Non-invasive fetal sex determination by maternal plasma sequencing and application in X-linked disorder counseling
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Objective
To develop a fetal sex determination method based on maternal plasma sequencing (MPS) and assess the performance and potential use in X-linked disorder counseling.

Methods
900 cases of MPS data from a previous study were reviewed, in which 100 and 800 cases were used as training and validation set, respectively. The percentage of uniquely mapped sequencing readings on Y chromosome was calculated and used to classify male and female cases. Eight pregnant women that are carriers of Duchenne muscular dystrophy (DMD) mutations were recruited, whose plasma were subjected to multiple sequencing and fetal sex determination analysis.

Results
In the training set, a sensitivity of 96% and false positive rate of 0% for male cases detection were reached in our method. The blinded validation results showed 421 in 423 male cases and 374 in 377 female cases were successfully identified, revealing sensitivity and specificity of 99.53% and 99.20% for fetal sex determination, at as early as 12 gestational weeks. Fetal sex for all 8 DMD genetic counseling cases were correctly identified, which were confirmed by amniocentesis.

Conclusion
Based on MPS, high accuracy of noninvasive fetal sex determination can be achieved. This method can potentially be used for prenatal genetic counseling.