

# Not-so-free testing for cell-free DNA

Darryl Huang MD Karen Lundgard MD CCFP Michael R. Kolber MD CCFP MSc

### Clinical question

Can cell-free DNA (CF-DNA) tests, also known as noninvasive prenatal tests (NIPTs), be recommended to women to screen for trisomies?

### Bottom line

Best evidence suggests that CF-DNA testing at 10 to 14 weeks' gestation is more sensitive (100%) and specific (99.9%) than current screening for trisomy 21 and approaches the accuracy of amniocentesis. Use might be limited by high cost and lack of provincial coverage.

### Evidence

A multicontinent prospective study of 18955 women with singleton pregnancies compared standard first-trimester screening (plasma protein A and  $\beta$ -human chorionic gonadotropin levels, nuchal translucency) with maternal blood CF-DNA tests for detecting trisomies 21, 18, and 13.<sup>1</sup>

- Patients and physicians were aware of standard test results (not CF-DNA). Decisions were made according to standard clinical practice.
- A CF-DNA test was done at 10 to 14 weeks' gestation by staff blinded to the other test results. Results were reported after delivery.
- Outcome assessors (blinded to test results) reviewed newborn examination and genetic test records.
- The CF-DNA results identified trisomy 21 in all 38 cases; standard screening identified 30 of 38 (79%).
- False-positive results were identified by standard screening in 5% of cases and by CF-DNA testing in less than 0.1%. The CF-DNA test had sensitivity of 100%, specificity of 99.9%, a positive likelihood ratio (LR+) of 1756, and a negative likelihood ratio (LR-) of 0. Standard testing had sensitivity of 78.9%, specificity of 94.6%, LR+ of 15, and LR- of 0.22.
- A CF-DNA test accurately detected trisomies 18 and 13 in 12 cases (LR+ >5000, LR- <0.1).
- In 3% of cases, unusable CF-DNA was found; this subgroup had a higher rate of aneuploidy (2.7% vs 0.4%).
- The CF-DNA test manufacturer supported the study.
- An earlier meta-analysis of 37 studies (N=22 659) found similar results.<sup>2</sup>

### Context

- Risk of trisomy 21 increases with maternal age.<sup>3</sup>
- Risk of pregnancy loss with amniocentesis is about 0.5% and with chorionic villus sampling is 1% to 2%.<sup>3,4</sup>
- The Society of Obstetricians and Gynaecologists of Canada recommends discussing screening for trisomies with all pregnant mothers<sup>5</sup>; CF-DNA testing could be

used instead of amniocentesis but termination decisions should not be based only on its results.<sup>6</sup>

- Coverage of CF-DNA varies across Canada, with self-pay costing about \$500. Compared with standard screening, CF-DNA testing is likely cost effective.<sup>7</sup>

### Implementation

Most pregnant women would use NIPTs if available,<sup>8,9</sup> including more than half who previously refused prenatal screening.<sup>10</sup> Studies cite test safety and accuracy, and a possible reduction in invasive procedures as reasons to offer NIPTs to all pregnant women.<sup>9</sup> In some areas of Canada, CF-DNA tests are covered for women who had a positive initial result, are older than 40 years, or had a previous trisomy pregnancy.<sup>3,8</sup> It takes time to perform a test, receive results, and discuss these results and explore patient preferences. Decision aids increase patients' involvement in health care decisions and improve risk estimates and patient satisfaction.<sup>11</sup>

Dr Huang was a family medicine resident at the University of Alberta in Fort McMurray. Dr Lundgard is a rural family physician in Peace River, Alta. Dr Kolber is Associate Professor in the Department of Family Medicine at the University of Alberta in Edmonton.

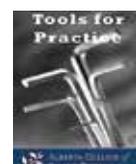
### Competing interests

None declared

The opinions expressed in Tools for Practice articles are those of the authors and do not necessarily mirror the perspective and policy of the Alberta College of Family Physicians.

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