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# Development and implementation of COVID-19 safety protocols for conducting a randomized trial in global mental health: Field report from Central India

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## ABSTRACT

The COVID-19 pandemic impacted ongoing clinical trials globally resulting in the suspension, cancellation or transition to entirely remote implementation of studies. In India, the first countrywide lockdown was imposed in phases starting from March 2020 to June 2020, followed by a continued restriction on in-person activities including study procedures, which halted the ESSENCE (Enabling translation of Science to Service to ENhance Depression CarE) trial activities such as recruitment, consenting, baseline assessment, digital training orientation, face to face training and end-line assessment evaluation. This situation made it imperative to amend procedures in order to mitigate the risk and address safety requirements for participants and the research team. This paper summarizes the need, development and implementation of the protocols focused on risk reduction and safety enhancement with an objective to resume and continue the research activities while ensuring the safety of study participants and research staff. These protocols are comprised of guidelines and recommendations based on existing literature tailored according to different components in each arm of the trial such as guidelines for supervisors, travellers, training/recruitment venue safety procedures, individual safety procedures; and procedures to implement the study activities. These protocols can be adapted by researchers in other settings to conduct research trials during pandemics such as COVID-19.

## 1. Introduction

Declared as a global pandemic by the World Health Organization (WHO) on 11th March 2020 (World Health Organization, 2020), the coronavirus disease (COVID-19) has infected millions of people worldwide and resulted in dramatic increases in morbidity and mortality (Gugnani and Gugnani, 2020). The COVID-19 pandemic has led to substantial disruptions in health-related risks, access to health care, daily interactions as well as created a unique challenge for the health research community. Aside from COVID-19 related studies and emergency medical services, most other non-essential activities including health research studies involving human subjects were suspended indefinitely, cancelled, or transitioned entirely to remote data collection in many places around the world. Data collection has remained suspended for many studies globally, even many months following the

initial implementation of national or regional lockdowns and restrictions. The impact of the pandemic resulted in unanticipated and rapid revisions to study protocols, which became unavoidable as most ongoing trials had to stop new enrollment, or modify consent procedures and their activities due to the measures adopted to control the pandemic such as lockdowns, travel restrictions, social distancing requirements, quarantine, and limited access to healthcare facilities especially for non-essential staff. This situation subsequently prompted regulatory authorities, investigators, institutional boards/ethics committees (IRBs) to implement new guidelines (ICMR, 2020), recommendations, review the status of ongoing studies and restructure the existing research protocols factoring in the conditions posed by the COVID-19 pandemic (Perez et al., 2020). With this kind of massive disruption and global impact on health research activities involving human subjects, we describe the COVID-19 impact on a randomized controlled trial in

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Madhya Pradesh, India as part of the US National Institute of Mental Health (U-19) funded ESSENCE (Enabling translation of Science to Service to ENhance Depression CarE) program, and the mitigation strategies adopted.

ESSENCE is a three-arm randomized trial evaluating the effectiveness and cost-effectiveness of digital technology with or without remote coaching support to train non-specialist health workers compared with traditional face to face method of training to deliver a brief evidence-based behavioral activation treatment for depression called the Healthy Activity Program in primary care settings in Sehore district of Madhya Pradesh, India (Naslund et al., 2021). It is jointly conducted by Sangath, India and Harvard Medical School (USA) in collaboration with the National Health Systems Resource Centre (NHSRC) and National Health Mission (NHM), Madhya Pradesh. Concerns around the pandemic started to enhance in early March 2020 in India, subsequently leading to the imposition of a countrywide lockdown, which was extended in phases for the next several weeks. This resulted in the ESSENCE research team working from home, the suspension of all in-person research activities under ESSENCE such as enrollment, recruitment, data collection, and endpoint assessments with participants. In addition, the new participants that were enrolled in the study prior to the restrictions coming into effect were not able to begin the training programs since it required in-person contact to collect the digital technology aids (devices) and initiate the program, all of which was postponed.

Eventually, as the restrictions and lockdowns in India were relaxed in June 2020, subsequently the local authorities allowed for re-initiation of residential/routine frontline health worker training. Trial sites and research offices were able to re-open; we subsequently started discussions internally within the team and with the government authorities to resume our research activities while following all regulatory and precautionary guidelines related to COVID-19. However, there was a sense of fear, apprehension and anxiety among the participants, as well as research staff given the potential risk of infection. Since the management of clinical trials and research activities demands critical consideration and maintenance of trial integrity, as well as risk minimization and prioritizing safety and wellbeing of research participants, and research staff, it was of utmost importance that our research team implements extra precautions to address this concern. This new situation made it imperative for us hence to conduct our research in a safe and effective way, while adhering to new revisions to our study procedures. In this paper, we outline our process of developing, adopting and implementing a COVID-19 safety protocol specifically for our research activities in primary care facilities in Madhya Pradesh, India aimed at mitigating potential risks of the pandemic for participants and research staff while also ensuring compliance with the good clinical practices (GCP) guidelines and the approved research protocol.

## 2. Materials and methods

### 2.1. Development and adaptation of the COVID-19 safety protocol

We started the development of the protocol on safety and operatory measures in July 2020 by convening digital meetings of the research team to strategize and discuss the necessary precautions and modifications. It was mutually decided by our team comprising of mental health professionals and public health researchers who were supervised by the site Principal Investigator that the protocol will be a live document (updated on a regular basis, subject to change as the national and international guidelines continued to be modified in response to the unfolding pandemic). As a first step, we identified existing guidelines, regulatory guidance, and published reports from the WHO, National Centre for Disease Control (NCDC), Ministry of Health and Family Welfare (Government of India), US National Institutes of Health (NIH), US Food and Drug Administration (FDA), United Nations International Children's Emergency Fund (UNICEF), United Nations Fund for

Population Activities (UNFPA), Harvard Medical School, Civil society organizations, and research groups. Secondly, we reviewed, summarized and adapted the best practices for the purpose of our trial to help standardize our processes. Thirdly, multiple iterative reviews were followed and the final protocol was shared with senior health system representatives at the district level, our independent trial Data and Safety Monitoring Board, and NIMH, and was approved by institutional review boards with Sangath, India, and Harvard Medical School, USA prior to finalization for deployment.

### 2.2. Components of the COVID-19 safety protocol

We classified the protocol under six subheadings: (1) guidelines for the research supervisor/coordinator; (2) travel guidelines; (3) training/recruitment venue safety procedures; (4) individual safety measures; (5) procedures for implementation of study activities such as data collection, providing orientation to participants for using the digital training program and attending residential training activities; and (6) additional child safety procedures for participants who bring their children with them to study activities (details in Supplementary Material). In accordance with various published guidelines described above, emphasis was given on mask usage, maintaining physical distance, thermal screening at first contact, frequent hand sanitization (for at least 20–40 seconds) during breaks and ensuring adequate ventilation during the implementation of the COVID-19 safety protocols for in-person research and training activities. Suggestions on sitting arrangement with six feet distance between individuals, and querying the participants if they might have come in contact with a COVID-19 patient or recently had any travel history to the COVID-19 affected areas to help identify potential exposure to COVID-19 were also included.

We also undertook preventive measures for children accompanying the non-specialist health workers (all women) of all age groups. Children of age 6 years and above were requested to wear a mask and undergo screening procedures, maintain physical distancing, sit at one place besides their mothers during recruitment and assessment, not to roam in the hall and avoid touching objects to prevent possible transmission. Children up to 5 years of age were not required to wear masks for source control; here, we were motivated by “do no harm” approach as advocated in the updated WHO guidelines (WHO, 2020) considering child developmental milestones, compliance challenges, and autonomy required to wear a mask properly.

Checklists and logs were other important components of the COVID-19 safety protocol. The checklist helped us to ensure that the research team carried all the required supplies before leaving for the field site and completing cleaning and sanitization at the activity venue. The advantage of using checklists was minimizing the chance of missing any supplies, and enhanced adherence to the protocol implementation. Using a checklist also reduces errors, improves care by avoiding communication errors within the team and ensures essential steps or processes that improves patient safety are followed (Early, 2010; Barlow, 2008). The details of the screening, mask usage, and sanitization of participants' belongings was documented in different logs prepared for research and training activities (see Supplementary material). Table 1 outlines key components of the COVID-19 safety protocol.

### 2.3. Planning for Implementation of safety protocol

Prior to resuming and implementing our trial activities, we did: (1) logistics preparation, i.e., procurement of adequate items like hand sanitizers, surgical face masks, thermal scanners, pulse oximeters, face shields etc.; (2) training of the study team on subjects like their roles and responsibilities, reporting structure, how to fill and maintain log sheets daily, keeping essential contact information, what to do and who to contact in case a participant, vehicle driver or team member reports COVID-19 symptoms, and timelines for each activity. Adherence to the protocols was ensured by periodic supervisory checks by research

**Table 1**  
Outline of the Covid-19 safety protocol components.

| Component of Safety protocol and Documentation              | Training Trial Activities (Recruitment and baseline assessment; Digital Training (DGT) Orientation; and Face to Face training)  |
|---|---|
| Use of Face Mask/Shield and Maintaining Physical Distancing | <ul style="list-style-type: none"> <li>• Mandatory use of face mask for the trial participants and research/training team.</li> <li>• Use of face mask for children as per the child safety procedures.</li> <li>• Use of face shield while conducting any research activity by the team.</li> <li>• Instructions to try to maintain physical distancing of approximately 6 feet.</li> <li>• Bedding arrangement in the dormitory was made with adequate distancing for Face to Face residential training.</li> </ul>   |
| Screening   | <p>Mandatory screening by checking the body temperature and oxygen saturation level (SpO2)</p> <p>3 screening points</p> <ul style="list-style-type: none"> <li>• Screening of research/training team and vehicle driver before starting the travel to the field site.</li> <li>• On the way to the field site when a new research/training team member joins midway.</li> <li>• At the field site, screening of trial participants and children of 6 years and above at the entrance of activity venue.</li> </ul> <p>Recruitment and Digital Training Orientation</p> <ul style="list-style-type: none"> <li>• Sanitization of research/training material (questionnaires, forms, mobile phones, folders, files, etc.) before leaving to and from the field site.</li> <li>• Instructions on following hand hygiene including frequent hand washing and use of sanitizer.</li> <li>• Sanitization of personal belongings of the research team and training trial participants.</li> </ul> |
| Cleaning, Sanitization, and Hand Washing                    | <ul style="list-style-type: none"> <li>• Disinfection, sanitization and cleaning of activity venue, chairs, tables, etc.</li> </ul> <p>Face to Face residential training</p> <ul style="list-style-type: none"> <li>• In addition to the above mentioned components, the training venue including training hall, reception, kitchen, dormitory, bathroom, and outer space was cleaned and sanitized twice a day on a regular basis for the 6 days of the training.</li> <li>• A provision for frequent hand washing at the entrance area, training hall and cafeteria.</li> </ul>   |

coordinators; and (3) telephonic orientation of participants by research assistants on the participant information sheet, which was reinforced during the actual visit during the consent process (to reduce the face to face interaction time between the participants and research team members during consent). We also ensured that on resumption of trial activities, participating non-specialist health workers were invited in small batches of 8–10 (as per government guidelines) to their nearest community health center or any other pre-decided convenient venue. Additionally, each team was asked to document their experiences and participants' feedback while implementing the safety protocol.

#### 2.4. Implementation of the safety protocol

The implementation of the developed safety protocol came into effect in October 2020 once the lockdown was lifted in a phase-wise manner. Fig. 1 describes our methodology of following the protocol at the training site. We started conducting our training activities (recruitment and baseline assessment; digital training orientation; and face to face training) at four different locations (health facilities and the field site office) at different time points. The duration of these activities ranged from 1 to 6 days. Since implementing these procedures, we have completed the recruitment and baseline assessment for a total of 113

participants across 12 working days, face to face training for 42 participants in three batches of six days each and digital orientation for 133 participants in a span of 18 days.

#### 2.5. Observations and challenges

For the purpose of improving our research procedures and use of the COVID-19 safety protocol, teams implementing the training programs and collecting data were asked to share their key observations and challenges. The observations were mainly related to participants' participation in activities (data collection, training, orientation etc.), use of face masks, cooperation in screening, and sanitization (see Table 2). All study participants' complied with required safety norms during the screening procedures. Majority of the participants were wearing a mask or had their faces covered with a cloth scarf, whereas those participants who did not have their faces covered were provided a mask at the entrance of the research activity venue. No participant denied participation in any of the mentioned activities related to these procedures. This was achieved as a result of informing the participants in advance about the safety procedures that will be followed in the field. Interestingly, one participant was hesitant to appear for the recruitment activity at a health center because she learned that a patient had reported COVID-19 positive in the same premises a day before. She however reported to the recruitment site at the center later in the day, and explained that she had reached out to the health center staff regarding the safety measures that were being undertaken during the research activity, and was reassured by the health facility staff that all necessary precautions are being followed, which gave her confidence to report for the research procedures.

Another observation was that the participating non-specialist health workers felt uncomfortable wearing masks for a long period of time, which resulted in them either removing the mask for some time or wearing it below the nose. This led to the research and training team members to frequently instruct the participants to wear their masks correctly. Several challenges were also faced while conducting the above-mentioned activities, which are described in Table 2. In addition, we have also described ways we addressed these challenges.

### 3. Conclusion

To successfully conduct clinical research activities involving human participants during pandemics like COVID-19 requires flexibility, endurance and adaptation. Creating a safe environment and conducting trials in a compliant and ethical manner is the way forward. Multiple guidelines have emerged around the prevention and consequences of COVID-19; however, not enough studies focused on the development and the experiences of research teams in implementing of COVID-19 safety protocols for conducting clinical trials. This paper can serve as a possible roadmap for researchers, investigators, and study teams working in similar situations or trials around the world about essential steps to prepare and implement their research during these challenging circumstances owing to the pandemic. These guidelines provide recommendations and provisions to assure quality through the use of checklists, and can be integrated into routine research, as well as adapted and contextualized by other research groups, depending on the unique needs of the study setting and context. Moreover, since we treated the protocol as a living document we were able to revise the same document periodically, and add the child safety procedures based on inputs from the DSMB members, which can serve as a good example of the nature of necessary iterations and revisions.

However, we also recognize that our trial does not include patients as participants, which would have required us to plan, develop and implement additional safety considerations given the additional risks of COVID-19 in health facilities and also, our 'intervention' i.e., training health workers (and not testing a treatment or other invasive therapy) is relatively low risk. In the case of studies looking at patients or direct

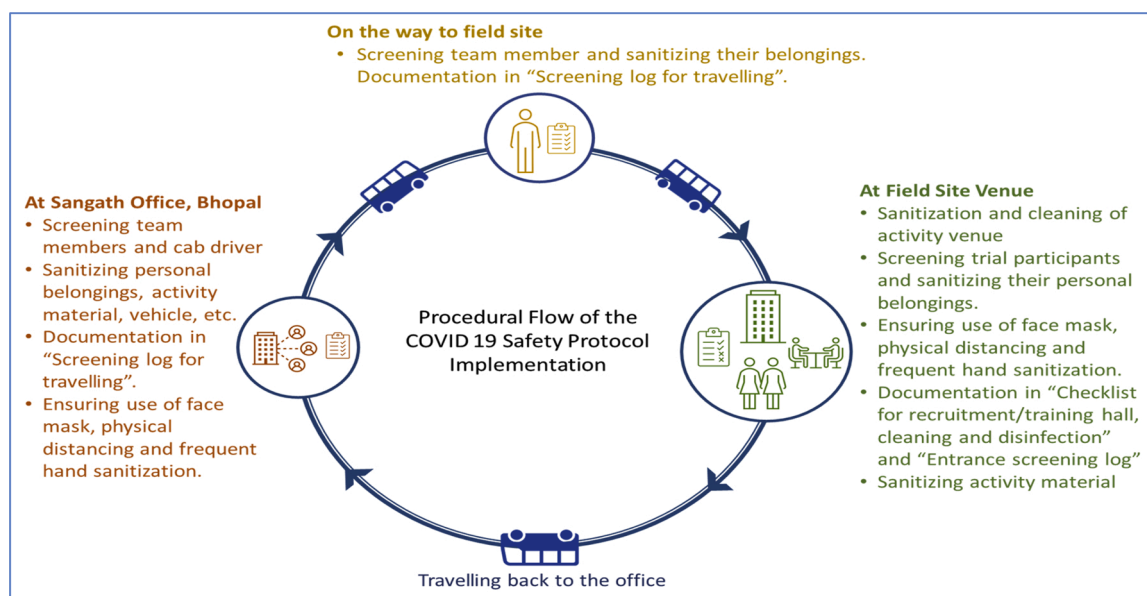


Fig. 1. The procedural flow of the Covid-19 safety protocol implementation.

**Table 2**  
Key challenges faced during implementing Covid-19 protocol.

| Challenges  | Ways to address challenges  |
|---|---|
| <ul style="list-style-type: none"> <li>Five team members were on occasion travelling in a single vehicle because of logistic reasons</li> <li>There was difficulty faced in hearing due to the use of mask and face shield (recruitment and digital orientation)</li> <li>Discomfort due to increasing weather temperature –high breathing while speaking, sweating, low intake of water, low level of energy (recruitment and digital orientation)</li> <li>Difficulty in maintaining physical distance while conducting group activities, role-plays (Face to Face training), and hands on training during digital orientation</li> <li>On completion of any activity or during breaks, participants were socializing amongst themselves which resulted in not maintaining physical distance</li> <li>Non-specialist health workers bringing their children without a mask</li> <li>Children wandering around in the training hall</li> </ul> | <ul style="list-style-type: none"> <li>We tried to plan in advance to minimize the number of vehicle occupants while travelling together</li> <li>By speaking loudly during orientation, use of portable mic and speakers</li> <li>Started speaking slowly, increased the intake of water for adequate hydration, ensured that all the windows were open for better airflow and ventilation</li> <li>Strict adherence to the usage of mask/face shield while maintaining physical distance to the extent possible</li> <li>Research and training team members frequently instructed and requested the participants to follow safety guidelines and maintain physical distance</li> <li>Incorporated the child safety procedures to our protocol for the trial activities</li> <li>Research and training teams requested the participants to adhere to the child safety procedures;</li> <li>Children were asked not to wander around in the hall and maintain physical distance from other participants and research/training team members</li> </ul> |

treatments, a careful review of guidelines mentioned in this paper will be needed and modifications to the guidelines will have to be made to contextually fit with study goals and objectives.

In India, considering the huge treatment gap in mental health (Murthy, 2017; Sagar et al., 2017) and increased prevalence of depression, the ESSENCE trial is a key step to building workforce capacity to provide evidence-based psychological treatment for depression in primary care. The economic consequences of the pandemic have further worsened the mental health of communities, and trials like ESSENCE

should resume to generate evidence in depression care. Therefore, reinforcing the need to use strategies such as the use of standard operating procedures and adherence to these protocols as a way of reducing infectious disease risk, as well as building confidence in all research team members to continue on-the-ground activities is critical. It is important to also highlight that we were able to resume research activities and finish recruitment, without any major adverse events linked to research activities. Major disruptive events such as the COVID-19 pandemic will likely occur again, and research teams must be prepared to meet the next challenge quickly with the lessons learned from this pandemic, to adjust to unforeseen threats and uncertainty.

**Ethics approval**

All procedures performed in this study were approved by the ethics review boards at Sangath, India, and Harvard Medical School, United States.

**Informed consent**

This paper describes modifications to study procedures for an ongoing study involving human participants who had been consented into the study to specifically address COVID-19 related risks. No separate consent was therefore required.

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**Declaration of Competing Interest**

The authors report no declarations of interest.

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#### Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:<https://doi.org/10.1016/j.ajp.2021.102750>.

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