Focus on Clinical Implementation

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REIMER
MARATHON

Implementation Science

What are the innovations?	• Interventions, tools, practices
What are the Implementation challenges?	• Underuse vs. overuse
Who/what is affected?	• Policy, community, health care system, provider, individual
How do we improve implementation?	• Interactive assistance, adapt and tailor, support practitioners, engage consumers
How do we know if implementation is successful?	• Acceptability, uptake, cost, fidelity, sustainment
What are the desired outcomes?	• Increased years of life, improved quality of life, health equity

adapted from cancer.gov

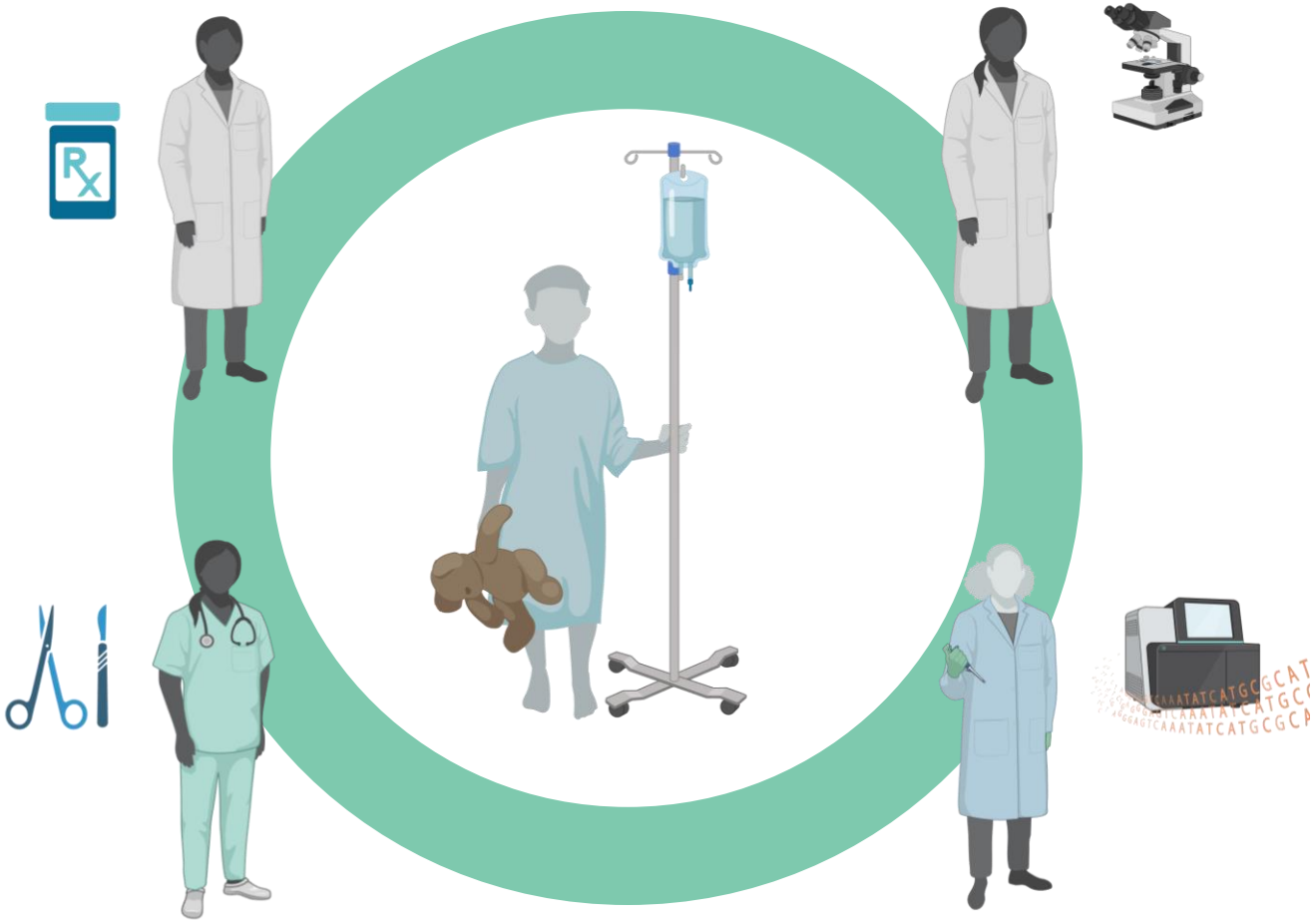
Challenges in Universal Adoption of Molecular Profiling for Children with Cancer

Ordering practices

Billing and payment

Laboratory regulations

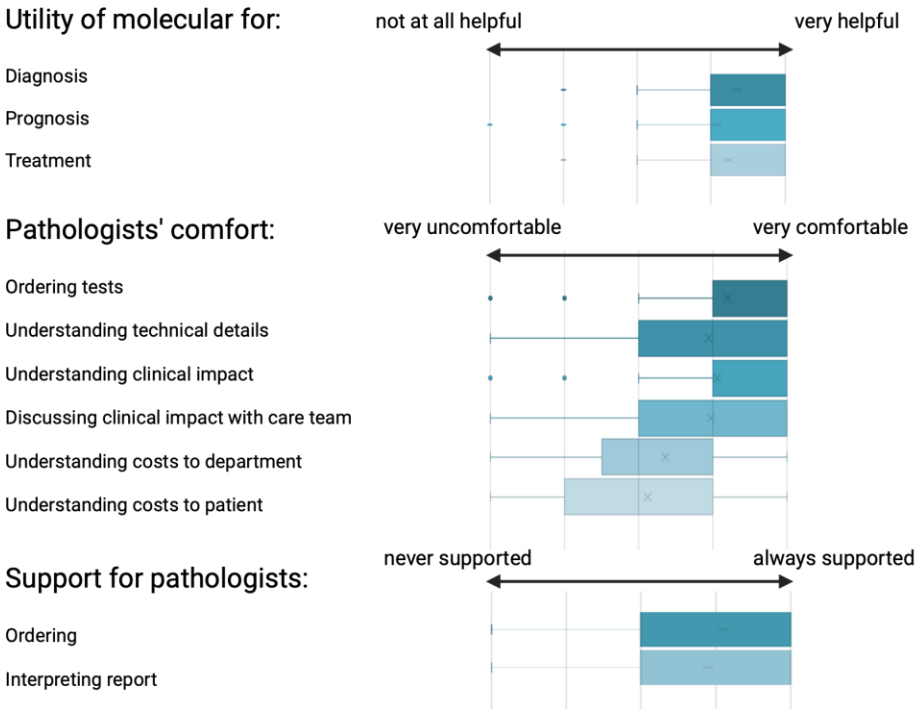
Clinical ordering practices

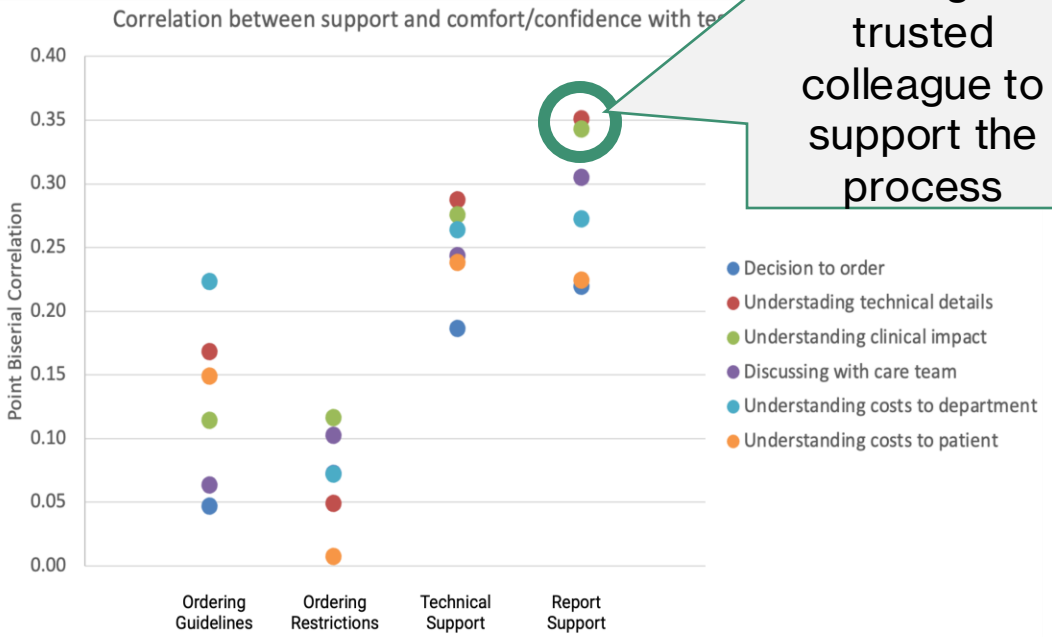


Right test at the right time

Some guidance in NCCN guidelines, but many gaps

Clinical ordering practices





Comfort with technical details and clinical impact correlates with having a trusted colleague to support the process

Gestrich C et al. *Pediatr Blood Cancer* 2025

Patient-centered integration of tumor and germline genetic results can improve cancer care

Alanna J. Church, Oindrila Bhattacharyya, Julie O. Culver, Yonatan Amzaleg, Erin Linnenbringer, Maeve Smart, Christina Ip-Toma, Adan Reinosa Rivera, Bethany Davis, Charité Ricker, Heinz-Josef Lenz, Stacy W. Gray, Heather Hampel & David W. Craig

Church et al. Nature Medicine 2025

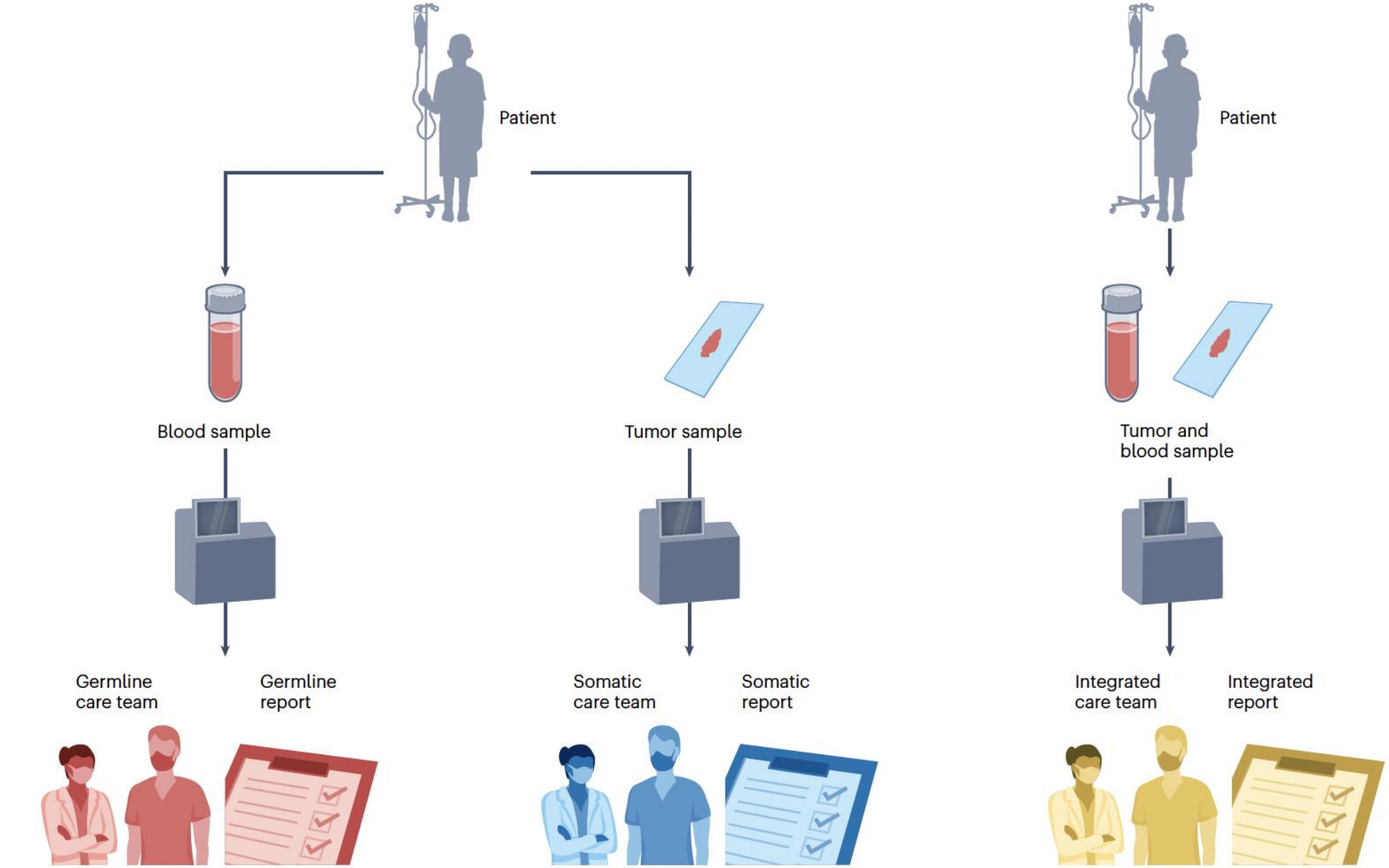


Fig. 1 | Models for reporting somatic and germline results. Infographic of the current siloed model (left) and an integrated patient-centered model (right).

Church et al. Nature Medicine 2025

Billing and payment for molecular tests

- Billing: CPT codes (81445, 81450, 81455); Z-codes (MolDX) often required
- Coverage: CMS reimburses under CLFS; Private insurers vary
  - CMS policy – reimburses NGS panel testing if:
    - The patient has recurrent, relapsed, refractory, metastatic, or advanced stage III or IV cancer.
    - The patient has not been previously tested with the same NGS test for the same cancer genetic content.
    - The patient has decided to seek further cancer treatment (e.g., therapeutic chemotherapy).
- Prior Authorization: Often needed; documentation critical
- Payment: Based on CMS Fee Schedules or negotiated rates
- Trends: Emphasis on clinical utility, value-based reimbursement

https://www.cms.gov/medicare-coverage-database/view/ncd.aspx?ncdid=372&ncdver=2&utm_source=chatgpt.com

SPROUT WORKING GROUP

SPROUT

Somatic Profiling for Pediatric Cancer,
Refining Our Understanding and Treatment

Key Findings from Existing Studies

Wide clinical utility shown for molecular profiling
Profiling approaches included DNA NGS, RNA NGS, WES, WTS, methylation profiling
Molecular profiling improves diagnostic yields, supports prognostic risk stratification and identifies opportunities for treatment with matched targeted therapies
RNA sequencing critical for fusion detection
Methylation profiling key for CNS tumors

Recommendations: at diagnosis [draft]

Target Population	Intervention	Recommendation Strength	Certainty of Evidence	Justification / Supporting Statement
Children, adolescents and young adults with newly diagnosed solid tumors	DNA-based next-generation sequencing (NGS) to assess sequence variants (point mutations and indels), copy number alterations, loss of heterozygosity, tumor mutational burden, and internal tandem duplications	Strong	Strong	Improves diagnostic precision, prognostic classification, risk-stratified therapy selection, and/or identifies targets for matched therapies.
Children, adolescents and young adults with solid tumors where fusions are common, diagnosis unclear, or no driver identified	RNA sequencing to detect fusions and internal tandem duplication (ITDs)	Strong	Strong	Fusions and ITDs are critical diagnostic and therapeutic biomarkers
Children, adolescents and young adults with central nervous system (CNS) tumors	DNA methylation-based tumor classification	Strong	Strong	Enhances diagnostic accuracy, prognostic classification and risk-stratified therapy selection

Recommendations: at relapse [draft]

Target Population	Intervention	Recommendation Strength	Certainty of Evidence	Justification / Supporting Statement
Children, adolescents and young adults with relapsed or refractory solid tumors	DNA-based next-generation sequencing (NGS) to assess sequence variants (point mutations and indels), copy number alterations, loss of heterozygosity, tumor mutational burden, and internal tandem duplications	Strong	Moderate	Comparison of molecular profile to the primary tumor can inform whether the patient has a true relapse or second malignancy. A subset will have newly identified alterations or signatures including tumor mutational burden associated with risk stratification, or matched targeted therapy.
Children, adolescents and young adults with solid tumors where fusions are common, original or relapsed diagnosis unclear, or no driver identified	RNA sequencing to detect fusions and internal tandem duplication (ITDs)	Moderate	Moderate	Comparison of molecular profile to the primary tumor can inform whether the patient has a true relapse or second malignancy. A subset of patients will present with novel fusions supported by high-level evidence – such as prospective clinical trials or tumor-agnostic FDA approvals – or by moderate evidence from case series indicating benefit from matched targeted therapy at recurrence.

REGULATION OF LABORATORY TESTS

- Local and national rules and regulations of clinical laboratory tests include:
  - State laws and regulations
  - Joint Commission
  - Clinical Laboratory Improvement Amendments (CLIA)
  - College of American Pathologists
  - [Food and Drug Administration]

Challenges and Opportunities

Challenges: Access, expertise, reimbursement variability

Opportunities: Clear guidance, education, policy advocacy

Importance of supporting our clinical colleagues and advocating for equitable universal adoption of molecular diagnostics and access to treatment for children with cancer

THANK YOU!

Elaine Mardis, Nationwide Children's Hospital
Jack Shern, National Cancer Institute
Jaclyn Biegel, Children's Hospital of Los Angeles
Marilyn Li, Children's Hospital of Philadelphia
Larissa Furtado, St. Jude Children's Hospital
Elli Papaemmaneouil, Memorial Sloan Kettering Cancer Center
Catherine Gestrich, University of Pittsburgh Medical Center
Maryam Fouladi, Nationwide Children's Hospital
Sarah Leary, Seattle Children's Hospital
Alberto Pappo, St. Jude Children's Hospital
Theodore Laetsch, Children's Hospital of Philadelphia
Andrew Kung, Memorial Sloan Kettering Cancer Center
Neal Shukla, Memorial Sloan Kettering Cancer Center
Erin Rudzinski, Indiana University
Adam Shlien, Hospital for Sick Children
David Malkin, Hospital for Sick Children
Katherine Janeway, Boston Children's / Dana-Farber Cancer Center
Jasper Shapiro, Boston Children's Hospital

PE-CGS

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