LOWERING COSTS THROUGH
Effective Hematologic Malignancy Diagnosis

DECEMBER 2014

Economic Burden of Inaccurate or Incomplete Hematologic Malignancy Diagnoses

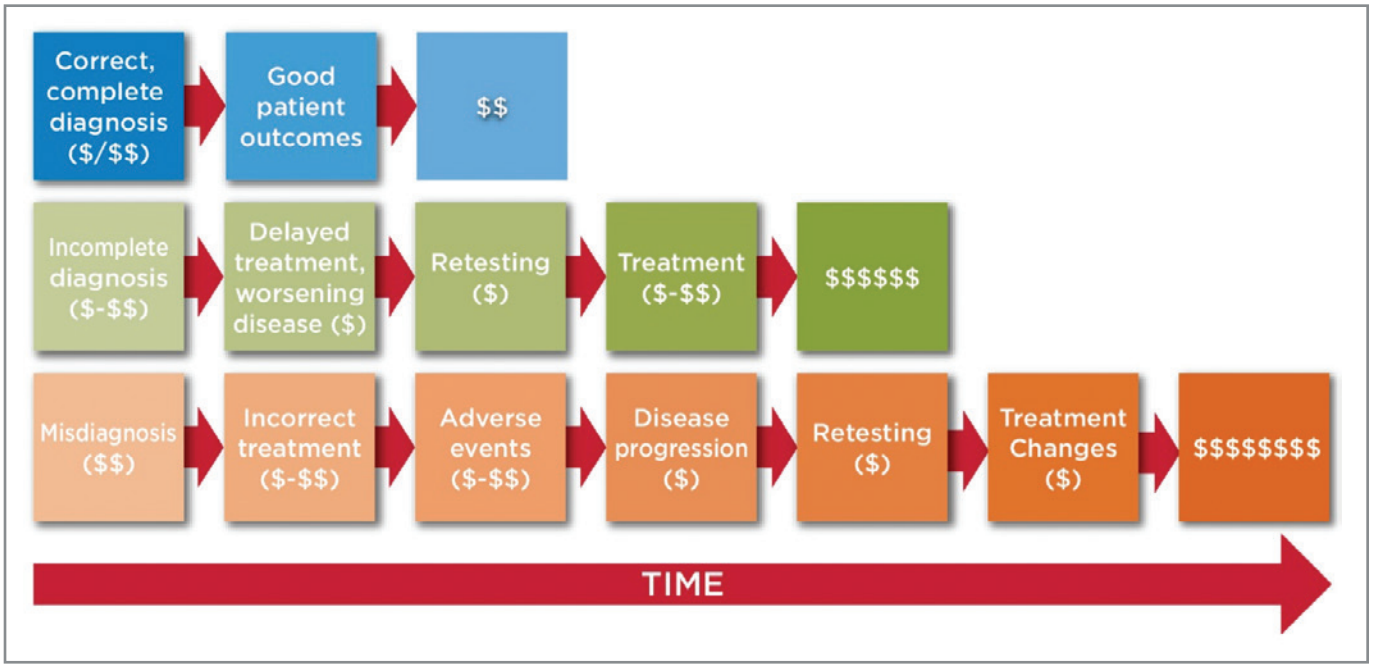
Optimal management of hematologic malignancies requires an early, accurate, complete, and clear diagnosis. Hematologic malignancies, however, are frequently misdiagnosed. Studies have demonstrated misdiagnosis in up to 27% of leukemia,[1] 18% of lymphoma,[2] and 75% of Burkitt lymphoma[2] cases. Often, there may not be enough information from an initial biopsy evaluation to generate a complete diagnosis.[3] A secondary review, further testing, and even additional biopsies may be required to establish a final diagnosis,[2-4] which could be delayed for >6 months.[5] Additionally, reports returned to the treating physician may not be integrated and/or correlated in a clear format that informs the treatment decision.

Incomplete diagnosis or misdiagnosis of hematologic malignancies may lead to suboptimal treatment and poor patient outcomes. In one study, 9.3% of lymphoid diagnosis reports provided insufficient information to initiate treatment.[6] In addition to delayed treatment, inappropriate treatment is a concern; in 5% to 11% of lymphoma patients, misdiagnosis led to incorrect treatment,[3,4] which could be needlessly toxic for the patients and costly to providers.[7] A misdiagnosis also causes patient anxiety,[8] associated with a reduced health-related quality of life.[9] Ultimately, diagnostic challenges can lead to disease progression because physicians may miss the optimal treatment window.[10]

Incomplete diagnosis may *necessitate* additional testing and delay the final diagnosis for more than 6 months.

The negative patient outcomes caused by incomplete diagnosis or misdiagnosis increase the economic burden of disease management (**Figure 1**). For example, the expense of a repeat bone marrow biopsy (BMB) and aspiration procedure is estimated to be $1722.[11] Inappropriate assignment to

Figure 1. Incorrect or Incomplete Diagnosis Increases Economic Burden



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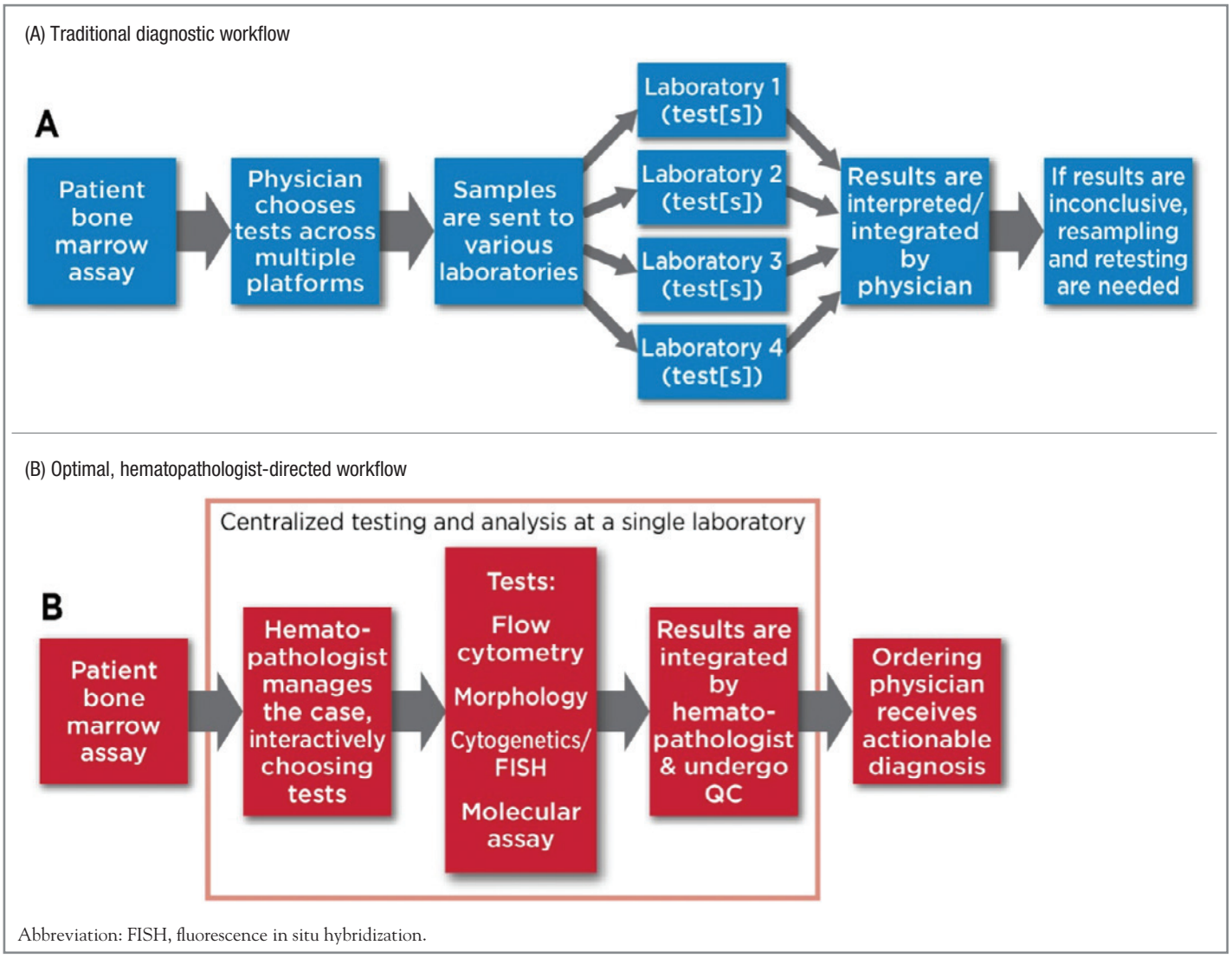
chemotherapy or changes to chemotherapy regimen are not only costly but can also increase the chances of side effects such as neutropenia, which often leads to hospitalization costing an average of $20,400 per stay.[12] Furthermore, progression of disease has an economic burden; progression of follicular non-Hodgkin lymphoma to more aggressive disease costs $2667 per patient per month (PPPM).[13]

Workflows for Diagnosing Hematologic Malignancies

In the traditional workflow for diagnosing hematologic malignancies, the onus of choosing tests falls to the clinician, as does identifying laboratories to perform the appropriate assays and integrating and interpreting data from reports across various laboratories.[14,15] Therefore, the patient's diagnosis is solely based on the ordering physician's familiarity/expertise with different diagnostic techniques and with interpretation of the resulting data, and clinicians may have difficulty maintaining up-to-date training on diagnostic technologies.[16] Issues associated with the traditional diagnostic process could be mitigated by an integrated and centralized workflow managed from initial diagnostic testing onward by a highly trained hematopathologist (**Figure 2**). In this method, final reports also undergo extensive quality control (QC) for consistency, continuity, and clarity; this results in more accurate actionable diagnoses.

Genoptix is a hematopathology specialty laboratory with a workflow tailored to oncology case management. Each case is

Figure 2. Workflow for Diagnosing Hematologic Malignancies



Abbreviation: FISH, fluorescence in situ hybridization.

Figure 3. Number of Days to Reach a Final Diagnosis

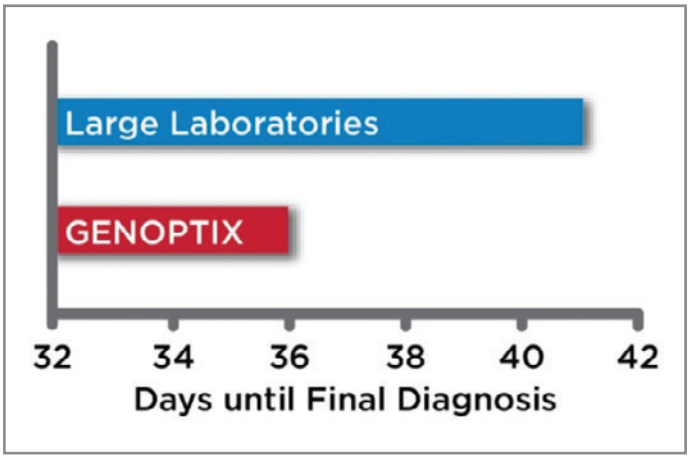


Figure 4. Diagnoses per Patient Over Time

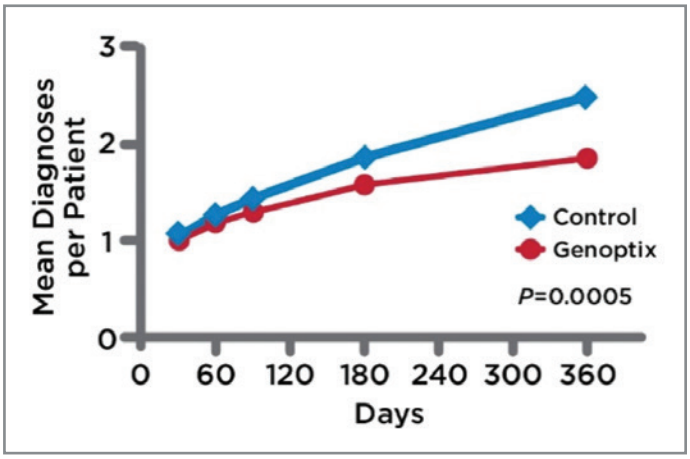
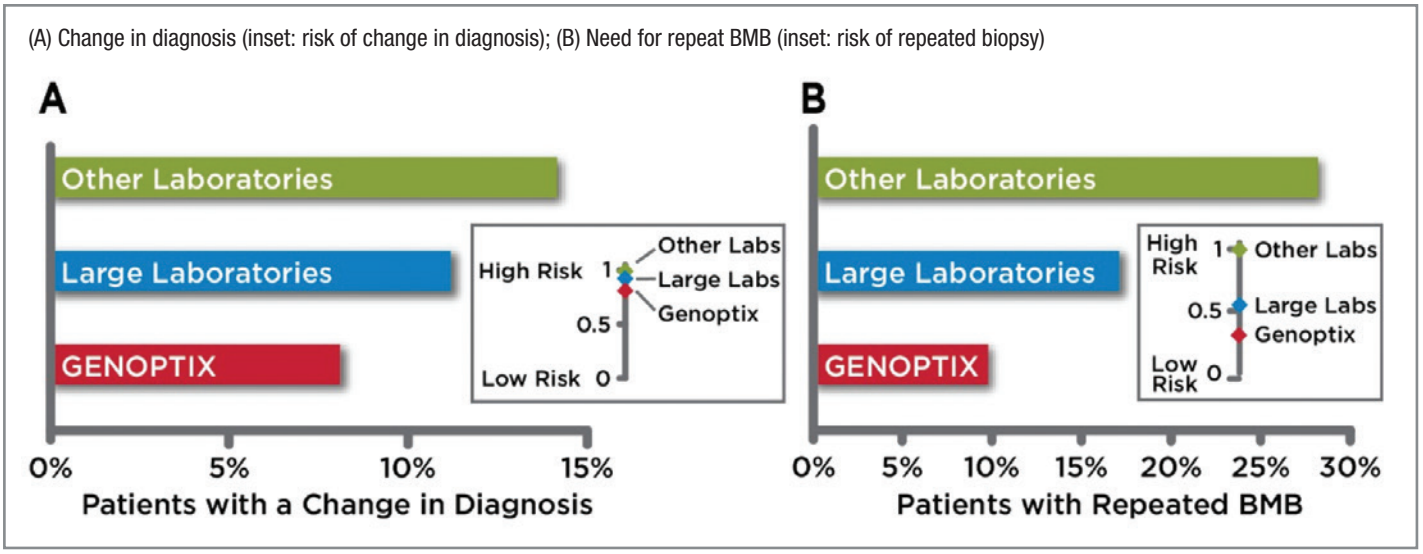


Figure 5. Stability of Diagnosis



supervised by a hematopathologist who chooses medically necessary tests, interprets the results, and integrates information into a comprehensive assessment. This optimized workflow provides an early, accurate, and clear diagnosis that leads to improved patient outcomes and reduced downstream costs compared with traditional diagnostic testing according to retrospective claims and electronic medical record (EMR) studies.[14,15,18] Initial diagnoses involve more complex diagnostic testing at Genoptix than at comparator laboratories. On average, a final diagnosis is established 5 days earlier at Genoptix than at other community laboratories (marginal difference, P=0.051; **Figure 3**).

In further support of a faster, more accurate diagnosis, significantly (P<0.001) fewer diagnoses per person were observed

Figure 6. Stability of Chemotherapy Regimens

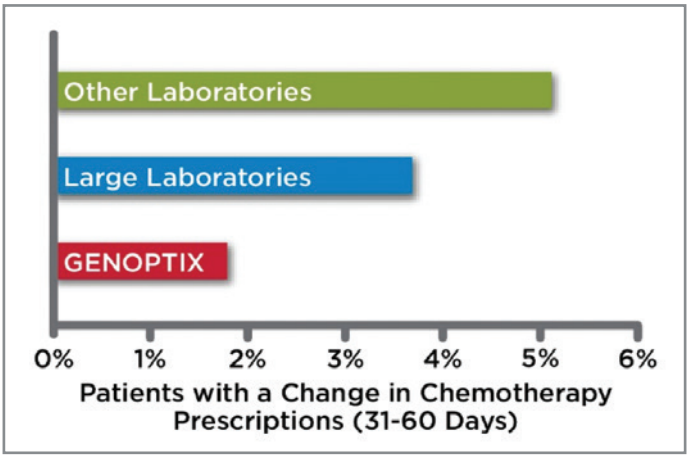
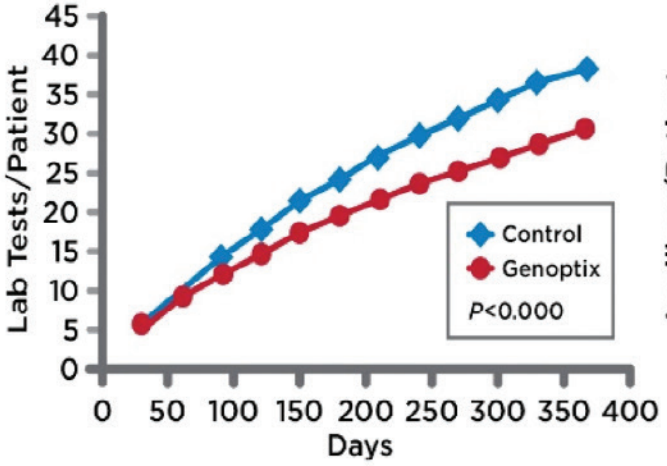


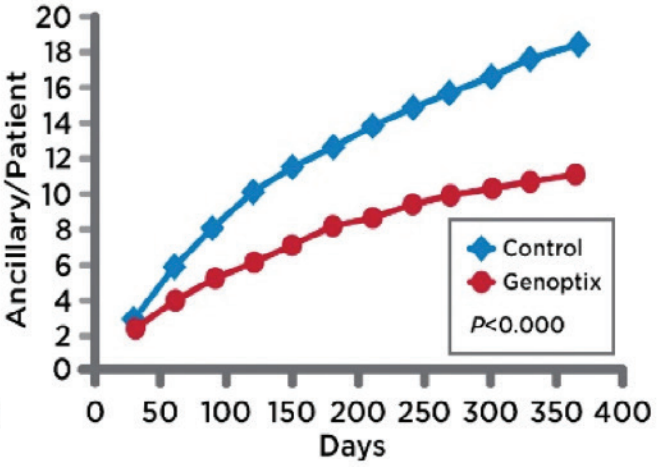
Figure 7. Resource Utilization per Patient per Month

Laboratory Tests



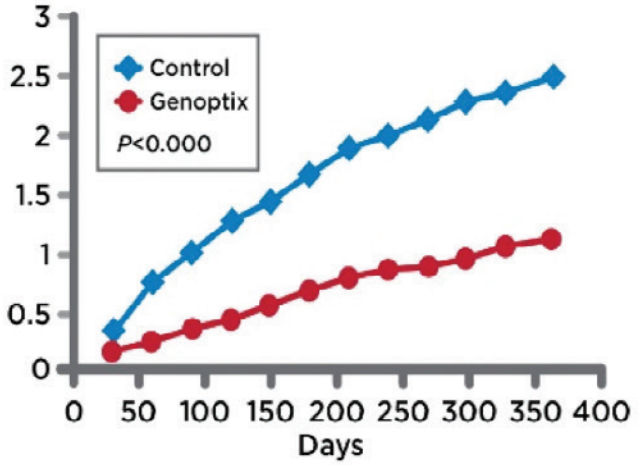
Days	0-30		0-365	
Cohorts	Test	Control	Test	Control
Mean values	5.6	5.6	30.4	38.9
P value	0.678		0.041	

Ancillary Procedures



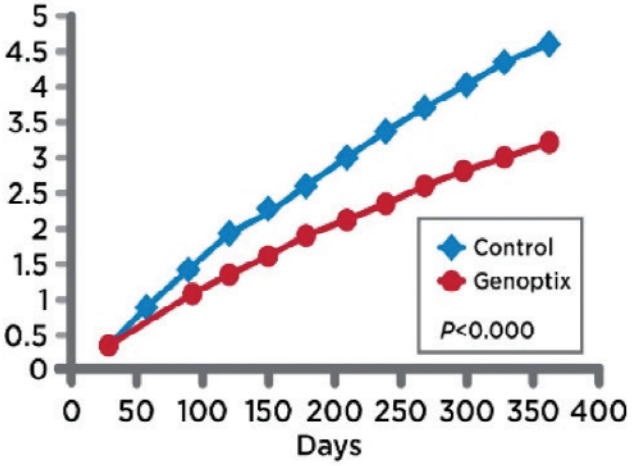
Days	0-30		0-365	
Cohorts	Test	Control	Test	Control
Mean values	2.2	2.9	11.2	18.6
P value	0.633		0.005	

Support Therapeutics



Days	0-30		0-365	
Cohorts	Test	Control	Test	Control
Mean values	0.1	0.3	1.1	2.5
P value	0.123		0.029	

ESAs*



Days	0-30		0-365	
Cohorts	Test	Control	Test	Control
Median values	0.3	0.3	3.3	4.6
P value	0.744		0.029	

*Erythropoiesis-Stimulating Agents

over a year with Genoptix analysis (**Figure 4**) versus traditional diagnostic testing methods in EMR data.[18] Further, Genoptix testing was associated with decreased risk of diagnosis change [odds ratio, 0.824 (95% confidence interval [CI]: 0.722-0.940); *P*=0.0040] and a reduced risk of costly and invasive repeated BMB [odds ratio, 0.307 (95% CI: 0.255-0.371); *P*<0.0001] compared with testing in other community laboratories[15] (**Figures 5A** and **5B**). Thus, Genoptix testing resulted in a fast, accurate diagnosis with a decreased need for follow-up testing compared with traditional workflows.[15]

Compared with other workflows, the Genoptix workflow resulted in a fast and accurate diagnosis with a reduced need for follow-up.

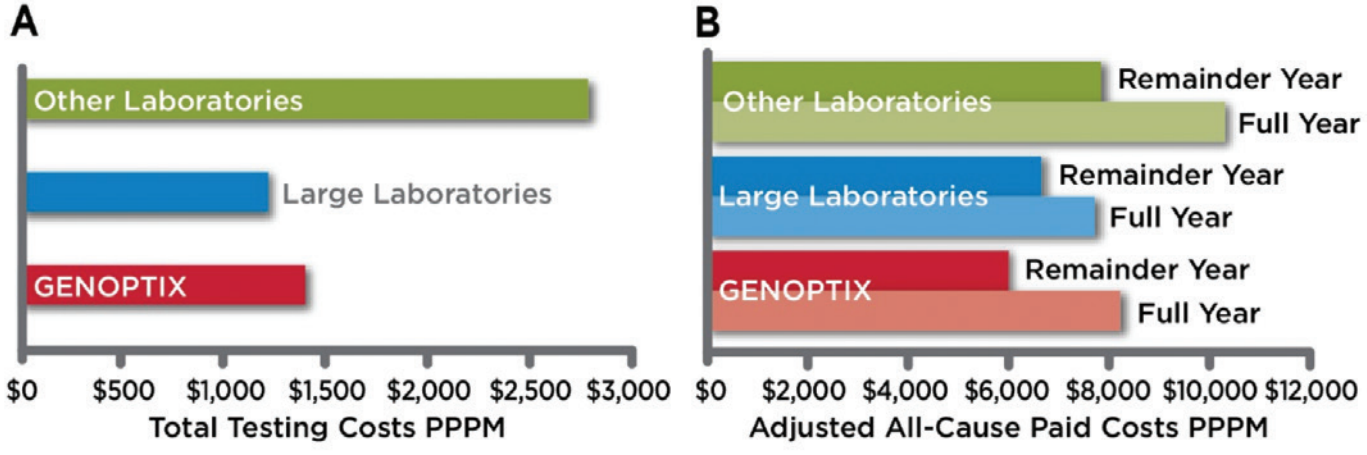
The Genoptix workflow also demonstrated promising results versus comparator laboratory strategies for transfusion dependence and change in treatment, which suggest a delay of disease progression. When diagnostic testing was performed by Genoptix, time to first transfusion was significantly later (*P*=0.009).[14,18] Additionally, change in chemotherapy prescriptions in the second month after treatment initiation was twice as likely when testing was performed at large laboratories versus at Genoptix and almost 3 times as likely with testing at community laboratories versus at Genoptix[15] (**Figure 6**). Consistent with improvement in patient outcomes, an analysis of EMR data highlighted the percentage of patients requiring hospital admission was lower among those undergoing Genoptix testing (8.9%) than among those undergoing traditional testing (9.9%); however, the difference was not significant (*P*=0.558).[18] These data suggest that diagnoses from the Genoptix workflow may enable improved intervention resulting in reduced disease progression.

An improved diagnosis with the Genoptix workflow saves valuable healthcare resources. Although short-term healthcare utilization (0-30 days) was not significantly different between laboratories, significantly (*P*<0.05) fewer office-based laboratory tests, ancillary procedures, support therapeutics, and erythropoiesis-stimulating agents (ESAs) were necessary over a year with Genoptix testing than with traditional laboratory analysis[14,18] (**Figure 7**).

These differences in healthcare utilization may translate into cost savings. Genoptix and large laboratories had similar total paid testing costs for the 1-year follow-up period (**Figure 8A**; $195 PPPM difference). However, adjusted all-cause paid costs for 1 year excluding the first 30 days were reduced with Genoptix compared with large laboratories (**Figure 8B**; $630 PPPM savings).[15] Additionally, compared with other community laboratories, Genoptix was associated with substantial total paid testing cost savings for the 1-year follow-up period ($1383 PPPM savings) and lower adjusted all-cause paid costs for 1 year excluding the first 30 days ($1782 PPPM savings)[15] (**Figures 8A and 8B**). For the full-year follow-up period, compared with services at large laboratories, Genoptix testing led to cost

Figure 8. Healthcare Costs Over Time

(A) Total testing costs in the 1-year follow-up period; (B) All-cause paid costs adjusted for patient characteristics across the full year or the remainder of the year, excluding the first 30 days



savings for BMB ($587 PPPM savings), cancer-related tests other than bone marrow testing ($90 PPPM savings), and hematologic tests other than bone marrow testing ($13 PPPM savings).[15] These analyses suggests that although Genoptix performs more diagnostic testing up front (i.e., in the initial 30-day period), significant cost savings are often discernable in the longer episode of care.

An improved diagnosis obtained from the Genoptix workflow saves valuable healthcare resources, which translates into cost savings.

Conclusions and Getting Started with Genoptix

In summary, the greater effectiveness of the Genoptix workflow compared with traditional testing workflows leads to more accurate diagnosis of hematologic malignancies. This benefit provides improved cost containment by eliminating unnecessary testing, treatment changes, and use of other healthcare resources during the episode of care. For additional information or to learn more about Genoptix, please visit our website at http://www.genoptix.com/.

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