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How will we know if the Enhanced Community Quarantine (ECQ) has been effective?

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Executive Summary

The objective of this briefer is then to provide a protocol for measuring the effectiveness of the ECQ and to guide decision-makers on how to move forward while balancing both the societal costs and health benefits of the interventions. A scoping review was done to achieve this.

Recommendations

- **A pre- and posttest quasi-experimental design can be undertaken** to determine the effectiveness of the ECQ, a social distancing intervention.
- **Any one of three or a combination of the following indicators can be measured.** Data for these indicators are already currently being collected by the DOH.
    - Number of confirmed cases
    - Proportion of critical care unit (CCU) beds per 100,000 population that are occupied (on a per province basis but with NCR taken a single unit)
    - Number of deaths
- **Measurement of the effect should be taken only after the latent period for the ECQ to act has elapsed.** This latent period depends on the indicator chosen.
- **Measurement should be taken at the subnational level** so that the withdrawal of the ECQ can be staged according to the outbreak stage each LGU is in.
- **The decision to lift or to impose ECQ, using the above indicators, can be based on reduction of the effective reproduction number, R(t) < 1.** This can be computed from surveillance data.

Introduction

Last March 16, 2020, the entire region of Luzon was placed under the “enhanced community quarantine (ECQ)” in the recommendation of the IATF. This policy enforced a total lockdown, with minimal to no movement for the whole population except for frontliners, businesses involved in essential services and products, and household representatives purchasing essential goods. As of writing (March 29, 2020), the ECQ has already been implemented for almost two weeks. However by looking at the epidemic curve, more new cases were detected after implementation. The 7-day moving average or the average of the reported cases for the past 7 days until March 28 shows that we have around 100 new cases each day.[1] These are based on dates of test reporting.

[1] EpiMetrics COVID-19 Dashboard (Accessed March 29, 2020)

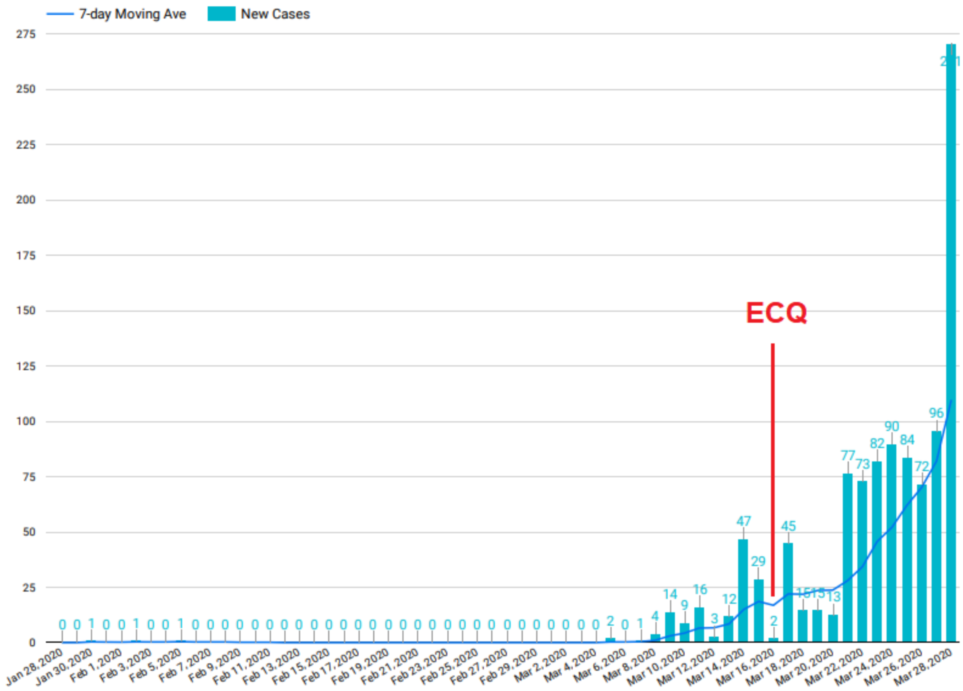

Figure 1. Epidemic Curve Based on Lab Confirmation (New Cases and 7-day moving average)

ECQ is one of the most common non-pharmaceutical interventions in controlling an outbreak. The restriction of movement delays the transmission of an infectious disease, inducing a lag time for health systems to respond to the growing number of cases. Nonetheless, such intervention takes a toll on the populations they are applied to. In a systematic review of literature on the psychological effects of quarantine and isolation for infection prevention, a high burden of mental health problems were found among individuals and populations who underwent such interventions. Psychosocial stressors that arise from restricted mobility and interactions were seen to contribute to long-term depression, PTSD, fear, stigmatization, anxiety, and other mental health disorders.[2]

According to the National Economic and Development Authority in the Philippines, ECQ is expected to result in a loss of gross value added of PHP298 billion to PHP1.1 trillion, equivalent to 1.5 to 5.3 percent of GDP and reduce employment by 61,000 to 1Million. At the start of the outbreak, it is also expected that the population in higher social standing will be directly affected due to the restriction on travel. However, social impact on the lower income classes will be from the containment measures undertaken. NEDA highlighted the need to balance the health benefits of the interventions with economic impact on the different socioeconomic classes.[3]

A recent study shows that containment mechanisms need to be implemented long-term (3 to 6 months) to ensure maximum benefits. However due to adverse concomitant effects of implementing such, an adaptive policy was explored. This means that a threshold can be set to act as a switch on when to enforce and lift containment measures. In the study, the number of critical care beds utilized served as the trigger.[4]

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[2] Hossain, Md Mahbub, Abida Sultana, and Neetu Purohit. "Mental health outcomes of quarantine and isolation for infection prevention: A systematic umbrella review of the global evidence." (2020).
[3] Addressing the Social and Economic Impact of COVID-19 Pandemic (NEDA, 2020)
[4] Ferguson, N., Daniel Laydon, Gemma Nedjati Gilani, Natsuko Imai, Kylie Ainslie, Marc Baguelin, Sangeeta Bhatia et al. "Report 9: Impact of non-pharmaceutical interventions (NPIs) to reduce COVID19 mortality and healthcare demand." (2020).

Methodology

A scoping review was done to provide a protocol for measuring the effectiveness of the ECQ and to guide decision-makers on how to move forward while balancing both the societal costs and health benefits of the interventions.

Results & Discussion

a. The evaluation of the expected effect of interventions applied during an ECQ is highlighted by several studies. A summary table of relevant literature is provided in the Appendix.
b. What requirements should the assessment's study design satisfy?[5] [6]
    i. The reasoning behind the causal mechanism and its link to the study design should be understandable .
    ii. The predicted event is clearly defined - The government should define what they would consider as the 'effect' of the ECQ. Do they value minimizing the number of infected cases (even though 80% of cases are mild) or do they value minimizing the severe cases such as patients on CCU beds (a better measure of health system capacity).
    iii. Temporal and spatial applicability is described
        1. There should be recognition of a latent period (from application of the ECQ to the onset of its action) before commencing the measurement of its effectiveness.
        2. Since ECQ has to be applied in successive on-and-off cycles until vaccine development, the outcome will need to be measured continuously and regularly in order to detect both on- and off-signals. There is already evidence from the 1918 pandemic that in the absence of a vaccine, social distancing policies have to be applied in on-and-off cycles until herd immunity, whether active or passive, develops.[7] [8] Thus, we should expect to apply ECQ in successive cycles until a vaccine is developed in 18-24 months.[9]
        3. The effect measure needs to be disaggregated into NCR and into individual provinces. Instead of a single outbreak, we are having unsynchronized outbreaks in different local government units (LGUs). Figure 2 below shows that the outbreaks started on different dates in the NCR and in each province. It also shows that the magnitude of the outbreaks and the trajectories are different among LGUs. Steeper lines represent faster doubling times.

[5] Nsoesie, Elaine O., John S. Brownstein, Naren Ramakrishnan, and Madhav V. Marathe. "A systematic review of studies on forecasting the dynamics of influenza outbreaks." Influenza and other respiratory viruses 8, no. 3 (2014): 309-316.
[6] The Ethics of Modeling
[7] Hatchett, Richard J., Carter E. Mecher, and Marc Lipsitch. "Public health interventions and epidemic intensity during the 1918 influenza pandemic." Proceedings of the National Academy of Sciences 104, no. 18 (2007): 7582-7587.. Accessed 23 Mar. 2020.
[8] Markel, Howard, Harvey B. Lipman, J. Alexander Navarro, Alexandra Sloan, Joseph R. Michalsen, Alexandra Minna Stern, and Martin S. Cetron. "Nonpharmaceutical interventions implemented by US cities during the 1918-1919 influenza pandemic." Jama 298, no. 6 (2007): 644-654.. Accessed March 23, 2020.
[9] Coronavirus vaccine: when will it be ready? | World news

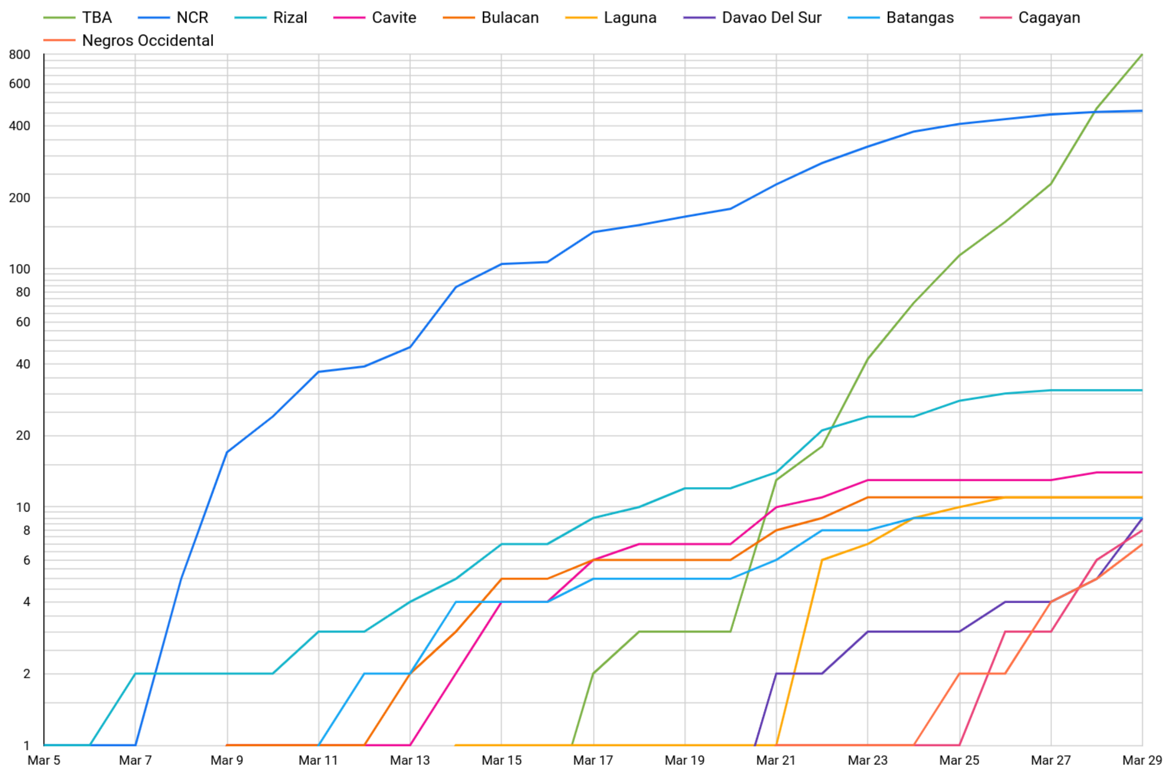

Figure 2. Epidemic curves across LGUs

iv. Assumptions are transparent
   1. There should be an attempt to present all the values contributing to the computation of the predicted event and a delineation of which are data-based and which are assumptions.
   2. Rationale for the assumptions should be explained.
   3. Sensitivity analysis of the assumptions should be performed.

v. Uncertainty is quantified and highlighted
   1. Confidence and/or uncertainty intervals around the point estimates should be presented and explained,
   2. The restrictions and limitations of the estimates should be explained.

vi. Unintended adverse consequences of the treatment, i.e., the ECQ, should also be considered, measured, and integrated into the evaluation. Negative consequences need to be weighed against the positive consequences.

c. What do we measure?

i. Who or what to count
   1. The government should make a choice as to its value preferences for different outcome indicators.
   2. As a social distancing measure, the ECQ's effect on the reproduction number, R, is on the contact rate or **K**. It separates the asymptomatic infected from the susceptible in the population.[10] There will be multiple effects of this intervention along a causal chain from case confirmation to death.
   3. The options for outcome indicator is compared in the Table 1 below.

[10] This is in contrast to the effect of other measures:
a. Transmission rate or **B** - hand hygiene, cough etiquette, frequent coughing
b. Duration of infectiousness or **D** - reducing the symptom to isolation interval

Table 1. Comparison of outcome indicators for measuring ECQ effectiveness.

Indicator	Advantages	Disadvantages
Number of confirmed cases	Measure of the magnitude of the outbreak	• 80% of cases are mild and will require only minimal health system resources • Mean number of days from symptom onset to lab confirmation is 10 days • Influenced by number of tests conducted
Proportion of CCU beds[11] per 100,000 population that are occupied (per geographical unit)	• Direct measure of the magnitude of health system strain • Addresses the public's anxiety	Mean number of days from symptom onset to hospitalization is 9 days[12]
Number of deaths	• Sensitive measure of the severity of the outbreak • Relatively insensitive to number of tests • Addresses the public's anxiety	Lagging indicator - duration from hospitalization to death is ___.

ii. Where?

1. The indicator selected above should be measured separately for each geographical unit. Based on the transportation network, these units should probably be:
    a. The whole NCR should be treated as one unit
    b. Each province should be treated as one unit
2. Each LGU should respond in proportion to its stage in the outbreak, e.g., no cases, single imported case, single local case, multiple cases, etc.[13] Instead of one national COVID 19 outbreak, we have a series of unsynchronized subnational outbreaks. See Figure 2 above.

iii. When do we measure it?

1. Depending on the indicator selected, the date on which to start measuring it will differ. There is a latent period during which the ECQ intervention will still be building up its effect. The measurement start date should start at the end of this indicator-specific latent period.
2. In addition, sufficient time should be given for the effect to be observed and analyzed. For example, if interrupted time series (ITS) analysis were to be done, the median number of observations would be 18 to 19 days pre- and post-intervention.[14]
3. Table 2 and Figure 3 below shows the different measurement start dates for three different indicators.

[11] Or some other medical countermeasure that is in short supply, i.e., ventilators
[12] Management of Patients with Confirmed 2019-nCoV (CDC)
[13] Updated Preparedness and Response Framework for Influenza Pandemics (CDC)
[14] Hudson, Jemma, Shona Fielding, and Craig R. Ramsay. "Methodology and reporting characteristics of studies using interrupted time series design in healthcare." BMC medical research methodology 19, no. 1 (2019): 137.

Table 2. Measurement start dates for each indicator

Interval	Definition	Mean or Median (days)	Minimum (days)	Maximum (days)
Incubation period (IP)	Duration from exposure to symptom onset	5.1	4.5	14.0
Symptom to confirmation interval (SCI)	Duration from symptom onset to test confirmation as positive	9.0	6.1	11.9
Latent period of ECQ (LP1)	IP + SCI	14.1	10.6	25.9
Date of Measurement, if # confirmed cases is preferred indicator (LP + 1 day)		**1 Apr 20**	**28 Mar 20**	**12 Apr**
Symptom to ICU interval (SII)	Duration from symptom onset to hospitalization	10.0	6.0	14.0
Latent period of ECQ (LP2)	IP + SII	15.1	10.5	28.0
Date of Measurement, if # CCU beds is preferred indicator (LP + 1 day)		**2 Apr 20**	**28 Mar 20**	**13 Apr**
Hospitalization to death interval (HDI)	Duration from hospitalization to death	TBD	TBD	TBD
Latent period of ECQ (LP3)	IP + HDI			
Date of Measurement, if # deaths is preferred indicator (LP + 1 day)				

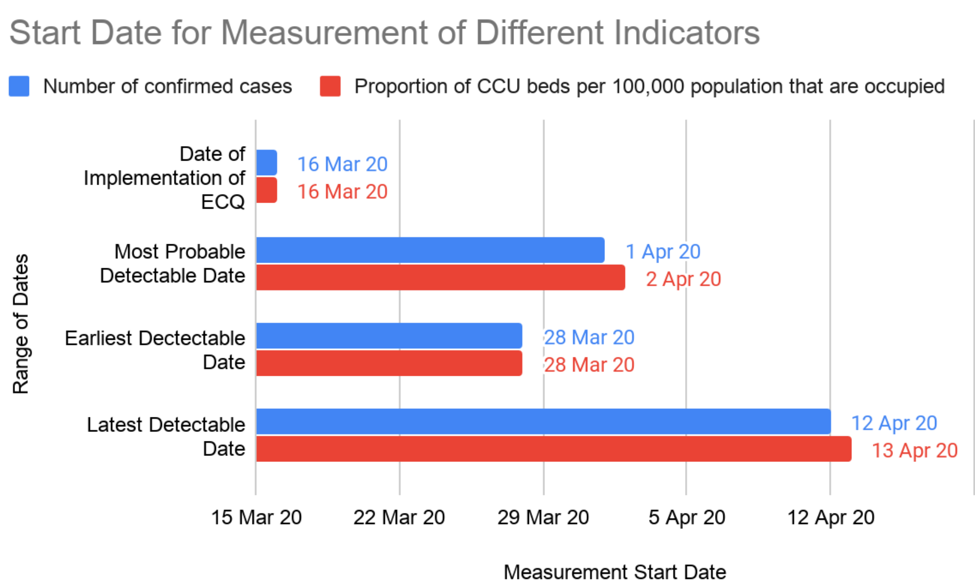

Figure 3. Start Date for Measurement of Different Indicators

d. What study design do we use?

i. Pre- and post-intervention design. The study should be a pre- and post-test quasi-experimental design. The intervention is the ECQ and is applied for at least a month. Depending on the indicator chosen, the indicator should be compared before and after the measurement start date listed above.

e. How do we measure?

i. Given the indicators, data collection must be comprehensive. Testing facilities and hospitals with COVID-19 patients must provide daily information on: a) new cases, b) number of CCU beds occupied[15], and c) new deaths.

f. How do we analyze the data?

i. The limited daily testing capacity will affect the evaluation since detection rates will be affected. Hence, an adjustment should be made during the evaluation. The positivity rate (or the number of laboratory-confirmed COVID-19 tests per 100 suspected cases examined) can be used as the indicator for this and such can be treated as a covariate in the statistical analyses to be done.

ii. To assess effectiveness, the use of the **effective reproduction number, R(t),** is proposed. Two thresholds should be set: (1) for triggering the end of the ECQ, i.e.., when the contact rate is likely to decrease the effective reproduction number, R(t) < 1 and (2) for triggering the start of the next cycle of ECQ, when the R(t) > 1. There are methods for computing the effective reproduction number, rather than just the theoretical Ro, based on observed surveillance data.[16,17,18,19] The data needed for this computation include: confirmed cases, hospitalizations, and

iii. **Interrupted time series** is a design that evaluates the effectiveness of population-level health interventions that have been implemented at a clearly defined point in time. To assess the effect of an intervention, a time series before and after its implementation is explored to check underlying trends. While there is no hard rule for the number of data points, the power depends on various other factors including distribution of data points before and after the intervention, variability within the data, strength of effect, and the presence of confounding effects such as seasonality. Nonetheless, model assumptions must be established apriori.[20,21] For this setting, the ITS for PH COVID-19 will use data before and after the indicator-specific measurement start date. *However, a statistically-significant decrease in the indicator may not necessarily result in the termination of the outbreak.*

iv. **Discrete events** like daily attack rates, peak attack rates, and delays in peak can be explored in time-series to see the trends pre-, during, and post-intervention implementation. These visualizations will closely follow the study of Ferguson et. al. (2006). See Appendix.

g. **Limitations**

i. Some of the selected indicators can be prone to bias:

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[15] The denominator will be derived from PSA estimates.

[16] Cao, Zhidong, Qingpeng Zhang, Xin Lu, Dirk Pfeiffer, Zhongwei Jia, Hongbing Song, and Daniel Dajun Zeng. "Estimating the effective reproduction number of the 2019-nCoV in China." medRxiv (2020).

[17] Nishiura, Hiroshi, and Gerardo Chowell. "The effective reproduction number as a prelude to statistical estimation of time-dependent epidemic trends." In Mathematical and statistical estimation approaches in epidemiology, pp. 103-121. Springer, Dordrecht, 2009.

[18] Cowling, Benjamin J., Max SY Lau, Lai-Ming Ho, Shuk-Kwan Chuang, Thomas Tsang, Shao-Haei Liu, Pak-Yin Leung, Su-Vui Lo, and Eric HY Lau. "The effective reproduction number of pandemic influenza: prospective estimation." Epidemiology (Cambridge, Mass.) 21, no. 6 (2010): 842.

[19] Yang, Fen, Lingling Yuan, Xuhui Tan, Cunrui Huang, and Jun Feng. "Bayesian estimation of the effective reproduction number for pandemic influenza A H1N1 in Guangdong Province, China." Annals of epidemiology 23, no. 6 (2013): 301-306.

1. Information bias - the daily number of confirmed cases is influenced by the number of tests conducted daily and by the date of reporting of the lab. Symptom-onset date is a better endpoint but there are ongoing problems in collecting this data.
2. External validity - the statistics for the symptom-to-hospitalization interval comes from a China study. The value may not hold in the Philippines.

ii. There is no information on the 'dose' of the intervention or % compliance with social distancing. Therefore, the 'most probable' onset date may be delayed.

iii. This protocol did not include in its design the measurement of the unintended adverse consequences of the ECQ. Although the ECQ may save lives, it may also cost lives through delayed or averted admissions like myocardial infarction or stroke.

iv. This design assumes no change in the other components of Ro when, in fact, they may also change. For example, R may also be decreased by reducing the symptom-to-hospitalization time, thereby reducing the duration of infectiousness of the patient.

Conclusion

We have described a protocol for measuring the effectiveness of the ECQ using currently collected data and the use of a threshold value for the effective reproduction number, R(t).

[20] Kontopantelis, Evangelos, Tim Doran, David A. Springate, Iain Buchan, and David Reeves. "Regression based quasi-experimental approach when randomisation is not an option: interrupted time series analysis." bmj 350 (2015): h2750.
[21] Bernal, James Lopez, Steven Cummins, and Antonio Gasparrini. "Interrupted time series regression for the evaluation of public health interventions: a tutorial." International journal of epidemiology 46, no. 1 (2017): 348-355.