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ORIGINAL RESEARCH

Using a Systems Engineering Approach to Build a PCR Testing System at a Medical School During the COVID-19 Pandemic

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Background: During the COVID-19 pandemic, there was an increasing need to expand diagnostic testing in hospitals. At Keio University Hospital (KUH), clinical staff were concerned that the demand for PCR testing might exceed the capacity of the Clinical Laboratory. In response, basic researchers at Keio University School of Medicine (KUSM) set out to build a new, collaborative, PCR testing system. To be authorized to perform such diagnostic PCR testing, KUSM registered its core laboratory as an external clinical laboratory (ECL).

Methods: In the pandemic, there was a pressure to build the PCR system quickly. Speed required discussions that developed a shared understanding of the unprecedented, new KUH/KUSM PCR system. To design, construct, and archive the new PCR testing system, we used a systems engineering (SE) approach. This included diagram visualization of functional flows and application of the Unified Architecture Framework (UAF), both of which are often used in system building. We considered daily demand for PCR testing at KUH and KUSM, and daily COVID-19 infections in Japan.

Results: We operated the collaborative PCR testing system from August 2020 to June 2022. Given public health insurance reimbursement policies, KUH focused on individuals with suspicious symptoms, while the ECL at KUSM screened samples from asymptomatic individuals. KUSM performed about half as many tests as KUH. Interviewing KUH staff revealed that diagrams helped promote a better understanding of the KUH/KUSM PCR testing system.

Conclusion: When designing temporary systems that may be repurposed in the future, we suggest using an SE approach with diagrams and UAF perspectives. This approach will enable stakeholders to understand what is being proposed to be built, and facilitate achieving an informed consensus on the proposed system. We suggest that SE approaches should be widely used in projects that involve building and operating complex, collaborative systems, and documenting the process.

Keywords: COVID-19, PCR test, clinical laboratory, systems engineering, diagram, temporary system

Introduction

In the early phases of the Coronavirus disease 2019 (COVID-19, severe acute respiratory syndrome coronavirus 2, SARS-CoV-2) pandemic, countries worldwide struggled to meet diagnostic testing demands.[1–3] Challenges in testing were due to various factors, including shortage of supplies, reagents, personnel, personal protective equipment (PPE), and/or instruments necessary to detect infections by quantitative reverse transcription polymerase chain reaction (RT-qPCR).[4] Some basic research laboratories in academic institutions, especially those associated with hospitals and those that had already developed expertise and infrastructure, built systems to run RT-qPCR diagnostic or screening tests to overcome the overall test shortages.[1,5–8] In Japan, institutions (other than hospitals, clinics, or institutions designated by the Minister of Health, Labour and Welfare or MHLW) must obtain registration from the prefectural governor with jurisdiction as an external clinical laboratory (ECL) to perform clinical diagnostic tests.[9] COVID-19 was first classified as a "designated infectious

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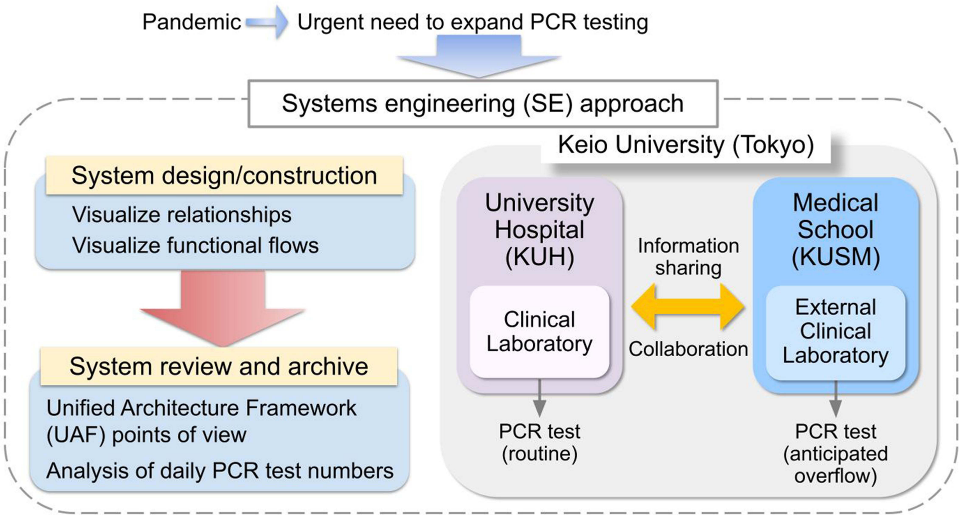
Graphical Abstract



disease" in February 2020, then in February 2021 as "the Novel Influenza and other diseases category (equivalent to Class 2)" under the Act on the Prevention of Infectious Diseases and Medical Care for Patients with Infectious Diseases (hereafter the Infectious Diseases Control Law) in Japan.[1,10] During these periods, strict measures were taken to prevent the spread of infection, based on the Infectious Diseases Control Law. Such measures may include notifiable disease surveillance (ie mandating medical facilities and Public Health Centers to report all new cases to the government); strong government involvement in the medical system, such as requesting hospitalization in the designated medical institutions, requesting that individuals take unified basic infection control measures in daily life (eg wearing masks, hand hygiene/ ventilation, avoiding the "Three Cs" of Closed spaces, Crowded places and Close-contact settings, and keeping a sufficient distance from others); and requesting that people who are infected with SARS-CoV-2, and those who have been in close contact with infected patients, refrain from going out. On May 8, 2023, the Japanese government reclassified COVID-19 as Class 5 (the same category as common infectious diseases, including seasonal flu, mumps, and measles), and eased its policies on infection control and restrictive measures.[10]

Keio University is one of more than 80 universities in Japan with its own hospital and medical school. Keio University Hospital (KUH) is a 960-bed tertiary care center in the center of metropolitan Tokyo. The Tokyo Metropolitan Government designated KUH as one of the medical institutions to admit COVID-19 patients. Its affiliated medical school, Keio University School of Medicine (KUSM) is known as one of the top medical schools in Japan,[11] and has world-leading research activities (in fields of stem cell biology, microbiomes, and multi-organ network analysis, among others). We anticipated that the capacity of the testing system at KUH alone would not meet the demand, and we considered expanding the capacity of the testing system with the cooperation of basic researchers from KUSM.[11] However, like all other medical schools in Japan, KUSM needed to register itself as an ECL to carry out clinical tests under the governmental regulations.

To build an agile and flexible cooperative testing system, it was necessary to build a consensus between the decision-makers at KUH and KUSM. To do so, we used a systems engineering (SE) approach. Systems engineering is an interdisciplinary approach that integrates all the disciplines and specialty groups into a team effort, creating a structured development process that moves from concept to product to operation.[12] SE has long been successfully applied to manage the development and operation of complex (and agile) defense and aerospace systems, and has been adopted in other fields, such as in establishing businesses or social programs.[12] Clarifying potentially complex interactions for stakeholders helps ensure that the expectations of all stakeholders will be addressed effectively, and that their respective roles will be clearly defined. However, to our knowledge, SE approaches have been rarely used in medicine, including risk management and policy decisions in health care. By applying SE to our case, we aimed to construct a new collaborative system in the most efficient way possible and to reach consensus in a smooth and transparent manner. Here, we outline how we quickly created an agile PCR diagnostic and screening test system for COVID-19 at KUSM. We demonstrate that our approach was effective in establishing a collaborative system and in identifying potential problems or bottlenecks. We anticipate that documenting our system-building experience should prepare us to respond more quickly and effectively to potential future health crises. To our knowledge, this is the first case study to show that SE is useful and applicable in the field of healthcare, and we believe that it will be a new focus of research in medical system management.

Materials and Methods

Study of COVID-19-Related Local Events

To visualize the timelines relevant to this study, we collected information on local events using online sources[13–15] for the period during which COVID-19 was declared as a global health emergency by the World Health Organization (WHO) (between March 2020 and May 2023) and published information from institutions such as the WHO[16] and the records from KUH and KUSM.

Description of Organizational Activities at Keio University

During the construction of the collaborative system between KUH and KUSM, we interviewed KUH staff to gain insights into their expectations from using the ECL as an auxiliary PCR testing system. Specifically, we interviewed and held discussions with five members of the Genomic Laboratory staff, three members of the Clinical Laboratory staff, four members of the Infectious Diseases and Infection Control staff, two members of the Dental and Oral Surgery staff, two members of the Preventive Medicine staff, and two members of the administrative staff. We reached a consensus with KUH staff by drawing, sharing, and discussing system diagrams, as described below. We then proceeded with the system construction. The senior author of this study and head of the ECL (KM) managed the system construction.

After we had built the PCR diagnostic system, we retrospectively reviewed and described the key points in the system construction process so that we would retain a record using the Unified Architecture Framework® (UAF®).[17] We used Summary and Overview, Strategic, Operational, Services, Resources, Standards, Personnel, and Security perspectives as references to describe what we had considered while developing the KUH/KUSM system.

Drawing Diagrams

We illustrated the flow of samples and information passed among the stakeholders involved in the PCR test system and the relationships among them using publicly-available online software "diagrams.net" (https://www.diagrams.net/). Utilizing the SE representation method, we created diagrams showing both the functional flows and the departments at KUH and KUSM that were responsible for the functions. In addition, we also made a diagram that described the steps we took in this study (Figure 1).

Number of PCR Tests and Daily New Cases in Japan

The number of PCR tests at KUH was obtained from the hospital's Department of Clinical Laboratory, while the numbers for KUSM were obtained from the ECL. The collection of PCR test data within Keio University received IRB approval from the Institutional Review Board of Keio University (IRB-ID: 20200344). The number of daily new cases in Japan was obtained from https://www.mhlw.go.jp/stf/covid-19/open-data_english.html. The numbers of PCR tests at KUH and KUSM and daily new cases in Japan were visualized using R (v4.1.1).

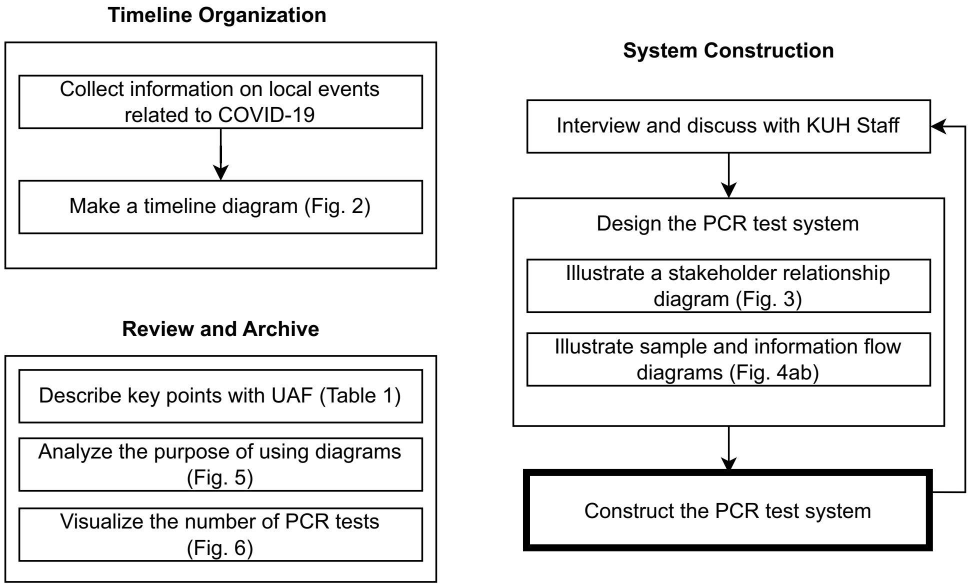


Figure 1 An overview of the study. The diagram describes an overview of the steps taken in this study.

Results

Exploration, Stabilized, and Idle Phases of the PCR System

From late March to early April 2020, KUH experienced a COVID-19 outbreak, which was accompanied by nosocomial (hospital-acquired) infections in patients and health-care workers.[18] A significant proportion of the viral transmission during this outbreak occurred among asymptomatic or presymptomatic individuals. To prevent another spike in nosocomial infections and to maintain hospital operation, KUH adopted universal COVID-19 PCR screening for asymptomatic patients before planned hospitalization due to non-COVID-19 reasons,[19] as well as for hospital staff. With the exponential increase in the demand for testing, there was a growing concern that KUH's Clinical Laboratory would become overwhelmed. KUH personnel communicated information about supply shortfalls, testing quantities and outcomes, and hospital bed occupancy to KUSM faculty members. To alleviate the burden on KUH staff, basic research laboratories in KUSM started to build a system to undertake PCR tests as a backup for KUH. To do so, we registered the Collaborative Research Resources at KUSM as an ECL (Figure 2). Contrary to what we had feared, KUH never

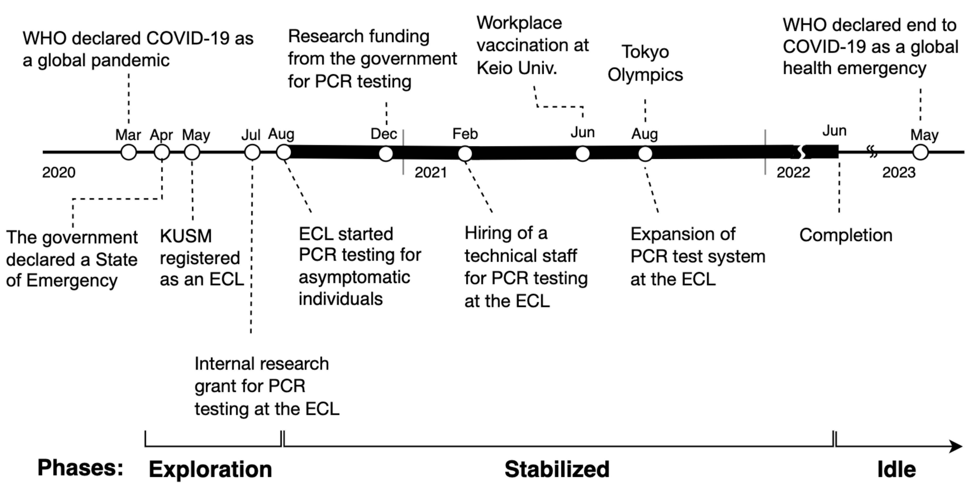


Figure 2 A timeline of the local events and the building process of the PCR test system at KUSM during COVID-19 pandemic. The thick black line indicates the stabilized phase (August 2020 to June 2022). Circles indicate local events that were relevant to the PCR test system. The exploration phase was defined as the period in which the test system at KUSM was created and developed (between March and August 2020); the stabilized phase as the period in which the PCR test system was in operation and was stabilized (between August 2020 and June 2022); and the idle phase as the period when the PCR test system was not in active use but could quickly be made executable.
Abbreviations: KUSM, Keio University School of Medicine; ECL, external clinical laboratory.

experienced an overflow. Instead, starting in late August 2020, KUSM began conducting non-urgent COVID-19 screening testing, ie, testing healthy and asymptomatic individuals who were at KUH for medical checkups or dental treatments. Starting from August 2021, this was extended to include Keio University students. Such measures allowed KUH to maintain its capacity to test recurring patients who had suspicious symptoms or a history of high-risk exposure, to manage patients already diagnosed, and to screen patients scheduled for hospitalization.[20] Over time, the PCR testing system at KUSM evolved. To report the system accurately, we defined three phases: (i) the "exploration" phase (between March and August 2020), the period in which the PCR test system at KUSM was created and developed; (ii) the "stabilized" phase (between August 2020 and June 2022), the period during which the PCR test system at KUSM was operated routinely; and (iii) the "idle" phase (after July 2022), the period in which the PCR test system was no longer in operation at KUSM (Figure 2).

Points Considered Within the UAF Framework for the PCR Testing System

In the SE field, a variety of "Enterprise Architectures" have been developed to establish different systems, such as in defense, government, and industry. Various enterprise architectures have been integrated into the UAF.[21] When creating a new system, UAF allows for a logical and systematic understanding of the relationships among the elements/components within the system from different perspectives, such as organizations, operations, services, resources, and personnel.[17] The UAF defines "ways of representing an enterprise architecture that enables stakeholders to focus on specific areas of interest in the enterprise while retaining sight of the big picture".[17] In general, the UAF is used before and during the creation of a system. This allows for prospective detailing of enterprise designs. However, in our case, we applied the UAF viewpoints retrospectively as a helpful tool for understanding and organizing important points in the PCR testing system at the ECL (Table 1).

At a cross-departmental leadership meeting in mid-March 2020 (ie during the "exploration" phase), leaders at Keio University, including the Dean of KUSM and the director of KUH, exchanged ideas for expanding the testing capabilities for SARS-CoV-2 infections. They shared the concern that KUH would become overwhelmed, which would result in the KUSM researchers needing to quickly establish a PCR test system to support the hospital (Table 1, Summary and Overview).

In early 2020, diagnostic PCR tests for COVID-19 were allowed only for those who had symptoms or were in close contact with infected individuals. To expand the overall capacity for testing, MHLW of Japan issued an ordinance in March 2020 to simplify the process of registering facilities (medical institutions, academic laboratories, or commercial

Table 1 Points of Consideration Based on the UAF Framework

Summary and Overview	**Pandemic-Driven Establishment of a PCR Test System at KUSM to Support KUH**	
	Exploration Phase	**Stabilized Phase**
Strategic	To create an agile/flexible PCR testing system at KUSM and accommodate "overflow" testing demands from KUH: - Registering as an ECL (registering The Collaborative Research Resources as ECL, KUH's request) - Applying for internal funding to buy necessary reagents and kits - Back-up for overflowed samples on standby - Allowing only inactivated samples to KUSM (KUSM's request)	To protect medical staff and patients and establish a stable examination system: - Performing PCR tests for healthy individuals at KUSM - Applying for external fundings - Allowing only inactivated samples into KUSM (at KUSM's request)
	Pursue academic value in analyzing the system construction process	
Operational	Collect samples, PCR test, record, report	
Services	- Set up reagents and devices - Collect samples at KUH - Nasopharyngeal swab samples - Inactivation at KUH - PCR testing of overflow samples* at ECL (planned)	- Procure reagents and devices - Self-collected - Saliva samples - Inactivation at KUH - PCR testing of samples from asymptomatic individuals at ECL

(*Continued*)

Table 1 (Continued).

<table>
<tr><th>Summary and Overview</th><th colspan="2">Pandemic-Driven Establishment of a PCR Test System at KUSM to Support KUH</th></tr>
<tr><th></th><th>Exploration Phase</th><th>Stabilized Phase</th></tr>
<tr><td>Resources</td><td>Facility: Clinical Laboratory (BSL3 level) at KUH
ECL (BSL2 level) for overflow samples (planned)
Virus inactivation was done in the Genome Laboratory (BSL2 level) at KUH.
Equipment: PCR machines for research
Reagents: Various emerging commercial kits
Only one kit was selected and used at the ECL.
There was a bottleneck for reagent supplies.
Internal Funding: the Keio University Global Research Institute (KGRI)</td><td>Facility: Center of Preventive Medicine or Department of Dentistry and Oral Surgery
Virus inactivation was done in the Genome Laboratory (BSL2 level) at KUH.
Equipment: Dedicated PCR machine
Reagents:
Only one kit was selected and used at ECL.
External Funding: Japan Agency for Medical Research and Development (AMED), Grants-in-Aid for Scientific Research (KAKENHI)
Internal Funding: Donner Project</td></tr>
<tr><td>Standards</td><td colspan="2">- Complying with laws/orders/regulations on infectious diseases
- Creating and validating a PCR protocol
- Registering The Collaborative Research Resources as an ECL
- Reporting PCR results to national and local governments</td></tr>
<tr><td rowspan="2">Personnel</td><td colspan="2">KUH: Clinical laboratory staff; KUSM: Staff from the ECL and the Genomics Unit</td></tr>
<tr><td>- Recruited volunteers among scientists and technical experts
Testing started to interfere with day-to-day work; thus, it became unsustainable to rely on volunteers.</td><td>Temporary staff from a job placement agency</td></tr>
<tr><td>Security and Safety</td><td colspan="2">Personal information protection was ensured by anonymizing samples.</td></tr>
</table>

Notes: *The ECL at KUSM did not receive overflow samples from the hospital because the Clinical Laboratory at KUH expanded its testing capacity within a short period.
Abbreviations: UAF, the Unified Architecture Framework; PCR, polymerase chain reaction; KUSM, Keio University School of Medicine; KUH, Keio University Hospital; ECL, external clinical laboratory; BSL, biosafety level.

clinical laboratories) as ECLs if the purpose was limited to COVID-19 PCR tests.[22] The Collaborative Research Resources, which served as a core facility at KUSM, provides PCR machines and other equipment for research activities. To perform PCR tests under quality control, we registered the Collaborative Research Resources with the Shinjuku City Public Health Center as an ECL, to be an auxiliary COVID-19 PCR testing site in Tokyo in early May 2020.

In retrospect, the main strategic goal during the exploration phase was to prepare KUSM for a possible “overflow” of test samples from KUH. Another goal was to create an agile and flexible PCR testing system at KUSM by considering various aspects, including ECL registration, securing internal funding, and setting up reagents and devices. The PCR kits used at KUH and approved by the Pharmaceuticals and Medical Devices Agency (PMDA) were obtained through internal funding. Once the system was established and stabilized at KUSM, the strategic emphasis shifted to protecting staff and patients (Table 1, Strategic).

The main functions of the established system included collecting samples, performing PCR testing, and recording and reporting the results (Table 1, Operational).

In the exploration phase, KUSM was to test nasopharyngeal swab samples from KUH as a backup, and these samples would be collected and virally inactivated within the hospital. We set up necessary reagents and devices at the ECL in preparation for performing PCR tests. In the stabilized phase, self-collected saliva samples from asymptomatic individuals were collected and inactivated at KUH, after which PCR was performed at the ECL (Table 1, Services).

We identified the assets (devices, rooms, etc.) available for PCR testing. Samples presumed to be infectious/contagious were handled at the hospital (in a safety cabinet). During the exploration phase, we anticipated that the primary site for PCR tests would be the Clinical Laboratory (Biosafety level 3, BSL3) at KUH, with the ECL (BSL2) serving as a contingency for sample overflows. However, there was no overflow, and, during the stabilized phase, the ECL performed PCR tests independently of the Clinical Laboratory. Specimens were collected at the Center for Preventive Medicine or the Department of Dentistry and Oral Surgery, and submitted to the ECL. Initially, a PCR device from the Collaborative Research Resources, intended for research, was repurposed for COVID-19 testing. Subsequently, a new PCR device was purchased using funding provided by the Japan Agency for Medical Research and Development (AMED). During the early phases of the pandemic, there was a supply bottleneck for reagents from other countries. To address this, we secured funding from the Keio University Global Research Institute (KGRI) to establish a system at KUSM that could support the expansion of PCR testing. Following the conclusion of KGRI funding, we received support from AMED and Grants-in-Aid for Scientific Research (KAKENHI) as external funding, and from the Donner Project as internal funding (Table 1, Resources).

We followed national laws/orders/regulations on infectious diseases, including the registration of the ECL and reporting of PCR results to national and local governments. PCR protocols were developed and provided by the National Institute of Infectious Diseases (Niid). A standard operating procedure (SOP) for COVID-19 diagnostic RT-qPCR was established for the newly registered ECL. Quality control was performed by the Clinical Laboratory at KUH (Table 1, Standards).

During the early stage of the pandemic, many scientists and technical experts from both KUH and KUSM volunteered to participate in the effort to address the health crisis. However, as time passed, this commitment began to encroach upon their regular responsibilities. Relying on volunteers who are hospital staff, scientists, and technicians, for the emergency response was thus unsustainable in the long run. Thus, during the stabilized phase, we engaged temporary staff through a job placement agency, enabling KUH and KUSM staff to do their own jobs (Table 1, Personnel).

Personal information protection was ensured by anonymizing the sample data. The collected samples were presumed to be infectious and were not allowed to be transferred directly to KUSM before being inactivated at KUH (Table 1, Security and Safety).

Stakeholder Relationships in the PCR Testing System

To design a new PCR-based COVID-19 testing system at KUSM, we first considered the stakeholders outside Keio University. This was because we needed to understand the relationships with outside stakeholders to better design the system from an SE perspective. Initially, KUH conducted PCR testing on patients and hospital staff suspected of infection. KUSM was ready to provide backup support in the event of specimen overflow at KUH, which could have been due to increased testing demands or decreased capacity due to a staff/supply shortage (Figure 3, red dotted line,

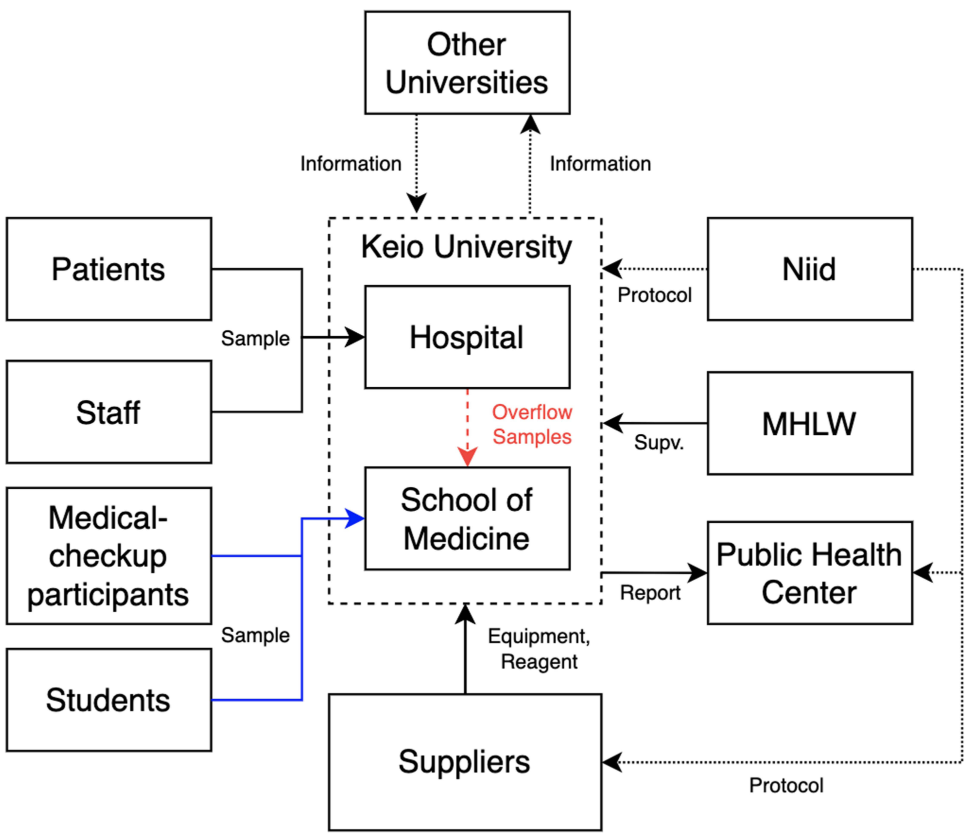


Figure 3 Shifts in stakeholder relationships in the PCR testing system during the exploration and stabilized phases. The squares indicate the stakeholders involved, and the arrows indicate the interfaces between the parties. The red dotted line represents an assumed emergency overflow due to demand for testing exceeding the capacity of KUH. Overflow samples were planned to be sent to KUSM for back-up COVID-19 testing. The blue line represents the actual PCR test flow performed at the KUSM, which was not initially planned.

Abbreviations: Niid, National Institute of Infectious Diseases; MHLW, Ministry of Health, Labour and Welfare; Supv., supervision.

Exploration Phase). When the ECL at KUSM started to provide PCR testing, it did not receive overflow samples, but instead started to take on PCR tests that were beyond the scope of the hospital, which prioritized patient care; that is, screening tests for asymptomatic individuals who were scheduled for medical check-ups, dental treatment, and students (Figure 3, blue line, Stabilized Phase). The blue line represents a flow that was not initially assumed but emerged and was addressed later. Niid provides standard protocols for hospitals, Public Health Centers, and suppliers. KUH conducted the tests using commercially available PCR test kits based on Niid's standard protocol and the U.S Centers for Disease Control and Prevention (CDC) guidelines. The role of the MHLW is to supervise hospitals and Public Health Centers under the Infectious Disease Control Law. Under the jurisdiction of prefectural governments, Public Health Centers have been central to COVID-19 responses, including conducting PCR testing, coordinating the treatment of COVID-19-positive patients, and identifying individuals who have been in close contact with COVID-19 patients through an epidemiological study of each positive case in Japan.[23,24] Hospitals and medical laboratories must report positive results to their Public Health Center, which collects and manages data on the total number of daily infections and occupied hospital beds that care for patients.

During the early stages of the COVID-19 pandemic, PCR reagents were often in short supply. Clinical laboratories introduced equipment that could perform a large number of tests, in preparation for situations in which the number of infections had increased. Thus, suppliers of reagents and equipment should also be recognized as important stakeholders.

Changes in the PCR System (Exploration to Stabilized Phases)

In the exploration phase, when the PCR system was being built, functional flow diagrams of the PCR testing systems at KUH and KUSM were created through discussions among stakeholders (Clinical Laboratory, Department of Division of Infectious Diseases and Infection Control, Genome Laboratory, and ECL). We used an SE approach to visualize the sample/functional flow (Figure 4a) to clarify which departments were responsible for a function and to support collaboration between departments. The Clinical Laboratory was responsible for testing patients who were scheduled to be hospitalized at KUH for non-COVID-19 purposes, outpatients with suspicious symptoms, and staff who had contact with PCR-positive individuals. In the exploration phase, the ECL prepared to take on testing overflow samples from KUH; in this scenario, samples from the Clinical Laboratory at KUH would undergo viral inactivation at the Genome Laboratory before being transferred outside of KUH to the ECL at KUSM; PCR test results for the overflow samples were expected to be returned to the Clinical Laboratory (Figure 4a, red dotted arrows).

In the stabilized phase, the ECL started to perform PCR testing for individuals who were scheduled for medical check-ups at the Center for Preventive Medicine as well as for patients who were scheduled for treatment at the Department of Dentistry and Oral Surgery but was still ready for a possible overflow from KUH. The Center for Preventive Medicine and the Department of Dentistry and Oral Surgery participated in discussions on the workflow diagram (Figure 4b, purple solid arrows). Early in the pandemic, the Clinical Laboratory continued to expand its PCR test capacity (eg purchasing more PCR devices, hiring staff, improving operational efficiency, etc.); therefore, there was never a sample overflow from KUH to the KUSM ECL (KUH found that it could handle its samples, and did not have to transfer samples to the ECL).

In both the exploration and stabilized phases, samples were inactivated at the KUH Genome Laboratory because the institutional policy mandated that samples that had any infectious/contagious risk had to be handled within the hospital.

For the period February 2020 to May 8, 2023, COVID-19 was classified as a "designated infectious disease" and then as a 'Novel Influenza and other diseases', (equivalent to a category 2 infectious disease under the Infectious Diseases Control Law in Japan[1,10]). Given this, the total number of positive cases had to be reported to local government, the Public Health Center, and the MHLW. Central and local governments have created digital tools (eg G-MIS of the MHLW and BC-Portal of the Tokyo Metropolitan Government) to report COVID-19 cases.

Diagrams Have Served Multiple Purposes

Figure 5 illustrates the transitions in the SE diagrams that describe the structures of the PCR testing system from the exploration phase to the stabilized and idle phases. During the exploration phase, the research team, including the KUSM director of the ECL, discussed with those who were in charge of the KUH Clinical Laboratory how to establish a back-up system in case the Clinical Laboratory became overwhelmed due to high PCR testing demands. We could determine the

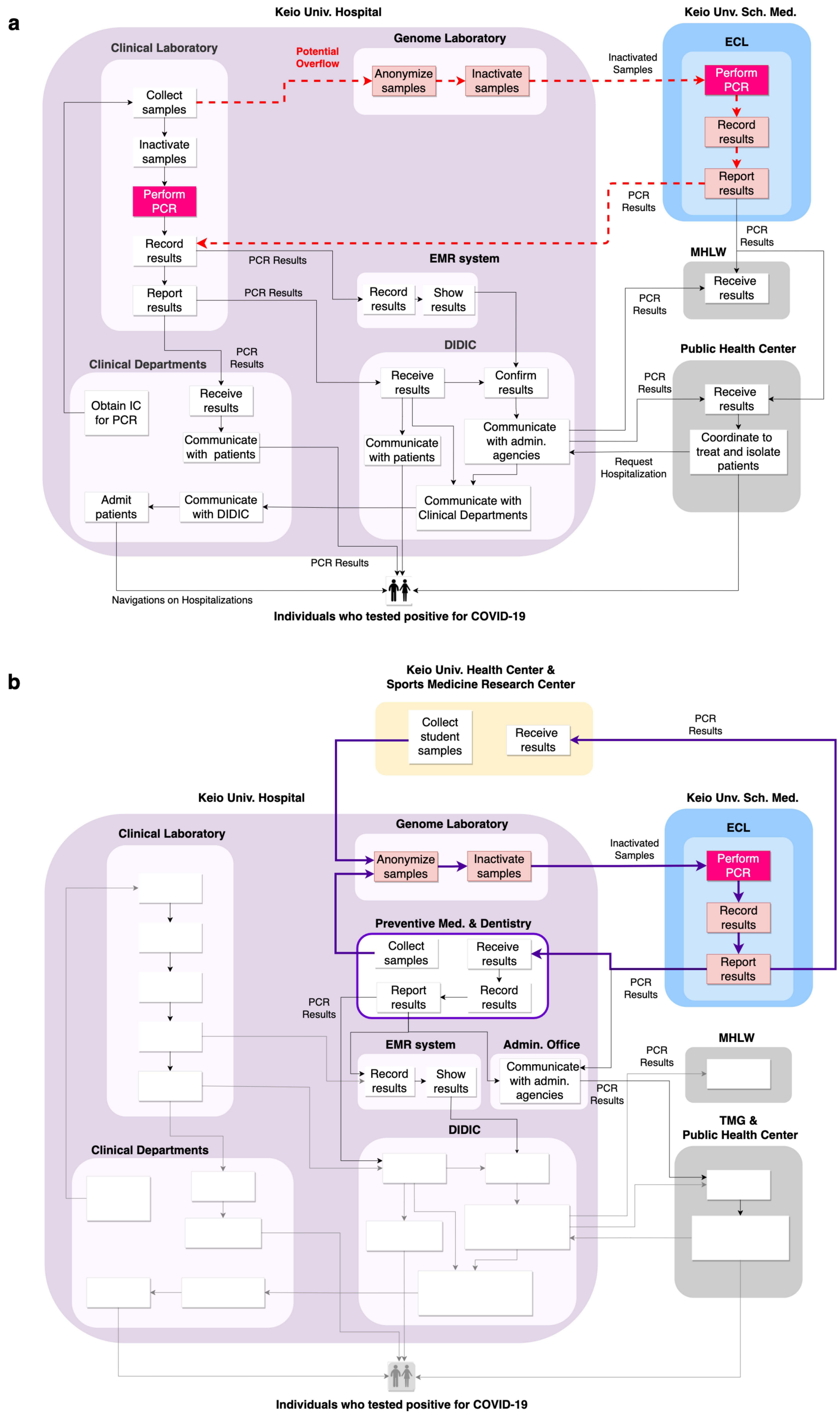


Figure 4 Functional flow diagrams of the PCR testing system. (**a**) Exploration phase. Red dotted arrows indicate the hypothetical overflowed PCR samples from KUH to KUSM. (**b**) Stabilized phase. Thick purple arrows indicate the actual flow of PCR samples from the Departments of Preventive Medicine and Dentistry to KUSM. Note that viral inactivation is performed at hospital before samples are sent to KUSM. The purple, light blue, and gray backgrounds represent the KUH, KUSM, and administrative agencies, respectively. Functions of each branch (within boxes) that did not change from the exploration phase to the stabilized phase were removed for simplicity.
Abbreviations: IC, informed consent; TMG, Tokyo Metropolitan Government; EMR, Electronic medical record; ECL, external clinical laboratory; DIDIC, Division of Infectious Diseases and Infection Control; MHLW, Ministry of Health, Labour and Welfare.

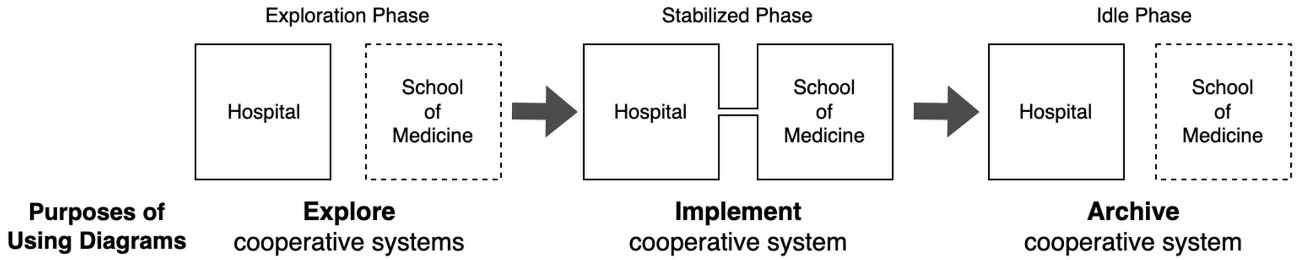


Figure 5 Transitions in the purpose of using diagrams changed over the three phases. Dotted squares indicate that KUSM ("School of Medicine") did not participate directly in the PCR testing.

details of the cooperative system by using an SE diagram, for example, where the responsibilities of the functions lie and the interfaces between organizations, such as specimen delivery and communication of PCR results. This diagram enabled us to implement the system promptly.

In the stabilized phase, no emergency demand exceeded the testing capacity of KUH Clinical Laboratory. However, the ECL performed PCR tests for individuals undergoing medical checkups at the KUH Center for Preventive Medicine and for patients who were scheduled for treatment at the KUH Department of Dentistry and Oral Surgery.

As shown in Figure 4b, the KUH and KUSM collaborations in PCR testing were fully realized in the stabilized phase. Such a diagram helped the Center for Preventive Medicine, Department of Dentistry and Oral Surgery, Genome Laboratory, and ECL understand the cooperative system structure for PCR testing. In the idle phase, the diagram served as an archive, so that the hospital and medical school could rapidly reestablish collaboration and immediately set up a system to expand PCR testing when a next pandemic occurs.

Figure 6 shows the number of PCR tests performed at KUH and KUSM, as well as the number of new infections reported daily in Japan from February 2020 to September 2022. The stabilized phase lasted from August 2020 to the end of June 2022, when the PCR tests were performed at KUSM. Prior to this period, there was an exploration phase during which the number of PCR tests at KUH increased (especially from May 2020). During the stabilized phase, approximately 100 PCR tests were performed at KUH per day. However, in October 2020, there was a significant increase in the

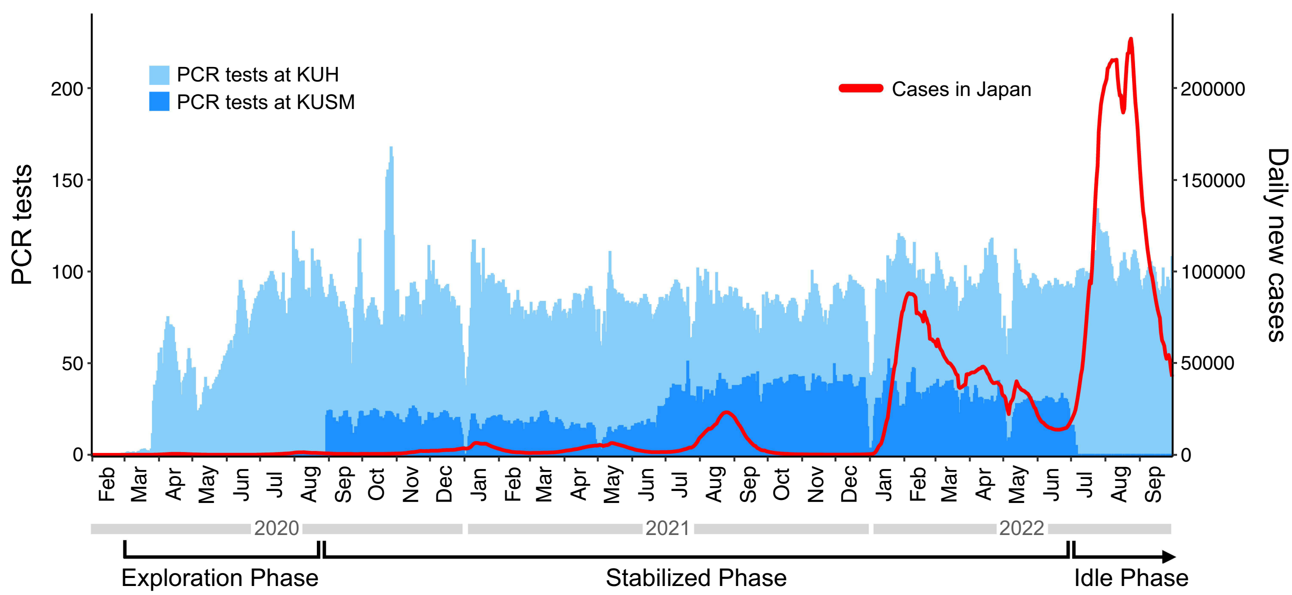


Figure 6 Number of PCR tests at KUH and KUSM, and daily new infections in Japan. Light blue bars indicate 7-day mean number of PCR tests performed at KUH; dark blue bars indicate 7-day mean number of PCR tests performed at KUSM; Red line indicates number of daily new confirmed cases in Japan. The number of PCR tests at KUH was obtained from the Department of Clinical Laboratory, and that of KUSM was obtained from ECL. The number of daily new cases in Japan was obtained from https://www.mhlw.go.jp/stf/covid-19/open-data_english.html.

Abbreviations: KUH, Keio University Hospital; KUSM, Keio University School of Medicine.

number of tests at the hospital, which was caused by the spread of infection among hospital staff. KUSM increased its PCR testing capacity from June 2021, when it began testing students in Keio University's sports clubs, and the number of tests almost doubled in July of the same year. After July 2022, PCR tests at KUSM were put on hold because of decreased demand; however, the ECL remained ready to perform PCR testing when necessary (idle phase). Finally, we compared the number of tests performed at KUH and KUSM with the number of SARS-CoV-2 infections reported in Japan to see if there was any relationship between them; we found no apparent correlation.

Discussion

The work reported here shows that the diagram-driven construction of a new system using an SE approach allowed the rapid implementation of a PCR-based COVID-19 testing system in a medical school during the COVID-19 pandemic.

Like many other institutions in many countries, KUSM initially faced the unprecedented health crisis of the COVID-19 pandemic with confusion and concern. In response, KUSM developed a PCR system to support medical care at KUH. We used an SE approach to build the new KUSM PCR testing system but also to analyze its structure and the building process. We developed the PCR testing system at KUSM in three phases: exploration, stabilized, and idle (Figure 2). In documenting this project, we leveraged the UAF to identify the aspects integral to the creation and deployment of the PCR testing system. As mentioned above, UAF is useful for identifying points that should be considered in detail when designing and building a new system. Within a diverse group of stakeholders, we were able to understand and share important points in our PCR testing system design. Further, it became evident that these considerations would evolve as the system transitioned from the exploration to the stabilized phase (Table 1).

The UAF not only helped us clarify the organizational structure and role allocation, which tended to be our focus of attention, but also helped document resources (facilities, equipment, reagents, and funding) and standards for rules and protocols, security, and safety. This record should enable us to swiftly refer to a wide range of points that should be considered when resuming the PCR testing system at Keio University or when creating a new diagnostic/screening system at the beginning of a next potential pandemic.

As for the obstacles of building the system in the early phase of the pandemic, global supply shortages coupled with a surge in demand made it challenging to obtain PCR reagents; thus, reagent supply was a major bottleneck in our PCR testing system. However, the reagent supply shortage was resolved over time, and it stopped being a limiting factor. Initially, we had expected shortages of manpower and equipment to become limiting factors, but this turned out not to be the case. We were able to hire technical staff through a job placement agency, and we repurposed a research PCR machine for COVID-19 testing. Subsequently, we purchased a new PCR machine that we dedicated to testing. The most difficult and rate-limiting challenge proved to be that we were designing and building a system that did not exist, and, for a while, we had little idea of which stakeholders to connect. Gradually, we came to understand that people in the medical school were unfamiliar with how different sections were organized and how information was shared/distributed within the hospital. In this context, the use of diagrams was helpful. It helped us build the new system because it allowed us, and a diverse group of collaborators, to grasp the whole picture.

In screening for an infectious disease, quality control is paramount. Facilities engaged in testing must meet the requirements imposed by the government. Requirements for an ECL included establishing SOPs, creating mechanisms for saving log data, setting up a reporting system, as well as periodic participation in quality control testing provided by the local government.

In addition, in order to protect medical school students, KUSM requested that raw samples, which were presumably infectious, should not be brought into the medical school. According to this policy, we allocated the role of sample inactivation to the hospital and arranged that inactivated samples be sent from KUH to KUSM (Figure 4a and b).

Figure 3 shows the relationships between the stakeholders in the PCR testing system. Given that the functions and structures of a system are determined by the relationships within and outside of the system, it is important to understand the relationships among stakeholders. During the exploration phase, we built a conceptual framework that would allow testing overflow samples from KUH using PCR. As we prepared personnel, equipment, and reagents, the need for samples became pressing. Concurrently, KUH was not screening individuals for COVID-19 who were visiting KUH for medical check-ups, while it routinely tested those who were scheduled for hospitalization. Thus, the KUSM ECL began analyzing samples from individuals who were scheduled for medical check-ups or dental treatments, as well as asymptomatic students.

The level of detail appropriate for a system flow diagram tends to vary with the intended purpose and the target audience. Early in the exploration phase, as we were planning the system, we created and used diagrams that were much more detailed, describing specific items and types of information communicated between stakeholders. These comprehensive flow diagrams facilitated discussions regarding field-level actions among different sections/departments at KUSM and KUH. They ensured a mutual understanding of the system, minimized ambiguities, and promoted collective decision-making. Additionally, the detailed diagrams also helped us find several established ways that would be worth reconsidering, such as analog communications (eg paper and/or telephone) within departments, and rules that would require us to report the same information (ie number of positive cases) to different levels of governments (eg MHLW and local governments). Reflecting on what we have learned, generating detailed flow diagrams may help improve the system structure, while broader diagrams might be more apt for conveying system overviews, for instance, when comparing systems across universities.

As described above, diagram visualization was useful both during the exploration and stabilized phases for establishing and refining a consensus on the new system. Currently, the KUSM ECL is in its idle phase, and is not conducting PCR tests. However, by preserving the diagrams and the UAF list (Table 1), we anticipate that it should be much quicker to restart the PCR testing system should another pandemic occur.

The number of PCR tests performed at KUH and KUSM remained relatively stable as compared to the daily positive cases in Japan. The increase in PCR tests at KUSM since June 2021 was due to the request from the Keio University's sports clubs to allow students to resume team sports activities and joint practice. With retrospect, the Keio PCR testing system has remained relatively unaffected by the domestic pandemic trends. This could be explained by the fact that KUH did not have a "fever clinic" for outpatients with fever or fever-related symptoms and that subjects for testing were mostly hospitalized inpatients and outpatients who visited each clinical department for their individual diseases — with no significant fluctuations in the patient population being tested. It should be noted, however, that an increase in the number of staff members affected by infection would result in an increase in the number of patients requiring testing — as we observed in October 2020.

In general, medical schools have resources for testing infectious diseases, but are not usually tasked with performing clinical diagnostic tests. Driven by the COVID-19 pandemic, we report here on how we generated a new collaborative system in which a medical school supported a hospital by conducting clinical diagnostic tests.

Although the SE approach allowed for efficient system building, it took a considerable amount of time to reach a consensus on PCR screening tests (most of which were negative). This was partly because, in the early phases of the pandemic, screening tests for asymptomatic individuals were controversial among some of the medical establishment in Japan from epidemiological and societal perspectives, as follows. For example, at the beginning of the pandemic, the epidemiological advice was that PCR testing should be focused on those who have suspicious symptoms or have been exposed, and should not be performed on asymptomatic subpopulations that have no known exposure. There were also concerns for false negative and false positive test results.[25] Further, there were concerns that screening tests might hinder the social and economic activities of individuals who tested positive via PCR but were otherwise healthy. There was also skepticism regarding the utility of testing subpopulations with anticipated low positive rates.

Ultimately, KUH tested patients who were either symptomatic (covered by health insurance) or scheduled to be hospitalized for the treatment of their disease, and KUSM screened asymptomatic individuals who would not have been eligible for PCR tests at KUH. This division of labor allowed the hospital to focus on its primary duties. In addition, the importance of screening asymptomatic individuals including medical check-up visitors and university students became more and more accepted within Keio University.

Over time, PCR testing gradually became more available at testing sites offered by local governments or clinics, eliminating the need for testing inside medical schools. Consequently, we transitioned our PCR testing system to the idle phase. Thus, medical schools supported the community when the social infrastructure was not ready for an emergency.

This study demonstrates a real-world example of building a new collaborative testing architecture in an agile and efficient manner by applying an SE approach. Commonly used narrative description and analysis is effective for recording target events as they occur. But it is difficult to directly apply the know-how to different situations and to convey information effectively. By contrast, our methods of using flow diagrams and UAF perspectives allowed us to extract abstract knowledge and communicate intuitively, and can easily be applied in different contexts. In addition, visualizing the system being created through diagrams enabled each stakeholder to quickly and more easily understand the big picture of the complex proposed system and reach consensus.

During the COVID-19 pandemic, the expansion of diagnostic testing systems through collaboration between medical schools and hospitals was observed in many other academic institutions. Support systems by medical schools have mostly finished by the end of 2023, but will likely be needed again when another health crisis emerges.

This study has several limitations. First, we focused on our institution (n of 1) and did not compare our case with other institutions. Second, we did not perform quantitative data analysis to validate the effectiveness or convenience of our SE approach. Future studies should compare the collaborative systems among multiple institutions using the SE approach. We suggest it may be worthwhile exploring the potential applications of SE methods in other healthcare management. Although COVID-19 is less of a global health emergency now, our methods may be useful in the future when another deadly infectious disease emerges.

Conclusion

The process of building a new system, especially a temporary one, can be forgotten if not recorded. We propose that SE approaches used to document the process of creating a new and temporary system can be applied to a variety of other purposes.

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Disclosure

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