the scope of this study, as you note, making this diagnosis can lead to early postnatal interventions that can improve outcomes, a unique aspect of prenatal diagnosis of 22q11.2DS.

You also suggested that screening for 22q11.2DS is not needed if the diagnosis of a fetal anomaly can be made by ultrasound. The same could be argued for many of the common aneuploidies, although in both situations, many cases are not detected by ultrasound. In our study, some anomalies were detected only after a high-risk cell-free DNA (cfDNA) result and it is possible that without screening, these anomalies would not have been identified. Furthermore, ultrasound findings were detected as early as cfDNA results could be obtained only in a relatively few number of cases.

Regarding your question on the common aneuploidies, the single nucleotide polymorphism—based cfDNA assay screened for the common aneuploidies and 22q11.2DS. The aneuploidy findings are reported separately.[3]

cfDNA screening has greatly advanced the field of prenatal diagnostics, and we welcome the debate on which disorders warrant screening. 22q11.2DS is associated with severe morbidity, has a reasonably high prevalence, is usually not otherwise reliably detected, can be confirmed with diagnostic testing, and outcomes can be improved with early diagnosis. It would seem that this disorder is an appropriate target for routine prenatal screening.   ∎

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Oxygen saturation in pregnant individuals with hemoglobinopathy and COVID-19

TO THE EDITORS: We would like to share a few thoughts regarding the interesting article entitled, "Oxygen saturation in pregnant individuals with COVID-19: time for re-appraisal?" The authors proposed that "maternal O_2 saturation should be maintained between 92% and 96% for admitted patients with acute respiratory failure who require supplemental O_2."[1]

We agree that maintaining a good O_2 saturation level is important in managing a pregnant patient with COVID-19. The current study did not discuss O_2 saturation history before admission to the hospital for COVID-19; without this information, it cannot confirm if the pregnant patient has an underlying low O_2 saturation. In our setting, located in Asia, hemoglobinopathy is common, and pregnant patients with thalassemia often have a very low O_2 saturation.[2] It is not possible to maintain a high O_2 saturation level in a pregnant patient with thalassemia compared with others. This additional evidence supported the proposed suggestion of Eid et al.[1]   ∎

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This article does not contain any study with human participants or animals performed by any of the authors.

Formal consent is not required for this type of study.

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Considerations in pregnant individuals with low baseline oxygen saturation: a response

We would like to thank the authors for their comments on our recent publication.[1] We agree that it is very important to interpret the oxygen saturation in the setting of underlying maternal disease. Targeting a higher oxygen saturation in pregnancy in certain patients with baseline low levels of oxygen is not always feasible from a physiological standpoint. In addition to patients with a hemoglobinopathy described by the authors, other populations with congenital cyanotic heart disease, such as Eisenmenger syndrome, have decreased oxygen saturation in the systemic circulation.[2] Maternal oxygen saturation in these patients should be assessed and optimized throughout the pregnancy to avoid adverse maternal and fetal outcomes. Hence, determining the baseline maternal parameters (including oxygen saturation) at the beginning of the pregnancy is crucial for guiding management, especially during this COVID-19 pandemic. ∎

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How can cell-free DNA screening best be incorporated into current prenatal screening algorithm?

TO THE EDITORS: In the past 20 years, great progress has been made in prenatal screening for fetal chromosome abnormalities. The detection rate continues to increase, whereas the false-positive rate (FPR) continues to decrease. Currently, cell-free DNA (cfDNA) in maternal plasma offers first-trimester screening with the greatest sensitivity and specificity and expansion in the scope of genetic disorders detectable.[1] Moreover, there is this question: should cfDNA screening be used for high-risk pregnant women only or the general obstetrical population?

Recently, Dar et al[2] assessed cfDNA performance using genetic confirmation in a large prospective obstetrical population. They found that in women at low previous risk of aneuploidy, cfDNA has high sensitivity and specificity and a positive predictive value (PPV) of 85.7% for trisomy 21 and a PPV of 74% for trisomies 21, 18, and 13 combined, similar to that in high-risk women who had a previous positive serum-based screen, a fetal nuchal translucency (NT) of >3.0 mm, an ultrasound-detected anomaly, or an advanced maternal age without other screening results. However, the study has raised some important issues that should be addressed.

The authors concluded that their study would add valuable information on test performance in women at low risk of aneuploidy. What did this mean? Did they recommend cfDNA screening in a low-risk population? The so-called "low-risk population" in their study is not low risk. For example, there were 18 cases of trisomy 21 in 12,836 low-risk women, with a prevalence of 1 of 713 women, which is about that of the general population. We can infer the performance of cfDNA screening for trisomy 21 in high-risk, general-risk, and low-risk groups from their study (Figure), and it was shown that the PPV (25%) in the low-risk group was remarkably lower than that in the other 2 groups.