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Interacting with Genomic Data: Clinician Requirements and Prototype Structure

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Abstract. Healthcare is currently being transformed by the introduction of genomic sequencing – a major advancement in personalised medicine. This advent provides new opportunities for clinicians to use genomic data in decision making about patient diagnosis and treatment, but this can only be achieved through access to data and support in its use. Engaging with clinicians in the development of decision support tools will optimise relevance and adoption of genomic sequencing in healthcare. In this study, existing data from clinician workshops and interviews together with horizon scanning of relevant technologies were used to define clinician portal specifications. We describe a preliminary structure of a decision support tool for use by clinicians and the manner in which the technology may be evaluated.

Keywords. Clinician decision support tool, genomic sequencing, clinician portal, data repository, human computer interaction, user centric design

Introduction

A revolutionary change in healthcare requires an established supporting infrastructure. In order to enhance patient care through improved diagnosis, treatment and care, the Melbourne Genomics Health Alliance will establish a genomic data repository to provide access to genomic data by patients, clinicians and researchers [1]. The repository in turn will meet information management needs for integrating genomics into clinical practice and allow interface with external systems, including those providing information to patients and to clinicians utilising genomic medicine.

The need for decision support in genome medicine arises in part from complexity and novelty of genomic science, workforce issues, limited proficiency of physicians in genomics and lack of clinical geneticists in the clinical workforce [2] as well as sheer velocity and rate of scientific discovery. Integrating decision support tools with genomic databases and e-health records will assist clinical care providers with personalisation of care, support access to and storage of data, and can simplify data exchange between systems [3].

A number of existing technologies store research genomic data, while other systems are dedicated to sharing of knowledge updates upon a change in the

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classification of a variant [5]. None of these systems, however, provide support or guidance for genomic decision making to clinicians. For example, a study database, REDCap, is a reusable tool for collection, storage, and dissemination of clinical and translational research data [4]; whereas Cpipe, is an open source variant detection pipeline designed specifically for clinical genetic diagnostics purposes [5]; LOVD 2.0, is an open source easy-to-set-up database installation tailored for storing information on gene sequence variations associated with phenotypes [6]; and ClinVar, is a public, freely available archive of reports of relationships among sequence variations and phenotypes [7].

In order to develop systems to interface with the repository, the preferences and user requirements of clinicians need to be determined. In this study, existing data from repository requirements workshops and clinician interviews together with horizon scanning of relevant technologies were used to define clinician portal specifications, including the design of a decision support tool for use by clinicians.

1. Gathering Clinician Requirements

Agile software development methodologies are based on iterative development, where requirements and solutions evolve through collaboration and consultation. Active stakeholder participation is a core practice of Agile Modelling. In order to inform information management system design specifications, the Melbourne Genomics Health Alliance conducted eight requirements gathering workshops with a range of system users in 2014. Eleven clinicians from across Alliance member organisations were invited to participate in a requirements gathering workshop. Clinicians were asked their perspectives on the necessary requirements for successful integration of genomic sequencing into future clinical practice, and specifically on a clinician portal. Agile methodologies rely on collection of 'user stories' to help define system requirements. As genomic testing is not routinely available in clinical care, the users selected for the workshop were clinicians leading a Melbourne Genomics clinical project with previous experience of using genomic testing in a research setting.

As part of the process evaluation of the Melbourne Genomics clinical project, all clinicians who attended at least two multidisciplinary review meetings of a Melbourne Genomics clinical project (n=35) were invited to participate in a semi-structured interview. In order to supplement data from the requirements gathering workshop, clinicians were asked to reflect on their experience of using genomic testing and discuss what resources/tools they felt would be needed to support clinicians using genomic sequencing in practice in the future. Thirty-two of the 35 clinicians approached consented to be interviewed.

During both phases of data collection, the clinicians expressed their need for an information system supporting management of genomic tests and data. The main system requirements included decision making around testing and treatment, tracking of patient samples and report annotation.

1.1. Decision Support Tool for Selecting the Appropriate Test

Clinicians expressed the need for a decision support tool that would assist them to determine the most appropriate test for any given patient. As a range of different personalised medical tests may be utilised in the future (whole genome sequencing,

whole exome sequencing, in addition to current costly panel tests and single gene tests), clinicians expected the need to seek guidance on the most appropriate test for a given patient. Clinicians favoured summarised information relating to each test, including general guidelines, success, costs involved, typical processing timeline, restrictions, previous evidence of the test, and appropriateness to the target patient.

1.2. Test Workflow Support

Once the desired test is identified, clinicians expressed the need for a workflow tool to allow them to order the tests in a standardised way; streamline all the required consents, authorisations and approvals for the test; manage test-related communication with the patient; enquire about the status of the test processing; and guide report preparation.

1.3. Test Report Annotation and Curation

Clinicians expressed interest in the development of an easy-to-use and intuitive tool that facilitates curation of the test results to facilitate communication with patients and to augment their own clinical records. Specifically, they mentioned the need for a functionality that allows generation of the result summaries and highlighting/extraction of the most important findings. Desired features included report content annotation, text extraction, easy-to-use visualisation, preparation of presentations, explanation of terms and complex cases, insertion of links to papers and further information.

1.4. Shared Repository of Past Tests Integrated with Other Clinical Data

The ability to share the tests (and possibly reports generated by the curation tool) in a centralised system of genomics tests and other medical patient records was considered important by clinicians. This idea was deemed important for allowing genomic data sharing with other clinicians. Clinicians also expressed the need for a search functionality that facilitates extraction of information from the patient's medical records and past genetic tests, identification of other patients that did the same test, and findings (or reports) of those past tests. They also were interested in a feature that would allow them to 'subscribe' for updates on new findings pertaining to a test, variant or phenotype. Together these features will allow enhanced decision making about treatment options for individual patients based on test results and outcomes for similar patients.

2. Clinician Interaction with the Decision Support Tool

Based on the clinician's articulated needs we have designed a web based decision support tool for integration into the Melbourne Genomics platform. The design assumes interoperability and that privacy and security are afforded by the repository. The clinician decision support tool provides guidance during the initial assessment and treatment planning with more administrative capabilities (sample tracking, interaction with report). Clinician interaction flow (Figure 1) would proceed as described in Sections 2.1–2.4. It should be noted that the decision support tool is seen to be an

application built upon the data repository, and functionality would not be replicated in the decision support tool.

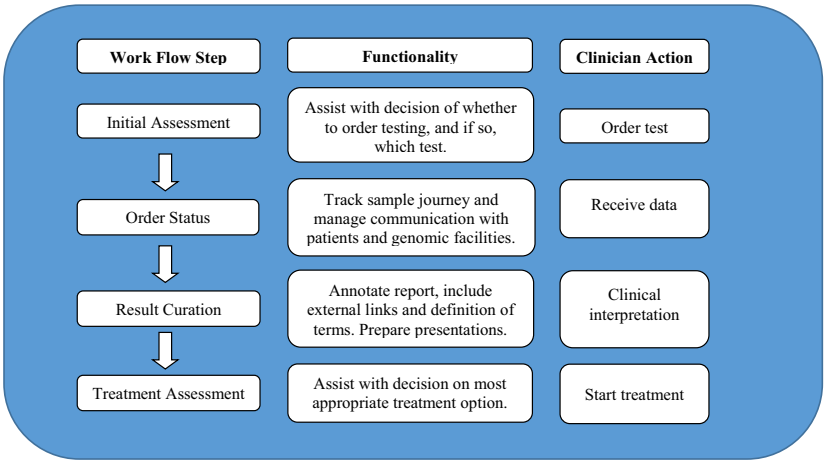

Figure 1. Clinician decision support tool requirements overview showing the work flow with functionality and clinician action for each step.

2.1. Test Selection Support

The goal of the initial assessment is to support clinician decision making in relation to the selection of appropriate tests, informed on a case by case basis. Test options include whole genome, whole exome (protein coding regions), panel (a number of genes), or single gene testing, all of which vary in cost and applicability to genetic conditions.

The user interaction would involve accessing the patient record and existing test results, including previous genomic sequencing, that may be able to be re-used; search for advice on whether genomic testing is indicated through curated/standard information on the phenotypes, symptoms and/or condition (e.g. clinical guidelines); search knowledge base of research; search patient treatments and outcomes. Information generated would include implicated variants, detection rates, treatment options, mitigating factors, variant treatment outcomes, applicability for intended patient, inclusion / exclusions criteria, other patients 'like' the one under review, with treatment and outcome, general guidelines, costs involved, processing time, consents, restrictions. The tool would automate and augment the current manual search process. Once the clinician has decided on the suitability of genomic testing, the test ordering protocol would be commenced through the decision support tool.

2.2. Test Order Tracking

In order to monitor and track the ordered test through the test ordering and result reporting cycle, clinicians would be provided with a visual indication of the status of the test and estimated length of sample processing as well as an alert when the test

result is available. This could take the form of a status 'dashboard' where status information for all current tests would be shown, including: ordering of tests, authorisation of tests, scheduling of tests, and viewing of sample status. Clinicians would also have the ability to manage communication with patients and with genomic facilities regarding sample journey.

2.3. Result Curation

Once genomic sequencing reports are generated, they need to be reviewed and prepared for discussion with the patient. This is a two stage process. Variants are annotated in the pipeline – annotations are reviewed to classify the variant. This requires multiple sources of data and may need multidisciplinary input. The results report is then modified. The resulting report is then reviewed by clinicians to decide on treatment. As test results can be intimidating and misleading to the patient, clinicians expressed a need for the ability to annotate test results before they are provided to patients. Annotations could be similar to Word's 'Track Changes' function. The original report would remain unedited with an auditable version created including clearly identifiable annotations that do not hide or alter the original content. All annotated versions of the document would be stored for audit purposes. Annotations would potentially include: content annotation, content highlight, insertion of external links (e.g. to papers), and explanation of terms.

In addition to patient provision, annotated reports would be used for multi-disciplinary team meetings. An ability to copy sections would facilitate the drafting of presentations.

2.4. Treatment Option Assessment

The treatment option assessment process is similar to the initial assessment, except that now the condition variant(s) has been identified from the genomic test, and the most appropriate treatment can be sought.

Clinicians would be able to search for advice on treatment options, through standard information on the condition variant (e.g. clinical guidelines), knowledge base of research and previous patient treatments and outcomes. This would provide them with information on variant detection accuracy, treatment options, mitigating factors, variant treatment outcomes, as well as being able to view other patients 'like' the one under review, with treatment and outcome. With this information at hand, clinicians would be best positioned to decide on the appropriate treatment pathway.

3. Evaluation of the Clinician Decision Support Tool

We have designed the clinician support tool based on articulated need. Feedback on the system in use will determine whether an automated system based on current need is sufficient, or if we need to develop new ways of interacting with genomic data. A protocol to evaluate the technology for efficacy and effectiveness would be developed based on the parameters of the population in which it is tested. This technology evaluation would be conducted with existing patients and clinicians involved in the

research conducted by the Melbourne Genomics Health Alliance and would involve three stages.

Stage 1: An early prototype version of the portal would be provided to a group of clinicians for feedback on individual components and usability of the portal as a whole.

Stage 2: A close-to-ready version of the portal will be provided in clinician focus groups to obtain qualitative feedback on the functionality of the portal, specifically on fine-grained aspects of user experience and user acceptance.

Stage 3: A version of the portal will be released for trial by a limited cohort of clinicians. Logs of their interaction with the portal would be analysed quantitatively. The analyses would address the uptake of the components (their use by clinicians), observable usability metrics (repeated actions, help requests), efficacy of decision support (uptake of suggestions), and overall contribution of the portal to patient care (reduced time and interoperability). Following this final stage, the portal would be ready for wide release.

4. Discussion

Here we describe the design of a potential prototype that would meet the requirements of clinicians as identified at this primary stage of genomic data integration into every day healthcare. The proposed portal provides clinicians with the ability to search the repository of past tests integrated with clinical data; make and track orders for genomic testing; share annotated reports with clinicians and genetic counsellors; build patient records by extracting information from health record and previous genetic testing where applicable; search 'people like this' to find similar cases, treatment options and where possible outcomes, and receive updates on new findings relating to past patients with specific variants, conditions, or treatments from files within the repository.

At this early stage, clinicians' views are both optimistic and limited. The ability to search for similar patients and their treatment outcomes seems beyond current resources, in that the data is not stored in a searchable format, and appropriate search tools have not been developed. As genomic medicine is in its infancy, the value and usability of a genomic repository will increase as the data within it grows and research on variants of unknown significance advances. The ability to leverage existing anonymised clinical data to search 'people like this' is a concept rapidly gaining popularity in big data frameworks and will be complemented by electronic health records. In the absence of published evidence on the implications of specific variants, the deployment of a comparative tool like Green Button [9] could facilitate improved patient care.

The ability to provide patient focused reports is another visionary aspect of clinician requirements on the verge of becoming reality. A recent US study looked at the family centred elements, language and format required to provide genomic reports to patients [10, 11]. Such a report is a good starting place to meet the needs of Australian clinicians in providing enhanced genomic information to patients, in addition to other resources clinicians identified as being of value.

Where the clinicians' views were limited, was in the realm of designing technology to support a health service of which we are just on the frontier. Genomic sequencing is likely to revolutionise personalised medicine in ways that we currently can only imagine. The requirements that clinicians have of the decision support tool are limited to those they can perceive to be of use today. As sequencing becomes more mainstream,

and used for a wider range of applications, the technology will require modifications to ensure the functionality is equal to the purpose to which it is applied.

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