# Whole genome and transcriptome sequencing can be introduced into the diagnostic workup of sarcoma and pediatric cancer patients

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## INTRODUCTION

Limited molecular diagnostics in pediatric cancers and sarcomas hinder accurate diagnosis and therapy selection, due to an inability to detect some clinically relevant large and rare rearrangements. This meta-analysis evaluates the potential of WGS/WGTS to overcome these limitations and improve personalized oncology care.

## METHODS

A systematic review and meta-analysis of English-language studies (PubMed; 01/08/2024-5/11/2024) was conducted per PRISMA guidelines to evaluate the clinical impact of WG(T)S in pediatric cancers and sarcomas. Included studies were primary research articles with data on clinical impact, validity, utility, and/or feasibility.

## RESULTS

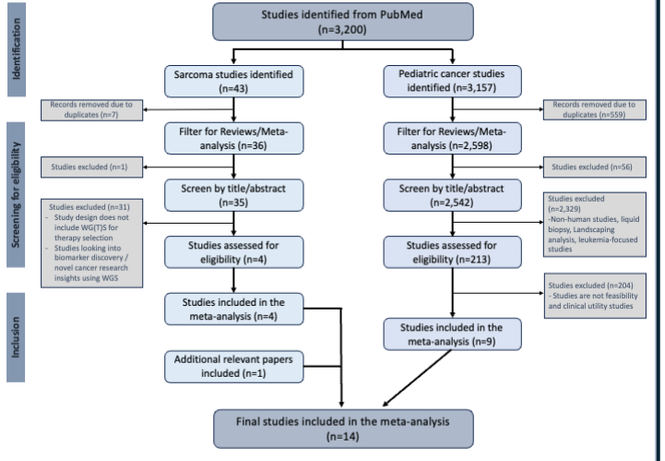



**Figure 1.** Screening process of published literature

## RESULTS

**Table 1.** Analytical utility of WG(T)S in sarcomas and pediatric cancers.

| Study | Feasibility, % (n/N) | Tissue type | Seq depth, X (T/N) | Tumor purity cut-off (%) | TAT (days) |
|---|---|---|---|---|---|
| Sarcoma | | | | | |
| Prendergast | 62 (597/957) | FF | 100/30 | 40 | 42 |
| Schipper | 100 (83/83) | FF | >90–100/30 | 20 | N/a |
| Watkins | 92 (67/73) | FF | 100/40 | 30 | 39 |
| Öfverholm | 99 (197/200) | FF | 90/30 | N/a | N/a |
| Andrew | 100 (15/15) | N/a | 80 or 100/40 | N/a | 45 |
| Pediatric cancer | | | | | |
| Wong | 100 (247/247) | FF | N/a | 25 | 52.5 |
| Newman | 82 (253/309) | N/a | 45/N/a | 40 | 49 |
| Trotman | 100 (36/36) | FF | 100/40 | N/a | 30 |
| Shukla | 57 (114/201) | FF | 80/30 | 20 | 9 |
| Villani | 94 (264/300) | FF + FFPE | 30–60/30 | 25 | N/a |
| Wadensten | 79 (117/149) | N/a | 90/30 | 40 | N/a |
| Hodder | 98 (281/286) | FF | 100/40 | N/a | 18 |
| Deyell | 90 (78/87) | N/a | 90/45 | N/a | 71 |
| Lau | 83 (319/384) | N/a | N/a | N/a | 46.2 |

- Feasibility: Range of 57%–100%; 64.2% of studies showed a feasibility of >90%
- TAT: 9–53 days; TAT calculations varied between studies

**Table 2.** WG(T)S leads to change or refinement of diagnosis in pediatric cancers.

| Study | CNS | Neuroblastoma | Sarcoma | Solid, Other | Heme | Other | Impact on Diagnosis | Germline Findings |
|---|---|---|---|---|---|---|---|---|
| Wong | 37 | 7 | 25 | 15 | 16 | 0 | 5.2 | 16.2 |
| Newman | 26 | 0 | 0 | 23 | 35 | 16 | N/a | 18 |
| Trotman | 47 | 0 | 20 | 30 | 0 | 3 | 17 | 8.3 |
| Shukla | 7 | 15 | 44 | 0 | 0 | 34 | 6 | 5 |
| Villani | 22 | 0 | 0 | 61 | 17 | 0 | 6.5 | 15 |
| Wadensten | 49 | 0 | 18 | 17 | 0 | 16 | 51 | 8.5 |
| Hodder | 13 | 4 | 8 | 21 | 54 | 0 | 38 | 7 |
| Deyell | 23 | 11 | 31 | 17 | 7 | 11 | N/a | 12 |
| Lau | 38 | 0 | 0 | 46 | 16 | 0 | N/a | N/a |

Values are percentages.

**Table 3.** WG(T)S leads to change or refinement of diagnosis in sarcomas.

| Study | Soft Tissue | Bone Tissue | Other | Impact on Diagnosis | Germline Findings |
|---|---|---|---|---|---|
| Prendergast | 56 | 44 | 0 | 3 | 1.7 |
| Schipper | N/a | N/a | N/a | 14 | 8 |
| Watkins | 31 | 17 | 52 | 37 | 4 |
| Öfverholm | 60 | 7 | 33 | 7 | 11 |
| Andrew | 80 | 0 | 20 | 32 | 13 |

Values are percentages.

**Sarcoma**: Refinement/change of diagnosis when compared to SoC ranged from 3%–37% (av 18.6%).

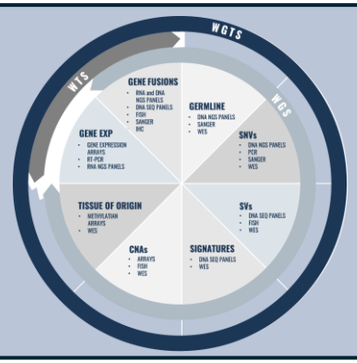
**Pediatric cancers**: WG(T)S impacts diagnosis in 5.2%–51% of patients (av 20.6%).

**Therapy-informing findings**: Ranged from 4%–67%.

**Germline findings**: Found in 7.35% of patients.

## CONCLUSIONS

WG(T)S enhances diagnostic yield by detecting large rearrangements (e.g., structural variants, gene fusions) critical for accurate diagnosis and risk stratification in pediatric cancers and sarcomas. Our meta-analysis demonstrates the clinical utility of WG(T)S, suggesting its potential for routine use in oncology.




## References

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