Covid-19 in Iceland

Timeline

- The discovery of the virus at the end of Dec 2019 in China
- Screening for the virus in Iceland began January 31 2020
- First case diagnosed in Iceland on Feb 28 2020
- The idea that deCODE should participate Mars 5
- The screening by deCODE began on Mars 13 (as well as sequencing of the virus)
- On May 26 deCODE had screened 38.635 volunteers (196+,0.50%)
- On May 26 deCODE had screened 3.925 randomly selected individuals (21+ 0.54%)
- On May 26 the National Hospital had screened 21.172 high risk individuals (1804+8.5%)
- 16.6 % of the population of Iceland had been screened on May 26
- June 15 the borders opened again

ORIGINAL ARTICLE

Spread of SARS-CoV-2 in the Icelandic Population

D.F. Gudbjartsson, A. Helgason, H. Jonsson, O.T. Magnusson, P. Melsted, G.L. Norddahl, J. Saemundsdottir, A. Sigurdsson, P. Sulem, A.B. Agustsdottir, B. Eiriksdottir, R. Fridriksdottir, E.E. Gardarsdottir, G. Georgsson, O.S. Gretarsdottir, K.R. Gudmundsson, T.R. Gunnarsdottir, A. Gylfason, H. Holm, B.O. Jensson, A. Jonasdottir, F. Jonsson, K.S. Josefsdottir, T. Kristjansson, D.N. Magnusdottir, L. le Roux, G. Sigmundsdottir, G. Sveinbjornsson, K.E. Sveinsdottir, M. Sveinsdottir, E.A. Thorarensen, B. Thorbjornsson, A. Löve, G. Masson, I. Jonsdottir, A.D. Möller, T. Gudnason, K.G. Kristinsson, U. Thorsteinsdottir, and K. Stefansson

ABSTRACT

BACKGROUND

During the current worldwide pandemic, coronavirus disease 2019 (Covid-19) was first diagnosed in Iceland at the end of February. However, data are limited on how SARS-CoV-2, the virus that causes Covid-19, enters and spreads in a population.

METHODS

We targeted testing to persons living in Iceland who were at high risk for infection (mainly those who were symptomatic, had recently traveled to high-risk countries, or had contact with infected persons). We also carried out population screening using two strategies: issuing an open invitation to 10,797 persons and sending random invitations to 2283 persons. We sequenced SARS-CoV-2 from 643 samples.

RESULTS

As of April 4, a total of 1221 of 9199 persons (13.3%) who were recruited for targeted testing had positive results for infection with SARS-CoV-2. Of those tested in the general population, 87 (0.8%) in the open-invitation screening and 13 (0.6%) in the random-population screening tested positive for the virus. In total, 6% of the population was screened. Most persons in the targeted-testing group who received positive tests early in the study had recently traveled internationally, in contrast to those who tested positive later in the study. Children under 10 years of age were less likely to receive a positive result than were persons 10 years of age or older, with percentages of 6.7% and 13.7%, respectively, for targeted testing; in the population screening, no child under 10 years of age had a positive result, as compared with 0.8% of those 10 years of age or older. Fewer females than males received positive results both in targeted testing (11.0% vs. 16.7%) and in population screening (0.6% vs. 0.9%). The haplotypes of the sequenced SARS-CoV-2 viruses were diverse and changed over time. The percentage of infected participants that was determined through population screening remained stable for the 20-day duration of screening.

CONCLUSIONS

In a population-based study in Iceland, children under 10 years of age and females had a lower incidence of SARS-CoV-2 infection than adolescents or adults and males. The proportion of infected persons identified through population screening did not change substantially during the screening period, which was consistent with a beneficial effect of containment efforts. (Funded by deCODE Genetics–Amgen.)

The authors' full names, academic degrees, and affiliations are listed in the Appendix. Address reprint requests to Dr. Stefansson at deCODE Genetics–Amgen, Sturlugata 8, Reykjavik 102, Iceland, or at kstefans@decode.is.

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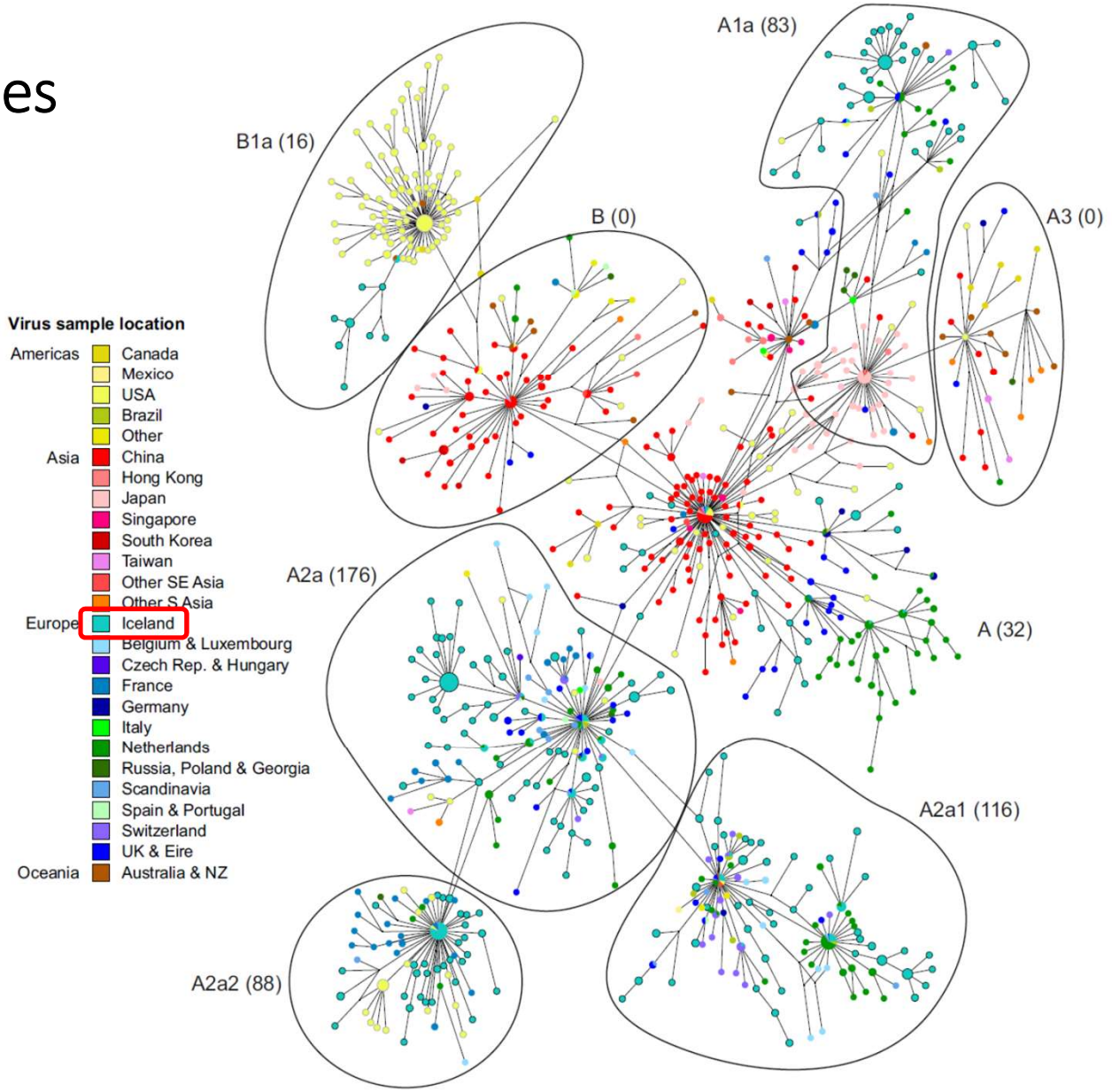
A phylogeny of cov2 sequences

Ancestral haplotype: center of A

Clear geographical structure:

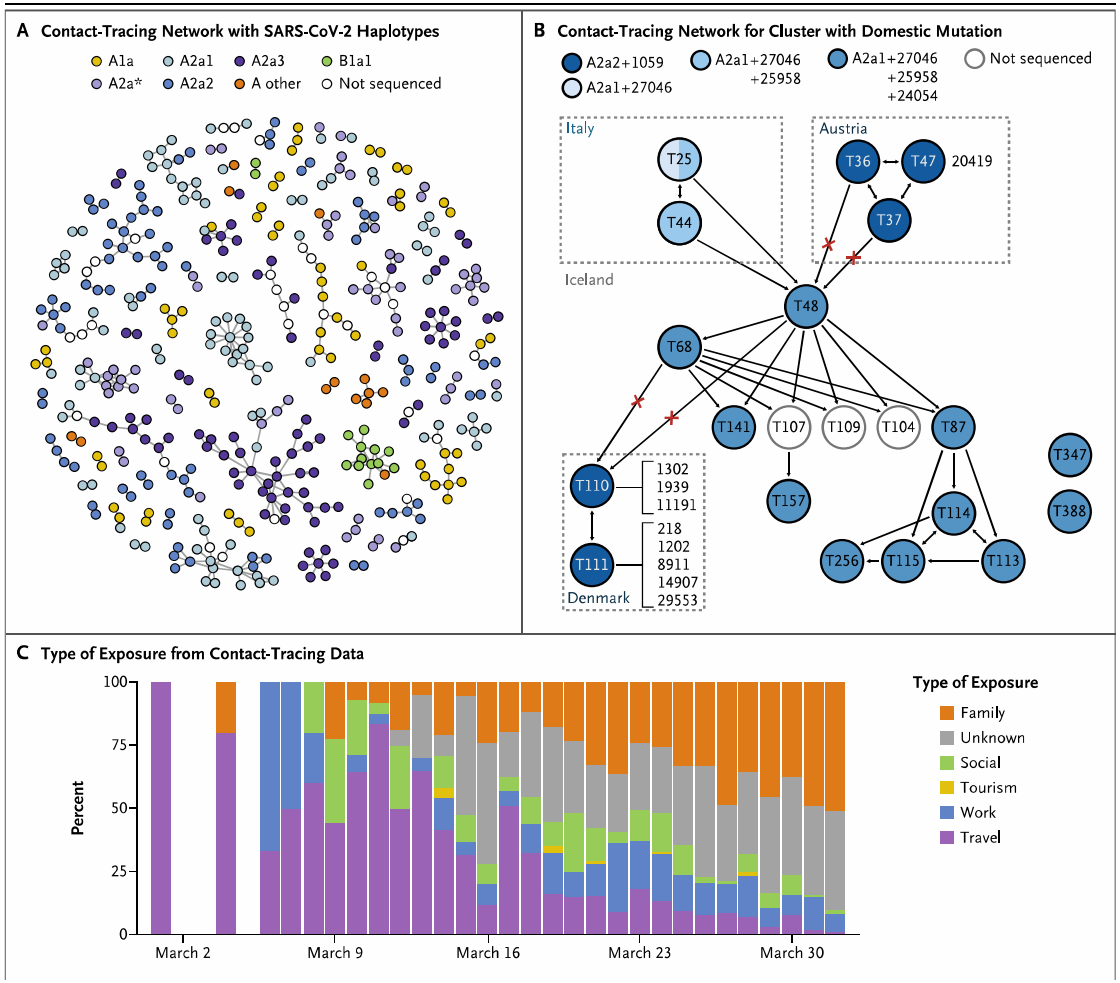
- A and B in China outbreak
- B1a in the USA (west coast)
- A2a, A2a1 and A2a2 primarily in Europe, from Italian outbreak
- Clear Iceland specific clusters



Circles: Sequence types (haplotypes)
Circle size: Number of viruses with haplotype
Lines: Mutations separating haplotypes
Colors: Sampling location of hosts

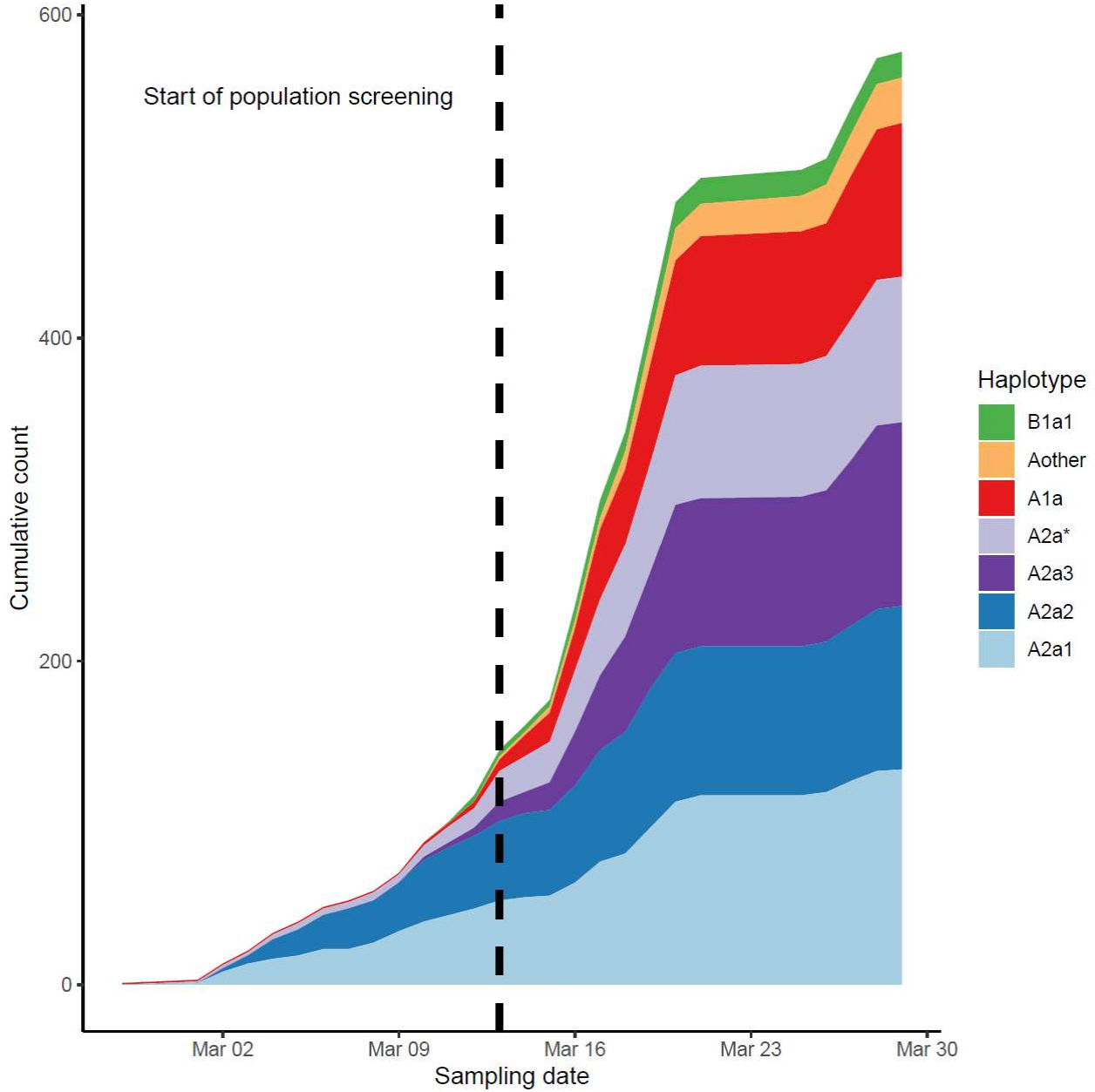
deCODE Genetics research of COVID-19

- Open invitation testing at deCODE began March 16
- Twelve days later the first manuscript was submitted and published April 14 in New England Journal of Medicine
- Open invitation testing of SARS-CoV-2, sequencing of viral genomes and connections with contact tracing data shed a new light on the pandemic in Iceland



Viral haplotypes

- How the viral haplotypes changed over time during the first wave



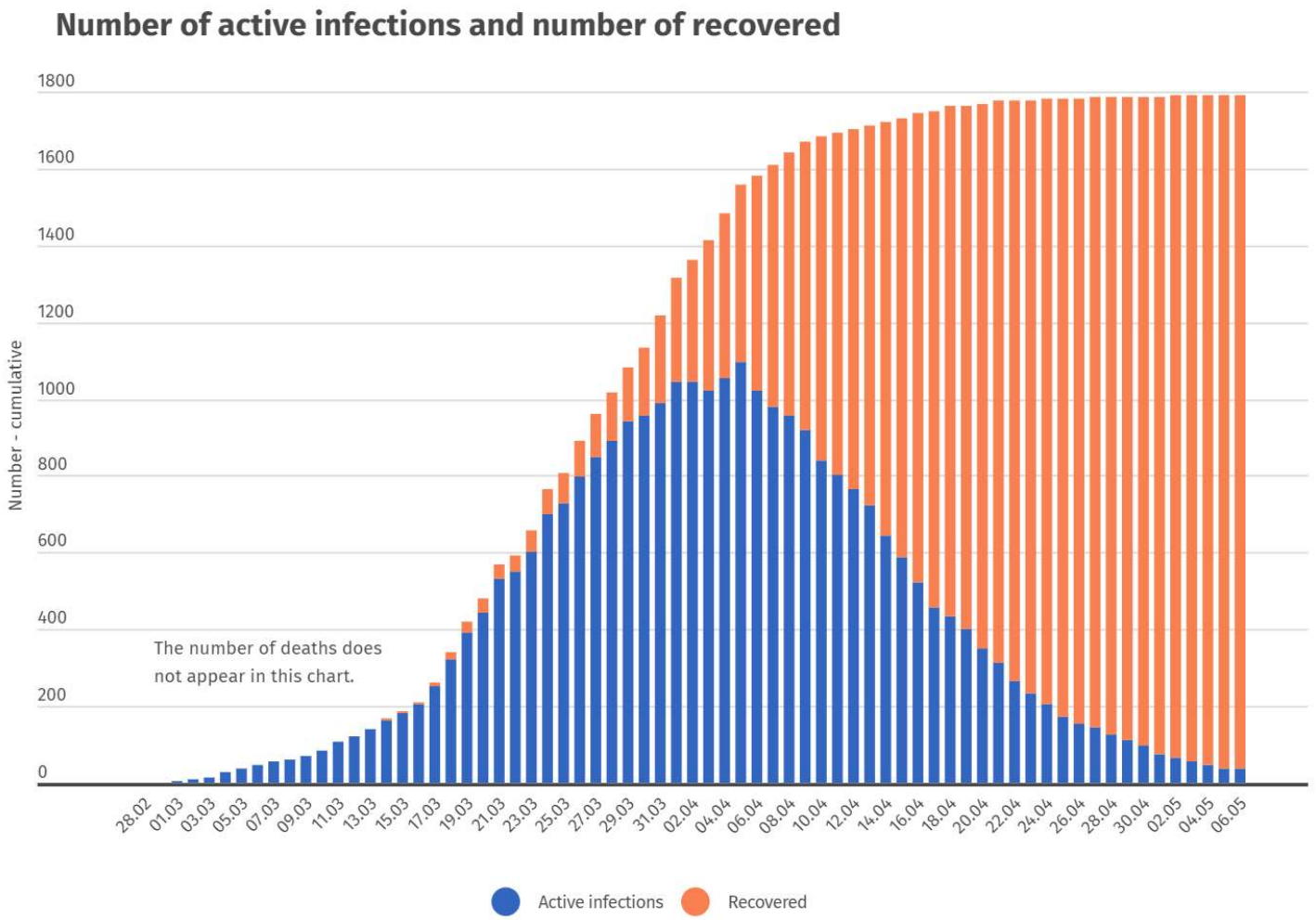
transmission to and from children

The probability of infection

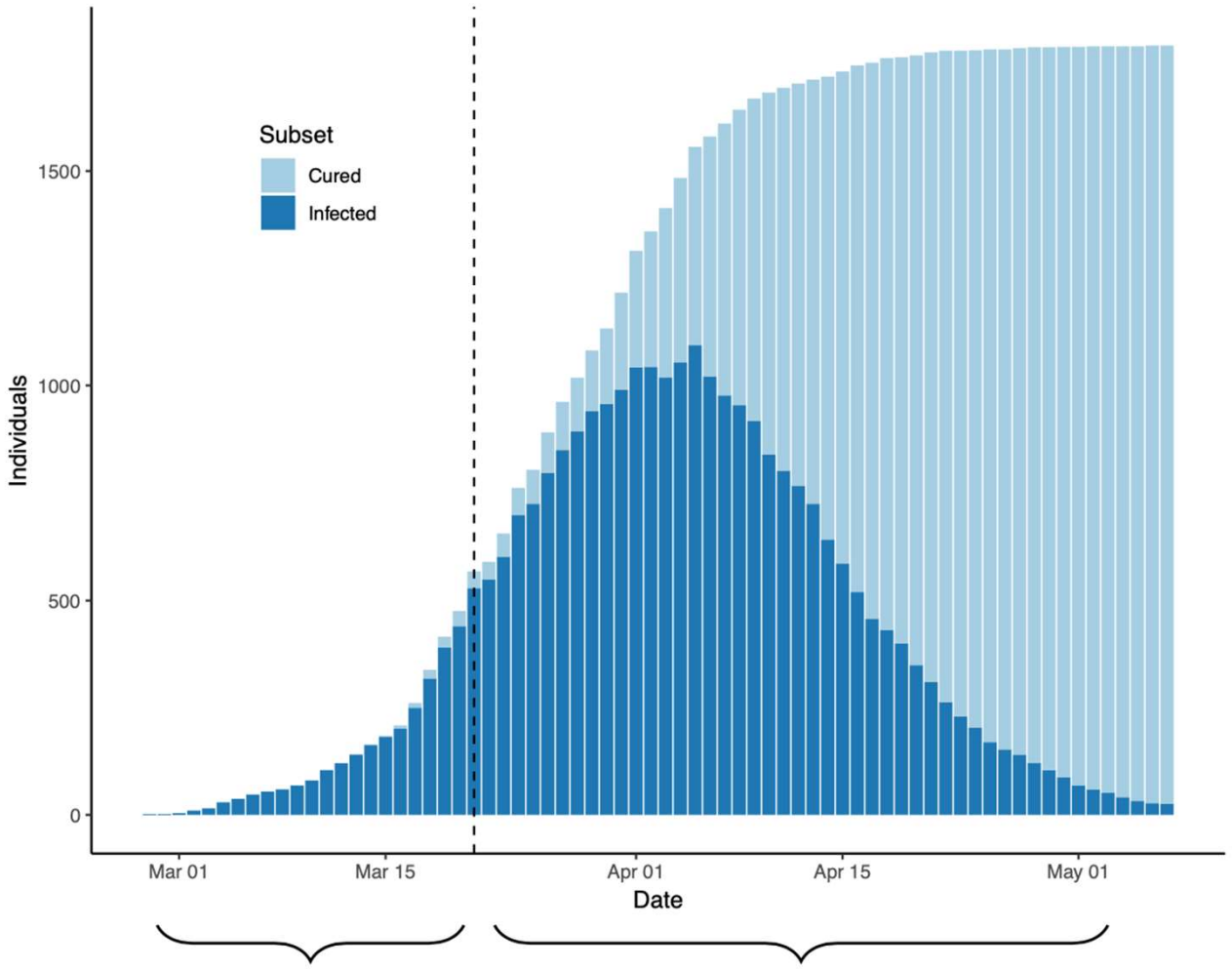
	N	Positive	Positive rate
Overall	1734	371	21.4%
Adult (>15)	1175	291	24.8%
Children (0-15)	559	80	14.3%
Index case over 20 years older	731	129	21.4%
Young adult (16-25)	243	58	23.9%
Children (0-15)	488	71	14.6%
Index case within 5y both >25	393	145	36.8%
Adults (26-50)	251	80	31.8%
Older adults (>50)	142	65	45.7%

Transmissions to and from children

	Adult to child			Child to adult	Child to child
Child age	0-5	6-12	13-15	0-15	0-15
Number	**25**	**47**	**38**	**8**	**6**
Same haplotype	11	22	20	6	4
Direction confirmed	4	12	9	1	2
Direction reversed	1	0	0	0	0
Incomplete data	7	8	8	1	0
Incompatible	**2**	**5**	**1**	**0**	**0**


Number of active infections and number of recovered
1800
1600
1400
1200
1000
800
600
400
200
0
Number - cumulative
The number of deaths does not appear in this chart.
28.02
01.03
03.03
05.03
07.03
09.03
11.03
13.03
15.03
17.03
19.03
21.03
23.03
25.03
27.03
29.03
31.03
02.04
04.04
06.04
08.04
10.04
12.04
14.04
16.04
18.04
20.04
22.04
24.04
26.04
28.04
30.04
02.05
04.05
06.05
Active infections
Recovered

May 7th 2020



Growth phase:

↑ High viral load

↑ Rapid accumulation of mutations

Containment phase:

↓ Low viral load

↓ Slow accumulation of mutations

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Humoral Immune Response to SARS-CoV-2 in Iceland

D.F. Gudbjartsson, G.L. Norddahl, P. Melsted, K. Gunnarsdottir, H. Holm, E. Eythorsson, A.O. Arnthorsson, D. Helgason, K. Bjarnadottir, R.F. Ingvarsson, B. Thorsteinsdottir, S. Kristjansdottir, K. Birgisdottir, A.M. Kristinsdottir, M.I. Sigurdsson, G.A. Arnadottir, E.V. Ivarsdottir, M. Andresdottir, F. Jonsson, A.B. Agustsdottir, J. Berglund, B. Eiriksdottir, R. Fridriksdottir, E.E. Gardarsdottir, M. Gottfredsson, O.S. Gretarsdottir, S. Gudmundsdottir, K.R. Gudmundsson, T.R. Gunnarsdottir, A. Gylfason, A. Helgason, B.O. Jensson, A. Jonasdottir, H. Jonsson, T. Kristjansson, K.G. Kristinsson, D.N. Magnusdottir, O.T. Magnusson, L.B. Olafsdottir, S. Rognvaldsson, L. le Roux, G. Sigmundsdottir, A. Sigurdsson, G. Sveinbjornsson, K.E. Sveinsdottir, M. Sveinsdottir, E.A. Thorarensen, B. Thorbjornsson, M. Thordardottir, J. Saemundsdottir, S.H. Kristjansson, K.S. Josefsdottir, G. Masson, G. Georgsson, M. Kristjansson, A. Moller, R. Palsson, T. Gudnason, U. Thorsteinsdottir, I. Jonsdottir, P. Sulem, and K. Stefansson

ABSTRACT

BACKGROUND

Little is known about the nature and durability of the humoral immune response to infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).

METHODS

We measured antibodies in serum samples from 30,576 persons in Iceland, using six assays (including two pan-immunoglobulin [pan-Ig] assays), and we determined that the appropriate measure of seropositivity was a positive result with both pan-Ig assays. We tested 2102 samples collected from 1237 persons up to 4 months after diagnosis by a quantitative polymerase-chain-reaction (qPCR) assay. We measured antibodies in 4222 quarantined persons who had been exposed to SARS-CoV-2 and in 23,452 persons not known to have been exposed.

RESULTS

Of the 1797 persons who had recovered from SARS-CoV-2 infection, 1107 of the 1215 who were tested (91.1%) were seropositive; antiviral antibody titers assayed by two pan-Ig assays increased during 2 months after diagnosis by qPCR and remained on a plateau for the remainder of the study. Of quarantined persons, 2.3% were seropositive; of those with unknown exposure, 0.3% were positive. We estimate that 0.9% of Icelanders were infected with SARS-CoV-2 and that the infection was fatal in 0.3%. We also estimate that 56% of all SARS-CoV-2 infections in Iceland had been diagnosed with qPCR, 14% had occurred in quarantined persons who had not been tested with qPCR (or who had not received a positive result, if tested), and 30% had occurred in persons outside quarantine and not tested with qPCR.

CONCLUSIONS

Our results indicate that antiviral antibodies against SARS-CoV-2 did not decline within 4 months after diagnosis. We estimate that the risk of death from infection was 0.3% and that 44% of persons infected with SARS-CoV-2 in Iceland were not diagnosed by qPCR.

The authors' full names, academic degrees, and affiliations are listed in the Appendix. Address reprint requests to Dr. Stefansson at deCODE Genetics–Amgen, Sturlugata 8, Reykjavik 102, Iceland, or at kstefans@decode.is.

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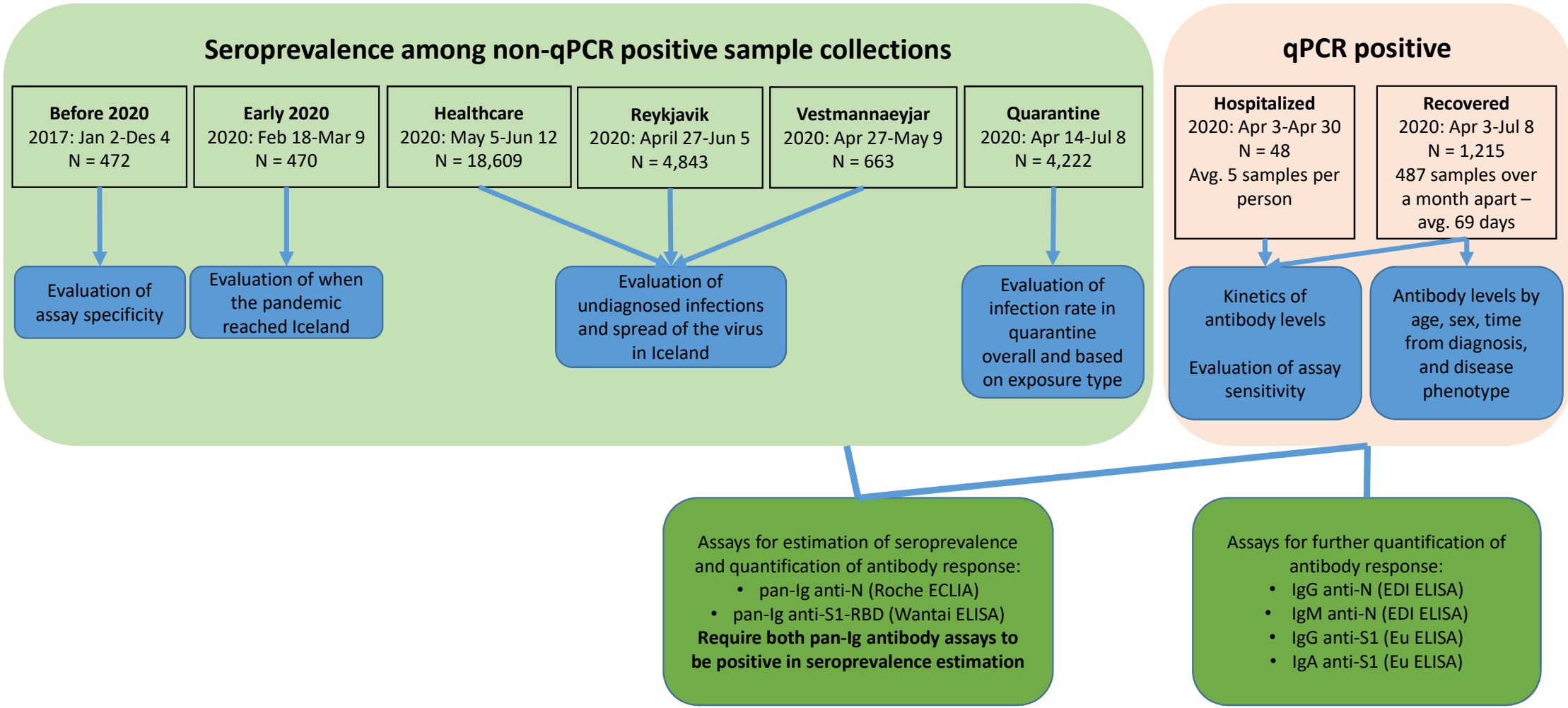

Seroprevalence among non-qPCR positive sample collections
Before 2020
2017: Jan 2-Des 4
N = 472
Early 2020
2020: Feb 18-Mar 9
N = 470
Healthcare
2020: May 5-Jun 12
N = 18,609
Reykjavik
2020: April 27-Jun 5
N = 4,843
Vestmannaeyjar
2020: Apr 27-May 9
N = 663
Quarantine
2020: Apr 14-Jul 8
N = 4,222
Evaluation of assay specificity
Evaluation of when the pandemic reached Iceland
Evaluation of undiagnosed infections and spread of the virus in Iceland
Evaluation of infection rate in quarantine overall and based on exposure type
qPCR positive
Hospitalized
2020: Apr 3-Apr 30
N = 48
Avg. 5 samples per person
Recovered
2020: Apr 3-Jul 8
N = 1,215
487 samples over a month apart – avg. 69 days
Kinetics of antibody levels
Evaluation of assay sensitivity
Antibody levels by age, sex, time from diagnosis, and disease phenotype
Assays for estimation of seroprevalence and quantification of antibody response:
• pan-Ig anti-N (Roche ECLIA)
• pan-Ig anti-S1-RBD (Wantai ELISA)
Require both pan-Ig antibody assays to be positive in seroprevalence estimation
Assays for further quantification of antibody response:
• IgG anti-N (EDI ELISA)
• IgM anti-N (EDI ELISA)
• IgG anti-S1 (Eu ELISA)
• IgA anti-S1 (Eu ELISA)

The 6 assays
Source, target and type

Source	Protein target	Ig
Roche	Nucleocapsid (anti-N)	pan-Ig
Wantai	Spike 1 RBD (anti-S1-RBD)	pan-Ig
EDI/Eagle	Nucleocapsid (anti-N)	IgG
EDI/Eagle	Nucleocapsid (anti-N)	IgM
Euroimmun	Spike subunit 1 (anti-S1)	IgG
Euroimmun	Spike subunit 1 (anti-S1)	IgA

Association of existing conditions and COVID-19 severity with quantitative measurements of SARS-CoV-2 antibody levels (adjusting for age, age squared, sex, and time from diagnosis)

Variable	max N	Log (pan-Ig anti-N) (95% CI)	pan-Ig anti-S1-RBD (95% CI)	IgG anti-N (95% CI)	IgM anti-N (95% CI)	IgG anti-S1 (95% CI)	IgA anti-S1 (95% CI)
Age (per 10 year)	1,254	0.15 (0.12, 0.19)**	0.1 (0.07, 0.14)**	0.2 (0.16, 0.23)**	0.04 (0, 0.07)+	0.09 (0.06, 0.13)**	0.02 (-0.01, 0.06)
Female sex	1,254	-0.07 (0.04, -0.18)	-0.19 (-0.08, -0.3)+	-0.05 (0.05, -0.15)	0.01 (-0.09, 0.11)	-0.1 (0.01, -0.21)	-0.26 (-0.16, -0.36)**
Body mass index	549	0.03 (0.02, 0.05)*	0.02 (0, 0.03)+	0.02 (0.01, 0.04)+	0.01 (0, 0.03)+	0.02 (0.01, 0.04)+	0.01 (0, 0.03)
Smoker	1,239	-0.57 (-0.31, -0.83)*	-0.58 (-0.31, -0.84)*	-0.63 (-0.39, -0.87)**	-0.15 (0.09, -0.38)	-0.66 (-0.4, -0.92)**	-0.54 (-0.3, -0.78)*
Anti-inflammation medication	545	-0.39 (-0.14, -0.64)+	-0.34 (-0.09, -0.59)+	-0.29 (-0.06, -0.53)+	0.00 (-0.25, 0.26)	-0.31 (-0.05, -0.56)+	-0.48 (-0.25, -0.71)*
Hospitalization	1,254	0.38 (0.18, 0.58)+	0.76 (0.56, 0.96)**	0.72 (0.53, 0.92)**	0.09 (-0.1, 0.28)	0.89 (0.69, 1.1)**	0.55 (0.36, 0.73)**
Max clinical stage	1,254	0.17 (0.09, 0.25)*	0.23 (0.15, 0.31)**	0.27 (0.19, 0.35)**	0.11 (0.04, 0.19)+	0.32 (0.24, 0.41)**	0.14 (0.06, 0.21)+
Temperature	406	0.38 (0.18, 0.58)+	0.45 (0.25, 0.65)*	0.49 (0.3, 0.68)**	0.18 (0, 0.36)+	0.52 (0.31, 0.72)**	0.27 (0.08, 0.45)+
Max Temperature	272	0.36 (0.22, 0.51)**	0.44 (0.3, 0.59)**	0.43 (0.29, 0.57)**	0.22 (0.09, 0.35)+	0.45 (0.3, 0.6)**	0.28 (0.14, 0.42)*
Loss of energy	552	-0.2 (-0.12, -0.29)*	-0.16 (-0.07, -0.25)+	-0.17 (-0.09, -0.26)*	-0.03 (0.05, -0.11)	-0.12 (-0.03, -0.21)+	-0.1 (-0.02, -0.18)+
Coughing	426	0.12 (0.02, 0.23)+	0.16 (0.05, 0.27)+	0.21 (0.12, 0.31)*	0.11 (0.02, 0.21)+	0.19 (0.09, 0.3)+	0.11 (0.01, 0.21)+
Loss of appetite	424	0.15 (0.07, 0.24)+	0.14 (0.05, 0.22)+	0.19 (0.11, 0.27)*	0.09 (0.02, 0.17)+	0.17 (0.08, 0.26)*	0.04 (-0.04, 0.12)

Comorbidity and COVID-19 severity

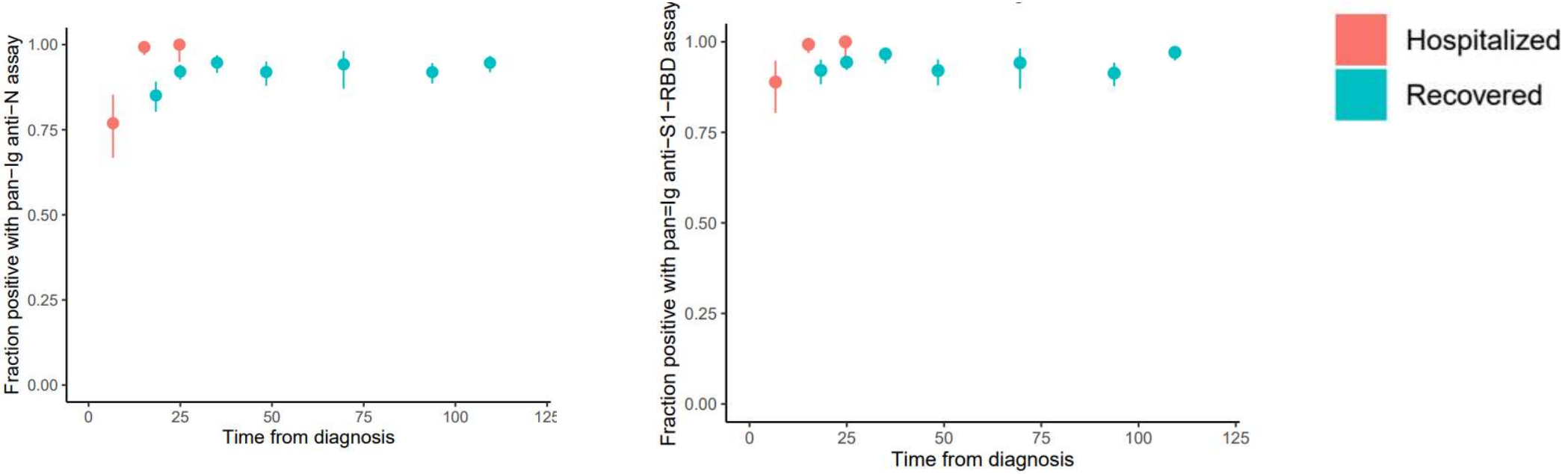
- Antibody levels go up with age and BMI
- Antibody levels are lower in females for two antibodies agains the spike protein
- Antibody levels are lower in smokers and users of anti-inflammation medication
- Antibody levels generally are higher in those who became more sick

SARS-CoV-2 qPCR and antibody positive rates among quarantined individuals by exposure type and presence of symptoms.

		qPCR				Both pan-Ig antibody assays			
	N	N	N pos	Pos%	OR (95% CI)	N	N pos	Pos%	OR (95% CI)
No household exposure	18877	6839	689	10.1		3,835	53	1.4%	
Household exposure	1889	1092	399	36.5	5.2 (4.5,6.1)	531	37	7.0%	4.9 (3.2, 7.7)
No reported symptoms	3439	1421	142	10.0		1,043	24	2.3%	
Reported symptoms	1639	1397	920	65.8	18.2 (14.8,22.4)	252	18	7.1%	3.4 (1.8, 6.3)

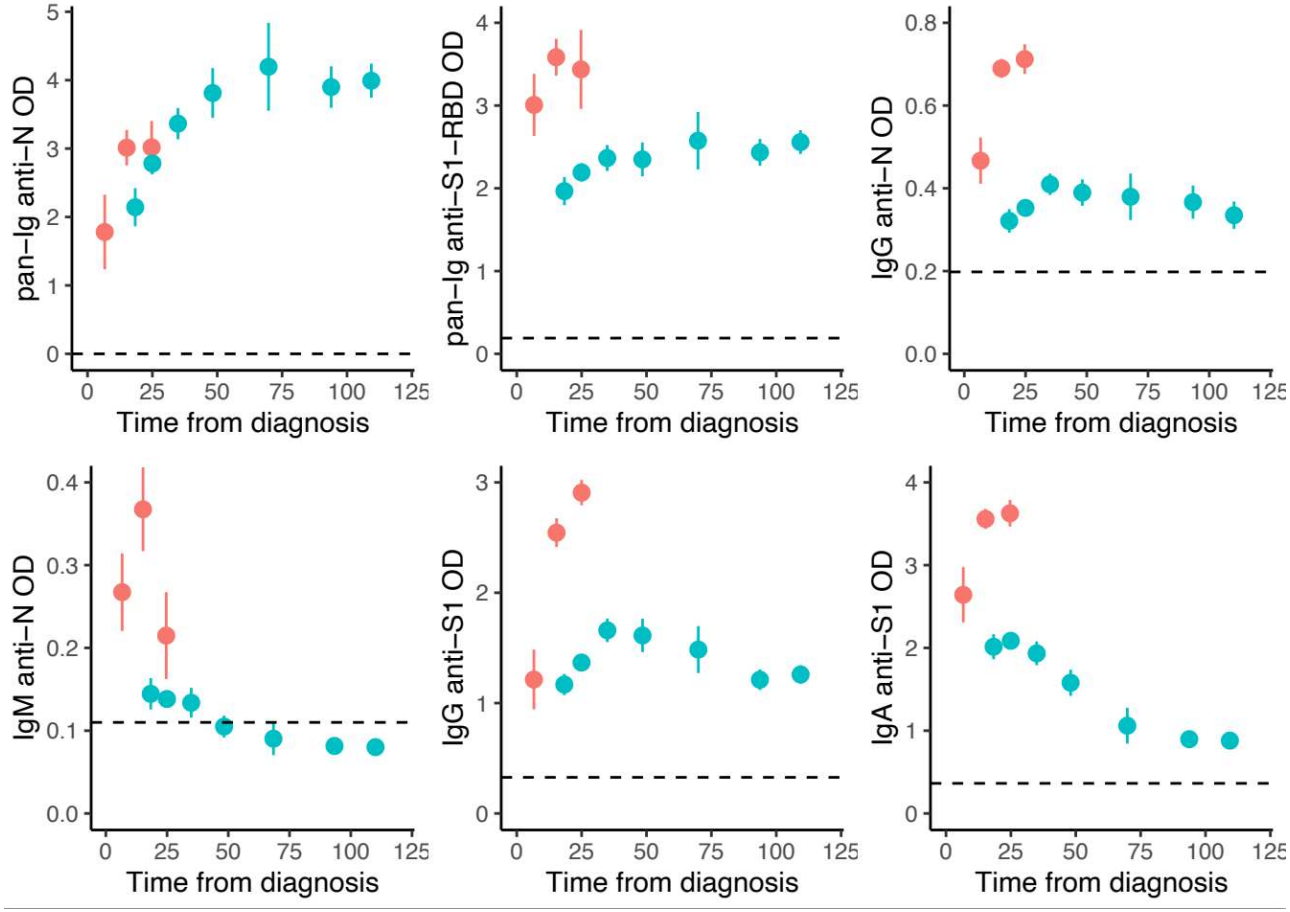
- 5.0% of quarantined individuals without household exposure were infected
- 26.6% of quarantined individuals with household exposure were infected

Fraction of individuals positive for two pan-Ig SARS-CoV-2 assays among individuals previously testing positive for qPCR.



25 days from qPCR diagnosis, over 90% of samples from recovered cases were positive in both pan-Ig antibody assays and after that the fraction of cases testing positive remained stable

Antibody levels among qPCR positive cases as a function of time from qPCR diagnosis



COVID-19 fatality rates in Iceland

- In Iceland, ten deaths have been attributed to COVID-19 corresponding to a nationwide death rate of 3 per 100,000
- Among the qPCR positive cases, the fatality rate was 0.6% (95% CI: 0.3%, 1.0%)
- Using the overall 0.9% frequency of SARS-CoV-2 infection in Iceland as the denominator, this yields an infection fatality rate of 0.3% (95% CI: 0.2%, 0.6%).

Summary of antibodies

- Serum from 30,576 individuals were measured for antibodies specific for either the nucleocapsid or spike proteins using six assays:
- Of the quarantined individuals not tested positive with qPCR, 2.3% were antibody positive in both pan-Ig assays
- 0.3% of random individuals and all-comers to the healthcare system who were neither quarantined nor PCR positive were antibody positive in both pan-Ig assays
- Of the recovered cases, 90% had antibodies with both assays, with very consistent results on repeated samples for up to 4 month after diagnosis
- Antibody levels measured with both pan-Ig increase for the first two months after qPCR diagnosis and then plateau for the remaining two months
- Antibody levels were substantially higher in males than females in two of the six assays, the pan-Ig anti-S1 and IgA ELISAs, both target the spike protein
- No decline in level of antibodies as measured with the two pan-Ig assays up to 4 months from diagnosis.
- Antibody levels are higher in sicker patients and in older individuals and males, mirroring the relationship between age, sex, and COVID-19 severity
- 0.9% of the population of Iceland was infected with SARS-CoV-2 but only half of them were diagnosed with qPCR, despite extensive qPCR testing in Iceland
- Infection fatality rate 1 in 300

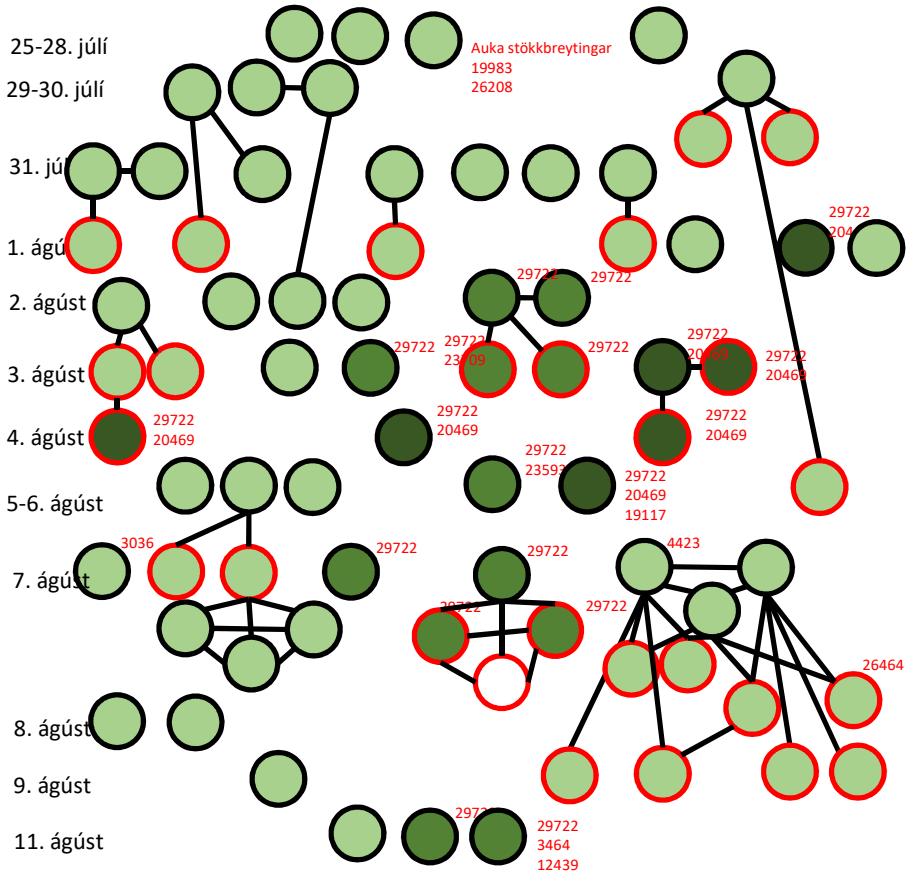
Screening at the borders

Overview

- From June 15 to August 11, a total of 88,170 tests were performed at the border
- Of those, 41 active infections were diagnosed, 14 of those were tourists
- Four outbreaks occured in Iceland
  - Two traced back to Icelandic travelers prior to the requirements of a second test
  - One traced back to a tourist, excempt from a second test
  - One large, uncontained outbreak that has not been traced, but must have come through the border
- For every 10 active infections caught at the border with a single test, we estimate that 3 are not caught and can start outbreaks.

Sequencing of viral genomes

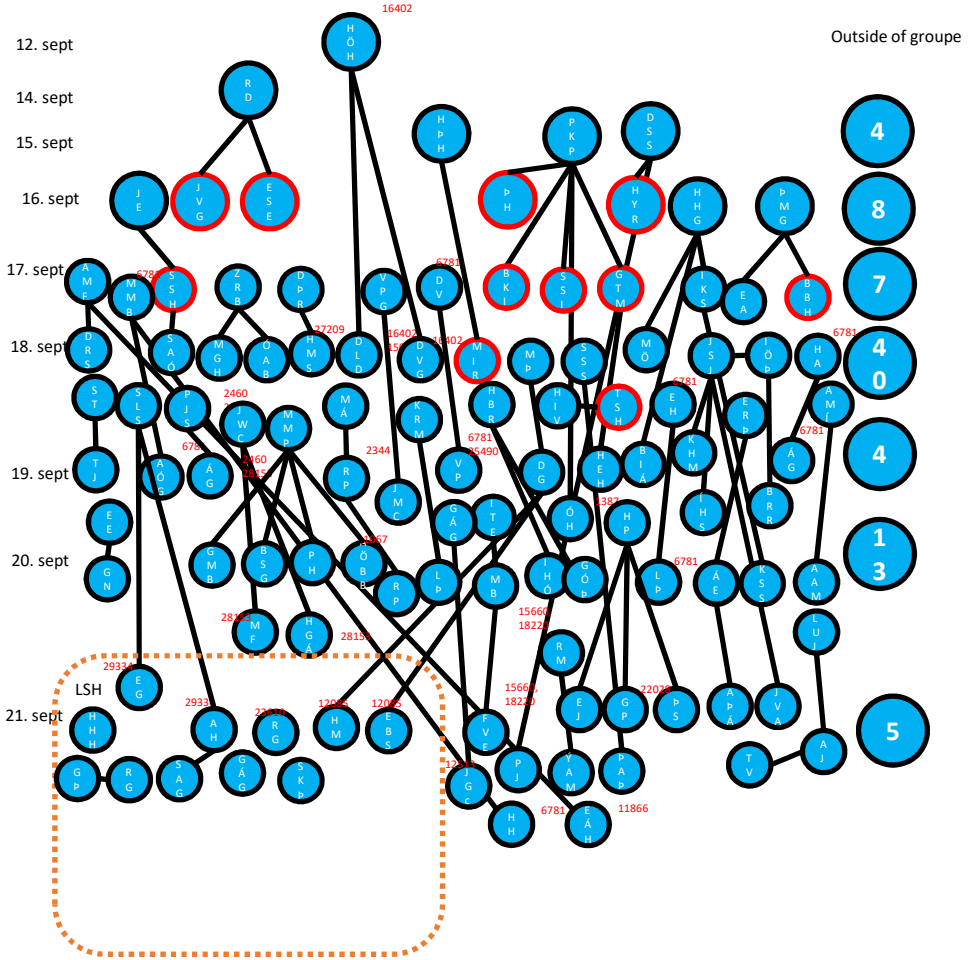
- Mutations in the viral genome can be used as a barcode to track the spread of the virus
- The second wave of infections began at the end of July and consisted of several epidemiologically disconnected groups that could not be traced but had a shared mutational signature (haplotype)
- The Chief epidemiologist and the contact tracing team receive information about haplotypes and an overview of the spread with a 48-hour turnaround time.

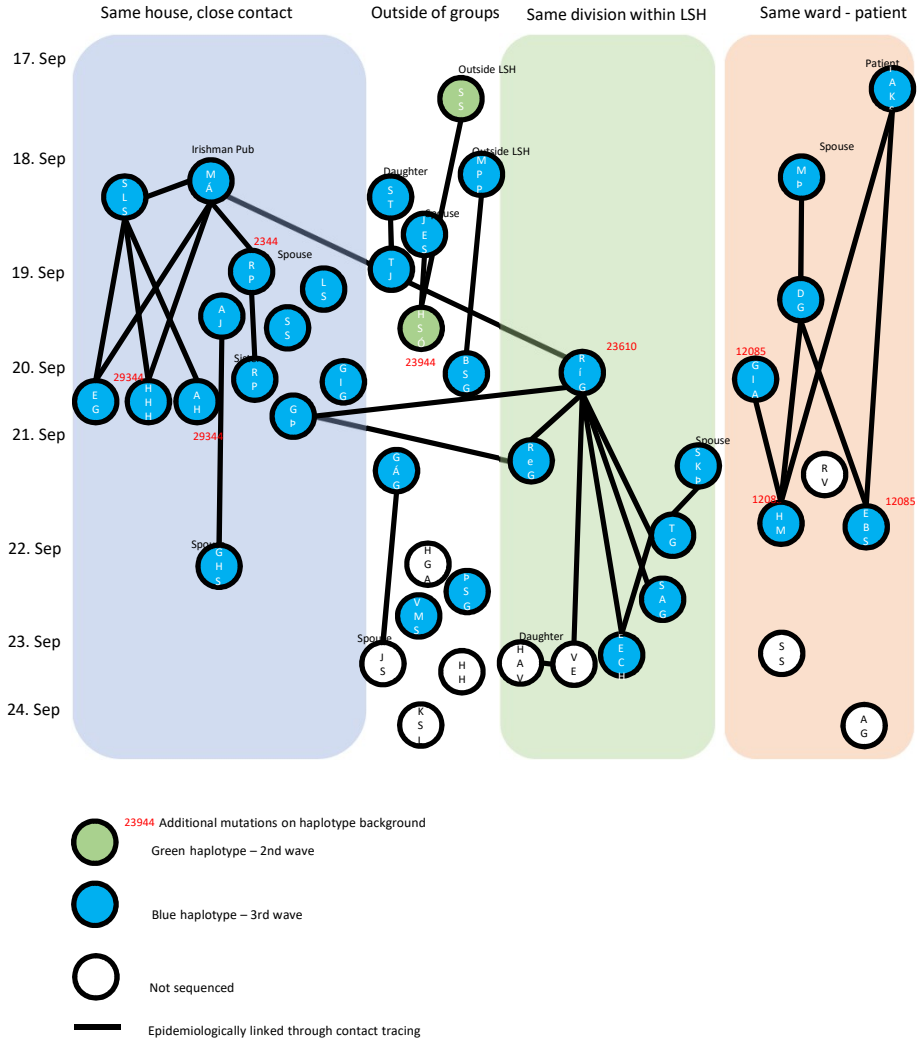


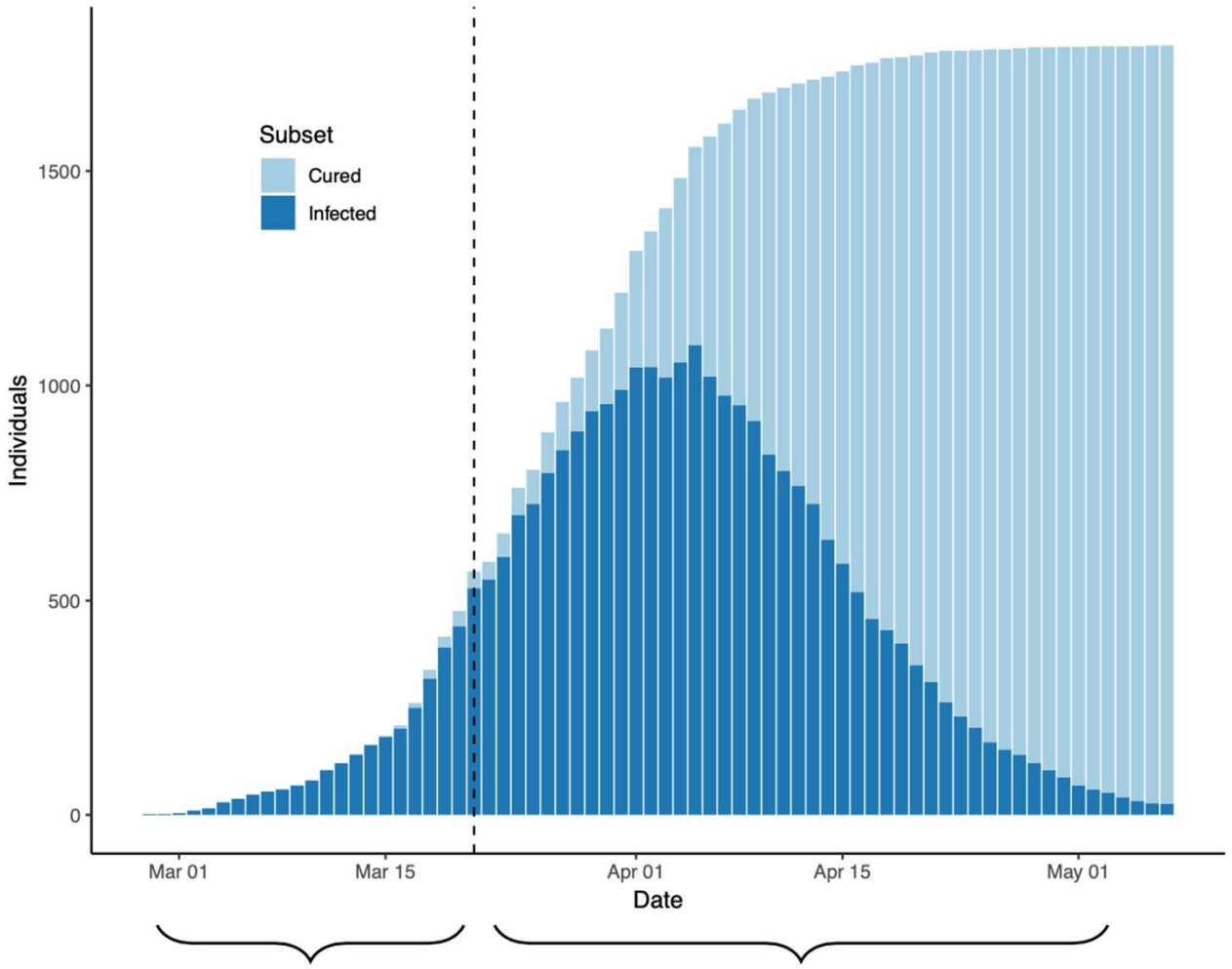
Since August 19th

- Screened a the border
- Five day quarantine
- Screened again

New outbreak with one haplotype




Same house, close contact
Outside of groups
Same division within LSH
Same ward - patient
17. Sep
18. Sep
19. Sep
20. Sep
21. Sep
22. Sep
23. Sep
24. Sep
Irishman Pub
Outside LSH
Outside LSH
Daughter
Spouse
2344
29344
29345
23944
23610
12085
12085
12085
Patient
Spouse
Spouse
Spouse
Daughter
23944 Additional mutations on haplotype background
Green haplotype – 2nd wave
Blue haplotype – 3rd wave
Not sequenced
Epidemiologically linked through contact tracing



Growth phase:

↑ High viral load

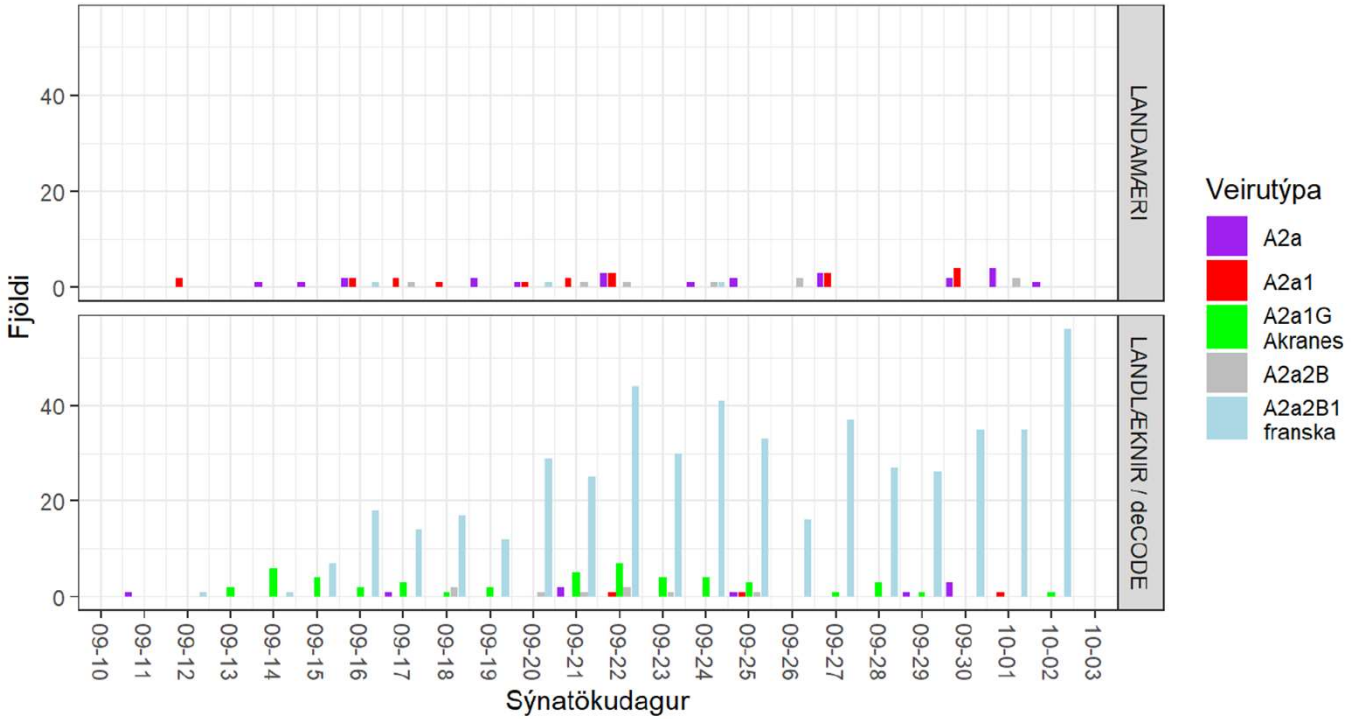
↑ Rapid accumulation of mutations

Containment phase:

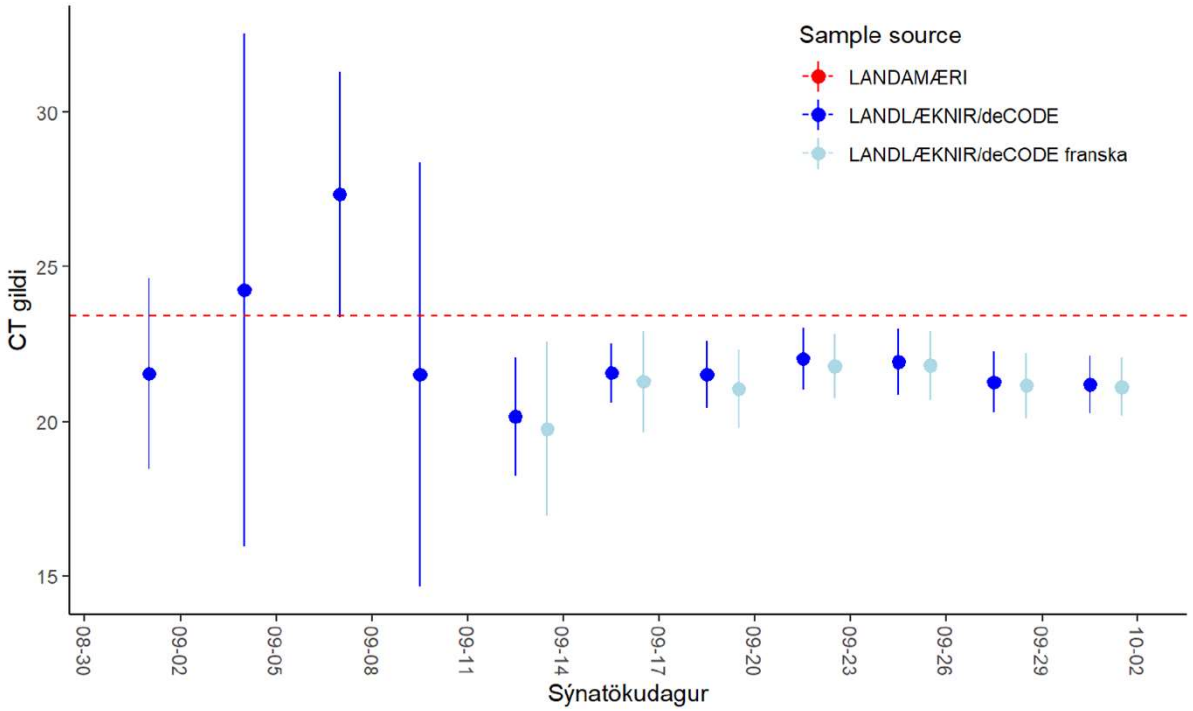
↓ Low viral load

↓ Slow accumulation of mutations

Haplotypes by day

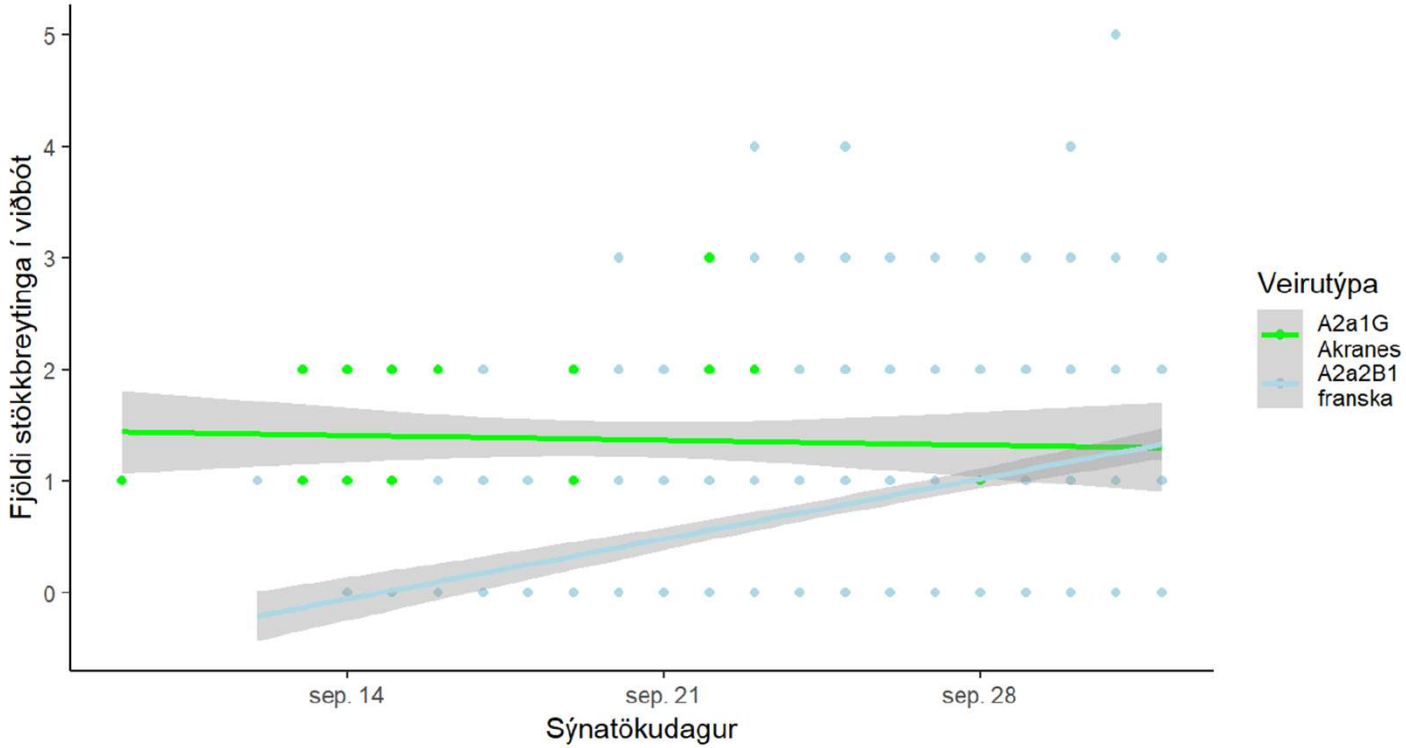


Viral load by day



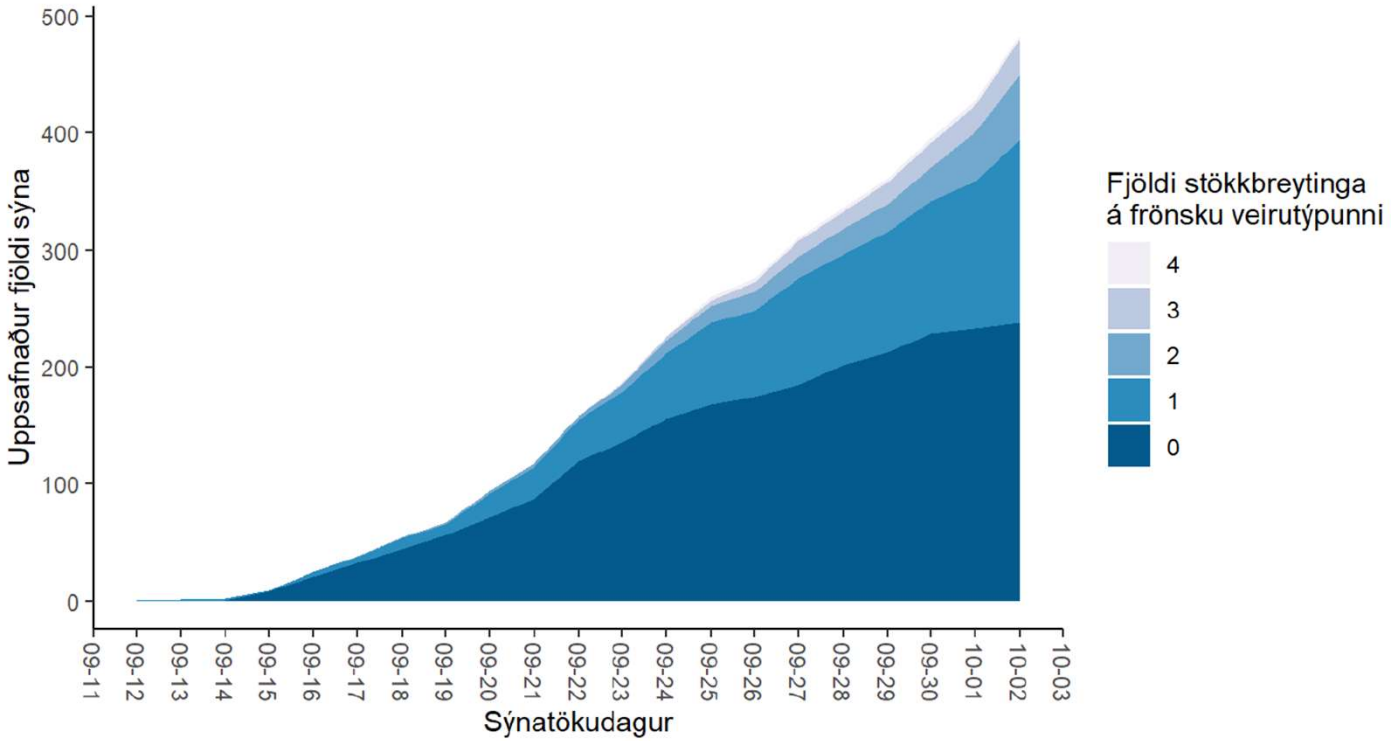
- Viral load in cases diagnosed in Iceland compared to those diagnosed at the border

Accumulation of mutations



In the growth phase of the epidemic the virus accumulates on mutation per 14 days

Number of mutations as a function of time



- The number of mutations is a measure of the number of cases since the original case with a specific haplotype. The accumulation is one new mutation every fourth case

18

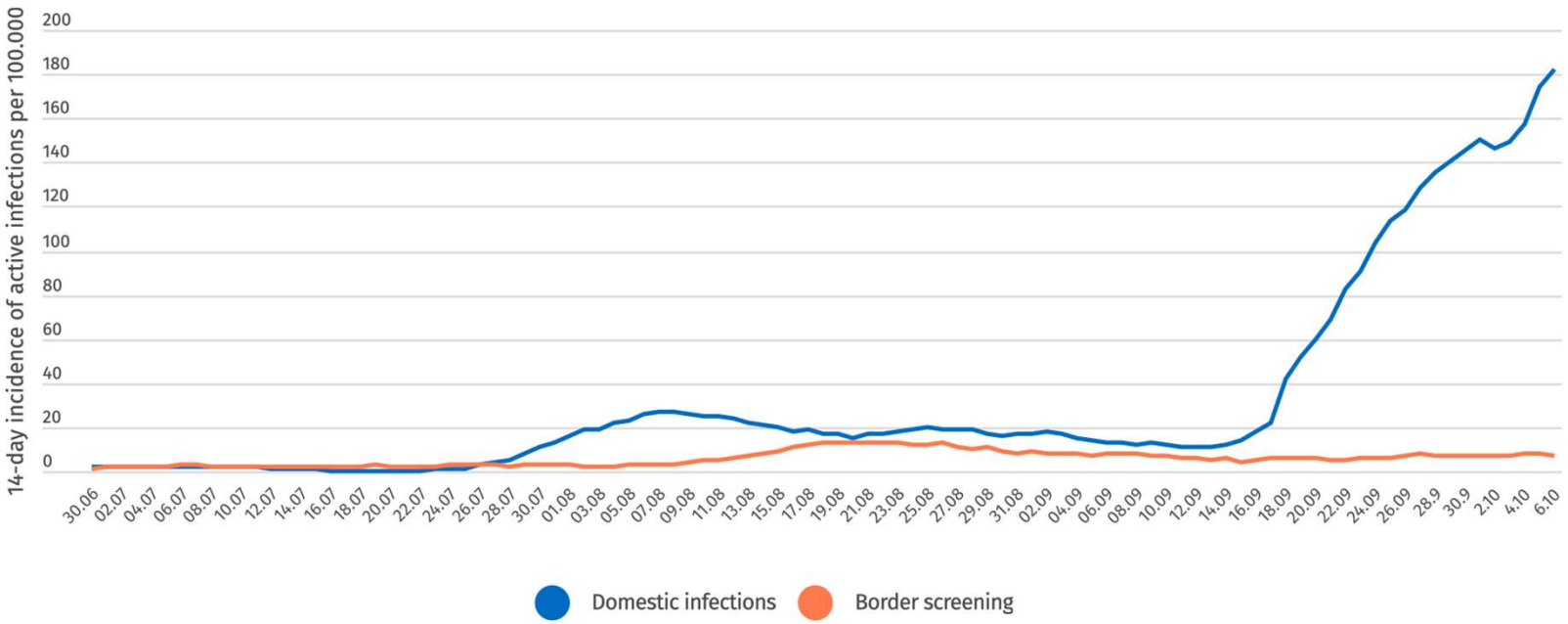
hospitalised

4

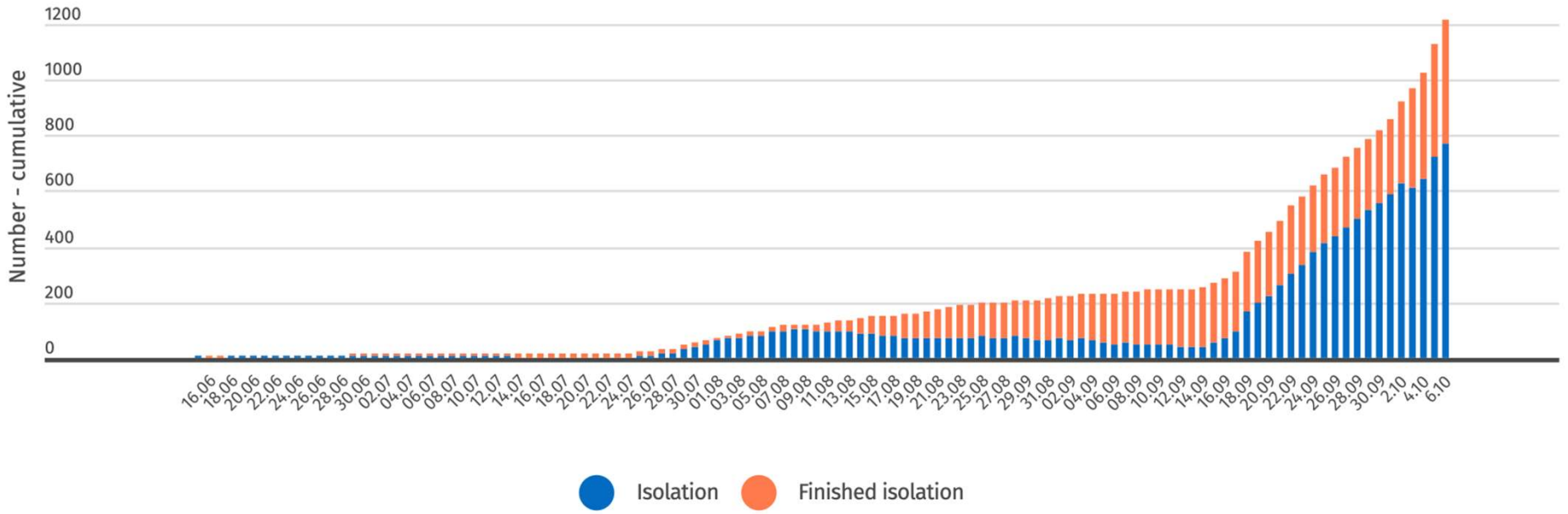
intensive care

Of those diagnosed with COVID-19, ten have died.

Incidence per 100 000 inhabitants



Number of domestic infections and those who have finished isolation



Updated everyday at 11:00

COVID-19 in Iceland – Statistics from 15 June 2020

- See also statistics from 28 February - 14 June on a separate page.

Current

Incidence, domestic infections
181.6
14-day incidence per 100.000 inhabitants

Incidence, border screening 7.4
14-day incidence per 100.000 inhabitants

795
in isolation

4 045
in quarantine

18
hospitalised

4
intensive care

Total figures from 28. February

3 172
confirmed infections

2 366
finished isolation

155 005
samples, border screening

139 925
samples, domestic

29 811
quarantine completed

Of those diagnosed with COVID-19, ten have died.