CASE DEFINITION OF A POSSIBLE COVID-19 CASE UPDATE SEPTEMBER

RAG 28/09/2020

Context

With the start of the autumn/winter season, physicians are worried that too many people (especially children) will have to be tested for COVID, based on the current case definition used for identification of people to be tested. Therefore, an evaluation of the case definition is requested.

Current case definition

In Dutch

De volgende definitie geldt als richtlijn om personen die mogelijk COVID-19 hebben te identificeren, zodat een PCR-test kan afgenomen worden.

Mogelijk geval

Een mogelijk geval van COVID-19 is een persoon met

- minstens één van de volgende hoofdsymptomen die acuut ontstaan zijn, zonder andere duidelijke oorzaak: hoest; dyspnoe; thoracale pijn; acute anosmie of dysgeusie;
  OF
- minstens twee[1] van de volgende symptomen, zonder andere duidelijke oorzaak: koorts; spierpijn; vermoeidheid; rhinitis; keelpijn; hoofdpijn; anorexia; waterige diarree[2]; acute verwardheid[2]; plotse val[2];
  OF
- verergering van chronische respiratoire symptomen (COPD, astma, chronische hoest…), zonder andere duidelijke oorzaak.

In French

La définition suivante sert de ligne directrice pour identifier les personnes potentiellement malades de COVID-19 et guider les indications de prélèvement.

Cas possible

Un cas possible de COVID-19 est une personne avec

- au moins un des symptômes majeurs suivants d'apparition aiguë, sans autre cause évidente : toux ; dyspnée ; douleur thoracique ; anosmie ou dysgeusie ;

[1] Bij kinderen is enkel koorts zonder duidelijke oorzaak voldoende om de diagnose van COVID-19 te overwegen tijdens deze epidemie.
[2] Deze symptomen komen vaker voor bij ouderen, waar een acute infectie zich atypisch kan uiten.

OU

- au moins deux des symptômes mineurs[3] suivants, sans autre cause évidente : fièvre ; douleurs musculaires ; fatigue ; rhinite ; maux de gorge ; maux de tête ; anorexie ; diarrhée aqueuse sans cause apparente[5] ; confusion aiguë[5] ; chute soudaine sans cause apparente[4] ;

OU

- une aggravation de symptômes respiratoires chroniques (BPCO, asthme, toux chronique...), sans autre cause évidente.

Elements of discussion

- The current guideline is more or less in line with the definition used in other countries and/or recommended by ECDC/WHO/CDC. It is even less extensive, since fever is often included as only symptom for a possible COVID-19 case (ECDC, The Netherlands, UK). The list of 2 minor symptoms in Belgium is in line with the recommendation of CDC; WHO uses 3 minor symptoms as criterion. Of note is that the proposed case definition by ECDC/WHO and some countries is meant for surveillance purposes; the indication for testing is often broader. In the UK anyone presenting symptoms can be tested (unspecified) and in France anyone can be tested (although priority is given to symptomatic persons, contacts and HCWs).
- Both the literature data and the data collected in Belgium on symptomatic index cases and high risk contacts confirms that the clinical manifestation of a symptomatic COVID-19 infection is aspecific.
- Fever is not added as only symptom sufficient for testing because it is very aspecific and mostly caused by other causes.
- General practitioners and pediatricians are very worried that they will not be able to cope with the workload if the current case definition/testing strategy is continued. A big part of the burden is administrative work (e-forms, making an appointment for the test, follow-up of the results…) and giving information to patients or their contacts. They are therefore insisting on changing de case definition (more restrictive).
- The majority of patients present with minor symptoms. A part concerns also people that do not fulfill the test criteria but are worried (e.g. low risk contact) or misinterpret the definition (a runny nose alone is not an indication for testing).
- The clinical evaluation by a physician is only important for persons presenting severe symptoms.
- Testing is important because it leads to contact tracing.
- Pediatricians are in favor of limiting the test indications for children aged 6 to 12 years, similar to the current testing strategy for children < 6 years old. This could also help reducing the burden of testing, both for pediatricians as general practitioners. The strategy for testing children 6-12 can be reassessed, but therefore, more data are needed on transmission of the virus in this age group (by the end of October).

[3] Chez les enfants, la fièvre seulement sans cause apparente suffit également pour envisager le diagnostic de COVID-19 pendant l'épidémie actuelle.
[4] Ces symptômes sont plus fréquents chez les personnes âgées qui peuvent présenter une infection aiguë de manière atypique.

- Shortening the quarantine to 7 days is a new element that will increase the risk of having contagious persons in the society. Therefor it seems not the wright time to further increase that risk by less testing symptomatic people.

Recommendation

- If the current national strategy is still to limit the virus circulation and thus protect the most vulnerable population (elderly and chronically ill) and to control the hospital capacity, it is important to maintain a low threshold for testing, through a large case definition, in order to detect as much as possible cases and perform contact tracing around these persons, followed by isolation/quarantine.
- However, the implementation of this large testing strategy needs to be adapted to reduce the workload for physicians. Alternative solutions should be sought to allow easier access to testing (without clinical evaluation) and reserve clinical evaluation by a physician to severe cases. In addition, the administrative burden must be shifted and reduced to manageable proportion. Without this, broad testing will not be feasible. A possible option is the use of a self-assessment tool to evaluate the indication for testing and the severity of the symptoms. For minor symptoms, a code could then be generated for a test in a test center/street/village, without consultation by a GP. However, in this case, a solution needs also to be found then for the certificates for work incapacity (normally done by GPs).
- In addition, the communication on the case definition to the general public/ in schools should he repeated and translated into an easily understandable description. See for example the work done by the Vlaamse Wetenschappelijke Vereniging voor Jeugdgezondheidszorg : https://www.vwvj.be/sites/default/files/infectieziekten/infectieziekten_-_info_en_brieven/beslisboom_covid-19_leerlingen_lo_so_20200818.pdf.

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Background

International guidelines for clinical criteria

ECDC

Case definition for coronavirus disease 2019 (COVID-19), as of 29 May 2020. Available at: https://www.ecdc.europa.eu/en/covid-19/surveillance/case-definition

Clinical criteria
Any person with at least one of the following symptoms [1]:

- cough
- fever
- shortness of breath
- sudden onset of anosmia, ageusia or dysgeusia

[1] Additional less specific symptoms may include headache, chills, muscle pain, fatigue, vomiting and/or diarrhoea.

WHO

WHO COVID-19 Case definition, updated in Public health surveillance for COVID-19, published 7 August 2020. Available at: https://www.who.int/publications/i/item/WHO-2019-nCoV-Surveillance_Case_Definition-2020.1

Clinical criteria:

A. Acute onset of fever AND cough;
OR
Acute onset of ANY THREE OR MORE of the following signs or symptoms:
fever, cough, general weakness/fatigue, headache, myalgia, sore throat, coryza, dyspnoea, anorexia/nausea/vomiting, diarrhoea, altered mental status

B. A patient with severe acute respiratory illness (SARI: acute respiratory infection with history of fever or measured fever of ≥38 C°;and cough; with onset within the last 10 days; and requires hospitalization)

CDC

Coronavirus Disease 2019 (COVID-19) 2020 Interim Case Definition, Approved August 5, 2020. Available at: https://wwwn.cdc.gov/nndss/conditions/coronavirus-disease-2019-covid-19/case-definition/2020/08/05/

Clinical Criteria

In the absence of a more likely diagnosis:

At least two of the following symptoms:

- fever (measured or subjective),
- chills,
- rigors,
- myalgia,
- headache,
- sore throat,

- nausea or vomiting,
- diarrhea,
- fatigue,
- congestion or runny nose

OR

Any one of the following symptoms:

- cough,
- shortness of breath,
- difficulty breathing,
- new olfactory disorder,
- new taste disorder

OR

- Severe respiratory illness with at least one of the following:
    - Clinical or radiographic evidence of pneumonia,
    - Acute respiratory distress syndrome (ARDS).

Case definition in surrounding countries

THE NETHERLANDS

Extracted from '*Inhoudelijke onderbouwing t.b.v. symptomatologie COVID-19 en consequenties voor testen en maatregelen; Bijlage bij de LCI-richtlijn COVID-19 | Definitief, vastgesteld in OMT 25 mei 2020*'. Available at: https://lci.rivm.nl/onderbouwing-symptomatologie

1. Bij welke symptomen van COVID-19 wordt geadviseerd dat de Nederlander thuis moet blijven, zelf geïnitieerd of door middel van externe triage/gezondheidscheck?
Bij de volgende symptomen wordt geadviseerd dat iedereen in Nederland thuis moet blijven, op basis van de huidige wetenschappelijke literatuur en expert opinion:

Verkoudheidsklachten, zoals neusverkoudheid, loopneus, niezen, keelpijn
EN/OF
(licht) hoesten
EN/OF
Plotseling verlies van reuk- en/of smaakvermogen (zonder neusverstopping)
EN/OF
Kortademigheid/benauwdheid
EN/OF
Verhoging óf koorts boven de 38 graden

Aangezien het alleen hebben van spierpijn, vermoeidheid, anorexie/verminderde eetlust en/of hoofdpijn voor de algehele populatie waarschijnlijk te weinig specifiek is, zijn deze symptomen alleen van belang in combinatie met een van de vijf bovenstaande symptomen.

De symptomen voor thuisisolatie van het hele gezin, indien de index nog niet getest is, zullen niet veranderd worden en blijven koorts en/of benauwdheid.

2. Bij welke symptomen van COVID-19 wordt geadviseerd dat de Nederlander zich laat testen?

De bovengenoemde symptomen worden gelijkgesteld voor thuisisolatie en testen. Echter, als iemand zich meldt met van een van de overige klachten uit het gehele brede palet aan klachten van COVID-19, dan zal dit waarschijnlijk minder discriminerend zijn voor COVID-19, maar dan kan deze persoon zich ook laten testen.

3. Bij welke symptomen van COVID-19 wordt geadviseerd dat de contacten van een COVID-19-patiënt zich laten testen?

Aangezien het huidige beleid gefocust is op intensief bron- en contactonderzoek zal een contact van een COVID-19 patiënt laagdrempelig getest worden bij aanwijzingen van een van de klachten uit het gehele brede palet aan klachten van COVID-19. Daaronder wordt dus onder andere verstaan: koorts, koude rillingen, hoesten, algehele malaise, vermoeidheid, algehele pijnklachten, oculaire pijn, spierpijn, hoofdpijn, keelpijn, buikpijn, pijn bij de ademhaling, duizeligheid, neusverkoudheid, kortademigheid, schorre stem, prikkelbaarheid/verwardheid/delier, anorexie/verlies van eetlust, diarree, overgeven, misselijkheid, hyposmie/anosmie, dysgeusie/ageusie, conjuctivitis en verschillende huidafwijkingen.

FRANCE

'*Définition de cas d'infection au SARS-CoV-2 (COVID-19) - Mise à jour le 07/05/2020'*. Available at https://www.santepubliquefrance.fr/dossiers/coronavirus-covid-19/covid-19-outils-pour-les-professionnels-de-sante.

Cas possible
Toute personne présentant des signes cliniques d'infection respiratoire aiguë avec une fièvre ou une sensation de fièvre.

Depuis le mois d'août, toute personne qui le souhaite peut se faire tester sans prescription médicale. Depuis le 11 septembre 2020, une stratégie de priorisation des tests de dépistage a été mise en place. Seront testés en priorité les personnes ayant des symptômes, les cas contacts et les personnels soignants ou assimilés. Pour ces publics, des plages horaires dédiées de test vont être mises en place dans les laboratoires. https://www.gouvernement.fr/info-coronavirus/tests-et-depistage.

GERMANY

Extracted from from COVID-19 case definition fact sheet. Available at (https://www.rki.de/DE/Content/InfAZ/N/Neuartiges_Coronavirus/Falldefinition.pdf?__blob=publicationFile). Translated from German by Google translate.

Clinical picture

Specific clinical picture of a COVID-19, defined as:

- inflammation of the lungs (pneumonia)

Nonspecific clinical picture of COVID-19, defined as at least one of the following two criteria:

- acute respiratory symptoms of any severity
- ► death due to illness

UNITED KINGDOM

Case definitions: possible case, as of 18 May 2020. Available at https://www.gov.uk/government/publications/wuhan-novel-coronavirus-initial-investigation-of-possible-cases/investigation-and-initial-clinical-management-of-possible-cases-of-wuhan-novel-coronavirus-wn-cov-infection

Possible case

1. *Patients who meet the following criteria (inpatient definition)*

requiring admission to hospital (a hospital practitioner has decided that admission to hospital is required with an expectation that the patient will need to stay at least one night)
and
have either clinical or radiological evidence of pneumonia
or
acute respiratory distress syndrome
or
influenza like illness (fever ≥37.8°C and at least one of the following respiratory symptoms, which must be of acute onset: persistent cough (with or without sputum), hoarseness, nasal discharge or congestion, shortness of breath, sore throat, wheezing, sneezing
or
a loss of, or change in, normal sense of taste or smell (anosmia) in isolation or in combination with any other symptoms
Note: Clinicians should consider testing inpatients with new respiratory symptoms or fever without another cause or worsening of a pre-existing respiratory condition.

2. *Patients who meet the following criteria and are well enough to remain in the community*

new continuous cough
or
high temperature
or
a loss of, or change in, normal sense of taste or smell (anosmia)
Individuals with any of the above symptoms but who are well enough to remain in the community should follow the stay at home guidance and get tested.
Clinicians should be alert to the possibility of atypical presentations in patients who are immunocompromised.
Alternative clinical diagnoses and epidemiological risk factors should be considered.

Who can be tested

Anyone with symptoms can get a coronavirus test, whatever their age.

SUMMARY INTERNATIONAL GUIDELINES

Symptoms taken into account to define a suspected Covid-19 case

	Belgium	ECDC	WHO	CDC	Netherlands	UK
One of these	Cough Dyspnea Breast pain Anosmia Dysgeusia	Cough Fever Shortness of breath Sudden onset of anosmia, ageusia or dysgeusia	None	Cough Shortness of breath, Difficulty breathing, New olfactory disorder New taste disorder	Verkoudheidsklachten (neusverkoudheid, loopneus, niezen, keelpijn) (licht) Hoesten Plotseling verlies van reuk- en/of smaakvermogen (zonder neusverstopping) Kortademigheid/benauwdheid Verhoging óf koorts boven de 38 graden	New continuous cough High temperature Loss of, or change in, normal sense of taste or smell (anosmia)
At least two	Fever Muscular pain Fatigue Rhinitis Sore throat Headache Anorexia Watery diarrhoea Acute confusion Sudden fall		Fever Cough	Fever Chills Rigors Myalgia Headache Sore throat Nausea or vomiting Diarrhoea Fatigue Congestion or runny nose	-	-
At least three			General weakness/fatigue Headache Myalgia Sore throat Coryza Dyspnea Anorexia/nausea/ Vomiting Diarrhoea Altered mental status		-	-

Other possible symptoms		Headache Chills Muscle pain Fatigue Vomiting and/or Diarrhea				

Clinical presentation of COVID-19

Literature

Symptoms of COVID-19

Several clinical studies have documented the occurrence of different symptoms of COVID-19. A recent review of 75 original articles (including 12 RCTs) and 33 systematic reviews or meta-analyses summarised that the most common symptoms were fever (78.0–91.3%), cough (52.0–72.2%), myalgia or fatigue (16.7–51.0%), dyspnoea (10.4–45.6%), expectoration (21.3–41.8%) and chest distress (31.2%)[1]. Gastrointestinal symptoms occurred in 9.8–17.6%, with diarrhoea (7.8–10.4%), nausea or vomiting (5.5–7.7%), abdominal discomfort/pain (3.0–6.9%) and loss of appetite (11%) being the most common symptoms. Fever, dyspnoea and gastrointestinal symptoms were more common in severely-ill patients than in mildly-ill patients. Olfactory and gustatory dysfunctions were also common (47–52%). In 20% of cases the loss of smell and taste preceded other symptoms and in 28% it was concomitant. Olfactory and/or gustatory dysfunctions were significantly more present in COVID-19 patients compared to patients with acute respiratory infection without detectable virus (OR=11.26) and patients with other respiratory viruses (OR=6.46). Four of the reviewed studies found ocular symptoms, mostly conjunctivitis, in 5 to 32% of COVID-19 patients and these sometimes appeared before the onset of respiratory symptoms. Some studies and case reports mention the occurrence of cutaneous symptoms
but without presenting prevalence figures. A review of these studies reported the skin lesions to be polymorph, with erythema, chilblain-like lesions and urticarial-like lesions as the most common[2].

Predictive value of symptoms

Studies assessing the predictive value of symptoms for the differential diagnosis between COVID-19 and other respiratory infections are still rare.

A study in The Netherlands among 803 health care workers (HCWs) with mild symptoms, of which 90 had tested positive with PCR for SARS-CoV-2, found that anosmia, muscle ache, ocular pain, general malaise, headache, extreme tiredness and fever were associated with positivity[3]. A predictive model based on these symptoms showed moderate discriminative value (sensitivity: 91.2%; specificity: 55.6%). The authors considered this insufficient for presumptive diagnosis, but possibly useful in screening strategies.

An American study among people who underwent a SARS-CoV-2 test (145 participants with positive and 157 with negative testing results) identified the presence of smell or taste change, unexplained body aches and fever or chills as the best predictors of COVID-19, and shortness of breath and sore throat as the best predictors of no COVID-19[4]. A model using all 5 symptoms had a predictive ability of 82% in discriminating between COVID-19 results. A model with only change in sense of smell or taste and fever had a lower discrimination accuracy (75%), but a higher sensitivity (70%).

An American retrospective study among 592 HCWs who underwent a SARS-CoV-2 test found that anosmia/ageusia, fever, and myalgia to be the strongest independent predictors of positive assays, and the absence of symptoms or symptoms limited to nasal congestion/sore throat predictors of negative assays[5].

A study using data from the UK and the US found loss of smell and taste to be the best predictor of COVID-19 among 18,401 participants who had undergone a SARS-CoV-2 test (OR=6.74)[6]. A combination of loss of smell and taste, fatigue, persistent cough and loss of appetite resulted

in the best predictive model. In the UK test set, the prediction model had a sensitivity of 65%, a specificity of 78%, a positive predictive value of 69% and a negative predictive value of 75%. Excluding loss of smell and taste from the model resulted in reduced sensitivity (33%) but increased specificity (84%). In the US cohort sensitivity was 66%, specificity 83%, the PPV 58% and the NPV 87%.

More recent studies have confirmed the strong predictive value of olfactory dysfunction. A meta-analysis of 12 studies found a positive predictive value of 61% for a positive COVID-19 result[7].

Children

Several reviews have been done of studies documenting symptoms in children (mostly 1-18 years old)[8,9,10,11]. The consensus is that the majority of children with COVID-19 presents with either no symptoms or mild symptoms. The most commonly reported symptoms in children have been similar to those in adults, although that some symptoms, such as olfactory and gustatory dysfunctions might be less frequent. Of particular concern is the occurrence of a multisystem inflammatory condition with some features similar to those of Kawasaki disease and toxic shock syndrome in some children with COVID-19. This condition is potentially fatal, but very rare and treatable[12].

A study in France among 446 pediatric patients in 4 hospitals found that the symptoms that most increased the likelihood to have a positive SARS-CoV-2 PCR were dyspnea (positive LR, 6.6), skin involvement (positive LR, 6.3), upper respiratory tract symptoms (positive LR, 2.9), and diarrhea or vomiting (positive LR, 2.3)[13].

A review of 77 studies in infants and neonates concluded that they were more vulnerable to more severe COVID-19 disease than older children, but that morbidity and mortality were still low[14]. Another review of 26 observational studies in newborns concluded that most neonates with SARS-CoV-2 infection were asymptomatic or presented mild symptoms, and had a good prognosis, but that large epidemiological and clinical cohort studies were needed[15].

Elderly

As in other infectious diseases, COVID-19 has in elderly, vulnerable patients often a more atypical start (delirium, sudden fall, syncope, acute loss of functions), followed by more serious symptoms[16]. Typical symptoms such as fever, cough or dyspnea can be absent and the mildness of the symptoms is often in contrast with the severity of the illness[17].

Belgian data

Symptoms in people tested for SARS-CoV-2 (eForms)

The current reporting form only reports if the person for whom a test was requested was symptomatic or asymptomatic, but does not specify the symptoms. The proportion of tested people who reported to have symptoms has increased over time. Still, information on symptomatic/asymptomatic is lacking for more than half of the patients with test results. For those of which information is available, the ratio was about 50/50 symptomatic/asymptomatic in the second and third week of September 2020, both for cases who tested positive and cases who tested negative. Test positivity has increased in asymptomatic people and was mid-September only slightly lower than among symptomatic people.

Symptoms in index cases and contacts contacted by the contact tracing center

Until 07/06/2020, index cases contacted by the contact tracing center were asked about symptoms. Since then, specific symptoms are no longer asked and the person is just classified as symptomatic or asymptomatic. The most frequently reported symptoms by index cases were ‘headache’ and ‘cough’.

Among 33,605 high-risk contacts tested in the period 11/05/2020-24/09/2020, and of whom both data on symptoms and the test result were available, 7,239 (21.5%) had reported symptoms. The most common symptoms were headache (8.5%), sore throat (7.5%), running nose (6.9%) and cough (6.5%). Among contacts who tested positive, the most common symptoms were headache (20.4%), cough (17.6%) and sore throat (15.6%).

The SARS-CoV-2 positivity rate in contacts reporting symptoms was 27.5%, against 9.3% in asymptomatic people. The symptoms most predictive of COVID-19 were anosmia and fever, (see table below). The least predictive were diarrhoea, running nose, sore throat and difficult breathing.

Positivity rate by reported symptoms

Symptom	Sole symptom	% positive	One of the symptoms	% positive
Anosmia	118	61,0%	634	58,7%
Fever	148	43,9%	895	55,1%
Cough	482	27,6%	2181	35,8%
Muscle joint pain	252	19,4%	1569	37,9%
Headache	750	18,5%	2859	31,6%
Running nose	649	17,4%	2528	27,3%
Sore throat	656	14,9%	2305	26,0%
Difficult breathing	98	14,3%	618	28,0%
Diarrhoea	272	5,1%	1050	17,5%

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