

Aggressive B-Cell Lymphoma Reporting After COVID-19 mRNA Vaccination: A Pharmacovigilance Signal in VAERS

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BACKGROUND

COVID-19 mRNA vaccines act within the germinal center, the compartment from which aggressive B-cell lymphomas arise. Case reports describe diffuse large B-cell lymphoma diagnosed or progressing within weeks of vaccination, at times as rapidly enlarging nodal disease near the injection site. Whether this reflects a true safety signal or coincident detection has not been examined systematically in national pharmacovigilance data.

AIM

To test whether lymphoma, and aggressive B-cell lymphoma in particular, is reported disproportionately after COVID-19 mRNA vaccination versus routine non-COVID-19 vaccines.

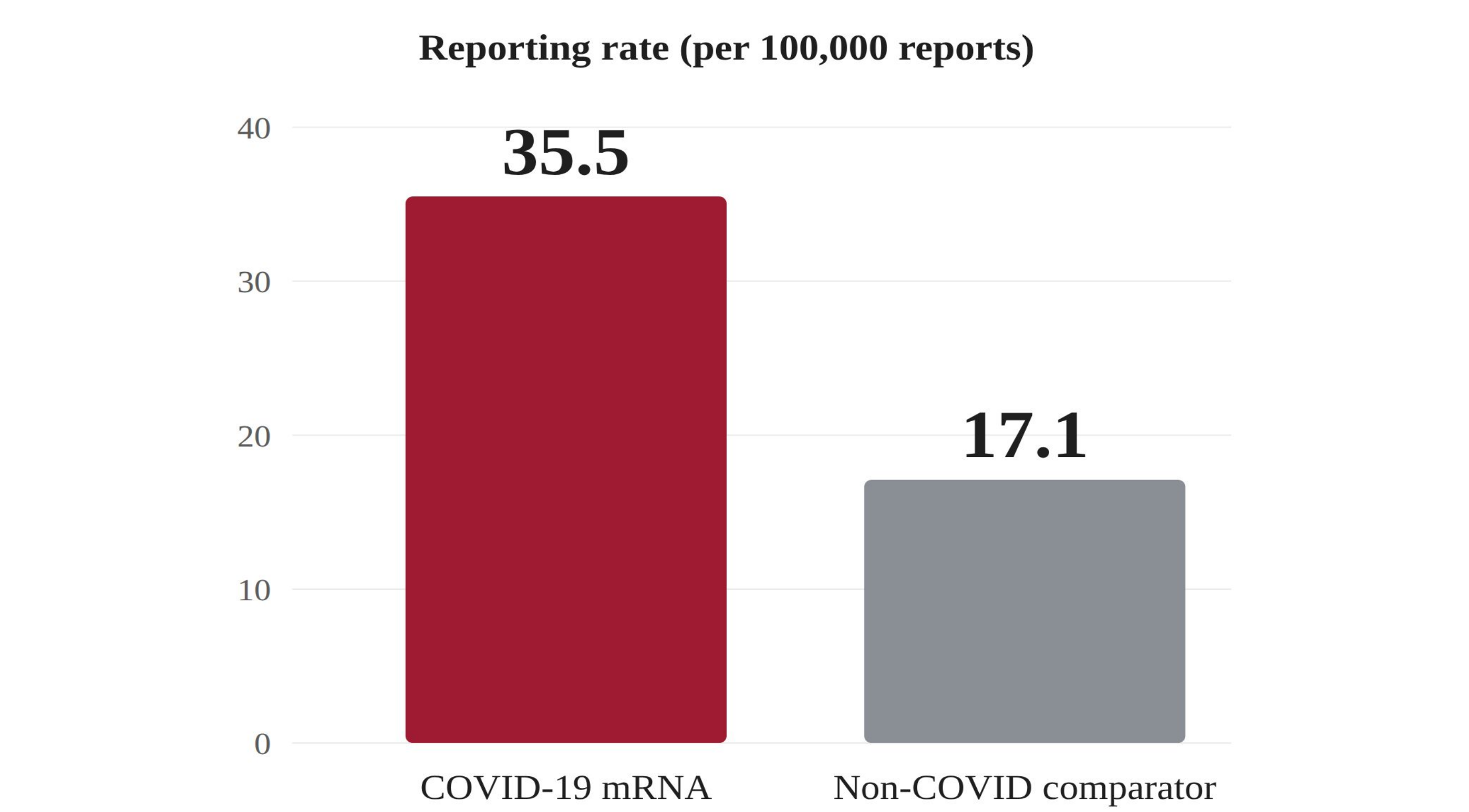
METHODS

- Design: We compared how often lymphoma was reported among COVID-19 mRNA vaccine reports versus reports for a fixed panel of routine vaccines. This is a disproportionality analysis, the standard method for detecting safety signals in spontaneous reporting data.
- Data source: US Vaccine Adverse Event Reporting System (VAERS), accessed through CDC WONDER. Reports received January 2020 through April 2026.
- Exposure group: Reports listing BNT162b2 or mRNA-1273.
- Comparator group: Reports listing routine non-COVID-19 vaccines: influenza, Tdap, HPV, MMR, pneumococcal, zoster, hepatitis B, varicella, or meningococcal.
- Case definition: A report counted as a case if it carried any lymphoma MedDRA Preferred Term. Diffuse large B-cell and related aggressive B-cell entities were the focus.

- Counting: Counts reflect Preferred Term mentions. A report listing more than one lymphoma term contributes to each, following standard VAERS methodology.
- Statistics: We calculated the Reporting Odds Ratio (ROR), the Proportional Reporting Ratio (PRR), and the Yates-corrected chi-square. A signal was defined by European Medicines Agency criteria: PRR at least 2, chi-square at least 4, and at least 3 reports.

RESULTS

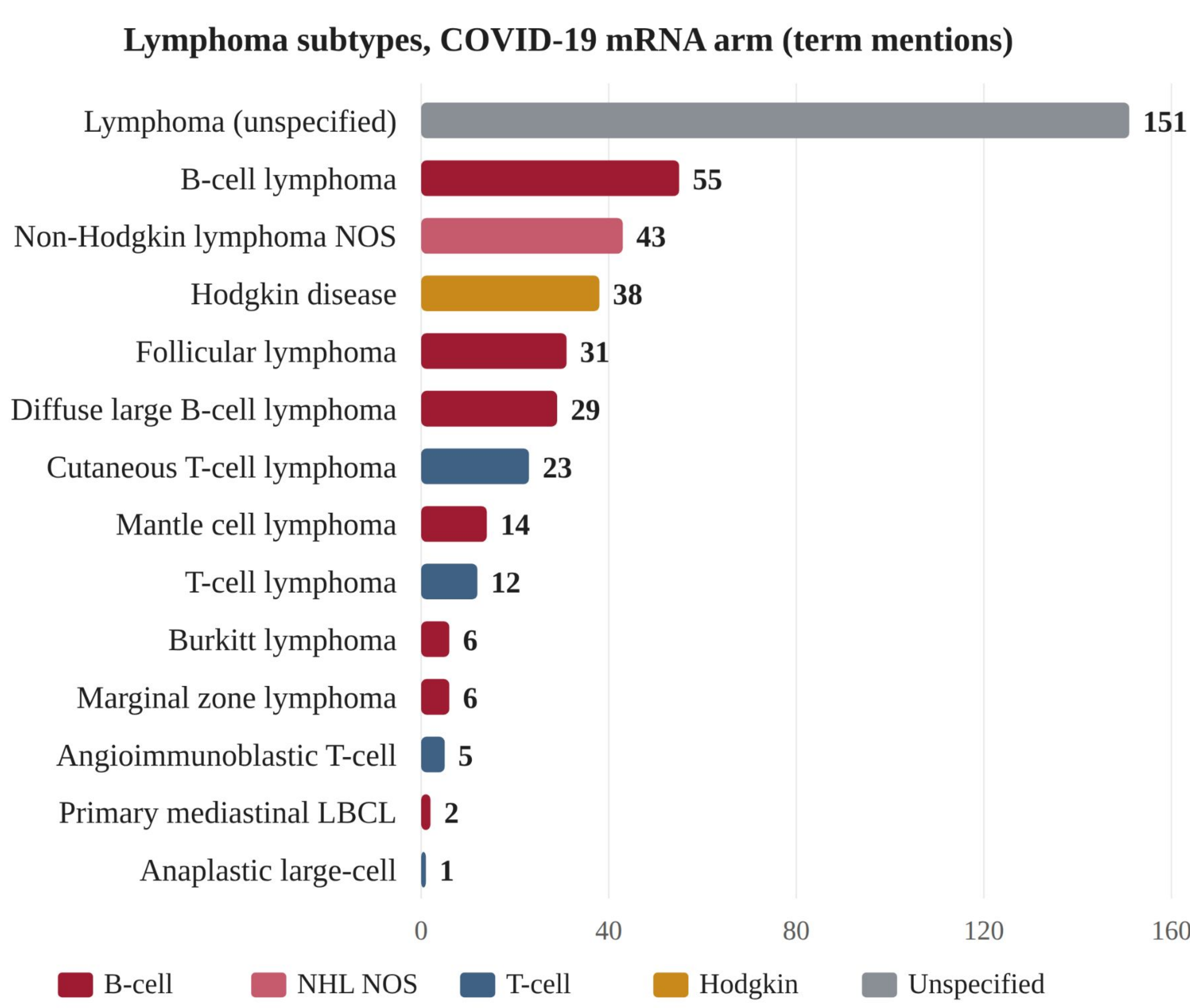
Lymphoma was reported about twice as often after mRNA vaccination as after the comparator vaccines. It appeared in 325 of 916,183 mRNA reports (35.5 per 100,000) versus 41 of 240,309 comparator reports (17.1 per 100,000).



COVID-19 mRNA reports were about twice as likely to carry a lymphoma term.

The disproportionality was clear and met all three signal criteria. ROR 2.08 (95% CI 1.50 to 2.88), PRR 2.08 (95% CI 1.50 to 2.88), and chi-square 19.82 (p < 0.0001).

B-cell entities dominated the categorizable signal: B-cell lymphoma 55, non-Hodgkin lymphoma NOS 43, follicular lymphoma 31, and diffuse large B-cell lymphoma 29. Both vaccines contributed.



Term mentions, mRNA arm (416 across 325 reports). B-cell entities dominate the categorizable signal. Comparator arm (48 across 41 reports): unspecified 18, Hodgkin 9, DLBCL 6, NHL NOS 4, B-cell 4, other 7.

CONCLUSION

A disproportionality signal for aggressive B-cell lymphoma reporting follows COVID-19 mRNA vaccination in VAERS. This is a signal, not proof of causation. Unmasking of pre-existing disease by post-vaccination lymphadenopathy, closer follow-up, and reporting bias remain credible explanations.

CONTACT INFORMATION

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