

## A Bayesian approach model to COVID-19 case definitions

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### Abstract

**Background:** Since December 2019, the novel coronavirus disease (COVID-19) has rapidly spread worldwide and caused a pandemic. Several case definitions have been released and revised by countries and organizations. However, the collectivization of case definitions has not been investigated.

**Methods:** The study was conducted in two phases. In the first phase, two review were conducted to detect current COVID-19 case definitions and their influential epidemiological features in the case definition. In the second phase, a dynamic case definition algorithm was applied using the Bayesian theorem models of diagnosis to represent case definitions.

**Results:** Our results showed categorization as suspected, probable, and confirmed cases, which is used in the majority of case definitions. Furthermore, the criterion for suspected cases and laboratory testing priority was a point of argument. Due to the pandemic situation and resource limitations, diagnostic tests were rationed and mainly administered to a selected population, thus it was shown that the fraction of positive test results do not reflect the total infection rate of the population. Case definitions for COVID-19 are changing as we learn more about the disease. RT-PCR and CT scan of lung seem to be beneficial in COVID-19 diagnosis and combing them with epidemiological criteria help us a better understanding of the disease.

**Conclusion:** Based on our results, in the current case definitions, only symptomatic patients categorized and tested as a susceptible case. While the majority of COVID-19 cases are asymptomatic carriers of the disease, thus making the prevention more challenging. Dynamic statistical models can provide new insights into surveillance systems.

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### Highlights

#### What is current knowledge?

Different COVID-19 case definitions of countries and organizations consist of clinical and epidemiological criteria. The deficiency of current case definitions is their focus on symptomatic patients and ignoring asymptomatic patients.

#### What is new here?

This study applied the Bayesian approach for case definition, which considers various criteria to calculate the probability scores of infection for each person.

### Introduction

On December 31, 2019, China announced the emergence of a new type of coronavirus, which later on January 12, 2020, was named COVID-19 by the World Health Organization (WHO). COVID-19 rapidly spread across China and other countries. On March 11, 2020, WHO declared COVID-19 as a pandemic (1). As of 28 April 2020, 2,954,222 confirmed cases, with 202,597 deaths of COVID-19 have been reported to World Health Organization. COVID-19 infection presents vary from being asymptomatic to mild or severe pneumonia. Monitoring the number of coronavirus infections is necessary in providing an appropriate epidemiological response (2). Simple counting the number of COVID-19 cases can be misleading due to difficulties with patient access and performing laboratory tests. Therefore, evidence suggests the necessity of a robust surveillance systems to active people monitoring for disease infection. The International Health Regulation (IHR) defines surveillance as “the systematic ongoing collection, collation, and analysis of data for public health purposes and the timely dissemination of public health information for assessment and public health response as necessary” (2).

One of the first steps in response to the novel Coronavirus pandemic in several countries was strengthening of surveillance systems for identifying different cases. In this regard, countries enhanced their laboratory systems and defined cases that needed the test (3). Case definitions have been recognized as one of the most important components of public health surveillance systems (4). A case definition determines necessary and sufficient findings for classifying an individual as having a disease. More commonly, however, determining whether an individual has the disease is left to the expert judgment of a clinician (5). Case definitions assure the comparability and consistency of surveillance data. Applying case definitions considered essential by the WHO to make surveillance

data comparable between countries. Transparent case definitions are necessary for effectively assessing an outbreak event. Applying a globally accepted case definition allows standardization of cases and provide comparisons inside and probably between outbreaks over time and in different geographical areas. Accepted case Definition includes defining and setting criteria for common demographic characteristics of Patients, location (Specific geographic area), time (Outbreak-related period), and clinical features (Clinical symptoms such as fever and cough) (6).

Case definitions can apply Boolean logical statements. These Definitions consist necessary and sufficient clinical findings with “AND” and “OR” operations. Also, case Definitions can use probabilistic statements that are based on conditional probabilities. In this approach, diagnosis will be categorized as confirmed, probable, or suspected. For example, If  $P(\text{Disease} | \text{Data}) > 0.99$  the cases will be categorized as a confirmed case. (5). Therefore, this study suggests that it is more likely that a probabilistic approach can be more useful in COVID-19 case definitions.

### Methods

This study was conducted in two phases. The first phase aimed at detecting different components, criteria, and categorizations of case definitions. Therefore, a rapid review of existing case definitions, was conducted. Also, a rapid review was conducted on the COVID-19 epidemiological studies. Also, to represent case definitions a dynamic case definition algorithm was applied using the Bayesian theorem models of diagnosis.

#### First phase: Rapid literature review

##### Search and databases

We conducted the review in two steps, in the first step a rapid review of existing case definitions conducted in PubMed and Google scholar from December 31, 2019, to April 3, 2020. Also, the Governmental websites of centers for disease control in different countries were searched to detect relevant document about countries case definitions. In this step, search strategy consisted of keyword that had similar meaning of “case definition” and “surveillance” along with “Coronavirus”, “Coronavirus”, “COVID-19”, “novel coronavirus”, “novel coronavirus disease”, “2019-nCoV”, “coronavirus disease”, “Severe acute respiratory syndrome”, “coronavirus 2” and SARS-CoV-2.

In the second step, the rapid review was performed on epidemiological review studies of the new coronavirus disease published from December 31, 2019, to March 26, 2020. The aim was to achieve a comprehensive definition of various dimensions of Gregg's model, including the characteristics of person, place, time, and clinical features of the disease. In this step the keywords include,

“Epidemiological characteristic”, “epidemiology”, “clinical features”, “incubation period”, “clinical description”, “clinical findings”, “clinical course”, symptoms, and surveillance, which used along with various new coronavirus keywords. The search strategy was conducted in Embase, PubMed and Google scholar databases.

Identified studies were screened by relevance of title and abstract and then full texts screened by inclusion and exclusion criteria.

**Inclusion and exclusion criteria**

Regarding case definitions, all types of evidence that provided case definitions of COVID-19, including reports of different countries and organizations were reviewed.

About the review of epidemiological studies, all English-language review articles that addressed the epidemiology of the new coronavirus disease, including clinical features, transmission methods, and demographic characteristics of COVID-19 cases were included. The studies that addressed the epidemiology of other coronaviruses or did not provide the required information excluded. Two researchers searched databases independently and two sets of studies compared and disagreements regarding the included studies resolved with discussion and third researcher’s opinion.

**Data extraction**

Based on Gregg’s framework, all the information related to symptoms and diagnostic tests, including clinical features, disease-related periods (Incubation period, etc.), places of the disease transmission, and demographic and physical characteristics of patients, were extracted.

**Second phase: Using the Bayesian approach**

The Bayesian approach was used to create a dynamic case definition, with this purpose we combine disease likelihood (Data), including symptoms, signs, and findings of a patient with a pretest probability distribution of disease (Disease). Consequently, the probability of disease is P (Disease | Data). Variables in the Bayesian approach are diagnosis and findings used for diagnosing, it includes all findings which have high specificity to rule in and high sensitivity to rule out in diagnosis (7,8).

This approach was carried out in three steps: in the first step, the aim was to generate the pretest probability using the method of objective probability estimates. Second step, the aim was to gather more information about the COVID-19 disease and its diagnosis. Therefore, we focused on the studies related to diagnostic tests on COVID-19 cases. The aim of third step was to modify and update the covid-19 case definition by using the results of previous stages. In this stage, we tried to update the initial probability estimation. The input for calculating the posttest probability of COVID-19 was the likelihood ratio calculated with the results of diagnostic tests and the Pretest probability based on the existing knowledge.

**Results**

The majority of case definitions categorized as suspected, probable, and confirmed cases (Table 1).

Table 1. Available case definitions

Country/ Organization (Cont.)	Suspected /reporting case of COVID-19 (Cont.)	Probable (Cont.)	Confirmed (Cont.)	Other categories (Cont.)
WHO (20 March 2020) (9)	<p>Suspect case</p> <p>A. A patient with acute respiratory illness (Fever and at least one sign/ symptom of respiratory disease, e.g., cough, shortness of breath), AND</p> <p>A history of travel to or residence in a location reporting community transmission of COVID-19 disease during the 14 days prior to symptom onset;</p> <p>OR</p> <p>B. A patient with any acute respiratory illness AND having been in contact with a confirmed or probable COVID-19 case (See definition of contact) in the last 14 days prior to symptom onset;</p> <p>OR</p> <p>C. A patient with severe acute respiratory illness (Fever and at least one sign/symptom of respiratory disease, e.g., cough, shortness of breath; AND requiring hospitalization) AND in the absence of an alternative diagnosis that fully explains the clinical presentation.</p>	<p>Probable case</p> <p>A. A suspect case for whom testing for the COVID-19 virus is inconclusive.</p> <p>OR</p> <p>B. A suspect case for whom testing could not be performed for any reason.</p>	<p>Confirmed case A person with laboratory confirmation of COVID-19 infection, irrespective of clinical signs and symptoms.</p>	-
US CDC (March 8)	<p>Clinical criteria</p> <p>Patients who have fever and/or symptoms of lower respiratory illness (e.g., cough, shortness of breath) + test for other causes of respiratory illness (e.g., influenza)</p> <p>And</p> <p>Epidemiologic criteria</p> <p>In the last 14 days before symptom onset, have a history of travel from Wuhan City, China, Hubei Province, and even mainland China</p> <p>OR</p> <p>Close contact with a person who is under investigation for COVID-19 while that person was ill or an ill laboratory-confirmed COVID-19 patient should be evaluated</p>	-	-	-
Taiwan (10)	<p>Reporting criteria</p> <p>Have any one of the followings:</p> <ol style="list-style-type: none"> <li>1. Fulfilling clinical criteria 1 or 2 and epidemiologic criteria 1 or 2</li> <li>2. Fulfilling clinical criteria 2 and epidemiologic criteria 3 or 4</li> <li>3. Fulfilling clinical criteria 3</li> <li>4. Fulfilling the laboratory criteria</li> </ol> <p>Clinical criteria</p> <p>Have any one of the followings:</p> <ol style="list-style-type: none"> <li>1. fever (&gt;38 C) or acute respiratory infection</li> <li>2. Cough with tachypnea or respiratory difficulty</li> <li>3. Radiologically- or pathologically diagnosed pneumonia, in case of community acquired pneumonia, without history of traveling to epidemic regions, excluding possible etiologic agents, highly suspected by the clinical physician</li> </ol> <p>AND</p> <p>Epidemiologic criteria:</p> <p>History of traveling to epidemic regions, contact with a person with fever or respiratory symptoms from epidemic regions currently include China, Hong Kong, Macau, Korea, Italy, and Iran (Will be updated whenever)</p> <p>Ever intimately contact with a probable or confirmed case, including 1: provide care or stay together without adequate personal protection equipment 2: direct contact with respiratory secretion or body fluids 3: Health care workers as profession</p> <p>OR</p> <p>Laboratory criteria:</p> <p>Have any one of the followings:</p> <ol style="list-style-type: none"> <li>1. SARS-CoV-2 identified from clinical specimens (Oropharyngeal swab, sputum, or lower respiratory aspirates) by virus culture</li> <li>2. Positive result for SARS-CoV-2 from clinical specimens by nucleic acid-based detection methods</li> </ol>	<p>A case satisfied clinical criteria, though not confirmed by the laboratory tests, and had intimate contact with a symptomatic confirmed case</p>	<p>Case satisfied the laboratory criteria</p>	-

<p>National Health Commission in China (Mar 3, 2020) (11)</p>	<p>Meet one of the epidemiological criteria AND two of the clinical manifestations, OR meet all three clinical manifestations if without epidemiological history:                      1. Epidemiological history:                      (1) Travelled to or had lived in Wuhan or the surrounding areas or other communities with reported COVID-19 cases within 14 days before illness onset;                      (2) Contacted with patient(s) infected with SARS-CoV-2 (Positive for SARS-CoV-2 nucleic acid) within 14 days before onset;                      (3) Contacted patients with fever or respiratory symptoms from Wuhan or the surrounding areas, or from communities with reported COVID-19 cases, within 14 days before illness onset;                      (4) Had clustering occurrence (<math>\geq 2</math> cases with fever and/or respiratory symptoms in a small area such as a family, an office, a school class, etc., within 2 weeks).                      2. Clinical manifestations:                      (1) Fever and/or respiratory symptoms;                      (2) Pneumonia indicated by chest radiograph;                      (3) Low or normal white blood cell count, or low lymphocyte count during early onset;</p>	<p>-</p>	<p>Confirmed case: A suspected case with one of the following etiological confirmations:                      1. Respiratory or blood specimens tested positive for the nucleic acid of SARS-CoV-2 by the real-time fluorescent RT-PCR;                      2. Viruses isolated from respiratory or blood specimens showing high homology with a known SARS-CoV-2 by whole genome sequencing;                      3. Serum tested positive for SARS-CoV-2 specific IgM and IgG antibodies; the serum SARS-CoV-2-specific IgG antibody test changed from negative (Undetectable) to positive (Detectable), or the IgG antibody level is 4 times higher in the convalescent serum than in the serum collected at the acute phase of the infection.</p>	<p>-</p>
<p>City of Toronto (April 2, 2020) (12)</p>	<p>-</p>	<p>A. A person with fever (Over 38 degrees Celsius) and/or onset of (Or exacerbation of chronic) cough AND any of the following within 14 days prior to onset of illness:                      • Travel to an impacted area or                      • Close contact with a confirmed or probable case of COVID-19 Or                      • Close contact with a person with acute respiratory illness who has been to an impacted area AND                      In whom laboratory diagnosis of COVID-19 is not available, inconclusive, or negative (If specimen quality or timing is suspect</p>	<p>A person with laboratory confirmation of COVID-19 infection using a validated assay, consisting of positive nucleic acid amplification test</p>	<p>-</p>
<p>Pakistan</p>	<p>A. A patient with acute respiratory illness (fever and at least one sign/symptom of respiratory disease, e.g., cough, shortness of breath), AND a history of travel to or residence in a location reporting community transmission of COVID-19 disease during the 14 days prior to symptom onset.                      OR                      B. A patient with any acute respiratory illness</p>	<p>A. A suspect case for whom testing for the COVID-19 virus is inconclusive.                      • Inconclusive being the result of the test reported by the laboratory                      OR                      B. A suspect case for whom testing could not be performed for any reason</p>	<p>A person with laboratory confirmation of COVID-19 infection, irrespective of clinical signs and symptoms.</p>	<p>-</p>
<p>New Zealand's Ministry of Health</p>	<p>A suspect case satisfies the following clinical criteria:                      Fever (<math>\geq 38^{\circ}\text{C}</math>) AND/OR any acute respiratory infection with at least one of the following symptoms: cough, sore throat or shortness of breath                      Symptomatic close contacts of suspect or probable cases should be considered suspect cases                      Suspect cases, where they or one or more of their household/bubble, meet one or more of the following criteria should be tested:                      • People meeting the clinical criteria who have travelled overseas in the last 14 days, or have had contact, in the last 14 days, with someone else who has recently travelled overseas                      • Hospital in patients who meet the clinical criteria                      • Health care workers meeting the clinical criteria                      • Other essential workers meeting the clinical criteria if they have had close or casual contact with a probable or confirmed COVID-19 case                      • People meeting the clinical criteria who reside in (Or are being admitted into) a vulnerable communal environment including aged residential care, or large extended families in confined household/ living conditions                      • People meeting the clinical criteria who may expose a large number of contacts to infection (Including barracks, hostels, halls of residence, shelters etc.) In addition, testing may be required                      on advice from the local Medical Officer of Health, when an outbreak or cluster is suspected, or being investigated</p>	<p>A close contact of a confirmed case (Epi-link) OR a case that meets the clinical criteria where other known etiologies that fully explain the clinical presentation have been excluded and either has laboratory suggestive evidence or for whom testing for SARS-CoV-2 is inconclusive</p>	<p>A case that has laboratory definitive evidence.                      Laboratory definitive evidence requires at least one of the following:                      • Detection of SARS-CoV-2 from a clinical specimen using a validated NAAT (PCR).                      • Detection of coronavirus from a clinical specimen using pan-coronavirus NAAT (PCR) and confirmation as SARS-CoV-2 by sequencing                      Significant rise in IgG antibody level to SARS-CoV-2 between paired sera (when serological testing becomes available).</p>	<p>Under investigation case: A suspect or probable case that meets the prioritization criteria for testing above, but information is not yet available to classify it as confirmed or not a case                      Not a case                      An 'under investigation' case who has a negative test.                      Not tested                      The key principle is to reduce transmission from person to person. That means reducing the contact that people who may have the virus have with others while they are infectious</p>

<p>Australian government</p>	<p>If the patient satisfies epidemiological and clinical criteria, they are classified as a suspect case.                      Epidemiological criteria                      • Travel to (Including transit through) a country considered to pose a risk of transmission in the 14 days before the onset of illness.                      OR                      • Close or casual contact in 14 days before illness onset with a confirmed case of COVID-19.                      Clinical criteria                      Fever OR acute respiratory infection (e.g. shortness of breath or cough) with or without fever.</p>	<p>–</p>	<p>A person who tests positive to a specific SARS-CoV-2 PCR test or has the virus identified by electron microscopy or viral culture, at a reference laboratory</p>	<p>–</p>
<p>Communicable Diseases Network Australia (CDNA). (26 March 2020)</p>	<p>Clinical criteria                      Fever (<math>\geq 38^{\circ}</math> C)1 or history of fever OR acute respiratory infection (e.g. cough, shortness of breath, sore throat)                      Epidemiological criteria                      Very high risk                      • Close contact (see Contact definition below) in the 14 days prior to illness onset with a confirmed or probable case                      • International travel in the 14 days prior to illness onset                      • Cruise ship passengers and crew who have travelled in the 14 days prior to illness onset                      High risk setting                      Two or more cases of illness clinically consistent with COVID-19 (See clinical criteria) in the following settings:                      • Aged care and other residential care facilities                      • Military operational settings                      • Boarding schools                      • Correctional facilities                      • Detention centers                      • Aboriginal rural and remote communities, in consultation with the local PHU                      • Settings where COVID-19 outbreaks have occurred, in consultation with the local PHU                      • Individual patients with illness clinically consistent with COVID-19 (See clinical criteria) in a geographically localized area with elevated risk of community transmission, as defined by PHUs                      Moderate risk                      • Healthcare workers, aged or residential care workers                      Background risk                      (No epidemiological risk factors)</p>	<p>–</p>	<p>–</p>	<p>–</p>
<p>UK guideline for GPs</p>	<p>Anyone requiring hospital admission with a flu like illness, acute respiratory distress syndrome, or either clinical or radiological evidence of pneumonia. Otherwise, consider covid-19 in anyone who has either had contact with someone with confirmed covid-19 infection or returned from a high-risk country in the 14 days before the onset of symptoms if they present with any of the following:                      • Acute respiratory infection of any degree of severity, including shortness of breath (Difficult breathing in children), or cough (With or without fever), OR                      Fever with no other symptoms.</p>	<p>–</p>	<p>–</p>	<p>–</p>
<p>French surveillance system for novel coronavirus (10 January)</p>	<p>Possible case:                      Patient with a severe acute lower respiratory infection requiring admission to hospital and with a history of travel to or residence in Wuhan, China in the 14 days before symptom onset,                      OR                      A patient with an acute respiratory illness whatever the severity and with a history of at-risk exposure, mainly to a confirmed case.</p>	<p>–</p>	<p>Confirmed case:                      A possible case with a positive SARS-CoV-2 RT-PCR on respiratory samples, performed by an accredited laboratory. Testing relied on the real-time RT-PCR procedure developed by the Charité as well as on the use of real-time RT-PCR specific for the RdRp gene (Four targets) designed at Institute Pasteur (RdRp-IP).</p>	<p>–</p>
<p>European Centre for Disease Prevention and Control (2 March 2020)</p>	<p>Based on WHO case definition</p>			

To define suspected cases, different organizations combined clinical criteria, which include the most common symptoms of COVID-19 patients (i.e. fever, cough, shortness of breath), with epidemiological criteria, including a history of travel to or residence in a location with reported community transmission of disease and a history of close contact with a confirmed case. In Taiwan, case definition classification is divided into reporting, probable, and confirmed cases. Patients with one of the clinical criteria and epidemiological criteria or one laboratory criteria are classified as reporting cases (10). In New Zealand, suspected cases are prioritized based on having some criteria which they or one or more of their household/bubble have for the test (13). The communicable Diseases Network in Australia (CDNA) divided suspected cases into Very high risk, High-risk setting, Moderate risk, and Background risk based on their epidemiologic criteria.

The definition's parameters are not conclusive in the Coronavirus literature because of the lack of available data. Data on prevalence, for example, is obtained from RT-PCR positive results of testing for the coronavirus, and tests have been rationed and almost entirely have been administered to a selected population mainly patients presenting with severe symptoms or vulnerable individuals. Thus, the fraction of positive test results does not reflect the total infection rate of the population. Although these tests were made available during the outbreak, their sensitivity and specificity were unknown because there are no “gold standard” laboratory or clinical definitions for the diagnosis of COVID-19. The disease definitions developed by the World Health Organization (WHO), the US Centers for Disease Control and Prevention, European Centre for Disease Prevention and Control (ECDC) care are broadly inclusive and nonspecific.

Also, data extracted from 10 epidemiological review studies in four dimensions of person, time, place, and clinical features showed that an important parameter is the asymptomatic individual rate (The fraction of the infected who are not tested under current guidelines). Therefore, estimation lacks in the literature because tests for the coronavirus have been targeted at the sick and vulnerable. However, a number of studies suggested an estimation by a general screening of the population. Furthermore, various studies showed the susceptibility and vulnerability of people to disease based on a variety of underlying conditions such as old age, hypertension, diabetes, cardiovascular diseases, immunosuppressive diseases, and male gender.

Following is our finding based on the literature review and using the Bayesian method.

**First stage (Pretest probability)**

By reviewing existing studies the pretest probability was generated based on three criteria:

(i) The presence or absence of a history of close contact with the COVID-19 case. Based on the result of the literature review, in this study close contact include:

- Living with a confirmed COVID-19 case
- Direct contact without protective equipment or contact with bodily fluids of a confirmed covid-19 case individual
- Direct or face to face contact with a confirmed COVID-19 case individual regardless of time
- Being less than two meters away from a confirmed COVID-19 case individual for more than 15 minutes
- Referral and visit to a medical center where people with COVID-19 have been admitted.
- Health care staff dealing with COVID-19
- Being otherwise advised by a public health agency that contact with a confirmed case has occurred

(ii) The presence or absence of typical clinical syndrome which respectively includes: Fever, dry cough, myalgia, fatigue, and normal or decreased white blood cells and decreased lymphocytes at the onset of the disease

(iii) History of Living in or traveling to an area with a high incidence or prevalence of COVID-19 case (An area that accounts for more than 30% of community infections).

**Second stage (Likelihood ratio)**

Evidence suggested that two medical tests seem to be beneficial in covid-19 diagnosis which were CT-Scan of lung and RT-PCR. Based on this result these two tests could be a key parameter to achieve a better understanding of COVID-

19 case definition. To measure the validity of these two tests, several studies were identified and reviewed leading to determining their specificity (Sp) and sensitivity (Sn), consequently the “Likelihood ratio” was calculated for CT-Scan and RT-PCR. The mentioned tests likelihood ratio was figured in the following terms:

CT scan of the lung

- Positive result (+)
- Negative result (-)
- Not-performed (NP) or inconclusive results

RT-PCR test

- Positive result (+)
- Negative result (-)
- Not-performed (NP)

Post-test probability was calculated as follows (Table 2):

**Table 2.** Post-test probability scores

Variables	Sn	Sp	LR+	LR-
CT	66	80	3.3	0.41
RT-PCR	0.6	99.6	150	0.4

$$\text{Pretest odds} = \frac{\text{pretest probability}}{1 - \text{pretest probability}}$$

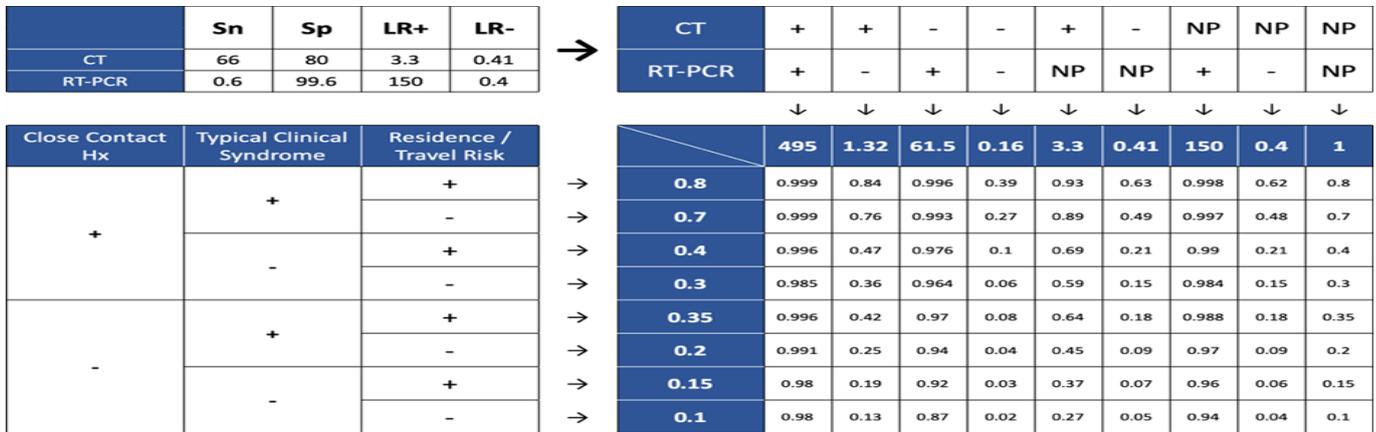
$$\text{Posttest odds} = \text{Pretest odds} \times \text{Likelihood ratio}$$

$$\text{Posttest probability} = \frac{\text{Posttest odds}}{\text{Posttest odds} + 1}$$

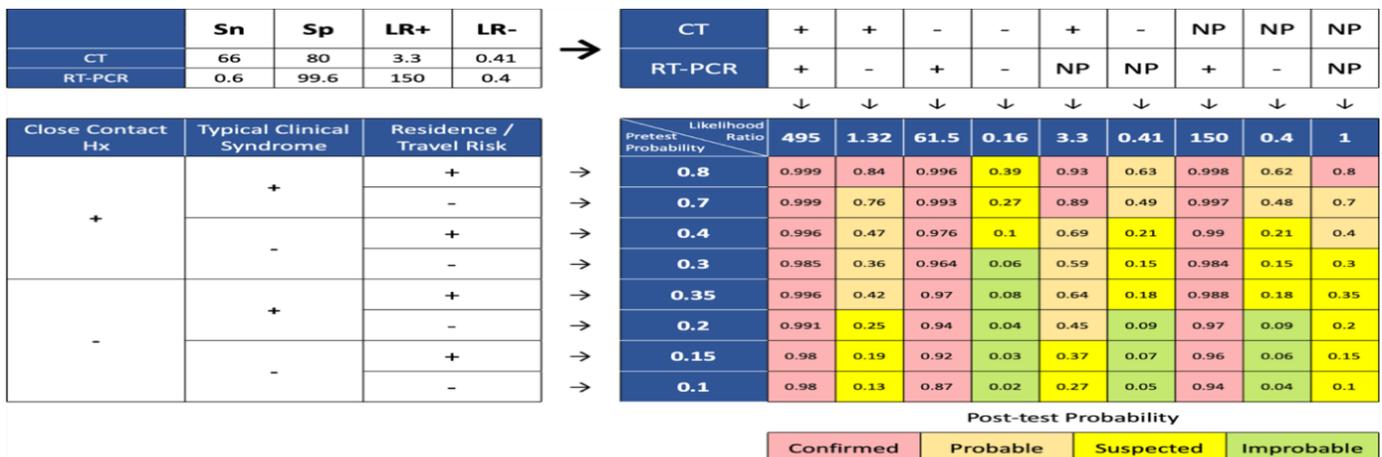
Accordingly, the simple clinical decision rule in Figure 1 will be used to determine the probability of COVID-19 infection.

**Third stage (Posttest probability):** This stage aimed to modify and update the COVID-19 case definition by using the results of previous stages. In this stage, we tried to update the initial probability estimation. The likelihood ratio calculated with Diagnostic test results and the Pretest probability based on the existing knowledge was the input for calculating the posttest probability of covid-19. Consequently, the probability of the covid-19 disease infection is classified into the following four categories (Figure 2):

- Confirmed cases (Over 80% probability)
- Probable cases (Probability between 40% and 79%)
- Suspected cases (Probable between 10% and 39%)
- Improbable cases (Less than 10% probability)



**Figure 1.** Probability of COVID-19 infection



**Figure 2.** Classification of the probability of the COVID-19 disease infection

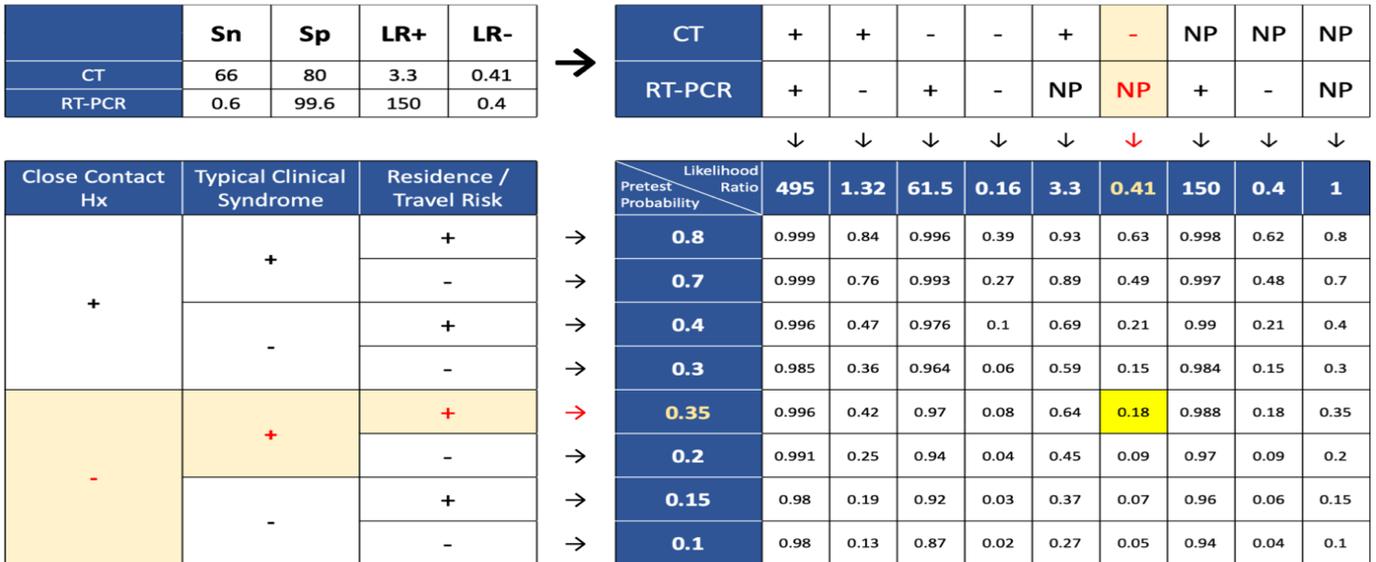


Figure 3. Post-test probability for CT (-), RT-PCR (NP), close contact (-), symptom (+), location (+)

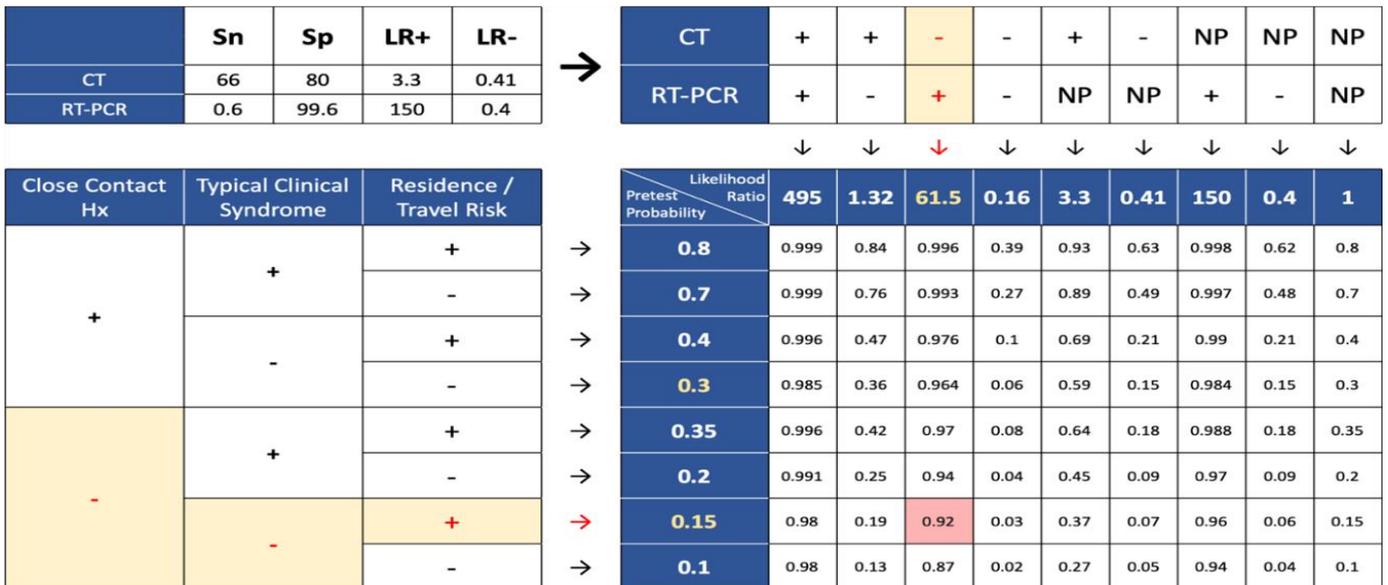


Figure 4. Post-test probability for CT (-), RT-PCR (+), close contact (-), symptom (-), location (+)

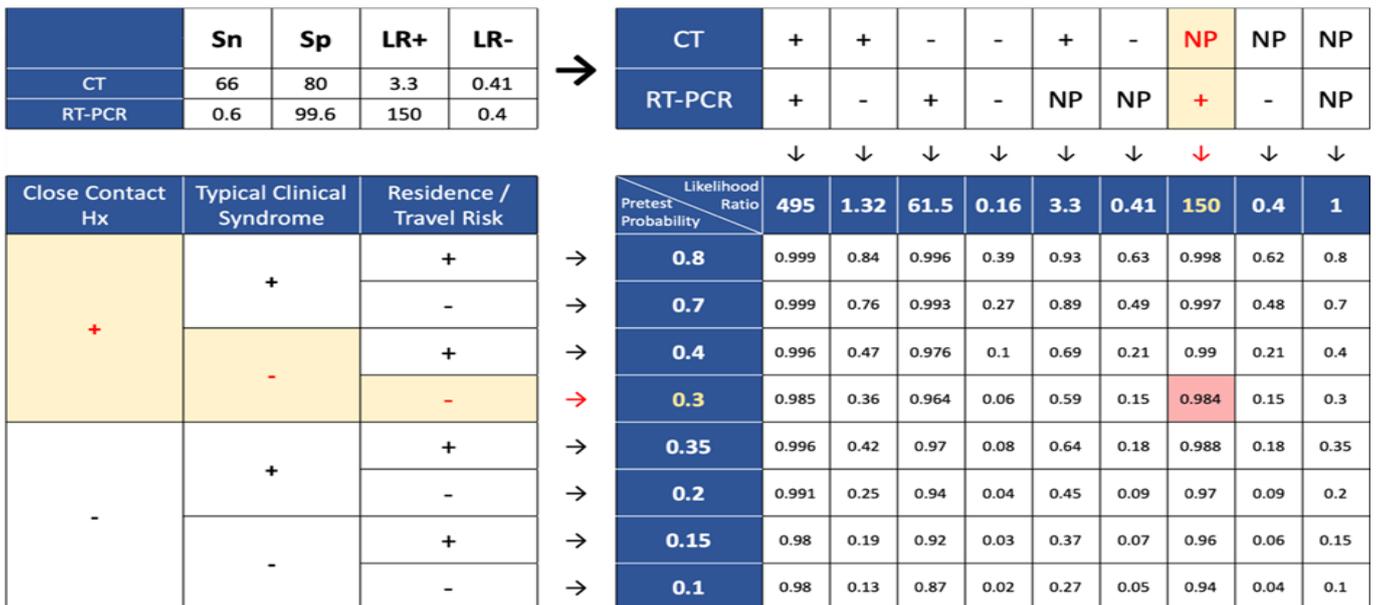


Figure 5. Post-test probability for CT (NP), RT-PCR (+), close contact (+), symptom (-), location (-)

## Discussion

Heretofore, there was no definitive treatment for COVID-19. Therefore, a robust surveillance system is necessary for monitoring infected people (14). Furthermore, to achieve early detection and isolation of COVID-19 cases, careful assessments within the surveillance system are essential at primary healthcare centers (15). An appropriate case definition can contribute to the efficient identification of infected patients (11). Health authorities in different countries should revise their case definitions based on available epidemiological information (16).

Different countries' and organizations' COVID-19 case definitions were applied clinical criteria, including the most common symptoms of the disease and epidemiological criteria, including the history of travel or residence in a location with a report of community transmission of the disease and a history of close contact with a confirmed case. Based on our results, current case definitions only categorized and tested symptomatic patients as susceptible cases. However, studies showed that most people are asymptomatic carriers of the disease. It remains a huge challenge in disease prevention (17). Especially this challenge is prevalent among people under 15 and pregnant women. The results of a study on February 17, 2020, suggested among 1732 travelers, 189 were asymptomatic patients whose tests for new coronavirus were positive. Based on the result of this study, we should consider people with a history of close contact and travel to the affected regions for performing tests. (18).

We use the Bayesian approach for creating our case definition. The first use of the Bayes approach for disease diagnosis was by Homer Warner in 1961 (19). This version of Bayes' formula is the mathematical equivalent of clinical diagnostic reasoning. We combine what we believe before doing the test with what we learn from the test to derive what we believe after doing the test. It makes use of the concepts of odds and likelihood ratio, which we define at this point. It also forms the basis for a simple pocket nomogram for rapidly working out post-test probabilities.

Based on our framework the possibility of a person from the affected region with typical clinical syndromes, normal chest CT, without a history of close contact, and in the absence of PCR test result, for COVID-19 is 18% and categorized as a suspected case (Figure 3).

Also, the possibility of a person from affected regions, without a history of close contact and disease symptoms, with normal chest CT and positive PCR for COVID-19 is 92% and categorized as a confirmed case (Figure 4).

The possibility of a person from a safe region, with history of close contact, in absence of disease symptoms, without chest CT, and with positive PCR is 98% and categorized as a confirmed case (Figure 5).

## Conclusion

Currently, multiple diagnostic tests with multiple categories and the independency of the diagnostic tests are the challenges of covid-19 case definition, which by using the Bayesian approach this challenges wares. The decision to isolate and screen cases can be made based on the probability score obtained through this technique.

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## Ethical statement

Ethical issues (Including plagiarism, informed consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc.) have been completely observed by the authors.

## Conflicts of interest

None.

## Author contributions

ShY: Conceptualization, Methodology, Writing - Original Draft, ZF: Writing - Review and Editing EK: Writing - Review and Editing, Conceptualization, Methodology. AH and HJ and AH and MHA: Writing - Review and Editing All authors read and approved the final manuscript.

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