Opinion

Clinical research during the COVID-19 pandemic: gastroenterology researchers' perspective

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INTRODUCTION

As the novel COVID-19 pandemic continues, its impact on healthcare institutions and the healthcare community is strongly felt. Researchers and research institutions around the world are trying to cope with the wide range of effects of the pandemic on clinical research.[1]

The impact of COVID-19 on clinical research will vary, depending on the disease under study, the study design and where the study is being conducted. While some clinical trials may have continued, recruitment to observational studies was almost ubiquitously stopped during the height of the pandemic in many countries. Lockdowns, site closures, quarantines, travel limitations, interruptions to the supply chain for investigational products, diversion of resources and site personnel or study subjects becoming infected with the virus will be major challenges.[1 2] All these factors might have an impact on clinical studies.

An issue specific to gastrointestinal (GI) research is the possibility of viral transmission through aerosol-generating endoscopic procedures and faecal to oral route. This will result in amendments to or unavoidable deviations from original study protocols and the need for additional precautions and protective equipment.[3] Many patients with COVID-19 can be asymptomatic or have mild symptoms.[4 5] Therefore, screening all participants for COVID-19, with real-time, reverse PCR (rRT-PCR) or a combination of antibodies and rRT-PCR, may be necessary for areas with a high prevalence of the disease.[6] If mandatory screening is to be implemented on all participants, this will have to be communicated to them and consent obtained from ethical review committees as this will involve collecting additional nasopharyngeal swabs and blood samples.

The safety of study participants continues to be the foremost consideration and should be emphasised at all times. Ongoing clinical trials could continue while complying with good clinical practice and minimising risks to trial integrity. Sponsors and regulatory authorities need to take into account the restrictions and new protective guidelines imposed on trial participants and staff, and their ability to perform visits, interviews, gather information and notify adverse effects.[2 3 7]

Although most funding agencies are committed to business continuity, to ensure processing applications and to award research grants where appropriate, given the present circumstances, there will be some loss of potential funding opportunities. This will be especially so from state funding agencies in the wake of the COVID-19 pandemic and its effects on the economy.[8] Furthermore, the charity sector is in crisis and this will affect the ability of specialist charities for specific diseases to continue funding during and after the pandemic.

INITIATING NEW RESEARCH

Most regulatory bodies have currently withheld or limited approvals for non-COVID-19-related research.[9] Newly approved studies have been advised to postpone enrolment. Even if recruitment is allowed, participation will be hindered during the pandemic situation.[10] Therefore, research teams should critically assess the feasibility and necessity of starting new studies or trials in the current environment.

Risk assessment should be included in all research protocols.[2 7] This should include additional risks to the participant and support staff due to COVID-19, and what additional precautionary measures are to be taken to mitigate these risks. This may include the risks of conducting any research, which should be weighed against its benefits to the participants and society by regulatory bodies and sponsors of clinical trials.[10]

In clinical research in gastroenterology, participants may be at increased risk of exposure to or spread of COVID-19. A definite risk of transmission is present when aerosol-generating procedures such as upper GI endoscopy is involved, and potential for transmission is also present during lower GI endoscopy and collection, handling and analysing stool samples for faecal microbiota or faecal transplantation studies.[11 12] There may also be increased risks to study participants who are already on or are to receive steroids, immunemodulators and biological therapies for GI diseases, such as inflammatory bowel disease.[13] These risks should be carefully considered before starting or continuing trials involving these drugs.

ONGOING CLINICAL RESEARCH

Continuing ongoing clinical research can also be restricted due to logistical problems, such as complete or partial lockdowns, closure of research facilities, restrictions on travel and disruption to supply chains.[2 10] A risk–benefit assessment is advised before deciding to continue. It is vital that participants are kept informed of any changes to study protocol and plans that could impact on their care. The decision about which projects can be stopped or paused will be best made by universities and research institutes themselves with guidance from their administrations and institutional review boards.[2 10]

Key points and recommendations

- The COVID-19 pandemic has had a strong impact on healthcare research.
- Non-COVID-19-related gastrointestinal (GI) research is almost at a standstill, mainly due to loss of funding opportunities.
- Essential GI research should continue after risk–benefit analysis.
- Safety of participants and investigators should be the highest consideration.
  - Screen participants; use personal protective equipment, especially for research involving endoscopy.
  - Consider discontinuing research involving immunosuppression.
  - Perform aspects of research remotely whenever possible.
  - Consider financial liabilities related to research.
- Research review boards should allow reasonable amendments and deviations from protocols

There will likely be liabilities related to research participants contracting COVID-19. Therefore, every precaution should be taken to minimise the exposure and risk of participants contracting COVID-19 due to study participation and interventions. Insurance policies may have to be amended with regard to this before restarting studies and recommencing recruitment.

Interruption and slowing down of recruitment of trial participants are very likely to occur. Worldwide, there has been a 65% decrease in new patient enrolments, year-on-year, during the month of March.[14] This challenge can be addressed, at least partially, by shifting the site mix to lower-impacted countries and regions. The virtualisation of studies using patient-facing technologies could allow research to be conducted remotely. A number of study aspects, including remote consent, remote randomisation, and remote data capture and reporting, can now be performed through web-based applications.[2 10]

In clinical trials, the scheduled visits to a trial the site may be significantly impacted. Certain investigational products that require self-administration may be amenable to home delivery. This may even include infusions. Where self-administration is not possible and monitoring is required, alternative methods of administration via home nurses or at smaller care facilities may be considered after obtaining approval from the local reviewing authorities.

Another major challenge will be of restarting halted research in the recovery phase of COVID-19. It may be safe to restart halted studies once a decreasing trend of new cases or lack of new cases are reported in the community.

NEED FOR REGULATORS TO BE FLEXIBLE

Research governing bodies and donors have to be flexible with funding, accepting delays and loss of data, allowing grants to run for longer, and letting institutions continue to charge salaries and stipends even when work has slowed down or stopped temporarily. Review boards should allow reasonable amendments and deviation from protocols and allow the use of innovative methods to continue or recommence studies. It must be acknowledged that variations will occur across countries, depending on the incidence of COVID-19 and the impact of the pandemic on each country.

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