VTE (1.29) for the modRNA products.

Similar analyses (p52/198 in Document 9 of (74)) showing near-threshold signals were shown to VaST before the April 23, 2021, ACIP meeting, along with an update on the CMS data describing a Pfizer-PE signal (p189/198 in Document 9 of (74)). This signal was evident as early as 2/27/21, flagged as an "outstanding issue" in a May 10, 2021 presentation ("VaST planning" - p209-211 in Document 10 of (74) ) disclosed by FDA in July 2021, (63) and published in December 2022.(4) (see also 9.1.2) Of note is CDC's statement (May 12 ACIP meeting) regarding the few cases of Janssen-related thrombosis events (VTE, PE) that *"No statistical signals* [were] *detected for any prespecified Rapid Cycle Analysis outcomes."* (slide 29 in (17) Even if technically true, the materially omitted analyses and subthreshold signals shared with VaST members were key components of the "totality" of evidence needed by ACIP members to generate hypotheses concerning vaccine-related clotting disturbances and to consider the policy question of recommending the Pfizer pro-vaccine for teenagers.

### 9.3.3 Inconsistent regulatory handling of signals for clotting disorders

It is therefore difficult to reconcile the following.

- On the one hand, just a few cases of TTS, an intuitively detected reporting imbalance, no formal statistical analysis, and no establishment of causality elicited regulatory actions and an acknowledgement of the importance of monitoring other clotting disturbances.

- On the other hand, by ACIP's second meeting on April 23, 2021, the number of reports of PE far exceeded (Pfizer 129, Moderna 155, Janssen 49) the number of action-triggering cases of CVST with thrombocytopenia (Supplemental Table 13). Further, EB05>2 and canonical PRR signals for PE were available about 12 weeks earlier for the Pfizer and Moderna products, and had just appeared for the Janssen pro-vaccine, despite its only recent authorization on February 27 (Figure 8). It is noteworthy that these signals, evident in the Oracle dataset and derived from US and foreign reports, appeared to go unnoticed by regulators, despite their willingness to allow foreign-sourced reports about a related vaccine (AstraZeneca) to influence regulatory actions regarding the Janssen product.

  Regardless of whether or not these signals would be dismissed after triage, their existence was material to the discussion as well as to a subsequent ACIP meeting on May 12, 2021 along with the aforementioned signals or borderline signals from CMS and VSD data, respectively.

### 9.3.4 Persistent imbalance of Janssen signals lacking regulatory action

The imbalance of Janssen EBGM signals in the FOIA dataset was evident before ACIP's second emergency meeting on April 23, 2021 and persisted over the next 14 months (Figure 3). Seventeen ACIP or VRBPAC meetings afforded opportunities for regulators to report their findings publicly, in the *"spirit of transparency."* (63) as to whether this imbalance reflected a truly greater use-normalized abundance of signals associated with the Janssen product, or a disproportionate truancy of signals associated with the Pfizer and Moderna products.

Aside from the relevance of this imbalance to ACIP discussions on the full approval of the Pfizer (August 2021) and Moderna (February 2022) products, three of these occasions were particularly germane to the Janssen product. Rather than considering whether the increased risk for the Janssen product was so great as to warrant revocation of its EUA, any discussion of risk excluded the EBDM data.

The first of these occasions was a VRBPAC meeting (October 15, 2021), which considered Janssen's booster dose. Janssen's briefing document (93) noted imbalances for embolic and thrombotic events (p56/117), specifically PE and DVT (p71/117). Noting their investigation of VAERS signals (p80/117), Janssen concluded that their data *"support a favorable benefit-risk profile"* for their booster dose. In an addendum, Janssen described real-world data indicating what they characterized (p7/10) as "slightly increased" risks of PE of 1.3 or 1.4-1.5 under different study designs. They reported no increased risk for DVT and a "slightly increased" relative risk of 1.17-1.33 for a composite VTE endpoint. Janssen concluded that *"Based on the review of the totality of data there is insufficient evidence to establish a causal relationship between Ad26.COV2.S and thromboembolic events."*

The reliability of this conclusion is questionable since FDA had indicated that in its review (94) of the Janssen submission, it had not verified Janssen's analyses, disclosed in 22 out of 26 data tables or figures. This included (slide 35) reports of thrombosis, PE, and venous thrombosis, and the annotation *"Narratives of SAEs were not submitted by the Sponsor (which limits FDA's assessment of causal relationship)."* Further, FDA acknowledged (slide 43) that interpretation of safety data was limited by the small sample size and short follow-up.

FDA's briefing document (95) and safety presentation (96) reported that *"Post-authorization surveillance of VAERS has identified a potential emerging safety concern for thromboembolic events (TEEs) with normal platelet counts,"* and noted a risk assessment by the EMA regarding VTE (p14/54). FDA further noted a signal for Immune Thrombocytopenia, but reported (slide 12 in (96)) finding no DVT or PE signals from near real-time surveillance within the BEST system. Given these acknowledgments, and FDA's admittedly limited review of Janssen's submission, there was a heightened need to disclose to VRBPAC members the material EBDM analyses from the FOIA dataset, given that they were asked to vote on whether *"**available data** support the safety and effectiveness of Janssen COVID-19 Vaccine for use under EUA as a booster dose…"* (emphasis added).

On the second of these occasions, an ACIP meeting (October 21, 2021) to consider the Janssen booster dose, discussion of the EBGM signal imbalance was absent from CDC's safety presentations (97) and the Evidence to Recommendation Framework. (98)

Lastly, the imbalance was not raised at the ACIP meeting of December 16, 2021 meeting to discuss policy options following FDA's addition of a contraindication for the Janssen product regarding TTS. The EBGM signal imbalance was again absent from CDC's Risk/ Benefit assessment (99) whose proposed policy options included a CDC recommendation (slide 50) against the use of the Janssen product *"for all persons."*

#### 9.3.5 Implications of regulatory inaction regarding Janssen signal imbalance

Other analyses have described a diversity of VAERS signals associated with all three pro-vaccines, including thrombo-embolic events over similar periods. Using data to April 30, 2021, Yan et al. (100) calculated Reporting Odds Ratios, a metric related to PRR. Likewise, Montano calculated Risk Ratios for VAERS (to October 10, 2021) and European data (to October 18, 2021). We previously noted (101) that there were many other signals associated with all three COVID-19 pro-vaccines that warranted investigation and action at least as urgently as TTS associated with the Janssen product.

Our findings suggest that the EBGM signal imbalance in the FOIA dataset reflects both a truly greater use-normalized abundance of signals associated with the Janssen product (4.8, 8.8-fold), and a disproportionate truancy (26, 11-fold) of signals associated with the Pfizer and Moderna products, respectively. This imbalance warrants regulatory action at least as extensive and transparent as those executed for TTS, the correction of deficiencies in data handling and interpretation, and addressing the consequences of the safety signals themselves. One notable example of a signal warranting special attention would be the signal for death (n=17) associated with the Janssen pro-vaccine in the FOIA dataset (Supplemental Table 2).

### *9.4 Did regulators dismiss the value of DSA?*

Implicit in the inclusion of DSA methods in the VAERS standard operating procedure for COVID-19 vaccines, (40) and the Federal expenditure on them, is the acceptance that these methods are valuable pharmacovigilance tools. However, these methods are seldom mentioned or integrated into discussions of safety at ACIP or VRBPAC meetings or in documents released under FOIA or Senate subpoena (e.g. Document 8 of (74)).

Indeed, although noting comments ascribing some value to EBDM, a VaST report (March 29, 2021) recorded that *"[m]ost members felt that proportional ratio would not be helpful due to the nature of the Covid-19 vaccination program"* (p7/202 in Document 8 of (74)). Only limited mention of DSA has been found so far. (pp41 & 189/194 in Document 11; pp10, 79, 94, 174 in Document 12 of (74); slides 12 and 26 of (16))

Table 13: Summary of deficiencies in the FOIA dataset

| Description | Consequence | Note |
|---|---|---|
| **PRR Analyses** | | |
| Janssen data missing | Unable to make between-vaccine and between-threshold criteria comparisons | |
| No separate analyses provided for Pfizer and Moderna: analyses | Unable to analyze PRRs for each pro-vaccine separately | |
| Limited date range supplied | Unable to compare the time dependence of signal generation with EBGM data | |
| Foreign-originating VAERS reports not included. | Although signals should be stratified by originating location, foreign-originating cases make a valuable contribution to the "totality of data" essential for an "early warning system. | |
| Canonical EVANS PRR arbitrarily set at 2. Ignores "alternative" criteria described in the original paper. (31) | Statistically and clinically meaningful signals may be missed. Use of a threshold of 2 constitutes filtering. | General comment on VAERS SOP |
| Use of chi-squared value in canonical criteria based on empirical considerations. | Method should be standardized using a confidence interval-based method, as proposed in the original paper.(31) | General comment on method |
| 90% intervals are used in EBDM, and CDC reports use of 95% intervals. | Intervals should be standardized across methods. | General comment on method |
| Data not corrected for masking | Signals may be masked by many AE reports for other COVID-19 vaccines (38) | |
| Delayed FOIA disclosure | Impedes timely analysis by the public | |
| Stratification is inconsistent with EBGM stratification | Impedes the "totality of evidence" assessment of adverse event signals | |
| PRR analysis performed by a different agency (CDC) than the EBDM analysis (FDA) | 1. Impedes the "totality of evidence" assessment of adverse event signals<br>2. Ineffective and inefficient use of public resources | |
| Unknown if analyses have been performed on groups of related events, e.g. thromboembolic events, cancer-related events, etc. | The same signal may be reflected in multiple Preferred Terms | Background info to FOIA dataset |
| | | |
| **EBGM Analyses** | | |
| Threshold set at 2 without justification. | Statistically and clinically meaningful signals may be missed. Use of a threshold of 2 constitutes filtering. | General comment on VAERS SOP |
| Data not corrected for masking, despite apparent availability of RGPS method to FDA. | Signals may be masked by high rates of other COVID-19 vaccines (38) | |
| Data supplied as poor-quality PDF-embedded text, not in spreadsheet form. Inconsistent format | 1. Possible errors in data extraction<br>2. Inability to perform quantitative analysis | |
| Data appear missing for 10 of the expected 79 weekly reports | Missing data impedes reliable analysis | |
| Foreign-originating VAERS reports not included. | Although signals should be stratified by originating location, foreign-originating cases make a valuable contribution to the "totality of data" essential for an "early warning system. | |
| Delayed FOIA disclosure | Impedes timely analysis by the public | |
| PRR analysis performed by a different agency (CDC) than the EBDM analysis (FDA) | 1. Impedes "totality of evidence" assessment of adverse event signals<br>2. Ineffective and inefficient use of public resources | |
| Unknown if analyses have been performed on groups of related events, e.g. thromboembolic events, cancer-related events, etc. | 3. The same signal may be reflected in multiple Preferred Terms | Background info to FOIA dataset |

Table 14: Summary of anomalies in the FOIA dataset

| Description | Consequence/ Detail | Note |
|---|---|---|
| **PRR Analyses** | | |
| The VIOLIN dataset contains 2837 canonical PRR signals for COVID-19 pro-vaccines (4/30/22). Adjusting for masking and threshold filtering yields between 6123 and 6889 signals | Either these analyses were not done by CDC, or they were not disclosed under FOIA. | 8.5.3<br>Table 11 |
| The number of signals for mRNA vaccines vs. non-COVID vaccines (878) is far lower than the 1904 signals estimated from the VIOLIN dataset. | This represents a 2.17 truancy factor and 54% signal loss. | 8.4.2 |
| **EBGM Analyses** | | |
| Disproportionate contribution of Janssen EBGM signals both by variety of type and category and by number (~88%) to total vs. Pfizer (~7%) and Moderna (~5%)<br>Extremely high use-normalized signal excesses for Janssen over Pfizer (99x) and Moderna (123x) (as of 4/29/22) | These fold excesses for EBGM signals in the FOIA dataset are inconsistent with excesses of Pfizer or Moderna over Janssen signals of:<br>1. 4.8-8.8 fold (canonical PRR signals, VIOLIN dataset)<br>2. 1.7 -3.8 fold (canonical PRR signals, Oracle dataset)<br>3. 1 to 2.3 fold (EBGM signals, Oracle dataset) | Table 1<br>Table 5<br><br><br><br>Table 8<br>Supp Tab 13 |
| Apparent truancy of EB05>2 signals by 26- (96.1% Pfizer) and 11- (91.1% Moderna) fold. | From alternative PRR criteria: the ratios are 25- (Pfizer 96%) fold and 19.4 (Moderna 94.7%) | Table 5 |
| Large contribution of product use-related events for the Moderna (63.9%) and Pfizer (35.3%) compared with the Janssen (3%) pro-vaccine. | Exacerbates the disproportionate excess of Janssen signals over Pfizer and Moderna. | Supplemental Table 12 |
| Expected correlation of EBGM (FOIA dataset) vs. PRR signals (VIOLIN dataset) not present. | Inconsistent with the correlation between PRR and EBGM signals found in the Oracle dataset. | Figure 4<br>Figure 5 |
| 7/8 (87.5%) of EB05>2 EBGM signals detected in the Oracle dataset were missing in the FOIA dataset (p=0.02). | EB05>2 signals missing for<br>1. Myocarditis - Pfizer<br>2. Bell's palsy – Pfizer<br>3. Tinnitus – Janssen<br>4. Appendicitis – Pfizer, Moderna<br>5. Pulmonary embolism – Pfizer, Moderna (present for Janssen) | Supplemental Table 13, Table 7 |
| Signals disproportionally missing from FOIA dataset for Pfizer > Moderna >> Janssen | May partly account for the disproportional excess of signals in the FOIA dataset for Janssen over Pfizer and Moderna. | |
| FOIA dataset misses EBGM signals using the EB05>1 threshold present in the Oracle dataset for:<br>1. Myocarditis - Moderna<br>2. Pericarditis, Moderna, Pfizer<br>3. Bell's palsy – Moderna<br>4. Tinnitus – Pfizer, Moderna<br>5. Appendicitis – Janssen | Arbitrary use of EB05>2 threshold (and not the EB05>1 threshold means that potentially important signals may be missed. Use of a threshold of 2 constitutes filtering. | Supplemental Table 13 |
| An estimated 763 (range 487-1898, 85-93%) signals are missing from the FOIA dataset. | Includes losses due to truancy, masking, and filtering. These represent largely uninvestigated potential risks FDA were required to consider. | 8.5.3 |
| Hematologic events (thrombo-embolic, coagulation) accounted for 30.1% of the signals for Janssen, but were absent from the AE signals associated with the Pfizer and Moderna pro-vaccines. | There are a large number of PRR signals for hematologic events for both modRNA, products, although they are outnumbered by those for the Janssen product. | Supplemental Tables 2 and 6 |
| Inconsistencies between FOIA, Oracle or VIOLIN datasets and FDA or CDC statements regarding safety signals | | Table 12 |

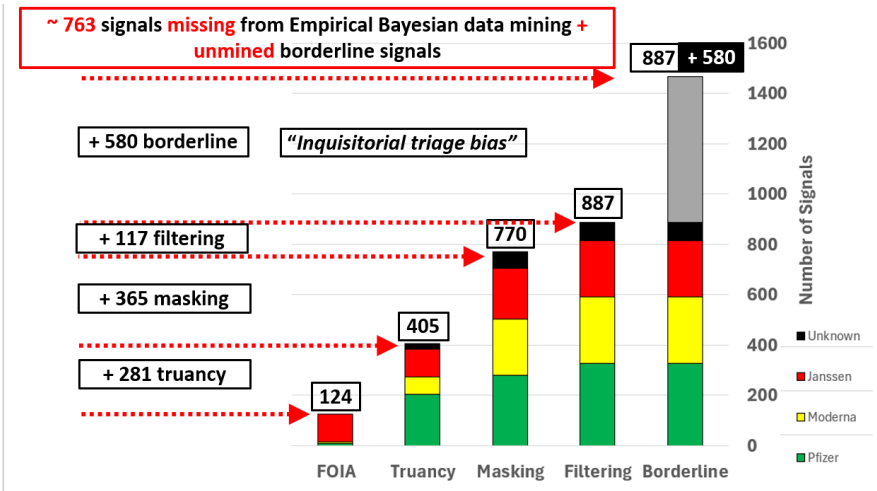
## 10 DISCUSSION

This study has revealed six main anomalies that challenge its reliability:

- A disproportionate use-normalized excess of the number of EBGM signals for the Janssen over the Pfizer (123x) and Moderna (99x) pro-vaccines.
- Lack of an expected correlation between the numbers of EBDM and PRR signals in the FOIA dataset suggests a disturbance of data integrity.
- An apparent absence of 96% (Pfizer) and 91% (Moderna) in the FOIA dataset, representing truancy factors of 26 and 11, respectively. 87.5% (7/8) of EB05>2 signals detected in the Oracle dataset were absent from the FOIA dataset (p=0.02).
- No adjustment appears to have been made for masking, which could account for 23-63% losses in the number of signals (Figure 6).
- The EBGM and PRR thresholds were set at 2 instead of 1, filtering out 13-69% of signals.
- The true excess of Janssen over Pfizer or Moderna signals is likely to be around 4.8, 8.8-fold, This anomaly should have warranted regulatory actions at least as extensive and transparent as those executed for Thrombosis with Thrombocytopenia Syndrome (TTS) associated with the Janssen product (9.3).

After correcting for biases due to signal truancy, filtering, and masking, these anomalies represent aggregate losses as of April 29, 2022, in the FOIA dataset of 763 (range 487-1898, 86% loss, range 85-93%) EBDM signals (Figure 9, section 8.5.3). Given the strong linear correlations found in the Oracle dataset (Figure 5) between the number of PRR signals and Empirical Bayesian signals, the loss of signals could be as high as 2713 (canonical PRR) to 6765 (demasked alternative criteria PRR signals) found by direct examination of the VIOLIN database, but not reported or retrieved by CDC.

Figure 9: Summary of EBDM estimated lost signals in FOA dataset as of 4/29/22




The total number of signals (unique AE-vaccine pairs with a statistical association) is shown in the boxes above each bar, each representing a additional level of bias correction. As of April 29, 2022, there were 124 EBDM signals in the FOIA dataset. Using similarly dated CDC vaccine use data and PRR data from the VIOLIN database, the number of signals expected after accounting for truancy (420), masking (770), and filtering (887) were calculated. Additionally, there were 580 borderline signals, with PRR >1, lower 5% CI <1, or PRR <1, lower 5% CI >1, from which an unknown number of *bona fide* signals may be discoverable. (See Supplemental Table 18 for source, and a similar graph that utilizes Oracle data).

Failure to adjust for masking and filtering are incompatible with the "Enhanced surveillance" of Adverse Events Special Interest (AESI) and the representation of VAERS as "*the nation's early warning system for vaccine safety.*"

Additionally, the PRR component of the FOIA dataset lacked separate analyses for Pfizer and Moderna products or any analysis for the Janssen product. The limited analysis for the mRNA vaccines aggregated against non-COVID vaccines appears deficient in 1026 (54%) PRR signals.

### *10.1 Deficiencies in DSA methodology applied to vaccine safety*

#### 10.1.1 The absurdity of failing to adjust for masking

In estimating the effect of masking in the FOIA and VIOLIN datasets, we have only addressed one form of masking, namely (38) where "*signals for a vaccine of interest are hidden by the presence of other reported vaccines."*

A second form of masking occurs where the PRR signal for an otherwise more frequent target AE is attenuated because the number of separate AE types reported for each unique VAERS case report for the target vaccine is greater than for its comparators. This form of masking is unavoidable, according to the original description of the PRR method (31) and the VAERS Standard Operating Procedure for COVID-19 vaccines.(40) which defines the PRR in terms of the number of "reactions of interest" and "all other reactions." This problem is avoided by using the number of unique VAERS case reports, rather than the total number of unique AEs reported, to calculate the PRR. To do otherwise would be absurd, and indeed, the Oracle and VIOLIN datasets used this improved method. Further, it is the method used by CDC in the PRR portion of the FOIA dataset, despite not complying with the standard operating procedure.(40)

CDC's avoidance of this second form of masking intensifies the question as to why regulators failed to avoid the first kind of masking by availing themselves of relatively simple spreadsheet calculations or features of the Empirica software it was using. The MHRA, also using Empirica software, does not appear to be availing itself of its demasking features.(54)

A third form of uncorrected masking occurs if, despite an increase in the number of cases of the target AE, there is a greater increase in the number of other AEs experienced by different patients, without an increase in the number of events reported per case.

Related to the issue of masking is the choice of comparator vaccine, as differences between its usage pattern and that of the target vaccine will lead to confounding. The VAERS SOP (p16/43 in (40)) required CDC to *"apply appropriate comparator vaccines (e.g., adjuvanted vaccines like Shingrix and/or Fluad for adjuvanted COVID-19 vaccines) and adjust for severity and age distributions where applicable."* It is unclear if this was done.

#### 10.1.2 PRR>2 and EB05>2 thresholds constitute filtering antithetical to "early warning" and "enhanced surveillance"

A presentation given by an FDA scientist to VaST on April 5, 2021, noted that *"Technically, any EBGM value above one indicates disproportionate reporting"* (p47/202 in Document 8 of (74)). Despite this, the presentation noted, a "standard" threshold of two was used in FDA's EBDM analyses, as reflected in the VAERS SOP.(40)

As we noted earlier (8.2.1), the use of the higher threshold does not change whether or not there is a statistical association for a particular vaccine-AE pair, it merely imposes a filtering condition, somewhat analogous to a "high-pass" filter used in electronics.

This distinction is an important one for regulatory transparency in the description of the totality of safety data. If, on the one hand, a statistical signal is only truly declared at a threshold of two, the enumeration of signals meeting this threshold fairly represents the universe of potential safety issues for a particular drug. If, on the other hand, the higher threshold is applied as a filter, this fact must be disclosed in any consideration of potential safety issues, else it would appear as an attempt to misrepresent the statistical axiom that a statistical association occurs once the null of one is crossed.

Using a threshold of two has become a widespread practice. The main justification appears to be the reduction of noise. According to a paper cited in the background materials accompanying the FOIA disclosure (35) and co-authored by one of the FDA-affiliated co-authors (Dr. Szarfman) in the paper by Harpaz et al., (38)

> *"using the criterion of EB05 greater than 2 ensures with a high probability that, regardless of the count size, the particular drug-event combination occurs in the database at least twice as often as expected under the assumption of randomly paired drug and event reports. The EB05 gives some assurance that potential signals are unlikely to be noise."*

Accordingly, a high threshold serves as a surrogate for further investigation of signals to determine whether or not causality can be declared.

Setting a threshold necessitates a trade-off between *"generating too many false positive signals if the threshold is too low or missing true signals if this threshold is too high."* (cited by (39)) Thus, as recognized by Szarfman et al. "*using an EB05 greater than 2 as a definition of a signal for all analyses is by no means always optimal."* Szarfman et al., proffer:

> "[The] *threshold should be chosen by the analyst depending on the severity of the event of interest or its clinical or public health importance."*

This sentiment is echoed by other FDA statisticians responsible for an open-source version of the EBDM software who note (Vignette 4 in (102,103)) that the "*value of 2 is arbitrarily chosen, and depends on the context."*

The consideration of the "*clinical or public health importance"* certainly pertains to the COVID-19 pro-vaccines. Further, Szarfman *et al*. (35) advise:

> "*When exploring severe adverse events (such as fatal outcomes), it might be appropriate to use the whole range of EBGM signal scores (positive and negative [EBGM > 0]) and confidence limits…"*

Despite effectively constituting a filter, the threshold of two for PRR analyses seems to have become canonized for more empirical reasons. As described earlier (8.2.1), in their original paper, Evans et al. (31) were not rigid in defining what became accepted as their "canonical" criteria. (38) Implicit in these criteria (PRR>2, chi-squared >4, N cases $\geq$ 3) is the ability to detect signals involving low case counts, an assumption reinforced by the use of Yates's correction, typically used when at least one of the input values is less than five. Thus, the canonical Evans PRR criteria appear to have been set empirically, such that with few AE cases, only PRR values exceeding 2 provide sufficient power to detect statistically significant ($p<0.05$) increases (associations) over the expected null value of 1 and reflected in a chi-squared value of approximately 4. Using a p-value, or confidence interval as the significance component of the signal criterion (10.1.4) avoids the problem of filtering by fixing the threshold at 2.

In the VIOLIN dataset, there were 5844 AE types with more than 20 case reports, and 2432 events with more than 100 case reports. These frequencies comfortably exceed those for which the canonical Evans criteria would need to be strictly applied. It is readily apparent that more AE reports provide sufficient power to detect smaller increases in the PRR for a particular AE. For some AEs, (e.g. death), increases of just a few percent would be clinically and epidemiologically meaningful.

There are notable exceptions to the widespread practice of using a threshold of two. In their paper providing the Oracle dataset, Harpaz *et al.* (38) use the EB05>1 threshold. The minutes of the April 5, 2021, VaST meeting noted that on a certain date, EB05 values for death, myocarditis, and facial paresis were less than 1, indicating that for some purposes, the value of 1 was considered an important threshold. A similar threshold was also applied to the Reporting Odds Ratio in a publication whose authors included the originator of the PRR method. (104)

In sum, given the rapid introduction of a novel class of drugs under emergency authorization, filtering signals by applying a threshold of two is:

- incompatible with the VAERS SOP (40) that describes conducting "Enhanced surveillance" of "adverse events of special interest" (AESI)
- incompatible with the representation that "*VAERS is the nation's early warning system for vaccine safety."* (15-18)
- incompatible with the "hypothesis-generating" objective of the EBDM analyses, as pointed out in the background materials provided with the FOIA dataset.
- mostly superfluous to the noise reduction already accomplished by EBDM

It therefore behooves investigators and regulators to not only justify the application of a threshold filter to DSA criteria, but to report its use along with the enumeration of unfiltered signals (i.e. meeting PPR >1 and EB05>1) *ab initio*.

### 10.1.3 "Inquisitorial triage bias"

FDA has referred to the PRR and EBDM methodologies as forms of data mining (40) which it defines (56) as the *"systematic examination of the reported adverse events by using statistical or mathematical tools."* FDA explains that data mining *"can provide additional information about the existence of an excess of adverse events reported for a product."* (56) "Inquisitorial triage bias" is introduced in the triage of DSA signals by mining for false positives, without equally zealous mining of "borderline" signals (false negatives among borderline threshold ratios whose confidence intervals cross the null). Such a bias is incompatible with the "enhanced surveillance" and "*early warning system"* goals of VAERS cited in the *Introduction*. Mining within borderline cases is essential to identify falsely negative or emerging signals.

Borderline signals in the Oracle dataset contributed an additional 17 to 21% to the number of signals possibly meeting the PRR, EB05 or ER05 criteria (Supplemental Table 13). In the VIOLIN dataset (Supplemental Table 5D), this contribution was between 87% and 181% (threshold of 2) and 65-84% (threshold 1).

Another source of potential signals is in the AEs for which the case count is >2, but for which the case count for comparator vaccines is zero, excluding them from consideration in the other analyses. In the VIOLIN dataset (Supplemental Table 22), there were 112 of these AEs (Pfizer 77, Moderna 34, Janssen 1).

### 10.1.4 Selection of the "significance component" of the signal criterion

There are limitations in declaring a PRR signal related to the selection of the significance component (i.e. a chi-squared value, a p-value, or a confidence interval) of the signal criteria. As described above (10.1.2), a chi-squared value of 4 appears to be an empirically set minimum value needed to provide sufficient power to detect PRR changes associated with low case counts. Since this is only an approximation, there will be a mismatch between the number of signals adjudicated by the canonical criteria and those that use a p-value calculated from a chi-squared value. Due to differences in the characteristics of the chi-squared and normal distributions, there is likely to be a further mismatch, especially with low case counts, in the number of signals generated using the chi-squared-derived p-value and a confidence interval based on the normal distribution.

In addition to providing chi-squared values, the PRR component of the FOIA dataset provides the upper and lower bounds of the 95% confidence interval. It is unknown if this interval informed any regulatory decision. This interval will yield fewer signals than the one used in the EBDM method, namely, the lower 5th percentile of the EBGM distribution (38) referred to by FDA as the lower bound of the 90% confidence interval. (40)

Given the variable selection of the significance component of the PRR criteria by FDA, CDC, and an NIH-funded database, the opportunity for confusion can be avoided by standardization. It seems that replacing the chi-squared-based canonical PRR criteria with a confidence interval-based method, as others have done,(105) would provide the most flexibility and consistency with Bayesian methods.

### 10.1.5 Shifting definitions of "signal." Is a signal of a signal a signal or a suspected adverse reaction?

Although a signal of statistical association (i.e. a PRR or EBGM value meeting signaling criteria) requires further investigation to establish causality, FDA sought to widen the distinction between signal and causality by stating in the FOIA disclosure that *"*[t]*he* [EBDM] *method is hypothesis-generating. Statistical signal of disproportional reporting (SSDR) ≠ safety signal*." Such a distinction would render "true" a report that certain safety signals had not been detected, without revealing the existence of signals of statistical association. This, at best, disingenuous distinction is not borne out practically in the use of the word "signal."

The pharmacovigilance literature attempts to discern between a "signal of disproportionate reporting" (SDR) and a "signal of suspected causality" (SSC). However, as can be inferred from references to "signals" in presentations by regulators, (40) this distinction is seldom made. (65,69) The term "safety signal" at best left undefined, but often tied to the findings of statistical signals without further qualification. (e.g. slide 23 in (15), slide 20 in (73), (106)

Both types of signals, SDR and SSC, are forms of "safety signal," the former being a precursor for the latter. As understood by Harpaz et al., (38) and from the context of work that includes the VSD lead.(70) "safety signal" represents a *"possible causal relationship between an AE and a product, of which the relationship is unknown or incompletely documented."* (38) Accordingly, paralleling its use by CDC (slide 31 in (17)), we have used the term "safety signal" generically to include both SDR and SSC.

Perhaps the clearest acknowledgement that a statistical signal is considered a “safety signal” comes from the VAERS SOP: *“MedDRA terms identified as **safety signals** due to elevated PRR and/or a statistically significant finding on data mining will be reviewed as appropriate.”* (p18/43, emphasis added)(40)

Regardless of the degree of triage or confirmation, a statistical signal is in essence a “suspected adverse reaction” (SAR) which, in the context of Investigational New Drugs, (107) means *“any adverse event for which there is a reasonable possibility that the drug caused the adverse event. For the purposes of IND safety reporting, “reasonable possibility” means there is evidence to suggest* [not establish] *a causal relationship between the drug and the adverse event.”*

#### 10.1.6 Other DSA improvements: surrogate estimates of exposure when coverage rates are known

Although DSA of spontaneously reported data (e.g. VAERS) is considered an important tool in pharmacovigilance, there is wide agreement, as evinced by a paper authored by British and European regulators, along with Astra-Zeneca and Pfizer scientists, that they *"are not easily interpretable in terms of clinical impact."* (39) The paper further noted that *"calculation of PRRs* […] *should not replace nor delay the performance of formal epidemiological studies."* (39)

It is for this, and other known shortcomings of VAERS, that the recently confirmed FDA Commissioner announced a transition away from VAERS towards Health Information Exchanges (HIEs) that access real-world data contained in electronic health records (EHR).(108) This is not without its own challenges, including public accessibility and transparency, and evidence that EHRs may fail to capture vaccine use adequately. (109) Limitations of EHR data, for example, in the comparison of myocarditis rates in vaccinated and SARS-CoV-2 infected cohorts, were noted in a paper authored, in his former capacity, by CBER Director Prasad.(110) Further, existing EHR or database-based systems monitor a limited number of events – 23 for VSD (69) and 17 in BEST. (111) VSD has lagged behind other systems in identifying myocarditis, PE, and stroke signals (9.1.2 , 9.1.3, 9.1.6).

There is therefore value in improving VAERS and related systems to provide an orthogonal view to that obtained from EHRs, and yielding analyses more rapid and reliable than at present. In the initial phases of vaccine introduction, the number of doses per person is fixed, with a known number of doses given to a known number of people (vaccine coverage). Hence, replacing surrogate measures of exposure with direct measures of vaccine coverage already available to CDC provides a more accurate incidence rate, *inter alia*, because individual signals are not diluted by a total number of events for that drug that is disproportionately greater than for comparator drugs.

Adopting this approach, used occasionally by FDA and CDC (61,112,113) and others,(114) we obtained “Normalized Event Ratio” (NER) signals referenced against influenza vaccine (115,116) that were more intense than their PRR counterparts. For example, the NER for death (all COVID-19 pro-vaccines) was 176 (by person vaccinated) and 97.5 (by number of doses) against a PRR of 5.2. For coagulopathy, the NER (by dose) was 276 against a PRR (by number of events) of 12.8.(116)

However, in the case of COVID-19 vaccines, booster dosing complicated the estimation of an incidence rate denominator, necessitating the use of DSA methods. Moreover, the advent of heterologous (“mix-and-match”) boosting further confounded safety data analysis.

### *10.2 Limitations*

A strength of our study is that it utilizes data from two well-pedigreed sources associated with NIH and FDA. (38,45) Our study has several limitations, described in the text, but largely related to inherent deficiencies in the quality and extent of the FOIA dataset (Table 13). Accordingly, verification of our analysis, with age and gender stratification, awaits full disclosure of EBGM and PRR signals by regulators. Although supported by an analysis based on the number of masked associations found by Harpaz et al. in VAERS. our finding of truant EBDM signals from the FOIA dataset awaits full disclosure of AE and vaccine coverage data to determine if this finding is generalizable beyond the seven AEs studied by Harpaz et al. Such disclosure will enable more accurate time-stratified estimation of the number of masked and otherwise concealed signals.

A general limitation is reflected in the background information accompanying the FOIA dataset relating to MedDRA constraints, namely that “*Signal X can be reflected in multiple PTs* [Preferred Terms] *that individually do not reach alert threshold.*” It is not known what analyses were performed by FDA or CDC on groups of related terms, such as thromboembolic events, cancer-related events, etc.

## 11 CONCLUSION

CDC has stated (17) that the *"U.S. vaccine safety monitoring system is able to rapidly detect rare adverse events following vaccination and quickly assess safety signals"* and that *"VAERS is the nation's early warning system for vaccine safety."* (15-18) Such attributes were critical to monitor the safety of arguably the most complicated medical products ever produced, authorized for emergency use after an accelerated research program whose development was characterized by the boast "*We flew the aeroplane while we were still building it."* (117)

However, regulators failed to recognize imbalances in the analysis of EBGM signals. They failed to act on a greater abundance of signals associated with the Janssen product and a truancy of signals associated with the Pfizer and Moderna products. Further, inappropriate threshold filtering, a failure to correct for masking, and an inquisitorial triage bias prevented the identification of signals.

Our primary finding, suggesting 763 missing signals in the FOIA dataset as of 4/29/22 is based on the correction of truancy, masking, and filtering biases. The robustness of this correction stems from the almost identically dated CDC and VIOLIN data used to calculate the correction factors, the completeness and size of the VIOLIN dataset, and the strong correlations between PRR and EBDM signal types derived from a well-pedigreed Oracle dataset. The estimate is supported by those obtained using dataset-date combinations. It is conservatively lower than that obtained by direct enumeration from the VIOLIN dataset of between 2713 and 6765 lost signals, and still lower than the 24971 US and foreign VAERS signals (total) reported by Harpaz et al.

Along with inconsistencies with statements made by regulators (9.1) and actions related to the Janssen product (9.3), our findings signal a failure to integrate the totality of safety data in the calculation of "potential risk." Suppressing 86% of Bayesian signals suppressed 86% of suspected adverse reactions, still uninvestigated "potential risks" that the FDA was required to consider, and impugning authorization, approval, and injury compensation decisions concerning the COVID-19 pro-vaccines (9.2). Most notable are those decisions relating to the safety of the Janssen product and the full approval of the Pfizer and Moderna products.

This compromise amplifies the erosion of trust in public health institutions, exacerbated by COVID-19 vaccination.(118) Despite their limitations, our findings warrant full disclosure of vaccine safety data and an investigation into inadequate signal detection and regulatory oversight. This must be consistent with the CDC's commitment to *"open and transparent communication of vaccine safety information."*(17) Possibly a harbinger for reform is the recent statement by FDA (84) *"The history of vaccine-associated myocarditis reflects missed opportunities for safety mitigation."*


## 12 ACKNOWLEDGMENTS

I wish to thank Ms. Marjorie Roswell for her assistance in data extraction and production of graphics, and Tom Yengst and Lizabeth Willner for their assistance in obtaining historical VAERS data. I also wish to thank several colleagues for their comments on this work, and the many collaborators on previous works, which have formed the foundation for this one.


## 13 REVISION HISTORY

083125
090125 Legend added for Figure 9
090525 Citations and associated text added (12,53,60,68)
Version number removed, and replaced exclusively with date (MMDDYY)
Keywords added

## 14 GLOSSARY

| | |
|---|---|
| ACIP | Advisory Committee on Immunization Practices (CDC) |
| AE | Adverse event |
| AESI | Adverse Event of Special Interest |
| AMI | Acute myocardial infarction |
| AR | Adverse reaction |
| CBER | Center for Biologics Evaluation and Research |
| CDC | Centers for Disease Control and Prevention |
| CI | Confidence interval |
| COVID-19 | Coronavirus disease 2019 |
| DIS | Disseminated intravascular coagulation |
| DSA | Disproportionality Signal Analysis |
| DVT | Deep venous thrombosis |
| EBDM | Empirical Bayesian Data Mining |
| EBGM | Empirical Bayesian Geometric Mean |
| EMA | European Medicines Agency |
| EUA | Emergency Use Authorization |
| FDA | Food and Drug Administration |
| GM | Geometric mean |
| HHS | Health and Human Services |
| IQR | Interquartile range |
| MedDRA | Medical Dictionary for Regulatory Activities |
| MHRA | Medicines and Healthcare products Regulatory Agency (UK) |
| NIH | National Institutes of Health |
| PE | Pulmonary embolism |
| PRR | Proportional Reporting Ratio |
| PT | Preferred term |
| RUR | Relative Use Ratio. The ratio of either:<br>(By dose): The number of Pfizer of Moderna to Janssen doses administered by a certain date.<br>(By people): The number of people receiving at least one dose of vaccine by a certain date. |
| SER | Signal Excess Ratio. The ratio of the number of Janssen to Pfizer or Moderna signals, unadjusted for usage. |
| TTS | Thrombosis with thrombocytopenia syndrome |
| UNSER | Use Normalized Signal Excess Ratio |
| VaST | ACIP's Vaccine Safety Technical (VaST) Work Group |
| VAERS | Vaccine Adverse Event Reporting System |
| VE | Vaccine efficacy |
| VRBPAC | Vaccines and Related Biological Products Advisory Committee (FDA) |
| VSD | Vaccine Safety Datalink |
| VTE | Venous thromboembolism |

## 15 READUS-PV CHECKLIST

The following checklist has been completed: Reporting of a Disproportionality Analysis for Drug Safety Signal Detection Using Individual Case Safety Reports in PharmacoVigilance (READUS-PV) (24)

| Section and topic | Item # | Checklist item | Location where item is reported |
|---|---|---|---|
| | | | |
| Title | | | |
| | 1a | If disproportionality analyses are a prominent component of the published study, the study should be identified as a "disproportionality analysis". The type of data and name of the database(s) should be specified. | Title |
| | 1b | Report the name of adverse event(s) and/or drug(s) under study, when applicable. | Title |

| | | | |
|---|---|---|---|
| Introduction | | | |
| Background | 2a | Describe the drug(s) and its utilization, the nature of the adverse event(s) under study and its frequency, and the existing knowledge on the drug-event combination. | Section 6.1 |
| | 2b | Specify the rationale for performing the analysis, e.g., as part of routine pharmacovigilance, to investigate an overall safety profile, or to assess a pre-specified hypothesis. | Section 6.1 |
| | 2c | Explain why ICSR databases and disproportionality analysis are suitable to fill the knowledge gap. | Section 6.1 |
| Objectives | 3 | State specific objectives, identifying the adverse event(s), the drug(s), and the reference group, including any pre-specified hypothesis, if applicable. | Section 6.2 |
| Methods | | | |
| Study design | 4a | Identify the study (i.e., “disproportionality analysis”) and the type of data used (e.g., “individual case safety reports”). | Section 7 |
| | 4b | Provide an outline of the entire study design, including primary and sensitivity analyses performed, and other designs such as case-by-case analysis or literature review. | Section 7 |
| Data description, access, and pre-processing | 5a | Specify the name of the database(s), the database(s) custodian, and the coverage. Specify the type/number of drugs included within the database and the thesaurus, taxonomies, or ontologies used for coding drugs and events. | 7.1.1, 7.1.2, 7.1.3 |
| | 5b | Specify the extraction dates and describe and justify all choices used for data pre-processing, including any data transformation or exclusion, if appropriate. | 7.1.1, 7.1.2, 7.1.3 |
| Variables definition | 6a | Describe the study population, including any restriction. | 7.1.1, 7.1.2, 7.1.3 |
| | 6b | Describe the nature and the meaning of key variables assessed in the work. | throughout |
| | 6c | Specify and justify any grouping of drugs or events. For drugs, specify and justify whether active ingredients/trade names/salts were considered and/or the selected role. | 8.1.2, 8.4.2, 9.1.3, 9.1.4 |
| | 6d | Describe any additional data source used, the type of data, and how they interact with ICSRs. | 8.1.3 |
| Statistical methods | 7a | Present any descriptive analysis performed, specifying variables investigated, statistical tests, and significance thresholds. | 8 |
| | 7b | Describe the measure(s) selected for the disproportionality analysis including any threshold used to identify signals of disproportionate reporting. Explain the reason for this choice if applicable. | 8 |
| | 7c | Clearly describe any sensitivity analysis and any tool to control confounding, including any restriction, subgroup, stratification, adjustment, or interaction. | 8 |
| | 7d | Specify the variables and methods used for the case-by-case analysis, including any algorithm or criteria used to assess causality, if performed. | NA |
| | 7e | Specify any statistical methods used for other data sources. | NA |
| Results | | | |
| Participants | 8a | Specify the number of individual case safety reports included at each stage, including reasons for exclusion. | NA |
| | 8b | Provide key demographic and clinical characteristics of cases, if possible comparing cases with any appropriate reference group. | NA |

| | | | |
|---|---|---|---|
| Disproportionality analysis | 9 | Present all results including confidence intervals. Present also results of sensitivity analyses, if performed. | CI's medians and range presented as appropriate |
| Case-by-case | 10 | Present the case-by-case analysis of key variables. Present the causality analysis assessment, if applicable. | NA |
| Discussion | | | |
| Key results | 11 | Discuss key results with reference to study objectives and contextualize them within the current literature and other consulted sources. Clearly discriminate between expected reactions and emerging safety signals. | 10, |
| External validity | 12a | Discuss the external validity of the results to the general population. | 10.2 |
| | 12b | Discuss the potential relevance of results in clinical practice | 9.1, 10.1 |
| | 12c | Propose further study designs if applicable | 10.1.4, 10.1.6 |
| Limitations | 13 | Present general limitations, making clear that disproportionality analysis alone cannot prove causation or measure incidence, and specific limitations, including confounding and reporting bias and efforts to mitigate them. | 10.2, 6.1 |
| Declarations | | | |
| | 14a | Provide the source of funding/sponsorship and the role of the funders/sponsors for the present study and for any original study on which the present article is based | Title page |
| | 14b | Clearly identify potential commercial and intellectual conflicts of interest (e.g., link to any drug/event investigated, whether financial, legal action, or software used). | Title page |
| | 14c | Declare any institutional approval needed or granted in the investigation. | 7.3 |
| | 14d | Include a statement on data availability, code availability (including the version of the statistical software used), and protocol registration. | Title page |

**The READUS-PV checklist for abstracts**

| | | | |
|---|---|---|---|
| Background | 1a | State the aim/rationale for performing the study. | X |
| | 1b | Specify the adverse event(s) and/or the drug(s) under study, when applicable. | X |
| | 1c | Specify the specific population or setting, when applicable. | X |
| Methods | 2a | Identify the study as a "disproportionality analysis" and specify the type of data used | X |
| | 2b | Specify the name of the database(s) used and the type of access. | X |
| | 2c | Specify the timeframe and geographical region, when applicable. | X |
| | 2d | Specify the disproportionality measure(s) used and their statistical significance threshold(s). | X |
| | 2e | Specify if a case-by-case analysis is performed. | NA |
| Results | 3 | Report main findings including their precision (e.g., 95% confidence intervals), together with a short summary of the case-by-case analysis. | X |
| Conclusion | 4a | Clearly report key conclusions. | X |
| | 4b | Acknowledge that the disproportionality analysis is a hypothesis generating or refinement approach. | X |
| | 4c | State the implications and clinical relevance of the findings. | X |

## 16 LIST OF SUPPLEMENTAL SOURCES

Supplemental Table 1: List of events that do not indicate an abnormality
Supplemental Table 2: EBDM signals by event type and category in FOIA dataset
Supplemental Table 3:
3A: Relative COVID-19 vaccine use by dose and users from January 6, 2021 to June 29, 2022, based on CDC statistics
3B: Ratios and normalized ratios of Pfizer or Moderna to Janssen signals, by doses, users
Supplemental Table 4:
4A: Numbers and relative occurrence (as SER) of AE reports made to VAERS for the COVID-19 pro-vaccines
4B: Reconciling case and event counts in Oracle and VIOLIN datasets, with VAERS Wonder
Supplemental Table 5:
5A: Number of PRR Signals in VIOLIN dataset (4/30/22), Pearson chi-squared: Masked.Alt Evans based on p value
5B: Number of PRR Signals in VIOLIN dataset (4/30/22), Yates chi-squared: Masked. Alt Evans based on p value
5C: Number of PRR Signals in VIOLIN dataset (4/30/22), Pearson chi-squared: Demasked. Alt Evans based on p value
5D: Number of PRR Signals in VIOLIN dataset (4/30/22), Yates chi-squared: Demasked. Alt Evans based on p value
5E: Number of PRR signals derived from the VIOLIN dataset and ratio compared with Janssen
Supplemental Table 6: PRR Hematologic Signals Extracted from VIOLIN database 4/30/22 (Yates chi-squared)
Supplemental Table 7: Cancer Signals for mRNA vaccines in FOIA PRR dataset meeting canonical criteria
Supplemental Table 8: PRR Cancer Signals Extracted from VIOLIN database 4/30/22 (Yates chi-squared)
Supplemental Table 9: Listing of EBGM EB05 >2 signals by report date
Supplemental Table 10: Shared Event Types in EBDM FOIA dataset
Supplemental Table 11: Data for histograms: accumulation of EBDM signals by time
Supplemental Table 12: Effect of masking and threshold filtering on the number of signals in the Oracle and VIOLIN datasets
Supplemental Table 13: Analysis of Oracle dataset from Harpaz et al, 2022
Supplemental Table 14: Figure 4 background data. Correlation between PRR (4/30/22 snapshot) and EBGM (4/29/22 snapshot) Signals Generated in VAERS (Yates chi squared)
Supplemental Table 15: Figure 6 background data Correlation between PRR and EBGM Signals Generated in VAERS Oracle dataset
Supplemental Table 16:
16A: Background data for Table 10: Number of canonical PRR signals present in CDC datasets released under FOIA
16B: Consolidated list of PRR signals in FOIA dataset (5-11, 12-17 and 18+ age classes) for 4/29/22
Supplemental Table 17: Vaccine-AE pair listing for PRR Signals in VIOLIN dataset (4/30/22), Yates chi-squared
Supplemental Table 18: Figure 9 source: Summary of EBDM estimated signal losses in FOA dataset as of 4/29/22
Supplemental Table 19: Canonical Signals in VIOLIN dataset for mRNA vacines combined vs. non-COVID vaccines
Supplemental Table 20: Effect of threshold on EB05 signal generation from a MHRA dataset
Supplemental Table 21: PRR Neurologic, or possibly neurologic signals extracted from VIOLIN database 4/30/22 (Yates chi-squared)
Supplemental Table 22: Listing of events in VIOLIN dataset (4/30/22) with >2 events in target product, but 0 events in comparator

| | |
|---|---|
| Table 2 Source | Categorized adverse event signals obtained by EBDM for COVID-19 pro-vaccines, in descending order of frequency |
| Table 11 Source | Aggregate effect of threshold and masking on loss of DSA signals |
| Supplemental Figure 1A | Correlation between PRR (4/30/22 snapshot) and EBGM (7/1/22 cumulative) Signals Generated in VAERS (Pearson chi squared) |
| Supplemental Figure 1B | Correlation between PRR (4/30/22 snapshot) and EBGM (7/1/22 cumulative) Signals Generated in VAERS (Yates chi squared) |
| Supplemental Figure 2 | Component and aggregate effects of masking and threshold filtering on signal generation in the Oracle and VIOLIN dataset, by pro-vaccine |

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