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Effect of large-scale testing platform in prevention and control of the COVID-19 pandemic: an empirical study with a novel numerical model — [Source link](#)

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1 **Effect of large-scale testing platform in prevention and control of the COVID-19**
2 **pandemic: an empirical study with a novel numerical model**

3

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16 **#These authors jointly supervised this work.**

17

18 **Background:** China adopted an unprecedented province-scale quarantine since
19 January 23rd 2020, after the novel coronavirus (COVID-19) broke out in Wuhan in
20 December 2019. Responding to the challenge of limited testing capacity, large-scale
21 standardized and fully-automated laboratory (Huo-Yan) was built as an ad-hoc measure.
22 There was so far no empirical data or mathematical model to reveal the impact of the
23 testing capacity improvement since the quarantine.

24 **Methods:** We integrated public data released by the Health Commission of Hubei
25 Province and Huo-Yan Laboratory testing data into a novel differential model with non-
26 linear transfer coefficients and competitive compartments, to evaluate the trends of

27 **NOTE: This preprint reports new research that has not been certified by peer review and should not be used to guide clinical practice.**
suspected cases under different nucleic acid testing capacities.

28 **Results:** Without the establishment of Huo-Yan, the suspected cases would increased
29 by 47% to 33,700, the corresponding cost of the quarantine would be doubled, and the
30 turning point of the increment of suspected cases and the achievement of “daily
31 settlement” (all daily new discovered suspected cases were diagnosed according to the
32 nucleic acid testing results) would be delayed for a whole week and 11 days. If the Huo-
33 Yan Laboratory ran at its full capacity, the number of suspected cases would decrease
34 at least a week earlier, the peak of suspected cases would be reduced by at least 44%
35 and the quarantine cost could be reduced by more than 72%. Ideally, if a daily testing
36 capacity of 10,500 could achieved immediately after the Hubei lockdown, “daily
37 settlement” for all suspected cases would be achieved immediately.

38 **Conclusions:** Large-scale and standardized clinical testing platform with nucleic acid
39 testing, high-throughput sequencing and immunoprotein assessment capabilities need
40 to be implemented simultaneously in order to maximize the effect of quarantine and
41 minimize the duration and cost. Such infrastructure like Huo-Yan, is of great
42 significance for the early prevention and control of infectious diseases for both common
43 times and emergencies.

44

45 **Keywords:** Coronavirus disease 2019 (COVID-19); modeling; testing capacity;
46 numerical simulation

47

48 **Introduction**

49 To cope with the outbreak of the coronavirus related disease (COVID-19) in Wuhan
50 since December 2019, the unprecedented province-scale quarantine since January 23rd
51 2020 was adopted to prevent the virus from spreading ^[1,2]. The numerical simulation of
52 Yang *et al.* ^[1] quantitatively explained the effectiveness of the series of unprecedented
53 measures taken by the Chinese government, such as extended the Spring Festival
54 holiday, encouraged people to self-quarantined and delayed the resumption of work and
55 school, which successfully reduced the population movement and thereby the virus

56 transmission.

57

58 The clinical testing method plays irreplaceable role in identifying the infected, cutting
59 off the transmission, and protecting the susceptible. The qRT-PCR based nucleic acid
60 testing is regarded as one of the gold standards for the detection of coronavirus related
61 disease (COVID-19). From January 3rd, the Chinese Center for Disease Control and
62 Prevention (CCDCP) began to distribute nucleic acid testing kits to hospitals and
63 medical institutions, and carried out testings according to their own capabilities.
64 However, the large-scale and standardization nucleic acid testing has always been a
65 problem that troubles the entire disease control system, including the CCDCP, hospitals
66 and clinical laboratories. Quality control of the sampling procedure, equipments, testing
67 kits and processes lack consistency amongst 97 institutions in Hubei Province and more
68 than 40 institutions in Wuhan, making it hard to centralize and scale-up the testings,
69 deliver the results and admit the infected on a timely manner. The above mentioned
70 technical issues of the clinical testing lead to the controversy about the effectiveness of
71 the nucleic acid testing by the doctors, experts and officials, which converted into the
72 social panic. On February 4th, the fifth edition of the diagnosis and treatment plan for
73 the novel coronavirus disease even adapted the imaging features of pneumonia (by CT-
74 scanning) as the diagnosis standard of COVID-19 in Hubei Province published by the
75 National Health Commission [3].

76

77 Though the province-scale quarantine is unprecedented, however the number of
78 suspected infections kept increasing due to a series issues with regard to the nucleic
79 acid testing, which leading to serious delay of both diagnosis and hospital admission.
80 To cope with that, the Wuhan government made another key strategic decision to build
81 an emergent clinical virus testing infrastructure on Jan 29th, i.e. the Huo-Yan Laboratory,
82 with a testing capacity over 10,000 per day (Figure 1). Huo-Yan was expanded into a
83 site of 2,000 m² within a week from an existing laboratory that continuously delivers

84 testing results. Since Huo-Yan put into use on Feb 5th, its testing capacity kept stably
85 increasing due to the automated nucleic acid extraction device and optimization of
86 procedure. Then Huo-Yan have achieved 14,000 testing capacity per day on Feb 9th
87 along with the original site and exceeded 20,000 testing capacity per day on Mar 1st.
88 And finally substantially contributed to achieve the “daily settlement” (no suspected
89 cases each day) raised by Hubei Provincial government starting by Feb 16th. On Feb
90 19th, the sixth edition of the diagnosis and treatment plan for the novel coronavirus
91 disease^[3] recalled the practice of using imaging features of pneumonia for the diagnosis
92 of COVID-19 in Hubei Province.

93

94 Testing is the key to the prevention and control of infectious diseases, for only by
95 identifying the infected can they be isolated and treated, as well as to stop the
96 transmission. So far, there was no empirical data and numeric model to clarify the
97 impact of standardized and large-scale clinical testing platform on the prevention and
98 control of contagion. Here we present a novel differential model with non-linear
99 transfer coefficients and competitive compartments to evaluate the trends of suspected
100 cases under different nucleic acid testing capacities.

101

102 **Methods**

103 *Data Source*

104 The number of daily received samples and the maximum testing capacity of Huo-Yan
105 Laboratory were taken into the model for the estimation of the testing (Figure 1) and
106 online available (<https://huoyan.bgi.com/#/>). The data of suspected cases, diagnosed
107 cases each day were acquired from the briefs released by the Health Commission of
108 Hubei Province (<http://wjw.hubei.gov.cn/>) were used for validation of the model.

109

110 *Estimation of the number of nucleic acid testing carried out in Hubei Province*

111 As the response to the rapid increment of suspected cases, the testing capacity of the

112 hospitals, the local disease control and prevention institutions and the clinical testing
113 laboratories in Hubei Province increased from c.a. 3,000 to over 30,000 tests per day.
114 In the period of simulation (Feb 25th-March 6rd), Huo-Yan had finished over 163,000
115 testings by March 6th, with a team of 130 personals. Besides, the 20 teams of 83
116 personals sent by CCDCP together with local lab professionals and supporting
117 personals, had finished 105,641 testings by the end of February. In Wuhan, the 23 most
118 qualified hospitals could perform over 7,000 tests per day. The specifics of the testing
119 carried out in Hubei Province were as follows:

- 120 1) From January 19th, since the testing kits became available to hospitals and medical
121 institutions, the daily testing capacity (TC) of Hubei Province was expected to be over
122 3,000;
- 123 2) From Jan. 26th to Feb. 11th, the daily testing capacity of clinical testing laboratories
124 increased rapidly. Testing capacity of the Huo-Yan Laboratory, $TC_{HY}(t)$ increased to
125 10,000 per day on Feb 4th, and Huo-Yan accounted for 30%-45% of the testing in Hubei
126 Province.
- 127 3) From February 11th to March 1st, $TC_{HY}(t)$ increased from 10,000 to 20,000 per day,
128 delivered 40%-50% of the testing results in Hubei Province.

129

130 *Estimation of the total infected population of novel coronavirus and other pathogens*

131 According to the modified SEIR model by Yang *et al* ^[1], after taken the whole province
132 quarantine measures in Hubei, the infected cases decreased from 43,000 on Feb 25th to
133 34,000 on Mar 6th. The suspected patents were usually with characteristics of fever and
134 influenza-like illnesses (ILIs), and the existing epidemiological data showed an
135 incremental trend of ILIs patients from 2015 to 2017 in Wuhan, along with annual ILIs
136 prevalence of 4.5% in Wuhan ^[4]. The ILIs cases in the 1st quarter of each year accounted
137 for about 20% (varying from 17% to 46%), therefore we estimated the annual total
138 infected patients of ILIs other than coronavirus could be over 460,000 in the first quarter

139 of 2020 in Hubei Province, which would lead to over 5,000 patients with similar
140 symptom of COVID-19 per day.

141

142 *Model for predicting suspected cases*

143 A novel model was used to illustrate the influence of testing capacity on the prevention
144 and control of COVID-19 (Figure 3). Unlike the common dynamic model used only
145 linear differential equations, this model applied the increasement of testing capacity
146 into account. Since the quarantine measures in Hubei, the contact probability among
147 people was reduced, which significantly reduced the possibility of large-scale
148 transmission. Meanwhile, due to quarantine, people were more alert to fever and other
149 symptoms, leading to more patients surged into the hospital and a continuous
150 increasement suspected cases. The purpose of nucleic acid testing was to 1) identify
151 patients with COVID-19 from the uninfected, and allow them to be hospitalized; 2)
152 after the symptoms disappear, the inpatient with more than twice negative testing results
153 (the interval must be more than 24 hours) could be discharged ^[3].

154

155 The conversion efficiency from suspected to hospital admission depended on the testing
156 capacity ($TC(t)$), the number of existing and newly discovered the suspected cases,
157 however there was a bottleneck of nucleic acid testing. As soon as the daily testing
158 capacity was greater than the existing suspected plus the newly suspected of the day,
159 the “daily settlement” of suspected cases could be achieved.

160

161 The differential equation derived from the following models:

162 $TR(t) = \sigma_{cov} \cdot E_{cov}(t) + \sigma_{other} \cdot E_{other}(t) + I_{cov}(t) + I_{other}(t)$

163 $PR(t) = (\sigma_{cov} \cdot E_{cov}(t) + I_{cov}(t))/TR(t)$

	$NTD(t) = \rho \cdot TC(t);$	<i>when $\rho \cdot TC(t) < TR(t)$</i>
	$NTR(t) = 0$	
	$NTD(t) = I_{sus}(t) + \sigma_{cov} \cdot E_{cov}(t);$	<i>when $TR(t) < \rho \cdot TC(t)$</i>

{	$NTR(t) = (1 - \rho) \cdot TC(t)$	<i>and</i> $TC(t) < (TR(t) + H(t))$
	$NTD(t) = I_{sus}(t) + \sigma_{cov} \cdot E_{cov}(t);$ $NTR(t) = H(t)$	<i>when</i> $TC(t) > (TR(t) + H(t))$

164 $\frac{dI_{cov}(t)}{dt} = \sigma_{cov} \cdot E_{cov}(t) - PR(t) \cdot NTR(t)$

165 $\frac{dI_{other}(t)}{dt} = \sigma_{other} \cdot E_{other}(t) - (1 - PR(t)) \cdot NTR(t)$

166 $\frac{dH(t)}{dt} = PR(t) \cdot NTR(t) - \gamma \cdot NTR(t) - \alpha \cdot H(t)$

167 $\frac{dR(t)}{dt} = \gamma \cdot NTR(t)$

168 $\frac{dD(t)}{dt} = \alpha \cdot H(t)$

169 The parameters in the model were as follows:

170 $TC(t)$: the testing capacity.

171 $TR(t)$: the testing requirement from existing and newly discovered suspected patients.

172 $PR(t)$: the positive ratio of the tests for diagnosis ($NTR(t)$).

173 $E_{total}(t)$: the number of COVID-19 latent patients and other diseases in the province.

174 $E_{cov}(t)$: the latent patients of COVID-19 in the province, including the asymptomatic
175 population.

176 $E_{other}(t)$: the latent patients that were not infected by the novel coronavirus.

177 σ_{cov} : incubation rate. Generally, the reciprocal of the disease cycle was taken (1/7).

178 $I_{sus}(t)$: the number of suspected cases of COVID-19 in the whole province.

179 $I_{cov}(t)$: the number of patients with novel coronavirus as suspected patients in the whole
180 province.

181 $I_{other}(t)$: the number of patients of other diseases as suspected cases of COVID-19 in
182 the whole province.

183 ρ : the rate of the test used for the diagnosis of the COVID-19 in the total nucleic acid
184 tests.

185 $NTD(t)$: the number of tests used for diagnosis suspected cases .

186 $NTR(t)$: the number of tests used for the discharge of the cases.

187 $D(t)$: the cumulative number of deaths caused by COVID-19.

188 $R(t)$: the cumulative number of discharged patients.

189 γ : the probability of recovery, generally taking the reciprocal of 20 days.

190 α : the mortality rate, which is 0.0035.

191

192 **Results**

193 The simulation result corresponded well with the trend of suspected cases by Health
194 Commission of Hubei Province, and the positive rate of the tests per day was around
195 50%, also consistent with the positive rate data from Huo-Yan. The effect of increased
196 testing capacity was significant, which was largely up to the government's decision and
197 the expansion of the hospitals and clinical testing laboratories (Figure 4).

198

199 Due to the insufficient testing capacity at the beginning of the province-scale quarantine,
200 the number of suspected cases rose to over 23,000, which became a "dammed lake" for
201 delayed diagnosis and led to social panic.

202

203 If the testing capacity did not rapidly increased, the suspected cases could have reached
204 a maximum of 33,700, resulting in a doubled isolation cost in term of room-days and
205 ten thousands medical personals in addition to the over 40,000 medical workers and
206 doctors which had been sent to Hubei Province. The diagnosis for over 30,000
207 suspected cases would be delayed, half of which are positive results and could cause
208 further transmission. The turning point of the increment of suspected cases would be
209 delayed for 6 days and the achievement of "daily settlement" would be realized at least
210 11 days later.

211

212 If the established testing capacity was fully used, over 22,800 suspected cases could be

213 diagnosed on time rather than being delayed, and accordingly, the isolation cost could
214 be reduced by at least 72%, the turning point of the increment of suspected cases could
215 arrive one week earlier, and “daily settlement” could be realized 12 days in advance.

216

217 Under the ideal scenario, if Hubei Province was capable of carrying out more than
218 10,500 tests per day at the very beginning of the epidemic, there would be no “suspected
219 cases” in the daily official COVID-19 epidemic report, but only the number of
220 diagnosed cases, i.e., either positive or negative, because all of the suspected cases
221 would be “settled” daily.

222

223 **Conclusions**

224 Novel coronavirus related diseases have been officially defined as pandemic on March
225 11th 2020 by WHO. The quarantine of an entire district, city or a region could be
226 adopted as part of the measures by the government. In Italy, more than 15 million people
227 were placed in the country-based quarantine on March 8th [5]. Spain has announced it is
228 placing its 47 million citizens under partial lockdown for 15 days. Hereby it would be
229 worth determining the required testing capacity, referring Huo-Yan as an example in
230 the public decision-making process. Timely and accurate clinical test is essential for
231 identifying the infected, cutting off the transmission, and protecting the susceptible. The
232 large-scale, precise, and reliable testing capacity is highly required to reduce the panic
233 accompanied by the drastic quarantine measures.

234

235 To increase the testing capacity is a systematic project, among which the qualified
236 laboratory spaces, the standardize of training medical panels, the supplement of the
237 equipment, reagents, consumables and protective materials, and the automation of the
238 testing procedure were of most importance. Here are the suggestions deduced from the
239 simulation:

240

- 241 1) The large-scale standardize testing platform and QC protocols were the premise of
242 in the quarantine, which were the prerequisite for the diagnosis of suspected cases,
243 isolate infectious patients, release isolation of convalescent and uninfected healthy
244 population, and also the screening of key communities and groups. The practice
245 from the centered platform could be summarized and replicated to other laboratories.
246 The quality of the diagnostic kits and the accuracy, timeliness, safeties of the
247 laboratories must be constantly compared and inspected. Unstandardized testing
248 process would cause inconsistency in testing results and led to distrust on the testing
249 results.
- 250 2) Encourage the laboratories to increase testing capacities and keep continues
251 delivery results at the same time. During emergencies, any changes in the testing
252 process could cause samples accumulation, and the best solution could be continues
253 applying new knowledge, know-hows in small scale and quickly replicate to the
254 whole testing assembly line. This principle works in deploying new laboratory
255 spaces, automation equipment, SOP and etc.
- 256 3) Keep the outsourcing clinical testing laboratory the same priority and responsibility
257 as the in-house laboratories. Despite of the high efficiency of the outsourcing
258 laboratory, some hospitals are not willing to perform the outsourcing diagnostic
259 tests just because they regard the risk of inaccurate testing results of the outsourcing
260 laboratories “incontrollable”.
- 261 4) Central planning of the diagnostic testing and comprehensive tracking of the
262 potential testing capability to achieve “daily settlement”. Once there are standardize
263 testing capacity, arrange the samples to fill the excess capacity immediately.
- 264 5) Sufficiently supplement the sampling kits and the corresponding trainings to the
265 medical panels. Other issues that require training on the sampling process including
266 the barcoding and information input of the samples, and the inactivation of the
267 pathogen before testing.
- 268 6) Large-scale and standardized clinical laboratory should be regarded as

269 infrastructure for both common time and emergencies against contagion, and should
270 be put into use as early as possible in any epidemic. A good estimation of the testing
271 capacity for nucleic acid testing of COVID-19 could be over 10,500 samples per
272 day for a region of 60 million population with over 43,000 infected patients.

273

274 With Huo-Yan Laboratory as a reference model, combining with high-throughput
275 sequencing, nucleic acid detection, immunoprotein analysis and other large-scale
276 standardized and automated analysis methods, we can build infrastructure in the field
277 of public health against the pandemic, so that large and small cities could have their
278 own detection capabilities of 100 to 1,000 or 10,000 people when facing various
279 epidemics, we can take it easy to ensure our life safety, biological safety and economic
280 safety.

281

282 **Disclaimer**

283 Huo-Yan is an ad-hoc COVID-19 clinical testing infrastructure owned by the Wuhan
284 East Lake High-tech Development Zone. BGI-Wuhan operates the laboratory, BGI
285 PathoGenesis Pharmaceutical Technology provides technical support for the whole
286 laboratory. This work is to serve as an empirical reference to regions where COVID-19
287 needs to be prevented and controlled as it is now spreading globally. All opinions
288 expressed are those of the authors and do not necessarily reflect the views of the Hubei
289 provincial government.

290

291 **Acknowledgement**

292 Wang Jian supervised the whole work, Qing Xie generated the simulation model, Qing
293 Xie, Jing Wang and Jianling You wrote the manuscript. We thank Dr. En Bo for his
294 technical support.

295

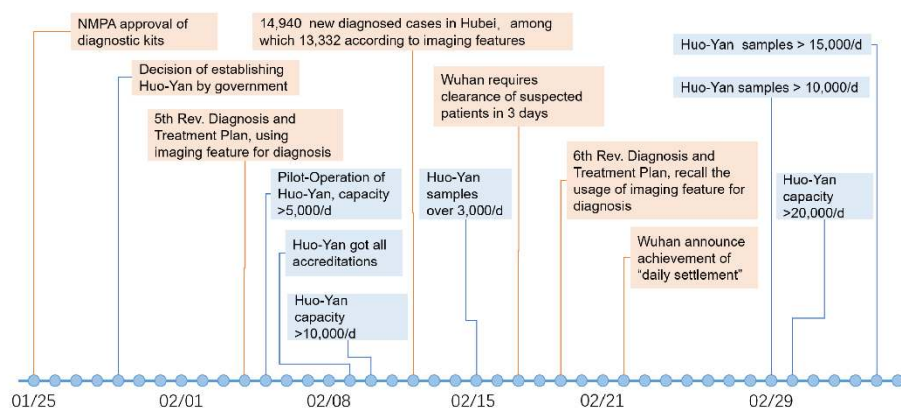
296 **References**

- 297 1. Yang Z, Zeng Z, Wang K. Modified SEIR and AI prediction of the epidemics trend
298 of COVID-19 in China under public health interventions[J]. J Thorac Dis, 2020.
- 299 2. Tang B, Wang X, Li Q, et al. Estimation of the transmission risk of the 2019-nCoV
300 and its implication for public health interventions[J]. Journal of Clinical Medicine,
301 2020, 9(2): 462.
- 302 3. Diagnosis and Treatment Plan for the Novel Coronavirus Disease (COVID-19) (1st -
303 7th Rev.), National Health Commission.
- 304 4. Ye Jiuhong, Cao Qian, Feng Ling, et al. Characteristics analysis of fever and
305 influenza-like patients in a tertiary hospital in Wuhan during 2015 to 2017[J] J of Pub
306 Health and Prev Med, 2019.
- 307 5. Anderson R M, Heesterbeek H, Klinkenberg D, et al. How will country-based
308 mitigation measures influence the course of the COVID-19 epidemic?[J]. The Lancet,
309 2020.

310

311 **Figures**

312 Figure 1. Timeline illustrating the establishment of Huo-Yan Laboratory as response to
313 the insufficient nucleic acid testing during the epidemic.

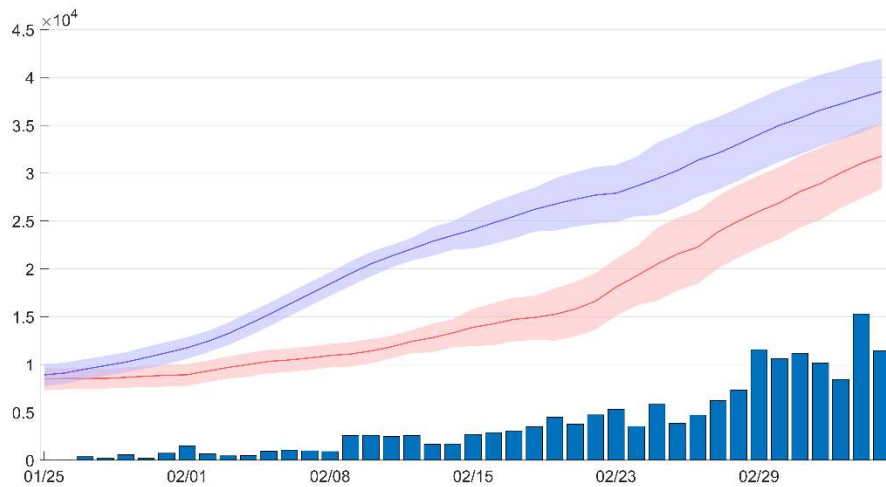


314

315 Figure 2. The trend of the nucleic acid testing performed in Hubei Province and by

316 Huo-Yan Laboratory.

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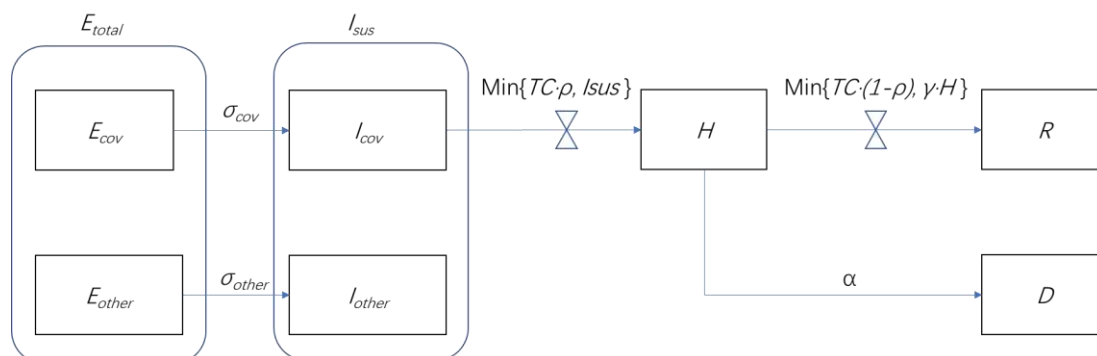


318

319 The number of samples sent to Huo-Yan Laboratory and the corresponding delivered
 320 testing results (bar with solid line, blue). Estimated testing capacity of the Hubei
 321 Province (red line and the corresponding envelop) and the corresponding potential
 322 testing capacity (blue line and the corresponding envelop).

323

324 Figure 3. The competitive, non-linear epidemic model of hospitalization and discharge
 325 of the suspected patients. Unlike the common epidemiologic models based on the linear
 326 transfer functions and constant transfer coefficients, the novel model has transfer
 327 coefficient restricted by the testing capacity.

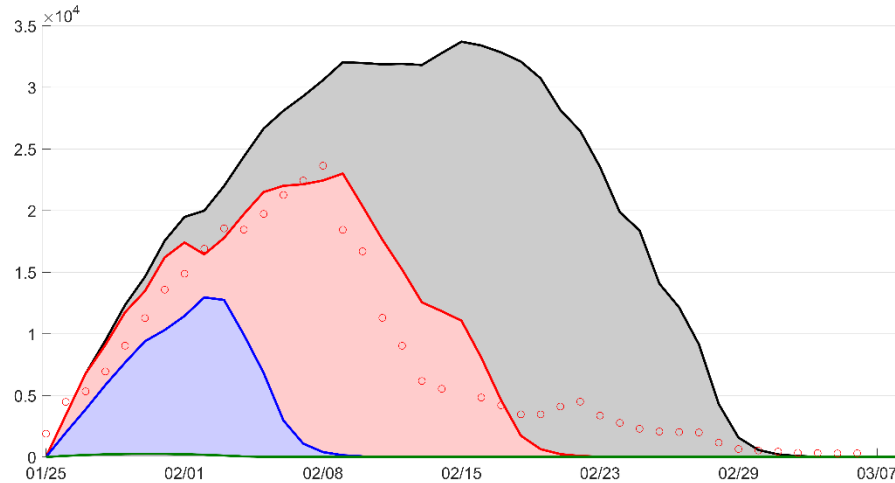


328

329 $E_{total}(t)$: the number of COVID-19 latent patients and other diseases in the region.

330 $E_{cov}(t)$: the latent patients of COVID-19 in the province, including the asymptomatic
 331 population.

- 332 $E_{other}(t)$: the latent patients that is not infected by the novel coronavirus.
- 333 σ_{cov} : incubation rate. Generally, the reciprocal of the disease cycle is taken (1/7 day).
- 334 σ_{other} : virtual incubation rate of other diseases that leads to symptom of suspected
335 patients. (1 day).
- 336 $I_{sus}(t)$: the number of suspected cases of COVID-19 in the whole province.
- 337 $I_{cov}(t)$: the number of patients with novel coronavirus as suspected patients in the whole
338 province.
- 339 $I_{other}(t)$: the number of patients of other diseases as suspected patients of COVID-19 in
340 the whole province.
- 341 ρ : the ratio of the test used for the diagnosis of the COVID-19 in the total nucleic acid
342 tests.
- 343 $TC(t)$: the testing capacity.
- 344 $NTD(t)$: the number of tests used for diagnosis suspected patients.
- 345 $NTR(t)$: the number of tests used for the discharge of the patients.
- 346 $D(t)$: the cumulative number of deaths caused by COVID-19.
- 347 $R(t)$: the cumulative number of discharged patients.
- 348 γ : the probability of recovery, generally taking the reciprocal of 20 days.
- 349 α : the mortality rate of COVID-19.
- 350
- 351 Figure 4. The simulation of the suspected patients under different testing capacity.
- 352



353

354 The simulation results using the Huo-Yan factual operation data (line, red) corresponds
355 with the open-access data from Health Commission of Hubei Province (circle, red). The
356 simulated results without the Huo-Yan laboratory (line, black) and the result using 100%
357 of the test capacity (blue). The ideal situation (line, green) would be achieved with a
358 testing platform of enough high capacity. The area under curve depicts the number of
359 isolated patients in term of rooms per person per day.

