COVID-19 Evidence Accelerator Collaborative

Lab Meeting # 41

Thursday, September 23rd, 2021, 3 - 4:00 pm ET

Call Summary

Overview of Lab Meeting 41

The focus of Lab Meeting 41 was Real World Data (RWD) for tracking the performance of COVID-19 vaccines. First, Dr. Richard Forshee of the Food and Drug Administration (FDA)'s Center for Biological Evaluation and Research (CBER), described how FDA uses data from claims and electronic health records (EHR) data in a rapid cycle analysis to identify potential adverse events (AE) of interest associated with COVID-19 vaccines. Second, Dr. Yinong Young-Xu of the White River Junction Veterans Affairs (VA) Medical Center showed how RWD was used to determine how the Delta variant impacted vaccine effectiveness.

FDA Monitoring COVID-19 Vaccine Safety

Dr. Richard Forshee & Dr. Steven Anderson, Office of Biostatistics & Epidemiology, CBER, FDA

FDA Active Surveillance Program for Vaccines Using RWD

- Uses population-based healthcare databases to conduct safety studies of vaccines including:
  1. Centers for Medicare & Medicaid Services (CMS) (>50 million persons – claims data, >= 65 years old in the US)
  2. CBER Biologics Effectiveness Safety (BEST) Program (>50 million persons (EHR data) and >100 million persons (claims data), <65 years old in US, includes Optum, CVS Health and HealthCore data sources)

Adverse Events of Special Interest (AESI)

- No causal relationship between events and receipt of vaccines at the time of the Emergency Use Authorization (EUA).
- Identified a list of potential AESI to include in rapid cycle analysis (RCA) based on previous experience with other vaccines and consultation with medical experts
- 16 AESI included in analysis, including: acute myocardial infarction, bell's palsy, anaphylaxis, narcolepsy, pulmonary embolism, etc.

Signal Detection Results from Rapid Cycle Analysis (RCA), CMS and Optum

- Results obtained from Near Real-Time Surveillance for CMS and Optum
- RCA detected several statistically-significant signals associated with four potential AESI for the Pfizer vaccine
  - Pulmonary embolism (RR = 1.54)
  - Acute myocardial infarction (RR = 1.42)
  - Disseminated intravascular coagulation (RR = 1.91)
  - Immune thrombocytopenia (RR = 1.44)

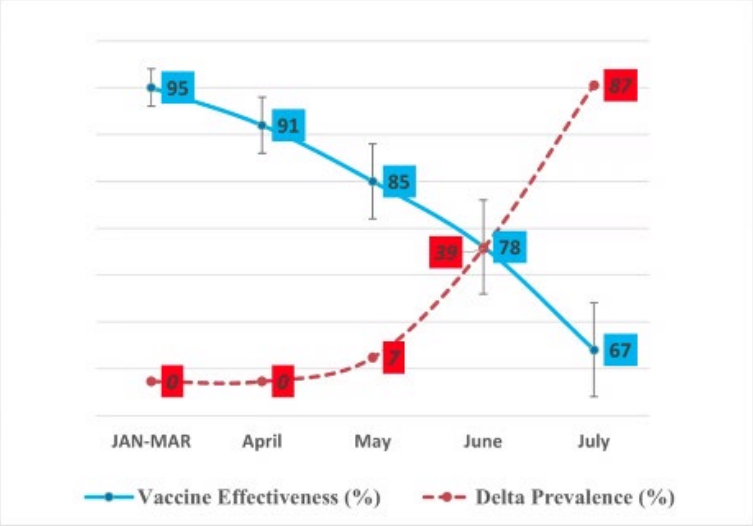
- Anaphylaxis (identified across all vaccines as an AESI) more expected than others, relatively common with receipt of vaccines
- Results indicate no signals for any vaccine with Near Real-Time Surveillance for Optum
- Near Real-Time Surveillance in CMS and Optum did not detect signals for Myocarditis/ Pericarditis, Thrombosis with thrombocytopenia syndrome (TTS), or Guillain-Barre Syndrome (GBS)
- FDA released public statement indicating there may be an elevated risk of four AESI for persons 65-years and older receiving the Pfizer vaccine.
    - May not be true safety concerns, conducting controlled follow-up analyses to determine whether events are actually linked to receipt of the Pfizer vaccine.
    - Need to carefully evaluate Pfizer signals because Pfizer was initially given to a target population of people with greatest COVID risk, also the group most vulnerable to AESI in analysis.
    - This analysis did not do anything to identify or control for risk factors for these AESI, signals could be due to the how the vaccines were rolled out among higher-risk populations.

<u>Impact of Delta on Vaccine Effectiveness: VA COVID Vaccine Surveillance</u>

Dr. Yinong Young-Xu, ScD, MA, MS, Clinical Epidemiology Program, White River Junction VA Medical Center

Veterans Health Administration (VHA) Nationwide Vaccine Effectiveness and Delta Prevalence Over Time

- As Delta prevalence grew, vaccine effectiveness (VE) decreased. Notified VHA leaders by June that the vaccine was not working as well against new variant.



Waning vs. Breakthrough

- Effectiveness of vaccines typically “wane” as they get older.
    - Estimated that COVID VE wanes an average of 3% points every one-month.
- Effectiveness of vaccines can also be challenged by variants that emerge over time --> Breakthrough infections

- Behaviors were also changing (mask-wearing decreasing, opening back up, etc.) while the variants were circulating
- Wanted to determine whether VE was waning or if it was due to Delta:
    - Compared a January cohort (February, March, April, pre-Rise in Delta variant) with a May cohort (June, July, August, post-Rise in Delta variant) to better isolate the effect of the variant
    - Observed 19-23% point drop in VE over time with increased prevalence of Delta.
    - When adjusting for age, observed a 29% point drop in VE due to Delta variant for populations over 65-years-old
- Estimated that the Delta variant causes an average of 21% point drop in VE

Adjusted VE (%, 95% Confidence Interval) against infection by Full Vaccination Month	(January cohort)	(May cohort)	Horizontal difference is due to "Delta"
1st month	Feb: 82 (79-85)	June: 63 (42-77)	-19
2nd month	Mar: 81 (75-85)	July: 58 (12-80)	-23
3rd month	April: 79 (74-84)	Aug: 55 (41-61)	-22
Vertical difference is due to WANING (duration of effectiveness)	-3	-8	
Adjusted VE against hospitalization	89 (80-94)	82 (78-86)	-7
Age 65+	87 (80, 91)	58 (41, 70)	-29
Age < 65	89 (75, 95)	83 (70, 91)	-6

Natural Immunity vs. VE Against Re-infection

- Higher incidence (per 1000 person/100 days) of re-infection among previously infected unvaccinated group (2.7) compared to vaccinated groups (Pfizer – 1.4, Moderna – .9) among ages 18+
- Highest rate of infection among unvaccinated, previously infected population ages 65+ (4.9) compared to vaccinated 65+ groups (Pfizer – 1.5, Moderna – 1.2)
- Possible that natural immunity protects against Delta more than or similarly to vaccines