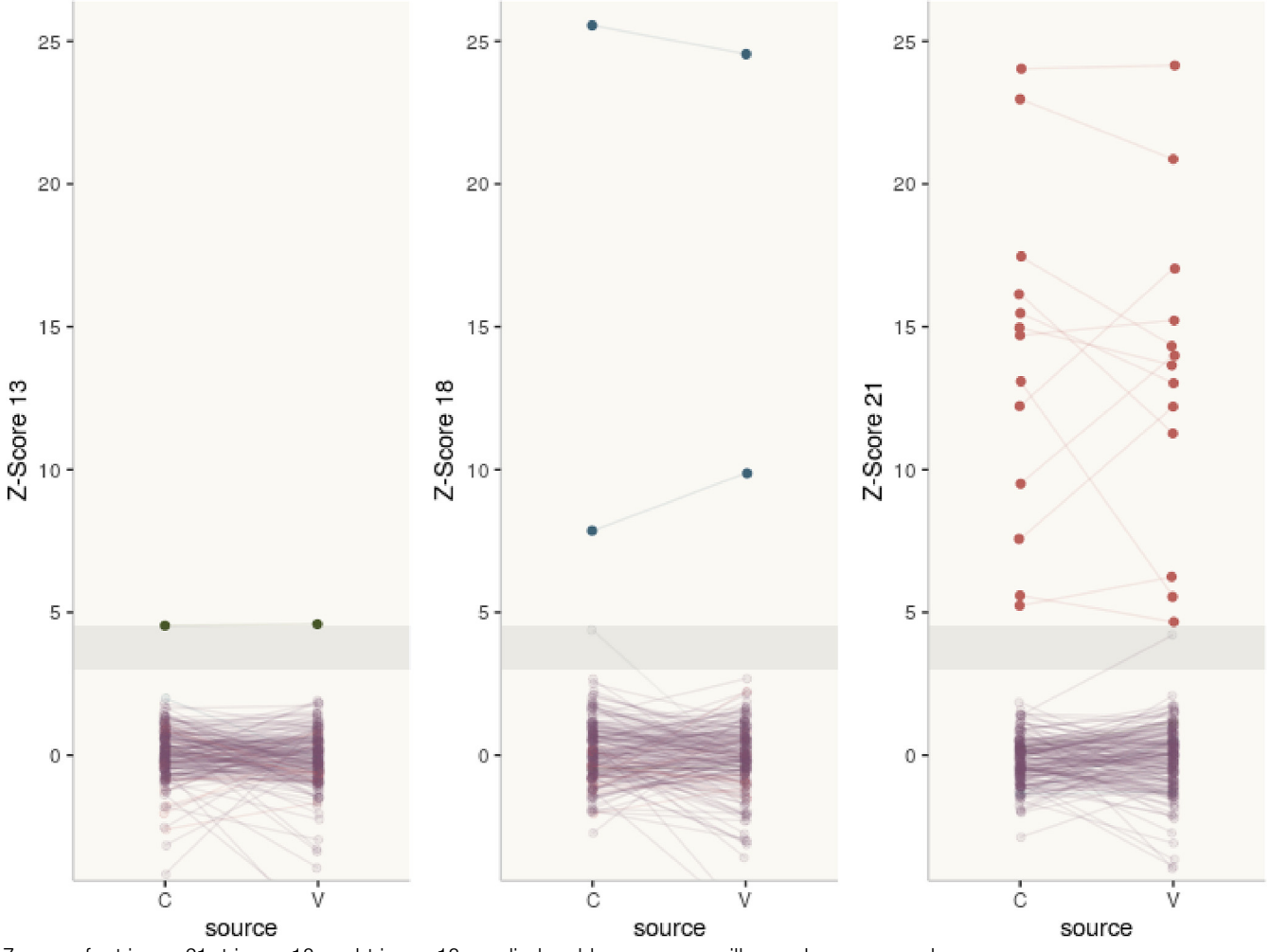
Capillary blood collection: exploring a new method to promote noninvasive prenatal screening access

OBJECTIVE: Noninvasive prenatal screening (NIPS) for aneuploidy using cell-free DNA (cfDNA) technology is endorsed for use across different pregnancy risk levels.[1,2] Yet, problems with NIPS access lead to the continued use of serum screening for some and thus produce aneuploidy screening disparities.[3,4] Enabling equitable access to NIPS requires an affordable approach that is attainable without additional office visits. To determine whether capillary blood collection is feasible for NIPS, in this study, we established a laboratory protocol for capillary blood samples and compared results from capillary and venous NIPS.

STUDY DESIGN: Our study was approved by the Aspire Independent Review Board (IRB #Juno-2017-0001). Across 4 United States sites, we prospectively recruited individuals aged 18 to 45 years with singleton or twin pregnancies between 6 and 40 weeks' gestation. Our cohort was enriched for previous positive aneuploidy screens. All participants contributed venous and capillary blood samples. In study arm 1, a trained professional (eg, phlebotomist) assisted with capillary blood collection, whereas samples were self-collected in study arm 2. Clinical and demographic data were collected.

A NIPS protocol was established based on published methods, and samples were analyzed using the Illumina NextSeq550 and

FIGURE
Z-scores for common autosomal trisomies



Z-scores for trisomy 21, trisomy 18, and trisomy 13 are displayed here across capillary and venous samples.

C, capillary; *V*, venous.

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NextSeq2000 platforms (San Diego, CA, USA).[5] Data analysis was performed using the R statistical package (R Core Team, Vienna, Austria) using a method validated in a separate set of >1200 maternal samples, including 326 samples with positive trisomy NIPS results. These samples were split into a training set (n=671; trisomy 21, n=84; trisomy 18, n=74; trisomy 13, n=21) and a test set (n=550; trisomy 21, n=75; trisomy 18, n=56; trisomy 13, n=6). Aneuploidy reporting thresholds were established using the training data set. The test data set was signed out by an outcomes-blinded laboratory director and used to establish sensitivity (>99%) and specificity (>99.9%).

RESULTS: Venous and capillary sample pairs were successfully collected from 202 participants. Neither cfDNA size profiles nor fetoplacental cfDNA contribution in plasma were significantly different between venous and capillary blood samples (Wilcoxon paired rank test, $P>.05$). Elevated Z-scores for trisomy 21 (n=13), trisomy 18 (n=2), or trisomy 13 (n=1) were concordant between venous and capillary samples in all 16 pairs (Figure). Results were inconclusive for capillary or venous pairs in 2 of the 202 pairs (1.0%); 1 of the pairs was venous euploid and capillary inconclusive, whereas the other was venous inconclusive and capillary euploid. Samples collected in the assisted study arm demonstrated a bimodal distribution clustered around first- and second-trimester in-office prenatal visit timing, whereas samples in the self-collected arm were more uniformly distributed across gestational ages.

CONCLUSION: We have demonstrated that with or without assistance from medical personnel, sufficient capillary blood volumes can be obtained for NIPS. Furthermore, capillary and venous cfDNA samples have comparable characteristics. Because NIPS results from capillary blood collections are equivalent to NIPS results obtained from venous blood, self-collected capillary blood samples are a prime candidate for a distributable NIPS system that promotes increased and convenient access to NIPS for all pregnant patients.

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