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Supplementary appendix

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APPENDIX

Omicron-adapted vaccines might require longer follow-up to reveal true benefits

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CONTENTS

SUPPLEMENTARY FIGURES AND LEGENDS

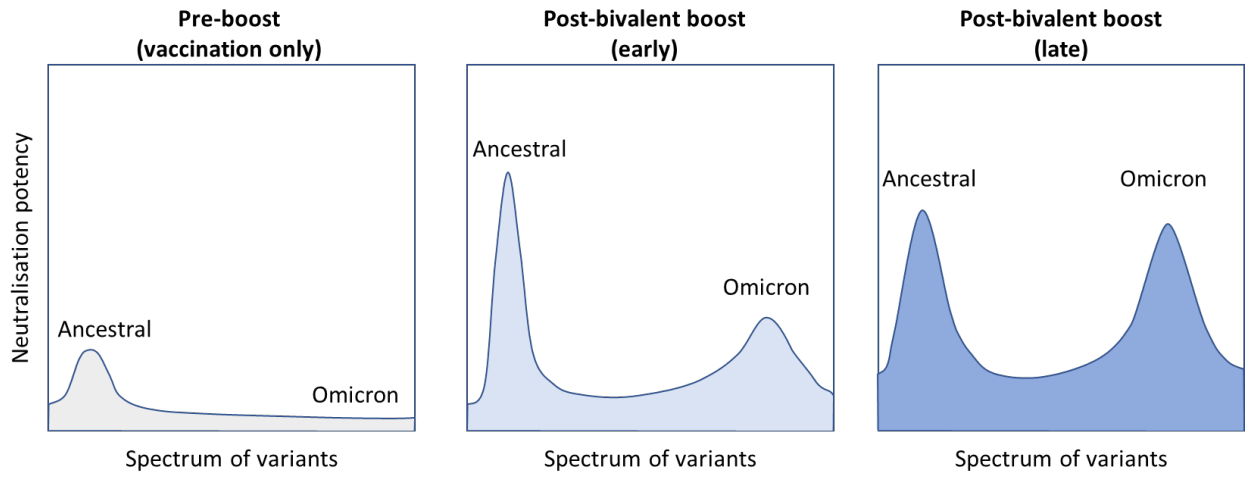

Figure S1. Simplified scheme of bivalent omicron-adapted booster-elicited expansion of neutralisation breadth.

These illustrations represent the authors' prediction of humoral immune response to bivalent boost vaccination. (**Left**) Pre-boost, vaccination only, and variant-naïve individuals would develop a B cell pool secreting highly potent neutralising antibodies against ancestral SARS-CoV-2 antigens and a broad spectrum of neutralising antibodies against variants, a typical outcome of long-term affinity maturation process.[1,2] (**Middle**) At early stage (e.g. within 30 days) after Wuhan-Hu-1/omicron bivalent boost vaccination, exposure to ancestral and omicron antigens would induce clonal expansion of B cells that recognize these antigens.[3] Due to the characteristics of the existing B cell pool, most high-potency neutralising antibodies would be derived from cells targeting Wuhan-Hu-1 antigens, whereas omicron-neutralising antibodies would only target epitopes shared with Wuhan-Hu-1 and have sub-optimal affinity to omicron-specific antigens.[4] (**Right**) At late stage (e.g. 30-90 days) after bivalent vaccination, B cells that recognize omicron antigens would undergo affinity maturation to improve antibody affinity and breadth, resulting in higher neutralisation potency against omicron (peak of the curve) and broad neutralisation breadth against other variants (valley of the curve).[2,5] Wuhan-Hu-1 neutralising antibodies already with high affinity due to long-term affinity maturation since first vaccination would thus benefit less from further affinity maturation after bivalent boost vaccination.[6] Instead, all neutralisation titers would undergo immune decay at this stage and later.[7]

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