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# Cost analysis of coronavirus disease 2019 test strategies using pooled reverse transcriptase-polymerase chain reaction technique

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## Abstract

**Background:** This study aimed to compare the testing strategies for COVID-19 (i.e., individual, simple pooling, and matrix pooling) in terms of cost.

**Methods:** We simulated the total expenditures of each testing strategy for running 10,000 tests. Three parameters were used: positive rate (PR), pool size, and test cost. We compared the total testing costs under two hypothetical scenarios in South Korea. We also simulated country-specific circumstances in India, South Africa, South Korea, the UK, and the USA.

**Results:** At extreme PRs of 0.01% and 10%, simple pooling was the most economic option and resulted in cost reductions of 98.0% (pool size ≥80) and 36.7% (pool size = 3), respectively. At moderate PRs of 0.1%, 1%, 2%, and 5%, the matrix pooling strategy was the most economic option and resulted in cost reductions of 97.0% (pool size ≥88), 86.1% (pool size = 22), 77.9% (pool size = 14), and 59.2% (pool size = 7), respectively. In both hypothetical scenarios of South Korea, simple pooling costs less than matrix pooling. However, the preferable options for achieving cost savings differed depending on each country's cost per test and PRs.

**Conclusions:** Both pooling strategies resulted in notable cost reductions compared with individual testing in most scenarios pertinent to real-life situations. The appropriate type of testing strategy should be chosen by considering the PR of COVID-19 in the community and the test cost while using an appropriate pooling size such as five specimens.

KEYWORDS
costs and cost analysis, COVID-19, COVID-19 testing, pooling test, RT-PCR

Eun Young Kim and Juyoung Kim contributed equally to this work and share the first authorship.

## 1 | INTRODUCTION

The World Health Organization (WHO) declared the outbreak of the novel coronavirus disease 2019 (COVID-19) as a pandemic on March 11, 2020.[1–3] The COVID-19 pandemic, caused by severe acute respiratory syndrome coronavirus (SARS-CoV-2), has been a tremendous threat to the global society. The number of COVID-19 cases has increased precipitously, with the global number of cases and deaths exceeding 250 million and 5 million in November 2021, respectively.[4] According to the International Monetary Fund, the global economy showed a downturn tendency in 2020 due to the enforcement of nationwide lockdowns and travel restrictions to prevent the spread of COVID-19, including temporary shutdown of workplaces and prolonged implementation of social distancing measures.[5] Moreover, a significant amount of budget has been spent on the care of COVID-19 patients, with the average cost of hospital care per patient being $8,400 in South Korea and $78,569 in the United States (US).[6,7] As such, the estimated health-care cost related to COVID-19 was about $300 million until December 2020; notably, the cost of diagnostic tests accounted for as much as 34.7% of the total health-care cost in South Korea.[6]

Reverse transcription-polymerase chain reaction (RT-PCR) tests have been recommended over antibody tests for detecting the presence of SARS-CoV-2 in specimens acquired from the upper respiratory tract.[8] Despite their affordability, antibody tests are not recommended for diagnosing COVID-19 because it takes several days or weeks for an individual to develop antibodies after infection.[9] Due to the limited availability of proven effective treatment, patients with COVID-19 are only given symptomatic treatments for alleviating pneumonia or acute respiratory distress.[8] Considering the sharp increases in morbidity related to COVID-19, an optimal way for managing the COVID-19 outbreak would be the implementation of multitudinous and simultaneous testing for early detection to prevent the transmission of the disease.

While many countries are conducting a considerable amount of testing on anyone showing symptoms, several countries such as South Korea adopted open public testing and testing asymptomatic people in order to quickly halt the disease spread by identifying patients in the early stages.[10] In the United States, nearly 300 million diagnostic tests had been conducted by January 2021.[11] In South Korea, the cumulative number of COVID-19 tests were over 15 million, or 300 per 1000 population, by October 2021.[12] To simultaneously carry out a vast number of RT-PCR tests, governments are allocating large budgets for testing; for example, the United Kingdom (UK) government planned to allot £100 billion for carrying out COVID-19 tests.[13] Taking into account the considerable surge in demand for COVID-19 testing, different tactics for diagnostic testing should be considered to optimize the use of economic resources.

Accordingly, strategies for pooling diagnostic specimens, which have been applied in screening donated blood samples for blood-borne pathogens such as hepatitis B virus,[14,15] were introduced to reduce the cost of screening large populations.[16,17] In addition to simple pooling testing (e.g., Dorfman testing or hierarchical group testing), more complicated methodologies such as nonhierarchical group testing or array testing have also been developed.[18–20] Recently, these pooling strategies have been adopted to efficiently detect SARS-CoV-2 by speeding up the tests and increasing the testing capacity, and have thus been recommended by the US FDA as well.[21]

Several simulation studies tried to determine the optimal pooling strategy by taking into account relevant parameters such as pool size and positive rate (PR).[22–26] However, no study has yet compared the pooling strategies by estimating the amount of cost reduction. Therefore, this study aimed to compare three testing strategies—individual testing, simple pooling, and matrix pooling—in terms of cost reduction in different scenarios with varying degrees of relevant parameters including PR, pool size, and cost per test. Based on the simulation results, we compared the costs between the two pooling strategies under plausible scenarios in South Korea. Also, we applied our models to real-life country-specific circumstances to illustrate how our model can be employed in the decision-making for testing strategies.

## 2 | MATERIALS AND METHODS

### 2.1 | Testing strategies

We compared three strategies for detecting SARS-CoV-2 using RT-PCR testing: individual testing, simple pooling, and matrix pooling. Individual testing is a classic way of detecting infected patients (Figure 1A), in which each specimen of the candidates undergoes all processes from sampling to DNA extraction and RT-PCR without pooling with other specimens. This typical testing strategy requires the same number of tests as the number of people who need to be tested, and can directly identify infected patients in a single round of testing.

The simple pooling strategy consists of two phases (Figure 1B). After collecting each specimen, a certain number of specimens (i.e., pool sizes) are placed in a single tube and undergo the PCR process.[22] If the pooled specimen produces a negative result, all of the individual specimens are considered negative; in cases of a positive result, the individual specimens are tested again in an individual manner.

The matrix pooling strategy also consists of two phases (Figure 1C), in which the specimens are pooled using a two-dimensional array (matrix).[18] Specifically, the samples are arranged in a square matrix, and then those in a single row or column are pooled for the test. In this way, each specimen is included in two different pooled sets. When the results from the pooled tests are negative, all specimens included in the matrix are considered negative and do not need additional tests as in the simple pooling strategy. However, samples with positive results from both the row and column sets undergo further testing to confirm the positivity.

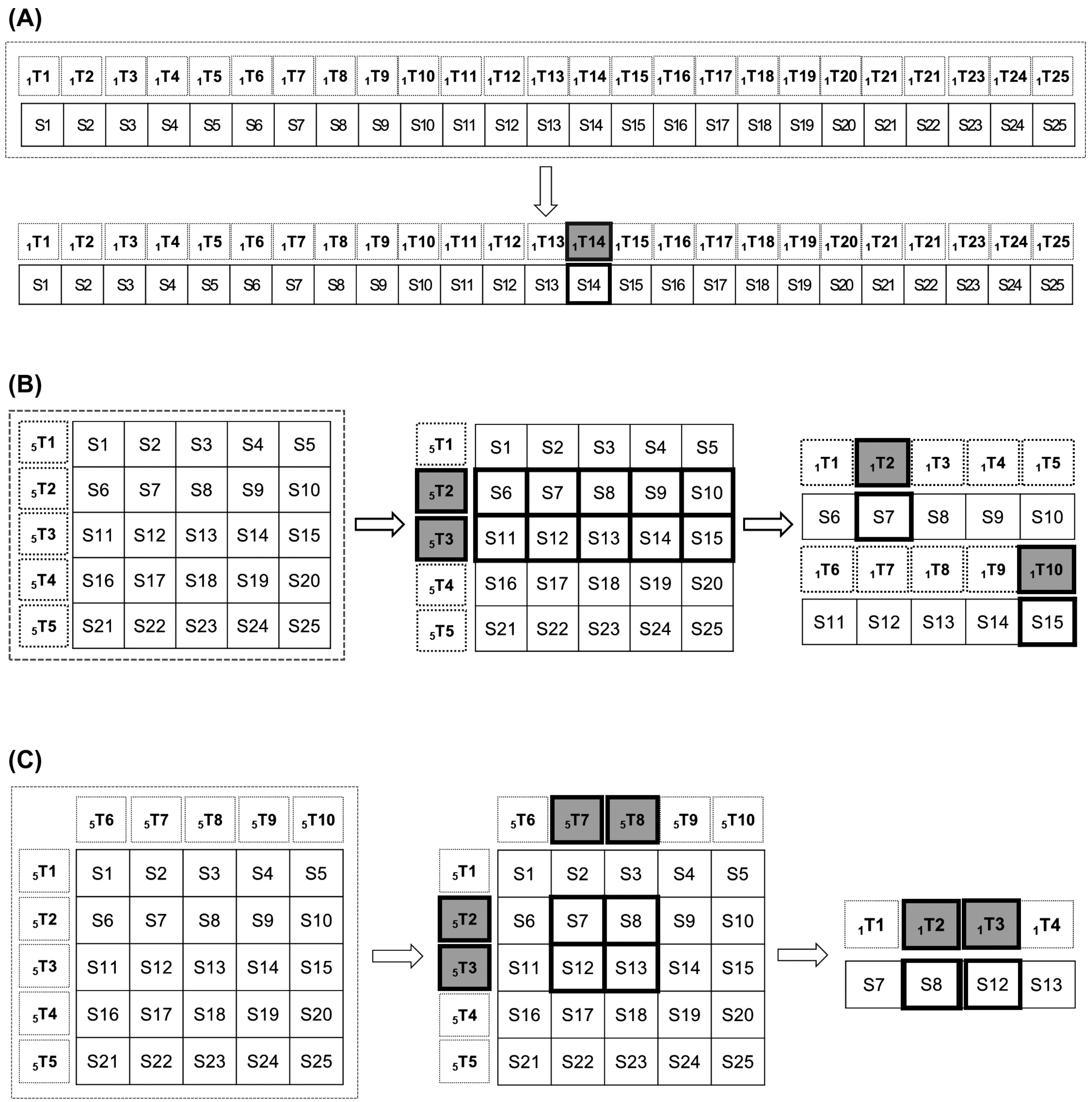



FIGURE 1 Types of testing strategies. (A) Individual testing†, (B) Simple pooling‡, and (C) Matrix pooling□. $_m$Tn: m, pool size; T, test tube; n, row or column numbering; Sk: S, specimen; k, the number of specimens in a unit. A dotted square surrounding specimens" is a unit for the test. †In the individual testing, 25 tests are carried out per unit (k = 25). ‡The simple pooling strategy consists of two phases. First, five tests are initially carried out per unit; then, positive pooled specimens are individually tested for verification. □The matrix pooling consists of two phases and uses a two-dimensional array (matrix) for pooling. First, samples in a single row or column in a square matrix are pooled and tested twice; then, to verify the results, positive pooled specimens are individually tested

## 2.2 | Pooling strategies

To identify individual specimen in a unit, we denoted the samples as $_m$Tn, where "m" refers to the pool size, "T" refers to the test tube, and "n" refers to the row or column number. In the figure describing the test strategies (Figure 1), a specimen is numbered as Sk, where "S" stands for "sample" and "k" refers to the series number of specimens in a unit. A total of 25 samples (pool size: 5) was chosen as the size of the initial unit. In individual testing, 25 tests are carried out per unit (Figure 1A). In the simple pooling strategy, 5 tests are initially carried out per unit (Figure 1B); then, in a hypothetical scenario in which $_5$T2 and $_5$T3 pooled tests are positive, 10 specimens (S6–S15) are individually tested for verification. Consequently, a total of 15 tests are needed in the simple pooling strategy for a single unit with two positive pooled samples. In the matrix pooling strategy, 10 tests are initially carried out per unit as each sample is tested twice in the row pool and the column pool (Figure 1C). Then, in a hypothetical scenario in which four pooled samples (e.g., ${}_5$T2, ${}_5$T3, ${}_5$T7, and ${}_5$T8) are positive, the samples at the intersections of the positive rows and columns (i.e., S7, S8, S12, S13) are individually tested for verification. Consequently, a total of 14 tests are needed in the matrix pooling strategy for a single unit with four positive pooled samples.

### 2.3 | Models and variables

We compared the total expenditure of each testing strategy with a conservative assumption of the maximum cost in a hypothetical scenario in which 10,000 specimens were required for tests at once. In the simulation model, there were three parameters: PR (%), number of pooled specimens (pool size), and cost per test. The range of PRs was decided considering the latest epidemiological measures and benchmark PRs lower than 10% for adequate testing as suggested by the WHO.[27] Until January 2021, the cumulative PRs for COVID-19 tests were less than 20% in 86.5% of countries worldwide. Therefore, we simulated the range of PRs from 0.01% to 20% with fixed pooled sizes (pool sizes: 5 and 10). We selected a pool size of 2–100 when the PRs are 0.01%, 1%, 2%, 5%, and 10%.[26] The cost varied from $40 to $1,280 with fixed variables of PRs and pool sizes. We assumed that the retest cost of the pooled test was the same as the individual cost, although it costs less in a real-life situation. There is no other collection of specimens for the retest due to the remnants obtained.[28,29]

### 2.4 | Simulation scenarios

The total expenditure was compared between the simple pooling strategy and the matrix pooling strategy under scenarios relevant to the degree of COVID-19 outbreak in South Korea. In the first scenario, we hypothesized a relatively low PR of 1% with a pool size of 5 and 2,000 cases requiring tests. In the second scenario, we assumed a PR of 2%, a pool size of 10, and 4,000 specimens requiring tests. In both scenarios, the cost per test was set as $70.[28]

### 2.5 | Country-specific circumstances

We applied our model of pool sizes 5 and 10 depending on the PRs relevant to country-specific circumstances in India, South Africa, South Korea, the UK, and the US. These countries were selected based on the availability of parameters including costs per test and PRs. The costs per test were as follows: $57.36 (Rs 2400) in India, $57.36 (R850) in South Africa, $66.43 (₩78,040) in South Korea, $103.26 (£75) in the UK, $148 in the US.[29–34] The currency rate on October 25, 2021, was applied to US dollars. We identified the points for changing the best cost-saving strategies in a series of PRs under country-specific circumstances. Then, the best cost-saving strategies were explored considering each country's PRs (daily PRs and 7-day rolling average PRs) recorded between October 4, 2021, and October 10, 2021.[35]

## 3 | RESULTS

### 3.1 | Testing cost according to PRs of COVID-19

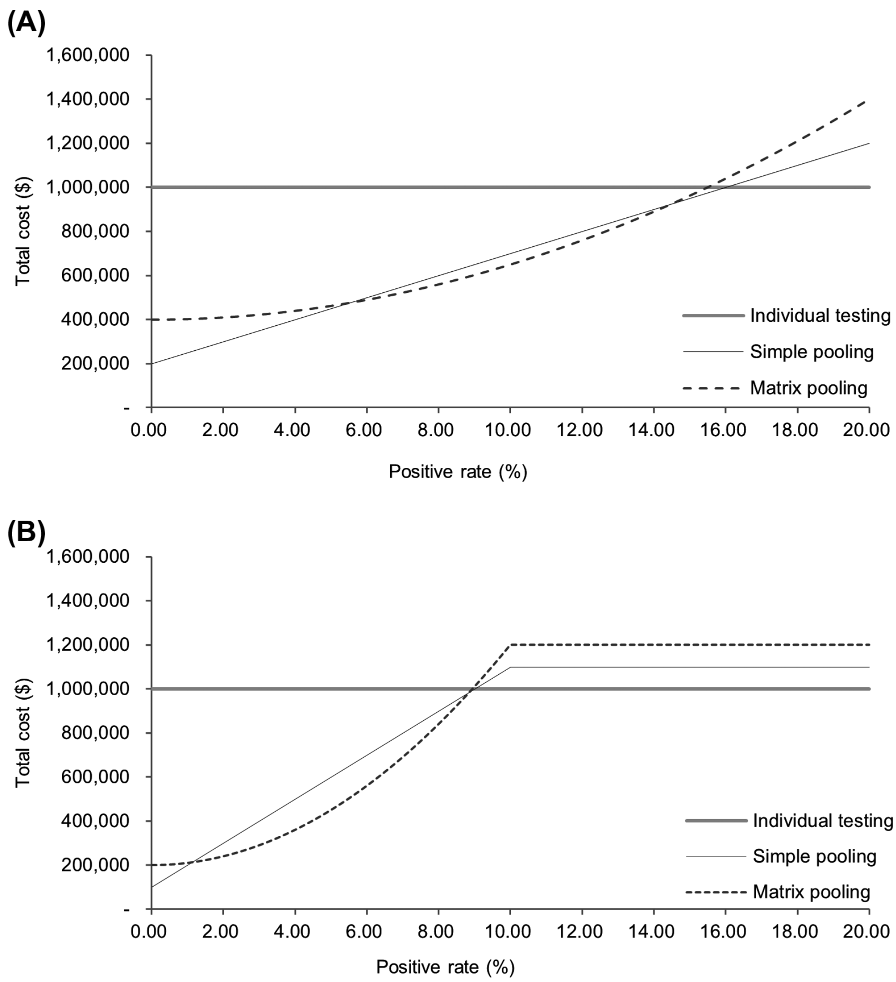
Under the assumption of pooling sample size ($n$ = 5, 10), cost per test ($100), and total number of cases tested ($N$ = 10,000), the total testing costs according to the PRs from 0.01% to 20.00% are shown in Figure 2. When five specimens were pooled, the simple pooling strategy was superior in terms of cost at PRs between 0.01% and 5.52% and between 14.48% and 16.00%, whereas the matrix pooling strategy was superior at PRs between 5.53% and 14.47% (Figure 2A). At PRs above 16.01%, the individual testing strategy was superior to both pooling strategies. The maximum cost-saving effect of the pooling strategy over individual testing was observed in the simple pooling strategy at a PR of 0.01% (80.0%), which was notably higher than that in the matrix pooling strategy (60.0%).

When 10 specimens were pooled, there were four intersection points among the three testing strategies in the plot (Figure 2B). The simple pooling strategy had the lowest total cost at PRs between 0.01% and 1.12% and also in a narrow range of between 8.88% and 9.00%. The matrix pooling strategy had the lowest total cost at PRs between 1.13% and 8.87%. At PRs above 9.01%, the individual testing strategy was superior to both pooling strategies. The maximum cost-saving effect of the pooling strategy over individual testing was observed in the simple pooling strategy at a PR of 0.01% (89.9%), which was notably higher than that in the matrix pooling strategy (80.0%).

### 3.2 | Testing cost according to pool size

The total testing costs according to different pool sizes (from 2 to 100) are shown in Figure 3, in which 10,000 tests were performed at $100 per test with six different PRs in the simulation: 0.01%, 0.1%, 1%, 2%, 5%, and 10%. The total expenditure of the individual testing strategy was $1,000,000 regardless of PRs and pool sizes; the individual testing strategy showed the highest cost at PR 0.01% (Figure 3A) and 0.1% (Figure 3B) regardless of pool sizes. In a scenario with a low prevalence of COVID-19 (i.e., PR = 0.01%), the simple pooling strategy resulted in a considerably low cost regardless of pool size, with the maximum cost reduction from individual testing being 98.0% at a pool size of 100. At a PR of 0.1%, the simple pooling strategy had the lowest cost in pool sizes 2–32, and the matrix pooling strategy had the lowest cost in pool sizes 33–100 (Figure 3B); the maximum cost reduction from individual testing was 97.0%, which was observed in the matrix pooling strategy at a pool size of 96.

FIGURE 2 Total testing costs according to different positive rates. (A) Pool size = 5, (B) Pool size = 10




At relatively high PRs from 1% to 10% (Figure 3C–F), the three strategies had three crossing points. The simple pooling strategy had the lowest total cost until the first crossing points, which involved pool sizes of 11, 8, 6, and 5 in PRs 1%, 2%, 5%, and 10%, respectively. Between the first and second crossing points, the matrix pooling strategy had the lowest total cost. After the second crossing points (i.e., pool sizes 99, 49, 19, and 9 in PRs 1%, 2%, 5%, and 10%, respectively), the individual testing had a lower total cost than did both pooling strategies. The highest cost reductions relative to individual testing were observed in the following conditions: PR 1% (86.1%, matrix pooling, pool size = 22), PR 2% (77.9%, matrix pooling, pool size = 14), PR 5% (59.2%, matrix pooling, pool size = 7), and PR 10% (36.7%, simple pooling, pool size = 3).

## 3.3 | Testing cost according to the cost per test

We calculated the total expenditure of 10,000 tests according to changes in the cost per test from $40 to $1,280 under the following assumptions: (1) PR = 0.1%, pool size = 8; (2) PR = 1%, pool size = 5; and (3) PR = 5%, pool size = 8. In all three scenarios, the testing cost showed a linear increase depending on the cost per test. In two scenarios (PR = 0.1%, pool size = 8; PR = 1%, pool size = 5), the simple pooling strategy resulted in the lowest total cost regardless of the cost per test (Figure 4A,B); specifically, the simple pooling strategy could reduce the cost by as much as 86.7% and 75.0% relative to individual testing in the two scenarios, respectively. In contrast, at a PR of 5% and a pool size of 8, the matrix pooling strategy resulted in the lowest total cost, reducing costs as much as 59.0% from the individual testing strategy (Figure 4C).

## 3.4 | Comparison between simple and matrix pooling strategies

The total costs of the simple and the matrix pooling strategies were compared under two hypothetical scenarios (Table 1), which were constructed based on COVID-19 statistics in South Korea. We selected the average PR of COVID-19 in South Korea during 2020[11] and 2,000 tests/day considering the capacity of a single laboratory (3,000–4,000 tests/day).[28] In terms of cost per test, the national insurance fee for testing in South Korea (~$70 per test) was used.[27] In scenario 1 ($N$ = 2,000, cost per test = $70, PR = 1%, and pool size = 5), the expected cost was higher in the matrix pooling strategy ($57,400) than in the simple pooling strategy ($35,000). Likewise, in scenario 2 ($N$ = 4,000, cost per test = $70, PR = 2%, and pool size = 10), the expected cost was higher in the matrix pooling strategy ($62,930) than in the simple pooling strategy ($60,900).

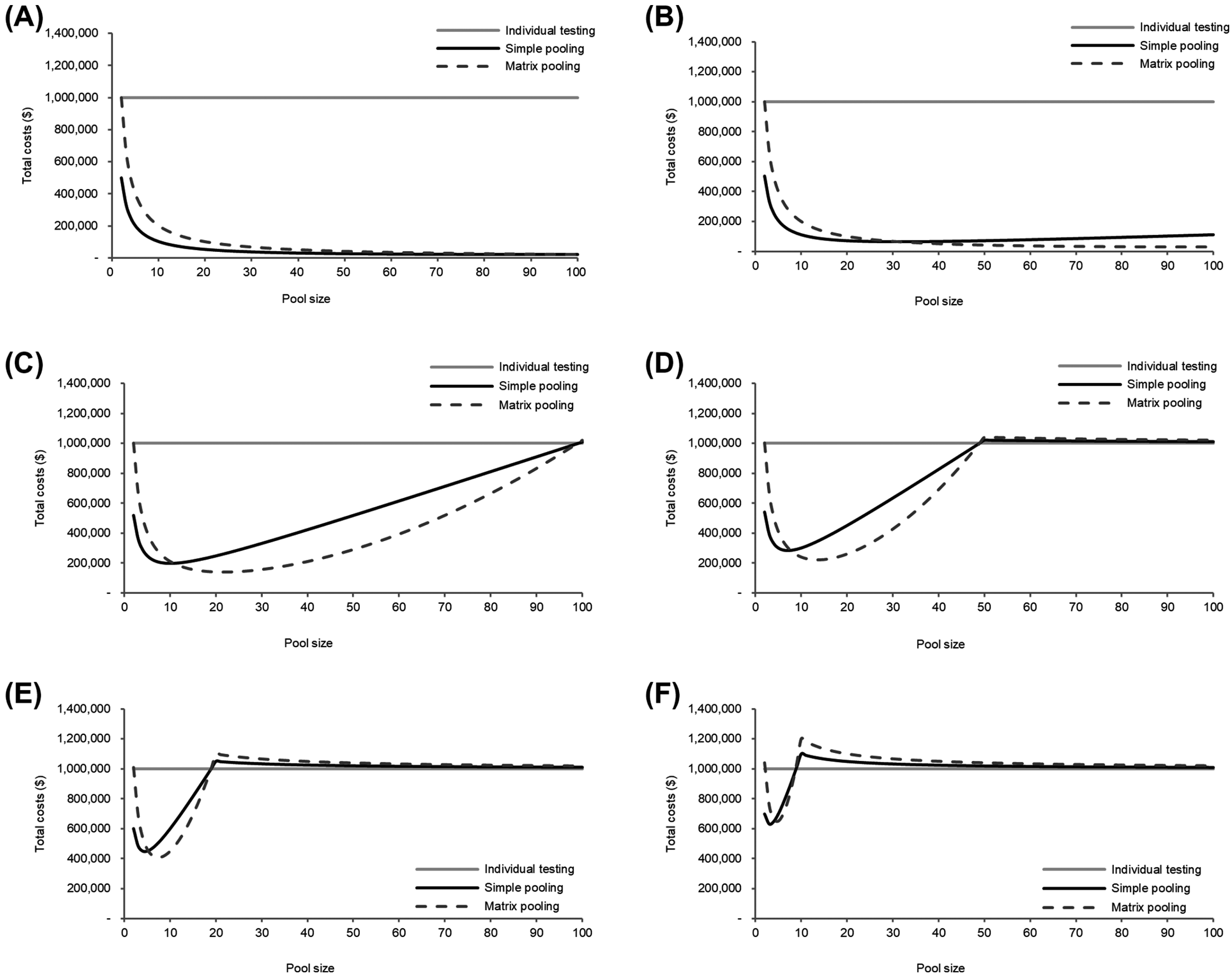



FIGURE 3 Total testing costs according to different pool sizes. (A) PR = 0.01%, (B) PR = 0.1%, (C) PR = 1%, (D) PR = 2%, (E) PR = 5%, (F) PR = 10%. PR, positive rate

## 3.5 | Application of country-specific circumstances

We applied the PRs of five countries (India, South Africa, South Korea, the UK, and the US) recorded between October 4 and October 10, 2021. In India, the daily PRs and 7-day rolling average PRs were 1.41%–1.85% and 1.50%–1.60%, respectively, during the study period (Figure S1A). The points of changing the best cost-saving strategies are illustrated in Figure S1B (pool size = 5) and Figure S1C (pool size = 10). While simple pooling can be a cost-saving strategy with a pool size of 5, matrix pooling was preferable when using a pool size of 10. When the daily PR was 1.41% (October 10, 2021), the cost-saving amount was 58.8% in simple pooling with a pool size of 5 and 60.6% in matrix pooling with a pool size of 10.

In South Africa, the daily PRs were 2.60%–3.22% and the 7-day rolling average PRs were 2.90%–4.60% (Figure S2A). Total costs of each strategy depending on the changes of PRs are presented in Figure 2B (pool size = 5) and Figure S2C (pool size = 10). Simple pooling with a pool size of 5 and matrix pooling with a pool size of 10 were shown to save 54.5% and 53.9% of the total cost compared with individual testing when applying the daily PR of 2.93% (October 10, 2021).

In South Korea, daily PRs ranged from 3.54% to 11.59%, whereas the 7-day average rates were between 6.10% and 7.10% (Figure S3A). The changes in the total costs according to the PRs are shown in Figure S3B (pool size = 5) and Figure S3C (pool size = 10). Considering the 7-day average PRs, the matrix pooling was cost saving at a pool size of 5. When using a pool size of 10, neither simple pooling nor matrix pooling were cost saving. Matrix pooling saved 35.6% of the total costs compared with individual testing, when the pool size was 5 and the PR was 6.56% (October 7, 2021).

In the UK, PRs ranged from 3.48% to 5.67% and the 7-day average rates ranged from 3.50% to 4.00% (Figure S4A). The changes in the total costs depending on the PRs are presented in Figure S4B (pool size = 5) and Figure S4C (pool size = 10). Within this range, either pooling strategies were cost saving compared with individual testing (pool size = 5, simple pooling; pool size = 10, matrix pooling). When the PR was 3.48% (October 10, 2021), matrix pooling with a

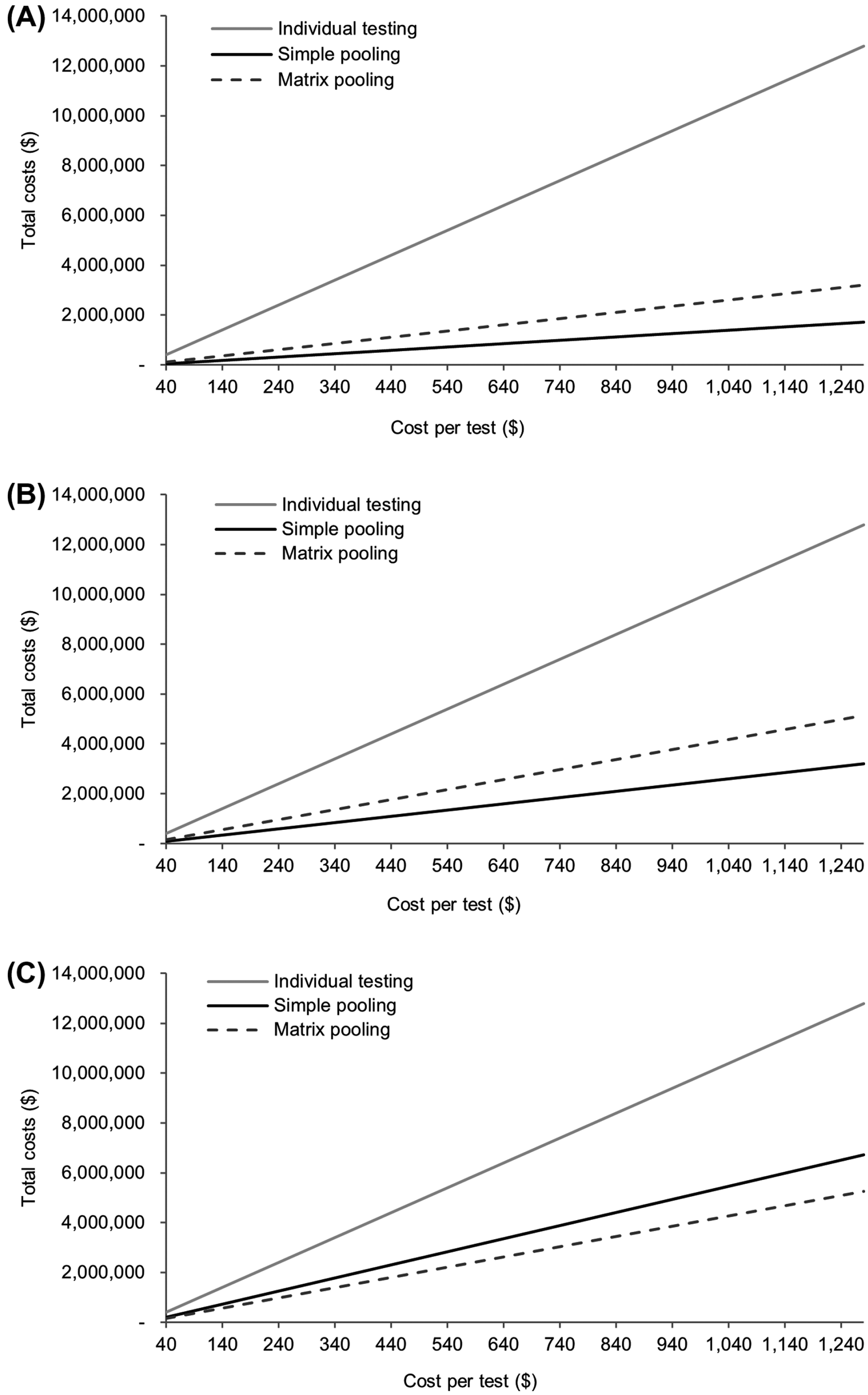



**FIGURE 4** Total testing costs according to different costs per test. (A) PR = 0.1% and pool size = 8, (B) PR = 1% and pool size = 5, (C) PR = 5% and pool size = 8. PR, positive rate

pool size of 10 was more cost-effective than simple pooling with a pool size of 5 (68.6% vs. 63.1%).

In the US, the daily PRs dropped from 13.66% to 2.31% during the same period, whereas the 7-day average PRs remained rather consistent at 6.20%–6.80% (Figure S5A). The points of changing the best cost-saving strategies depending on PRs between testing strategies are shown in Figure S5B (pool size = 5) and Figure S5C (pool size = 10). When using a pool size of 5, simple pooling was more cost saving than matrix pooling; however, when using a pool size of 10, matrix pooling resulted in a greater degree of cost reduction compared with individual testing. When the daily PR was 5.27% (October 5, 2021), the matrix pooling strategy (pool size = 10, 67.3%) has saved more costs than the simple pooling strategy (pool size = 5, 62.2%).

## 4 | DISCUSSION

This study calculated the cost savings amounts of two pooling strategies over individual testing for COVID-19 by considering wide

| | Scenario 1 | | Scenario 2 | |
|---|---|---|---|---|
| | Simple pooling | Matrix pooling | Simple pooling | Matrix pooling |
| Total number of tests | 2,000 | | 4,000 | |
| Cost per test | $70 | | $70 | |
| Positive rate | 1% | | 2% | |
| Pool size | 5 | | 10 | |
| Total cost | $35,000 | $57,400 | $60,900 | $62,930 |

**TABLE 1** Total testing costs of the simple and matrix pooling strategies under different numbers of tests, positive rates, and pool sizes

ranges of PR, pooling size, and cost per test. We found that when using a pooling size of 5, both simple and matrix pooling strategies were cheaper than individual testing if the PR is below 16.00%. In countries with a low PR of 1.5%, the simple pooling strategy would be the most cost-saving option, reducing as much as 72.5% of the cost compared with individual testing.

In the simulations using different PRs, the matrix pooling strategy showed a U-shaped trend, whereas the simple pooling strategy showed a linear trend. In moderate levels of PRs (5.53%–14.47%, pool size = 5; 1.13%–8.87%, pool size = 10), the matrix pooling strategy resulted in the lowest total testing cost. Notably, at PRs higher than 16.01% or 9.01%, both pooling strategies did not result in any cost reduction over individual testing when using pool sizes of 5 or 10, respectively.

In terms of pool size, the points at which pooling strategies did not confer reduced cost were lower in scenarios with higher PRs (Figure 3C–F). This result suggests that neither simple nor matrix pooling strategies have the potential for saving cost when using larger pool sizes in communities with higher PRs. When using a pooling size of 10 considering previous simulation or field experience studies, the simple pooling strategy was the best cost-saving option in situations with low PRs of up to 1%.[25,26] In situations with relatively higher PRs such as 2%, 5%, and 10% (Figure 3D–F), the difference between simple pooling and matrix pooling strategies seems meaningful when using pool sizes smaller than 10.

In terms of cost per test, all strategies showed linear rising tendencies. Regardless of the cost per test, the simple pooling strategy was the most cost-saving option in relatively lower PRs of 0.1% and 1%, whereas the matrix pooling strategy was the most cost-saving option in higher PRs of 5% and a pool size of 8.

In the analysis of two plausible scenarios regarding COVID-19 (total number of tests = 2,000, cost per test = $70, PR = 1%, pool size = 5; total number of tests = 4,000, cost per test = $70, PR = 2%, pool size = 10), the simple pooling strategy was more cost-effective than the matrix pooling strategy in both scenarios. In each scenario, the simple pooling strategy could save $22,400 and $2,030 compared with the matrix pooling strategy, respectively. Moreover, the simple pooling strategy could save the cost of 10,000 tests by up to approximately $100,000 and $200,000 in each scenario compared with individual testing, respectively.

The cost simulation was applied to country-specific circumstances in India, South Africa, South Korea, the UK, and the US that were recorded between October 4, 2021, and October 10, 2021. Depending on the cost per test and PRs of each country, the preferable strategies for achieving cost savings were different. Each country had different cutoff points at which both pooling strategies did not show cost-saving effects over individual testing. Particularly, these cutoff points of PRs were higher when the costs per test were higher. The cutoff points having no cost-saving effect of pooling strategies were PR 5.11% (pool size = 5) and PR 2.87% (pool size = 10) in India (cost per test, $31.98), whereas the points were PR 23.67% (pool size = 5) and PR 13.32% (pool size = 10) in the US (cost per test, $148). In South Africa, pooling strategies had no cost-saving effect when the PR was 9.17% and more (pool size = 5) or 5.16% and more (pool size = 10). In South Korea, pooling strategies were preferable when the PRs were less than 10.62% (pool size = 5) and 5.97% (pool size = 10) considering costs. At these cutoff points, pooling strategies were worth considering with cost simulation to determine the best cost-saving strategy.

There are some limitations to this study. First, this study did not consider the mixed use of individual testing and pooling strategies. The combination of testing strategies (e.g., individual testing for symptomatic people and simple or matrix pooling testing for asymptomatic people for massive group testing, often applied to soldiers or students) can be simulated in further studies. Second, the total amount of cost saving might have been overestimated because we used the same cost per test for individual testing and pooling strategies. In some countries, the fee might have been designated depending on the testing strategies. Lastly, we did not consider the contribution of human errors occurring during the pooling process. In case of human error, additional costs can be incurred and the time to diagnosis delayed.

In conclusion, our study simulated the cost of COVID-19 testing strategies including two types of pooling strategies in scenarios with different PRs, pool sizes, and costs per test. Both pooling strategies showed cost-saving effects over individual testing depending on the PRs and pooling sizes, especially in situations with low PRs. In real-life situations with low PRs of COVID-19, simple or matrix pooling strategies may be worth considering to counter the high costs of screening at the population level.

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## CONFLICT OF INTEREST

The authors have no conflict of interest to disclose.

## DATA AVAILABILITY STATEMENT

The authors confirm that the data supporting the finding of this study are available from the corresponding author upon reasonable request.

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## SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

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