






ORIGINAL ARTICLE

ESTIMATED CONDITIONS TO CONTROL THE COVID-19 PANDEMIC IN PERUVIAN PRE- AND POST-QUARANTINE SCENARIOS

Charles Huamaní ^{1,2,a}, Raúl Timaná-Ruiz ^{3,b}, Jairo Pinedo ^{4,5,c}, Jhelly Pérez ^{5,d}, Luis Vásquez ^{5,e}¹ Hospital Nacional Adolfo Guevara Velasco, Cusco, Perú.² Universidad Andina del Cusco, Cusco, Perú.³ Instituto de Evaluación de Tecnologías en Salud e Investigación, EsSalud, Lima, Perú.⁴ Politécnico de Milán, Italia.⁵ Universidad Nacional Mayor de San Marcos, Lima, Perú.^a Neurologist, Master of Science in Epidemiological Research; ^b Physician specialized in Public Management; ^c Mechanical fluid Engineer; ^d Bachelor's degree in Scientific Computing, Master of Applied Mathematics with mention in Computer Science; ^e Bachelor's degree in Mathematics, Master of Applied Mathematics.

ABSTRACT

Objectives: To determine the probability of controlling the outbreak of COVID-19 in Peru, in a pre- and post-quarantine scenario using mathematical simulation models. **Materials and methods:** Outbreak simulations for the COVID-19 pandemic are performed, using stochastic equations under the following assumptions: a pre-quarantine population R_0 of 2.7 or 3.5, a post-quarantine R_0 of 1.5, 2 or 2.7, 18% or 40%, of asymptomatic positives and a maximum response capacity of 50 or 150 patients in the intensive care units. The success of isolation and contact tracing is evaluated, no other mitigation measures are included. **Results:** In the pre-quarantine stage, success in controlling more than 80% of the simulations occurred only if the isolation of positive cases was implemented from the first case, after which there was less than 40% probability of success. In post-quarantine, with 60 positive cases it is necessary to isolate them early, track all of their contacts and decrease the R_0 to 1.5 for outbreak control to be successful in more than 80% of cases. Other scenarios have a low probability of success. **Conclusions:** The control of the outbreak in Peru during pre-quarantine stage demanded requirements that were difficult to comply with, therefore quarantine was necessary; to successfully suspend it would require a significant reduction in the spread of the disease, early isolation of positives and follow-up of all contacts of positive patients.

Keywords: Coronavirus Infection; Outbreaks; Surveillance; Decision Modelling (source: MeSH NLM).

INTRODUCTION

Controlling an epidemic depends, among other factors, on the current knowledge about the disease and how this information is used in decision-making. Therefore, knowing the contagion periods, the number of people susceptible, the spread speed, among others, is necessary to predict the progression of the disease. The problem with the coronavirus disease (COVID-19) pandemic is that such new information is being generated constantly and decisions are based on highly uncertain assumptions ⁽¹⁾.

Once the epidemic in China was first reported, preventive measures took several weeks to be established worldwide. In Peru, social distancing was implemented once the first cases were detected ⁽²⁾. Other mitigation measures followed, but due to their low effectiveness, the Government was forced to decree national quarantine on March 16, 2020. These measures (mitigation and suppression strategies) were possibly implemented based on the recommendation of experts who generated mathematical models to simulate the impact of the epidemic ⁽³⁾. However, when the national quarantine was decreed, some local groups rejected the idea.

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Correspondence to: Charles Augusto Huamani Saldaña; Av. Arriba Perú 1154, Lima 42, Perú; huamani.ca@gmail.com

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Mitigation and suppression measures proposed by the Government of Peru required citizen participation; nonetheless, there have been societal difficulties in complying with these. Other measures directed towards the health sector included increasing the number of hospital beds and health personnel, as well as the timely detection of people with COVID-19. Early diagnosis is intended to promote isolation in order to cut off the spread of disease and carry out contact tracing. Our study aims to determine the probability of controlling the COVID-19 outbreak in Peru, in a pre- and post-quarantine scenario with mathematical simulation models, and without the effect of social mitigation measures. Considering only the isolation of positive cases and the tracing of their contacts, in scenarios with greater or lesser supply of beds in intensive care units (ICU).

MATERIALS AND METHODS

The Centre for Mathematical Modelling of Infectious Diseases at the London School of Hygiene & Tropical Medicine (4) designed a model available for free download in the Rproject software, based on the disease assumptions known up to 5 February 2020 (Table 1).

Stochastic differential equations

The study designed by Hellewel *et al.* (4) was based on a mathematical model which originated from stochastic differential equations, and has the following modeling concepts.

If $x_{(t)}$ is the number of infected persons in a day, the equation in linear stochastic difference associated with $x_{(t)}$ is described in Figure 1, where $p+q=1$. When in contact with an infected person; p represents the probability of a person becoming infected, while q is the probability of not becoming infected.

This is one way of explaining the speed of the virus' spread which is usually done using the R_0 (basic reproductive number). That being said, the sequence for the number of new infections per day would be:

KEY MESSAGES

Motivation for the study: Mathematical modeling at the beginning of the COVID-19 pandemic was carried out to estimate the number of cases, but not the conditions for starting or suspending quarantine.

Main findings: The COVID-19 pandemic would only have been controlled if all patients were detected and isolated from the start. To be successful in controlling the post-quarantine pandemic, the spread of the virus must be significantly reduced, all cases must continue to be isolated, and the percentage of contacts traced must be close to 100%.

Implications: Control of the pandemic is not possible without slowing the spread of the disease. This is a matter of a societal nature. In the health sector, it is necessary to identify all cases, isolate them and trace their contacts. Scenarios with less active participation have a high probability of failure.

$$1; 2 * p; 4 * p^2; 8 * p^3; 16 * p^4; 32 * p^5$$

x_1 = Infected at the beginning

$x_2=R_0 p x_1$

$x_3=R_0^2 p^2 x_1$

$x_4=R_0^3 p^3 x_1$

$x_{(t+1)}=R_0^t p^t x_1$

Infected at the beginning

Among other variables, the R_0 varies according to the disease, the mechanism of contagion, and the population interaction (5). There are several R_0 estimates for the COVID-19 epidemic, some studies indicate that it varies from 3.5 in person-to-person contact, or 2.5 in person-to-reservoir/fomite contact (6). R_0 variability ranges from 1.4 to 6.5 (7,8), with a median of 2.7. When this study concluded, a Peruvian R_0 was not yet available neither for the pre-quarantine or quarantine stage.

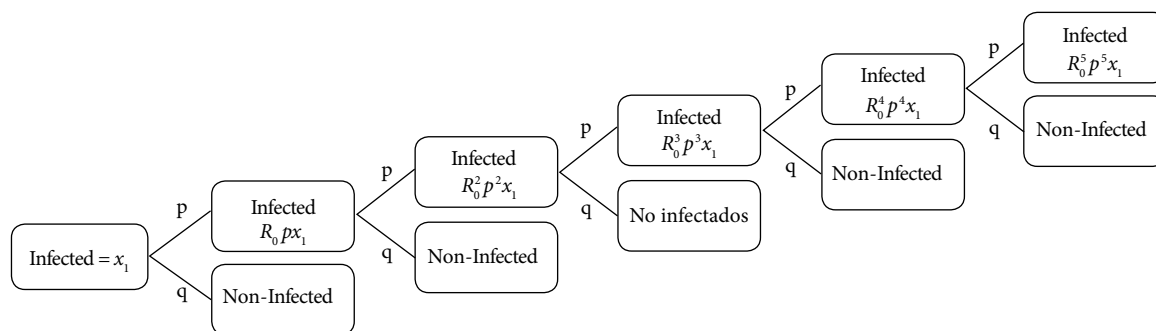


Figure 1. Disease spread according to the probabilities established in the stochastic difference equation model

Assumptions for mathematical modeling

The study by Hellewell *et al.* ⁽⁴⁾ used the following assumptions for its mathematical modeling: 1) if a positive case was detected, it was sent into early isolation for 3.43 days; 2) the incubation period of the disease was 5.8 days; 3) the R0 was 2.5 in the community and 0 in isolation; 4) the percentage of subclinical infected cases was 0%; and 5) most importantly, they defined success in controlling an outbreak if the spread did not exceed 5,000 cases. These assumptions were tested in scenarios where positive case isolation measures were initiated after 5, 10 or 20 cases had been detected.

We updated the disease behavior data according to the new information available. While the spread of the disease and the response of the health system are variables. In Peru we do not have any data on this matter, so we carried out the modeling based on the following assumptions:

Pre-quarantine scenario: In which the R0 would be 2.7 and 3.5. The R0 of 2.7 corresponds to the median of the R0 values calculated from 12 studies ⁽⁷⁾. Nonetheless, a second R0 of 3.5 was posed ⁽⁶⁾, which would correspond to an adverse scenario. In this adverse scenario, the positive case isolation measures and the contact follow-up, are assumed to begin with 1, 5 or 10 cases. Higher values for R0 are not assumed, due to the fact that in such models, control of the outbreak would be unsustainable.

Post-quarantine scenario: A scenario where the R0 could be 1.5, 2.0 or 2.7. Starts with a R0 value of 1.5 because it would be the best-case scenario after quarantine (assuming that the learned and reinforced behaviors in quarantine will diminish the interaction with the decrease in the spread dynamic). Another modeling with a R0 of 2.7 was made, which would be the starting scenario with no learning from the pandemic. In the latter modelling it is assumed that the quarantine is lifted when 20, 40 or 60 cases are registered per day.

The percentage of patients with subclinical infection was modified in both scenarios, the current being 18 ⁽⁹⁾. This information originates from what happened at the Diamond Princess Cruise, which was kept quarantined and tested every passenger. In a real scenario, the subclinical or asymptomatic infected cases would not be tracked, and could continue to spread the disease. On the other hand, symptomatic cases would spread the disease until being isolated. A second analysis is carried out, with 40% asymptomatic cases ⁽¹⁰⁾, which corresponds to a pretty bad asymptomatic infection scenario.

The incubation time estimates for the disease ($5,8 \pm 2,6$ days) were maintained ⁽¹¹⁾, as well as the fact that 15% of the

contagion occurred before the symptom onset, and the assumption that isolation decreases the R0 to 0.

The duration of the time to isolation was chosen based on findings from the severe acute respiratory syndrome (SARS-CoV) pandemic and from the initial stage of the COVID-19 pandemic, both of these measures were used in the original study. The time to isolation in the SARS-CoV 2003 outbreak was of 3.43 days (2.02-5.23) ⁽¹²⁾ and it is referred to as "early isolation". During the initial stage of the COVID-19 pandemic the time to isolation was of 8.09 days (5.52-10.93) ⁽⁴⁾ and is referred to as "late isolation". Given that the first case in Peru was isolated 10 days after being reported, baseline calculations are made considering "late isolation". In the post-quarantine analysis, "early isolation" is considered, as it is assumed that the epidemiological surveillance and control measures were improved, thus reducing the delay.

Finally, "outbreak control" was defined as the absence of new infections from 12 to 16 weeks after detecting the initial cases. The original study assumed that outbreaks reaching over 5,000 cumulative cases were too large to be controlled. However, this European assumption does not reflect the case-resolving capacity of Peru, where there are a limited number of ICU beds for management of patients with COVID-19.

The original study based the outbreak control on the maximum number of cases detected, we made the modeling considering the maximum number of beds in the ICU required, in scenarios where there are 50 or 150 beds in the pre-quarantine stage, and 150 beds in the post-quarantine stage. The modeling

Table 1. Assumptions used in mathematical modeling

Concept	Values	Reference
Patients with subclinical infection	18% and 40%	Mizumoto ⁽⁹⁾ , Nishiura ⁽¹⁰⁾
Incubation time (days)	5.8 ± 2.6	Li ⁽¹¹⁾
Isolation time (days)		
Early	3.43 (2.02-5.23)	Donnelly ⁽¹²⁾
Late	8.09 (5.52-10.93)	Hellewell ⁽⁴⁾
R0		
Pre-quarantine	2.7 and 3.5	Liu ⁽⁷⁾ , Chen ⁽⁶⁾
Post-quarantine	1.5, 2.0 and 2.7	
Number of ICU beds	50 or 150	Assumed
Initial number of cases		
Pre-quarantine	1, 5 or 10	Assumed
Post-quarantine	20, 40 or 60	

R0: basic reproductive number; ICU: intensive care unit

with 50 beds is done to try to reflect what could happen in provinces or cities other than Lima, with less case-resolving capacity.

RESULTS

Pre-quarantine scenario

Two scenarios are proposed according to the propagation dynamics, considering that the basal R_0 is of 2.7 and the unfavorable R_0 is of 3.5 (Figure 2).

In the baseline scenario, if measures are implemented from the first case onward, the probability of success in controlling the outbreak is close to 80%, even without the need for contact tracing. If isolation measures are implemented when there are already 5 cases detected, 100% of the contacts should be traced to obtain a success rate of 40%. Implementing measures when there are more than 10 cases detected, in all scenarios, shows a probability of success in controlling the outbreak of less than 20%. The effect from the asymptomatic people percentage barely changes the outbreak control scenarios when measures are implemented from the first case detected.

In the worst-case scenario ($R_0=3.5$), if measures are implemented from the first case onward, isolation measures by themselves would be enough to obtain a success rate of at least 60% in controlling the outbreak. Contact tracing increases the probability of success in controlling the outbreak up to 80%. But, if isolation measures are implemented when there are 5 or 10 cases detected, success rate decreases to less than 40%, even when tracing 100% of the contacts.

Post-quarantine scenario

It is assumed that when quarantine ends the R_0 decreases to 1.5, 2 or 2.7 in the worst-case scenario, furthermore, the assumption of "late isolation" could be updated and changed to "early isolation".

From all of the scenarios shown in Figure 3, the one with a success rate of 80% is the one that integrates early isolation of positive cases, 100% of contacts traced, and a R_0 of 1.5; regardless if the quarantine ends with 20, 40 or 60 cases (Figure 3).

In a more conservative scenario, where the R_0 decreases to 2, quarantine could end with 20 positive cases; but 100% of contacts traced should be guaranteed to obtain approximately a success rate of 60% in controlling the outbreak.

If early isolation of positive patients is not yet achieved, there would still be a 60% chance of success in controlling the outbreak if the R_0 decreases to 1.5 and quarantine ends with 20 positive cases and 100% of contacts traced.

DISCUSSION

Public health decisions are recommended to be based on evidence and to have technical support. At the onset of the COVID-19 pandemic, information was either absent or uncertain⁽¹⁾, so several initiatives emerged to provide epidemiological and clinical information to help make better decisions. In this studies, mathematical modeling was used to simulate scenarios that predict the pandemic development to be able to make decisions ahead of time^(13,14). We decided to show part of a scenario that is still under development. This scenario evaluates, in an isolated way, the effectiveness of epidemiological surveillance by identifying cases, isolating them and tracing their contacts. All of this depends on the health system logistics, so these would be scenarios where social participation would only be reflected in the R_0 variation.

In Peru, although the first positive case was isolated and the contacts were traced, the process of identification and isolation of the case was late. In the ideal scenario of "early isolation" from the first positive case, a low percentage of contacts traced would have been required. But that ideal scenario would have involved a more rigorous migration control from the beginning and having the correct control of all possible suspects and their subsequent follow-up. Changing the scenario to five cases to implement the isolation or tracing of cases can be interpreted as if the detection measures were surpassed and five cases went undiagnosed, in this scenario the probability of controlling the outbreak would be less than 40%. Perhaps that is why countries such as Russia and South Korea, both of which took very quick but different decisions, such as closing borders or strictly monitoring confirmed and suspected cases^(15,16), have had better results in controlling the pandemic.

European models about propagation dynamics represented by the R_0 could not be applied to Peru, because it has greater social interaction and low healthcare case-resolving capacity. This is why a greater number of cases for a reduced supply of ICU beds is expected, therefore, the main objective would be to minimize the number of cases that require mechanical ventilation⁽¹⁷⁾. Taking action with only a few cases detected could seem less important. Nonetheless, late decision-making has a low probability of success in controlling the outbreak, even at 20 cases. In this context, from a mathematical modeling perspective, a measure of mandatory social isolation such as quarantine was the only option for timely control of the epidemic⁽¹⁸⁾, a measure that was finally adopted in Peru⁽¹⁹⁾. Since this scenario is similar to several other countries with high social interaction and low case-re-

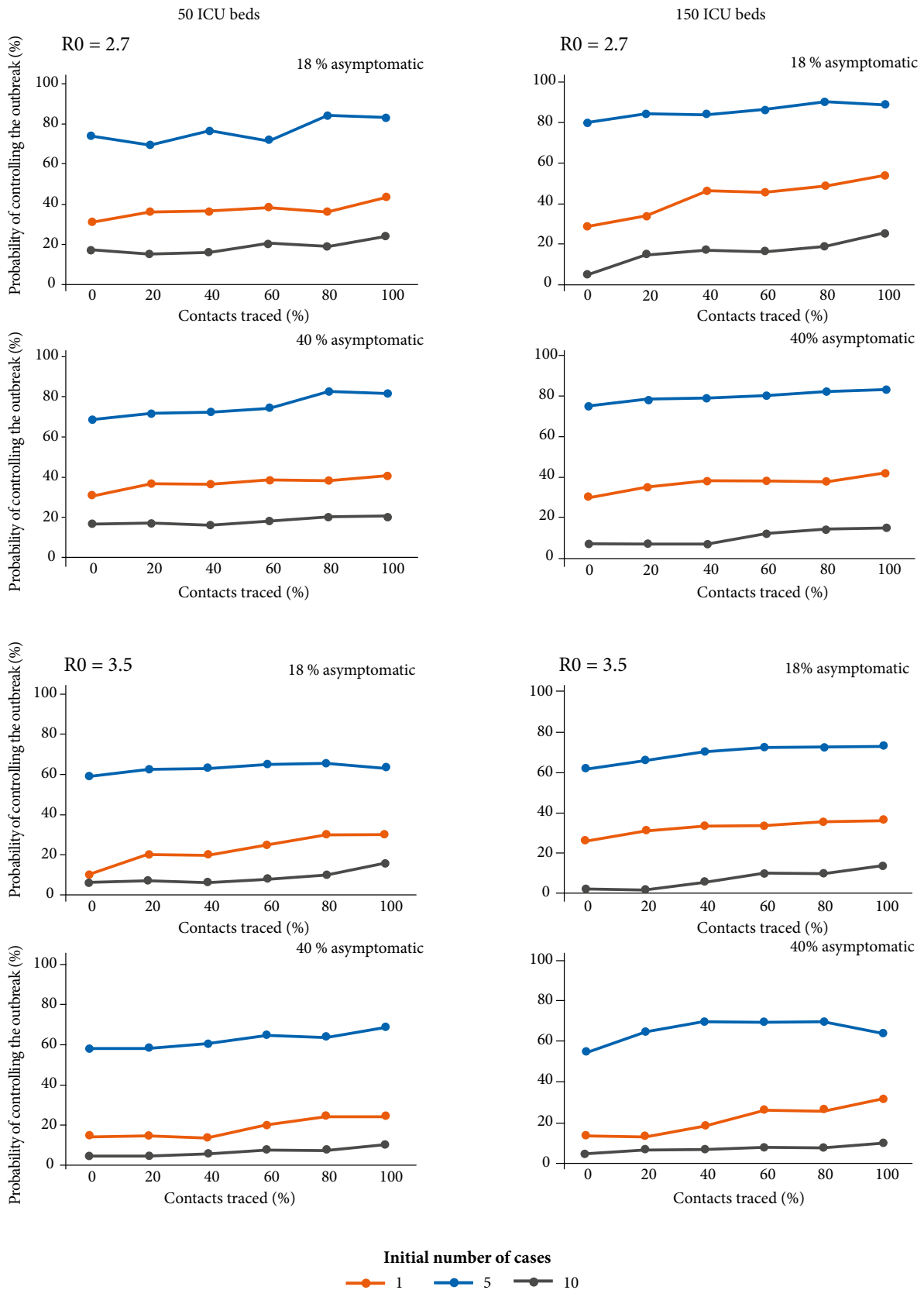


Figure 2. Probability of controlling simulated outbreaks according to different numbers of initial cases, different propagation scenarios (R_0) and with different proportions of asymptomatic cases. The R_0 used represents an ordinary ($R_0=2.7$) or unfavorable ($R_0=3.5$) scenario for Peru. Both scenarios are performed considering late isolation for positive cases (average 8.1 days), and 15% transmission before the onset of symptoms.

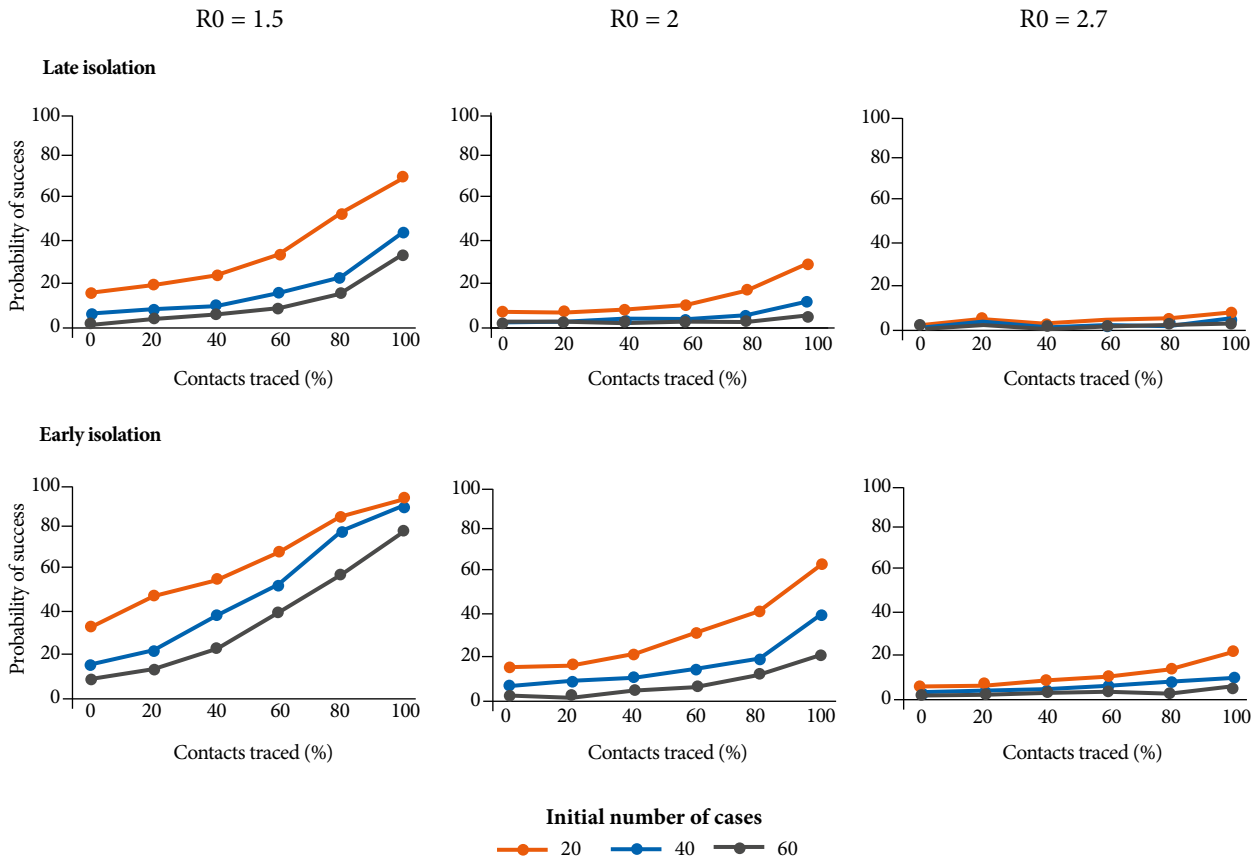


Figure 3. Probability of success in controlling the outbreak in different scenarios, starting with 20, 40 or 60 cases. In this differentiated propagation scenarios (R0), the percentage of asymptomatic people is 18%. It is differentiated according to early (average 3.4 days) or late isolation (average 8.1 days)

solving capacity ⁽²⁰⁾, quarantine in countries like ours would be the only viable way to control the epidemic.

However, several questions remain. When is the right time to lift the quarantine or what conditions must be met to lift the quarantine? It is foreseeable that after quarantine ends many people will increase their social interaction disproportionately; if the control measures are decreased, it is possible that the post-quarantine R0 could be higher than pre-quarantine. In this case, the pandemic re-emergence would be uncontrollable, since it would no longer be based on one case, but on many more, as shown by some simulations in other contexts ⁽²¹⁾. What happened in China is a very instructive example, in this case the epidemic mitigation measures have not been lifted in a drastic, immediate manner, but rather gradually ^(22,23).

A very optimistic scenario is one where social interaction is reduced and accordingly the capacity of contagion decreases with R0 values of 1.5 or even less, this could be interpreted as a high probability of controlling of the epidemic

post-quarantine. However, this optimistic scenario is not likely to take place, as it implies reducing social interaction and increasing case-resolving capacity in just a few weeks. In a more conservative scenario, where the R0 is 2, if we interrupt quarantine with 20 positive cases, we would need to track all contacts and early isolate people who test positive for COVID-19.

Therefore, it is understood that measures taken after quarantine will result in the control of the epidemic, or in the failure of the health system and the epidemic re-emergence. Everything will depend on how much the value of the post-quarantine R0 decreases. In the conservative scenario, aggressive case and contact identification measures, border closure, home and hospital isolation, identification and quarantine of high-risk populations, and measures for mass events assessment may not increase the R0 after quarantine ⁽²⁴⁾.

This analysis has several limitations, for example, it is based on a mathematical model that assumes that the disease spreads in a single closed society. On the contrary, Peru is divided into

several regions that can be isolated from each other and thus, each one can have a different type of propagation dynamics. For each region, different problems arise when implementing and executing the control measures in a differentiated manner, which could generate confusion and inadequate preparation for the epidemic. Another limitation of this study is that it is based on assumptions that may not actually be verified, such as the number of cases. Without a mass screening test, the number of infected cases may not be accurate; however, such approximation can be determined by evaluating trends in epidemiological curves. This study recommends adequate logistics to guarantee effective contact tracing. This type of logistics varies in the case of a symptomatic or a non-symptomatic contact. Due to the lack of resources to guarantee such a measure, this is considered a limitation. Finally, the spread dynamics of COVID-19 in Peru is unknown, although the necessary calculations could be made. However, given the high level of under-report of COVID-19 cases, we would obtain an underestimated result. This is why we need to refer to values described in other studies.

The results are intended to be applicable to Peru, but are relevant for any region or country with similar case-resolving

capacity, because the starting point is considering the maximum number of cases that can be supported and not the amount of affected population. Therefore, a region or country with less than 150 ICU beds will have to take more restrictive measures if it estimates to have over 3,000 cases. Likewise, the post-quarantine scenario we modeled could be equivalent to a pre-quarantine scenario in places with a late response.

In conclusion, social isolation of positive cases and contact tracing required many assumptions that were quickly exceeded, and if appropriate measures had not been taken, the probability of failing to control the epidemic would have been high. Our results justify the decision of implementing quarantine. The concern lies in the scenarios for the end of the quarantine. It is imperative that low social interaction is promoted in a sustained manner to avoid a new post-quarantine outbreak, as well as to continue with social isolation and the tracing of contacts of patients with COVID-19. Only then could there be a high probability of controlling the pandemic. In scenarios where mitigation measures are loosened and the spread of the disease returns to “normal” the probability of failure to control the pandemic is very high.

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