

# **Diagnostic system for COVID-19 in South Korea**

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# SARS-CoV-2

- Novel coronavirus reported in December 2019 in Wuhan, China
- Genetic similarity (80%) with SARS-CoV reported in 2003 → SARS-CoV-2

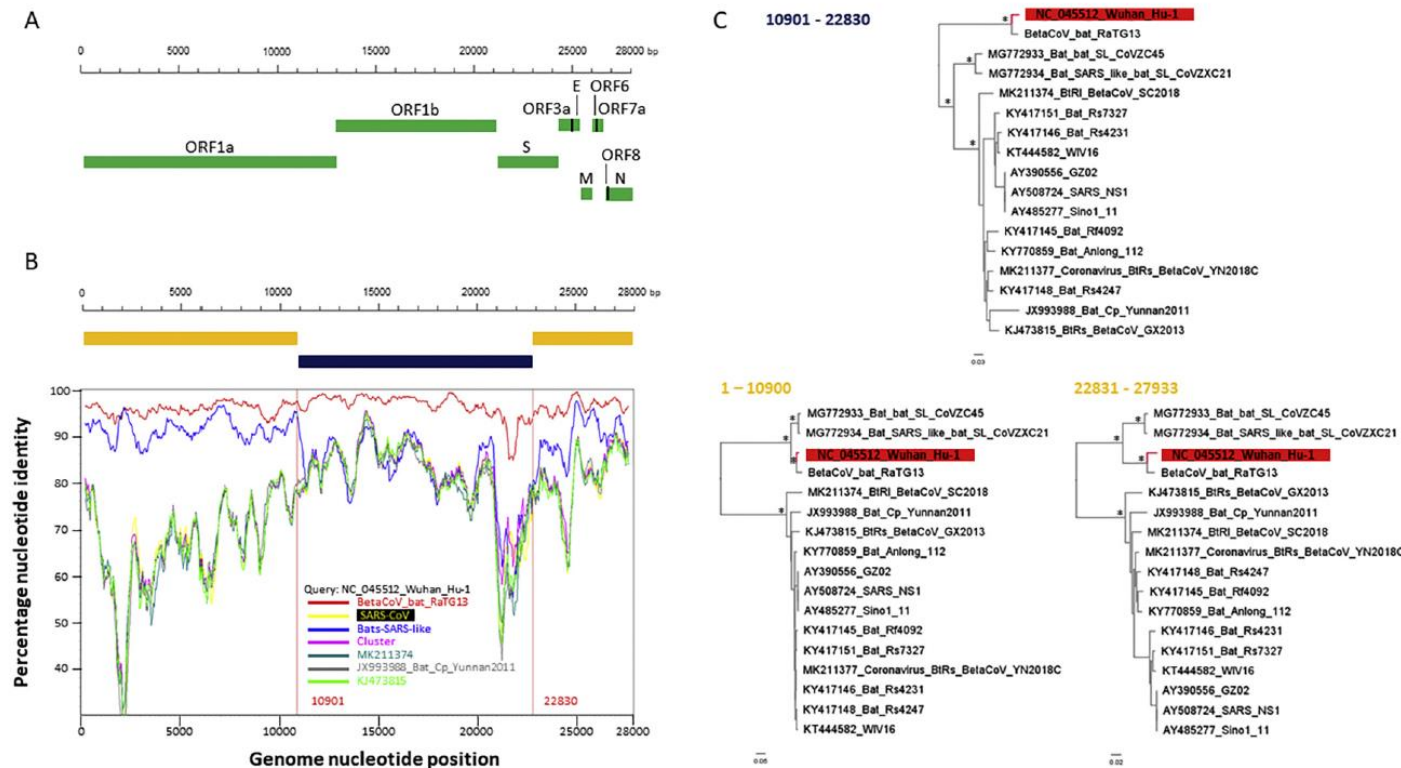


Fig. 1. **A. Genomic organization of the novel coronavirus** (2019-nCoV) according to the positions in the edited alignment. **B. Simplot of 2019-nCoV (NC\_045512\_Wuhan\_Hu-1)** against sequences within the subgenus sarbecovirus. Different colours correspond to the nucleotide similarity between the 2019-nCoV and different groups. The regions with discordant phylogenetic clustering of the 2019-nCoV with Bats\_SARS-like sequences are shown in different colours. **C. Maximum likelihood (ML) phylogenetic trees** inferred in different genomic regions as indicated by the Simplot analysis. The genomic regions are shown in numbers at the top or at the left of the trees. The 2019-nCoV sequence is shown in red and stars indicate important nodes received 100% bootstrap and 1 posterior probability support. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

## Coronavirus Cases:

# 10,395,463

[view by country](#)

Deaths:

## 507,411 (4.9%)

Recovered:

## 5,646,007

### ACTIVE CASES

#### 4,242,045

Currently Infected Patients

4,184,535 (99%)  
in Mild Condition

57,510 (1%)  
Serious or Critical

[Show Graph](#)

### CLOSED CASES

#### 6,153,418

Cases which had an outcome:

5,646,007 (92%)  
Recovered / Discharged

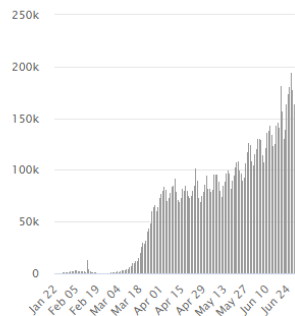
507,411 (8%)  
Deaths

[Show Graph](#)

daily linear logarithmic

### Daily New Cases

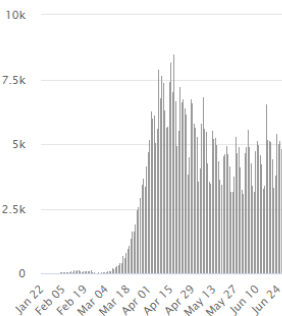
Cases per Day  
Data as of 0:00 GMT+0



daily linear logarithmic

### Daily Deaths

Deaths per Day  
Data as of 0:00 GMT+0



#	Country, Other	Total Cases	New Cases	Total Deaths	New Deaths	Total Recovered	Active Cases	Serious, Critical	Tot Cases/ 1M pop	Deaths/ 1M pop	Total Tests	Tests/ 1M pop	Population
1	<a href="#">Qatar</a>	95,106	+693	113	+3	80,170	14,823	203	33,872	40	352,659	125,600	2,807,805
2	<a href="#">San Marino</a>	698		42		656	0		20,571	1,238	5,669	167,074	33,931
3	<a href="#">Bahrain</a>	26,239	+534	84	+1	20,928	5,227	43	15,432	49	543,790	319,814	1,700,330
4	<a href="#">Vatican City</a>	12				12	0		14,981				801
5	<a href="#">Chile</a>	275,999	+4,017	5,575	+66	236,154	34,270	2,090	14,439	292	1,096,443	57,360	19,115,048
6	<a href="#">French Guiana</a>	3,774	+313	15	+3	1,352	2,407	27	12,641	50	8,061	27,000	298,557
7	<a href="#">Andorra</a>	855		52		799	4		11,066	673	3,750	48,534	77,265
8	<a href="#">Kuwait</a>	45,524	+582	350	+2	36,313	8,861	145	10,662	82	382,842	89,660	4,269,925
9	<a href="#">Mayotte</a>	2,560	+52	32		2,325	203	5	9,387	117	8,800	32,268	272,715
10	<a href="#">Peru</a>	282,365	+2,946	9,504	+187	171,159	101,702	1,183	8,565	288	1,661,324	50,393	32,967,364
11	<a href="#">Armenia</a>	25,127	+482	433	+7	13,297	11,397	10	8,480	146	110,571	37,314	2,963,223
12	<a href="#">USA</a>	2,678,357	+41,280	128,762	+325	1,104,171	1,445,424	15,841	8,092	389	33,109,490	100,031	330,991,690
13	<a href="#">Oman</a>	39,060	+910	169	+6	22,422	16,469	115	7,652	33	188,291	36,887	5,104,563
14	<a href="#">Singapore</a>	43,661	+202	26		37,985	5,650	1	7,463	4	684,359	116,984	5,850,036
15	<a href="#">Panama</a>	31,686		604		15,470	15,612	140	7,345	140	125,570	29,107	4,314,039
16	<a href="#">Luxembourg</a>	4,256	+14	110		3,997	149	2	6,800	176	178,422	285,080	625,866
17	<a href="#">Sweden</a>	67,667	+125	5,310	+12	N/A	N/A	171	6,700	526	444,607	44,025	10,098,898
18	<a href="#">Belarus</a>	61,790	+315	387	+4	45,213	16,190	89	6,539	41	992,007	104,982	9,449,331
19	<a href="#">Brazil</a>	1,368,195	+22,941	58,314	+656	757,462	552,419	8,318	6,437	274	3,017,350	14,196	212,549,934
20	<a href="#">Spain</a>	296,050	+200	28,346	+3	N/A	N/A	617	6,332	606	5,162,909	110,425	46,754,725

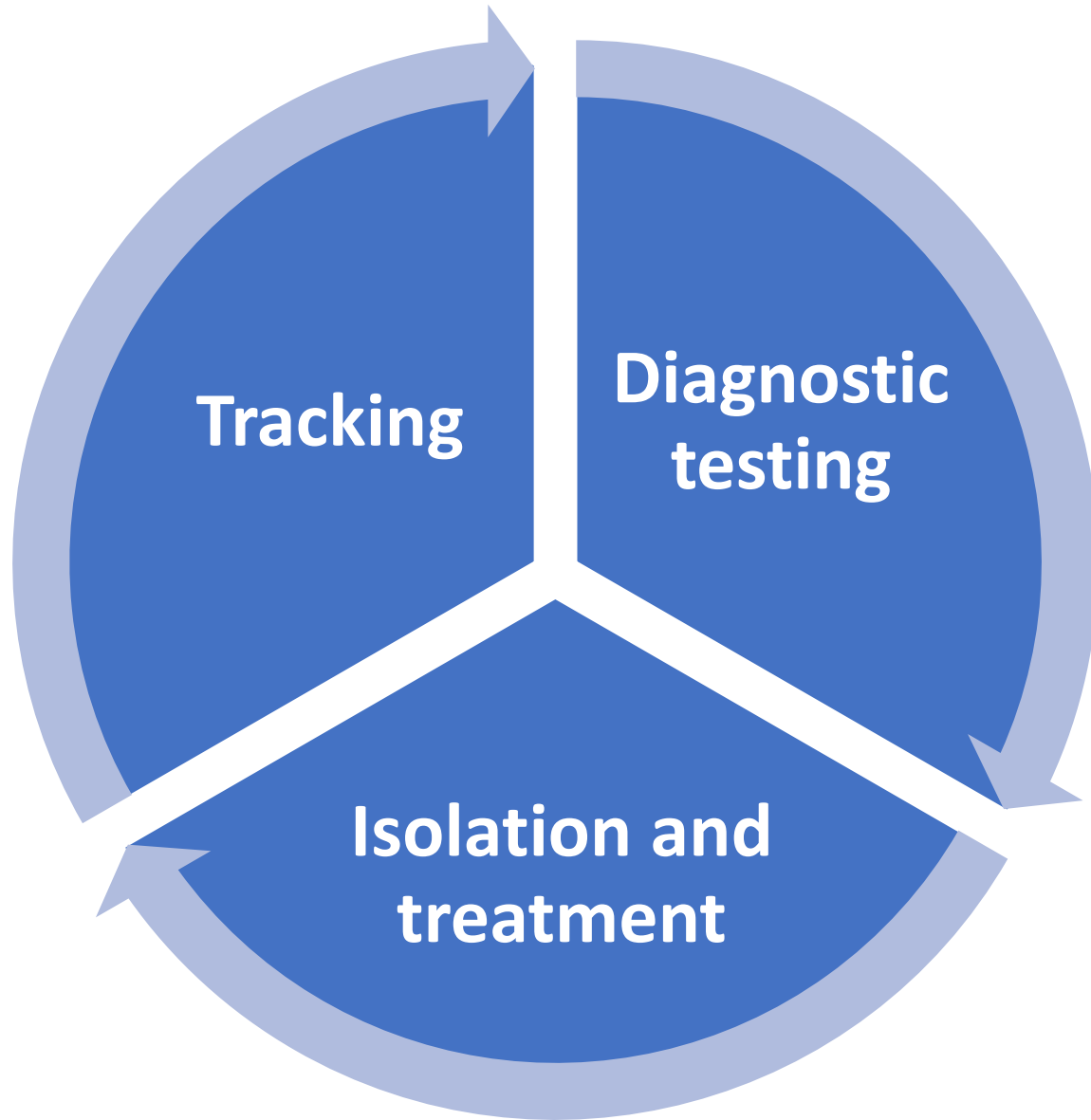
164	<a href="#">S. Korea</a>	12,757	+42	282		11,429	1,046	15	249	6	1,259,954	24,575	51,269,046
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# Characteristics of COVID-19 transmission

- Asymptomatic transmission (Arons M.M., et al., NEJM 2020)
  - 76 residents in long-term care residency participated in PPS in US
  - 48 (63%) were positive for COVID-19 → 27 (56%) patients were asymptomatic
  - Among 27 asymptomatic patients, 24 (89%) patients became symptomatic
- Very mild symptom even in symptomatic patients (Guan W., et al., NEJM 2020)
  - The percentage of patients who showed high BT ( $>38^{\circ}\text{C}$ ): 21.7%
  - Low prevalence of sore throat (13.9%) and shortness of breath (18.7%)
- Massive viral shedding in early stage of infection by droplet → Droplet transmission

# Characteristics of COVID-19 transmission

- Asymptomatic transmission
  - Very mild symptom even in symptomatic patients (Common cold)
  - Massive viral shedding in early stage of infection by droplet
- Hard to screen by symptom in community
- Massive screening by epidemiological tracking



- **Early implementation**
- **Capacity for massive testing**
- **Exact testing**
- **Rapid turnaround time**

## Daily infections and testing ⓘ

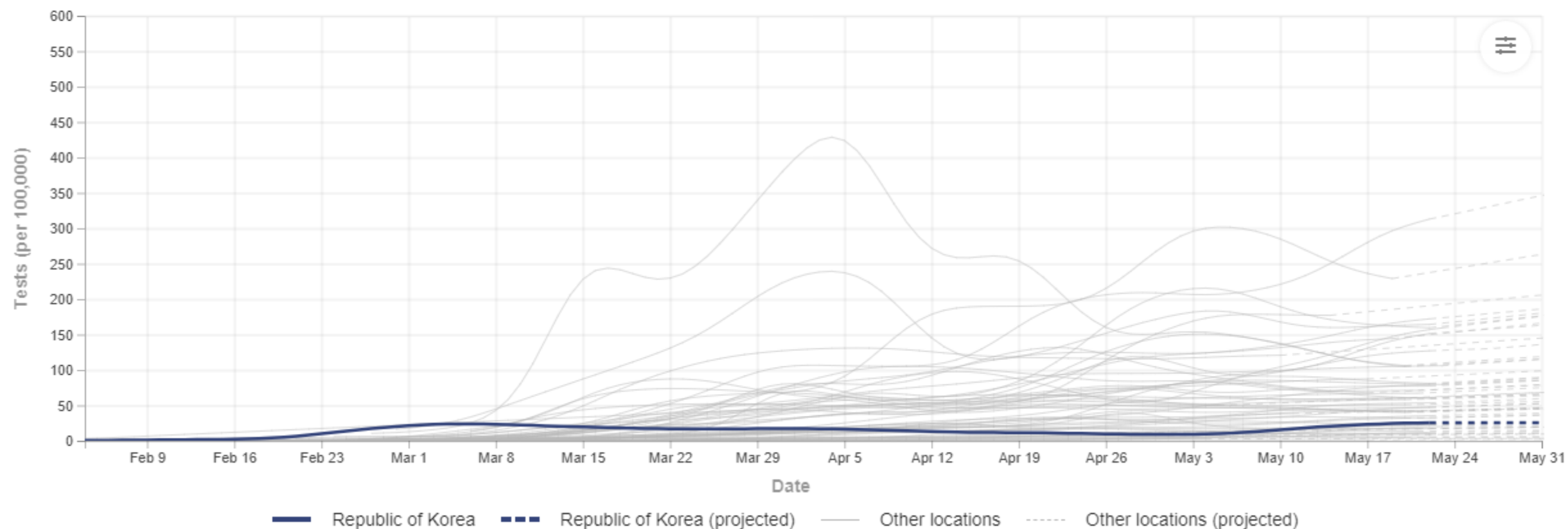
(per 100,000)

Compare Republic of Korea to:

Estimated infections

Confirmed infections

Tests



# Early implementation of nationwide diagnostic system

- **Transmissibility of COVID-19**

- China data:  $R_0$  2.4-2.7, Doubling time 6.7 days
- USA data:  $R_0$  5.7, Doubling time 3 days

- **Exponential increase of COVID-19 (Logarithmic elevation)**

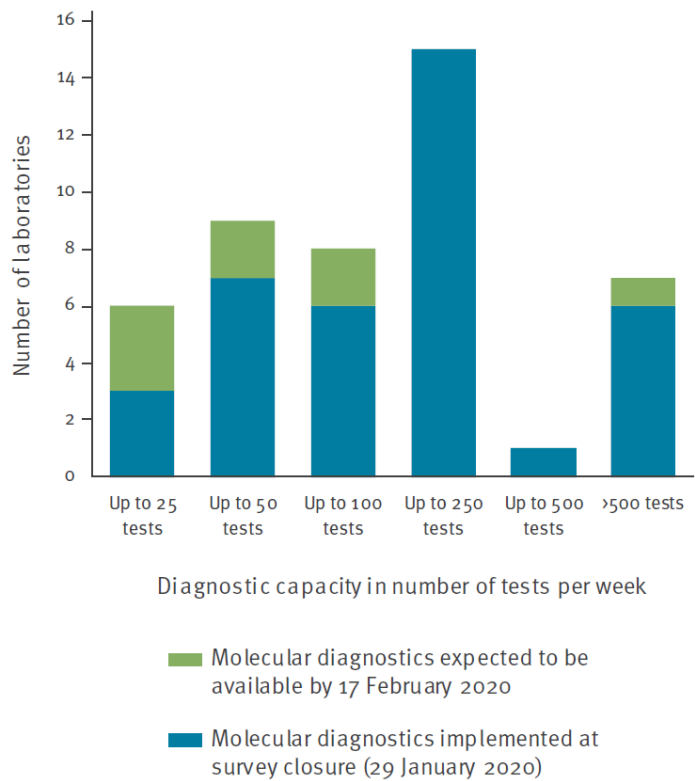
- 10 patients on Jan 20: The number of estimated patients by  $R_0$  (China data)
- Feb 20 =  $10 \times 2^4 = 160$
- Mar 20 =  $160 \times 2^4 = 2,560$
- April 20 =  $2,560 \times 2^4 = 40,960$
- May 20 =  $40,960 \times 2^4 = 655,360$
- Jun 20 =  $655,360 \times 2^4 = 10,485,760$

2,560 new patients/week -> 366 new patients/day  
Test, tracing and isolation: Possible (Flattening or decrease)

40,960 new patients/week -> 5,851 new patients/day  
Test, tracing and isolation: Impossible → Lock down



**FIGURE 3**  
 Diagnostic capacity of specialised laboratories with molecular tests available or forthcoming for novel coronavirus (2019-nCoV), EU/EEA, January 2020 (n = 46)<sup>a</sup>



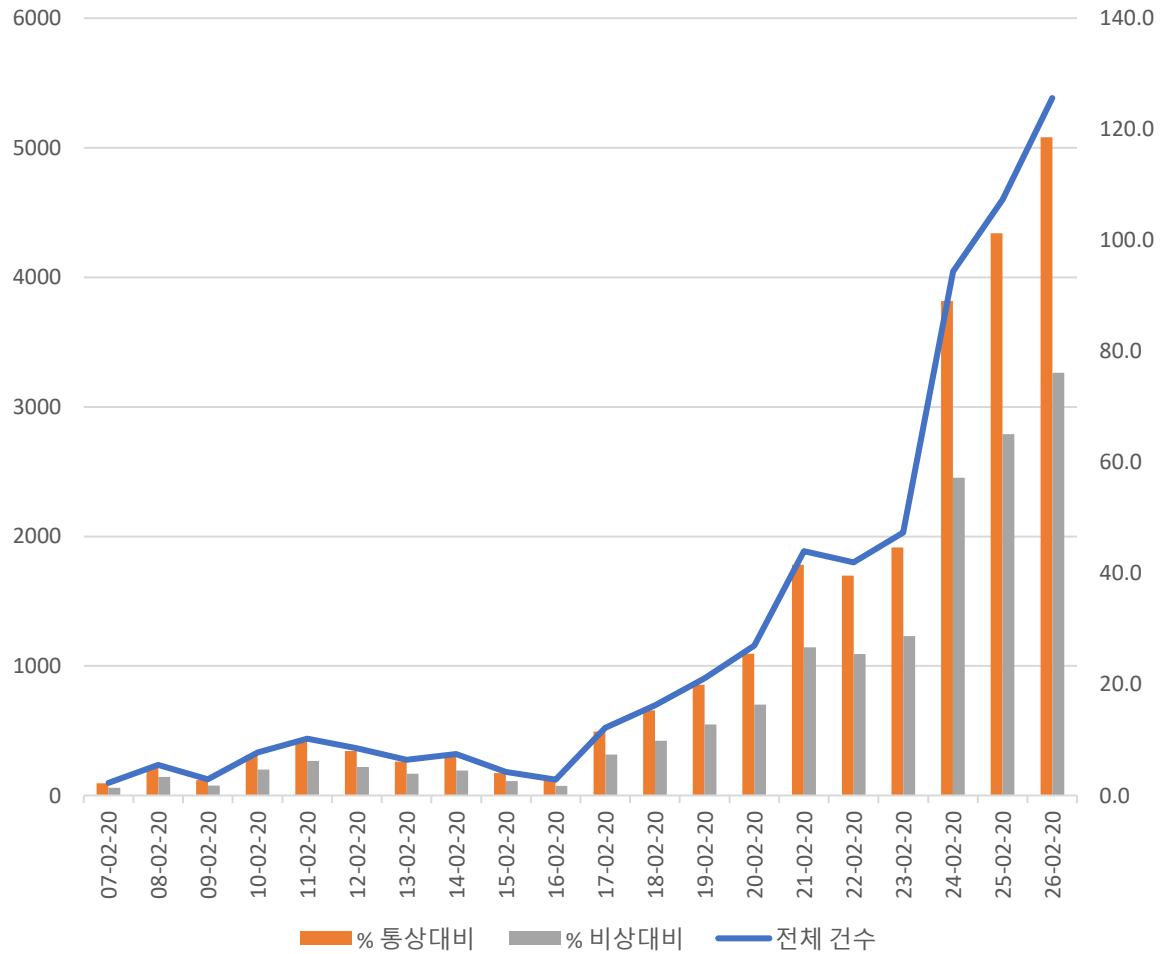
EU/EEA: European Union/European Economic Area.

<sup>a</sup> One laboratory of the 47 included in the current study did not indicate when its molecular diagnostics would be available.

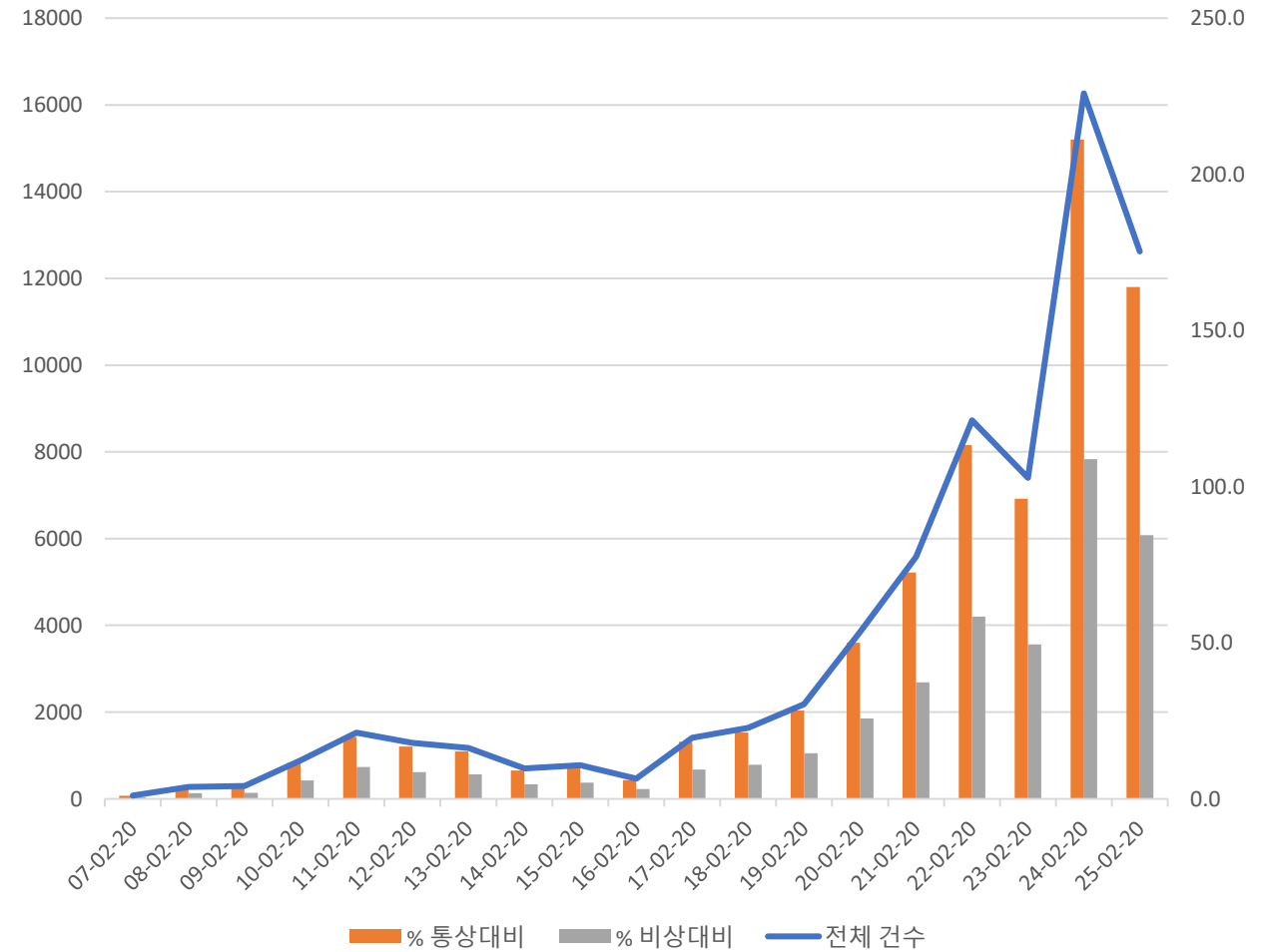
Date	No. of laboratories which can test for COVID-19	Available No. tests/day
Feb-7	25	8,000
Mar-1	65	22,000
April-1	94	35,000
May-1	94	50,000
Jun-1	103	55,000

- **The number of countries in EU = 30**
- **Total population = 740 M**
- **8,275 test/week ≈ 1,200 tests/day**

# The number of COVID-19 tests and capacity in February



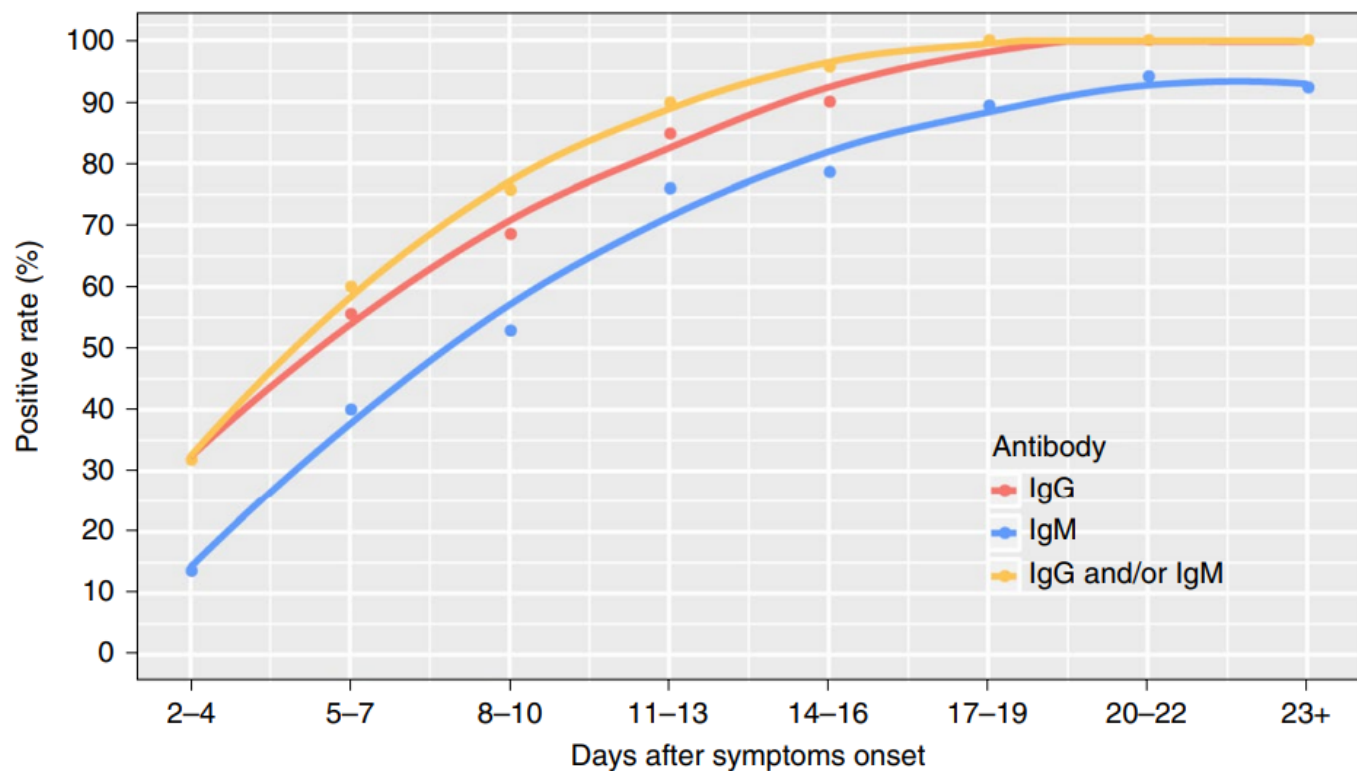
Hospitals



Commercial laboratory center

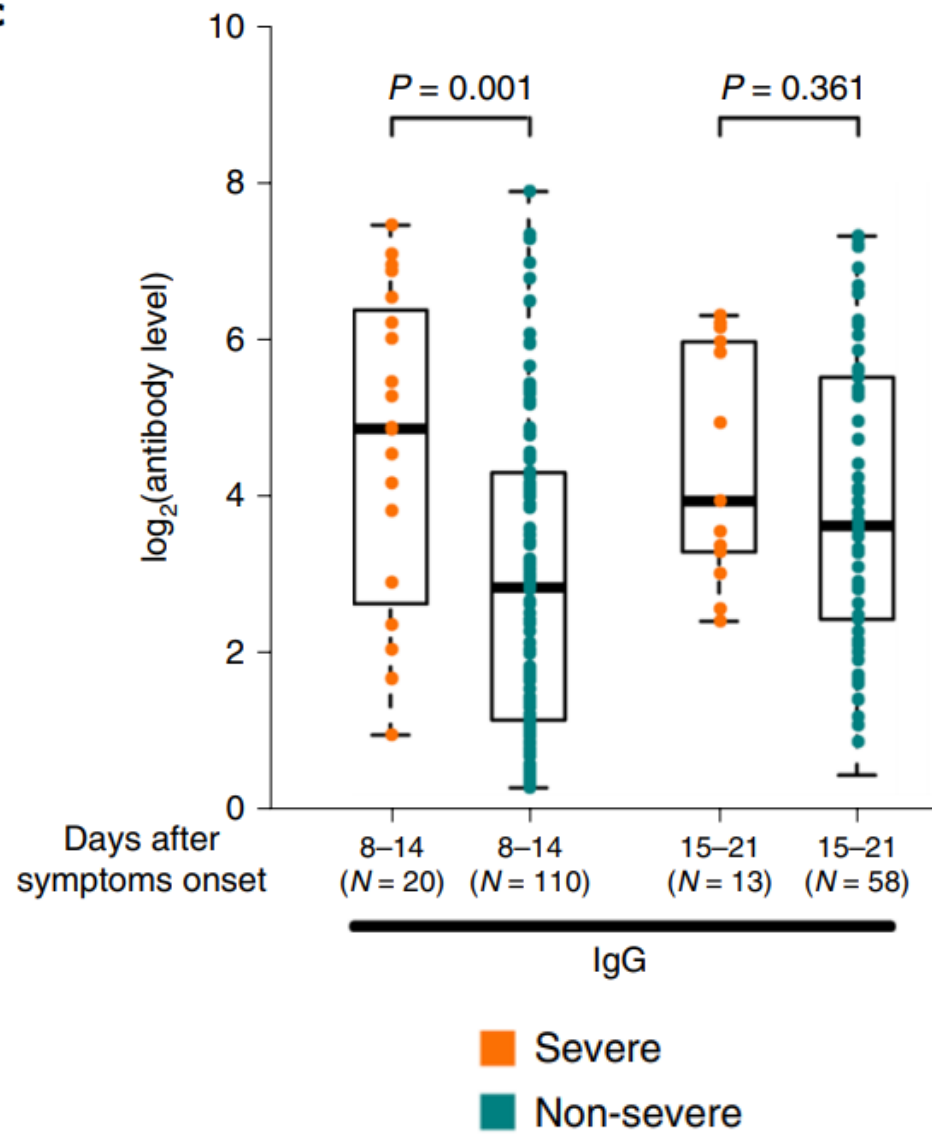
# Comparison of diagnostic methods for COVID-19

Comparison	Molecular diagnosis	Immunoassay (Rapid assay)	
		Antigen assay	Antibody assay
Detection target	Genes (E, RdRp, S, N, etc)	Antigen	Antibody
Detection period (From Sx onset)	From early to late (Guide to isolation)	Mid-term (Medium sensitivity compared with molecular assay)	7-28 days (Low-Medium sensitivity during early 2 weeks)
Sensitivity	≥ 95%	50-70% (?) (Currently not evaluated)	≥ 95% (Currently not evaluated)
Specificity	≥ 95%	>70% (?) (Currently not evaluated, and possibility of cross-reaction from the other coronavirus)	?% (Currently not evaluated, and possibility of cross-reaction from the other coronavirus)
Asymptomatic patient detection	From early stage	May be different according to antigen amount	Late stage
Cost	High	Low	Low
Purpose	Diagnosis for treatment and containment	Pandemic situation with insufficient molecular diagnostic capacity	Epidemiologic study for missing link or seroprevalence, Pandemic situation with insufficient molecular diagnostic capacity
Current situation for use	Worldwide (Including WHO and CDC)	Part of China	Part of China

**a**

Days *	2-4 (N = 22)	5-7 (N = 45)	8-10 (N = 70)	11-13 (N = 79)	14-16 (N = 70)	17-19 (N = 47)	20-22 (N = 17)	23+ (N = 13)
IgG	7	25	48	67	63	47	17	13
IgM	3	18	37	60	55	42	16	12
IgG and/or IgM	7	27	53	71	67	47	17	13

\* Number of serum samples with positive results

**c**

# Diagnostic capacity for COVID-19 in Korea

Characteristics	Clinical laboratory network	Public laboratory network
Management	Korean Society for Laboratory Medicine	Center for laboratory control of infectious diseases in KCDC
Component	<ul style="list-style-type: none"> <li>• 2<sup>nd</sup>- or 3<sup>rd</sup> care hospital (91)</li> <li>• Clinical laboratory center (12)</li> </ul>	<ul style="list-style-type: none"> <li>• Center for laboratory control of infectious diseases in KCDC (1, central)</li> <li>• Research institute of health and environment (17, Local)</li> </ul>
Lab. capacity	55,000 tests/day (Normal)	3,000-4,000 tests/day (Normal) 15,000-20,000/day (Pooling)
Turnaround time	3-24 hours	3-24 hours

- The amount of testing kits per day in Korea:  $\geq 500,000$  tests/day (five companies)
- The number of testing kits which can be exported:  $\geq 450,000$  tests/day (2020 JUN)

# Establishment of diagnostic laboratory network

Problem	Solution
<ul style="list-style-type: none"><li>• Lack of primers/probes</li><li>• Lack of positive control</li><li>• Lack of panel to assess specificity</li><li>• Absence of commercial tests</li></ul>	<ul style="list-style-type: none"><li>• Development and approval of commercial tests for emergency use (EUA)</li><li>• Storage of positive clinical specimen for evaluation</li></ul>
<ul style="list-style-type: none"><li>• Lack of personnel/time</li><li>• Lack of equipment</li><li>• Absence of proper BSL laboratory</li></ul>	<ul style="list-style-type: none"><li>• Expansion of laboratory tests for many laboratory (Private health system)</li><li>• Recruit for COVID-19 testing among accredited private laboratory</li></ul>
<ul style="list-style-type: none"><li>• Lack of funds</li></ul>	<ul style="list-style-type: none"><li>• Insurance</li></ul>
<ul style="list-style-type: none"><li>• Implementation according to quality control system</li><li>• Need for specific training</li></ul>	<ul style="list-style-type: none"><li>• Collaboration with academic society (private healthcare system) and KCDC</li></ul>

# Approval process for EUA in Korea

Process	Description
Application	<ul style="list-style-type: none"><li>• Analytical sensitivity and cross-reaction check should be required (transcript RNA and various virus)</li></ul>
Evaluation	<ul style="list-style-type: none"><li>• Clinical evaluation should be done by several laboratory (1 public laboratory and 4 public laboratories)</li><li>• Clinical specimen collected from patients have been stored in deep freezer for evaluation</li><li>• Negative specimen showing positivity for other respiratory viruses should be tested for specificity</li></ul>
Decision	<ul style="list-style-type: none"><li>• The evaluation results should be reviewed by board members consisting of public and private laboratory directs and other experts</li><li>• Final decision for approval should be made by agreement between board members</li><li>• The testing kits showing the same results in all laboratories can be approved for EUA</li><li>• Currently, about 30 testing kits have been evaluated and 6 testing kits have been approved.</li></ul>

# Strategy for laboratory testing

Testing capacity	Strategy
High molecular testing capacity	<ul style="list-style-type: none"> <li>• Diagnosis: Only molecular testing</li> <li>• Mass screening: Molecular testing with pooling (5X)</li> <li>• Seroprevalence: Antibody testing (ELISA)</li> </ul>
Low molecular testing capacity with antibody testing (high Sn after 14 days, high Sp)	<ul style="list-style-type: none"> <li>• Diagnosis: Sx onset 1-7 days – Molecular Sx onset 7-14 days – Antibody (1<sup>st</sup>) + Molecular (2<sup>nd</sup>) Sx onset 14 days - Antibody</li> <li>• Mass screening: Antibody (Targeting) Molecular testing with/without pooling (5X)</li> <li>• Seroprevalence: Antibody testing (ELISA)</li> </ul>
Low molecular testing capacity with antigen testing (moderate Sn, high Sp)	<ul style="list-style-type: none"> <li>• Primary testing: Antigen testing</li> <li>• Secondary testing: Molecular testing (Primary testing negative)</li> <li>• Mass screening: Antigen testing (Targeting)</li> <li>• Seroprevalence: Antibody testing (ELISA)</li> </ul>

Diagnosis for treatment and containment



**Table 1: Considerations for laboratory testing for each transmission scenario\***

	No Cases	Sporadic Cases	Clusters of Cases	Community Transmission
<b>Transmission scenario</b>	No reported cases	One or more cases, imported or locally acquired	Most cases of local transmission linked to chains of transmission	Outbreaks with the inability to relate confirmed cases through chains of transmission for a large number of cases, or by increasing positive tests through sentinel samples (routine systematic testing of respiratory samples from established laboratories)
<b>Public health aim</b>	Stop transmission and prevent spread	Stop transmission and prevent spread	Stop transmission and prevent spread.	Slow transmission, reduce case numbers, end community outbreaks
<b>Testing strategy guidance documents</b>	<p>Test all individuals meeting the suspected <a href="#">case definition</a></p> <p>Test a subset of samples from SARI/ILI surveillance for COVID-19</p> <p>Test patients with unexpected clinical presentation or an increase in hospital admissions in a specific demographic group that could be COVID-19</p>	<p>Test all individuals meeting the suspected <a href="#">case definition</a></p> <p><a href="#">Considerations in the investigation of cases and clusters of COVID-19</a></p> <p><a href="#">Clinical management of severe acute respiratory infections when novel coronavirus is suspected.</a></p> <p>SARI/ILI surveillance for COVID-19 and reporting: see <a href="#">Interim operational considerations for COVID-19 surveillance using GISRS.</a></p>	<p>Test all individuals meeting the suspected <a href="#">case definition</a></p> <p><a href="#">Considerations in the investigation of cases and clusters of COVID-19.</a></p> <p><a href="#">Clinical management of severe acute respiratory infections when novel coronavirus is suspected.</a></p> <p>SARI/ILI surveillance for COVID-19 and reporting: see <a href="#">Interim operational considerations for COVID-19 surveillance using GISRS.</a></p>	<p>If diagnostic capacity is insufficient, implement prioritized testing and measures that can reduce spread (e.g. isolation)., including:</p> <ul style="list-style-type: none"> <li>people who are at risk of developing severe disease and vulnerable populations, who will require hospitalization and advanced care for COVID-19 (see <a href="#">Clinical management of severe acute respiratory infections when novel coronavirus is suspected</a>).</li> <li>health workers (including emergency services and non-clinical staff) regardless of whether they are a contact of a confirmed case (to protect health workers and reduce the risk of nosocomial transmission)</li> <li>the first symptomatic individuals in a closed setting (e.g. schools, long term living facilities, prisons, hospitals) to quickly identify outbreaks and ensure containment measures</li> </ul>

\*In all scenarios, if feasible, test for treatable diseases (according to local protocols)

# **Conclusion**

- **COVID-19 can easily spread in community**
- **Three cycle for COVID-19 containment is important**
- **Early implementation and expansion of capacity for COVID-19 diagnostic testing is essential**
- **Collaboration of private and public health system is required to establish the laboratory capacity**