

SUPPLEMENTAL DIGITAL CONTENT 2. Humoral immunity, measured as spike-specific antibody response against the receptor-binding domain (RBD) and S1/S2

Trimer. To quantify the humoral response at the three time points day of first vaccination (V1D0), 5 weeks after primary vaccination (V2D35), and one year after vaccination (V2M12) against SARS-CoV-2, spike-specific antibodies directed against the RBD (**A-B**) were measured in serum using the Elecsys® Anti-SARS-CoV-2 Ig assay (Roche, Mannheim, Germany), at a cut off of 0.8 U/mL. Analyses were performed according to in vitro diagnostics criteria on the cobas e411 system (Roche) (Montalvo Villalba et al 2022), as recommended by the manufacturer. We observed RBD-specific antibody responses 5 weeks after vaccination in all participants, which increased on V2M12, most likely due to hybrid immunity acquired as a result of natural Omicron infection (booster). While antibodies directed against the viral nucleocapsid (Roche Elecsys® Anti-SARS-CoV-2 Ig assay, cut off 1.0 U/mL) to identify SARS-CoV-2 natural infection were positive in only 2 children on V1D0, all were positive on V2M12. To detect IgG antibody responses against S1/S2 Trimer (**C-D**), the LIAISON® SARS-CoV-2 S1/S2 IgG assay (DiaSorin) was performed as a confirmatory assay using a Liaison XL system, following the manufacturers' recommendations. A cut-off value of 10 AU/mL was used for positivity. Assay specificity has been reported at 98.5 %, according to the manufacturer, for detection of IgG antibodies against the spike protein S1 and S2 subunits. Panel A and C depict boxplots, indicating median, IQR and min-max range. Panels B and D show dot plots indicating individual responses.

