Reportable Actionability Versus Pragmatic Actionability: Implementing Precision Medicine at Three Large Health Systems

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BACKGROUND

Precision medicine (PM) molecular panel (MP) testing labs report actionable findings with associated targeted therapies (including immunotherapies). However, the "reported actionability", or associated treatment recommendations provided by MP testing labs, are often not realized as "pragmatic actionability", or delivering these recommended treatments in the real world setting. The Syapse platform was leveraged to explore the concordance among PM MP therapy recommendations and subsequent drug treatment orders by clinicians at Aurora Health Care (AHC), Henry Ford Health System (HFHS), and Hoag Memorial Hospital Presbyterian (HMHP).

METHODS

Structured de-identified clinical history, pathology, radiology, and treatments were obtained from the Syapse platform, sourced from health system databases. Subsequent treatment order was defined as the medication order placed at any time after MP testing. MP refers to somatic NGS-based testing performed at a CLIA-certified commercial lab where the test report contains annotations including treatment recommendations. Syapse integrates structured MP test results via a direct real-time feed with MP labs along with associated therapy and clinical trial recommendations. MP test results are normalized into a standard ontology, or data model, allowing for comparisons across multiple health systems and multiple labs.

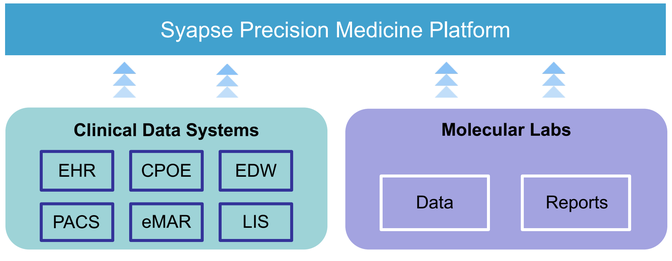

Figure 1. The Syapse platform aggregates patient clinical data and receives structured molecular data through direct integration with MP testing labs.

METHODS (cont.)

At AHC, HFHS, and HMHP, we identified 996 patients who received MP testing between 2014 and 2018.

Health system	# of patients with med order after MP testing	# of patients with MP testing	% of patients who received med order after MP testing
Aurora	398	420	95%
Henry Ford	43	50	86%
Hoag	307	458	67%
Total	748	996	75%

Table 1. Syapse database query identified 748 patients who received MP testing and had a medication order placed after testing.

RESULTS

713 MP reports had "reported actionable" (positive) treatment recommendations and a subsequent treatment order across all 3 health systems.

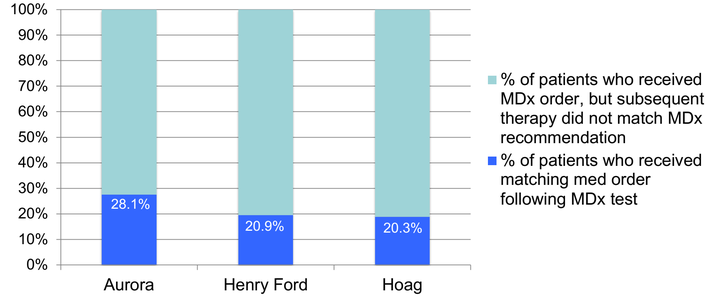

Figure 2. Concordance between treatment orders and MP therapy recommendations was relatively consistent across all 3 health systems.

RESULTS (cont.)

24.4% (174/713) of MP reports were followed by a treatment order that matched to at least one reported actionable treatment. The translation from a MP-reported actionable finding to a prescribed treatment order was 28.1% (105/374) at AHC, 20.9% (9/43) at HFHS, and 20.3% (60/296) at HMHP, which has borderline statistical significance (p=0.0563) for differences between sites. Of the 713 MP reports analyzed, there was an average of 7.8 therapy recommendations per MP report. When limiting the analysis to patients who received a targeted therapy recommendation, the number of recommendations per report dropped to 3.4, and only 14% of patients with a positive targeted therapy recommendation had a matching treatment order. The match rate of individual therapy recommendations to ordered therapies was consistent between targeted therapies (4%) and chemotherapies (5%). There were no significant rate differences in actionability between the two molecular testing vendors examined.

Health system	# of MP reports with positive actionability	# of MP reports with treatment order matching therapy recommendation	% of MP reports with matching treatment order
Aurora	374	105	28.1%
Henry Ford	43	9	20.9%
Hoag	296	60	20.3%

Table 2. MP reports were followed by a lab-recommended therapy in 24.4% of cases across these three health systems, on average.

CONCLUSIONS

The translation of reported actionability to pragmatic actionability was consistent across all 3 health systems. Of all 996 MP reports in the initial sample, only 17.5% resulted in a treatment order which matched a MP report recommendation. This may reflect different definitions of "actionable" between molecular testing companies and clinicians as well as patient performance status changes over time, insurance coverage for off-label use, or referral to a clinical trial. These findings support the need for independent clinical decision support that takes into account the full patient care journey. Both molecular findings and comprehensive clinical information are critical factors in determining optimal treatment. Further research is warranted to understand the issues involved.