Improving Data Surveillance Resilience Beyond COVID-19: Experiences of Primary heAlth Care quAlity Cohort In ChinA (ACACIA) Using Unannounced Standardized Patients

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We analyzed COVID-19 influences on the design, implementation, and validity of assessing the quality of primary health care using unannounced standardized patients (USPs) in China. Because of the pandemic, we crowdsourced our funding, removed tuberculosis from the USP case roster, adjusted common cold and asthma cases, used hybrid online–offline training for USPs, shared USPs across provinces, and strengthened ethical considerations.

With those changes, we were able to conduct fieldwork despite frequent COVID-19 interruptions. Furthermore, the USP assessment tool maintained high validity in the quality checklist (criteria), USP role fidelity, checklist completion, and physician detection of USPs. Our experiences suggest that the pandemic created not only barriers but also opportunities to innovate ways to build a resilient data collection system.

To build data system reliance, we recommend harnessing the power of technology for a hybrid model of remote and in-person work, learning from the sharing economy to pool strengths and optimize resources, and dedicating individual and group leadership to problem-solving and results. (*Am J Public Health*. Published online ahead of print April 28, 2022:e1–e10. https://doi.org/10.2105/AJPH.2022.306779)

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As the COVID-19 pandemic swept through the world,[1] it has resulted in severe work disruption in all walks of life. National health and health care surveillance efforts are no exception. A resilient health surveillance system is critical for dealing with the current as well as future pandemics. Primary heAlth Care quAlity Cohort In ChinA (ACACIA) was launched in 2017 to longitudinally track the quality of primary health care (PHC).[2,3] The initial round of ACACIA data collection coincides with the pandemic. The pandemic interrupted every step of ACACIA's work. However, despite the COVID-19 challenges, we have remained agile in adapting to the pandemic environment and maintaining our fieldwork. Our experiences in making and implementing those decisions can be helpful for other complex nationwide data collection efforts. Meanwhile, as we intend to make the ACACIA data publicly available, fully disclosing the COVID-19–related changes and their impact on data validity is critical for future users to interpret the data in context.

After presenting a brief review of the history of ACACIA, we discuss the influences of COVID-19 on a full implementation spectrum of the program and the resultant program adjustments. We

then report the preliminary results of the study and discuss the influence of COVID-19 on the validity of our quality assessment tool. Finally, we discuss the lessons learned and our recommendations to build a resilient data collection system during and beyond COVID-19.

HISTORY AND OVERVIEW

ACACIA was conceptualized in 2017 in response to an increasing call for improving the quality of PHC toward the realization of universal health coverage. China has made substantial progress in developing its PHC since the 2009 national health reform, having achieved universal health insurance coverage.[4] However, universal health coverage goes beyond access to care; it also includes quality of care.[5] There has been scanty information about the quality of China's PHC,[6] although the limited studies so far suggest that the overall quality is unsatisfactory.[4,7,8] ACACIA used unannounced standardized patients (USPs) to assess PHC quality with a nationally representative sample of primary care providers across 7 provinces in China.[2,3] ACACIA involves 10 multidisciplinary teams: from Southern Medical University, Guizhou Medical University, Lanzhou University, Sun Yat-sen University, Sichuan University, Central South University, Inner Mongolia Medical University, Xi'an Jiaotong University, China Pharmaceutical University, and Guangzhou University.

Standardized patients (SPs) are healthy people who, after rigorous training, simulate the symptoms and emotions of an actual patient with certain conditions in a consistent fashion.[9] The USP case includes 3 critical components: a decoy plan (methods to conceal the true identity of the USP), a script (standardized lines for the USP–clinician conversation), and a quality checklist (evidence-based guideline-suggested items for consultation, medical exams, diagnosis, and treatment plans). The USP as a quality assessment tool has 3 distinct advantages: it (1) directly assesses quality in actual practice,[9–11] (2) minimizes the Hawthorne effect,[12] and (3) inherently controls patient-level variations.[13] To the best of our knowledge, ACACIA was the first attempt to nationally use USPs for quality assessment, probably because of the complexity of developing USP cases and recruiting, training, and fielding USPs on a national scale.

USPs have been increasingly used in quality assessment for PHC in recent decades.[14] The implementation experiences of ACACIA can help other USP projects to cope with COVID-19 challenges. We here discuss a few unique features of ACACIA to put the lessons learned in context. First, we used 11 USP cases to represent common conditions in PHC in China, whereas prior studies generally used 1 to 5 cases.[9,15] Second, we constructed a nationally representative sample of PHC providers, whereas most studies restricted their samples to a health system or several cities.[9,15] Third, we comprehensively validated each USP case and USP player, whereas many studies assumed the validity of the USP as an assessment tool. Fourth, we voice-recorded each USP–clinician encounter, which enabled us check the implementation quality of each USP visit. Fifth, we used USPs to check multiple quality dimensions, including technical quality (adherence to guidelines for effectiveness and safety), patient-centered care, and efficiency (cost). Finally, we plan to conduct ACACIA every 5 years for the same sample to track the evolution of China's quality of PHC over time.

COVID-19 CHALLENGES AND RESPONSES

As of August 17, 2021, both the number of COVID-19 cases (32 574) and the death toll (959) were relatively low in China.[16] Over the past 12 months, life in China has generally returned to normal. However, because China adopted a zero-COVID policy, a handful of COVID-19 cases would lead to rapid region-wide mass testing for COVID-19 and widespread restrictions on movements.[17] This new normal directly and indirectly affected almost all phases of ACACIA implementation. In the rest of the article, we describe COVID-19 challenges and corresponding program responses.

Funding

The USP tool was perceived to be an expensive data collection method.[18] Government funding in China prioritizes biomedical research rather than health service research. The pandemic has resulted in a substantial cut in funding opportunities globally.[19] Consequently, we took a 2-pronged approach. On the one hand, we tightly controlled cost through process optimization and resource sharing, as discussed in several of the following sections. On the other hand, we turned to crowdsourcing to pool funds. We encouraged and assisted interested researchers in using the ACACIA platform to prepare grant proposals for different research questions; in return, a proportion of their funds help finance the core USP data collection. ACACIA collaborators succeeded in obtaining 7 ACACIA-related competitive grants.

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Case Development

We developed and validated a total of 12 USP cases: angina, asthma, child diarrhea, common cold, gastritis, hypertension, lower back pain, migraine, postpartum depression, stress urinary incontinence, tuberculosis (TB), and type 2 diabetes. We selected those conditions based on 2 national surveys of the common conditions at PHC. Because of the pandemic, PHC providers were put on high alert for COVID-19–related symptoms. Patients with a body temperature above 37.3°C were directed to a specialized fever clinic. Testing for COVID-19 nucleic acid was also required. To avoid harming USPs and interrupting the COVID-19 response system, we dropped TB cases (as fever was among the symptoms) and retained 2 other cases with respiratory symptoms (common cold and asthma) after necessary modifications. For the common cold, we updated its quality checklist per the government's COVID-19 guideline to include whether the clinician checked the USP's epidemiological history related to COVID-19. We strengthened the asthma-related features after a clinician, in an asthma USP's validation visit, suspected that the asthma was actually COVID-19. For all cases, we added a script for the USPs to report no exposure to the COVID-19 high-risk population over the past 2 weeks.

Recruitment

We intended to have 132 USPs for the entire project, with the USPs being recruited from their home provinces (which were part of ACACIA). The pandemic created a substantial hurdle for recruiting and retaining USPs. Many people perceived visits to a medical facility as putting them at risk of acquiring COVID-19. Also, China's zero-tolerance policy for COVID-19 subjected residents or passersby in any affected area to various degrees of quarantine, leading to travel concerns. To meet this shortage of USPs, we selected some capable USP players to take on 2 USP roles. In addition, we shared our USPs across the 7 provinces to support other regions after the USPs had completed their home-province visit. To date, through a combined online–offline interview procedure, 357 people have applied for USP positions, 77 candidate USPs have entered training, and 41 people (taking the roles of 77 USPs, with 36 playing 2 roles) have participated in official ACACIA visits (Figure 1). During the visit, each USP player was accompanied by a USP facilitator. The facilitators went through the entire training with the USPs and were tasked with coordinating onsite logistics and data collection, and sometimes played the role of family members or friends of the USPs. Additionally, 58 rigorously trained health sciences students served as quality controllers, who listened to the recording of each USP visit to verify USP role fidelity and double-check the checklists. Furthermore, 11 researchers involved in case development worked as "case tutors" who guided USP role-play in the field, and 12 students working toward a master's degree in health sciences acted as provincial coordinators who organized USP recruitment, training, and site visits.

Training

In response to the pandemic, we adapted our in-person training (originally planned for Jiujiang City) to a competency-based and hybrid online–offline approach. People entering the training at different times experienced slightly different procedures as the methods evolved over time. Our most recent training started with prerecorded online self-learning modules, which were followed by online one-on-one tutoring and offline training visits. Figure 2 provides more training details. The trainees learned at their own pace but had to pass exams to move from one module to another. The candidate USPs became USPs only when they achieved 90% role fidelity in 4 consecutive unannounced visits or a mean 90% over the 6 visits.

Clinician Visits

Both validation visits and official visits were significantly interrupted by the pandemic. We originally planned to complete the official visits within 6 months. Our official visits started on March 30, 2021, and we had completed 817 (37%) of the 2200 visits as of August 14, 2021. The interruptions of the field visits were mainly caused by lockdowns in the targeted destinations due to regional COVID-19 outbreaks, a shortage of USPs (or of both USPs and USP facilitators) due to challenges in recruiting and retaining them, precautionary restrictions imposed on travel outside of the home cities, and precautionary closure of PHC services even in low-risk municipalities. However, disruption of the USP visits had been restricted to individual provinces until July 20, 2021, when the delta variant of COVID-19 swept through several provinces in China.

Ethics

ACACIA received ethical approval from several universities (see "Human Participant Protection" statement). However, the pandemic warranted 2 additional concerns. First, our use of fake patients

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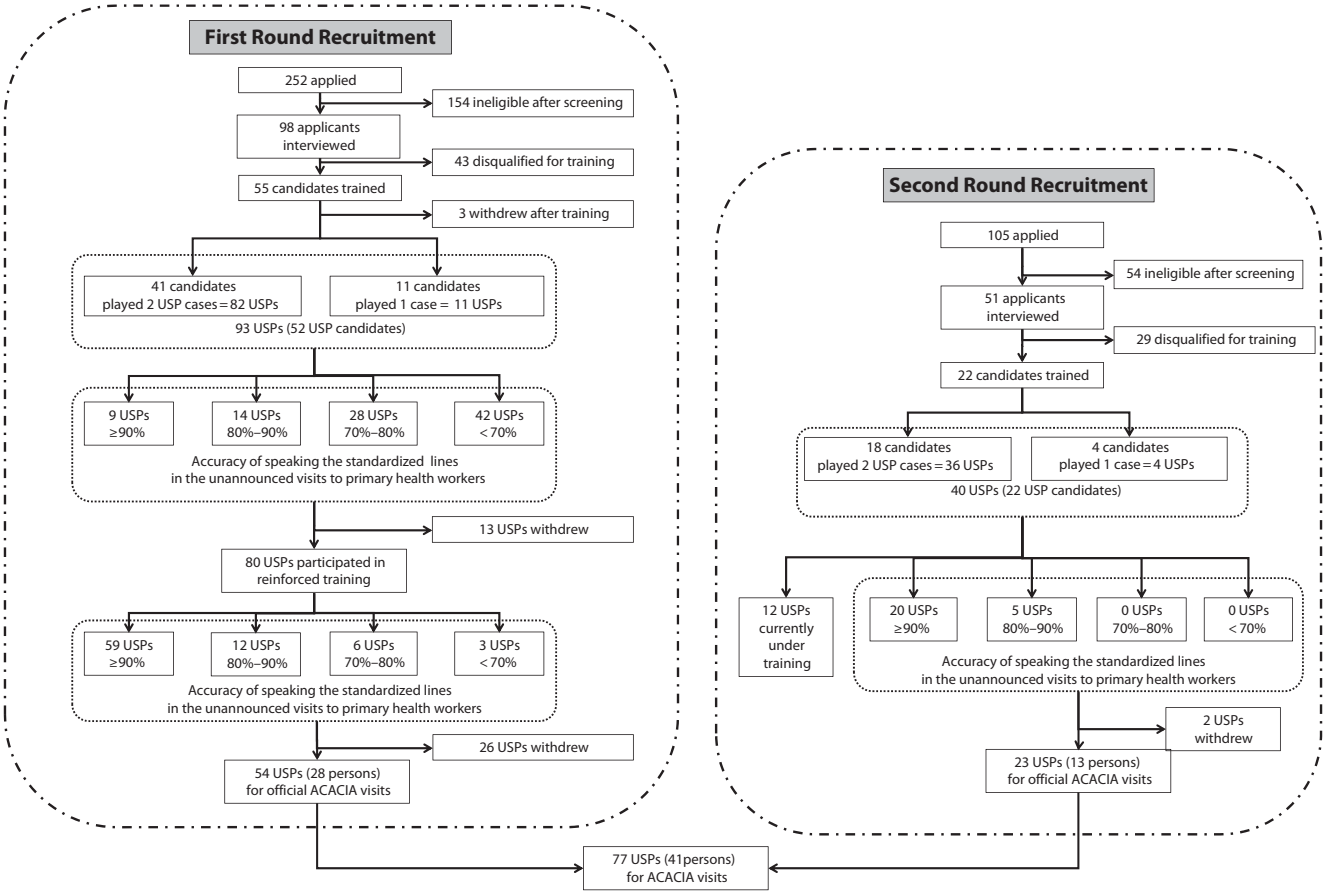

FIGURE 1— Flow of Unannounced Standardized Patient (USPs) Participants: Primary heAlth Care quAlity Cohort In ChinA (ACACIA), March 30, 2021–August 14, 2021

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might divert the already constrained medical resources to nonessential work. Second, the USPs and facilitators might be subject to risk of COVID-19 transmission. To address these concerns, we suspended activities in any municipalities and surrounding areas whose government-designated pandemic level was medium or above. For any municipality that had more than 1 locally transmitted COVID-19 case but had not yet received a medium-risk designation, we allowed ongoing USP visits to proceed with caution while suspending new visits. As of August 14, 2021, none of our field-workers had been infected with COVID-19.

PRELIMINARY RESULTS

We have so far conducted 817 visits (45.8% urban vs 54.2% rural), including 235 (28.8%) hospital outpatient visits, 163 (19.9%) community or township health center visits, and 419 (51.3%) heath station or clinic visits. Only 27.3% of the USP visits resulted in a perfect diagnosis, whereas 19.2% were completely wrong. On average, of the guideline-recommended quality checklist items, the PHC clinicians completed only 16.0% (95% confidence interval [CI] = 15.5, 17.1) of those for consultation, 10.0% (95% CI = 9.1, 11.1) of those for physical and laboratory exams and 23.0% (95% CI = 21.0, 24.8) of those for treatment (Table 1). By comparison, the 2007 systematic review of USP studies reported that doctors were performing 40% to 60% of guideline recommendations.[9] The average total expenditure of a PHC visit was renminbi (RMB) 35.45 (95% CI = 30.63, 40.27), or US $4.49 (95% CI = 4.74, 6.23). The median medicine expenditure was RMB 12.00 (interquartile range [IQR] = 41.07 – 0 = 41.07), or US $1.86 (IQR = 6.36 – 0 = 6.36). A surprising finding is that 61 of the 817 visits (7.5%) were not completed because the facilities had closed down, even though they were listed on the government registry.

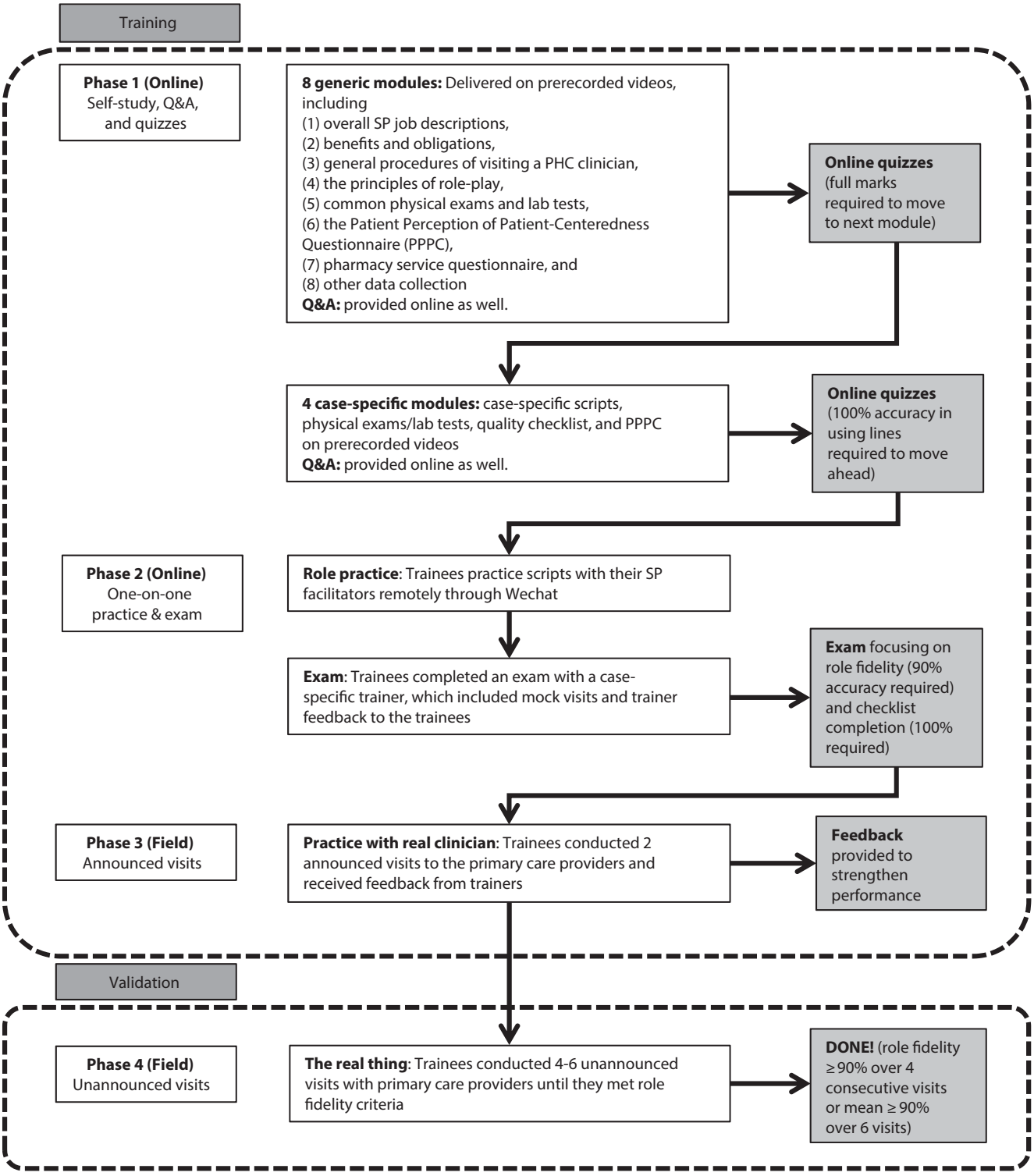

FIGURE 2— Procedures of Training and Validating Unannounced Standardized Patient Participants: Primary heAlth Care quAlity Cohort In ChinA (ACACIA), March 30, 2021–August 14, 2021

Note. PHC = primary health care; Q&A = questions and answers; SP = standardized patient.

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COVID-19 IMPACT ON ASSESSMENT VALIDITY

A major concern of the implementation's deviation from the original protocol was its potential impact on the validity of the USP assessment tool. We now discuss several negative and positive aspects.

First, we initially selected the TB case to serve as a tracer condition for major infectious diseases and to enable easier international comparisons, as TB was widely used in USP studies in China,[20] India,[21–23] Kenya,[24] and South Africa.[23,25] Dropping TB thus affected the overall representativeness of our case roster. Second, some USPs were sent from their home bases to other provinces with distinct cultures and dialects, possibly increasing the risk of exposing their true identities. Incognito visits are critical for minimizing the Hawthorne effect. However, recruiting "local" USPs was not feasible even in the same province because of the diversity of cultures and dialects. In the cities, speaking Mandarin was common for medical consultations; in rural areas, however, we trained the USPs to use various decoys to minimize suspicions, such as posing as a student who was conducting thesis fieldwork. Third, the in-person training was completely revamped into a hybrid online–offline modality.

We considered this approach superior and preferable to the conventional training. Meanwhile, because of our competency-based training approach, we had higher confidence in those trainees in playing their roles. Finally, the pandemic substantially prolonged the length of the program's fieldwork. As the duration of data collection gets longer, external quality-related policy changes that could introduce bias are more likely to occur. However, so far, we have not observed any major national policy changes related to PHC. ACACIA had an embedded validation study for the USP tool. The full results of the validation will be reported in a separate article. However, the preliminary analysis suggested high validity of the USP assessment even against the background of the pandemic. Table 2

TABLE 1— Clinician Completion of Essential Guideline-Suggested Items: Primary heAlth Care quAlity Cohort In ChinA (ACACIA), March 30, 2021–August 14, 2021

Conditions and Provinces	Visits, No.	Consultations, % (95% CI)	Exams, % (95% CI)	Perfect Diagnosis, %	Treatment, % (95% CI)
Condition					
Postpartum depression	67	16.6 (13.6, 19.7)	0	49.3	26.3 (21.0, 31.5)
Hypertension	91	11.7 (9.9, 13.6)	6.2 (4.9, 7.4)	19.8	10.4 (7.5, 13.4)
Migraine	71	19.1 (16.2, 22.0)	3.6 (2.5, 4.7)	12.7	38.8 (30.5, 47.1)
Common cold	64	17.0 (13.9, 20.0)	17.4 (13.5, 21.3)	37.5	13.8 (9.8, 17.8)
Type 2 diabetes	89	9.6 (7.6, 11.6)	8.0 (5.6, 10.4)	0.0	27.9 (21.8, 34.0)
Gastritis	44	23.4 (20.0, 26.7)	16.5 (11.4, 21.7)	34.1	34.4 (27.8, 41.0)
Asthma	52	17.6 (13.5, 21.8)	9.6 (5.2, 13.9)	25.0	27.5 (14.8, 40.1)
Child diarrhea	47	18.1 (14.0, 22.2)	7.1 (3.5, 10.6)	0.0	25.6 (20.5, 30.8)
Angina	52	16.2 (13.4, 19.0)	22.7 (15.6, 29.8)	51.9	28.8 (20.0, 37.7)
Stress urinary incontinence	118	15.3 (13.3, 17.4)	4.8 (2.6, 6.9)	20.3	32.9 (28.1, 37.8)
Lower back pain	122	19.3 (17.5, 21.1)	18.4 (16.4, 20.5)	49.2	3.2 (1.9, 4.6)
Province					
Gansu	84	19.4 (16.6, 22.3)	10.3 (6.7, 13.9)	31.0	26.0 (19.4, 32.5)
Guangdong	60	17.6 (14.5, 20.6)	11.6 (8.3, 14.9)	28.3	18.8 (12.6, 25.1)
Guizhou	58	14.4 (11.7, 17.2)	11.3 (7.9, 14.6)	17.2	18.1 (13.0, 23.2)
Hunan	38	14.1 (10.0, 18.2)	10.8 (5.8, 15.8)	21.1	15.7 (8.4, 23.0)
Inner Mongolia	7	20.6 (4.9, 36.4)	8.2 (–5.6, 22.0)	28.6	41.8 (1.8, 81.9)
Shaanxi	157	14.1 (12.3, 15.8)	10.5 (8.1, 12.9)	31.2	22.8 (18.0, 27.6)
Sichuan	513	16.7 (15.6, 17.9)	9.5 (8.1, 10.9)	26.9	23.9 (21.2, 26.6)
Total	817	16.0 (15.5, 17.1)	10.0 (9.1, 11.1)	27.3	23.0 (21.0, 24.8)

Note. CI = confidence interval.

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summarizes the results of the 4 most important areas of validity.

IMPLICATIONS AND RECOMMENDATIONS

As societies transition from lockdowns to partial or sporadic restrictions, our experience will be especially relevant for other complex national data collection efforts. COVID-19 will not be the last pandemic. We need to learn from the past to build resilient data surveillance actively.

What Went Well

Crisis often creates momentum and conditions for changes. Several approaches that we were forced to take have become preferred ones even under normal conditions. As an example, our hybrid training model had many advantages over the initial in-person training. It allowed trainees to learn repeatedly at their own pace, saved trainers' workload, shared trainers' resources across provinces, enhanced communications between instructors and trainees, and saved substantial travel costs. It also enabled a rolling training process, indispensable to addressing USP attrition. Similarly, sharing our USPs across the provinces has become more efficient and effective than training more USPs. The direct cost of the hybrid training was RMB 1680 (US $260) per USP, less than the cost of moving a USP to a neighboring province. The USP role-playing improved with more visits as well. The pandemic also created new research opportunities. We have now begun to use the same USPs to assess the quality of eHealth in China, which has become increasingly popular during the pandemic.

Our second lesson concerns maintaining team morale and interests during the pandemic. The frequent disruptions from the pandemic could be baffling and disheartening for the project team. There were almost 200 fieldworkers of diverse backgrounds working for ACACIA at any time. Notably, 117 undergraduate and master's degree students of health sciences worked as USP facilitators, quality controllers, and provincial coordinators. We maximally matched the students' interests with the project objectives to stimulate their self-motivation for the project work. For instance, we prospectively discussed a range of ACACIA-based thesis opportunities with the master's degree students. We also specifically targeted undergraduates who intended to gain

TABLE 2— Validity of the Unannounced Standardized Patient (USP) Assessment Tool: Primary heAlth Care quAlity Cohort In ChinA (ACACIA), March 30, 2021–August 14, 2021

Validity	Measures	How	Why It Matters	Results
Content validity of the quality checklist	Scale-level content validity index with averaging calculation method (*S*-CVI/Ave)	Agreement of a multidisciplinary expert panel on the relevance of the checklist via a Delphi process	Checklist serves as the evidence-based criteria for the evaluation of the quality	12 USP cases ranging from 0.92 to 1, >0.90 threshold
Fidelity of USP role-playing	Proportion of accurately used lines during an unannounced USP visit	Quality controllers listened to each voice-recording of the USP visit to verify the accuracy of the USP line use[a]	Consistently and accurately using the lines is critical to maintaining the standardization of the USP visit	Average 94%, >90% criterion
Accuracy of checklist completion by USPs	Agreement of checklist items completed between the USP and the quality controllers	Using the checklist completed by quality controllers listening to the voice-recording of the visits as the gold standard[a]	USPs must accurately recall and identify the details of clinician consultation, exams, diagnosis, and treatment	88% agreement
Detection of USP	Proportion of USPs detected by the clinicians	Clinicians reported on any suspected USP visits over the past 2 weeks	Maintaining the fake identity during the visit is critical to avoid the Hawthorne (observation) effect	0.68%[b]

Note. Scale level content validity index/average (S-CVI/Ave) = 0.96.

[a]We required the field team to upload the voice recording before 7 p.m. of the same day of the visit. The quality controller checked the accuracy of the standardized patient (SP) rendition of the lines (>90% accuracy required) and the completion of the checklist and provided feedback to the field team. The SPs who did not meet the quality requirement would take an online refresher course on scripts before resuming their visit.
[b]In the development and validation phase, 147 doctors returned survey forms and 25 reported their suspicion of at least 1 USP visit. However, only 1 reported suspicion was actually linked with our USP visits.

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research experiences through ACACIA. Likewise, for the 14 ACACIA researchers from the 10 universities, we prospectively and mutually agreed upon one another's benefits and obligations in the project. We successfully aligned the participants' interest with ACACIA to the extent that all researchers volunteered their time in the research. The high self-motivation of the entire team was the core for building project resilience under the pandemic.

The third thing we learned is to use technology and tools well. We leveraged the societal drive for remote work for all phases of ACACIA. As described in the "Recruitment" and "Training" sections, we used remote means for USP interviews and training. Moreover, the cloud-based Research Electronic Data Capture (REDCap) system[26] provided us with a sophisticated, customizable, secured, and efficient tool for remote collaborations.[27] For example, our USPs and facilitators used REDCap to upload all data forms, audio recordings, and images on the same day as their visits, whereas the quality controllers, who were spread over different universities, used the same system to remotely check missing data, assess USP role-play fidelity, and verify the quality of the checklist completion. The remote means improved the efficiency and validity of the data as mistakes were promptly rectified.

Finally, we should emphasize the importance of ethical considerations at the implementation level. The method of USP was ethically controversial because of the use of deception and the absence of consent.[28–30] The pandemic further complicated the issue, as mentioned in the "Ethics" section. However, the currently prevailing opinion is that USP studies are justifiable as long as there is (1) minimum risk to the clinicians (ACACIA analysis will be at the aggregated level and only on de-identified data), (2) the necessity of a waiver of consent to produce scientifically valid data (obtaining clinician consent will lead to self-selected bias), and (3) the potential for substantial social value of the knowledge gained from the research (ACACIA is a rare attempt to monitor the quality of PHC in China).[31,32] We carefully observed those conditions in our preparation of the study protocol[2] and took extra care to deal with the pandemic-related risks as discussed in "Case Development" and "Ethics."

What Could Be Improved

We had great difficulty in recruiting USP players. Recruitment news was distributed mainly through social media and word of mouth. In hindsight, we should have explored other recruitment avenues, such as popular job search Web sites. Identifying and establishing partnerships with hospital medical education departments that have standardized patients might be another recruitment shortcut for recruiting the USPs.

Meanwhile, pandemics such as COVID-19—as well as future public health crises—highlight the importance of PHC. Although we tactically dealt with this issue—for example, we adjusted the quality checklist of the common cold to include a COVID-19–related item—we did not have a strategic and overarching design to examine the preparedness and resilience of PHC systematically. It was a missed opportunity.

Recommendations

We would like to share the 3 most important recommendations to foster resilient data surveillance during and beyond the COVID-19 pandemic. First, the hybrid remote and in-person work is highly recommended. One of the lasting legacies of the pandemic is probably the realization of how much can be achieved remotely without compromising quality. Data collection teams need to pursue technological tools to actively facilitate this hybrid model, which can be implemented across all phases of the project, not only the fieldwork.

Second, we should learn from the sharing economy to pool strengths and optimize resources. An individual is powerless against the pandemic, but collectively we are strong. In ACACIA, we shared ideas, funds, expertise, resources, and intellectual properties. Sharing entails more than the passive availability of resources for the group; it also involves dynamically optimizing individual resources for group needs. Sharing makes the group not only stronger but also more efficient.

Third, individual and group leadership is critical for a resilient system. It was a bold vision, not the availability of a grant, that initially led to the ACACIA group's launch. Several core members of ACACIA, from students to researchers, exercised exceptional leadership in harnessing the group strengths for a shared goal. Without the intrinsic call of the team members to take initiatives, ACACIA would not have been maintained during the pandemic.

CONCLUSIONS

COVID-19 brought crisis but also opportunities. With leadership and innovation, we adopted hybrid work and dynamically shared resources to fund, design, validate, and implement this complex national data effort with

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unannounced standardized patients. Our experiences may encourage like-minded researchers to build resilient data systems during and beyond the pandemic. AJPH

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CONTRIBUTORS

D. Xu conceptualized the study. Y. Y. Cai and X. H. Wang coordinated the daily implementation of this study in the 7 provinces. Y. Y. Cai conducted the data analysis. Y. Y. Cai, X. H. Wang, Y. L. Chen, W. J. Gong, J. Liao, J. F. Zhou, Z. L. Zhou, N. Zhang, C. X. Tang, and J. Pan were the project leaders in each province and were responsible for the implementation of the project in each province. B. B. Mi was the chief data manager of the project. Y. Lu took charge of online training. R. X. Wang, Q. Zhao, W. J. He, and H. J. Liang were project assistants. D. Xu prepared the first draft of the manuscript and Y. Y. Cai and X. H. Wang developed the second draft. All authors substantially contributed to the implementation of the project and the iterative revisions of this manuscript.

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CONFLICTS OF INTEREST

The authors have no conflicts of interest to report.

HUMAN PARTICIPANT PROTECTION

Ethical approval for this project was issued by the institutional review boards of Sun Yat-sen University (2017-011 and 2019-024), Xi'an Jiaotong University (2020-1288), Guizhou Medical University (2020-201), and Lanzhou University (2020-0901).

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