SPECIAL ARTICLE | Genetics inMedicine

My46: a Web-based tool for self-guided management of genomic test results in research and clinical settings

Holly K. Tabor[1,2], Seema M. Jamal[3,4], Joon-Ho Yu[1], Julia M. Crouch[2], Aditi G. Shankar[1], Karin M. Dent[5], Nick Anderson[6], Damon A. Miller[7], Brett T. Futral[7] and Michael J. Bamshad[1,8]

A major challenge to implementing precision medicine is the need for an efficient and cost-effective strategy for returning individual genomic test results that is easily scalable and can be incorporated into multiple models of clinical practice. My46 is a Web-based tool for managing the return of genetic results that was designed and developed to support a wide range of approaches to disclosing results, ranging from traditional face-to-face disclosure to self-guided models. My46 has five key functions: set and modify results-return preferences, return results, educate, manage the return of results, and assess the return of results. These key functions are supported by six distinct modules and a suite of features that enhance the user experience, ease site navigation, facilitate knowledge sharing, and enable results-return tracking. My46 is a potentially effective solution for returning results and supports current trends toward shared decision making between patients and providers and patient-driven health management.

Genet Med advance online publication 15 September 2016

Key Words: exome sequencing; genome sequencing; incidental; results return; secondary results

INTRODUCTION

Every person is predicted to have hundreds of genetic risk variants associated with both Mendelian and complex phenotypes that can be identified via exome sequencing (ES) or whole-genome sequencing (WGS).[1–4] Increasingly, such risk variants are of clinical, reproductive, and personal utility and afford individuals greater opportunities to make more informed health-related decisions.[1,5–9] Empirical data about whether individuals want such results are limited, but there seems to be a general preference for increased disclosure of and access to the broad scope of results available from ES/WGS.[10–13]

Conventional strategies for the return and interpretation of genetic test results (e.g., face-to-face interview with a genetic counselor, physician, or researcher) are often costly, inefficient, and typically require substantial personnel, resources, and infrastructure.[3,4,14,15] Such challenges to the return of genetic test results are magnified in the context of ES/WGS results for several reasons, including (i) the wide breadth and incomplete knowledge of phenotypes[16]; (ii) the relatively large number of risk variants in ES/WGS data[1,2]; (iii) the varied and dynamic utility associated with many risk variants[1,8]; and (iv) the increasingly fragmented expert knowledge about rare conditions to support conventional models for returning genetic test results. Collectively, these barriers to the return of genetic results can limit the benefits of ES/WGS and can compromise the satisfaction with genetic services and the safety of both patients and research participants.[17]

Recognizing these challenges and anticipating their increasing impact as ES/WGS became more commonplace, in 2010 we conceived a person- or family-centric model of "self-guided results management" in which an individual undergoing genetic testing or their parent chooses whether and when to receive genetic test results offered by their care provider or a researcher.[18] We implemented this model via an interactive Web-based information management system called My46 (www.My46.org) that is designed to enable clinicians and researchers to offer patients and participants, respectively, the opportunity to receive their individual genetic test results while maintaining data security and confidentiality, in a setting that emphasizes convenience, autonomy, and flexibility in the process of results return (**Figure 1**). Moreover, My46 provides comprehensive tracking of user navigation, decision making, and disclosure confirmation to advance education and user experience at the point of use. More broadly, My46 represents a model of education about and management of results that is consistent with current trends toward shared decision making between patients and providers and patient-driven health management.[19,20]

The first two authors contributed equally to this work.
[1]Department of Pediatrics, University of Washington, Seattle, Washington, USA; [2]Treuman Katz Center for Pediatric Bioethics, Seattle Children's Research Institute, Seattle, Washington, USA; [3]Department of Molecular Genetics, University of Toronto, Toronto, Ontario, Canada; [4]Department of Paediatric Laboratory Medicine, Hospital for Sick Children, Toronto, Ontario, Canada; [5]Department of Pediatrics University of Utah, Salt Lake City, Utah, USA; [6]Department of Public Health Sciences, University of California, Davis, Sacramento, California, USA; [7]Catalyst IT Services, Beaverton, Oregon, USA; [8]Department of Genome Sciences, University of Washington, Seattle, Washington, USA.
Correspondence: Michael J. Bamshad (mbamshad@uw.edu)

Submitted 11 May 2016; accepted 19 July 2016; advance online publication 15 September 2016. doi:10.1038/gim.2016.133

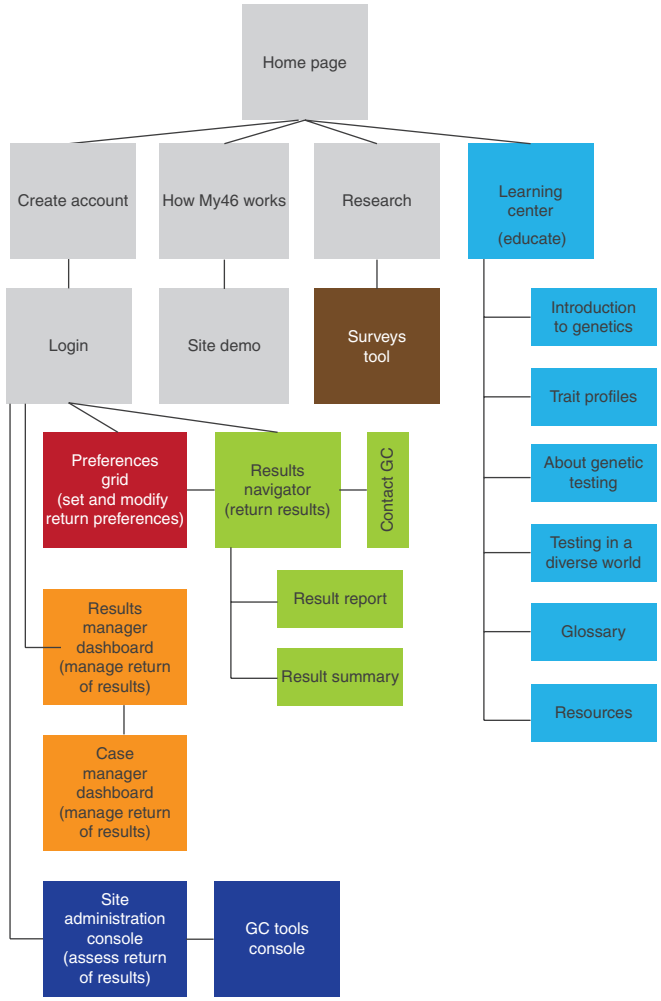

Figure 1 Abbreviated site diagram of the structure of My46. Labeled boxes indicate individual pages of the six modules of My46, including the learning center (light blue), surveys tools (brown), preferences grid (red), results navigator (green), results management dashboards (orange), and site administration console (dark blue). Shown in parentheses are the five major functions of My46 supported by pages and modules. Lines between boxes represent links between pages.

Herein we define the core functions, modules, and features of My46 and describe how it can be deployed in support of a wide variety of results-return workflows. It is important to note that My46 was explicitly developed as a tool to facilitate education and results return. It cannot and does not replace the expert interpretation and medical management offered by care providers (e.g., genetic counselors, clinical geneticists). Indeed, My46 should be viewed as a tool to support and extend the services offered by care providers; the amount of information (e.g., education about genetics, results, and different diseases) provided to a patient or research participant can be extensive[14] and therefore may diminish the time available for care providers to concentrate on results interpretation (e.g., addressing a family's adaptation and response to results or personalizing the implications for the family and relatives) and medical management during a clinical encounter.

A CONCISE DESCRIPTION OF MY46

My46 has five key functions: set and modify results-return preferences, return results, educate, manage the return of results, and assess the return of results. Six modules enable these functions: a preferences grid, a results navigator, a learning center, results management dashboards, a site administration console, and survey tools. Cross-functional features include intuitive site navigation; accessible audio-assisted guidance; use of family-friendly language for summaries, reports, and trait profiles; tools to facilitate knowledge sharing (i.e., reports) between users and their care providers or family members; online access to a genetic counselor; and results tracking, including delivery confirmation. An embedded site demonstration provides the full range of capabilities for training and evaluation without requiring registration on the site.

The back-end infrastructure and management of My46 (e.g., processing of results information, management of results-return workflows) are supported by a site coordinator, results administrator, and results manager. Each of these roles is assigned a different, albeit overlapping, set of site responsibilities and permissions (**Supplementary Table S1** online). Genetic counselors and clinicians also have roles in My46: to counsel users and review and approve results for return, respectively. A site auditor oversees site security, can audit site activity, and can view all user activities. My46 also includes an integrated secure messaging system for users to communicate with results managers, clinicians, and genetic counselors. Users are alerted via e-mail when a message is available for review.

MY46 FUNCTIONS

Set and modify results-return preferences

A key component of My46 is the ability of users to select whether to view a result that has been offered for return (i.e., to select their preferences for results return), whether a single result or hundreds of results. The former differs little conceptually and operationally from standard online patient portals for the return of targeted genetic test results or other laboratory test results. Accordingly, My46 can support relatively conventional workflows. By comparison, developing an effective and user-friendly tool that enables users to make informed and dynamic decisions (i.e., a "no" decision can subsequently be changed to "yes") about the return of tens to hundreds of results offered represents a major challenge. Moreover, enabling a person to review categories of possible results that may be offered at a future time and to select preferences, independent of knowing what individual results have been identified and offered for return, is critically important to the meaningful operationalization of preferences.

To address these challenges, we developed a module called the "preferences grid," which organizes results that could potentially be offered for return into nine phenotype labels or "trait" categories, each denoted by a differently colored square (**Figure 2**). Trait categories in the grid include "genetic syndromes," "metabolic disorders," "disease risk," "medication

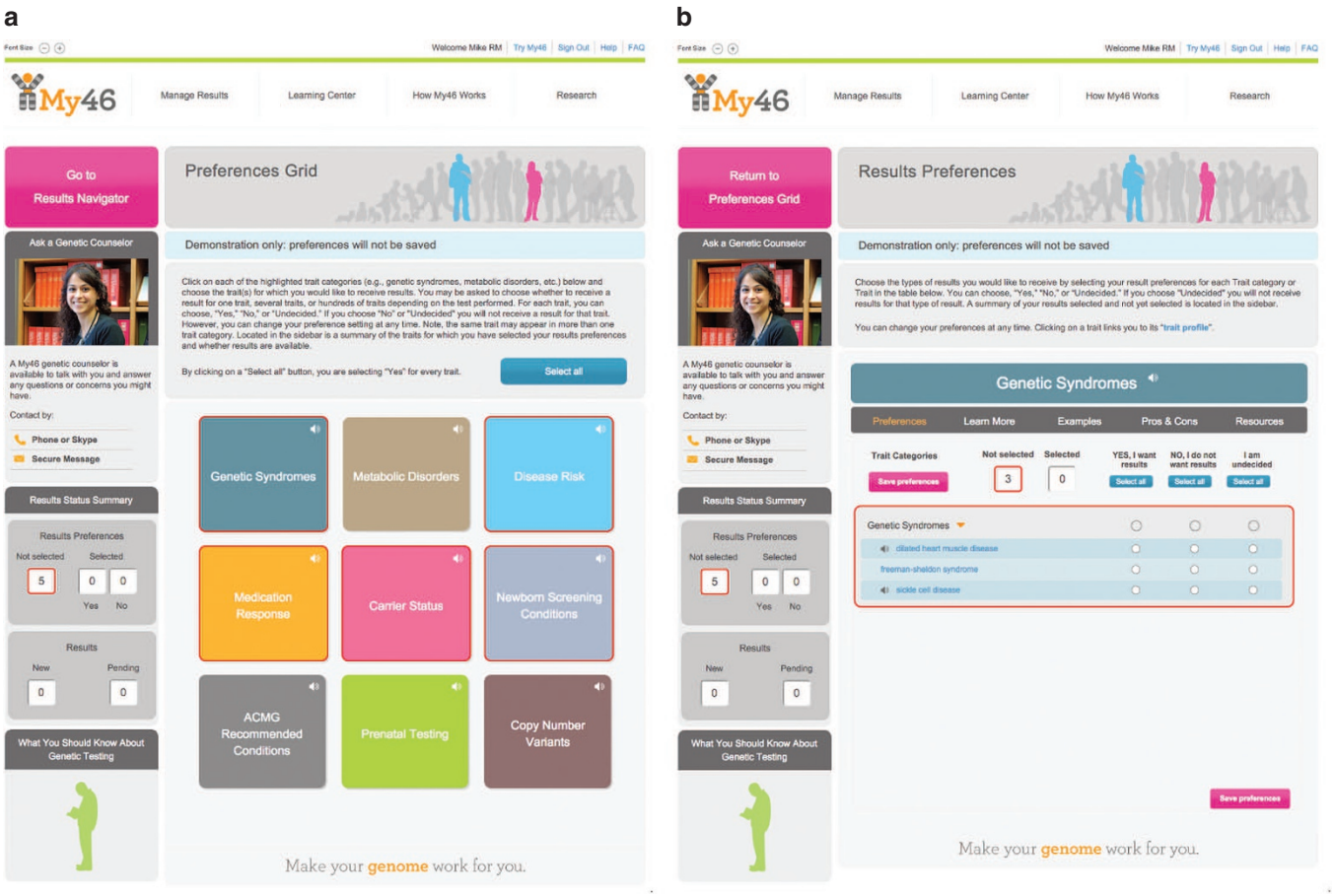

Figure 2 Preferences grid module of My46. (**a**) A "preferences grid" organizes results that could potentially be offered for return into nine phenotype labels or "trait" categories, each denoted by a different colored square. Category names were selected to offer intuitive choices in simple language and based in part on feedback from focus groups and interviews with mock users. (**b**) Traits within categories are further organized into individual conditions (e.g., genetic syndromes) or subcategories (e.g., disease risk is divided into subcategories representing different organ systems) to facilitate both navigation and decision making. The number of results offered for return, the preferences selected, and the results available for review are indicated in a sidebar.

response," "carrier status," "newborn screening conditions," "ACMG recommended conditions,"[21] "prenatal testing," and "copy number variants." Within categories, traits are further organized into subcategories (e.g., disease risk is divided into subcategories representing different organ systems, such as "heart and lungs") to facilitate both navigation and decision making. Category names were selected to offer intuitive choices in plain language. Nevertheless, the specific categories in the preferences grid are simply a heuristic and can be easily adapted to other conceptual approaches to results organization that might better reflect the perspective of an institution or reference laboratory and/or be adapted to delivery within specific populations of patients or research participants.

To inform users about the type of traits in each category, and therefore the impact of setting preferences, headers in each trait category banner are linked to a general explanation of the traits included ("Learn More"), "Examples" of included traits (e.g., Lynch syndrome/colon cancer for "Cancer," long QT syndrome/sudden death for "Heart and Lungs"), "Pros" and "Cons" of receiving results, and "Resources" that include hyperlinks to external sources of information about the trait category. For a specific result preference, a user may choose to receive results, not to receive results, or to remain undecided (Figure 2). If a user selects undecided, results are not offered for return. Whereas a choice to receive a result is final, selecting "no" or "undecided" does not preclude the user from changing their selection to "yes" at some later date. The ability to reflect indecision allows users to experience preference setting as a flexible rather than static decision-making process.

Return results

Perhaps the most formidable challenge to self-guided results management is developing an effective and efficient strategy for returning genetic test results that can be easily scaled for the return of tens to hundreds of results. To address this challenge, My46 organizes results available for return into a module called the "results navigator" (Figure 3), which displays all results selected for review by the user (i.e., results not selected for return by the user are not presented in the results navigator). The metaphor of a navigator is used because once a user has selected at least one preference for results return, the results

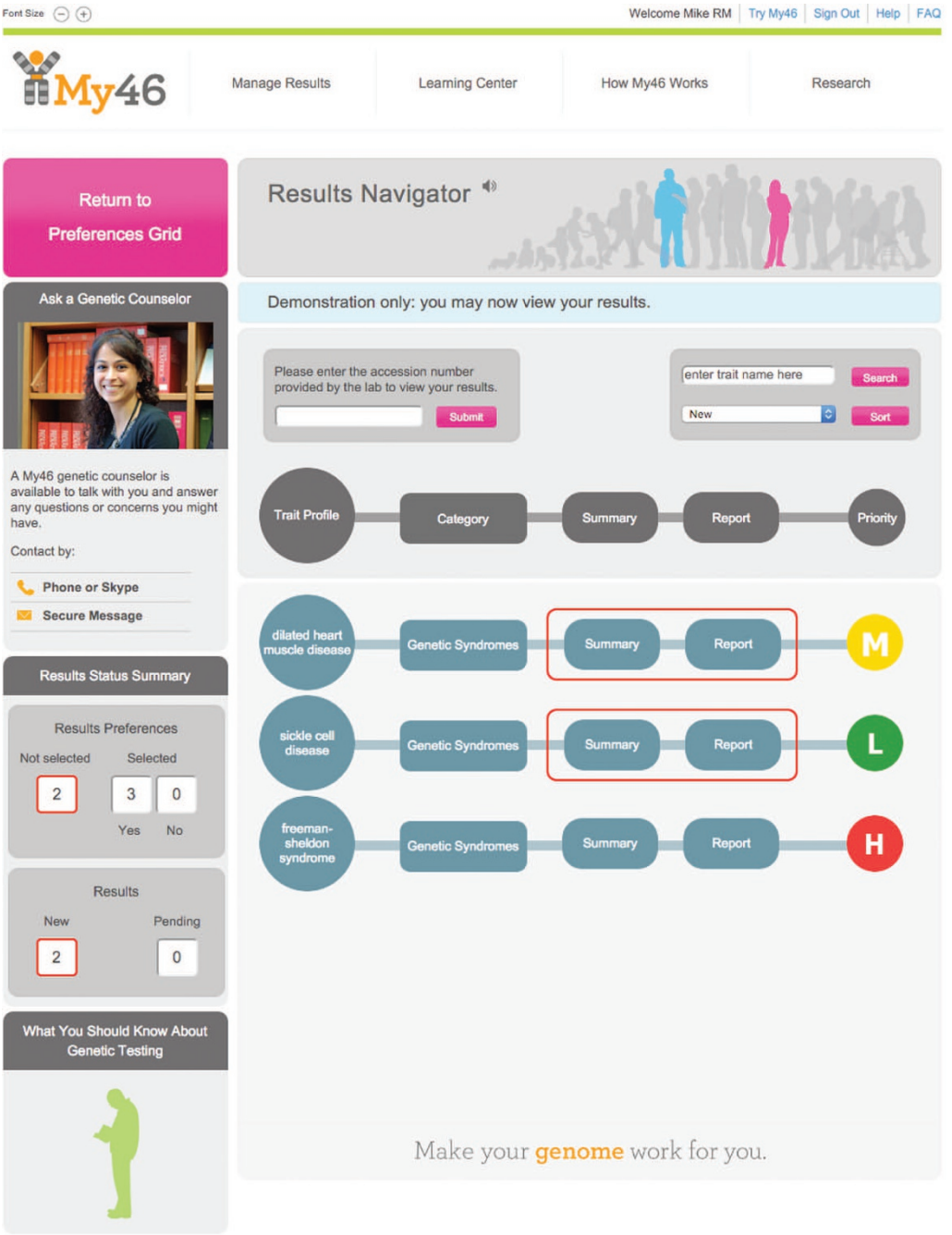

Figure 3 Results navigator module of My46. My46 organizes results into a module called the "results navigator" that displays all results selected for review by the user (i.e., results not selected for return by the user are not presented in the results navigator). Detailed information about each result is presented as a "result summary" and a "result report" and labeled by trait, trait category, and a "priority," the latter ranging between low, medium, and high corresponding to green, yellow, and red circles, respectively. The buttons representing unopened result reports and summaries are highlighted in red so they can be easily recognized by the user. Users can filter results by trait category, priority, or review status (i.e., unopened or opened).

navigator page becomes their de facto home page for accessing information about results.

Detailed information about each result is presented as a "result summary" and a "result report" and labeled by trait, trait category, and "priority," ranging between low, medium, and high corresponding to green, yellow, and red circles, respectively (Figure 3). The content of summaries and reports as well as the criteria used to define the range of priorities and distinguish among them can be customized by a laboratory, institution, or researcher. The buttons representing unopened result reports and summaries are highlighted in red so they can be easily recognized by the user. Users can filter results by trait category, priority, or review status (i.e., unopened or opened). Result summaries provide information about a result in simple,

family-friendly language with a logical flow that includes the identity of the variant(s), the gene, a concise interpretation, trait information, what to expect next (e.g., the potential benefits and disadvantages of knowing a result), and links to resources for patients. Result reports provide information intended to facilitate interpretation by a care provider, including a brief interpretation, guidance, clinical and epidemiological characteristics of the trait, genetic characteristics, population prevalence, testing limitations, and links to additional resources for clinicians. Both summaries and reports can be exported as PDF files to facilitate sharing with family members and care providers.

Educate

Lack of access to accurate genetic information is a major barrier to the pursuit of appropriate care of families/patients with a genetic condition.[22] In conventional approaches to the return of genetic test results, educational information about a result is typically provided by face-to-face discussion with a clinician (e.g., a clinical geneticist or a genetic counselor). While this is arguably ideal, this approach is also extremely labor-intensive, inefficient, and costly, and it cannot be sustained, particularly with increasing use of ES/WGS, given the size of the existing workforce and the austerity of economic constraints.[23,24] Development of alternative strategies to facilitate the return of genetic test results that are similarly effective is thus imperative. There are now numerous examples of models in which information to educate a patient, research participant, or the general public about genetics is provided by alternative strategies, most notably self-guided review of Web-based content (e.g., the National Organization of Rare Diseases and the Genetic and Rare Disease Information Center). With these precedents in mind, we aggregated educational resources for My46 users into a publicly accessible module called the "Learning Center."

Information in the learning center is organized into six sections: "Introduction to genetics," "Trait profiles," "What you should know about genetic testing," "Genetic testing in a diverse world," "Glossary," and "More resources." Information in the learning center is linked—often via a pop-up or by hovering over—to elements of both the preferences grid and the results navigator and is integrated into the results preferences setting and results-return functions. Information in the section entitled, "What you should know about genetic testing" was referenced frequently in usability studies, so access to it was made permanent in a sidebar of the preferences grid and results navigator.

The trait profiles are a centralized repository of knowledge of all the conditions for which test results could be available. They are a major resource of the learning center, and all trait profiles are part of the publicly accessible website. A trait profile summarizes information about a condition, including a description of its characteristic clinical features, options for genetic testing, general comments on major issues of management, the mode of inheritance of the trait, risks to family members, special considerations, and links to additional resources. Trait profiles are written by genetic counselors and clinical geneticists. The profiles were edited to improve readability based in part on previous studies of communicating genetic risk information to families.[25] The standardized information within each trait profile is intended to benefit both a lay audience and healthcare professionals. Eventually, a trait profile for every known genetic condition will be included in this resource. Notably, there is currently no such public resource of concise, standardized information about every known genetic condition, written in family-friendly language, and its development seems to be a compelling proposition for the medical genetics community.

Manage return of results

Efficient management of the process of returning results, particularly when returning a large number of results, requires tools that provide a results manager (e.g., a care provider or researcher) options to easily preview results, monitor the return process, prompt users to action, and confirm receipt of results (i.e., result summaries and reports). My46 fulfills this requirement and consolidates access to all of these tools into a module called the "results management dashboard" (**Figure 4**). From this dashboard a results manager can view the name, identifier, and results offered for return; whether a preference for return for each result has been selected and, if so, the preference chosen; and the dates that a result was offered, a result summary or report was opened, and a result summary or report was read. Clicking on the name of a person tested links a result manager to the case manager page for that person (**Figure 4**). On this page a results manager can view all tests offered a person, including those monitored by other results managers. From the case manager page, a results manager can upload and review result reports from third parties (e.g., reference labs) linked to the person tested, preview result summaries and reports, set intervals for automated reminder e-mail messages, and contact other clinicians or the user via secure messaging.

Assess return of results

Because ES/WGS is integrated into a broader range of clinical and research settings, tools for results return such as My46 need to undergo continuous improvement and development, in part via assessment of the user experience (e.g., usability and workflow) and outcomes of result return (e.g., patient-reported outcomes and clinical and personal utility). While the specific metrics to be used will, of course, partly depend on the context of return (e.g., research vs. clinical, type of result, or population served), a major function of My46 is to facilitate the assessment of results return. A module consisting of survey tools accomplishes this goal. Surveys can be implemented at all major decision points in the results-return process (e.g., before and after setting preferences, changing preferences, or after returning results). Additionally, Web metrics such as page use and navigation can be captured.

MY46 FEATURES

The creative team that developed My46 consisted of experts in graphic design, medical informatics, Web development, genetic

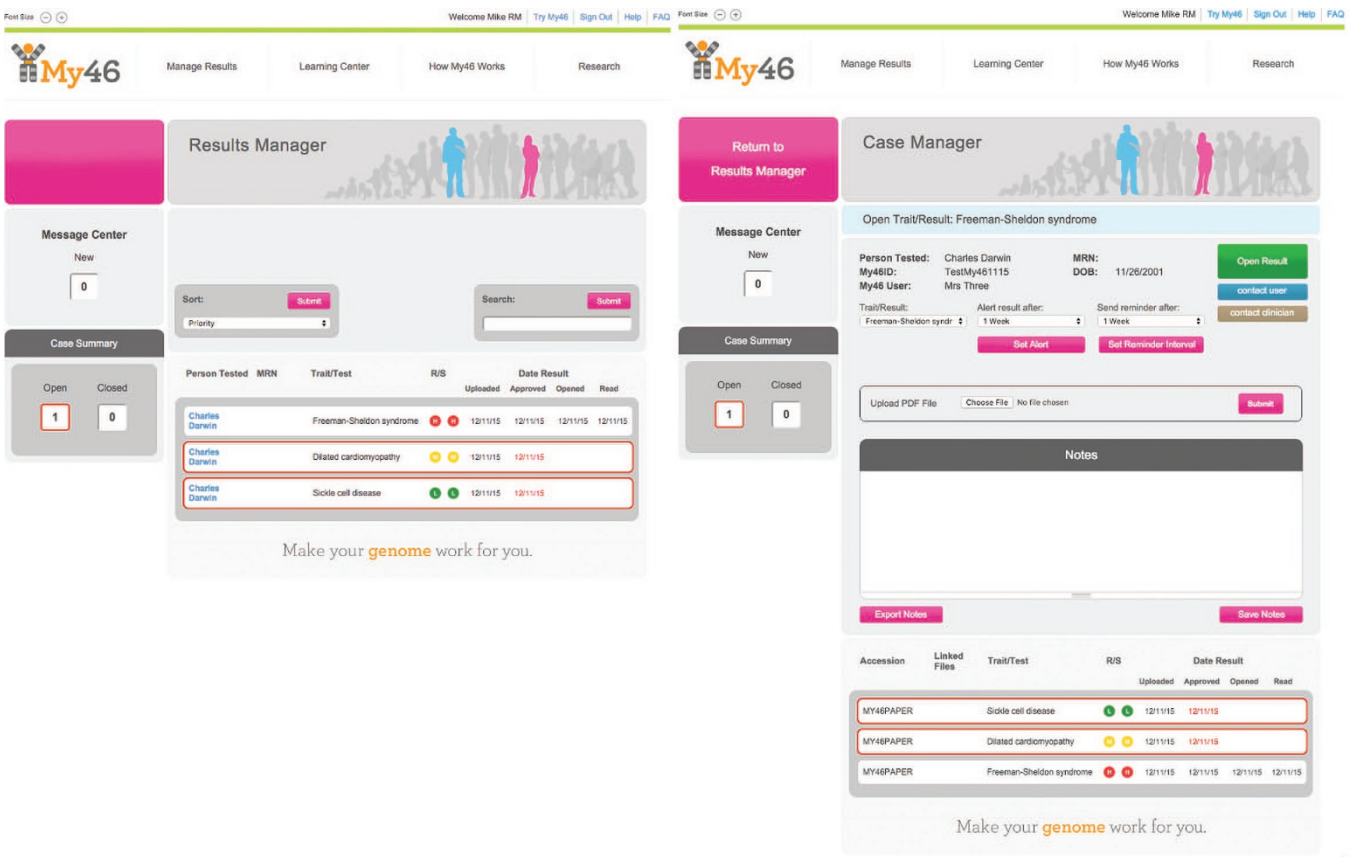

Figure 4 Results management dashboard module of My46. My46 consolidates access tools that provide a care provider or researcher with options to easily preview results, monitor the return process, prompt users to action, and confirm receipt of results (i.e., result summaries and reports) into a results management dashboard consisting of (**a**) a "results manager" page and (**b**) a "case manager" page. From these pages a results manager can view all results offered for return; whether a preference for return has been selected and, if so, the preference chosen; and the dates that a result was offered, a result summary or report was opened, and a result summary or report was read.

counseling, medical genetics, and biomedical ethics. A major emphasis of the team was to develop features of My46 that maximized its usability. Foremost was the creation of an intuitive workflow navigated with the assistance of textual (e.g., pop-ups), visual (e.g., shapes and colors), and auditory guidance and landmarks. Content throughout the site was written in family-friendly language, including a glossary to explain the meaning of many terms.

Consultation with a genetic counselor is essential for meaningful interpretation of genetic test results (e.g., psychosocial counseling to help a person and their family understand what a result means in the context of their values, mores, and perceptions of health and life), assessment of risk for other family members, and development of optimal strategies for further testing. My46 was envisioned and designed to return genetic test results and educate users about genetic traits, but not to interpret results for users. To this end, My46 should be viewed as a tool to extend the services offered by genetic counselors, which is particularly important given the relative labor shortage of genetic counselors and clinical geneticists. Nevertheless, distinguishing between return and interpretation can be challenging, and not all questions and/or concerns about return can be addressed without expert assistance. For this reason, a feature of My46 is online access to a genetic counselor (i.e., "Ask a genetic counselor") whereby users can send queries to and set up conferencing via video or telephone with a genetic counselor.

My46 has several features to ensure data security, including differentiated user roles and privileges, user authentication and authorization security, secure sockets layer encryption, and comprehensive auditing to record and monitor access and data changes. In addition, information on the site informs and prompts users to take steps to minimize risks to security and confidentiality (e.g., not sharing passwords and logging off and quitting the Internet browser after using My46).

USES OF MY46

My46 is designed for use under different structural contexts of return, each distinguished by a number of variables: research versus clinical care, a self-guided versus traditional model of return involving different providers to varying degrees, return of one (e.g., a primary result) versus several hundred (e.g., secondary results from ES/WGS) results. Here we present several result return scenarios to illustrate how My46 can be implemented.

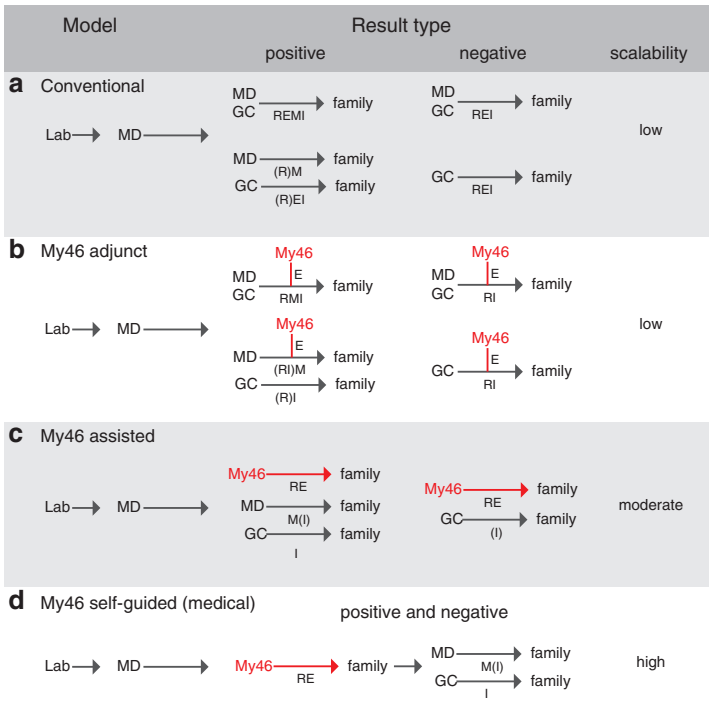

Figure 5 Options for integrating of My46 into different models of results return. (**a**) In a conventional results-return workflow, return (R), education (E), interpretation (I), and medical management (M) are provided by a clinical geneticist (CG), genetic counselor (GC), or a combination thereof. (**b**) In its most basic implementation, My46 can be used simply as an adjunct to conventional results return by facilitating education of a family/patient. (**c**) In assisted results return, My46 is used for education and results return, but a CG and/or GC meet with every family/patient to provide interpretation and management of positive results and interpretation of negative results. In the immediate future, My46-assisted return (and variations thereof) is perhaps the model most easily adapted to most current clinical settings. (**d**) In My46 self-guided return in a medical setting, results to be offered for return are curated by expert review but families/patients select their preferences for return and pursue evaluation by a CG or GC at their discretion.

Clinical applications

In a clinical setting, My46 can be used in myriad ways. These range from My46 serving simply as an adjunct educational tool in conventional models of results return to supporting the self-guided return of results offered for return by a provider (**Figure 5**). In conventional models of return, a diagnostician (e.g., a physician or nurse practitioner) and a genetic counselor work together or in tandem to offer a result for return, educate a family about the result, interpret the result with the family, and discuss medical management of persons with a positive result (**Figure 5**). This is the gold standard of results return and, although effective, it is labor-intensive, and scaling beyond the return of a primary result is typically inefficient and costly.[23]

In its most basic application, My46 can be used as an adjunct educational tool before, during, or after a clinical encounter to provide general genetics information and/or information about a specific trait(s). This is a convenient way to provide educational support and may reduce the time a provider spends face-to-face with a family or allow a provider(s) to focus their time on results return, interpretation, and medical management. However, it is not a highly innovative alternative or supplement to other approaches currently used to educate patients/families about genetics and genetic traits. Additionally, scalability for the return of additional results remains low.

Using My46 for both results return and for educational support (i.e., assisted by My46) is the most straightforward way to take broader advantage of My46 in the workflow of conventional models of results management in a clinical setting (**Figure 5**). In this scenario, after a provider determines which result(s) should be offered for return, a family is provided instructions for creating a My46 account and a My46 identifier via e-mail, text, telephone call, or letter. The combination of My46 identifier, medical record number, surname, and date of birth of the person tested represents a unique and secure identifier of that person. Patients/families use My46 at their convenience to set their preferences for each result offered for return. Users who elect to receive results are provided with a unique accession number that links a result(s) to the person tested. Preloaded results are immediately made available in the results navigator, along with a recommendation for further evaluation by a physician-provider and genetic counselor (i.e., for all positive results) or only by a genetic counselor (i.e., for all negative results). Primary and secondary results can be stratified for return, but at a minimum each positive result requires further evaluation by a clinical provider. Nevertheless, scalability for the return of a large number of results using a My46-assisted model in a clinical setting is good.

My46 was designed to support the implementation of self-guided management of results in a clinical setting (**Figure 5**). In

this case each result a user is to receive is presented in the results navigator, along with a recommendation for further evaluation. However, families/patients are provided more latitude such that mandatory evaluation is required only for positive results of moderate and high priority. Thus the major distinction between My46-assisted and My46 self-guided results return is that families/patients have greater autonomy over the results for which they seek further evaluation by a physician-provider or genetic counselor. Scalability for the return of a large number of results in a clinical setting is high.

Research settings

Return of results in research settings is recapitulated in the My46 self-guided workflow in which one or more results are offered for return. In this case research participants are made aware, via e-mail, text, telephone call, or letter, that results are being offered for return and provided instructions for creating a My46 account and a My46 identifier. Users who elect to receive results are provided with a unique accession number that links a result(s) to the person tested. Preloaded results are immediately made available in the results navigator. Study participants have access to a genetic counselor via My46 and staff for technical assistance at any point in the process.

My46 can also be used as a tool to study both the process and outcome of results return. The surveys tool provides examples of surveys that have been used in various studies completed to date. Such surveys can be fully integrated into My46 or at researcher-selected time points in the results-return process. My46 can also be set to direct users via e-mail to external survey tools.

FURTHER DEVELOPMENT OF MY46

Testing My46

The effectiveness of any information systems–based tool revolves, in part, around usability and user satisfaction. The design and implementation of My46 was guided by intermittent assessments of user satisfaction and usability for returning targeted and secondary results from ES/WGS using several standardized measures. However, continued testing will be integral to the successful ongoing development of My46 and its effective integration into clinical workflows.

It is unclear to what extent My46 could be used as a decision aid in the process of selecting preferences for return versus simply as a tool to facilitate the communication of results. If return of the vast majority of genetic tests ordered generally does not require additional consideration by families/patients, then decision-making aids in general may be of limited value. Alternatively, the degree to which patients opt to receive results from large panels or ES/WGS will motivate the development of additional features to aid in decision making, such as the integration of pop-ups into results-return workflows to confirm preferences or selections. Questions about communication more narrowly focus on whether My46 modules such as the preferences grid and the results navigator provide an enhanced systematic approach to capturing and communicating preferences and accessing results, respectively. For instance, some people may prefer alternative taxonomies of results that incorporate factors such as age at onset of a condition, disease severity, or clinical actionability.

It will be important to investigate the extent to which receiving genetic results using My46 or any information systems–based approach in general affects health-related outcomes such as patient satisfaction, cost of care, sharing of information with family members and other health-care providers, increased utilization of genetic information for screening, surveillance, and medical management.[26] Study of these outcomes is complete, and a manuscript(s) reporting the results is in preparation. In a society dominated by social media, it might be hypothesized that the use of such a system could facilitate the sharing of personal genetic information. Studies of direct-to-consumer genetic testing suggest that Web-based access to genetic test results is changing the notion of "personal." Indeed, some studies suggest that individuals who receive results online are less likely to share results.[27]

General challenges to adoption of Web-based tools

In the context of ES/WGS, the annotation and curation of variants remain perhaps the most substantial challenges to returning results, partly because of the dynamic nature of information about variant pathogenicity and difficulties in warehousing and managing such information. My46 is intentionally agnostic regarding such issues, yet such challenges and the general uncertainty surrounding the validity and utility of genetic results may lead to a nervous enthusiasm for any form of automated disclosure of genetic information.[18] As with other Web-based tools for sharing sensitive information (e.g., credit card information and heath records), such discomfort will likely diminish with increased familiarity and use. This predictable course of technological diffusion suggests a need to step back from a traditionally paternalistic approach to returning results and invest in fostering patient and family capacity to engage with their providers as partners in managing their genetic information and related care.

The development of My46 is partially driven by the increasing use of digital technologies in health management. Consequently, My46 is also subject to broader technological forces and trends such as digital divide(s) and the prospective fragmentation and stratification of technology and access.[28] Beyond ensuring the ability to use My46 on multiple platforms, perhaps more important will be considering how a model of self-guided management can operate across different technological infrastructures in an evolving environment where the point of care is shifting away from traditional clinical encounters to patient-owned devices and industry-supported Web applications. In anticipation of such challenges, further study is needed of the applicability and utility of self-guided results management for populations that experience technological disparities.

CONCLUSIONS

Translating discoveries in genomics research into effective precision health care depends in part on the development of highly

accessible and useful information systems that help individuals manage their own, or a parent manage their child's, health information, including genetic test results.[20] My46 offers a potentially user-friendly, convenient, secure, generalizable, and relatively cost-effective tool for managing genetic test results that can support multiple models for returning genetic test results in either clinical or research settings and returning secondary results from ES/WGS, and the ability to study the return of results. My46 also allows health-care providers to efficiently manage and monitor the return process and affords institutions assurance that results are received and in a timely manner, which should in turn improve patient satisfaction and safety. My46 will be licensed to academic and nonprofit research organizations at no charge. The integration of health data management tools such as My46 in clinical genetics service workflows will necessarily change the roles of genetics health professionals and perhaps the very practice of care. Clinical geneticists and genetic counselors will play lesser roles as educators and gatekeepers in the process of results return but even more important roles in the translation and interpretation of results information, including meeting the emotional needs of families/patients and providing psychotherapeutic support.

SUPPLEMENTARY MATERIAL

Supplementary material is linked to the online version of the paper at http://www.nature.com/gim

ACKNOWLEDGMENTS

The authors thank the many research participants and families who provided input on the design and function of My46. Our work was supported in part by grants from the National Institutes of Health/National Human Genome Research Institute (R01HG006618 to H.K.T.; 1U54HG006493 to M.B., Debbie Nickerson; 5R000HG004316 to H.K.T.; and K99HG007076 to J.Y.) and the National Institute of Child Health and Development (HHSN 267200700023C and HHSN27500503415C). The authors thank each genetic counselor who contributed a trait profile(s). The authors also thank the design team at Cognition Studio and the development team at Catalyst IT Services, as well as Ellen Kuwana and Jacquie Stock for their editorial work on the site content and Kevin McCullough for his work on early site development.

DISCLOSURE

M.J.B., H.K.T., and J.Y. have a patent application pending on My46. The other authors declare no conflict of interest.

REFERENCES

1. Tabor HK, Auer PL, Jamal SM, et al.; NHLBI Exome Sequencing Project. Pathogenic variants for Mendelian and complex traits in exomes of 6,517 European and African Americans: implications for the return of incidental results. *Am J Hum Genet* 2014;95:183–193.
2. Tennessen JA, Bigham AW, O'Connor TD, et al.; Broad GO; Seattle GO; NHLBI Exome Sequencing Project. Evolution and functional impact of rare coding variation from deep sequencing of human exomes. *Science* 2012;337:64–69.
3. Dewey FE, Grove ME, Pan C, et al. Clinical interpretation and implications of whole-genome sequencing. *JAMA* 2014;311:1035–1045.
4. McLaughlin HM, Ceyhan-Birsoy O, Christensen KD, et al.; MedSeq Project. A systematic approach to the reporting of medically relevant findings from whole genome sequencing. *BMC Med Genet* 2014;15:134.
5. Parsons DW, Roy A, Yang Y, et al. Diagnostic yield of clinical tumor and germline whole-exome sequencing for children with solid tumors. *JAMA Oncol* 2016; e-pub ahead of print 28 January 2016.
6. Yang Y, Muzny DM, Xia F, et al. Molecular findings among patients referred for clinical whole-exome sequencing. *JAMA* 2014;312:1870–1879.
7. McBride CM, Bryan AD, Bray MS, Swan GE, Green ED. Health behavior change: can genomics improve behavioral adherence? *Am J Public Health*. 2012;102:401–405.
8. Foster MW, Mulvihill JJ, Sharp RR. Evaluating the utility of personal genomic information. *Genet Med* 2009;11:570–574.
9. Facio FM, Eidem H, Fisher T, et al. Intentions to receive individual results from whole-genome sequencing among participants in the ClinSeq study. *Eur J Hum Genet* 2013;21:261–265.
10. Middleton A, Wright CF, Morley KI, et al.; DDD study. Potential research participants support the return of raw sequence data. *J Med Genet* 2015;52:571–574.
11. Jarvik GP, Amendola LM, Berg JS, et al.; eMERGE Act-ROR Committee and CERC Committee; CSER Act-ROR Working Group. Return of genomic results to research participants: the floor, the ceiling, and the choices in between. *Am J Hum Genet* 2014;94:818–826.
12. Middleton A, Morley KI, Bragin E, et al.; DDD study. Attitudes of nearly 7000 health professionals, genomic researchers and publics toward the return of incidental results from sequencing research. *Eur J Hum Genet* 2016;24:21–29.
13. Yu JH, Harrell TM, Jamal SM, Tabor HK, Bamshad MJ. Attitudes of genetics professionals toward the return of incidental results from exome and whole-genome sequencing. *Am J Hum Genet* 2014;95:77–84.
14. Hartmann JE, Veach PM, MacFarlane IM, LeRoy BS. Genetic counselor perceptions of genetic counseling session goals: a validation study of the reciprocal-engagement model. *J Genet Couns* 2015;24:225–237.
15. Mayer AN, Dimmock DP, Arca MJ, et al. A timely arrival for genomic medicine. *Genet Med* 2011;13:195–196.
16. Hennekam RC, Biesecker LG. Next-generation sequencing demands next-generation phenotyping. *Hum Mutat* 2012;33:884–886.
17. Bowdin SC, Hayeems RZ, Monfared N, Cohn RD, Meyn MS. The SickKids Genome Clinic: developing and evaluating a pediatric model for individualized genomic medicine. *Clin Genet* 2016;89:10–19.
18. Yu JH, Jamal SM, Tabor HK, Bamshad MJ. Self-guided management of exome and whole-genome sequencing results: changing the results return model. *Genet Med* 2013;15:684–690.
19. Biesecker LG, Biesecker BB. An approach to pediatric exome and genome sequencing. *Curr Opin Pediatr* 2014;26:639–645.
20. Precision Medicine Initiative (PMI) Working Group. The Precision Medicine Initiative Cohort Program—building a research foundation for 21st century medicine. 2015 https://www.nih.gov/precision-medicine-initiative-cohort-program.
21. Green RC, Berg JS, Grody WW, et al.; American College of Medical Genetics and Genomics. ACMG recommendations for reporting of incidental findings in clinical exome and genome sequencing. *Genet Med* 2013;15:565–574.
22. Levy HP, LoPresti L, Seibert DC. Twenty questions in genetic medicine–an assessment of World Wide Web databases for genetics information at the point of care. *Genet Med* 2008;10:659–667.
23. Ormond KE, Wheeler MT, Hudgins L, et al. Challenges in the clinical application of whole-genome sequencing. *Lancet* 2010;375:1749–1751.
24. Berg JS, Khoury MJ, Evans JP. Deploying whole genome sequencing in clinical practice and public health: meeting the challenge one bin at a time. *Genet Med* 2011;13:499–504.
25. Lautenbach DM, Christensen KD, Sparks JA, Green RC. Communicating genetic risk information for common disorders in the era of genomic medicine. *Annu Rev Genomics Hum Genet* 2013;14:491–513.
26. Gray SW, Martins Y, Feuerman LZ, et al.; CSER Consortium Outcomes and Measures Working Group. Social and behavioral research in genomic sequencing: approaches from the Clinical Sequencing Exploratory Research Consortium Outcomes and Measures Working Group. *Genet Med* 2014;16:727–735.
27. Kaufman DJ, Bollinger JM, Dvoskin RL, Scott JA. Risky business: risk perception and the use of medical services among customers of DTC personal genetic testing. *J Genet Couns* 2012;21:413–422.
28. Kontos E, Blake KD, Chou WY, Prestin A. Predictors of eHealth usage: insights on the digital divide from the Health Information National Trends Survey 2012. *J Med Internet Res* 2014;16:e172.