



COST-EFFECTIVENESS ANALYSIS OF GENETIC TESTING FOR STILLBIRTH: BALANCING COST AND DIAGNOSTIC RATE

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Introduction

- The most cost-effective algorithm for genetic testing for stillbirth is unknown
- Addition of whole exome sequencing (WES) complicates cost-benefit analysis
- Objective: to perform cost-effective analysis for various algorithm of genetic testing for stillbirth

Methods

- Literature review for yield rate, cost, failure rate of karyotype, chromosomal microarray (CMA) and WES on stillbirth
- 12 approaches for stillbirth testing algorithms using karyotype, CMA and WES (**Table 1**)
- Point simulations using 12 algorithms to calculate expected annual total diagnosis, hit-rate, cost/diagnosis and missed diagnosis assuming birth rate of 3,788,235 births/year
- Monte-Carlo simulation for 4 highest hit-rate algorithms without WES and 2 algorithms with WES by letting yield rate, cost, failure rate of karyotype, CMA and WES vary
- One-way ANOVA to compare cost/diagnosis for each algorithm

Results

- The four algorithms with the highest hit-rate without WES are; **1) universal karyotype AND CMA 2) Universal CMA 3) Universal karyotype with reflex CMA 4) Universal karyotype with reflex CMA for culture failure only (Table 1)**
- Results of Monte-Carlo simulation shown in **Figure 1**
- Of the highest hit-rate algorithms, universal karyotype with reflex CMA for culture failure only and universal CMA have the lowest median cost/diagnosis at \$7,112.61 and \$9,863.61

Discussion

- From a cost-effectiveness perspective, CMA is likely reasonable to be performed in the case of karyotype culture failure
- Cost of WES is likely still prohibitive for widespread usage in the evaluation of stillbirth though the addition of WES results in 58.9% increase in yield rate to universal karyotype and CMA
- To aid health systems and policy makers, we have created a calculator to show the calculation result using different birth rate and cost of testing <http://bit.ly/StillBirthCalc> (download and click to open the file to access the calculator)

Universal karyotype for all stillbirths followed by reflex CMA in the case of culture failure ONLY results in the lowest cost/diagnosis among highest hit-rate algorithms



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Table 1. Point simulations of genetic testing algorithms

No	Algorithm	Annual Genetic Diagnosis	Hit Rate	Cost/Diagnosis	Annual Missed Genetic Diagnosis
1	Universal, karyotype	1318.30	5.80%	\$4,978.45	1986.4
2	Universal, karyotype, reflex CMA	1706.52	7.51%	\$13,883.17	1598.1
3	Universal, CMA	1886.54	8.30%	\$5,903.61	1418.1
4	Universal, karyotype + CMA	2093.37	9.21%	\$11,821.39	1211.3
5	Anomalous only, karyotype	621.74	2.74%	\$1,488.40	2682.9
6	Anomalous only, karyotype reflex CMA	625.41	2.75%	\$3,525.25	2679.3
7	Anomalous only, CMA	956.67	4.21%	\$2,680.00	2348.0
8	Anomalous only, karyotype + CMA	956.67	4.21%	\$3,623.04	2341.6
9	Universal, karyotype reflex CMA for culture failure only	1702.51	7.49%	\$7,005.68	1602.2
10	Anomalous only, karyotype, reflex CMA for culture failure only	681.97	3.00%	\$2,132.20	2622.7
11	Universal, karyotype + CMA, reflex WES	3304.67	14.54%	\$35,266.33	0.0*
12	Anomalous only, karyotype + CMA, reflex WES	1176.7	5.18%	\$9,159.07	2128.0

*Algorithm 11 is used as the gold standard to calculate missed diagnoses

