

**Article:**

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*Alternative Sample Matrices Supporting Remote Sample Collection during the Pandemic and Beyond*

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**Guest:** Dr. Khushbu Patel is the director of Clinical Chemistry and Point of Care Testing at the Children's Hospital of Philadelphia. She is also an assistant professor of pathology and laboratory medicine at the University of Pennsylvania's Perelman School of Medicine.

Bob Barrett:

This is a podcast from *Clinical Chemistry* sponsored by the Department of Laboratory Medicine at Boston Children's Hospital. I'm Bob Barrett.

Medical testing that occurs outside a physician's office or laboratory is not a new concept. Measurement of temperature, blood pressure, heart rate, weight, as well as measurement of blood glucose and urine HCG occur quite frequently. However, an area that is growing is remote sampling that allows patients to collect samples in the privacy of their own homes and then send it to a clinical lab for analysis. This type of testing is particularly advantageous to patient populations that need frequent monitoring or have limited access to hospital clinics and laboratories.

In conjunction with the increased growth of telemedicine, remote sampling can allow for expansion of services to reach these patient populations. The COVID-19 pandemic has caused a dramatic increase in Telehealth visits and as telemedicine becomes increasingly popular, it is anticipated that at-home sample collection for routine laboratory testing may as well.

A Q&A feature appearing in the February 2022 issue of *Clinical Chemistry* examines this very matter. Five expert laboratorians and technology developers weigh in on the advantages, hurdles and technological improvements needed for laboratories to incorporate the use of these alternate specimen types into their workflows.

We are pleased to have one of the Q&A moderators in this podcast. Dr. Khushbu Patel is the director of Clinical Chemistry and Point of Care Testing at the Children's Hospital of Philadelphia. She is also an assistant professor of pathology and laboratory medicine at the University of Pennsylvania's Perelman School of Medicine. So, first of all, Dr. Patel, what types of specimen matrices can be used for at-home or remote sample collection? And how do these differ from the samples usually collected in traditional hospital or laboratory settings?

Khushbu Patel: Yes. So, the traditional model of blood collection usually requires a venipuncture draw by a trained professional, usually in proximity to a testing or processing site. And before I go into specifics of sample types that can be used or collected at home, the typical characteristics that you would want in a specimen matrix that's used for this purpose would be, first and foremost that, the sample be easy to collect at home by just following simple instructions.

Second, the matrix should be easy to transport by mail or post. And third, that the analyte being measured is stable in the matrix from the period of time that is collected to when it is analyzed. Meaning it is not sensitive to temperature and other environmental factors that can be imposed during transit. Therefore, matrices such as dried blood or plasma spots from a finger prick or other micro sampling devices and other matrices that require minimally invasive collection techniques such as saliva or dried urine are ideal for this model. And aside from newborn screening programs, such collection methods have not been used in clinical settings thus far.

Bob Barrett: What are some of the advantages of using specimen types that can be collected at home?

Khushbu Patel: Yeah. So, there are several advantages of at-home collection that are mostly convenient and access related. Some of the key advantages that the experts in the Q&A commented on are increased accessibility for populations that live in remote or limited resource setting that may not have access to health care facilities.

Opening up access through such means can help address healthcare inequalities and allow us to understand the true prevalence of certain medical conditions that often go unscreened for. Additionally, it alleviates the burden of having to take time off from work or school and traveling to a specimen collection site.

Getting blood draws is often a stressful and anxious time for patients and the family. So, having the ability to do sample collection in the comfort and familiarity of their own home is also an added convenience factor. All in all, increased access and convenience to testing has many benefits. It can help people with chronic conditions comply with the need to have frequent labs or as well as having providers better tailor plans based on their lab results.

Also, there are benefits of using micro sampling and finger sticks which only requires small volumes of sample which is attractive to everyone, but particularly for small children with limited blood volume.

Bob Barrett: Well, the advantages of using these alternative specimen types for remote collection are fairly obvious. Given these advantages, why are these techniques not used more frequently and what are some of the limitations?

Khushbu Patel: Yes. So, for one, pre-analytical factors can have implications on the end quality of test results. For example, failure to adhere to proper collection techniques and shipping conditions can lead to test cancellations or erroneous results. In dried blood samples, variability and hematocrit can impact certain analytes. Dr. Dickerson pointed out potential interferences that can be matrix specific.

In their experience at Seattle Children's, they have observed variability with different filter papers and collection devices. Dr. Russell Grant in his response to the question also noted that the quality of results (meaning the expected bias and imprecision of the results) is not truly disclosed for most home collection approaches. This can lead to confusion as to how dependable the results are and may require additional laboratory testing as well as clinical follow-up.

Additionally, offering such testing directly to patients without appropriate medical oversight, in some cases, can cause unnecessary anxiety for patients and family. There are also analytical challenges associated with the illusion of extracted dried blood and plasma samples. This can put constraints on both the sample volume needed to do a full panel of testing as well as adhering to the sensitivity and other analytical requirements needed for automated chemistry and immunoassay analyzers.

Additionally, not to forget saliva samples, which are used commonly for genetic testing also have inherent limitations. The overall quality and yield of DNA is lower and is associated with a higher failure rate compared to DNA extracted from blood or bone marrow. All these issues can lead to higher sample rejection rates and need for repeat collections. Also, there is the issue of unintentional or intentional sample swaps with the family.

Bob Barrett: What are the major hurdles involved for laboratories wanting to offer options for at-home sample collection?

Khushbu Patel: The operational hurdles are really the biggest challenge in implementing such programs. These include creating a system for training patients or families and proper collection techniques, having resources and personnel dedicated to assembling and mailing these sample collection kits.

Additionally, there are other workflow issues dealing with accessioning of samples, the informatics of resulting, as well as billing and reimbursement of at-home collected tests that

need to be considered. Working out all these pieces requires close collaboration with the laboratory, the clinical teams as well as the informatics and finance teams within the hospital.

Bob Barrett: So, doctor, what are some of the regulatory challenges laboratory as an IVD manufacturers face when offering testing on samples collected at home?

Khushbu Patel: That is a great question. It is important to remember that many of these tests will ultimately be classified as a laboratory test or an LDT if the validation of the alternative matrix has not already been conducted by the manufacturer. Thus, the test should be validated as an LDT which currently fall under discretionary enforcement oversight with the FDA.

There are specific recommendations that were referred to in the Q&A Article by Dr. Dickerson that I would encourage listeners to visit. The European Bioanalysis Forum recommends validating five key parameters which are the effective hematocrit, testing sample stability to simulate the environmental transport conditions, establishing the bias between capillary versus venous collection, the matrix effects from the filter paper or matrix, and finally, variation in blood spot homogeneity.

Bob Barrett: And what should laboratories consider when validating alternative matrices?

Khushbu Patel: Yes. So, to quickly summarize all the issues discussed: I think most labs will find that it's not the analytical validation that is the challenging part, but really the operation and workflows, especially with the current staffing challenges that laboratory should consider. However, I do not want to underscore that a thorough analytical validation is important to ensure that all the pre-analytical and analytical parameters are thoroughly tested before launching the program.

Considering a pairwise sample collection study to compare the true variability between venous and at-home collected samples that go through the transit process is essential. The variability that exists in our controlled lab environment looks much smaller when other external factors are introduced. Also, most of the experts in the Q&A pointed out that there is a need to establish strict acceptance and rejection criteria for the matrix to ensure that the results are clinically acceptable.

Bob Barrett: Well, finally, Dr. Patel, it sounds like there's still much work and planning needed for laboratories and hospitals to offer remote collection services. Looking ahead, what do you think the future holds for these as healthcare systems rebound from the pandemic and in-person visit start to increase?

Khushbu Patel: Yeah. This is definitely an interesting time to observe the rapid developments in both telemedicine and at-home testing. The COVID-19 pandemic has accelerated many technological improvements that were impending in health care. As we see technological advancements on all fronts with lower costs, self-collection technologies, better quality indicators, sample transportation, and ability of laboratories to handle micro samples, it is anticipated that this field will definitely grow. But these technological barriers will likely need to be overcome first before their broad scale implementation.

Bob Barrett: That was Dr. Khushbu Patel. She is director of Clinical Chemistry and Point of Care Testing at the Children's Hospital of Philadelphia and an assistant professor of pathology and laboratory medicine at the University of Pennsylvania's Perelman School of Medicine. She was a moderator of a Q&A feature in the February 2022 issue of *Clinical Chemistry* on Alternate Sample Matrices Supporting Remote Collection and she's been our guest in this podcast on that topic. I'm Bob Barrett. Thanks for listening.