Improving Cancer Diagnosis and Care: Patient Access to Oncologic Imaging and Pathology Expertise and Technologies: A Workshop

Diagnostic Management Teams (DMT)
The Vanderbilt University Medical School Experience

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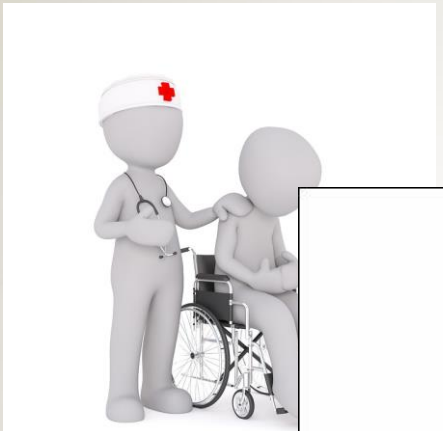
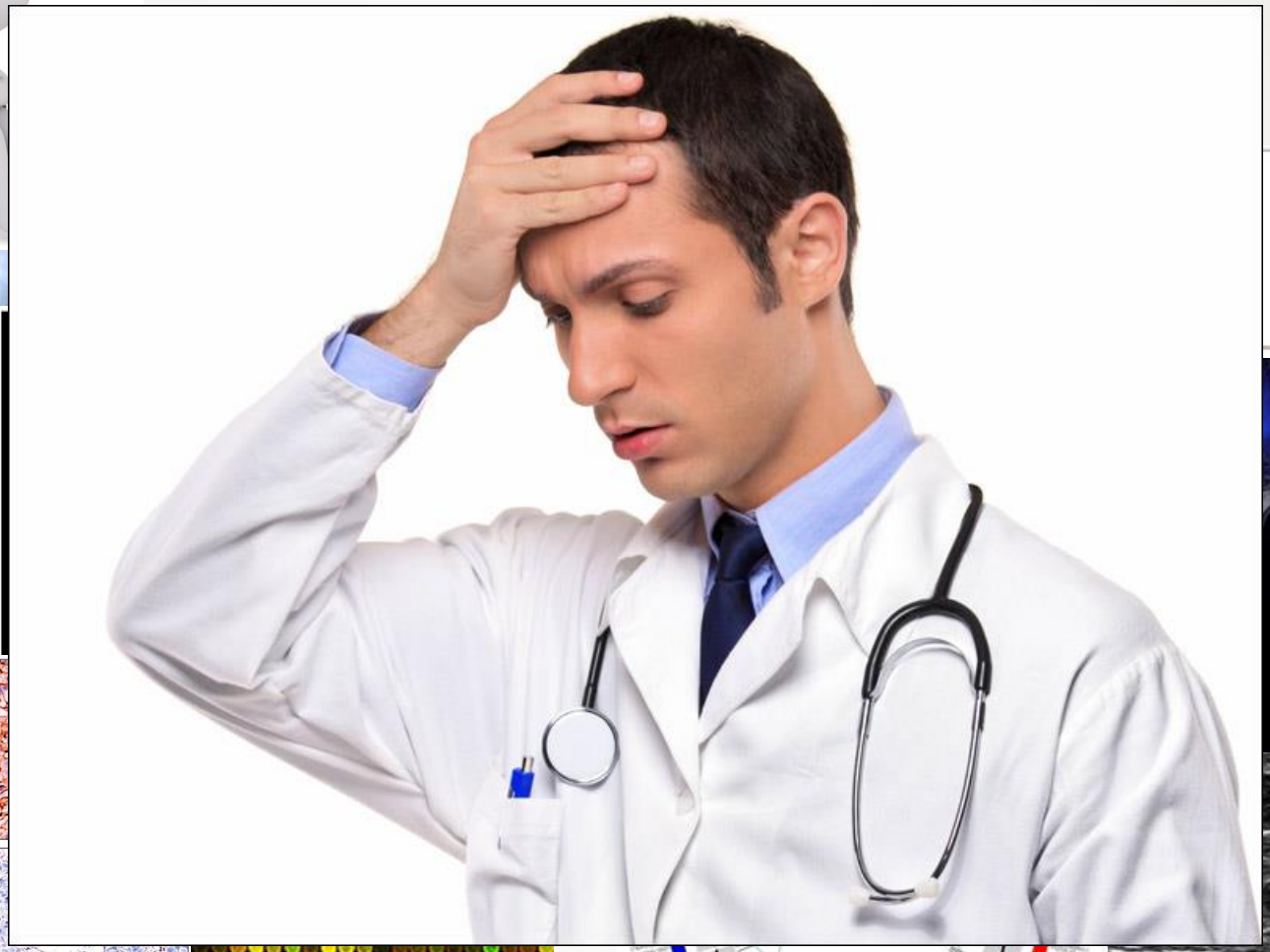
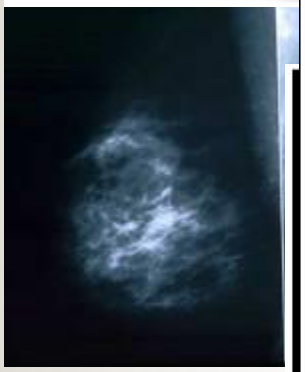
Cancer Diagnosis and Management

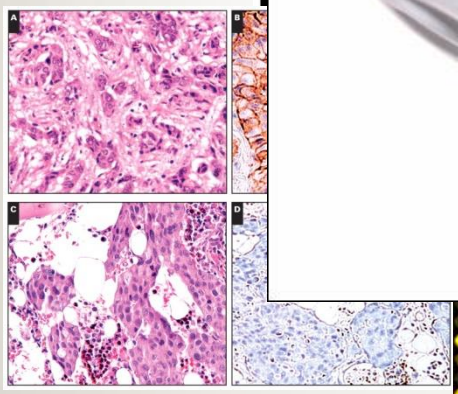
- Where we are today
- Vanderbilt “end-to-end” process engineering examples
  - Diagnostic Management Teams for cancer
- The future: Where we want to go
- Lessons and recommendations

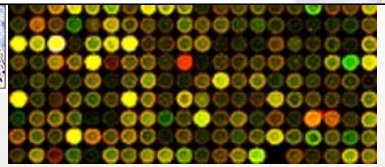
Different Views of Cancer

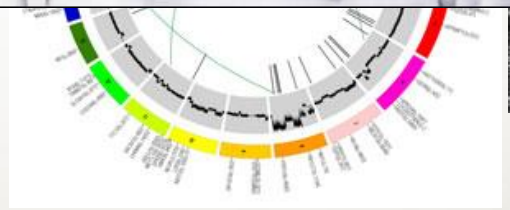


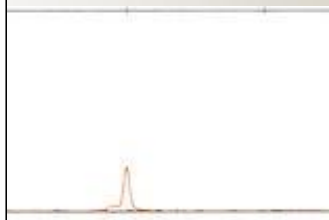


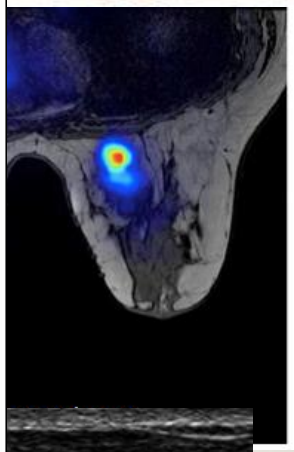


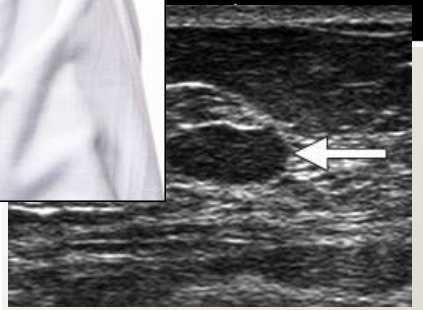












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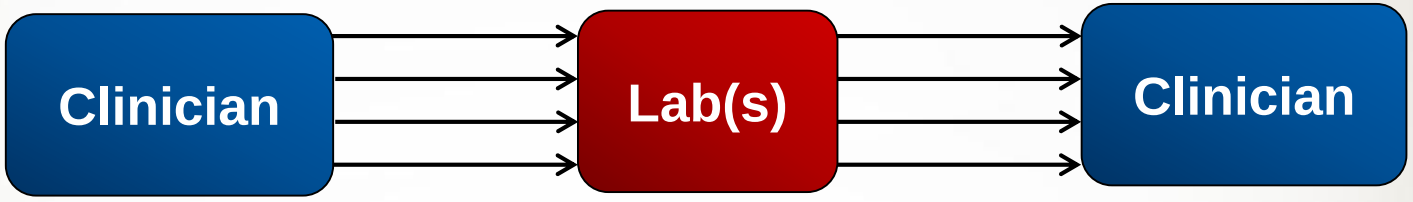
The Traditional Model of Pathology: Limitations for Modern Medicine

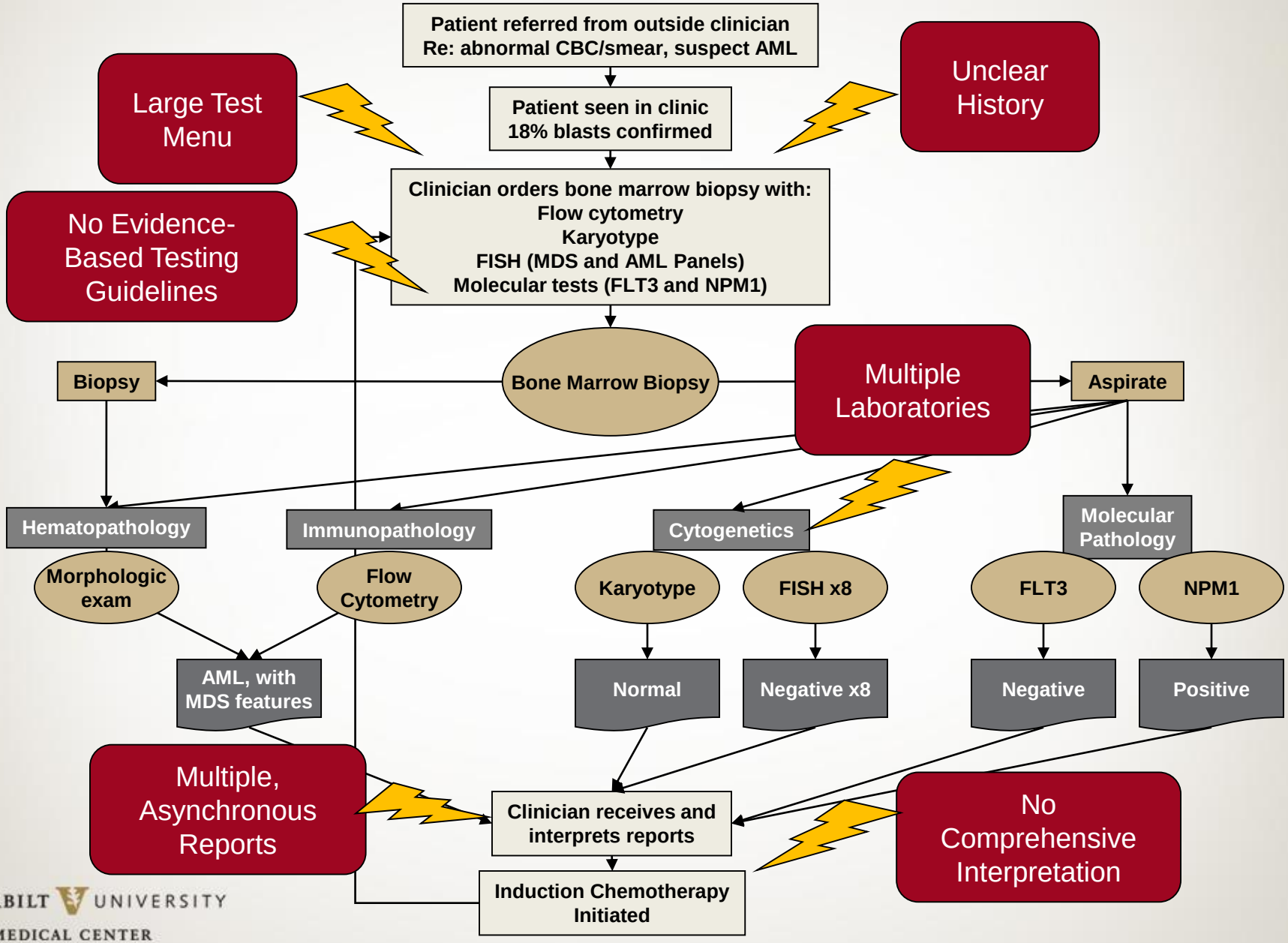


Clinician orders individual tests

Lab(s) perform ordered tests and return simple results

Clinician collates and interprets results alone

Diagnostic Complexity Example – Hemato-Malignancy



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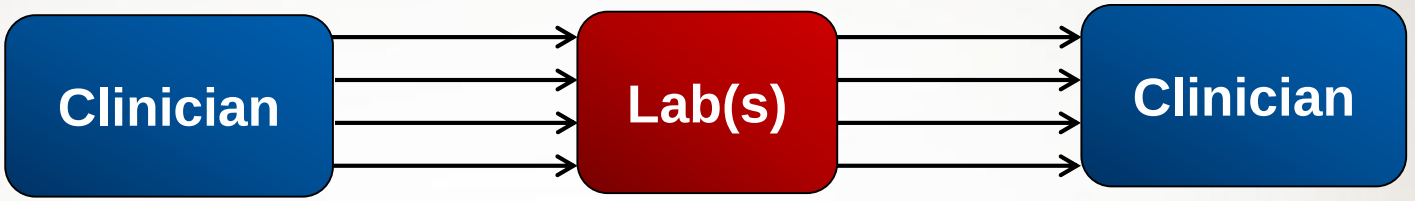

Clinician orders individual tests

Lab(s) perform ordered tests and return simple results

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Challenges	Consequences
• Large, complex, rapidly expanding test menus • Few if any evidence-based guidelines for test selection	• Unnecessary tests = increased costs
• Multiple laboratories • Multiple asynchronous reports	• Inefficient work-flow = wasted time
• Complex diagnostic outcomes.	• Difficult to correlate and interpret results

The Diagnostic Management Team (DMT)

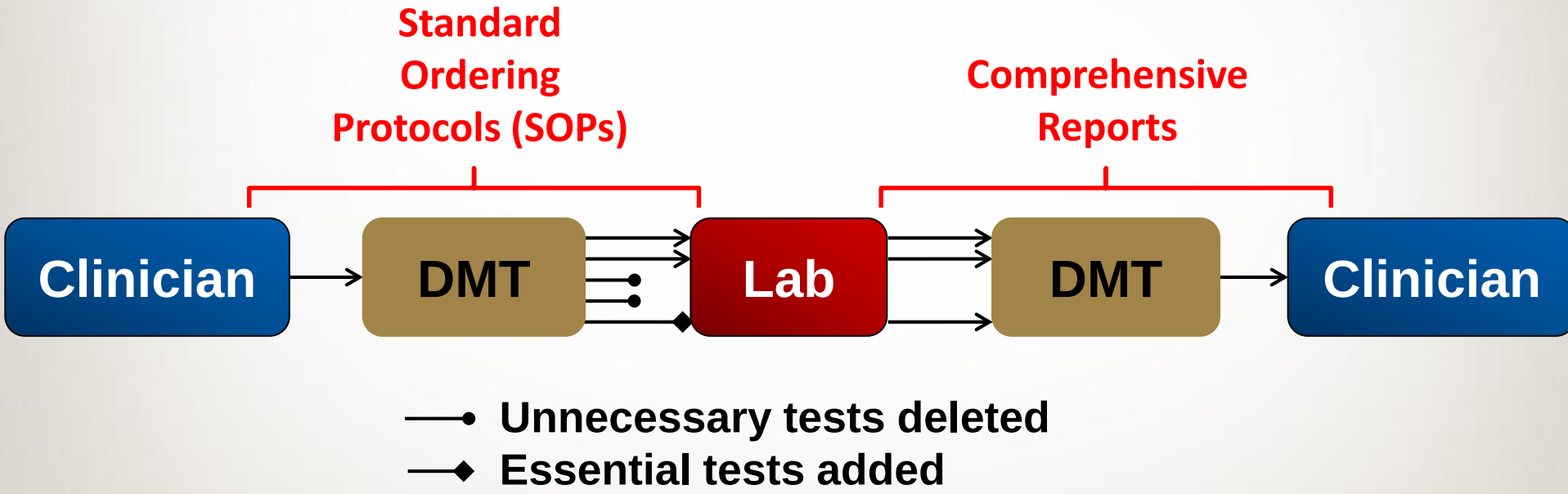
A collaborative effort amongst pathologists, clinicians, and biomedical informatics.

1. To develop the right pattern of diagnostic testing for the patient, using **standard test ordering algorithms.**

2. To create a single, evidence-based, **comprehensive report** of integrated diagnostic data to guide therapy and disease monitoring.

3. To iteratively improve the algorithms as evidence based practices evolve and change.

The Diagnostic Management Team (DMT)



Secondary Testing Standards: MDS/AML

Diagnosis or Morphologically Overt Disease	No Overt Disease (multiple encounters)	Pre-SCT	Post-SCT
Flow Cytomet			
Karyotype			
FISH			
Molecular			

**AML or MDS

**AML

SOPs Developed for:

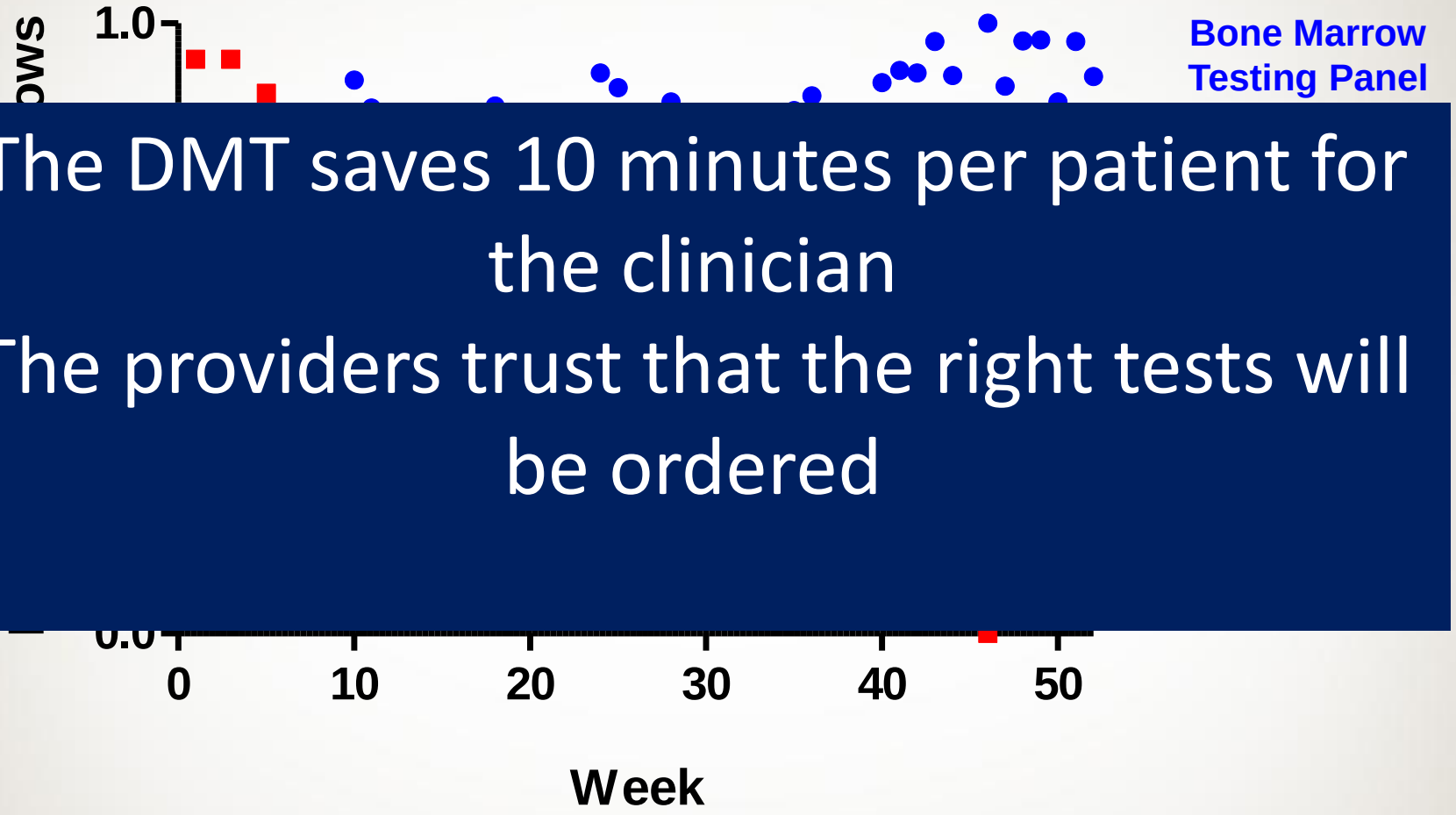
- Acute Myeloid Leukemia
- Myelodysplastic Syndrome
- Acute Lymphoblastic Leukemia
- Myeloproliferative Disorders, including CML
- B cell, Acute lymphoblastic leukemia
- T cell, Acute lymphoblastic leukemia
- Non-Hodgkin and Hodgkin Lymphoma
- Multiple Myeloma
- Bone Marrow Failure Syndrome

**AML includes MDS in evolution to AML

The hematologist retains the option to order tests "a la carte."

Comprehensive Diagnosis	Acute myeloid leukemia (47% blasts) with myelomonocytic differentiation, positive for NPM1 and FLT3-ITD mutations
Clinical History	73-year old male with new onset cytopenias and circulating blasts
Morphologic Diagnosis	Hypercellular marrow (80-90% cellularity) with decreased trilineage hematopoiesis; involved by acute myeloid leukemia (47% blasts) with myelomonocytic differentiation
Flow Cytometry	Increased myeloblasts Gating on blasts (47% of total cells) identified on CD45/side scatter histograms, immature cells have the following immunophenotype: CD2 (negative), CD4 (heterogeneous dim), CD7 (dim), D11b (partial moderate), CD13 (dim), CD14 (negative), CD15 (dim), CD16 (negative), CD19 (negative), CD33 (bright), CD34 (partial moderate), CD45 (dim), CD56 (partial dim), CD64 (moderate), CD117 (partial moderate), HLA-DR (bright), MPO (partial moderate)
Karyotype	Abnormal male karyotype 46,XY,del(9)(q13q22)[12]/46,XY[8]
FISH	Normal for the tested MDS and AML panels nuc ish 8q22(RUNX1T1x2),21q22(RUNX1x2)[200] nuc ish 15q22-24(PMLx2),17q21(RARAx2)[200] nuc ish 16q22(CBFBx2)[200] nuc ish 11q23(KMT2Ax2)[200] nuc ish 5q15.2(D5S23,D5S721x2),5q31(EGR1x2)[200] nuc ish 7cen(D7Z1x2),7q31(D7S486x2)[200] nuc ish 8cen(D8Z2x2)[200] nuc ish 20q12(D20S108x2)[200]
Molecular Studies	NPM1 mutation detected 0.73 FLT3-ITD mutation detected 0.12 CEBPA mutation not detected c-KIT mutation not detected

Hemato-malignancy DMT was accepted by users and “a la carte” ordering fell significantly



The DMT saves 10 minutes per patient for the clinician

The providers trust that the right tests will be ordered

Fractional weekly utilization of the bone marrow testing panel vs. a la carte ordering after DMT implementation.

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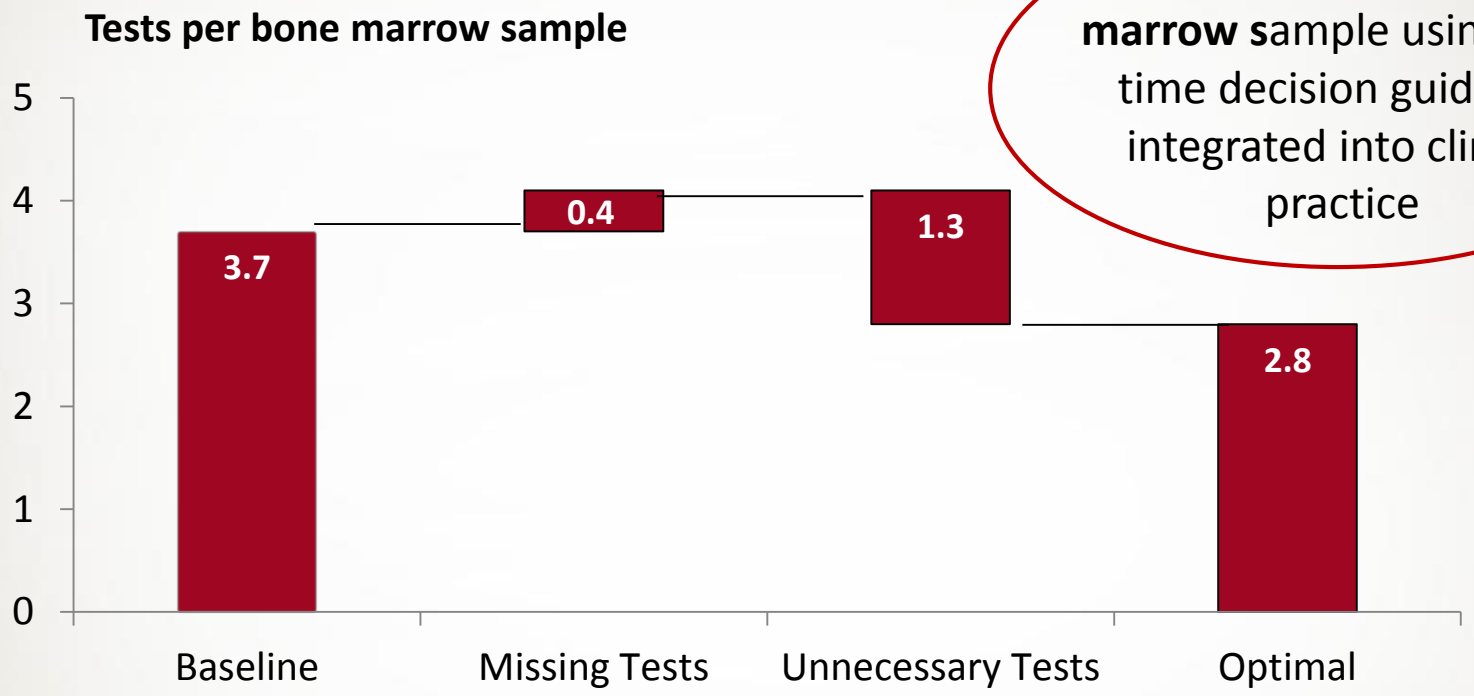
Seegmiller AC, Kim AS, Mosse CA, et al. Optimizing personalized bone marrow testing using an evidence-based, interdisciplinary team approach. Am J Clin Pathol 2013;140:643-650.

A retrospective analysis predicted that DMT guidance of laboratory testing improves concordance and reduces testing

Saves ~1 test per bone marrow sample using real-time decision guidance integrated into clinical practice



140,000 Americans will be newly diagnosed with **leukemia, lymphoma or myeloma** this year, while 1,000,000 are in remission/actively treated

Scaling nationally, this represents **a $0.5B/year savings opportunity**

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Seegmiller AC, Kim AS, Mosse CA, et al. Optimizing personalized bone marrow testing using an evidence-based, interdisciplinary team approach. Am J Clin Pathol 2013;140:643-650.

Using the DMT to guide testing continues to improve test concordance and reduces testing year after year

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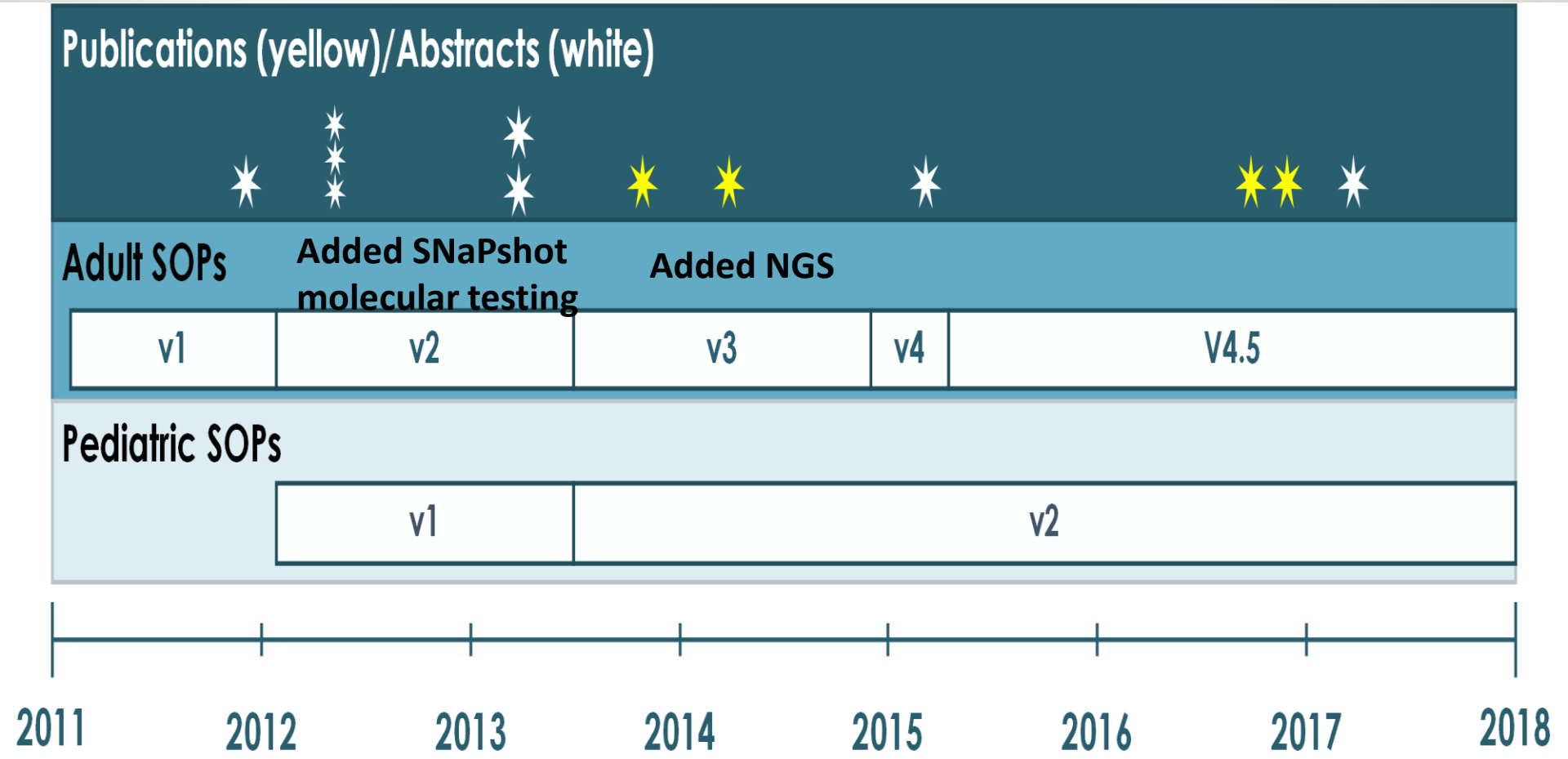
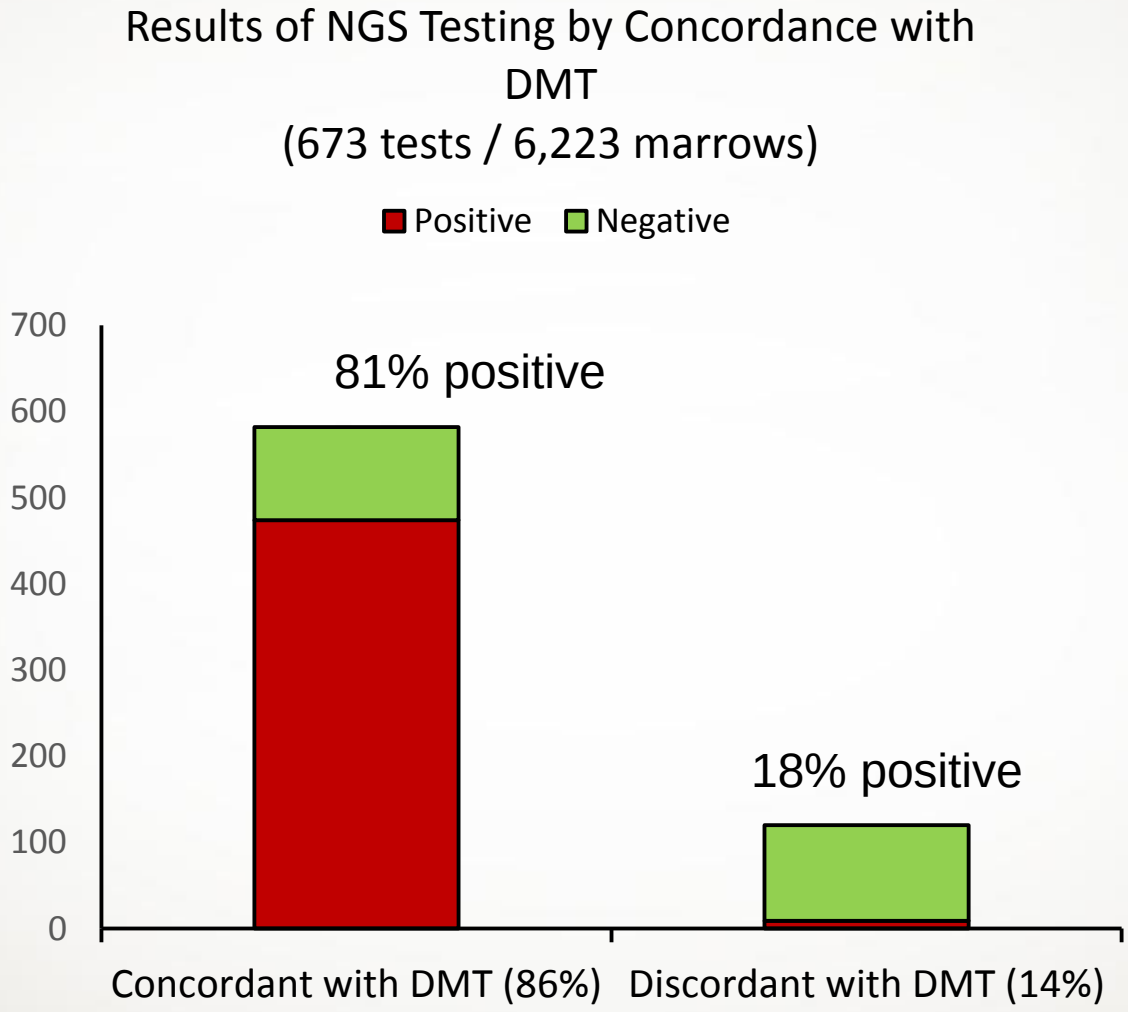
Seegmiller AC, Kim AS, Mosse CA, et al., Data-driven iterative refinement of bone marrow testing protocols leads to progressive improvement in cytogenetic and molecular test utilization. Am J Clin Pathol 2016;146:585-593.

Evolution of the SOPs:
An Example of a Learning Health Care System



Mutation testing for 36 genes by NGS was incorporated into the DMT algorithms in 2014:

Only cases with suspected myeloid malignancies



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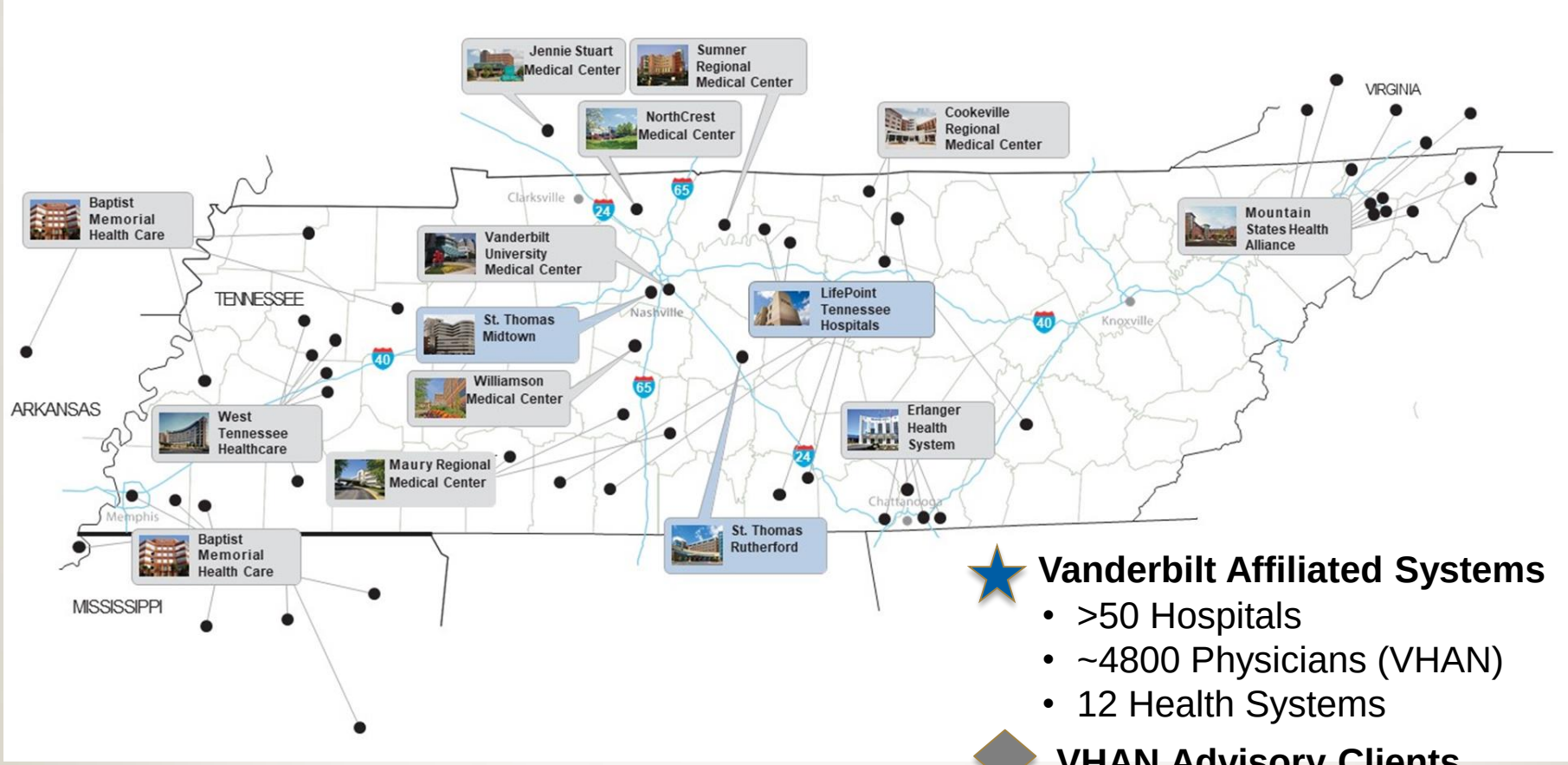
Seegmiller AC (Unpublished results)

Ongoing Work:

- Scale to Vanderbilt Health Affiliated Network Partners

  First partner: Jackson Madison Hospital in Jackson, TN

  Implemented Hematopathology DMT in 2014



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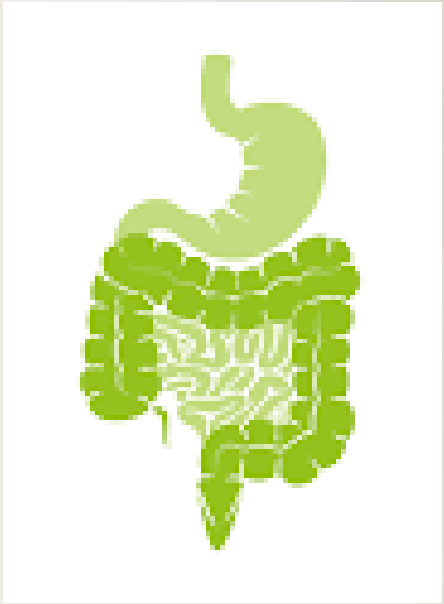
Next Steps and Challenges:



- Develop similar processes
  - Currently developing: GI
  - On deck: lung and breast
- Challenges of solid tumors
  - Imaging is critical
  - Metastatic and non-metastatic disease
  - Multiple time points of entry into system
  - Multiple different tumor sites with different characteristics:
    - **Colorectal, Stomach, Small intestine, Pancreas, Liver**
  - Multiple providers involved:
    - **Gastroenterologists, Surgeons, Radiologists, Oncologists,**
  - Multiple different sample types:
    - **Biopsies of primary or metastatic lesions, Full or partial resections,**

In Summary

- Introduction
  - Discussed traditional pathology practice.
  - Developed the use case for innovation in practice.

- Description of the Hematopathology Diagnostic Management Team (DMT)
  - Defined the requirements for a DMT
  - Highlighted the team approach
  - Reviewed a “learning health care” system approach

- Presented on-going work and next steps

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