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Sequential Coupling of Dry and Wet COVID-19 Screening to Reduce the Number of Quarantined Individuals

Yen Po (Harvey) Chin, Wenyu Song, Md Mohaimenul Islam, David W. Bates, Li Zhou, Yu Chuan (Jack) Li

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Highlight

- This viewpoint article discusses the potential benefits of sequential coupling of digital checker (Dry screening) and Rapid Antigen Test (Wet screening) at a population level for COVID-19 positive test to reduce the number of people who require quarantine and alleviating stress on the overburdened healthcare systems during the COVID-19 pandemic.
- We concluded that sequential coupling of a digital checker and a Rapid Antigen Test could significantly reduce the number quarantined by around 1 million in a hypothetical country with 10 million people.
Title: Sequential Coupling of Dry and Wet COVID-19 Screening to Reduce the Number of Quarantined Individuals

Yen Po (Harvey) Chin, MD, MBI\textsuperscript{1,2,3}, Wenyu Song, PhD\textsuperscript{1,2}, Md Mohaimenul Islam, PhD\textsuperscript{3}, David W. Bates, MD, MSc\textsuperscript{1,2}, Li Zhou, MD, PhD\textsuperscript{1,2}, Yu Chuan (Jack) Li, MD, PhD\textsuperscript{1,2,3*}

1. Division of General Internal Medicine & Primary Care, Brigham and Women's Hospital, Boston, MA, USA
2. Harvard Medical School, Boston, MA, USA
3. Graduate Institute of Biomedical Informatics, Taipei Medical University, Taipei, Taiwan

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*Corresponding author:

Prof. Yu Chuan (Jack) Li, MD, PhD

Professor, Graduate Institute of Biomedical Informatics, Taipei Medical University

Dermatology Dept, Wan Fang Hospital, Taipei, Taiwan

President-elect, International Medical Informatics Association (IMIA)

Editor-in-Chief, BMJ Health and Care Informatics

Address: 15F, No. 172, Sec. 2, Keelung Rd., Da’an Dist., Taipei City, Taiwan

Email: jack@tmu.edu.tw
Abstract

Introduction: Currently, several countries are facing severe public health and policy challenges when designing their COVID-19 screening strategy. A quantitative analysis of the potential impact that combing the Rapid Antigen Test (RAT; Wet screening) and digital checker (Dry screening) can have on the healthcare system is lacking.

Method: We created a hypothetical COVID-19 cohort for the analysis. The population size was set as 10 million with three levels of disease prevalence (10%, 1%, or 0.1%) under the assumption that a positive test result will lead to quarantine. A digital checker and two RATs are used for analysis. We further hypothesized two scenarios: RAT only and RAT plus digital checker. We then calculated the number of quarantined in both scenarios and compared the two to understand the benefits of sequential coupling of a digital checker with a RAT.

Result: Sequential coupling of the digital checker and RAT can significantly reduce the number of individuals quarantined to 0.95-1.33M, 0.86-1.29M, and 0.86-1.29M, respectively, under the three different prevalence levels.

Conclusion: Sequential coupling of digital checker and RAT at a population level for COVID-19 positive test to reduce the number of people who require quarantine and alleviating stress on the overburdened healthcare systems during the COVID-19 pandemic.
Introduction:

COVID-19 caused by SARS-CoV-2, a new coronavirus, was declared a pandemic by the World Health Organization in 2020. Rapid diagnosis of COVID-19 patients is critical to control the pandemic. While RT-PCR is the gold standard in diagnosing COVID-19, it is less than an ideal tool for screening at a population level due to time and cost constraints.\(^1\) Currently, a Rapid Antigen Test (RAT) is still the first-line screening tool. However, in a low prevalence population, RATs will have a high proportion of false-positives due to their low positive predictive value (as low as 0.39\(^1\)), resulting in a large number of unnecessary self-quarantines and hospital quarantined, which can be a significant challenge to the overburdened healthcare system.\(^2\) Currently, several countries are facing severe public health and policy challenges when designing their COVID-19 screening strategy. Some COVID-19 digital checkers, such as the US CDC checker, has shown promise in helping the publics to make decisions about seeking appropriate medical care.\(^3\) However, while some countries have been using digital checkers and RATs, sequential coupling of the two screening tools (dry and wet) is not yet a common strategy, and a quantitative analysis of the potential impact that combing the two approaches can have on the healthcare system is lacking.

Method:

To examine the benefits of coupling the two screening tools, we created a hypothetical
COVID-19 cohort for the analysis. The population size was set as 10 million with three levels of disease prevalence (10%, 1%, or 0.1%) under the assumption that a positive test result will lead to quarantine. We used the digital checker designed by the US CDC (Sensitivity: 0.94; Specificity: 0.29). For the RATs, we utilized one reported by Cento et al. from Italy (Sensitivity: 0.85; Specificity: 0.97) as RAT 1, and the other reported by Kim et al. from Korea (Sensitivity: 0.90; Specificity: 0.98) as RAT 2. We further hypothesized two scenarios: RAT only and RAT plus digital checker (digital checker as the first-stage screening test). We then calculated the number of quarantined in both scenarios and compared the two to understand the benefits of sequential coupling of a digital checker with a RAT.

Results

With RAT 1 only, the number of individuals requiring quarantine under three different prevalence levels (10%, 1%, 0.1%) are 2.32M, 1.58M, and 1.51M. Sequential coupling of the digital checker and RAT 1 can significantly reduce the number of individuals quarantined to 1.33M, 1.29M, and 1.29M, respectively, under the three different prevalence levels.

With RAT 2 only, the number of quarantined under three different prevalence levels for are 1.88M, 1.09M, and 1.01M. Similarly, sequential coupling of the digital checker and RAT 2 can substantially reduce the number of individuals quarantined to 0.95M, 0.86M, and 0.86M, respectively.

Discussion
Our results showed that sequential coupling of a digital checker and a RAT could significantly reduce the number quarantined by around 1 million in a hypothetical country with 10 million people. One negative of this approach is that combining screening tests might slightly increase the number of missed COVID patients (detailed numbers in supplementary Table 1). However, this approach still has merit since reducing the number quarantined by 1 million would hugely alleviate the stress on the RT-PCR capacities and healthcare systems. Notedly, the benefit of this combination is even more evident when the prevalence is low since there will be a minimal increase in the missed cases and still has the potential to reduce the number quarantined. This article has potential limitations. Since this is a conceptual analysis, a real-world study would be needed to further prove the strategy's effectiveness. The sensitivity and specificity of the digital checker and RATs used in this article may differ from the actual numbers when applied to different ethnic groups, which warrants careful consideration before extrapolating the numbers from this article directly to other countries.

**Conclusion:**

Sequential coupling of digital checker and RAT at a population level for COVID-19 positive test to reduce the number of people who require quarantine and alleviating stress on the overburdened healthcare systems during the COVID-19 pandemic. Consider the benefit and the low-cost and easy-to-repeat features of the digital checker, combining the two approaches is a promising strategy that should be considered by governments around the
globe as a realistic and feasible strategy for COVID-19 screening on general populations.

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**Conflict of interest:**

None of the authors declared any potential conflict of interest.
References

1. Mak, G. C. et al. Evaluation of rapid antigen test for detection of SARS-CoV-2 virus. *J Clin Virol* **129**, 104500 (2020).

2. Peek, N., Sujan, M. & Scott, P. Digital health and care in pandemic times: impact of COVID-19. *Bmj Heal Care Informatics* **27**, e100166 (2020).

3. Munsch, N. et al. Diagnostic Accuracy of Web-Based COVID-19 Symptom Checkers: Comparison Study. *J Med Internet Res* **22**, e21299 (2020).

4. Cento, V. et al. Frontline Screening for SARS-CoV-2 Infection at Emergency Department Admission by Third Generation Rapid Antigen Test: Can We Spare RT-qPCR? *Viruses* **13**, 818 (2021).

5. Kim, D. et al. Development and Clinical Evaluation of an Immunochromatography-Based Rapid Antigen Test (GenBody™ COVAG025) for COVID-19 Diagnosis. *Viruses* **13**, 796 (2021).
Table 1: The impact of sequential coupling digital checker and rapid antigen detection test in a hypothesized 10 million population cohort.

|                | Scenario 1: RAT | Scenario 2: Digital checker + RAT |
|----------------|-----------------|----------------------------------|
|                | RAT 1 | RAT 2 | RAT 1 | RAT 2 | RAT 1 | RAT 2 |
| Number of quarantined | 2.32  | 1.88  | 1.58  | 0.09  | 1.51  | 1.01  |

|                | RAT types | RAT 1 | RAT 2 | RAT 1 | RAT 2 | RAT 1 | RAT 2 |
|----------------|-----------|-------|-------|-------|-------|-------|-------|
| Number of quarantined | 0.99  | 0.93  | 0.29  | 0.23  | 0.22  | 0.15  |
| Reduced quarantined   | 1.33  | 0.95  | 1.29  | 0.86  | 1.29  | 0.86  |

RAT = Rapid Antigen Test. RAT 1: from Italy (Sensitivity: 0.85; Specificity: 0.97). RAT 2: from Korea (Sensitivity: 0.90; Specificity: 0.98). Digital checker: from US CDC (Sensitivity: 0.94; Specificity: 0.29). Number of quarantined = True positive + False positive. Reduced quarantined = Number of quarantined in Scenario 1 - Number of quarantined in Scenario 2. All numbers showed in millions and rounded off to the second decimal. Detailed calculation processes were demonstrated in supplementary Table 1.