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The Undiscovered Country: The Future of Integrating Genomic Information into the EHR

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The papers in this special issue take advantage of the research and experience of the eMERGE network and are designed to provide operational and academic leaders a "getting started" guide for integrating genomic information into the EHR. As noted in the paper by Gottesman, et al., [1] the eMERGE network has been actively researching issues that shed light on the integration of genomic information into the EHR However, as the authors in this special issue have indicated, many questions and challenges remain. We have completed mapping of terra incognita and have now arrived at the shores of the undiscovered country.

Additional discussion, education, and research need to occur in order to determine the placement and role of genomic results in the EHR. One challenge is that guidelines for the interpretation and use of genomic results in clinical care need to be established. Additionally provider education on the interpretation and value of genomic results in clinical care is sorely needed. Germline genetic results were previously the province of geneticists and involved extensive counseling, while genomic results which have the potential to impact care in multiple specialties involves providers who are not geneticists. How much education then is required? Enough to interpret results and, if necessary facilitate referral to experts for further evaluation of the test and treatment like an echocardiogram and cardiology, or more like lab test results where providers know what the result is and are given reference ranges that guide action on it? There is the added wrinkle of DTC (Direct to Consumer) testing that will require additional provider understanding and education [2]. As Hartzler et. al [3] noted in their paper, there are many discussions that need to take place among the various stakeholders. The complex ethical issues among the stakeholders were well covered by Hazin et al. [4]

Hartzler et. al. [3] also touched upon genomic results being available in Personal Health Records or Patient Portals (PHRs). Will genomic information obtained at medical centers be available in the PHR? Test results in PHRs can either be manually released in which case the provider must release the result to the patient or autoreleased in which case the result is automatically sent to the patient after a fixed interval of time. Most sites have found that autorelease of lab test results is well accepted by patients and does not generate excessive

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phone calls or PHR messages[5]. The underlying assumption is the patient will ask questions and/or the provider will contact to discuss any abnormal results. Can the same approach for release of lab results in the PHR be used for genomic results? Are genomic results more equivalent to sensitive tests such as HIV? In New York State HIV test results require counseling which precludes autorelease. Current standards for the reporting of single gene test results recommend genetic counseling[6] and certain extremely sensitive test results such as presymptomatic testing for Alzheimer or Huntington diseases require extensive pre- and post-test counseling[7,8]. Alternatively are genomic results more akin to radiology results which many centers are wrestling with given that the reports are written for providers and are not easily interpretable by the lay public? These reports also include incidental findings that may or may not have been discussed with the patient by the ordering clinician. Radiology results as well as pathology results are not routinely autoreleased at many sites[5] although one of the authors (MSW) notes that radiology reports as well as patient-controlled image downloads are now available at Geisinger Health System.

It is difficult to prognosticate how much direct access to genomic test results patients will have because of two developments. Unlike the diagnostic testing discussed above, (i.e., laboratory, imaging, and pathology) patients can order and view their own results through Direct-to-Consumer (DTC genomic testing. How DTC testing will interact with provider ordered testing, viewable in the PHR, is unclear. It also remains an open question of whether or not there will be widespread uptake of DTC genomic testing. Nevertheless, companies involved in the DTC space have developed innovative ways to represent genomic test results that have been shown to be comprehensible and accessible to consumers[9,10]. These methods may be instructional to PHR designers. The appropriately named Open Notes research project, is releasing all progress notes to the patient and the initial results are encouraging[11]. This would make any discussion of which test results to autorelease in the PHR potentially moot as progress notes may contain test interpretations by providers.

It remains unclear which diagnostic tests genomic results are most analogous to in terms of provider reporting and interpretation [12,13]. Papers in this issue have discussed delivering the raw data, the result and the interpretation. Genomic education of both providers and patients remains a pressing need as results and interpretation of results may be confusing or meaningless to many providers[14–18] as well as most patients[19]. To date, other than the specialty of genetics and the need for counseling, few providers seem to want to see the raw genomic data let alone have the means to understand it[20]. As in the setting of other complex tests, most providers want interpreted reports though as noted earlier challenges remain with education. Laboratory tests are generally stored in EHRs as discrete, interpreted results. The raw data are not presented as healthcare providers do not want to read spectrograms to determine the patient's electrolyte levels. In contrast imaging presents the raw data, images, and interpretation to EHR users. Imaging uses links to a Picture Archival Communication System (PACS) and the interpretation is stored as a text blob. In the case of imaging, specialists prefer reading their own imaging with assistance available as needed from radiologists etc. Pathology is somewhere in between in that the interpreted free text reports are always stored in an EHR but viewing pathology specimens requires going to pathology to view them.

Like pathology, genomic test results are returned as unstructured text. The near future evolution of pathology reporting may be a guide to what could happen to genomic test reports. To improve the utility of the reports, the College of American Pathologists has recommended the use of synoptic reporting for certain cancers[21,22]. Synoptic reporting incorporates free text into a structured format that allows for the data to also be represented as discrete elements. This concept has been expanded to create documents that are both human and machine readable through the use of clinical document architecture (CDA). From their 2006 article Dolin et al. [23] state, "CDA is a … standard that specifies the structure and semantics of a clinical document … for the purpose of exchange. A CDA document is a defined and complete information object that can include text, images, sounds, and other multimedia content. It can be transferred within a message and can exist independently, outside the transferring message."[23] Some have suggested that CDA documents could be used for genetic and genomic test reporting, and the Health Level 7 clinical genomics workgroup has created a CDA implementation guide for genetic testing reports[24]. This prototype is now available for testing and the model is being extended to support genomic data. Chute et al. [25] discuss this in more detail. Is this the solution to the reporting conundrum?

Overby's [26] and Marsolo's [27] papers address the use of Clinical Decision Support (CDS) to facilitate the use of genomic information in healthcare as well as the current state of CDS in eMERGE sites. Many sites have focused their CDS work on pharmacogenomics which provides prescribing recommendations based on genomics and for which there are published guidelines[28]. Use of this information has become increasingly routine. For clopidogrel the FDA has a black box warning that recommends genomic testing be considered as "an aide for determining therapeutic strategy"[2930–34]. For Abacavir the FDA has a black box warning requiring HLAB*5701 testing[35]. Denny's[36] paper in this special issue describes pharmacogenomics in an internally developed EHR. Besides clinical utility and focused use, CDS for pharmacogenomics has one other advantage which is the use of structured data; drug information such as name and dose. Use of structured data also lends itself to capture of outcomes data, which is critical to the development of robust evidence of utility.

CDS will require actionable discrete data that can be stored and represented in the EHR[13]. Papers in this issue and others have noted representation and storage of genomic information in the EHR has remained challenging as most commercial EHRs are not up to the task. While the data needs to be stored in a structured form the paper by Kho et al.[37] summarizes where we are today with the storage of discrete phenotypic data that can be linked to genomic data which is equally important to CDS. The paper by Tarczy-Hornoch highlights the needs for standard representation in test resulting in addition to CDS[38]. Even when sites used the same sequencing technology and commercial EHR, customized solutions were required at each site. As Chute et al.[25] note the standards to make this happen are still evolving and as a result commercial EHR vendors have been slow to incorporate genomic results.

By its very nature, CDS depends on a knowledge base and rules engine[3940]. This makes CDS challenging for genomic test results in that both the knowledge and the rules around this knowledge are rapidly changing[41]. As a result both the knowledge base and rules engine

require frequent and rapid revisions. Ury[42] in his paper explores this problem. It is the long-held belief of the authors that interpreted results residing in EHR, the CDS rules, and the knowledge itself will need to be "versioned". This paper defines the term versioning as the creation of a standardized and systematic methodology for dating and numbering the rules and knowledge in a consistent way as well as systematically recording changes in content. Older versions of the CDS rules and knowledge would be archived indefinitely in a yet to be developed knowledge maintenance schema. Without versioning it will be impossible to tell why possibly contradictory actions were taken on what seems to be the same genomic results at different times. Versioning would tie the decision to the knowledge available to the clinician *at that specific point in time* which is critical for liability and quality improve purposes.

Since challenges remain for storing genomic results in an EHR as discrete data as well as the need to rapidly update the knowledge base and the decision rules, several sites have begun developing external CDS. In external CDS, the knowledge base and rules engine reside outside of the EHR. This methodology has begun to be used to help standardize knowledge and implementation of rules across multiple sites[39,43] and has the potential to accelerate implementation. Efforts to facilitate the adaptation of external CDS have focused on producing agnostic extensible CDS that could be shared by multiple sites[44,45]. The challenge with external CDS for genomic results is to make the genomic CDS actionable. Without standards many sites are challenged with presenting little more than recommendations at the point of care which ask the user to consider the information and take action if the user feels appropriate. The approach of presenting CDS as FYI (For Your Information) is not desirable as David Bates and others have noted[46]. Chute et al.'s[25] paper calls attention to the need for standard representation and notes that taxonomy and development of these standards as well as others might solve this conundrum. It is the belief of the authors that within the next few years, we will see researchers develop external CDS capable of generating messages that trigger specific actionable items in a commercial EHR. Until standard representation of genomic results occurs, widespread adaptation of CDS by commercial EHRs will continue to be challenging irregardless of value propositions by providers and patients.

CDS for Genomic Testing will also have to address issues of confidentiality and privacy. In contrast to other forms of diagnostic testing (i.e., laboratory, imaging, pathology), genomic testing is somewhat unique regarding its privacy and confidentiality issues[17,47]. There remains significant concern about the impact of genomic test results on a patient's health insurance and perhaps even employment[48], despite the passage of the Genetic Information and Nondiscrimination Act[49,50]. While both Hartzler[3] and Hazin[4] addresses this much still needs to be discussed and done. The age of whole genome sequencing is rapidly approaching and patients will be presented with results that they neither want nor understand and for which providers struggle to interpret[20,51]. Unless we provide a secure and trustworthy environment for the storage of genomic information and combine this with public policies that protect against the misuse of this information, there will be concern about the routine use of this information for health care, even when it has been shown to improve outcomes.

In conclusion, we have completed an initial mapping of terra incognita with this special issue summarizing the knowledge, experience and wisdom of eMERGE consortium members. While much has been learned, many questions remain. A concerted and collaborative effort involving all groups working on these daunting problems will help to generate solutions that will allow genomics to move into clinical care. We have arrived on the shores of the future, the undiscovered country and though much remains to be resolved, the future looks so bright we ought to be wearing shades.

References

1. Gottesman O, Kuivaniemi H, Tromp G, et al. The Electronic Medical Records and Genomics (eMERGE) Network: Past, Present and Future. Genet Med. 2013; 15(10) in press; this issue.
2. Powell KP, Christianson CA, Cogswell WA, et al. Educational needs of primary care physicians regarding direct-to-consumer genetic testing. J Genet Couns. Jun; 2012 21(3):469–478. [PubMed: 22207397]
3. Hartzler A, McCarty CA, Rasmussen LV, et al. Stakeholder Engagement: A Key Component of Integrating Genomic Information into Electronic Health Records. Genet Med. 2013; 15(10) in press; this issue.
4. Hazin R, Brothers KB, Malin BA, et al. Ethical, Legal and Social Implications of Incorporating Genomic Information into Electronic Health Records. Genet Med. 2013; 15(10) in press; this issue.
5. Kannry J, Beuria P, Wang E, Nissim J. Personal health records: meaningful use, but for whom? Mt Sinai J Med. Sep; 2012 79(5):593–602. [PubMed: 22976365]
6. Matsuda I, Niikawa N, Sato K, et al. Guidelines for genetic testing. The Japan Society of Human Genetics, Council Committee of Ethics. J Hum Genet. 2001; 46(3):163–165. [PubMed: 11310587]
7. Goldman JS, Hahn SE, Catania JW, et al. Genetic counseling and testing for Alzheimer disease: joint practice guidelines of the American College of Medical Genetics and the National Society of Genetic Counselors. Genet Med. Jun; 2011 13(6):597–605. [PubMed: 21577118]
8. Craufurd D, Tyler A. Predictive testing for Huntington's disease: protocol of the UK Huntington's Prediction Consortium. J Med Genet. Dec; 1992 29(12):915–918. [PubMed: 1479607]
9. 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. Jun; 2012 21(3):413–422. [PubMed: 22278220]
10. Vayena E, Gourna E, Streuli J, Hafen E, Prainsack B. Experiences of early users of direct-to-consumer genomics in Switzerland: an exploratory study. Public Health Genomics. 2012; 15(6): 352–362. [PubMed: 23154382]
11. Delbanco T, Walker J, Bell SK, et al. Inviting patients to read their doctors' notes: a quasi-experimental study and a look ahead. Ann Intern Med. Oct 2; 2012 157(7):461–470. [PubMed: 23027317]
12. McGuire AL, Cho MK, McGuire SE, Caulfield T. Medicine. The future of personal genomics. Science. Sep 21.2007 317(5845):1687. [PubMed: 17885116]
13. Starren J, Williams MS, Bottinger EP. Crossing the omic chasm: a time for omic ancillary systems. Jama. Mar 27; 2013 309(12):1237–1238. [PubMed: 23494000]
14. Nickola TJ, Green JS, Harralson AF, O'Brien TJ. The current and future state of pharmacogenomics medical education in the USA. Pharmacogenomics. Sep; 2012 13(12):1419–1425. [PubMed: 22966890]
15. Bonter K, Desjardins C, Currier N, Pun J, Ashbury FD. Personalised medicine in Canada: a survey of adoption and practice in oncology, cardiology and family medicine. BMJ Open. Jan 1.2011 1(1):e000110.
16. Babyatsky, M.; Giovanni, M.; Murray, M. Clinical Genomics: Practical Applications in Adult Patient Care. McGraw Hill; 2013.
17. Liaw ST. Genetics and genomics in general practice. Aust Fam Physician. Sep; 2010 39(9):689–691. [PubMed: 20877778]

18. Gullapalli RR, Desai KV, Santana-Santos L, Kant JA, Becich MJ. Next generation sequencing in clinical medicine: Challenges and lessons for pathology and biomedical informatics. J Pathol Inform. 2012; 3:40. [PubMed: 23248761]
19. Brewer NT, Tzeng JP, Lillie SE, Edwards AS, Peppercorn JM, Rimer BK. Health literacy and cancer risk perception: implications for genomic risk communication. Med Decis Making. Mar-Apr;2009 29(2):157–166. [PubMed: 19050227]
20. Manolio TA, Chisholm RL, Ozenberger B, et al. Implementing genomic medicine in the clinic: the future is here. Genet Med. Apr; 2013 15(4):258–267. [PubMed: 23306799]
21. Hassell L, Aldinger W, Moody C, et al. Electronic capture and communication of synoptic cancer data elements from pathology reports: results of the Reporting Pathology Protocols 2 (RPP2) project. J Registry Manag. Winter;2009 36(4):117–124. quiz 163–115. [PubMed: 20795553]
22. Baskovich BW, Allan RW. Web-based synoptic reporting for cancer checklists. J Pathol Inform. 2011; 2:16. [PubMed: 21572504]
23. Dolin RH, Alschuler L, Boyer S, et al. HL7 Clinical Document Architecture, Release 2. J Am Med Inform Assoc. Jan-Feb;2006 13(1):30–39. [PubMed: 16221939]
24. Groups HCGaSDW. CDA Implementation Guide: Genetic Testing Report (GTR). 2013. http://www.hl7.org/documentcenter/public_temp_20DA1AE7-1C23-BA17-0CCEBE0F4D95D6A8/wg/clingenomics/presentations/CDA%20IG%20for%20Genetic%20Testing%20Report%20-%20May%202013%20-%20Shabo.pdf
25. Chute CG, Ullman-Cullere M, Wood G, Lin SM, He M, Pathak J. Some Experiences and Opportunities for Big Data in Translational Research. Genet Med. 2013; 15(10) in press; this issue.
26. Overby CL, Kohane I, Kannry JL, et al. Opportunities for Genomic Clinical Decision Support Interventions. Genet Med. 2013; 15(10) in press; this issue.
27. Marsolo K, Spooner SA. Clinical Genomics in the World of the Electronic Health Record. Genet Med. 2013; 15(10) in press; this issue.
28. PharmaGKb CPICC. [Accessed July 2, 2013] CPIC Gene-Drug Pairs. http://www.pharmgkb.org/page/cpicGeneDrugPairs
29. FDA. [Accessed July 11, 2013] Black Box Warning for Plavix. 2010. http://www.accessdata.fda.gov/drugsatfda_docs/label/2010/020839s042lbl.pdf
30. Goswami S, Cheng-Lai A, Nawarskas J. Clopidogrel and genetic testing: is it necessary for everyone? Cardiol Rev. Mar-Apr;2012 20(2):96–100. [PubMed: 22293861]
31. Kim KM, Murray MD, Tu W, et al. Pharmacogenetics and healthcare outcomes in patients with chronic heart failure. Eur J Clin Pharmacol. Nov; 2012 68(11):1483–1491. [PubMed: 22543981]
32. Mette L, Mitropoulos K, Vozikis A, Patrinos GP. Pharmacogenomics and public health: implementing ‘populationalized’ medicine. Pharmacogenomics. May; 2012 13(7):803–813. [PubMed: 22594512]
33. Bartlett MJ, Green DW, Shephard EA. Pharmacogenetic testing in the UK clinical setting. Lancet. Jun 1.2013 381(9881):1903. [PubMed: 23725729]
34. Turner RM. From the lab to the prescription pad: genetics, CYP450 analysis, and medication response. J Child Adolesc Psychiatr Nurs. May; 2013 26(2):119–123. [PubMed: 23607823]
35. FDA. [Accessed July 11,, 2013] Ziagen (abacavir) Safety Warning. 2008. http://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm079913.htm
36. Peterson JF, Bowton E, Field JR, et al. Electronic Health Record Design and Implementation for Pharmacogenomics: a Local Perspective. Genet Med. 2013; 15(10) in press; this issue.
37. Kho AN, Rasmussen LV, Connolly JJ, et al. Practical challenges integrating genomic data into the electronic health record. Genet Med. 2013; 15(10) in press; this issue.
38. Tarczy-Hornoch P, Amendola L, Aronson SJ, et al. A survey of informatics approaches to whole exome and whole genome clinical reporting in the electronic health record. Genet Med. 2013; 15(10) in press; this issue.
39. Wright A, Sittig DF. A framework and model for evaluating clinical decision support architectures. Journal of Biomedical Informatics. 2008; 41(6):982–990. [PubMed: 18462999]

40. Kannry, J. Computerized Physician Order Entry and Patient Safety: Panacea or Pandora's Box?. In: Ong, KR., editor. Medical informatics : an executive primer. Vol. xviii. Chicago, IL: HIMSS; 2007. p. 316
41. Evans JP, Khoury MJ. The arrival of genomic medicine to the clinic is only the beginning of the journey. Genet Med. Apr; 2013 15(4):268–269. [PubMed: 23306801]
42. Ury A. Storing and Interpreting Genomic Information in Widely Deployed Electronic Health Record Systems (EHR's). Genet Med. 2013; 15(10) in press; this issue.
43. Wright A, Sittig DF. A Four-Phase Model of the Evolution of Clinical Decision Support Architectures. International journal of medical informatics. Oct; 2008 77(10):641–649. [PubMed: 18353713]
44. Kawamoto K, Del Fiol G, Orton C, Lobach DF. System-agnostic clinical decision support services: benefits and challenges for scalable decision support. Open Med Inform J. 2010; 4:245–254. [PubMed: 21603281]
45. Hongsermeier T, Maviglia S, Tsurikova L, et al. A legal framework to enable sharing of Clinical Decision Support knowledge and services across institutional boundaries. AMIA Annu Symp Proc. 2011; 2011:925–933. [PubMed: 22195151]
46. Bates DW, Kuperman GJ, Wang S, et al. Ten commandments for effective clinical decision support: making the practice of evidence-based medicine a reality. J Am Med Inform Assoc. Nov-Dec;2003 10(6):523–530. [PubMed: 12925543]
47. McGuire AL, Fisher R, Cusenza P, et al. Confidentiality, privacy, and security of genetic and genomic test information in electronic health records: points to consider. Genet Med. Jul; 2008 10(7):495–499. [PubMed: 18580687]
48. Allain DC, Friedman S, Senter L. Consumer awareness and attitudes about insurance discrimination post enactment of the Genetic Information Nondiscrimination Act. Fam Cancer. Dec; 2012 11(4):637–644. [PubMed: 22890887]
49. Clifton JM, VanBeuge SS, Mladenka C, Wosnik KK. The Genetic Information Nondiscrimination Act 2008: What clinicians should understand. J Am Acad Nurse Pract. May; 2010 22(5):246–249. [PubMed: 20500738]
50. Feldman EA. The Genetic Information Nondiscrimination Act (GINA): public policy and medical practice in the age of personalized medicine. J Gen Intern Med. Jun; 2012 27(6):743–746. [PubMed: 22314637]
51. Ginsburg GS, Willard HF. Genomic and personalized medicine: foundations and applications. Transl Res. Dec; 2009 154(6):277–287. [PubMed: 19931193]