This is the promise of digital health. With its unique position in the palette of medical specialties, cardiology could be a leading example paving the road for others in how to adopt advanced technologies while focusing on the real-life relationships they can build with patients through compassionate care.

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# The need for ethical and pragmatic strategies for sample and data collection during public health emergencies—minimizing missed opportunities

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## What the COVID-19 pandemic has revealed to clinical researchers

The magnitude of the success in vaccine and countermeasure research to address the pandemic of SARS-CoV-2 in 2020 cannot be overstated.[1] Within a short period of time, the international community teamed up to address one of the greatest challenges in history, leading to unprecedented achievements such as 'Project Lightspeed',[2,3] in which a highly efficient vaccine against SARS-CoV-2 was developed within months. In parallel, other investigators and companies developed with great efficiency successful vaccines and therapies against SARS-CoV-2, trying to meet the high demand for protection of our society and for return to 'normal' life.[4,5]

While these great successes received extensive media coverage, other scientists have faced challenges due to delayed institutional approvals of their COVID-19 research projects.

Certainly, the role of the ethics committee in ensuring the balance between scientific progress and the protection of patients' rights, privacy, and clinical care is of utmost importance. While the review of a research project application by an ethics committee frequently takes several months during 'normal times', this delay may lead to avoidable loss of valuable samples and data during an outbreak of a pandemic. Time is of the essence for the research community during a pandemic as scientists race to elucidate the pathophysiology of the disease and provide guidance to those designing potentially lifesaving public policies. A new pragmatic balance between regulation and productivity in science must be found in such scenarios.

In this article, we suggest a two-step consent algorithm, in which we separate the institutional approval process for sample acquisition from the approval process of sample analysis, allowing sample collection to start immediately during an outbreak of a public health emergency.

## Lost samples during the first peak of the COVID-19 pandemic

Our motivation for writing this article arose from anecdotal evidence of missed opportunities during the first peak of the COVID-19 pandemic observed by our international colleagues and by ourselves. In this small-scale collection of data, we found that, on average, 70% of COVID-19 minimal-risk biosamples such as blood or plasma could not be collected during the first wave of the pandemic and were therefore lost due to delays in approvals across many institutions. These delays were caused by an overwhelming number of applications to the ethics committees by investigators aiming to study COVID-19.[6] The lost samples could have potentially provided insights into the pathophysiologic mechanisms of COVID-19 in spring 2020 to better prepare the public and clinical facilities for the second peak in autumn 2020.

The increased volume of applications required institutions to adjust their review and approval practices.[6] While ethical decisions on investigational trials are complex and require a comprehensive and often lengthy review, we suggest a simple and time-efficient approach during a public health crisis for studies that are solely analytical.

Early analytical and observational studies are highly relevant as they seek to generate a better understanding of the pathophysiology of a novel disease such as COVID-19 and to improve diagnosis and risk assessment.[6] In that regard, relevant discoveries had been made in analytical studies concerning the nature of COVID-19, active viral replication of SARS-CoV-2 in the respiratory tract, and how this affects infectivity of patients during the course of the illness.[7] Those findings had a relevant impact on public health procedures.

Given the importance of analytical studies, the low health risk they pose to patients, and the observed delays in their approval process, we suggest a two-step consent process that separates sample collection

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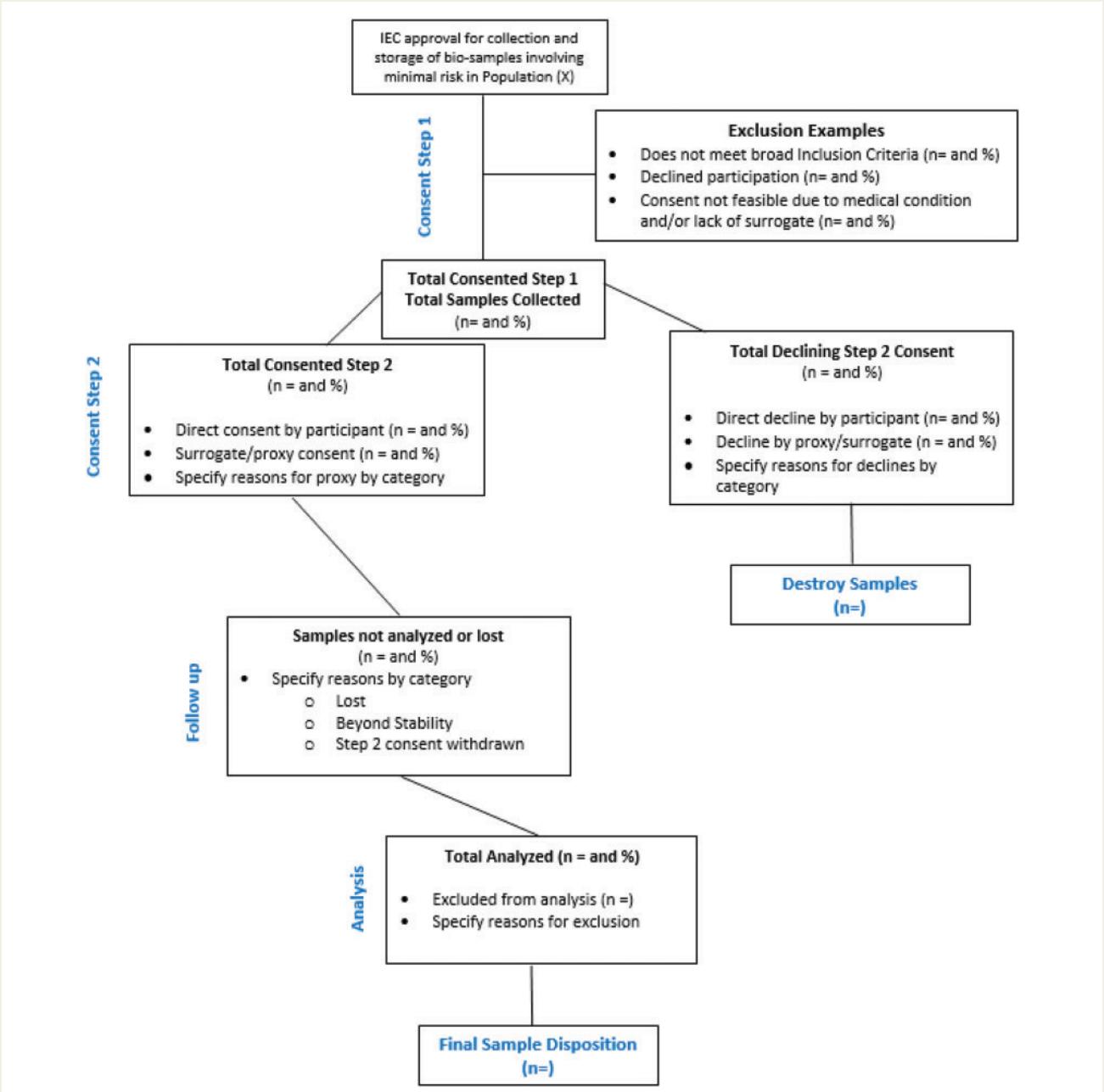


**Figure 1** Proposed 2-step consent process for collection of bio-samples in public health emergencies.

and sample processing, enabling sample collection immediately from the start of the outbreak.

## Proposal for two-step consent process and exploratory sample collection

We suggest a rapid, simple, independent ethics committee (IEC) approved, two-step process to consent for collection of biosamples that involve minimal risk to the donor.

Step 1 obtains a consent limited to collection, proper storage, description of the level of personal identifiability, and process for withdrawing consent for donated routine bio-samples such as (blood, plasma, sputum, and urine) until the public health emergency eases. This consent must be approved *a priori* by the local ethics committee for general health emergencies and may be applied anytime an outbreak such as the current pandemic occurs without requiring an additional approval process. This allows storage of samples right from the start of an outbreak and commits the investigator to proper stewardship of the biosamples.

Step 2 of consent is approved as part of the application for a specific analytical analysis, which is submitted to the IECs at a time when the

system is less acutely burdened. After approval by the IECs, the Step 2 consent is collected retrospectively from patients whose samples have already been stored and includes more specific details of research objectives and the analyses to be done on their samples. Step 2 consent may be a broad consent, but it must contain adequate details on present and future analyses, storage, data sharing, and rights to discontinue use.[8,9] If a patient died between Steps 1 and 2, the Step 2 consent is sought from the nearest family member. If the analyses involve genetic testing, local regulations have to be taken into consideration. If proper consent at Step 2 cannot be obtained, samples are destroyed (*Figure 1*).

With the algorithm of a two-step consent, we would like to offer guidance to institutions who may have experienced similar barriers during the outbreak of the pandemic, when rapid data and sample collection was most needed to obtain insights into this novel disease.

Clinical Scientists/Investigators have a(n ethical) responsibility to pursue research which may urgently reduce morbidity and mortality, as well as to be diligent stewards of their ongoing research projects involving human subjects, even during public health emergencies. Any process which slows, halts or handicaps valid and ethical scientific research, affects research utility and integrity. Likewise, academic, public, and private institutions have a similar responsibility to create a policy and offer guidance to investigators on the benefits and risks of approving new, continuing, suspending, or terminating existing research projects during public health emergencies.

With our suggested algorithm, we hope that in the future similar clinical scenarios can be addressed more promptly so that the entire scientific community will be able to address these challenges from Day 1 of the outbreak.

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