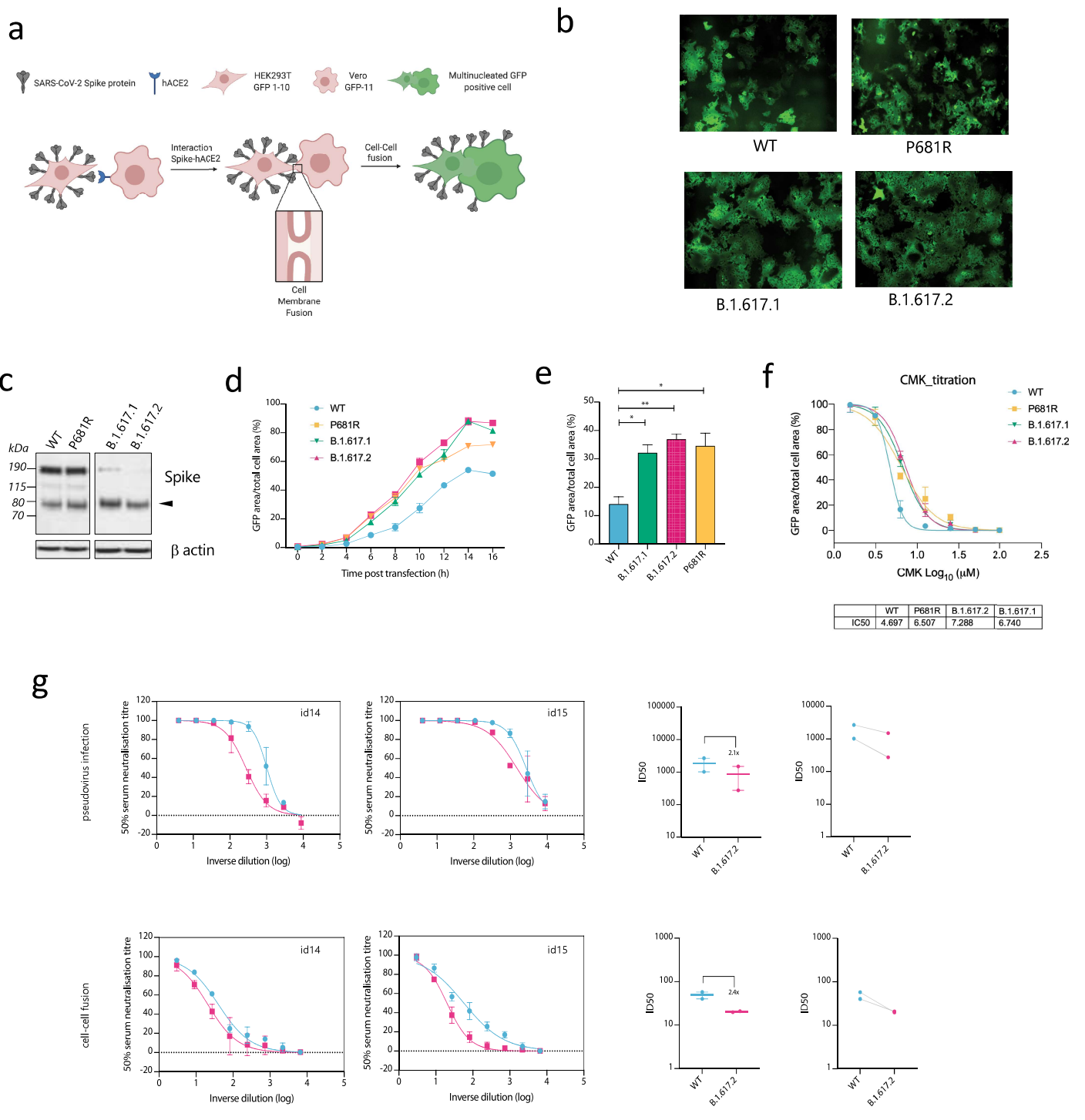


**Extended Data Figure 1. Breakthrough SARS-CoV-2 infections amongst vaccinated health care workers (HCW)** **a**. A heatmap of pairwise SARS-CoV-2 SNP differences of vaccinated HCW samples at hospital 1. The B.1.617.2 lineage is in the upper-left quarter, with fewer than 2 SNP difference between them. **b**. Maximum likelihood phylogeny of vaccine breakthrough SARS-CoV-2 B.1.617.2 sequences from hospital 1 in context of closest Indian B.1.617.2 sequences. Phylogeny was inferred with IQTREE2 with 1000 bootstrap replicates. Rooted on Wuhan-Hu-1 and annotated with the lineage designated by pangolin v.3.0.5. **c-e**. Frequency graphs for cluster size at each hospital 1-3. **f**. Comparison of IgG antibody titres between a control group of vaccinated individuals receiving two doses of ChadOx-1 who have not been infected with SARS-CoV-2, with vaccinated healthcare workers who had received two doses and subsequently tested positive for SARS-CoV-2. **g**. Ct values (N gene target) of vaccinated healthcare workers at three Delhi hospitals who tested positive for SARS-CoV-2.



**Extended Data Figure 2: B.1.617.2 Delta variant spike confers accelerated cell-cell fusion activity that can be blocked by anti-spike neutralising antibodies in sera.** **a.** Schematic of cell-cell fusion assay. **b.** Reconstructed images at 10 hours of GFP positive syncytia formation. Scale bars represent 400 mm. **c.** western blot of cell lysates 48 hours after transfection of spike plasmids. Anti-S2 antibody. **d,e.** Quantification of cell-cell fusion kinetics showing percentage of green area to total cell area over time. Mean is plotted with error bars representing SEM. **f.** Sensitivity of fusion kinetics to furin inhibitor CMK as shown by titration of drug and measurement of fusion after 10hrs. Mean is plotted with error bars representing SEM. **g.** comparison of impact of post vaccine sera ( $n=2$ ) on PV neutralisation (top) and cell-cell fusion (bottom), comparing WT and Delta variant B.1.617.2.

**Extended Data Table 1.** Sensitivity analysis for the two strain model: B.1.617.2 and non-B.1.617.2 strains under different combinations of starting dates for B.1.617.2 strain and extent of underreporting. The inferred changes in epidemiological characteristics of B.1.617.2 are presented via the estimated posterior mean and Bayesian 50% credible interval.

<b>Starting Date</b>	<b>Under-Reporting Of Deaths</b>	<b>Evasion of protection from previous SARS-CoV-2 Infections (%)</b>	<b>Transmissibility Increase from B.1.617.2*</b>
<b>31st Jan 2021</b>	<b>30%</b>	32% (18%-48%)	2% (-19%-18%)
	<b>50%</b>	38% (20-55%)	26% (12%-41%)
	<b>70%</b>	35% (17%-50%)	39% (29%-51%)
<b>1st Jan 2021</b>	<b>30%</b>	17% (9%-25%)	18% (0%-35%)
	<b>50%</b>	24% (7%-34%)	34% (20%-50%)
	<b>70%</b>	32% (19%-45%)	37% (28%-47%)
<b>15th Dec 2020</b>	<b>30%</b>	10% (5%-15%)	28% (17%-42%)
	<b>50%</b>	28% (11%-29%)	27% (16%-41%)
	<b>70%</b>	26% (9%-38%)	40% (31%-50%)
<b>1st Dec 2020</b>	<b>30%</b>	5% (3%-7%)	39% (31%-47%)
	<b>50%</b>	14% (4%-21%)	40% (33%-50%)
	<b>70%</b>	24% (9%-35%)	39% (31%-49%)

\*Inferred transmissibility advantage for B.1.617.2 is against the background of a mixture of all previous circulating variants in Mumbai.

**Extended Data Table 2:** Clusters of SARS-CoV-2 infections in three hospitals with near universal staff vaccination during first half of 2021.

	B.1.617.2 Delta Variant (N= 98)	Non-Delta Variant (N=35)	P value
Median age <i>years</i> (IQR)	37 (27-50)	34 (27-49)	0.83 <sup>a</sup>
Female %	48.0 (47)	54.3 (19)	0.52 <sup>b</sup>
Hospital %			0.11 <sup>b</sup>
1	11.2 (19)	22.9 (8)	
2	52.0 (51)	34.3 (12)	
3	36.7 (36)	42.9 (15)	
Median Ct value (IQR)	16.5 (13.2- 19.0) <sup>c</sup>	19 (17.1- 23.0) <sup>d</sup>	0.0006 <sup>a</sup>

<sup>a</sup> Wilcoxon rank-sum test. <sup>b</sup> Chi square test. <sup>c</sup> 47 of 98 available. <sup>d</sup> 22 of 35 available. <sup>e</sup> 12 of 98. <sup>f</sup> 5 of 35.

**Extended Data Table 3** Demographic information of individuals undergoing two dose vaccinations with ChAdOx-1 or BNT162b2

	ChAdOx-1 (N=33)	BNT162b2 (N=32)	P. value
Female (%)	18 (54.5)	13 (40.6)	0.38 <sup>a</sup>
Median Age <i>Years</i> (IQR)	67 (64 - 71)	71 (46 -83)	0.74 <sup>b</sup>
Median time <i>in Days</i> since dose 2 (IQR)	31 (21 -38)	27 (24 -29)	0.15 <sup>b</sup>
Serum Geometric Mean Titre <i>GMT</i> for delta variant (95% CI)	654 (313 -1365)	3372 (1856 - 6128)	0.0006 <sup>b</sup>
Serum Geometric Mean Titre <i>GMT</i> for WT (95% CI)	2625 (1492 - 4618)	7393 (3893 - 14041)	0.0030 <sup>b</sup>

<sup>a</sup>Chi-square test, <sup>b</sup> Mann-Whitney test