

Supplementary information

Figure S1A and B. Maximum-likelihood phylogenetic tree of swine and human influenza A viruses isolated in North America between 2002-2019 and downsampled to retain 98% sequence identity. Tips are coloured by country of origin of swine strains (S1A) and host species the strain was isolated from (S1B).

Figure S1A

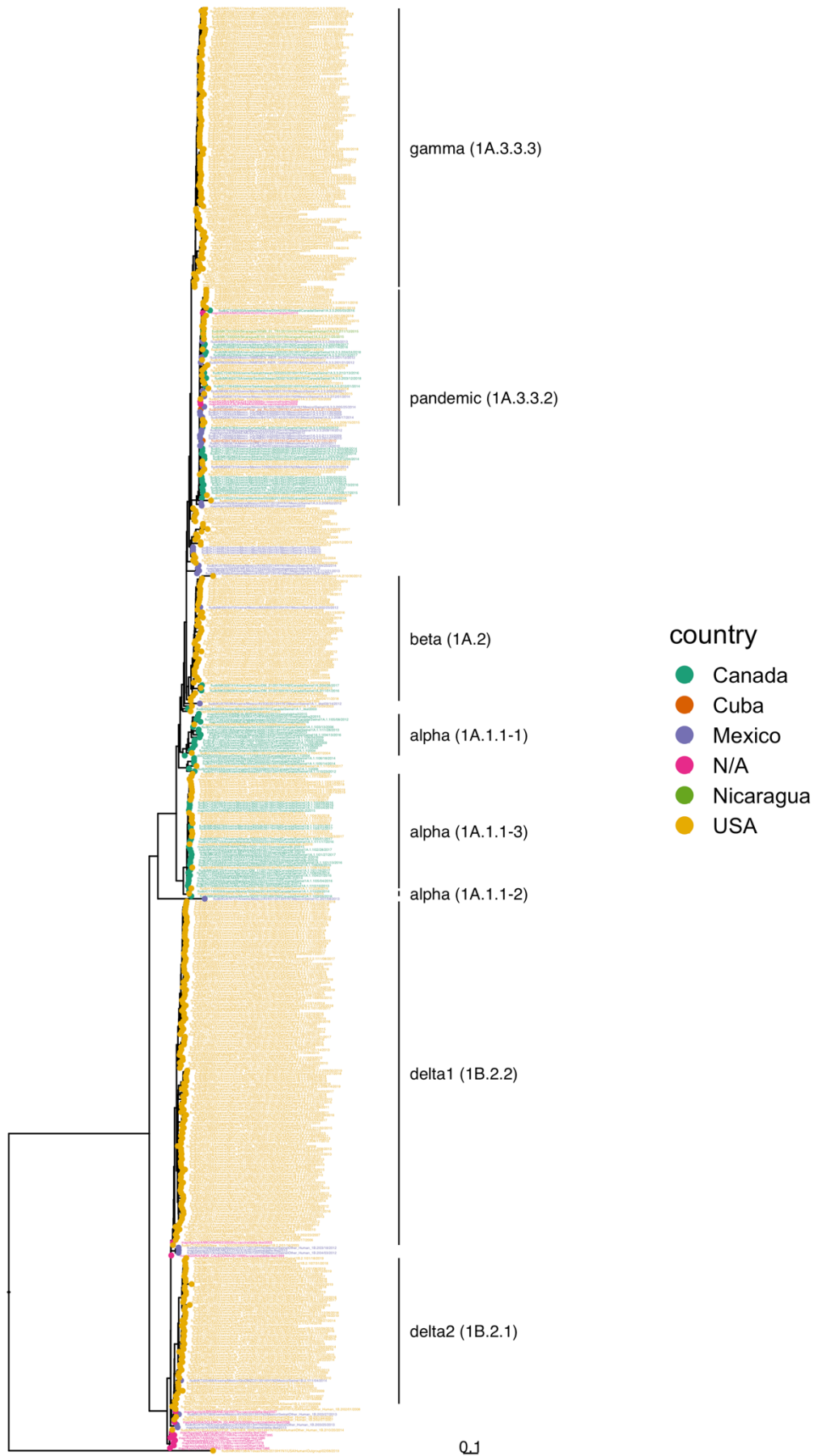


Figure S1B

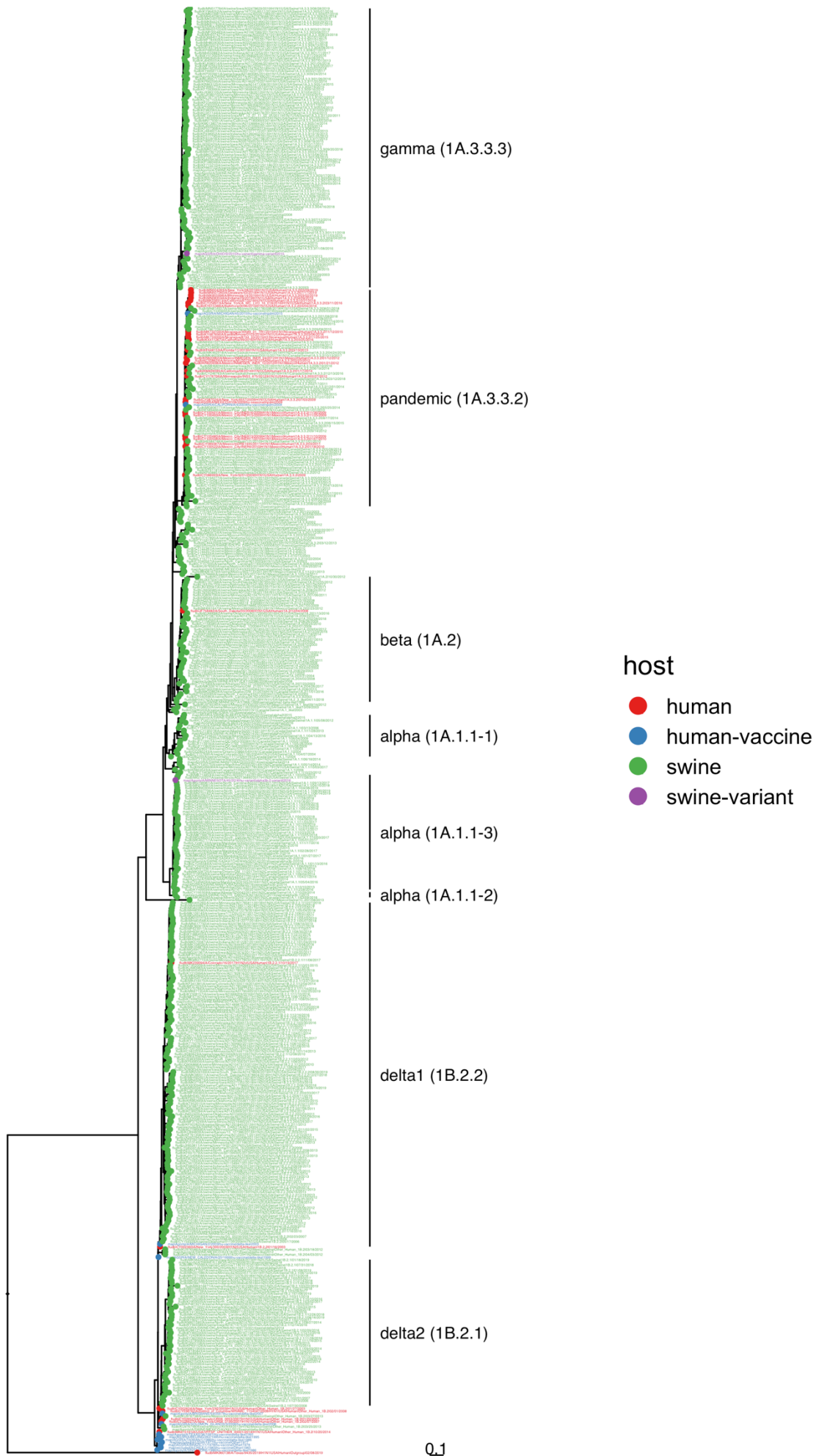


Figure S2. A scatterplot of genetic (amino acid) versus antigenic distance between viruses within the 1A and 1B lineages with a linear model regression line fitted to the data.

Figure S2

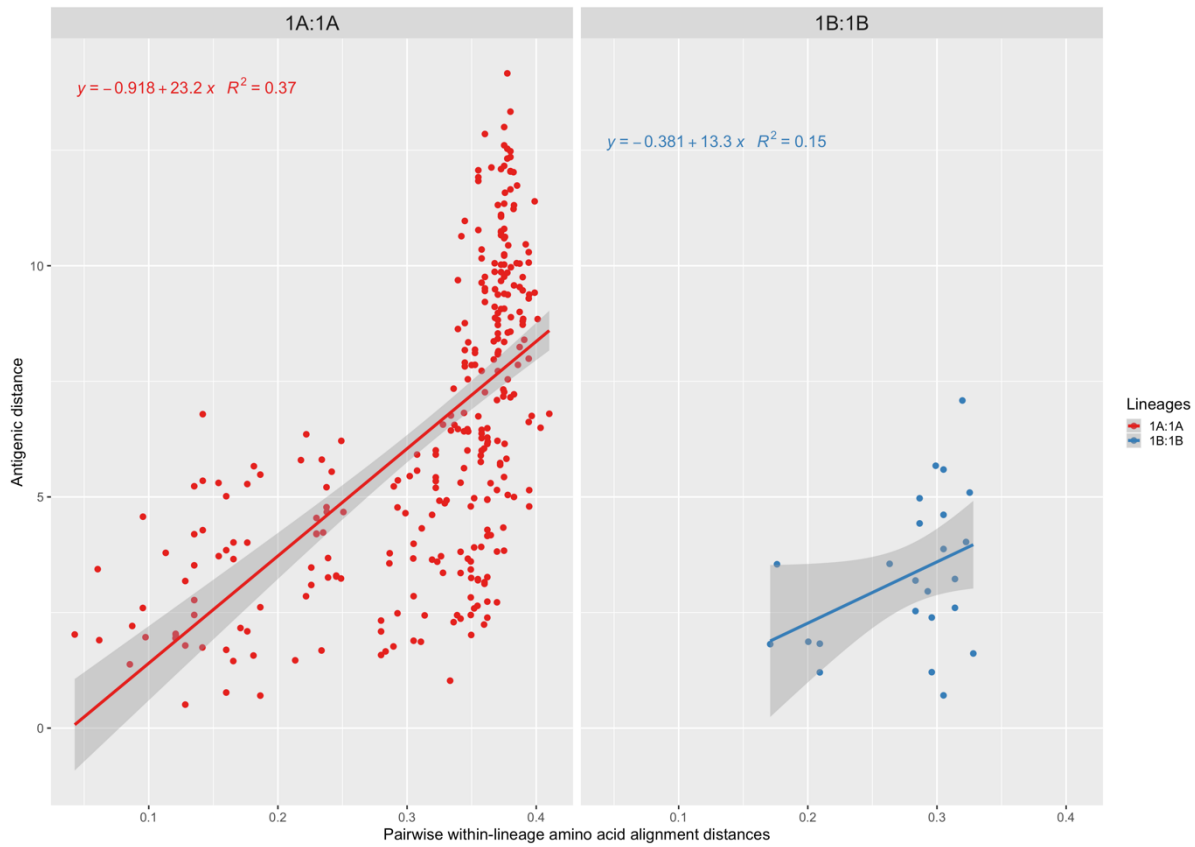
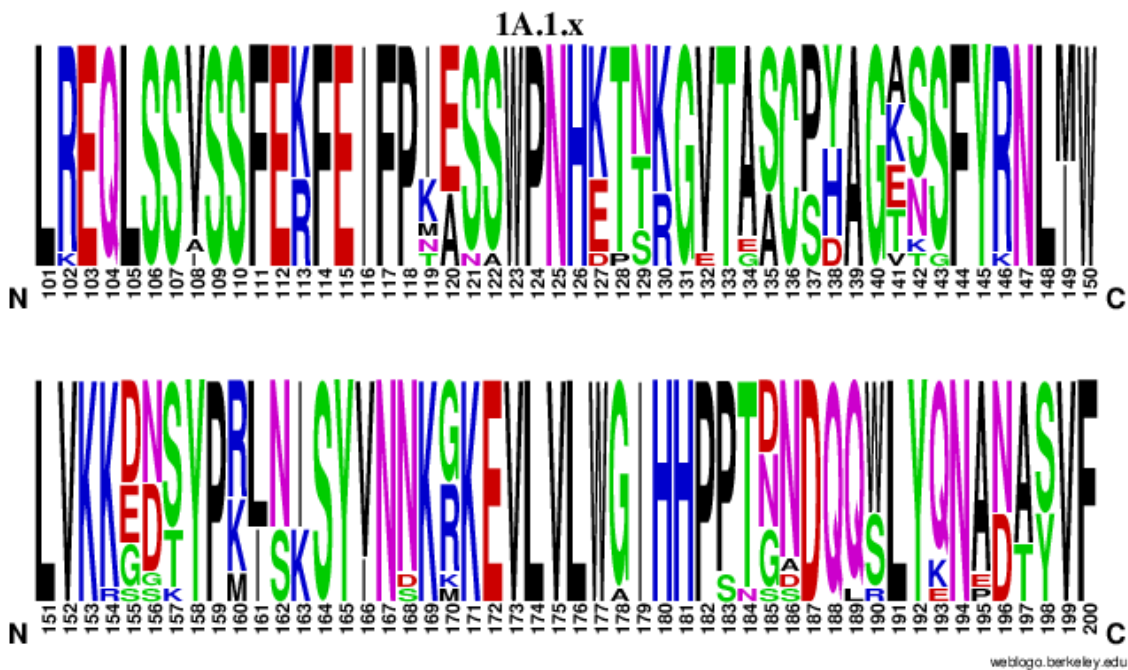
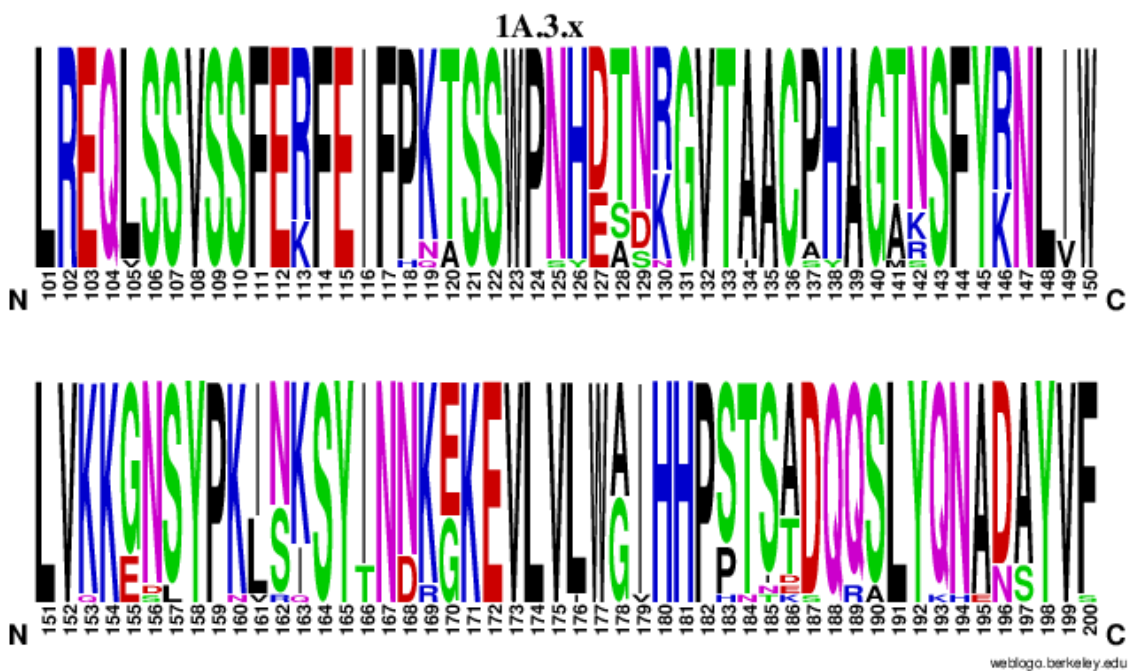


Figure S3 (A-D). Web-logo of the amino acid alignment (101-200) of each sub-lineage of North American swine influenza A virus: A (1A.1.x), B (1A.3.x), C (1B.2.1) and D (1B.2.2.1). Logo shows variation at each amino acid residue in a region of the protein in which largely determines antigenicity (recognised by host antibodies). (Crooks et al. 2004)

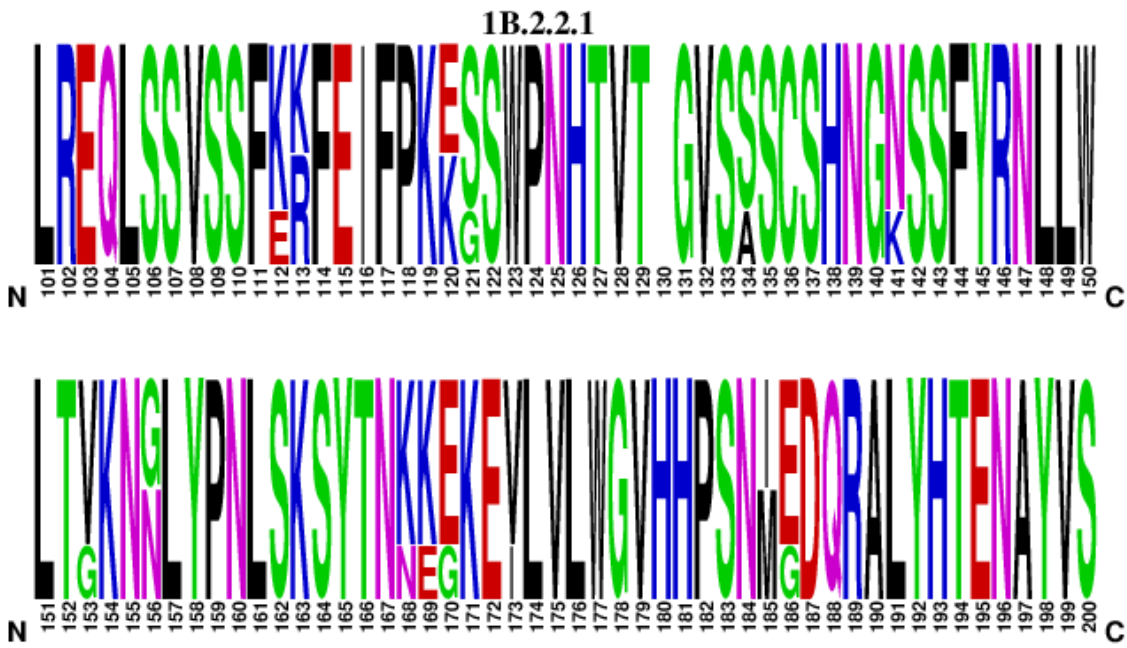
A



B

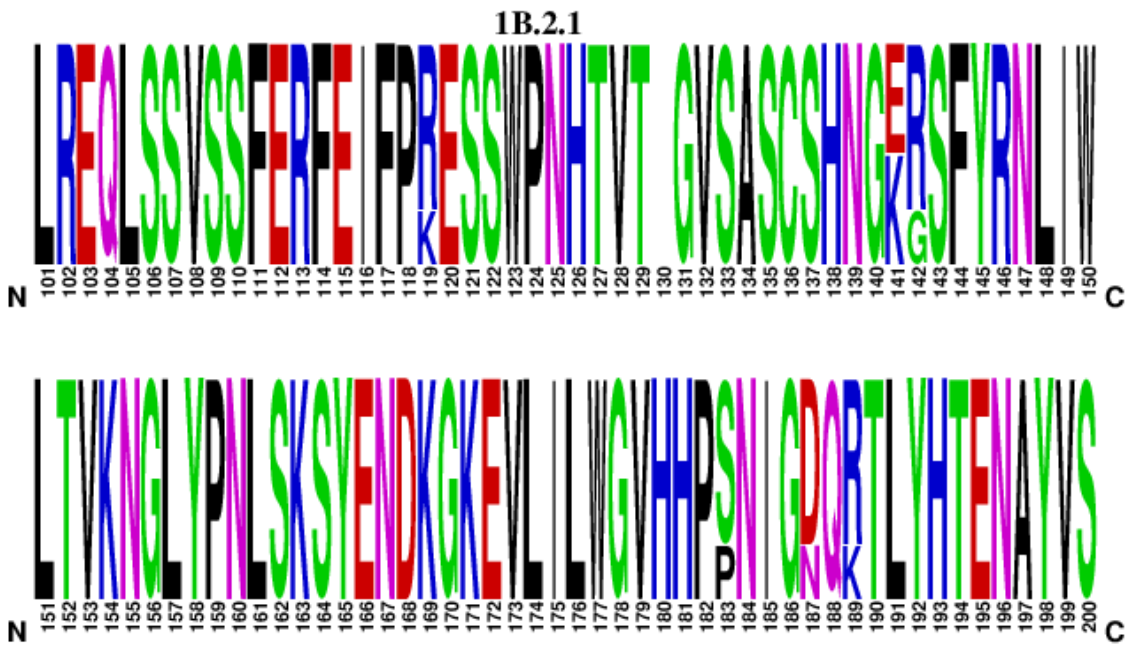


C



weblogo.berkeley.edu

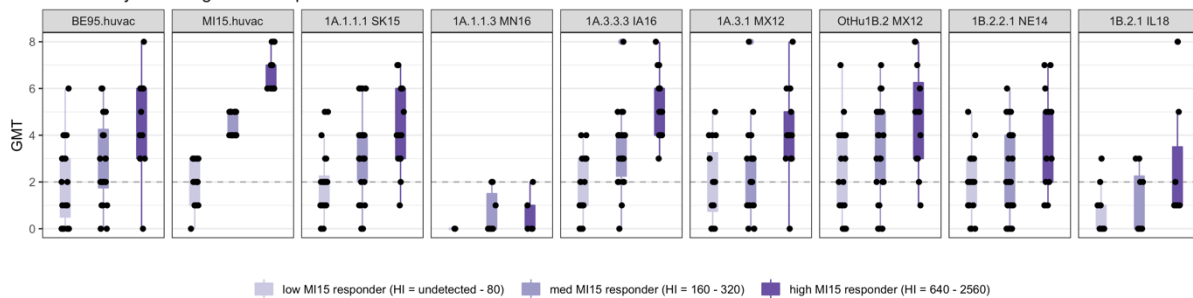
D



weblogo.berkeley.edu

Figure S4 (A-B). Combined post-exposure and post-vaccination titres of human sera against representative swine strains, stratified by (A) low – to – high responders to MI15 (A/Michigan/45/2015) vaccine strain, (B) low – to – high responders to MI15 and period of birth (1945-76, 1977-88, 1989-96). Violin box plots show the median of aggregated HI titres against H1N1 strains with 5th and 95th percentile and standard deviation. Each dot represents the GMT: geometric mean titre, \log_2 (HI titre /10) of human sera on the y-axis against each strain (shown on x-axis). Cohorts are combined as results are similar for individual cohorts).

A HI Titers by low to high MI15 responders



B HI Titers by low to high MI15 responders

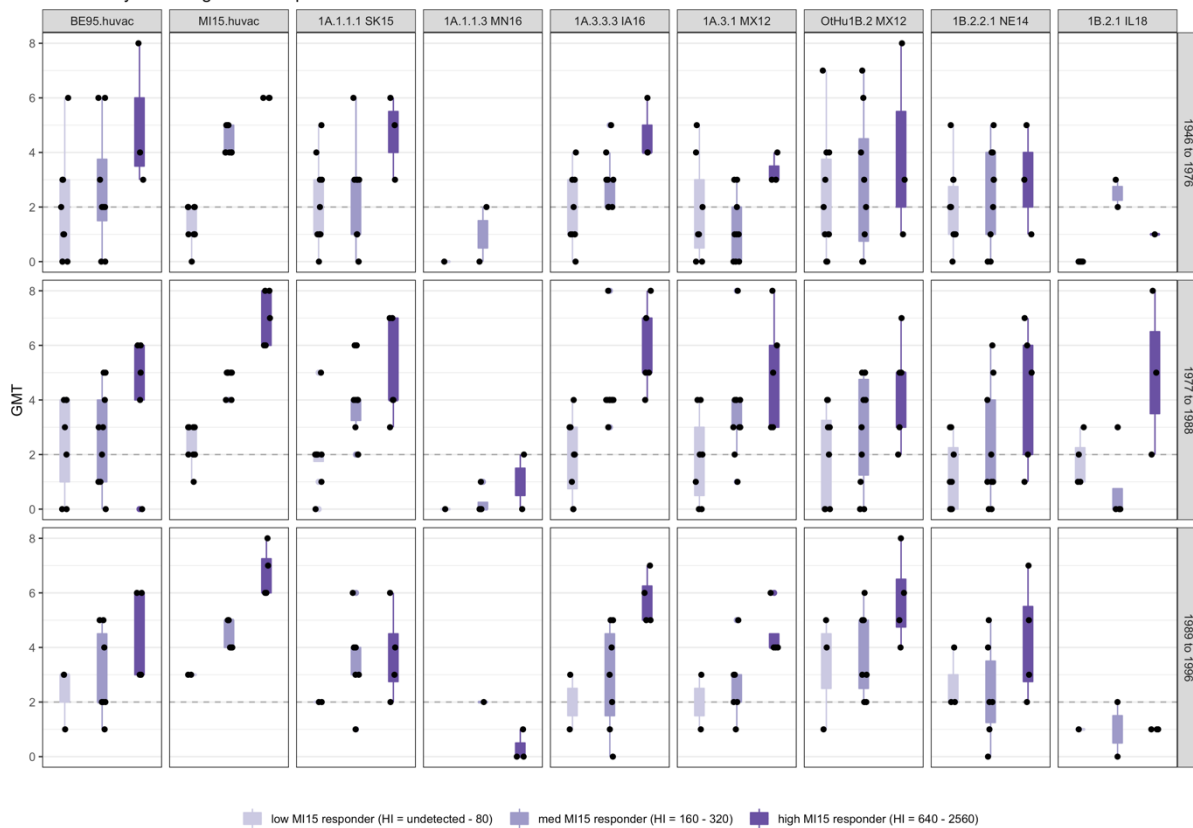


Figure S5. Spearman's correlation between HI titers against North American H1 swine strains and human seasonal H1 vaccine strains of post-exposure convalescent and post-vaccination human sera cohorts (combined as results similar to individual cohorts).

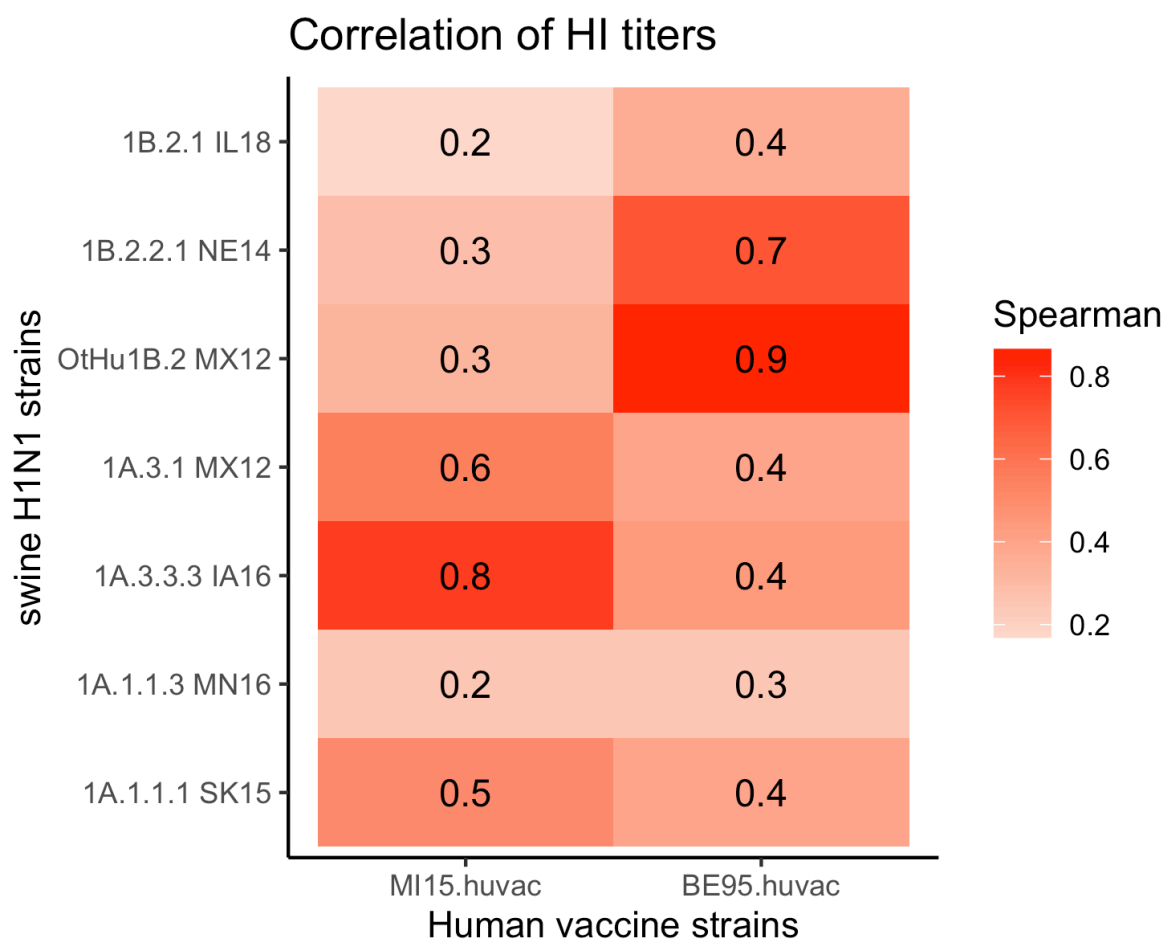


Table S1. A list of swine and human influenza A viruses and sera raised against them that have been used in this study.

Viruses tested against swine sera	virus clade	virus subtype	HA reference	Swine sera raised against virus	virus clade	virus subtype	HA reference
A/swine/Alberta/SD0125/2015	1A.1.1	H1N1	MF768555	A/swine/Iowa/1973	1A.1.1	H1N1	EU139826
A/swine/Saskatchewan/SD0094/2015*	1A.1.1	H1N1	MF768483	A/swine/Alberta/SD0125/2015	1A.1.1	H1N1	MF768555
A/swine/Alberta/SD0014/2013	1A.1.1	H1N1	CY195078	A/swine/Alberta/SD0014/2013	1A.1.1	H1N1	CY195078
A/swine/Alberta/SD0154/2016	1A.1.1	H1N1	MF768523	A/swine/Alberta/SD0154/2016	1A.1.1	H1N1	MF768523
A/swine/Manitoba/D0333/2014	1A.1.1	H1N2	CY195575	A/swine/Manitoba/D0333/2014	1A.1.1	H1N2	CY195575
A/swine/Manitoba/D0392/2015	1A.1.1	H1N2	MF768531	A/swine/Minnesota/02053/2008	1A.1.1	H1N1	HM461762
A/swine/Saskatchewan/SD0102/2015	1A.1.1	H1N2	MF768539	A/swine/Manitoba/D0392/2015	1A.1.1	H1N2	MF768531
A/swine/Manitoba/SD0114/2015	1A.1.1	H1N2	MF768507	A/swine/Saskatchewan/SD0102/2015	1A.1.1	H1N2	MF768539
A/swine/Alberta/SD0191/2016	1A.1.1	H1N2	MF768475	A/swine/Manitoba/SD0114/2015	1A.1.1	H1N2	MF768507
A/swine/Saskatchewan/SD0200/2016	1A.1.1	H1N2	MF768547	A/swine/Saskatchewan/SD0142/2016	1A.1.1	H1N2	MK462362
A/swine/Manitoba/D0348/2014	1A.1.1	H1N2	CY195295	A/swine/Minnesota/A01781045/2016	1A.1.1	H1N2	KX928680
A/Minnesota/45/2016	1A.1.1	H1N2	EPI760602	A/swine/Minnesota/37866/1999	1A.2-3-like	H1N1	EU139827
A/swine/Minnesota/A01781045/2016*	1A.1.1	H1N2	KX928680	A/swine/South Dakota/A01349306/2013	1A.3.2	H1N1	KC844200
A/swine/Mexico/AVX23/2012*	1A.2-3-like	H1N1	KU976649	A/swine/Minnesota/1192/2001	1A.3.3-like	H1N2	EU139828
A/swine/Illinois/A01493472/2014	1A.3.3.2	H1N1	KJ701784	A/Mexico/4108/2009	1A.3.3.2	H1N1	GQ223112
A/California/04/2009	1A.3.3.2	H1N1	GQ280797	A/swine/Illinois/A01493472/2014	1A.3.3.2	H1N1	KJ701784
A/Mexico/4108/2009	1A.3.3.2	H1N1	GQ223112	A/California/04/2009	1A.3.3.2	H1N1	GQ280797
A/Michigan/45/2015*	1A.3.3.2	H1N1	KU933493	A/Michigan/45/2015	1A.3.3.2	H1N1	KU933493
A/swine/Mexico/AVX31/2012	1A.3.3.2	H1N1	KU976950	A/swine/Minnesota/00194/2003	1A.3.3.3	H1N2	EU139830
A/swine/Mexico/AVX44/2012	1A.3.3.2	H1N1	KU976796	A/swine/Kansas/00246/2004	1A.3.3.3	H1N2	CY081680
A/swine/North Carolina/A02076926/2015	1A.3.3.3	H1N1	KT429540	A/swine/OH/511445/2007	1A.3.3.3	H1N1	EU604689
A/swine/North Carolina/A01841602/2015	1A.3.3.3	H1N1	KR088267	A/swine/Missouri/02060/2008	1A.3.3.3	H1N1	CY082655
A/swine/Ohio/A01847657/2015	1A.3.3.3	H1N1	KR780630	A/swine/North Carolina/02023/2008	1A.3.3.3	H1N1	HM461818
A/Ohio/09/2015	1A.3.3.3	H1N1	EPI587643	A/swine/Ohio/02026/2008	1A.3.3.3	H1N1	CY082631
A/swine/Minnesota/A01567490/2014	1A.3.3.3	H1N1	KP662638	A/Ohio/09/2015	1A.3.3.3	H1N1	EPI587643
A/swine/North Carolina/A01797415/2015	1A.3.3.3	H1N1	KU357008	A/swine/Iowa/A01731653/2016	1A.3.3.3	H1N1	KU877398
A/swine/Iowa/A01731653/2016*	1A.3.3.3	H1N1	KU877398	A/swine/Illinois/00685/2005	1B.2.1	H1	CY081899
A/swine/North Carolina/A01730369/2016	1A.3.3.3	H1N1	KU695684	A/swine/Oklahoma/A01409770/2014	1B.2.1	H1N2	KJ437589
A/swine/Oklahoma/A01409770/2014	1B.2.1	H1N2	KJ437589	A/swine/Minnesota/A01134353/2011	1B.2.2.1	H1N2	JQ906881
A/swine/Illinois/A02139356/2018*	1B.2.1	H1N2	MG917068	A/swine/Nebraska/A01492366/2014	1B.2.2.1	H1N2	KJ549771
A/swine/Michigan/A01104117/2018	1B.2.1	H1N2	MH758776	A/Brazil/11/1978	Other-Human	H1N1	CY020293
A/swine/Minnesota/A01134353/2011	1B.2.2.1	H1N2	JQ906881	A/Taiwan/1/1986	Other-Human-1B.2	H1N1	X17224
A/swine/Nebraska/A01492366/2014*	1B.2.2.1	H1N2	KJ549771	A/Beijing/262/1995	Other-Human-1B.2	H1N1	AJ457900
A/swine/Illinois/A01644323/2018	1B.2.2.1	H1N2	MG825101	A/New Caledonia/20/1999	Other-Human-1B.2	H1N1	EU103824
A/Brazil/11/1978	Other-Human	H1N1	CY020293	A/Solomon Islands/3/2006	Other-Human-1B.2	H1N1	EU124135
A/New Caledonia/20/1999	Other-Human-1B.2	H1N1	EU103824				
A/swine/Mexico/AVX18/2012*	Other-Human-1B.2	H1N2	KU976609				
A/swine/Mexico/AVX61/2013	Other-Human-1B.2	H1N2	KU976596				
A/Solomon Islands/3/2006	Other-Human-1B.2	H1N1	EU124135				
A/Singapore/6/1986	Other-Human-1B.2	H1N1	CY020477				
A/Taiwan/1/1986	Other-Human-1B.2	H1N1	X17224				
A/Texas/36/1991	Other-Human-1B.2	H1N1	AJ457908				
A/Beijing/262/1995*	Other-Human-1B.2	H1N1	AJ457900				
A/Michigan/2/2003	Other-Human-1B.2	H1N2	CY016324				
A/Brisbane/59/2007	Other-Human-1B.2	H1N1	KF009550				

*viruses tested against human sera

Table S3. Risk ranking scoring system used to prioritize representative swine H3N2 strains for the assessment of human immunity for pandemic potential.

strain	global lineage	blast_USA 2yr	blast_global 10yr	revblast_USA 2yr	revblast_global 10yr	Sequence Factor	ABRAZIL/11/1978	ASINGAPORE/1986	ATAWAN/1/1986	ATEXAS/36/1991	ABELJUNG/262/1995	ANEW_CALEDONIA/20/1999	AMICHIGAN/2/2003	ASOLOMON_ISLANDS/3/200	ABRISBANE/59/2007	ACALIFORNIA/4/2009	AMICHIGAN/45/2015	all_vaccine	stdev	>3	Antigenic Factor	Summed Factor
A/SWINE/SASKATCHEWAN/SD0094/2015	1A.1.1-1	0.00	0.18	0.00	23.67	40.40	5.77	3.65	5.82	5.62	6.40	5.69	5.09	6.15	7.81	3.54	2.56	5.28	1.49	10	14.48	54.89
A/SWINE/ALBERTA/SD0154/2016	1A.1.1-1	0.00	0.06	0.00	0.06	0.20	6.96	4.91	6.62	6.41	7.56	6.25	6.27	6.69	7.79	2.12	1.85	5.77	2.01	9	15.04	15.25
A/SWINE/ALBERTA/SD0125/2015	1A.1.1-1	0.00	0.06	0.00	9.45	16.11	6.03	5.29	6.05	6.09	7.99	7.37	6.77	7.34	8.65	3.12	1.75	6.04	2.05	10	16.16	32.27
A/SWINE/ALBERTA/SD0014/2013	1A.1.1-1	0.00	0.06	0.00	0.06	0.20	6.91	5.54	8.09	8.08	8.23	7.83	6.93	8.79	10.56	4.35	2.47	7.07	2.24	10	16.71	16.92
A/SWINE/MANITOBA/D0333/2014	1A.1.1-3	0.00	0.06	0.00	0.18	0.41	9.33	5.22	9.49	8.96	6.89	5.00	5.72	7.43	8.87	5.87	5.92	7.15	1.74	11	16.21	16.62
A/SWINE/SASKATCHEWAN/SD0200/2016	1A.1.1-3-del	0.00	0.12	0.00	0.18	0.51	6.17	3.33	7.13	6.75	2.97	5.34	2.77	6.42	9.32	9.62	8.65	6.22	2.44	9	16.33	16.84
A/SWINE/MANITOBA/D0348/2014	1A.1.1-3-del	0.00	0.24	0.22	1.65	3.50	5.82	3.38	6.90	6.56	2.96	5.64	2.86	6.49	9.45	9.80	8.75	6.24	2.47	9	16.40	19.90
A/SWINE/MANITOBA/SD0114/2015	1A.1.1-3-del	0.00	0.41	3.51	1.06	7.29	5.70	4.29	7.65	7.52	4.83	7.11	4.42	8.05	10.97	9.75	8.34	7.15	2.17	11	17.51	24.80
A/SWINE/ALBERTA/SD0191/2016	1A.1.1-3-del	0.00	0.12	0.15	0.41	1.10	6.35	3.90	7.61	7.28	3.62	6.01	3.46	7.11	10.02	10.00	8.92	6.75	2.38	11	18.13	19.24
A/SWINE/SASKATCHEWAN/SD0102/2015	1A.1.1-3-del	0.00	0.12	0.15	0.83	1.81	7.38	5.82	8.91	8.66	4.88	7.73	5.18	8.64	11.61	12.07	10.89	8.34	2.47	11	18.42	20.24
A/SWINE/MINNESOTA/A01781045/2016	1A.1.1-3-del	0.00	0.18	2.71	1.36	6.31	3.25	4.13	5.14	5.21	4.10	7.39	4.19	7.01	10.02	10.30	8.90	6.33	2.53	11	18.59	24.91
A/MINNESOTA/45/2016	1A.1.1-3-del	1.10	0.00	5.34	0.47	9.60	4.77	5.29	6.18	6.15	4.25	7.95	4.84	7.53	10.56	11.86	10.59	7.27	2.67	11	19.00	28.60
A/SWINE/MANITOBA/D0392/2015	1A.1.1-3-del	0.00	0.12	0.00	0.24	0.61	8.06	7.03	8.07	7.69	4.53	7.95	5.81	7.50	10.20	13.91	13.14	8.54	2.85	11	19.54	20.15
A/SWINE/MEXICO/AVX23/2012	1A.3.1	0.00	0.24	2.71	7.14	16.21	7.35	6.23	6.25	6.15	8.64	7.34	7.51	6.93	7.42	2.79	3.20	6.35	1.81	10	15.43	31.64
A/SWINE/MEXICO/AVX31/2012	1A.3.3.2	0.00	0.06	0.00	3.25	5.61	7.75	5.66	7.05	6.80	8.20	6.51	6.93	6.87	7.55	1.45	2.27	6.10	2.20	9	15.61	21.21
A/SWINE/MEXICO/AVX44/2012	1A.3.3.2	0.00	0.12	0.00	0.18	0.51	7.73	4.59	7.95	7.62	7.08	5.62	5.72	7.12	8.57	3.58	3.21	6.25	1.83	11	16.50	17.00
A/SWINE/ILLINOIS/A01493472/2014	1A.3.3.2	0.00	0.35	6.88	30.70	62.00	9.14	7.22	8.42	8.21	9.73	7.77	8.46	8.19	8.44	0.71	2.72	7.18	2.82	9	17.45	79.45
A/SWINE/NORTH_CAROLINA/A01797415/2015	1A.3.3.3	0.00	0.00	0.22	0.30	0.81	7.33	5.00	5.59	5.14	7.02	5.24	5.97	4.83	5.23	3.74	4.53	5.42	1.04	11	14.12	14.93
A/SWINE/IOWA/A01731653/2016	1A.3.3.3	1.68	0.00	36.21	0.12	52.00	6.82	5.54	5.05	4.81	7.63	6.43	6.64	5.53	6.00	4.09	4.49	5.73	1.09	11	14.26	66.26
A/SWINE/NORTH_CAROLINA/A01730369/2016	1A.3.3.3	0.00	0.00	0.00	0.00	0.00	6.19	2.77	6.53	6.18	5.33	4.69	3.98	5.95	7.96	4.86	4.08	5.32	1.44	10	14.32	14.32
A/SWINE/MINNESOTA/A01567490/2014	1A.3.3.3	0.07	0.00	2.56	1.53	6.19	8.40	6.39	6.98	6.66	8.63	6.65	7.49	6.53	6.55	2.51	3.88	6.42	1.79	10	15.38	21.56
A/OHIO/09/2015	1A.3.3.3	0.00	0.00	0.00	0.06	0.10	9.26	5.38	8.00	7.35	7.09	3.99	5.97	5.40	5.59	4.14	5.43	6.14	1.62	11	15.85	15.95
A/SWINE/NORTH_CAROLINA/A02076926/2015	1A.3.3.3	0.07	0.00	1.46	0.06	2.19	10.44	7.07	8.92	8.34	8.86	5.74	7.76	6.64	6.02	3.75	5.68	7.20	1.89	11	16.68	18.88
A/SWINE/NORTH_CAROLINA/A01841602/2015	1A.3.3.3	0.00	0.00	0.80	0.00	1.09	10.84	7.00	8.98	8.23	8.18	4.67	7.30	5.68	4.62	5.62	7.29	7.13	1.91	11	16.72	17.81
A/SWINE/OHIO/A01847657/2015	1A.3.3.3	0.00	0.00	0.00	0.06	0.10	10.82	6.62	9.30	8.53	7.74	4.09	6.83	5.80	5.31	5.80	7.28	7.10	1.93	11	16.78	16.88
A/SWINE/MICHIGAN/A01104117/2018	1B.2.1	1.83	0.00	5.41	0.00	9.90	4.32	2.01	4.75	4.38	1.94	4.91	1.71	4.91	7.91	8.84	7.90	4.87	2.48	8	15.44	25.34
A/SWINE/OKLAHOMA/A01409770/2014	1B.2.1	0.15	0.00	2.56	2.01	7.11	3.60	2.89	4.84	4.70	3.00	6.10	2.90	5.94	8.96	9.37	8.16	5.50	2.43	9	16.29	23.40
A/SWINE/ILLINOIS/A02139356/2018	1B.2.1	0.37	0.00	8.34	0.00	11.91	4.84	4.51	6.47	6.37	3.85	7.29	4.15	7.36	10.43	11.02	9.72	6.91	2.55	11	18.65	30.55
A/SWINE/ILLINOIS/A01644323/2018	1B.2.2.1	0.07	0.00	6.36	1.06	10.59	5.37	1.68	5.81	5.45	4.24	4.39	2.92	5.40	7.79	5.90	5.01	4.91	1.61	9	13.83	24.42
A/SWINE/NEBRASKA/A01492366/2014	1B.2.2.1	0.07	0.00	8.71	0.65	13.10	4.42	0.53	4.62	4.20	2.73	4.20	1.61	4.51	7.29	7.24	6.38	4.34	2.15	8	14.44	27.54
A/SWINE/MINNESOTA/A01134353/2011	1B.2.2.1	0.00	0.00	5.71	0.00	7.81	6.64	3.28	6.85	6.49	5.82	4.81	4.46	6.13	7.93	4.32	3.70	5.49	1.47	11	15.41	23.22
A/SWINE/MEXICO/AVX18/2012	Other_Human_1B.2	0.00	0.12	0.00	12.63	21.60	6.87	2.65	5.71	4.88	1.96	1.89	1.60	2.65	5.29	8.23	8.15	4.53	2.52	6	13.56	35.16
A/SWINE/MEXICO/AVX61/2013	Other_Human_1B.2	0.00	0.06	0.00	0.59	1.10	5.01	1.21	5.53	5.16	3.65	4.36	2.39	5.23	7.80	6.55	5.62	4.77	1.84	9	14.52	15.62

