Investigating Cancer Diagnoses after Atypical Findings on Prenatal Cell-Free DNA (pcfDNA) Screening

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Background

- Incidental findings of maternal malignancy on noninvasive prenatal cell-free DNA (pcfDNA) screening have been previously reported, with autosomal monosomy and multiple positive aneuploidy results potentially associated with increased risk of cancer.

OBJECTIVE: We evaluated the proportion of patients with a new cancer diagnosis in the 180 days following results from a prenatal whole genome sequencing-based pcfDNA screening test using a novel approach of linking to insurance claims data.

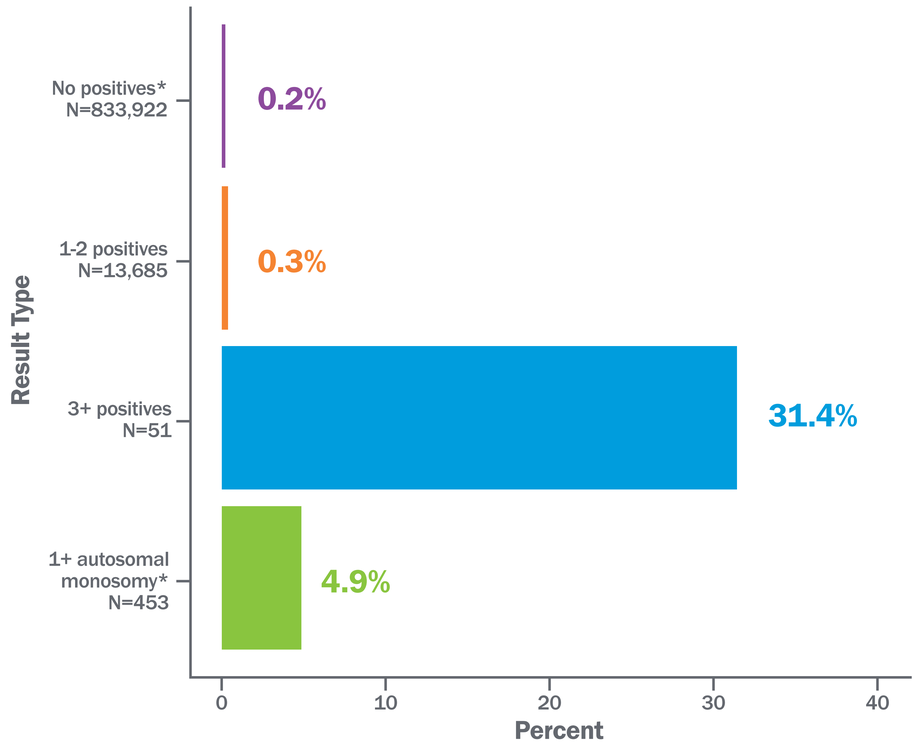
Methods

- Patients who received Prequel[1] between 2015 and 2023 were were eligible. Patients were excluded if they were aged <18 years, opted out of research, resided in New York State, or had any cancer diagnosis code in the 180 days before pcfDNA testing.
- De-identified Prequel data were linked to de-identified insurance claims data from the Komodo Healthcare Map[2] using Datavant tokenization.[3]
- A positive result was defined as screening positive for a trisomy or monosomy of any autosome, any of five microdeletions (15q11.2, 1p36, 22q11.2, 4p, or 5p), or a sex chromosome abnormality.
- Positive results were summed per patient per test and grouped by number of positive results; patients with 1+ positive autosomal monosomy result were also flagged.
- The odds of being newly diagnosed with cancer during follow-up was estimated based on any new cancer ICD-10 diagnosis code in the 180 days after Prequel testing for each result group using logistic regression with adjustment for maternal age.

Results

- A total of 847,658 pregnancies met the eligibility criteria.
- 31.4% (16/51) of pregnancies with 3+ positive results and 4.9% (22/453) of pregnancies with 1+ positive autosomal monosomy result had a new cancer diagnosis during follow-up, versus 0.2% (1,510/833,922) of those with 0 positive results **(Figure 1)**.

Figure 1. Frequency of cancer diagnoses in the 180 days after pcfDNA testing by result group



*The autosomal monosomy group is not mutually exclusive to the other categories.

References: 1. Myriad Genetics, Inc., Salt Lake City, UT. Prequel® Prenatal Screen. https://myriad.com/womens-health/patient-prequel/. **2.** Komodo Health, Inc. https://www.komodohealth.com/healthcare-map. **3.** Datavant. https://www.datavant.com/. **4.** Goldring G, et al. *Obstet Gynecol.* 2023 Apr 1;141(4):791-800. **5.** Bianchi DW, et al. *JAMA.* 2015 Jul 14;314(2):162-9. **6.** Carlson LM, et al. *Obstet Gynecol.* 2018 Mar;131(3):464-468.

Results

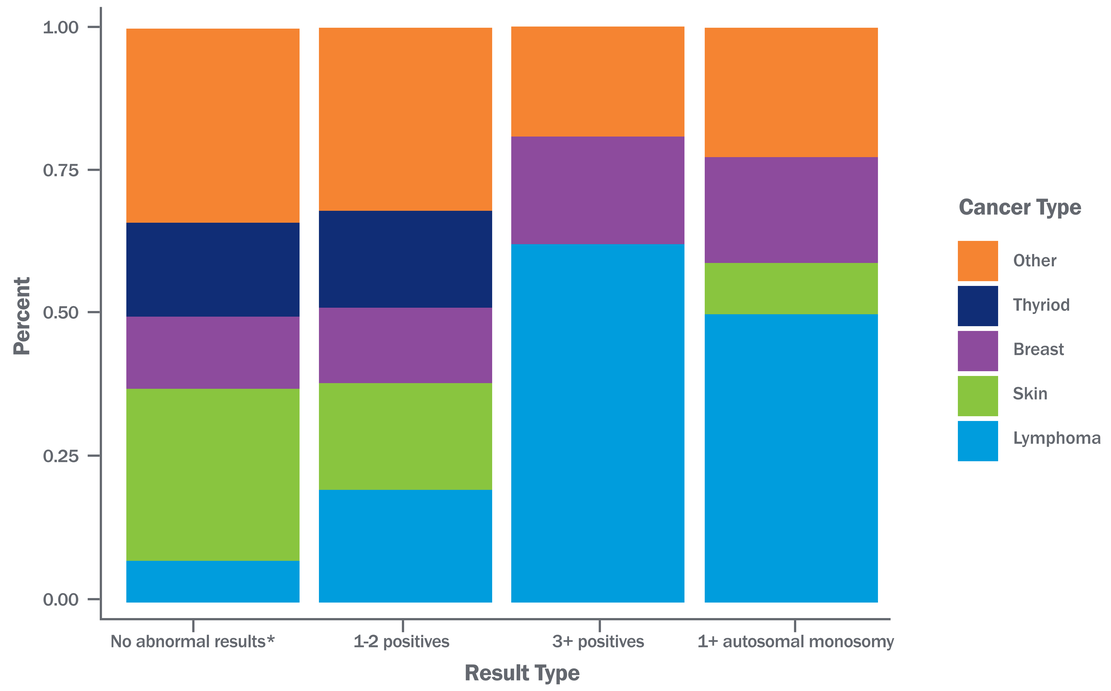
- Patients with 3+ positive results and patients with 1+ positive autosomal monosomy result had higher odds of cancer diagnosis vs those with 0 positives **(Table 1)**.
- Among patients with 3+ positives or an autosomal monosomy, the most common cancer types were lymphoma and breast **(Figure 2)**.

Table 1. Logistic regression results on the association of pcfDNA result and odds of incident cancer diagnosis

	Result type	OR (95% CI)	P-value
Number of positive results	No positive results*	Reference	
	1 positive result	1.4 (1.0 – 1.9)	0.027
	2 positive results	3.7 (0.9 – 10.2)	**0.030**
	3+ positive results	82.1 (36.4 – 176.0)	**<0.0001**
Autosomal monosomy result	None	Reference	
	At least one	9.1 (4.8 – 16.2)	**<0.0001**

Model was adjusted for maternal age. *The autosomal monosomy group is not mutually exclusive to the other categories.
CI, confidence interval; OR, odds ratio.

Figure 2. Most common cancer subtypes, stratified by pcfDNA result



Unable to report subgroup sample sizes due to privacy restrictions.
*Autosomal monosomy results were excluded from the 'No abnormal results' group.

Conclusion

Consistent with previous studies,[4-6] these results suggest that patients with an autosomal monosomy or multiple aneuploidies on pcfDNA have higher risk of a cancer diagnosis in the pregnancy and postpartum periods than those with no abnormal results.

Disclosures: All authors were employees of Myriad Genetics, Inc. at the time of this study and received salaries and stock as compensation.