Adapting Clinical Systems to Enable Adolescents' Genomic Choices

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Abstract

Background—We offered adolescents personalized choices about the type of genetic results they wanted to learn during a research study and created a workflow to filter and transfer the results to the electronic health record (EHR).

Methods—We describe adaptations needed to ensure that adolescents' results documented in the EHR and returned to adolescent/parent dyads matched their choices. A web application enabled manual modification of the underlying laboratory report data based on adolescents' choices. The final PDF format of the laboratory reports was not viewable through the EHR patient portal, so an EHR form was created to support the manual entry of discrete results that could be viewed in the portal.

Results—Enabling adolescents' choices about genetic results was a labor-intensive process. More than 350 hours was required for development of the application and EHR form, as well as over 50 hours of a study professional's time to enter choices into the application and EHR. Adolescents and their parents who learned genetic results through the patient portal indicated that

they were satisfied with the method of return and would make their choices again if given the option.

Conclusion—Although future EHR upgrades are expected to enable patient portal access to PDFs, additional improvements are needed to allow the results to be partitioned and filtered based on patient preferences. Furthermore, separating these results into more discrete components will allow them to be stored separately in the EHR, supporting the use of these data in clinical decision support or artificial intelligence applications.

Keywords

clinical information systems; implementation and deployment; general aspects; facilitators and barriers; electronic health records and systems; patient records; specific types

Background and Significance

In pediatric clinical settings, when diagnostic genome sequencing is ordered,[1,2] parents typically have the choice to opt in or opt out of learning about their children's secondary results for genes recommended by the American College of Medical Genetics for opportunistic analysis.[3,4] This raises two concerns: (1) the child may not have been engaged in an active assent conversation about learning results that convey the child's risk for diseases[5] and (2) the additional results that may become useful in the child's future are embedded in a diagnostic report rarely searchable by discrete gene or risk condition.[6]

Phase III of the Electronic Medical Records and Genomics Network (eMERGE III) required that each participating member conduct a site-specific genomic implementation project using a gene panel of 109 genes and 1,551 single nucleotide variants to support network-wide discovery.[7] Cincinnati Children's Hospital Medical Center (CCHMC's) project sought to engage adolescents in a multistep decision-making process about the type of genomic results that they wanted to learn about themselves.[8–10] The implementation focused on a subset of the eMERGE III panel, with institutional review board (IRB) approval to return adolescents' genomic results for up to 84 clinically actionable and returnable genes that informed risk for 55 conditions, including adult-onset conditions. The adolescent decision-making process gave them private time to make independent choices followed by a facilitated joint decision-making process with the parent. Adolescent/parent dyads then had 2 weeks following the study visit to change their joint choices. While our multistep process provided considerably more engagement than in current clinical situations, it did result in our having to return customized results based on those individualized choices.[8,9] The purpose of this paper is to describe the required informatics solutions to ensure that only the results desired by the dyads were returned, that they were easily findable and searchable within the EHR and also accessible via the EHR patient portal.

Methods

Harvard's Broad Institute and the Laboratory of Molecular Medicine (LMM) was CCHMC's assigned eMERGE III sequencing center and CLIA approved, CAP-certified laboratory, respectively. Results were provided in XML format, which included both an

embedded PDF document of the report as well as the raw report text and underlying variant data. Two hurdles prevented the native LMM reports from being directly returned to the participant. The first was that LMM's infrastructure was set up to report results for all of the IRB-approved genes, regardless of participants' choices. Second, PDF-based results could not be viewed through MyChart.

CCHMC's Division of Biomedical Informatics (BMI) was asked to create an application in which adolescents' choices would be entered into a web interface, and when LMM results were ready, the application would use those choices to extract the relevant elements of the XML laboratory report, which would then be transferred to the EHR (Epic) in a format viewable via the patient portal (MyChart). Unfortunately, this idealized workflow could not be achieved. Complexities in the structure of the XML laboratory report limited the ability to easily identify and filter the adolescents' choices, resulting in a need to review and further customize the report before it could be transferred to Epic. In addition, the study timeline and budget did not permit the development of a direct interface between the application and the EHR. The final solution required more manual intervention as described below.

The application developed by BMI fulfilled several aspects of the proposed workflow. First, screens were created that replicated the content and structure of the decision tools, allowing for documentation of participants' choices (Fig. 1). Second, LMM's secure file transfer site could be queried for newly published laboratory reports, which were then downloaded as they became available. Third, it supported actions that allowed the XML-based data to be manually parsed and modified based on participants' choices. For example, the methods section of the LMM report listed all analyzed IRB-approved genes, necessitating deletion of genes associated with conditions about which the dyads did not want to learn, even if all results were negative. The final stock LMM report (if a participant wished to learn about all results) or the modified version (taking into account specific preferences) were then available for download so the information could be transferred to Epic. The connections between systems are shown in Fig. 2. The application was developed in Java, utilizing Java enterprise edition-related technologies/standards, and runs on JBoss Enterprise Application Platform.

The application produced a PDF file that served as the "official" result, which was scanned into the EHR's Media tab by Health Information Management staff. This content was not accessible via MyChart, so an Epic form was created that listed all of the conditions associated with the 84 genes potentially reportable by LMM (rows could be deleted for the conditions about which the participant did not want to learn). A drop down menu of nine result options was available for each condition, reflecting the potential values reported by LMM. A comment field was available for each condition to list specific variant(s) if the result was anything but negative. A narrative section was used to address the meaning, clinical implications, and limitations of negative and positive results and changing knowledge of genetics. After the completed Epic form was submitted, it was immediately viewable in the providers' results review tab and in the patient's MyChart.

While participants could set up their MyChart accounts to send automatic alerts when new content became available, the participants' providers had no reason to actively look for

results not generated during the course of clinical care. The first author therefore sent a standard message to CCHMC providers who provided routine or specialty clinical care to the participant within 1 year prior to the returned result. The standard message alerted providers about their patient's participation in the eMERGE III study, their patient's overall study result (negative/positive), how the result was returned, and where providers could find the report. Participants' primary care providers outside of CCHMC were mailed the original LMM or modified report with a cover letter describing their patient's participation in the study.

Results

Enabling adolescents' choices was labor intensive. Application development and testing took approximately 350 hours. Development time for the Epic form is unknown as the developers are no longer at CCHMC. A single study investigator with clinical genetics expertise entered all participants' choices into the application and all results into the Epic abstract forms.

Of the $n = 163$ dyads who chose the type of results they wanted to learn, 70% ($n = 115$) jointly chose to learn about all of the available results. Data entry into the application for these participants was straightforward, taking no more than 10 minutes each. Two dyads chose not to learn any results, and thus, their choices were not entered into the application. Data entry took significantly longer for the remaining participants that made tailored choices ($n = 46$, 28.2%), with the overall time dependent on the complexity and granularity of their selections. The majority who made tailored choices chose to only learn the category of preventable conditions rather than both preventable and not preventable conditions, thus excluding 25 (45.5%) conditions for which they could learn results. Analysis of the range of participant choices has been previously published.[8]

DNA samples were obtained for 160 adolescents. Reports were not downloaded from the study application or returned for 17 dyads (two who chose not to learn any results and 15 who were lost to follow-up when results were available for return). Epic forms for the remaining 143 dyads were manually completed, with results available in MyChart for participants to view. The process of accessing the application, downloading the LMM report, blacking out study-related IDs, completing the Epic form, and sending staff messages to CCHMC providers took an estimated 33 total hours for participants who chose to learn all results and to whom results were returned ($n = 114$). The amount of time required per result for the remaining participants was dependent on the complexity and granularity of their choices.

Participants received results through MyChart ($n = 137$, 95.8%) or phone ($n = 6$, 4.2%). A 1-month post return-of-results (RoR) survey was completed by 71 adolescents and 91 parents who received results through MyChart. Most adolescents ($n = 65$, 91.5%) and parents ($n = 84$, 92.3%) indicated that they would choose to learn the same conditions, and 64 (90.1%) adolescents and 82 (90.1%) indicated that they were satisfied learning the adolescent's results through MyChart (Fig. 3).

Discussion

Our decision tools and clinical system adaptations enabled research participants to individualize their preferences for learning nondiagnostic genomic results beyond the standard "all or none" approach. Our custom reports required manual steps for every participant. Time, budget, and technological constraints prevented the generation of highly personalized reports using fully automated processes. Two major improvements are needed for this to occur: the generation of customized results from genetic laboratories and the ability to provide those results back to patients.

The eMERGE III central laboratories were not able to individualize reports to reflect participants' customized choices. This limitation impacted four other eMERGE III sites that also offered participants' choices beyond receiving all or none of the possible results.[11] Some commercial laboratories are offering customized next-generation sequencing panels that allow ordering providers to build a diagnostic panel or to remove genes from an existing diagnostic panel. There has been less progress on customization for secondary results. One clinical center previously reported offering clinical patients or their parents the ability to learn some, but not all secondary results when sequencing was used for diagnostic purposes but did not address how reports were individualized according to patients' choices.[12]

As analysis of sequence data for diagnostic purposes has been described as distinct and separate from analysis of variants in genes for secondary results,[13] we encourage laboratories to add selection flexibility. Such a service would avoid the need to filter out unwanted results from laboratory reports. Our findings suggest adolescent and parent participants who were allowed to make tailored choices would do so again if given the option, and that they are satisfied with an automated return of results that considers more nuanced choices.

Given the continued evolution of commercial EHRs, the inability to provide PDF reports through the patient portal is likely an issue that will be fixed through a future system upgrade. However, to more fully leverage the potential use of genetic results, particularly for decision support or as part of artificial intelligence/machine learning algorithms, these data will need to be stored more discretely instead of being embedded within a PDF report.[14,15] Future wide-scale adoption of structured and standards-compliant reports by genetic laboratories, which represent individual results as discrete data points, and more widespread incorporation of patient preferences into clinical practice should make the process of documenting this information in the EHR more efficient.

Beyond the technical challenges noted above, the inclusion of secondary results in the EHR for children and adolescents can raise ethical challenges. Once documented, the data are part of the medical record and accessible for future use. While theoretically protected via federal antidiscrimination legislation,[16] having results stored longterm based only on patient assent raises questions. We have attempted to mitigate this as best as possible. Unlike clinical settings, we used a multistep process to prioritize adolescent engagement, providing several opportunities to learn information and ask questions to enable informed decisions.[8,9] Also unlike clinical settings, we gave dyads the option to change their choices up to 2 weeks after

the study visit. Analysis of our RoR survey data are underway as are qualitative interviews with dyads who received results to learn the adequacy of our methods and responses to receiving results, which will yield recommendations for future studies in this area.

Conclusion

During eMERGE III, significant manual processing was needed to ensure that patient's preferences were taken into consideration. Given the growing recognition of the need to be more cognizant of patient preferences when providing care, we believe that the need for manual interventions will be greatly reduced or removed with cost-effective technology advances.

Funding

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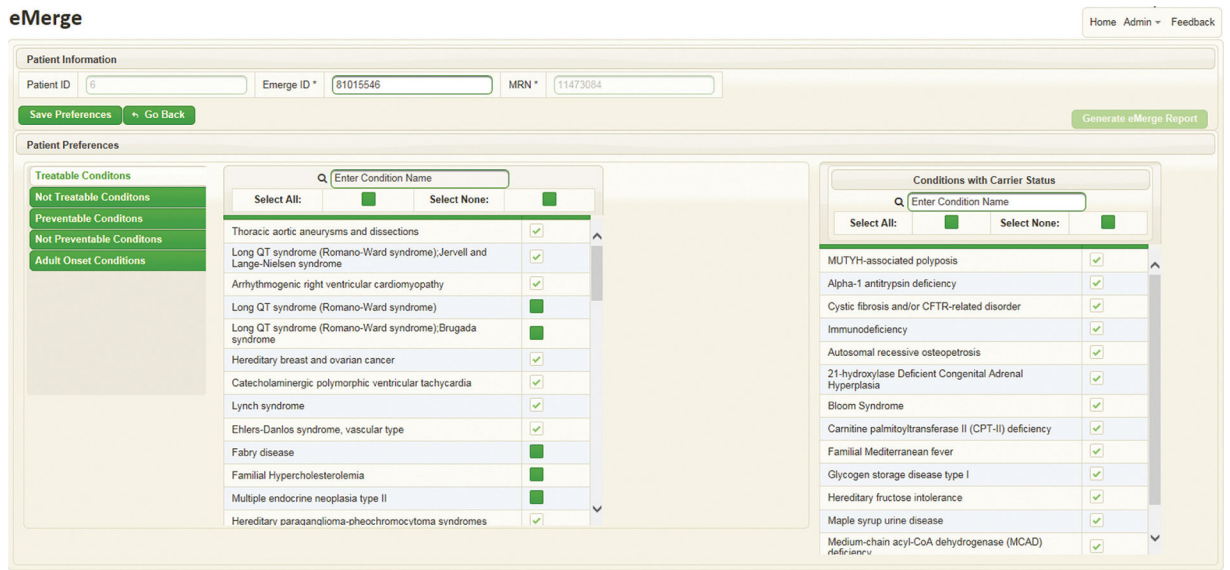
Fig. 1.
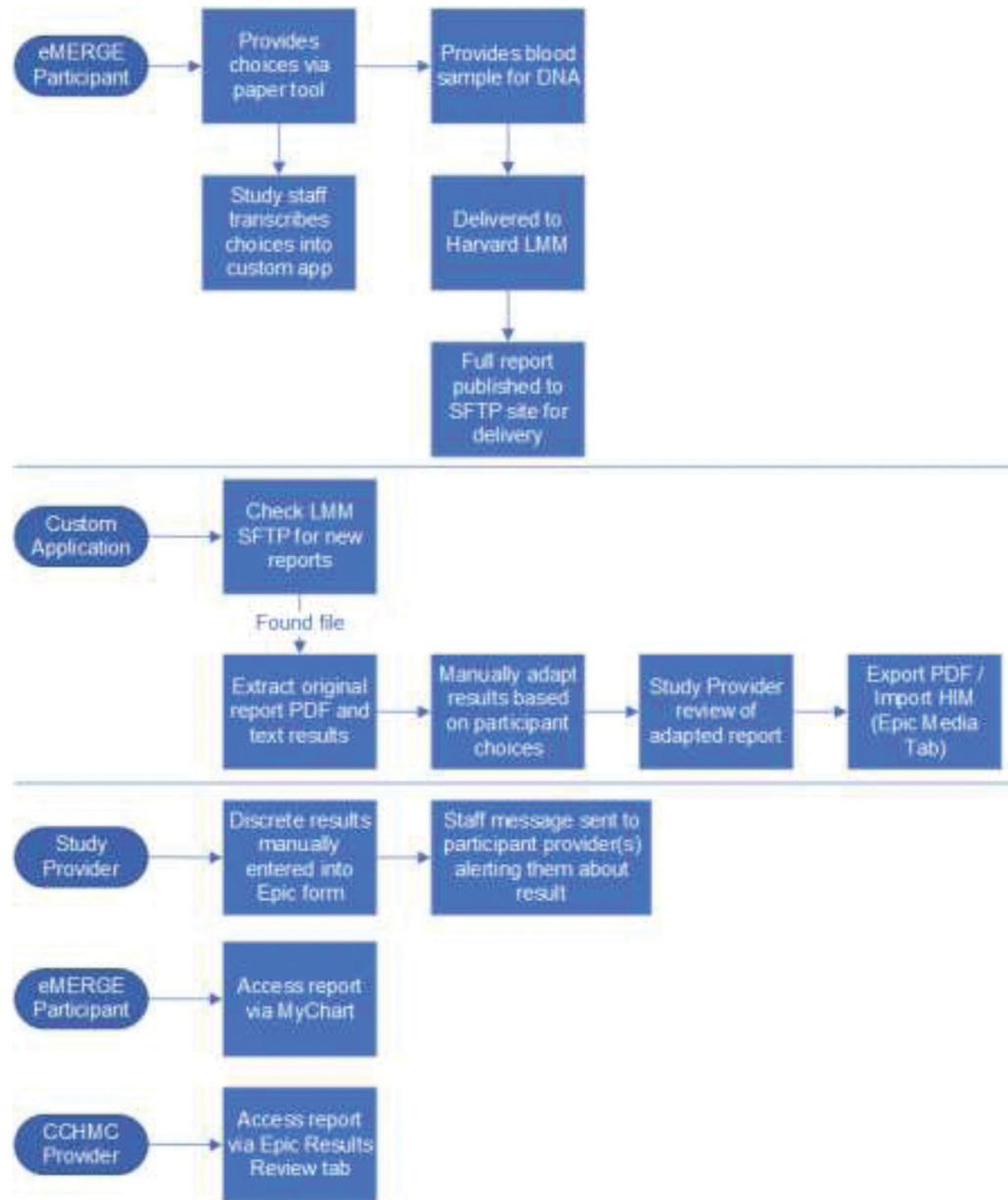Screenshot of application for participant who made customized choices.

Fig. 2.
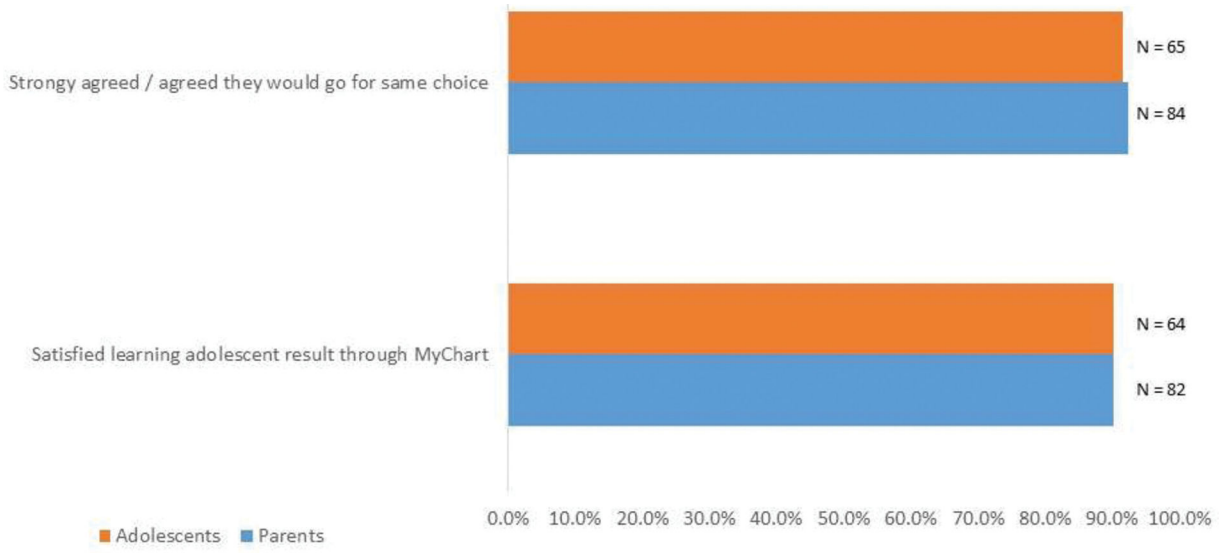Information flow between research participant and systems

Fig. 3.
Participants' satisfaction with adaptations to clinical systems and choices.