Humoral Responses to Bivalent vs Monovalent Vaccine Boosters in Canada: A Stop the Spread Ottawa Comparative Analysis

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Introduction

Bivalent COVID-19 vaccines contain mRNAs that code for two different spike proteins: the ancestral strain and one of the newer variants. In contrast, monovalent COVID-19 mRNA vaccines express the ancestral spike protein.

The advantage of bivalent COVID-19 vaccines is that they may provide better and broader protection against different variants of the virus. By targeting two different spike proteins, the vaccine may be more effective at preventing infection from different strains of the virus.

Objectives

Evolving SARS-CoV-2 variants have necessitated updates to vaccines. In Sept 2022, Canadians began receiving Moderna (Omicron BA.1) and Pfizer (Omicron BA.4/BA.5) bivalent vaccines. The relative efficacy of these bivalent vaccines compared to previously established monovalent vaccines remains unclear. By leveraging the ongoing Stop the Spread Ottawa (SSO) longitudinal cohort, we will conduct a comparative analysis of these vaccine strategies through the lens of humoral responses.

Methods

SSO is an ongoing prospective cohort of individuals at risk for or with prior SARS-CoV2 infection. SSO cohort demographics and infection histories are well-characterized, and blood specimens are collected and banked every 2 months. Of the 300 participants currently enrolled, over half of the cohort has received a 4th dose of COVID-19 vaccine, and of these, 30% have received a bivalent vaccine (equal Moderna/Pfizer representation). To assess differences between monovalent and bivalent vaccines, serum samples prior to and following 4th dose vaccinations were examined for levels of IgG, IgA and IgM reactive to Spike and receptor-binding domain of Spike (RBD), as well as neutralizing capacity against wild-type and Omicron (subvariant XBB.1.5) Spike proteins. Antibody levels and neutralizing capacity were measured on an automated, high-throughput platform for in-house chemiluminescent ELISA and ELISA-based neutralization assays.

Results

Table 1. Cohort characteristics.

Variable	Participants (n=165)
Age (median, IQR) Range (min, max)	56 (43, 63) 57 (22, 79)
Sex, n (%) Male Female	 55 (33.3) 110 (66.7)
Past COVID-19 Infection, n (%) Yes No	 111 (67.3) 54 (32.7)
4th dose type, monovalent vs bivalent; n (%) Bivalent, Moderna Bivalent, Pfizer Monovalent, Pfizer Monovalent, Moderna Monovalent, Novavax	 28 (17.0) 23 (13.9) 52 (31.5) 61 (37.0) 1 (0.6)

Figure 2. Neutralization activity of antibodies produced by monovalent and bivalent mRNA vaccines before and after third booster shot (V4). Assays were performed on the ancestra (WU) spike and on the Omicron XBB.1.5 spike.

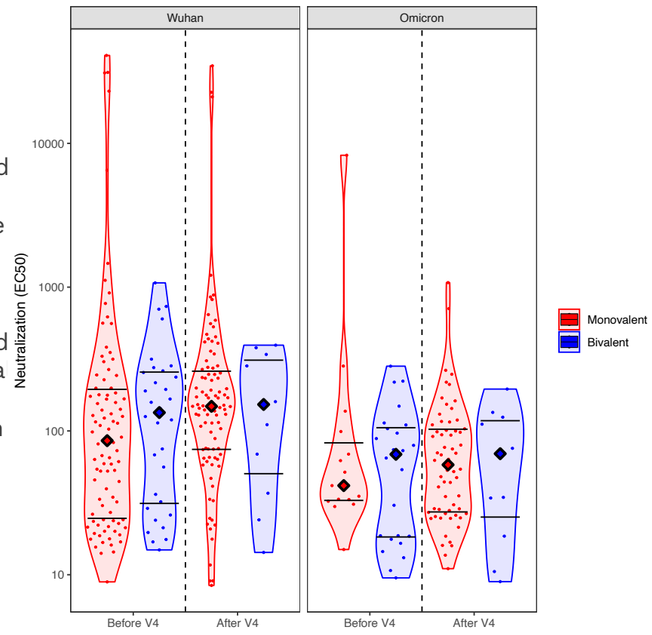
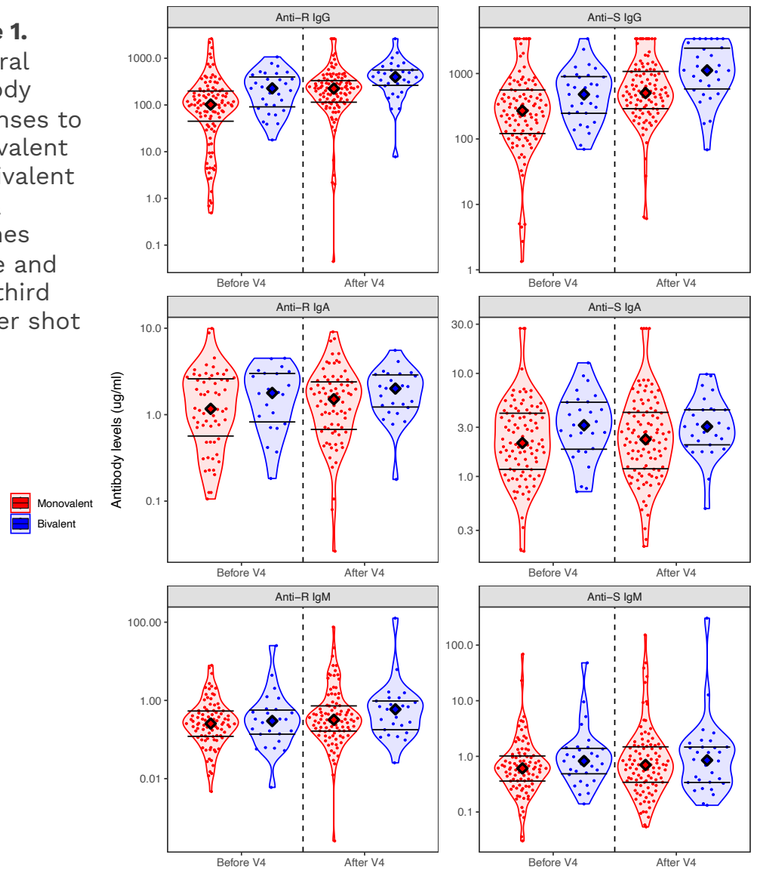


Figure 1. Humoral antibody responses to monovalent and bivalent mRNA vaccines before and after third booster shot (V4).



Conclusions

- Our SSO cohort data supports existing published studies and show that bivalent vaccines induce a marginal increase in IgG antibody responses against spike and RBD.
- However, neutralizing antibody levels against Omicron XBB.1.5 were not significantly increased in this preliminary dataset.