

## Supplementary Online Content

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**eTable 1.** Results of Mixed-Effect Binary Logistic Regression Model, Examining the Odds of Experiencing a Given Symptom or Symptom Group by Variant of Concern

**eTable 2.** Comparison of Symptom Profiles by Method of Variant of Concern Assignment (Reported vs Imputed)

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This supplementary material has been provided by the authors to give readers additional information about their work.

**eTable 1.** Results of Mixed-Effect Binary Logistic Regression Model, Examining the Odds of Experiencing a Given Symptom or Symptom Group by Variant of Concern

	Variant of Concern (VoC)				Sex		Age			Illness Duration			Hospitalized	
	Omicron	Delta	Alpha	Original type	Female	Male	≥ 4 yrs	1-3 yrs	< 1 yr	≥ 4 days	2-3 days	≤1 day	Yes	No
<b>Core Symptom</b>	2.19 (1.37, 3.51) P=0.001	2.09 (1.25, 3.49) P=0.005	0.69 (0.43, 1.08) P=0.11	ref.	1.18 (0.83, 1.67) P=0.35	ref.	0.45 (0.30, 0.68) P<0.001	1.03 (0.63, 1.69) P=0.89	ref.	1.24 (0.81, 1.88) P = 0.32	1.34 (0.87, 2.07) P = 0.18	ref.	0.57 (0.36, 0.93) P = 0.08	ref.
<b>Fever</b>	2.00 (1.43, 2.80) P<0.001	1.93 (1.33, 2.78) P<0.001	0.76 (0.53, 1.09) P=0.14	ref.	1.22 (0.95, 1.57) P=0.12	ref.	0.59 (0.44, 0.79) P<0.001	1.23 (0.88, 1.73) P=0.22	ref.	0.85 (0.63, 1.16) P=0.31	1.19 (0.86, 1.63) P=0.29	ref.	0.74 (0.51, 1.08) P=0.12	ref.
<b>Cough</b>	1.42 (1.06, 1.91) P=0.02	1.57 (1.13, 2.17) P=0.007	1.13 (0.80, 1.58) P=0.48	ref.	0.88 (0.71, 1.10) P=0.26	ref.	0.57 (0.44, 0.74) P<0.001	0.88 (0.66, 1.16) P=0.36	ref.	2.56 (1.93, 3.38) P<0.001	1.54 (1.17, 2.02) P=0.002	ref.	0.67 (0.47, 0.94) P=0.02	ref.
<b>Conjunctivitis</b>	0.41 (0.22, 0.78) P=0.007	1.32 (0.75, 2.33) P=0.33	0.40 (0.17, 0.95) P=0.04	ref.	0.70 (0.44, 1.11) P=0.13	ref.	0.70 (0.42, 1.16) P=0.16	0.47 (0.25, 0.85) P=0.01	ref.	1.43 (0.80, 2.58) P=0.23	2.07 (1.18, 3.65) P=0.01	ref.	1.19 (0.60, 2.38) P=0.61	ref.
<b>Upper Respiratory Symptoms</b>	1.32 (0.97, 1.80) P=0.07	1.96 (1.38, 2.79) P<0.001	0.72 (0.51, 1.02) P=0.07	ref.	1.06 (0.84, 1.33) P=0.62	ref.	0.65 (0.49, 0.85) P=0.002	0.84 (0.62, 1.12) P=0.24	ref.	2.50 (1.88, 3.34) P<0.001	2.04 (1.53, 2.70) P<0.001	ref.	0.62 (0.43, 0.88) P=0.008	ref.
<b>Lower Respiratory Symptoms</b>	1.42 (1.04, 1.92) P=0.03	0.96 (0.69, 1.36) P=0.83	1.05 (0.74, 1.50) P=0.77	ref.	0.89 (0.71, 1.12) P=0.31	ref.	0.94 (0.72, 1.24) P=0.68	0.98 (0.73, 1.31) P=0.88	ref.	1.83 (1.38, 2.42) P<0.001	1.48 (1.12, 1.97) P=0.007	ref.	0.96 (0.66, 1.40) P=0.85	ref.
<b>GI</b>	0.89 (0.65, 1.21) P=0.45	0.80 (0.57, 1.13) P=0.21	0.84 (0.59, 1.20) P=0.34	ref.	1.37 (1.09, 1.72) P=0.007	ref.	1.54 (1.18, 2.02) P=0.002	1.57 (1.18, 2.09) P=0.002	ref.	1.79 (1.35, 2.37) P<0.001	1.77 (1.34, 2.35) P<0.001	ref.	1.54 (1.07, 2.23) P=0.008	ref.
<b>Neurologic</b>	1.12 (0.76, 1.65) P=0.57	1.18 (0.79, 1.77) P=0.41	0.91 (0.59, 1.40) P=0.66	ref.	1.39 (1.05, 1.85) P=0.02	ref.	33.65 (19.69, 57.49) P<0.001	6.09 (3.46, 10.73) P<0.001	ref.	1.50 (1.06, 2.14) P=0.02	1.26 (0.88, 1.82) P=0.21	ref.	1.09 (0.68, 1.73) P=0.91	ref.
<b>MSK</b>	0.56 (0.36, 0.87) P=0.009	0.65 (0.42, 1.02) P=0.06	0.56 (0.34, 0.90) P=0.02	ref.	1.59 (1.16, 2.18) P=0.004	ref.	12.87 (7.55, 21.94) P<0.001	3.77 (2.12, 6.72) P<0.001	ref.	1.69 (1.14, 2.51) P=0.01	1.59 (1.06, 2.39) P=0.02	ref.	0.68 (0.38, 1.21) P=0.19	ref.
<b>Rash, oral</b>	0.63 (0.44, 0.91)	0.77 (0.51, 1.14)	0.65 (0.42, 0.98)	ref.	1.09 (0.83, 1.43)	ref.	0.84 (0.61, 1.16)	0.65 (0.46, 0.92)	ref.	1.69 (1.21, 2.35)	1.18 (0.84, 1.67)	ref.	0.93 (0.59, 1.46)	ref.

changes,	P=0.01	P=0.19	P=0.04		P=0.54		P=0.30	P=0.01		P=0.002	P=0.34		P=0.75
GU/dehydration	1.28 (0.93, 1.76)	1.08 (0.76, 1.54)	1.21 (0.84, 1.74)		1.34 (1.06, 1.70)		0.72 (0.54, 0.95)	1.03 (0.76, 1.38)		1.42 (1.06, 1.91)	1.50 (1.12, 2.01)		1.76 (1.20, 2.57)
	P=0.14	P=0.67	P=0.31		P=0.01		P=0.02	P=0.86		P=0.02	P=0.007		P=0.004
Systemic	1.77 (1.24, 2.52)	1.19 (0.82, 1.72)	0.70 (0.48, 1.01)		1.05 (0.81, 1.35)		0.60 (0.44, 0.81)	0.86 (0.62, 1.2)		1.37 (1.00, 1.87)	1.36 (0.99, 1.87)		0.91 (0.61, 1.36)
	P=0.002	P=0.37	P=0.06		P=0.71		P=0.001	P=0.38		P=0.05	P=0.06		P=0.65
Anosmia/ageusia	0.18 (0.07, 0.43)	0.74 (0.39, 1.42)	0.48 (0.23, 1.005)		1.5 (0.91, 2.46)		69.63 (9.5, 510.47)	12.89 (1.66, 100.0)		1.98 (1.04, 3.77)	2.09 (1.08, 4.04)		0.76 (0.31, 1.85)
	P<0.001	P=0.37	P=0.05		P=0.11		P<0.001	P=0.02		P=0.04	P=0.03		P=0.54

Data are adjusted for age, sex, number of days of illness at ED presentation, and hospitalization status. Data are reported as odds ratios (95% CI).

a - Symptoms were grouped as follows: upper respiratory = rhinorrhea and/or sore throat, lower respiratory = shortness of breath, pleuritic or non-pleuritic chest pain, wheezing and/or sputum production, GI = abdominal pain, vomiting, diarrhea and/or anorexia, neurologic = headache and/or seizures, MSK= joint and/or muscle pain, dehydration = decreased urine output and/or refusal to drink, systemic = irritability, lethargy, apnea and/or drowsiness, rash/oral changes = rash to skin, hands, feet and/or oral or extremity changes.

**eTable 2.** Comparison of Symptom Profiles by Method of Variant of Concern Assignment (Reported vs Imputed)

	Original-type Imputed (n=409)	Original-type Reported (n=0)	P-value <sup>a</sup>	Alpha Imputed (n=84 <sup>c</sup> )	Alpha Reported (n=158 <sup>d</sup> )	P-value <sup>a</sup>	Delta Imputed (n=144)	Delta Reported (n=177)	P-value <sup>a</sup>	Omicron Imputed (n=422 <sup>e</sup> )	Omicron Reported (n=46 <sup>e</sup> )	P-value <sup>a</sup>
<b>Age, years, median (IQR)</b>	1.3 (0.6, 6.0)	N/A	N/A	2.0 (1.0, 7.0)	1.7 (0.8, 7.0)	0.95	2.0 (0.9, 7.0)	3.0 (0.8, 9.0)	0.67	1.0 (0.3, 6.0)	3.0 (1.0, 7.0)	0.13
<b>Age groups</b>		N/A	N/A			0.93			0.28			0.13
< 1 year	135 (33.0)			18 (21.4)	47 (29.7)		38 (26.4)	49 (27.7)		190 (45.0)	10 (21.7)	
1 to 3 years	133 (32.5)			33 (39.3)	55 (34.8)		50 (34.7)	43 (24.3)		97 (23.0)	15 (32.6)	
≥ 4 years	141 (34.5)			33 (39.3)	56 (35.4)		56 (38.9)	85 (48.0)		135 (32.0)	21 (45.7)	
<b>Sex, male, n (%)</b>	227 (55.5)	N/A	N/A	51 (60.7)	97 (61.4)	0.99	80 (55.6)	96 (54.2)	0.94	221 (52.4)	29 (63.0)	0.47
<b>Days of illness, median (IQR)</b>	2.0 (1.0, 4.0)	N/A	N/A	2.0 (1.0, 5.0)	2.0 (0.5, 4.0)	0.55	4.0 (2.0, 6.0)	3.0 (1.5, 5.0)	0.03	3.0 (1.0, 4.0)	2.0 (0.5, 3.0)	0.27
<b>Days of illness</b>		N/A	N/A			0.93			0.12			0.37
≤1 day	158 (38.6)			31 (37.3)	69 (44.8)		24 (16.7)	44 (24.9)		126 (29.9)	21 (45.7)	
2 to 3 days	130 (31.8)			23 (27.7)	44 (28.6)		39 (27.1)	62 (35.0)		158 (37.4)	15 (32.6)	
≥ 4 days	121 (29.6)			29 (34.9)	41 (26.6)		81 (56.3)	71 (40.1)		138 (32.7)	10 (21.7)	
<b>Core COVID Symptoms<sup>b</sup></b>	55 (13.4)	N/A	N/A	68 (81.9)	127 (82.5)	0.99	130 (90.3)	164 (92.7)	0.71	390 (92.4)	44 (95.7)	0.77
Fever	290 (70.9)	N/A	N/A	50 (60.2)	106 (68.8)	0.93	106 (73.6)	146 (82.5)	0.20	341 (80.8)	38 (82.6)	0.94

Cough	211 (51.6)	N/A	N/A	43 (51.8)	86 (55.8)	0.9 8	90 (62.5)	107 (60.5)	0.9 2	245 (58.2)	29 (64.4)	0.77
Conjunctivitis	31 (7.6)	N/A	N/A	2 (2.4)	5 (3.2)	0.9 9	9 (6.3)	23 (13)	0.2 1	17 (4.0)	1 (2.2)	0.99
<b>Upper Respiratory Symptoms</b>	241 (58.9)	N/A	N/A	42 (50.6)	77 (50)	0.9 9	101 (70.1)	127 (71.8)	0.9 4	259 (61.5)	29 (64.4)	0.89
Rhinorrhea	215/408 (52.7)	N/A	N/A	36 (43.4)	65 (42.2)	0.9 9	89 (61.8)	109 (61.6)	0.9 9	234 (55.6)	22 (48.9)	0.77
Sore throat	76 (18.6)	N/A	N/A	14 (16.9)	24 (15.6)	0.9 9	33 (22.9)	58 (32.8)	0.2 0	92 (21.9)	18 (40.0)	0.13
<b>Lower Respiratory Symptoms</b>	145 (35.5)	N/A	N/A	33 (39.8)	52 (33.8)	0.9 3	45 (31.3)	67 (37.9)	0.4 5	177 (42)	26 (57.8)	0.30
Shortness of breath	88 (21.5)	N/A	N/A	23 (27.7)	30 (19.5)	0.9 3	24 (16.7)	44 (24.9)	0.2 4	131 (31.1)	23 (51.1)	0.13
Chest pain	38 (9.3)	N/A	N/A	8 (9.6)	11 (7.1)	0.9 6	10 (6.9)	13 (7.3)	0.9 9	22 (5.2)	2 (4.4)	0.99
Chest pain (pleuritic)	14 (3.4)	N/A	N/A	3 (3.6)	3 (1.9)	0.9 3	2 (1.4)	4 (2.3)	0.9 2	12 (2.9)	2 (4.4)	0.83
Wheezing	55 (13.4)	N/A	N/A	15 (18.1)	14 (9.1)	0.5 5	24 (16.7)	20 (11.3)	0.3 8	70 (16.6)	9 (20)	0.82
Sputum	38 (9.3)	N/A	N/A	7 (8.4)	15 (9.7)	0.9 9	20 (13.9)	20 (11.3)	0.7 5	57 (13.5)	4 (8.9)	0.77
<b>GI</b>	272 (66.5)	N/A	N/A	56 (67.5)	90 (58.4)	0.9 3	94 (65.3)	107 (60.5)	0.6 4	254 (60.3)	33 (73.3)	0.39
Abdominal pain	109 (26.7)	N/A	N/A	21 (25.3)	29 (18.8)	0.9 3	27 (18.8)	35 (19.8)	0.9 4	81 (19.2)	11 (24.4)	0.77
Vomiting	114 (27.9)	N/A	N/A	28 (33.7)	34 (22.1)	0.5 5	38 (26.4)	42 (23.7)	0.8 5	110 (26.1)	11 (24.4)	0.97
Diarrhea	107 (26.2)	N/A	N/A	21 (25.3)	27 (17.5)	0.9 3	30 (20.8)	33 (18.6)	0.8 7	86 (20.4)	6 (13.3)	0.72
Anorexia	155 (37.9)	N/A	N/A	37 (44.6)	58 (37.7)	0.9 3	59 (41)	71 (40.1)	0.9 8	148 (35.2)	22 (48.9)	0.37
<b>Neurologic</b>	100 (24.4)	N/A	N/A	19 (22.9)	39 (25.3)	0.9 9	34 (23.6)	65 (36.7)	0.1 1	91 (21.6)	15 (33.3)	0.37
Headache	93 (22.7)	N/A	N/A	17 (20.5)	36 (23.4)	0.9 9	31 (21.5)	58 (32.8)	0.1 7	86 (20.4)	12 (26.7)	0.72

Seizures	10 (2.4)	N/A	N/A	3 (3.6)	3 (1.9)	0.93	4 (2.8)	8 (4.5)	0.84	10 (2.4)	3 (6.7)	0.42
<b>MSK</b>	83 (20.3)	N/A	N/A	12 (14.5)	21 (13.6)	0.99	16 (11.1)	39 (22.0)	0.11	48 (11.4)	7 (15.6)	0.77
Muscle pain	80 (19.6)	N/A	N/A	12 (14.5)	21 (13.6)	0.99	15 (10.4)	34 (19.2)	0.18	43 (10.2)	6 (13.3)	0.77
Joint pain	50 (12.2)	N/A	N/A	6 (7.2)	16 (10.4)	0.93	13 (9.0)	29 (16.4)	0.20	29 (6.9)	6 (13.3)	0.42
<b>Rash or oral changes</b>	105 (25.7)	N/A	N/A	13 (15.7)	30 (19.5)	0.95	20 (13.9)	38 (21.5)	0.24	76 (18.1)	8 (17.8)	0.99
Skin rash	52 (12.7)	N/A	N/A	6 (7.2)	19 (12.3)	0.93	12 (8.3)	16 (9.0)	0.94	33 (7.8)	6 (13.3)	0.63
Rash to hands	10 (2.4)	N/A	N/A	2 (2.4)	2 (1.3)	0.99	2 (1.4)	2 (1.1)	0.99	8 (1.9)	1 (2.2)	0.99
Rash to feet	14 (3.4)	N/A	N/A	3 (3.6)	6 (3.9)	0.99	1/143 (0.7)	3 (1.7)	0.87	6 (1.4)	1 (2.2)	0.77
Extremity changes	8 (2.0)	N/A	N/A	1 (1.2)	3 (1.9)	0.99	2 (1.4)	3 (1.7)	0.99	9 (2.1)	0 (0)	0.99
Oral changes	56 (13.7)	N/A	N/A	5 (6.0)	7 (4.5)	0.99	8 (5.6)	21 (11.9)	0.20	43 (10.2)	4 (8.9)	0.99
<b>Dehydration</b>	126 (30.8)	N/A	N/A	28 (33.7)	48 (31.2)	0.99	47 (32.6)	48 (27.1)	0.54	142 (33.7)	13 (28.9)	0.77
Decreased urine output	69 (16.9)	N/A	N/A	15 (18.1)	23 (14.9)	0.98	32 (22.2)	29 (16.4)	0.40	60 (14.3)	9 (20.0)	0.67
Refusal to drink	102 (24.9)	N/A	N/A	25 (30.1)	39 (25.3)	0.93	37 (25.7)	37 (20.9)	0.55	127 (30.2)	12 (26.7)	0.83
<b>Systemic</b>	273 (66.7)	N/A	N/A	40 (48.2)	96 (62.3)	0.55	82 (56.9)	117 (66.1)	0.26	295 (70.1)	34 (75.6)	0.77
Apnea	4 (1.0)	N/A	N/A	1 (1.2)	3 (1.9)	0.99	0 (0)	4 (2.3)	0.33	4 (1.0)	0 (0)	0.99
Irritable	194 (47.4)	N/A	N/A	21 (25.3)	76 (49.4)	0.02	58 (40.3)	68/176 (38.6)	0.94	186 (44.2)	27 (60.0)	0.30
Lethargic	174 (42.5)	N/A	N/A	29 (34.9)	57 (37.0)	0.99	54 (37.5)	66 (37.3)	0.99	194/420 (46.2)	19 (42.2)	0.83
Drowsy	147 (35.9)	N/A	N/A	28 (33.7)	49 (31.8)	0.99	49 (34.0)	70/176 (39.8)	0.54	193 (45.8)	19 (42.2)	0.83
<b>Loss of</b>	35 (8.6)	N/A	N/A	6 (7.2)	6 (3.9)	0.93	5 (3.5)	20 (11.3)	0.11	5 (1.2)	2 (4.4)	0.42

<b>smell/taste</b>												
Loss of smell	21 (5.1)	N/A	N/A	4 (4.8)	3 (1.9)	0.93	1 (0.7)	13 (7.3)	0.10	3 (0.7)	0 (0)	0.99
Loss of taste	30 (7.3)	N/A	N/A	6 (7.2)	5 (3.2)	0.93	5 (3.5)	17 (9.6)	0.20	4 (1.0)	2 (4.4)	0.42
<b>Number of symptoms at index visit, median (IQR)</b>	6.0 (4.0, 9.0)	N/A	N/A	5.0 (3.0, 8.0)	5.0 (3.0, 8.3)	0.99	6.0 (3.0, 9.0)	7.0 (3.0, 9.0)	0.38	6.0 (3.0, 9.0)	7.0 (4.0, 9.3)	N/A
<b>Number of symptoms at index visit</b>			N/A			0.99			0.52			0.63
≤ 3	88 (21.5)	N/A		31 (37.3)	54 (35.1)		39 (27.1)	45 (25.4)		112 (26.5)	9 (19.6)	
4 to 6	140 (34.2)	N/A		24 (28.9)	43 (27.9)		44 (30.6)	42 (23.7)		126 (29.9)	11 (23.9)	
≥ 7	181 (44.3)	N/A		28 (33.7)	57 (37)		61 (42.4)	90 (50.8)		184 (43.6)	26 (56.5)	

All data are n(%) unless otherwise indicated.

a Adjusted P-value for multiple comparisons via Benjamini-Hochberg method, within the set of tests

b  $\geq 1$  of fever, cough, and/or loss of smell or taste

c missing data in one patient

d missing data in four patients

e missing data in one patient

**eTable 3.** Comparison of Clinical Course and Outcomes at Index ED Visit or Within 14-Day Follow-up Period, by Method of Variant of Concern Assignment (Reported vs Imputed)

	Original-type Imputed (n=389)	Original-type Reported (n=31)	P-value <sup>b</sup>	Alpha Imputed (n=54)	Alpha Reported (n=170)	P-value <sup>b</sup>	Delta Imputed (n=128)	Delta Reported (n=205)	P-value <sup>b</sup>	Omicron Imputed (n=430)	Omicron Reported (n=62)	P-value <sup>b</sup>
<b>OUTCOMES</b>												
<b>Admitted</b>	N/A	N/A	10/84 (11.9)	8/158 (5.1)	0.18	18/144 (12.5)	15/177 (8.5)	0.59	51/422 (12.1)	10/46 (21.7)	0.36	N/A
<b>Admitted to ICU</b>	N/A	N/A	1/84 (1.2)	2/158 (1.3)	0.99	0/144 (0)	2/177 (1.1)	0.67	1/422 (0.2)	0/46 (0)	0.99	N/A
<b>Any Revisit</b>	N/A	N/A	18/76 (23.7)	50/138 (36.2)	0.18	36/118 (30.5)	36/149 (24.2)	0.59	107/364 (29.4)	9/33 (27.3)	0.99	N/A
<b>Revisit to ED</b>	N/A	N/A	10/76 (13.2)	27/138 (19.6)	0.47	12/118 (10.2)	15/149 (10.1)	0.98	68/364 (18.7)	7/33 (21.2)	0.99	N/A
<b>Hospitalized at revisit</b>	N/A	N/A	1/84 (1.2)	2/158 (1.3)	0.99	1/144 (0.7)	4/177 (2.3)	0.67	7/422 (1.7)	2/46 (4.3)	0.66	N/A
<b>Mechanical ventilation<sup>a</sup></b>	N/A	N/A	0/84 (0)	1/158 (0.6)	0.99	0/144 (0)	2/175 (1.1)	0.67	2/416 (0.5)	0/46 (0)	0.99	N/A
<b>Died</b>	N/A	N/A	0/84 (0)	0/158 (0)	N/A	0/144 (0)	0/175 (0)	N/A	0/419 (0)	0/46 (0)	N/A	N/A
<b>Chest x-ray/MANAGEMENT</b>												
<b>Chest x-ray</b>	69/407 (17.0)	N/A	N/A	13/84 (15.5)	14/158 (8.9)	0.29	21/142 (14.8)	14/175 (8.0)	0.56	89/421 (21.1)	8/46 (17.4)	0.99
<b>IV fluid</b>	50/406 (12.3)	N/A	N/A	9/84 (10.7)	5/158 (3.2)	0.13	15/142 (10.6)	16/177 (9.0)	0.77	60/417 (14.4)	11/46 (23.9)	0.36
<b>Oxygen</b>	5/406 (1.2)	N/A	N/A	0/84 (0)	1/158 (0.6)	0.99	4/143 (2.8)	3/175 (1.7)	0.77	8/416 (1.9)	1/46 (2.2)	0.99
<b>Antibiotics</b>	62/406	N/A	N/A	16/84 (19)	11/158 (7.0)	0.05	27/143 (18.9)	27/176 (15.3)	0.67	64/420 (15.2)	6/46 (13.0)	0.99



	(15.3)											
<b>Corticosteroids</b>	38/405 (9.4)	N/A	N/A	10/84 (11.9)	19/158 (12)	0.9 9	17/143 (11.9)	14/175 (8.0)	0.5 9	69/418 (16.5)	13/46 (28.3)	0.3 6
Co-detection of a respiratory pathogen	2/63 (3.2)	N/A	N/A	1/14 (7.1)	2/16 (12.5)	0.9 9	9/16 (56.3)	5/19 (26.3)	0.5 6	16/94 (17)	0/10 (0)	0.8 5

All data are n (%).

ED, emergency department; ICU, intensive care unit; IV, intravenous

a Invasive or non-invasive

b Adjusted P-value for multiple comparisons via Benjamini-Hochberg method, within the set of tests

**eFigure.** Chronological Depiction of Timing of Identification of Variants and Proportional Breakdown of Identification Through Testing or Imputation Based on Known Dominant Strains

