

LETTERE

Public health strategies for a safe releasing of isolated persons following SARS-CoV-2 infection

Strategie di sanità pubblica per un rilascio in sicurezza delle persone isolate a seguito di un'infezione da SARS-CoV-2

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At the very beginning of the COVID-19 pandemic, on 12th January 2020, the World Health Organization (WHO) recommended that SARS-CoV-2 infected persons be discharged from isolation, regardless of isolation location or disease severity, following both clinical recovery and two sequentially negative RT-PCR swab tests performed at least 24 hours apart; on 27th May 2020, the WHO turned to a different approach, taking into consideration, for symptomatic cases, the time elapsed from the symptom onset and the symptom-free time or, for asymptomatic cases, the time elapsed after positive testing.¹

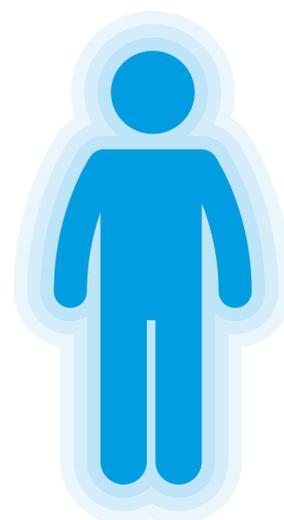
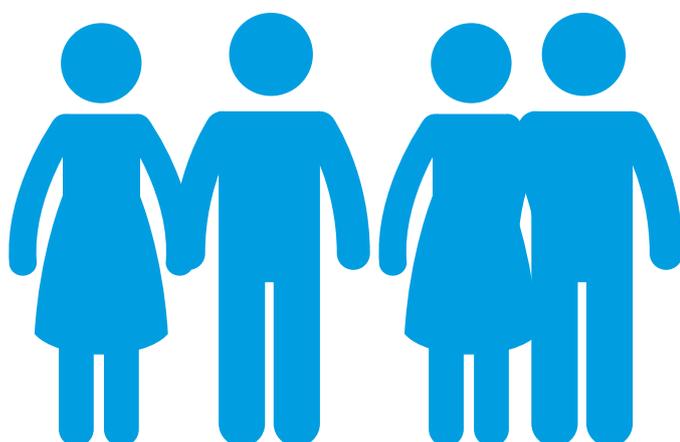
On 16th October 2020, the European Centre for Disease Prevention and Control (ECDC) emitted a technical report stating the absence of sufficient evidence for a qualified answer to the question: "What is the longest documented transmission of SARS-CoV-2 from an asymptomatic person?", and assuming a combined approach for the discharge of hospitalized COVID-19 patients, based upon clinical criteria, laboratory evidence of SARS-CoV-2 clearance in respiratory samples, and serology.²

Over the months, different national criteria have been adopted worldwide aiming at a safe release of isolated persons following SARS-CoV-2 infection (i.e., aiming at avoiding that still infectious subjects return into the communities), whilst

considering the necessity of sparing superfluous repeated tests and redundant limitations imposed to no longer infectious subjects.³ Public health strategies are continuously evolving at this regard, also under the pressure of the circulation of SARS-CoV-2 variants of concern (VOC) possibly boosting the viral loads and prolonging the viral shedding compared to the wild-type.^{4,5} The sanitary systems are challenged by emerging cases of SARS-CoV-2 infection both in previously infected⁶ and in vaccinated⁷ subjects, their management requiring to consider possible peculiarities related to the grade and the duration of infectiousness too.

The duration of infectious period of SARS-CoV-2 has been repeatedly inferred, based upon the cycle threshold (Ct) values of the semi-quantitative RT-PCR too and related to different parameters (age, time from symptom onset, symptom pattern, severity of the full-blown disease); two reviews published even in the days of July 2020 summarized the evidence at that time.^{8,9}

Starting from a now classic study (targeted on RdRp gene) published on 13th August 2020,¹⁰ a robust relationship repeatedly emerged between the Ct values of semi-quantitative RT-PCR tests (targeted on N, E, and S genes too) and the ability to recover infectious virus from the clinical specimens, this one representing a relatively rare event in the



presence of Ct values of 35 or more. Recently, in a series of 121 consecutive cases, differential kinetics of Ct values between asymptomatic SARS-CoV-2 infected subjects and mild COVID-19 patients have been clearly defined and the Ct values at the discharge of the COVID-19 patients resulted significantly higher (38 or more) in the IgG-positive subgroup in the respect of the IgG-negative subgroup.¹¹

Given the multiple uncertainties afflicting the sanitary systems in front of the evolving COVID-19 pandemic, particularly in the areas where the vaccination campaigns achieve insufficient levels of population coverage, an application of the precautionary principle appears to be mandatory when managing the isolation of SARS-CoV-2 infected subjects too. Wherever an adequate laboratory support is available, RT-PCR Ct values may represent a useful tool accompanying the time-based approaches for a safe release of isolated people following SARS-CoV-2 infection. In the daily public health practice, lower Ct values can be assumed as a reliable proxy for higher virus loads, and vice-versa. Ct values do not result from additional tests (whose viability could reveal extremely hard in scenarios of sustained viral transmission and in any case in low income countries), but only from additional records on ordinary reports when an RT-PCR has been performed. Accordingly, the discharge of asymptomatic patients from isolation just following (when possible) the evidence of a negative swab test or, at least, of a reasonably high RT-PCR Ct value (i.e., 35 or more) may constitute a prudent and sustainable public health strategy.

Conflicts of interest: none declared.

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