A statistical method of batch screening entrying population from abroad by stages and groups in COVID-19 nucleic acid testing

Author:

Cheng Yuan yuan

Address for correspondence:

E-mail:henuhh@outlook.com

Affiliation

Henan University Huaihe hospital, Kaifeng City, Henan Province, China.

Abstract

Objective: To screen out COVID-19 patients in entrying population from abroad with the minimum number of nucleic acid testing (*NAT*).

Methods: In the first stage, the nasopharyngeal swab samples of the entrying population are numbered and grouped. After the samples in the group are mixed together, one *NAT* was performed. When the test result is negative, it shows that all of the peple in the group are not infected and the test for the group is complete. On the contrary, when the test result is positive, the group enters the second stage. In the second stage, all samples in the positive group will be tested one by one using the *NAT*.

Results: The advantages and precautions of the method were discussed. The incidence rate of entrying population is the determinant of the number of samples in the group. The lower the incidence rate, the larger the number of samples in the group, and the greater the percentage saved.

Conclusion: The method has obvious efficiency and cost advantages in *COVID-19* testing. It can also be used to screen other populations such as community populations, high risk of infection populations.

Key words: COVID-19, NAT, nucleic acid testing, screening, nasopharyngeal swab

Background

Since *WHO* declared *COVID-19* (Corona Virus Disease 2019) as a pandemic all of the world on 11 March 2020[1], the number of people entrying China has reached 600,000 to 15 March 2020[2], and 44 newly confirmed cases were found out from the entrying population[3-7]. Starting from 19 March 2020, the cities such as Shenzhen, Guangzhou, Shanghai and Beijing have successively performed the policy which nucleic acid testing (*NAT*) covers the whole entrying population from abroad[8-11].

Methods

The formula equation used is the following:

$$p = \frac{d}{t} = \frac{1}{q} \quad \cdots\cdots (1)$$

$$y = \frac{1}{p * x} + x \quad \cdots\cdots (2)$$

$$y_{min} = \sqrt{q} + x \approx 2\sqrt{q} = 2x \quad \cdots\cdots (3)$$

R software (Version 3.6.3) code to calculate y is the following:

```
1 p<-                    #input value of Incidence Rate
2 x<-c(2:(1/p))
3 y<-1/(p*x)+x
4 t<-data.frame(x,y)
5 View(t)
```

where p is the incidence of entrying population, d is the number of confirmed cases of entrying population, t is the number of entrying population in the same period, q is the number of entrying population which bring one *COVID-19* patient, y is the number of *NAT*, x is the number of sample each group, y_{min} is the minimum number of the *NAT*. According to formulas (1), when d = 44, t = 60,000, then p = 0.7333(1/10,000), and q = 13637. The incidence of entrying population is 0.7333 (1 / 10,000). On average, there is 13637 entrying persons which bring one *COVID-19* patient. In order to find out this patient, 13637 entrying persons must be performed *COVID-19* fluorescent *RT-PCR* testing, 13637 *NAT* are required. At the cost of *RMB* 160 per testing, the cost of 13637 *NAT* are 2.18 million. In order to achieve the same detection result with the minimum number of *NAT*, we recommend using the methods of batch screening by stages and groups (Figure 1).

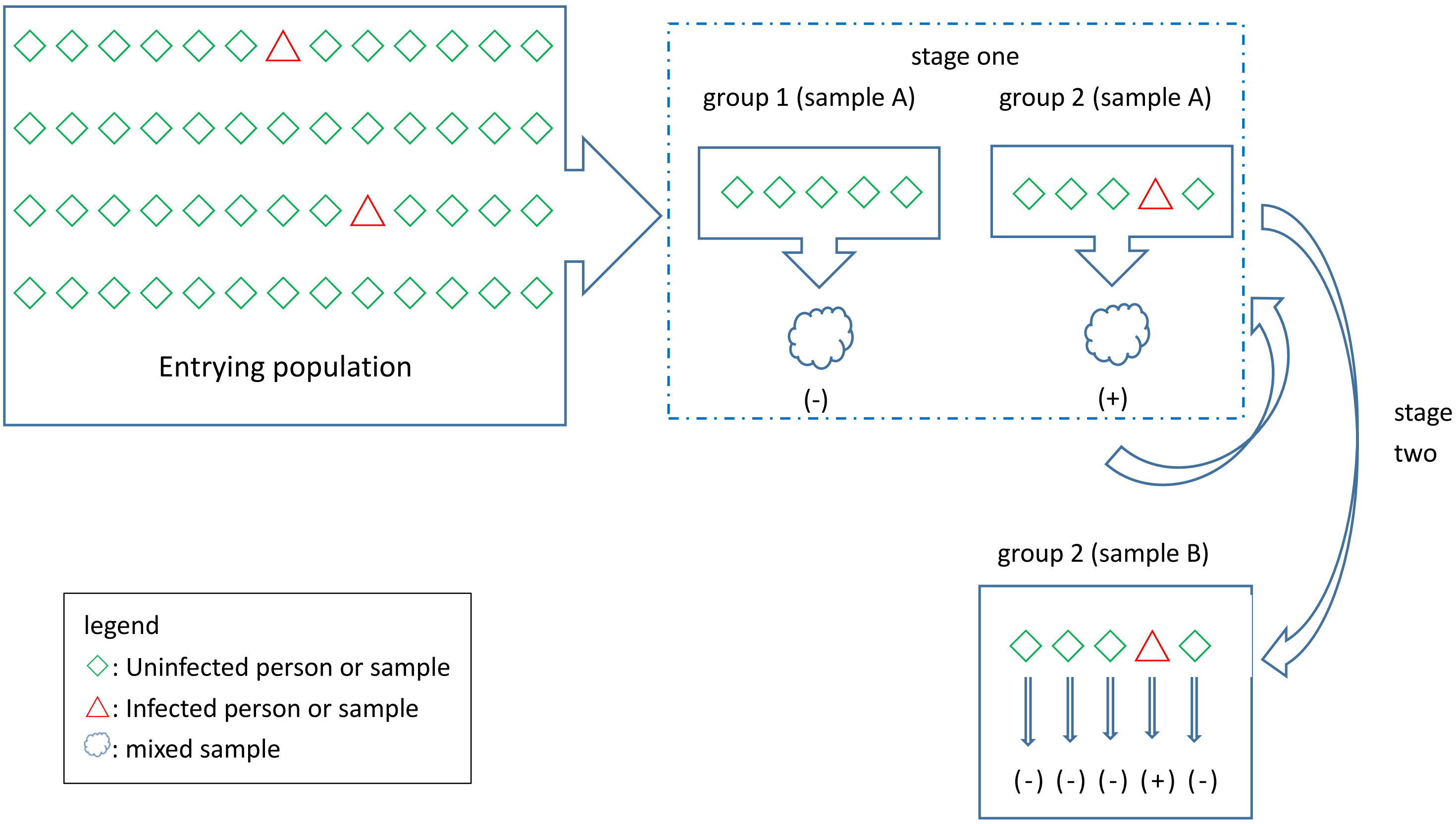

Figure 1　Schematic flow chart of batch screening by stages and groups

At the first stage, all the entrying persons through customs are numbered and grouped, each group has *x* persons. In a same group, the double nasopharyngeal swabs of each person's are extracted and called sample A, sample B. All of the sample A in a group are mixed together as one sample for a *NAT*. When the test result is negative, it shows that all of the peple in the group are not infected and the test for the group is complete. On the contrary, when the test result is positive, it indicates that at least one of the samples in the group is positive, and the postive group will enter the second stage of test.

At the second stage, all of the sample B in the positive group are performed for *NAT* one by one, to find out the corresponding patient which sample caused the positive result. In this way, *y* times *NAT* required. when a patient are found out , *q-y* times of the *NAT* will be saved. We calculate *x* to get the minimum value of *y* and the more times of *NAT* could be saved.

For example, where *p* is 0.733 per 100,000, *q* is 13637, according to formulas (1), (2) , (3) and code of R software 3.63, when *x* is 117, the groups are 117, the minimum value of *y* is 234 times, that is, 117 persons a group, 13637 persons are divided into 117 groups, the minimum number of *NAT* is 234 instead of 13637. In each group, the double samples per person are collected, and 234 nasopharyngeal swabs are extracted who called sample A and sample B， each group has 117 sample A and 117 sample B. A *NAT* is performed after the sample A of the same group are mixed together, to all groups, 117 tests are performed. When the test result is negative, it indicates that the test results of all 117 people are negative, and the test of the group is complete. When the test result of the group is positive, it indicates that at least one of the 117 people has a positive test result. All the sample B in the positive group are subjected to the second stage test. In the second stage, all samples B in the positive group will be tested one by one using the NAT, and 117 tests performed. As a result, 234 *NAT* required. When a patient are found out from 13637, the average every entrying person pays only *RMB* 2.8 instead of *RMB* 160 for the *NAT*. Compared with 13,637 times of *NAT*, 13,403 times tests are saved, equivalent to saving 2.14 million in costs. The percentage saved is 98.3% of the number of *NAT* (or costs). If two or more patients are found in a same group, or the statistical method is performed again in positive groups, more costs can be saved. With an average daily detection volume of more than 6,000 people in Beijing, the cost of *NAT* is at least *RMB* 960,000. Using the method, Beijing can save *RMB* 940,000 testing costs per day, and can save *RMB* 28.2 million in 30 days. Based on an average of 120,000 people entrying China through land ports, seaports and airports every day, it can save *RMB* 18.83 million in test costs per day and *RMB* 565 million in 30 days.

Conclusion

This method is not only limited to entrying population detection, but also can be used in community poplation detection and close contact population detection[12-28].

It should be noted that *p* is the determining factor for the number of persons in each group. To find out the patients, the lower the *p*, the greater the value of *x* and the greater the value of *q*-*y* ,and vice versa (Table 1, Figure 2, Figure 3).

Table 1. Realaship of the incidence rate, number of sample and percentage saved

p(1/10,000)	*q*	*x*	y_{min}	*Percentage saved*（%）
10.00	1000	32	64	93.6
5.00	2000	45	90	95.5
3.33	3000	55	110	96.3
2.50	4000	64	128	96.8
2.00	5000	71	142	97.2
1.67	6000	78	156	97.4
1.43	7000	84	168	97.6
1.25	8000	90	180	97.8
1.11	9000	95	190	97.9
1.00	10000	100	200	98.0
0.91	11000	105	210	98.1
0.83	12000	110	220	98.2
0.77	13000	115	230	98.2
0.71	14000	119	238	98.3
0.67	15000	123	246	98.4

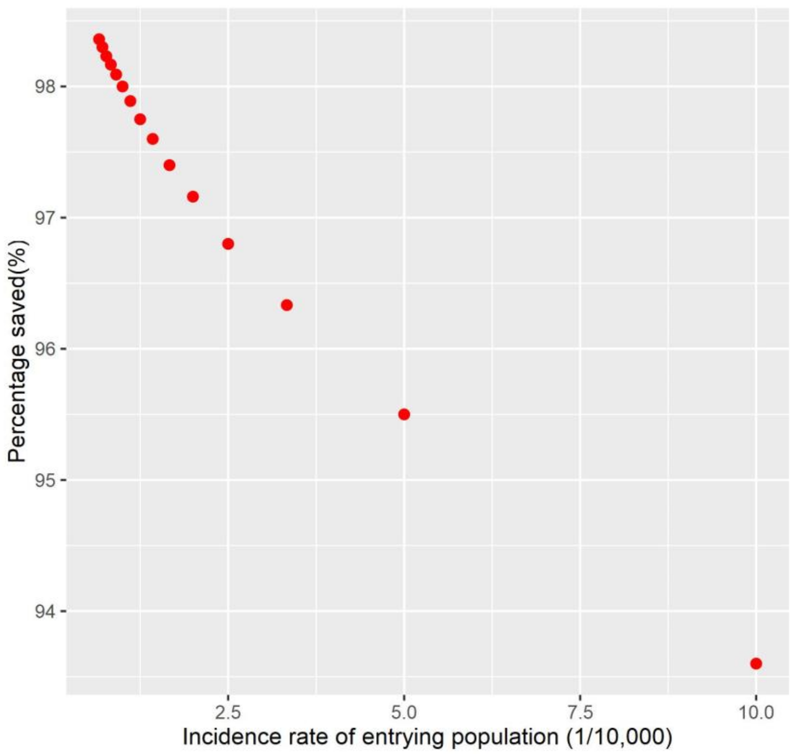

Figure 2 Scatter plot of incidence rate of entrying population and Percentage saved. It shows that the relationship between incidence rate and percentage saved, the lower incidence rate, the greater the percentage saved.

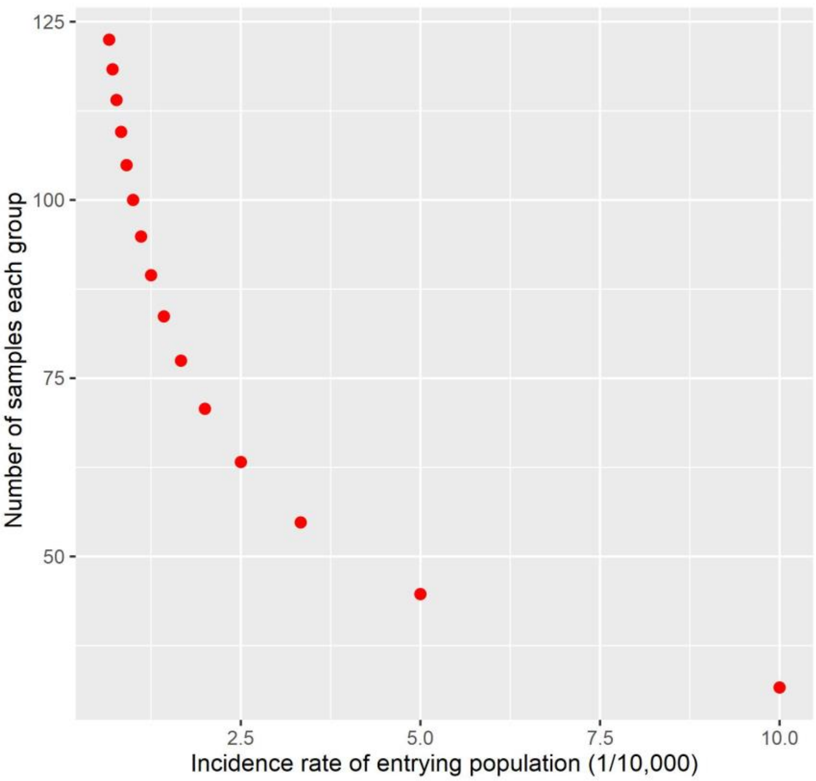

Figure 3 Scatter plot of incidence rate of entrying population and Number of samples each group. It shows that the relationship between incidence rate and number of samples each group, the lower incidence rate, the greater the number of samples each group, more *NAT* can be saved.

There are many factors that affect *p*, such as the international situation, country, city, observation period, customs policy, and characteristics of the entrying population. Sometimes it will cause large fluctuation of *p*. It is necessary to monitor *p* in time and adjust *x* in accordance with formula (2). When *p* fluctuates within a certain range, *x* should be adjusted according to the maximum value of *p*.

Reference:

[1] WHO Director-General's opening remarks at the media briefing on COVID-19 - 11 March 2020. https://www.who.int/dg/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19---11-march-2020.[11 March 2020]

[2] http://news.cyol.com/app/2020-03/16/content_18516985.htm.[2020-03-16]

[3] http://www.nhc.gov.cn/xcs/yqtb/202003/37c1536b6655473f8c2120ebdc475731.shtml. [2020-03-12]

[4] http://www.nhc.gov.cn/xcs/yqtb/202003/816e6f71236b4dca96378df5f6f4ae53.shtml. [2020-03-13]

[5] http://www.nhc.gov.cn/xcs/yqtb/202003/ec0119a5881543288efd5b5c8008387b.shtml. [2020-03-14]

[6] http://www.nhc.gov.cn/xcs/yqtb/202003/8331f126d3854413b6ea323009fbbcc5.shtml.[2020-03-15]

[7] https://www.sznews.com/news/content/2020-03/19/content_22979893_0.htm.[2020-03-19]

[8] http://www.nhc.gov.cn/xcs/yqtb/202003/114113d25c1d47aabe68381e836f06a8.shtml.[2020-03-16]

[9] http://economy.southcn.com/e/2020-03/25/content_190640969.htm.[2020-03-25]

[10] http://www.gov.cn/xinwen/2020-03/24/content_5494829.htm#1.[2020-03-24]

[11] http://www.xinhuanet.com/local/2020-03/24/c_1125762120.htm.[2020-03-24]

[12] Ye B, Fan C, Pan Y, Ding R, Hu HX, Xiang ML. Zhonghua Er Bi Yan Hou Tou Jing Wai Ke Za Zhi. 2020;55(0):E003. doi:10.3760/cma.j.cn115330-20200223-00116

[13] Ai T, Yang Z, Hou H, et al. Correlation of Chest CT and RT-PCR Testing in Coronavirus Disease 2019 (COVID-19) in China: A Report of 1014 Cases [published online ahead of print, 2020 Feb 26]. Radiology. 2020;200642. doi:10.1148/radiol.2020200642

[14] Zhao W, Zhong Z, Xie X, Yu Q, Liu J. Relation Between Chest CT Findings and Clinical Conditions of Coronavirus Disease (COVID-19) Pneumonia: A Multicenter Study [published online ahead of print, 2020 Mar 3]. AJR Am J Roentgenol. 2020;1–6. doi:10.2214/AJR.20.22976

[15] Xie X, Zhong Z, Zhao W, Zheng C, Wang F, Liu J. Chest CT for Typical 2019-nCoV Pneumonia: Relationship to Negative RT-PCR Testing [published online ahead of print, 2020 Feb 12]. Radiology. 2020;200343. doi:10.1148/radiol.2020200343

[16] Corman VM, Landt O, Kaiser M, et al. Detection of 2019 novel coronavirus (2019-nCoV) by real-time RT-PCR. Euro Surveill. 2020;25(3):2000045. doi:10.2807/1560-7917.ES.2020.25.3.2000045

[17] Lippi G, Simundic AM, Plebani M. Potential preanalytical and analytical vulnerabilities in the

laboratory diagnosis of coronavirus disease 2019 (COVID-19) [published online ahead of print, 2020 Mar 16]. Clin Chem Lab Med. 2020;/j/cclm.ahead-of-print/cclm-2020-0285/cclm-2020-0285.xml. doi:10.1515/cclm-2020-0285

[18] Udugama B, Kadhiresan P, Kozlowski HN, et al. Diagnosing COVID-19: The Disease and Tools for Detection [published online ahead of print, 2020 Mar 30]. ACS Nano. 2020;10.1021/acsnano.0c02624. doi:10.1021/acsnano.0c02624

[19] Peto Julian. Covid-19 mass testing facilities could end the epidemic rapidly BMJ 2020; 368 :m1163

[20] Hellewell J, Abbott S, Gimma A, et al. Feasibility of controlling COVID-19 outbreaks by isolation of cases and contacts [published correction appears in Lancet Glob Health. 2020 Mar 5;:]. Lancet Glob Health. 2020;8(4):e488–e496. doi:10.1016/S2214-109X(20)30074-7

[21] Burke RM, Midgley CM, Dratch A, et al. Active Monitoring of Persons Exposed to Patients with Confirmed COVID-19 - United States, January-February 2020. MMWR Morb Mortal Wkly Rep. 2020;69(9):245–246. Published 2020 Mar 6. doi:10.15585/mmwr.mm6909e1

[23] Jin YH, Cai L, Cheng ZS, et al. A rapid advice guideline for the diagnosis and treatment of 2019 novel coronavirus (2019-nCoV) infected pneumonia (standard version). Mil Med Res. 2020;7(1):4. Published 2020 Feb 6. doi:10.1186/s40779-020-0233-6

[24] http://www.nhc.gov.cn/yzygj/s7653p/202001/f492c9153ea9437bb587ce2ffcbee1fa.shtml. [2020-01-23]

[25]http://www.nhc.gov.cn/yzygj/s7652m/202001/7450028ab6084101ae8110f0aaf81271.shtml. [2020-01-28]

[26] http://www.nhc.gov.cn/yzygj/s7653p/202002/d4b895337e19445f8d728fcaf1e3e13a.shtml. [2020-02-08]

[27] Diagnosis and Treatment Plan for COVID-19 (Trial Version 6) [published online ahead of print, 2020 Mar 17]. Chin Med J (Engl). 2020;10.1097/CM9.0000000000000819. doi:10.1097/CM9.0000000000000819

[28] http://www.nhc.gov.cn/yzygj/s7653p/202003/46c9294a7dfe4cef80dc7f5912eb1989.shtml. [2020-03-04]