

1 Cell-Free Fetal DNA Testing (Green-Top Guideline No. XX)

3 Final Scope

5 This is the first edition of this guideline, and has been produced jointly with the British Maternal and
6 Fetal Medicine Society.

- 8 1. Purpose and Scope
- 9 2. Introduction and background
 - 10 2.1 Antenatal screening in the first trimester
 - 11 2.2 Screening tests for trisomies 21, 18 and 13
 - 12 2.3 Diagnostic testing with chorionic villous sampling and/or amniocentesis
 - 13 2.4 Policy and performance of aneuploidy screening in NHS England
- 14 3. Identification and assessment of evidence
- 15 4. Cell-free fetal DNA as a screening tool for chromosomal anomalies
 - 16 4.1 Cell-free fetal DNA
 - 17 4.2 What are the different approaches that can be used for screening with cell-free fetal DNA?
 - 18 4.2.1 Universal screening for trisomies 21, 13 and 18
 - 19 4.2.2 Contingent screening for trisomies 21, 13 and 18
 - 20 4.2.3 Based on clinical indication for pregnancies considered at a-priori high risk
 - 21 4.3 What do women need to know before choosing to have screening with cell-free fetal
22 DNA?
 - 23 4.4 What is the screening performance of cell-free fetal DNA in low-risk and high-risk
24 populations?
 - 25 4.5 How is fetal fraction defined, and what is its significance?
 - 26 4.6 What are the patient factors known to affect the performance of cell-free fetal DNA
27 screening?
 - 28 4.6.1 Maternal factors
 - 29 4.6.2 Fetal factors
 - 30 4.6.3 Placental factors
 - 31 4.7 What is the recommended patient pathway in cases where cell-free fetal DNA screening
32 fails to yield a result?
- 33 5. Expanding the use of cell-free fetal DNA screening beyond the detection of trisomies 21, 13 and
34 18
 - 35 5.1 Fetal sex
 - 36 5.2 Sex chromosomal aneuploidies
 - 37 5.3 Copy number variants
 - 38 5.4 Rare autosomal trisomies
 - 39 5.5 Single gene disorders
- 40 6. Potential indications for offering cell-free fetal DNA screening
 - 41 6.1 Women who have had the combined test with a high chance result for trisomy 21, 18 or
42 13 because of raised nuchal translucency or abnormal serum biochemistry
 - 43 6.2 Women who have had a high chance result from the quadruple test for trisomy 21
 - 44 6.3 Fetal anomalies detected by ultrasound
 - 45 6.4 Women with a previous diagnosis of trisomy 21, 13 or 18
 - 46 6.5 Women who have conceived with in vitro fertilisation/intracytoplasmic sperm injection
47 and had pre-implantation genetic screening
 - 48 6.6 Women who have had cell-free fetal DNA screening with a low chance result and a
49 subsequent finding of:
 - 50 6.6.1 Elevated nuchal translucency

51	6.6.2 Fetal anomalies detected by ultrasound
52	6.6.3 High risk result from the combined test
53	7. Caring for women with a high chance cell-free fetal DNA screening result who choose to
54	continue with their pregnancy
55	8. Cell-free fetal DNA screening in multiple pregnancies
56	8.1 What is the screening performance of cell-free fetal DNA in monochorionic and
57	dichorionic twins?
58	8.2 Can cell-free fetal DNA screening be offered in a twin pregnancy in the setting of a single
59	empty sac or vanishing twin syndrome?
60	8.3 How should a high chance cffDNA screening result be managed in twin pregnancies?
61	8.4 Is there a role for cell-free fetal DNA screening in triplets and higher order pregnancies?
62	8.5 Is there a role for cell-free fetal DNA screening in multiple pregnancy discordant for nuchal
63	translucency (≥ 3.5 mm)?
64	8.5.1 Monochorionic
65	8.5.2 Dichorionic
66	8.6 Is there a role for cell-free fetal DNA screening in multiple pregnancy discordant for fetal
67	anomalies?
68	9. Follow-up care after a high chance cell-free fetal DNA screening result and post-test counselling
69	9.1 What is the optimal diagnostic test for singleton pregnancies?
70	9.1.1 High chance result for trisomy 13 or 18
71	9.1.2 High chance result for trisomy 21
72	9.2 What is the optimal diagnostic test in twin pregnancies?
73	9.2.1 High chance result for trisomy 13 or 18
74	9.2.2 High chance result for trisomy 21
75	9.3 How should discordant results between cell-free fetal DNA screening and chorionic villous
76	sampling/amniocentesis be managed?
77	9.4 What is the role of support groups in this setting?
78	10. Recommendations for future research
79	10.1 What is the role of cell-free fetal DNA in universal screening?
80	10.2 What is the role of cell-free fetal DNA in screening for genetic conditions other than
81	trisomies 21, 13 and 18?
82	10.3 How can we improve our understanding of womens' perspectives around cell-free fetal
83	DNA screening?
84	10.4 Future technologies
85	11. Auditable topics
86	12. Useful links and support groups
87	13. Quick reference flow diagram – Management pathway: Care of women opting for cell-free fetal
88	DNA screening
89	14. References