

## **DIAGNOSTIC TEST MODULE**

### **DNA sequencing of maternal Plasma to detect down syndrome**

#### **Objectives:**

At the completion of this session you will be able

1. To assess the validity of an article about a diagnostic test
2. To calculate a Likelihood ratio (LR)
3. To interpret a Likelihood Ratio (LR) in relation to a specific diagnostic test
4. To determine the applicability of a diagnostic test to a particular situation

#### **Assignment:**

1. Read the Clinical Scenario.
2. Compose a well-built clinical (foreground) question about the clinical problem.
3. Complete a literature search using the headings from your well-built clinical question, and bring the results to the session.
4. Read the EBCP Manual reference articles.
5. Complete the attached EBCP Worksheet.
6. Determine whether the result of this diagnostic test should change your approach to the patient.

#### **Clinical Scenario:**

You are a busy primary care physician and one of your well-known patients presents with early pregnancy. Mrs. McKay is a pleasant 36 year old G2P1, who is healthy without any significant past medical history, and no family history in she or her husband for Down syndrome. She takes no regular medications, and has no allergies to medications. She notes that she would like to pursue genetic testing but is fearful of invasive tests as a neighbor suffered a miscarriage after amniocentesis. She has a friend in British Columbia who had DNA sequencing for Down syndrome, and wonders if this is an option she could pursue. You promise to look into this option and get back to her in a couple of days.

You go to PUBMED and check the MESH terms. You search Prenatal Diagnosis/methods\* and Down syndrome/diagnosis and Mass Screening. The second hit is an interesting debate about current controversies in the area (Bianchi, 2014). You review the article and decide to read the primary study by Palomaki and colleagues.

### **Recommended Material:**

1. Guyatt G, Roman Jaeschke, Mark Wilson, Victor Montori, and Scott Richardson. What is evidence-based medicine. In Guyatt G, Rennie D, Meade MO, Cook DJ. Users' Guides to the Medical Literature: A Manual for Evidence-based Clinical Practice. 3rd ed. New York, NY: McGraw-Hill; 2015.
  - a. The Process of Diagnosis. Section 16.
  - b. 18 Diagnostic Tests. Section 18.
  - c. Advanced Topics in Diagnosis – 19.1 Examples of Likelihood Ratios. Section 19.2
2. Palomaki GE, *et al.* DNA sequencing of maternal plasma to detect Down syndrome: An international clinical validation study. *Genetics in Medicine* 2011; 13(11): 913-920. (methods appendix attached)
3. Bianchi DW, Oepkes D, Ghidini A. Current controversies in prenatal diagnosis 1: should noninvasive DNA testing be the standard test for Down syndrome in all pregnant women? *Prenatal Diagnosis* 2014; 34: 6-11.