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Managing Expectational Language: Translational genetic professionals consider the clinical potential of next-generation sequencing technologies

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This paper is about managing expectations in translational medicine involving next generation sequencing (NGS) through whole genome/exome sequencing (WG/ES) tests for the clinic. Translational medicine, put colloquially, is the concept of moving bench science to the bedside, that is, moving research from the laboratory to the clinic. Similar to other biotechnologies, NGS (for medicine) is shot through-and-through with rhetoric of anticipation, promises, skepticism, pessimism, hope, and hype. For more than a decade since the draft sequence of the Human Genome Project (HGP), we have seen these articulated, debated, and represented often through discussions about and efforts to deliver on (personalized) genomic medicine (PGM). Since then, scientists, policy makers, entrepreneurs, and other proponents have made some great strides to develop research, infrastructure, resources, and social imagination to make this vision of medicine happen. Sequencing has been an important component. Here, it hasn't only been new developments in the life sciences at the intersection of computer science and information technology or efforts to reduce cost and time to sequence that have allowed for the current state of whole genome sequencing. Developing vision across disciplines, professionals, and environments for which these sequencing technologies could be used for health and medical purposes has also been vital.

Through focus group data concerned with genomics in the clinical environment with diverse professionals, we examine and explore how these actors manage expectations, especially promissory ones, just as these technologies enter in some early ways into their work environment. These are actors who are not, as Harry Collins (2002) and others describe, in the *core set* of researchers or expectation producers of NGS, but are still relevant. Such an examination and exploration can help us not only understand the function of expectations about emerging-to-new technologies, but make expectations more explicit as well as, perhaps, help find areas of accord for the diverse actors, or stakeholders, involved. This analysis is informed by the growing field of sociology of expectations (SE) and, to lesser extents, research on public understanding of science (PUS) and user design. Initially

emerging out of a concern with innovation in the sociology of technology (Borup *et al.* 2006, Rappert 1999, van Lente and Rip 1998), SE emphasizes, in particular, the performativity of representations of the future. Projects of the future are performative (Brown *et al.* 2000, Rappert and Brown 2000, Rosengarten and Michael 2009) in that the aims of representations or assemblages of the future are to construct a particular present. Many case studies have shown how expectation producers, for instance, persuade other actors in the present to align themselves with that future in a variety of ways (e.g. facilitating collaboration). Researchers have studied new bio(medical) technologies including human embryonic stem cell research (Michael *et al.* 2007), regenerative medicine (Martin *et al.* 2008a); xenotransplantation (Brown and Michael 2003), biobanking (Tutton 2007), pharmacogenetics and personalized medicine (Hedgecoe 2004), avian flu (Nerlich and Halliday 2007) as well as nanotechnology (Selin 2007; 2008).

A central focus in SE has been contests over the status of such futures. Adam Hedgecoe showed how those outside the core set of Alzheimer's research specialists were enrolled, for instance, into expectation making in his study of Alzheimer's (Hedgecoe 2006). These (biomedical) entities, for which expectations are generated, are then always in transformation as are their expectational efforts. As we pick up on this thread of SE, we view such objects, in our case, NGS for medicine as WG/ES tests, undergoing such translational processes. Efforts are being made to turn NGS into workable clinical tests, but simultaneously expectations are in translation. This paper examines and explores this situation. Specifically, we examine the articulations of this diverse group of professionals, on the border of the core set, and show how they view expectations for NGS and WGS tests for the clinical environment. Our contribution to the literature on expectations is aimed, then, at illuminating expectations and how expectational representations orient themselves to the matter of translation discursively. On this order, this analysis is informed by the literature of SE that examines expectations as representations of the future and puts these in conversation with PUS literatures discussed further below, but first we turn to introduce NGS.

Next-generation sequencing (NGS) and clinical genomics

For our purposes, we are defining NGS as all post Sanger sequencing methods, from approximately 2004 to present. This is important to point out, because in the technical literatures today, sequencing technologies are still in formation. Advances in NGS technologies have sparked much speculation about the clinical opportunities that might be enabled by these new tools (Klee *et al.* 2011, Meyerson *et al.* 2010, Ross and Cronin, 2011, Ware, 2011). NGS methods are widely understood in the sequencing literature and propounded to wider circles to increase output, cut costs to sequencing, and be more versatile than Sanger methods. They enable large-scale genotyping such as whole exome sequencing/whole genome sequencing (WES/WGS) that many sequencing proponents are prospecting for the clinical arena. These clinical opportunities might include, for example, new diagnostic tools for identifying genetic causes of Mendelian and common diseases; population-based tests to facilitate preventive interventions; and tools for driving down the costs of genetic testing (Tucker *et al.* 2009). These new technologies currently are not a routine part of patient care, however, even for specialists in medical genetics.

NGS are (*re*)-*emerging* technologies, that is, there currently is considerable re-visioning in their development and analytic methods (Kingsmore and Saunders 2011). The reiteration and serial re-production with some technical and cost-efficiency tweaking as in the third generation systems, and as referenced as ‘next-next generation sequencing,’ (improvements after the 2nd) help highlight this point (Schadt *et al.* 2010). While technical literatures present NGS’ development, they also present its soon-to-be value in the clinical arena. We have seen and continue to see the promissory representations of NGS for WGS tests for population and individuals in technical, trade, and popular literatures (ten Bosch & Grody 2008; Zhao and Grant 2011). Genomic researchers such as ten Bosch and Grody, from UCLA, wrote,

“The impact that these “next-generation” sequencing innovations will have in clinical genetics will certainly be substantial.... Eventually, the perceived clinical benefit of whole-genome sequencing will outweigh the cost of the procedure, allowing for these tests to be performed on a routine basis for diagnostic purposes....” (484)

While promissory, the representation is not uncontested within the research community, e.g. Ku *et al.* (2012), Roberts *et al.* (2012), and Voelkerding *et al.* (2010). However, promissory statements and similar comments (to the one above) about NGS’ eventual impact on clinical genetics are often found in introductions or conclusions of NGS papers e.g. Baudhuin *et al.* (2012), reviews, e.g. Koboldt *et al.* 2013 and editorials e.g. Drmanac (2012), and it has led to critique from within biomedical and healthcare communities and without to tone down the promises (Evans *et al.* 2011, O’Rourke 2013). These critics often point out that more realistic language is necessary considering that there have been little wide advancements in translational medicine.

From the clinical literature, NGS is widely seen as an *unproven* technology for normal patient care settings, although at the time of this focus group study, a number of suggestive illustrations of its clinical potential were published (Ashley *et al.* 2010, Lupski *et al.* 2010). Yet it has become common to state that genomic science or, rather, NGS development is moving rapidly, clinical use soon-to-be (Choi *et al.* 2009), and its clinical improvement dependent on its broad use (Raffan and Semple 2011, Kreiner and Buck 2005, Pettersson *et al.* 2008). Many of these sequencing researchers seem to play the fence that clinical tools coming out of NGS should be viewed as both research (‘discovery’) and clinical (‘diagnostic’) tools (Ku 2012). This can be read as promissory, but it also engenders some tension.

This paper takes as its point of departure the promissory narrative around NGS and the contest to it. Building on SE research that considers how different groups manage expectations (Tutton *et al.* 2008, Wainright *et al.* 2006, Webster 2009), in this paper, we show the tensions in this situation and efforts of some translational genetic professionals – who together cross boundaries of bench, clinical research, clinic, and policy – to manage this situation in light of what many of the focus group participants saw as linked to the impending inevitability of WG/ES tests as the norm in clinics.

Conceptual framework

This study on expectations in translational medicine sits at the intersection of user studies that examine how users are made or enrolled (Akrich 1992), public understanding of science (PUS), and sociology of expectations in the area of biomedicine and biotechnology. With few exceptions (McGowan *et al.* 2010, Bloss *et al.* 2011), much of the recent US ELSI research on users and genomic medicine has focused on studying lay awareness, perspectives, and experience of the new personal genomics for medicine (McBride *et al.* 2010, McGuire *et al.* 2009), often defining lay as non-experts or consumers. This important research follows social research in the lead up to the HGP and after, on PUS and genetics (Condit 1999, Condit 2012, Bates *et al.* 2005). This research primarily studies attitudes and perspectives as well as level of technical knowledge of the general public in the area of genetics, while science studies research on ‘users,’ such as those of Madeleine Akrich and colleagues (2008), show consumers or patients as (co)-producers of knowledge. This latter signals an important growth in our insight to our understanding of knowledge production, but we need as well to continue our study of others (here a group of diverse professionals whose work concerns translational genomics into the clinic) who may also be involved. We have seen some studies on health care professionals’ views specifically on direct-to-consumer (DTC) genetics (Powell *et al.* 2011, Hock *et al.* 2011), or technical experts’ own attitudes and motivations for using genomics tests (O’Daniel *et al.* 2010), but few have examined and explored with translational genetics’ and allied professionals’ their views on NGS and genomic testing, even though they will no doubt be vital in shaping forms of ‘clinical genomics’ and ‘personalized medicine.’ The focus group (FG) study used in this analysis was an attempt to fill this gap.

We follow on user-studies that problematize ‘public’ by interrogating the boundaries between user (often represented as ‘consumer’/producer) and expert/lay (Oudshoorn and Pinch 2003). From our perspective, these professionals might be considered users (consumers of these tools) and (potential) producers who may tweak or be earlier designers of genomic tests and concepts embedded within them. They convey that they provide different expertise from the core researchers of NGS and bench genomics or manufacturers of WE/S.

Furthermore, while not in the core set of researchers or expectation producers, this study not only examines and explores some of their views about NGS and WG/ES tests, it argues through the frame of SE that their representations can be viewed as constitutive to expectation creation. Representations of science are often viewed as the purview of PUS, but SE allows us to think about discourse, and specifically representation, as performance and so material in the sense of being action-oriented. Many SE studies show the role of expectation as representations of future building through news media (Horst, 2007, Nerlich and Halliday 2007, Kitzinger and Williams 2005) as well as commercial entities (Petersen and Sear 2011, Tutton 2011), while others show how scientists’ representations can be implicated in the production of expectations (Harvey 2009, Hedgecoe 2006). SE allows us to move from studying these representations as only ephemeral rhetoric, language, or representation to something more material, performative.

It is also important to recognize the PUS research on representations of science (Nelkin 1995, Nelkin and Lindee 1995, Petersen 2001, Turney 1998, van Dijck 1997). This research convincingly showed the production of hype evident amongst genetic and biotechnology enthusiasts as well as sensationalizing in media reporting and popular culture. Despite this research, we continue to see what we may call the ‘hype’ frame even by genomic scientists e.g. Friend and Ideker (2011). In the area of biomedicine and biotechnology SE researchers have shown not only that much of this rhetoric has been framed in terms of generating crass hype or developing a vision of acceptable hope but that these particular expectational discourses have function (Martin *et al.* 2008b, Moreira and Palladino 2005, Petersen and Seear 2011, Novas 2006). While acknowledging the existence and importance of making visible hype in this arena, SE and allied scholars suggest that we need to take a more nuanced and critical look at the *functions* of this ‘hype’ as well as other expectational (e.g. promissory and pessimistic) language in genomic sciences today (Fortun 2001, Hedgecoe and Martin 2003, Tutton 2011). They show, for examples, how expectational, speculative, and promissory narratives about genomics travel discursively and can become instantiated institutionally, organizationally, and individually (Fortun 2008, Rajan 2006, Brown 2003).

To some extent we saw this promissory trajectory, especially about NGS, in the data. While not wholeheartedly accepting this type of expectational talk, many of the focus group participants were aware of the importance of future talk, even if somewhat hyped. However, this paper contributes to SE precisely by showing explicitly discursive examples of some responses such embedded promissory expectational talk in NGS for clinical genomic testing as well as showing the material force of discourse. In other words, expectations can generate further attempts to represent and so create, by other stakeholders, here, the translational experts in these FGs, new visions about emerging-new technologies and, in doing so, they can co-envision (new) representations about themselves and their work environment.

Methods & Approaches

For our article, we drew on data from a series of four focus group sessions of Expert Advisory Panels (EAP), across six regional medical sites (Baltimore, Cleveland, Denver, Ann Arbor, Philadelphia, Seattle) across the US. These 24 focus groups (4 rounds; 6 groups) were held over a 20-month period (07.2009-03.2011). These EAPs (designed using focus group methodology) were established to explore the impact of highly multiplexed genetic testing (commonly refers to testing for multiple mutations that give rise to a single disorder but, as here, includes tests for multiple conditions on a single panel) on clinical practice. Focus groups were selected for the following reasons: group interaction can reveal points of agreement, conflict, and uncertainty; they can yield data on meaning, especially its co-construction; and they allow participants a great degree of control over their own interaction.

The sites were selected based on their geographic diversity, their well established programs in human and molecular genetics and genetic counseling, their local translational research programs. The research team and site coordinators identified participants from various backgrounds including specialists in medical genetics, pediatric genetics, genetic counseling, public-health genetics, primary care medicine, laboratory medicine, health communication, law, and bioethics. Participants also assisted in the identification of

alternates in the event of their unavailability at certain sessions. While participants were encouraged to attend all four EAP sessions, the number of sessions attended varied depending on their availability. The make-up of the focus groups was chosen to create potential for new perspectives. In total there were 61 individuals and 9-11 individuals per focus group.

The major topics discussed in the EAP included: 1) the utility of clinical applications; 2) challenges associated with the interpretation and communication of results; 3) ethical and legal implications of use in clinical practice; and 4) participants' overall level of enthusiasm or concern about the introduction of genomic testing into clinical practice. The research team developed semi-structured moderator guides which included open ended questions and case studies that asked participants to give their opinions on a range of multiplexed genetic tests and issues associated with genetic testing. Clinical case scenarios, created by the research team, based on anonymized test results from (then) currently available testing platforms, which could be offered to patients/clients were also included. Participants were provided a folder of materials, consisting of the case scenarios and articles, at the start of each session to review. The articles were characterized as 'non-essential' so participants may or may not have read them for each session. The principal investigator (PI) acted as the moderator for each panel, at times, asking probing questions to direct the discussion during the groups. Participants were not asked to identify themselves professionally when they spoke. Generally, they were asked to discuss how they would respond as clinical genetic professionals in these cases or what they thought of these specific tests with these given scenarios. The approaches used here – of including this diverse set professionals as well as the semi-structured, but open ended conversation – enabled these professionals to react to and build on responses from their colleagues. These resulted in novel opportunities for the production of ideas (Stewart, et al, 2007; Kitzinger, 1994). Conducting several rounds of focus groups over time allowed the collection team to incorporate new research findings, technological developments, industry events, policy initiatives, and media stories in the question guide. For further details of these scenarios we direct readers to Uhlmann and Sharp (2012).

Each expert advisory panel was audio recorded. These recordings were transcribed, and transcriptions were reviewed for accuracy by a research team member. We used two analytic approaches in reviewing the transcripts for this paper. First, we coded for pre-structured and emergent themes. Two coders, JH and MBM, independently coded the transcripts using NVivo. Consensus was reached on the structure of the coded tree. The coders met to compare results and identify and discuss any differences in their coding. Later on, led by PK, the data set was put to further analysis. PK read all the transcripts and conferred with the research team from time to time. While highly multiplexed genetic tests were the organizing theme of this focus group study, clinical applications of NGS technologies were a concern among the participants and discussed. For us, this phenomenon warranted description, analysis, and reflection. This analysis focused in on Rounds 1 and 4 where most of the discussion about WG/ES occurred. This latter analysis and interpretation drew on interpretive, constructivist approaches from STS, specifically sociology of expectations, and focused on discussions about whole genome testing.

Reflexivity

Our analysis follows on other researchers on sociology of expectations who recognize and acknowledge that social researchers' themselves are implicated (Barr and Rose 2008, Selin 2008, Tutton 2011). Following on Barr and Rose, we also acknowledge that by necessity, how genomics and NGS in the clinic were presented must influence responses. Discussions were primarily structured around case scenarios using different genetics/genomic tests in the clinic. When news events, especially noteworthy professional events, such as relevant research or important speeches were made, participants were encouraged to discuss genomics in the clinic in relation to these. In creating these scenarios and in our question frames, researchers are playing some role in contributing to the production of expectations, be it hope, skepticism, etc., surrounding the possible success of these technologies (Hedgecoe and Martin 2003). However, we suggest that the semi-structured and focus-group approach allowed for some more participant-driven discussion.

Troubling & Managing Expectations: from the focus groups—Our primary concern in this article is on how these professionals in the clinical arena were seeking to make sense of NGS technologies in a formative period. While NGS was not a term used by our moderator, the clinical case scenarios were used to facilitate discussions that involve the use of these technologies. We found that participants' views showed complexity, ambivalence, and effort to re-negotiate visions of how NGS could be used as a tool in patient care. At the same time, we found that many participants expressed their frustrations about certain discourses about 'genomics' and 'genomic tests,' specifically as they relate to expectations. We present articulations explicitly on this topic because, in our analysis of the data, we saw a recurrent tension in many of our respondents accounts between what we call an insider's (basic science/researcher) and an outsider's (public/media) view about genomic medicine. Following, we present ways in which participants managed promissory expectations about NGS for clinical use. In analyzing the data, we saw different ways in which they situate WGSTs, which we present here: WGSTs were articulated in relation to work environment, other clinical tool, and professional identity. By no means do we argue that there was consensus. However, we do want to argue that, through these accounts, they construct their own expectations of NGS as WG/ES tests in the clinical environment and attempt to manage these as well. [Note: Throughout this paper we use quotation marks around 'genomics' and 'genomic test' to emphasize that there was no consensus about what these mean.]

'Genomics' and 'Whole Genome Tests': managing 'insider'-'outsider' representations

At the start of the first round of focus groups (R1), participants were asked to reflect upon and define 'genomics' and 'genomic tests.' Defining these terms was not a straightforward task for participants. On the one hand, when probed for definitions of 'genomic test,' some participants responded with characterizations that were bounded by perspectives from the basic, life sciences, as in this example:

P: So a genomic test would be a test of all the DNA, a complete sequence...

P2: Not necessarily [a complete sequence], right, but it's exploratory in nature because it's not predefined. [Round 1, Group 5]

Others elaborated. In the example below, this participant explains that when he hears the term ‘genomic’ test ‘two things’ come to mind and goes on to explain:

P: ...One is scale and the other is completeness. So a genome is a scale. It's a very large combination of genetic elements that interact and so a genomic test to me is something that, um, at least samples broadly from among those and it's more than – and then the completeness bit...one of the definitions that people use in basic science is it's all of the genetic information in an organism. It contains *all of it* and so it's not just *a lot* – but genomic, I think too many people in the field mean all that there is. So, there's not only the size and scale but the completeness of the test. We're not leaving anything out. [Round 1, Group 4]

In this context, participants presented what we might call an insider's or basic science expert's perspective on the meaning of ‘genomic’ and ‘genomic tests.’

These participants made these comments when asked for their ‘global’ or more general view of ‘genomics.’ As discussions turned to particular examples of multiplexed genetic tests, they often framed their views of ‘genomic’ and ‘genomic tests’ in terms that reflected their perceptions of how non-genetic professionals’ viewed these technologies. For instance, many stated that they had not heard patients use the term ‘genomic test’ but that they had heard primary care physicians (PCPs) use the term. As discussions shifted to more specific examples of emerging clinical tools, participants tended to discuss ‘genomic’ and ‘genomic tests’ within what we are calling an ‘outsider’ representation that reflected a socio-technical concept for genomics. For example, many participants believed that non-genetic professionals, especially lay people equated the term ‘genome’ with *the whole genome* and even the Human Genome Project, for example,

P: ...I think a lay person first thinks of genome as in ‘Human Genome Project,’ as in the original term when that was introduced to the public and what that means. And there they see it as an enterprise, whether it's led by, you know, government agencies, whether it's by private entities...and I, I think they tend to – the lay person tends to see it as the whole thing – the whole kit and caboodle. [Round 1, Group 3]

Further, for many participants, the term ‘completeness’ was used in the public's understanding of ‘genomics’ and ‘genomic test’ (what we call ‘outsider’ view) as well as the basic/bench scientists (‘insider’). However, their meanings differed. They articulated that publics and non-genetic professionals have an overly simplified view of the complete ‘genome’ and ‘genomic test,’ thinking about them in terms of the *‘whole thing,’* making reference to the biomedical *‘enterprise,’ ‘Human Genome Project,’* and the whole *‘kit and caboodle.’* In contrast, genetic professionals’ (or *‘researchers’*) ‘insider’ views about completeness were some participants said more about a *‘comprehensive’* genome test. These participants drew on more technical usage of ‘genomic’ in the basic life sciences. Not surprising, participants also stressed how the larger public's understanding of genetics is often filtered by lack of knowledge and inaccurate media and marketing portrayals.

However, participants also described their understanding of genomic tests in ways that distinguished their expert perspectives as clinicians from others, including basic researchers,

but especially patients and promoters of personalized medicine. Further, they were especially concerned about how to explain the complexity of genomic tests to patients. In expressing their perspectives, some participants envisioned a part of their emerging professional role to include the education of non-geneticists, but when asked specifically about the meaning of the term ‘genomic’ they themselves expressed ambivalence about the meaning of a ‘whole genome test.’

In these discussions ‘completeness’ was a term that many participants differentiated within insider’s and outsider’s views and, we suggest, linked to their effort of managing the expectations and the future of WGS as tool in the present. ‘Completeness’ in ‘basic’ science was in some ways more flexible. One participant said that what “‘whole genome meant” in their current discussion, “in the future” may “lack currency,” because what they discussed here about completeness and genomes “may be different than what we see in maybe two or three years’ in science (R1 G2).”

For many of the participants, they sat at the border of the inside and outside. They saw themselves as identifying with some basic scientists who were, as one participant stated, “trying to be careful....(R1 G3),” but their articulations revealed the tension to navigate these views about genomics, NGS, and medicine with patients and work environments. Not only was there an ‘outsider’ discourse, there was an outside world which they simultaneously had to navigate. We can read these discussions as efforts to resist what genetic professionals consider a naïve public understanding of WGSTs. Drawing on SE, we can read this differently. The focus shifts: less to seeing these framings as mere rhetorical strategy and more towards participants’ efforts to reconcile the promissory expectations that they describe as public – emerging from DTC and media into their own expectations by re-articulating these in their accounts. In the next section, we present another way in which genetic professionals attempted to negotiate these expectations and visions associated with them.

Managing promissory expectations: research-clinical boundaries

While the hype or promissory expectation from the outsider’s understanding of whole or ‘complete’ genome and genomic tests were at least in part managed by attempting to bring in an insider’s perspective, a new expectation, perhaps more negative emerged in discussions. This followed on many participants’ views that these tests are/were coming into the clinic soon. Following more general or global discussions about the meaning of ‘genomics’ and ‘genomic’ tests, the facilitator asked participants to consider several specific forms of genomic testing in clinical scenarios that involved genomic analysis. In these contexts as well as impromptu discussions based often on current events or local experiences, participants also discussed the prospect of using NGS and WGS in patient care. Many participants deflated the high expectations by putting the promissory ‘outsider’ idea of WGS tests in the research category, such as this participant:

P: I just think that NIH isn’t appropriately stepping to the plate to curate the kind of resource required for the responsible implementation of what the NIH likes to advertise: ‘Genetics is now, genetics is here.’ Um...so, you know, I think too much

is done as clinical medicine that is really research...Um, and I think patients are suffering. [Round 4, Group 2]

We found that discussions about research/clinical boundaries – either the articulations of clear boundaries or the ambivalence about how or if to draw boundaries with WGS – turned into a recurring theme across sites and rounds. Some were less convinced about the existence of sharp boundaries between these spheres of activity and attempted to work through them. In the following, based on a case scenario of a person who's adopted and comes in for a genomic test, these participants discuss whether whole genome assessment in the clinic is really a research project or a clinical tool:

P: ...you can get a real bombshell that might change your life. I think that's – I mean you said, "What if Huntington's shows up?" What if, uh, the person has FAP or, you know, I mean...

P2: Right...but you know, at some point this type of test will actually have some statistics around. If you have and you come in and you're 25 years old and you have no other problems and this is all you know, these are your chances for having something.

P: Provided there's a collection, a follow-up collection {right} of prospective data collection {yes} and repository. {yeah}

P2: So, are you suggesting maybe that the only way this [genomic] should be offered is as part of, "I'm volunteering to participate in a registry and I will...agree to be – to contribute my health data in the future so that we can understand better what my tests mean?"

P:That's right, I mean as a research project to, to have a longitudinal study for subjects to agree and consent to that information being collected...yeah.

P2: So if it diagnoses my kid's mental retardation right now, that's wonderful. If it just tells us a bunch of things that we aren't sure...what will happen then I'm part of the research project. [Round 1, Group 3]

These participants were not directly addressing the promissory expectation of WGS but, in such tests arriving at their door, perhaps an expectation more about work-place disruption. Above, the participants are in some ways contributing to such an expectation, but in the following discussion, a participant suppresses somewhat the expectation of major disruption to their work practices, presenting a WGST as simultaneously a research test and an emerging technology in a clinical environment:

P: ...I think that as genetics professionals, we do this routinely, we introduce, you know, novel testing options...we talk about research testing in our practice. It's the non-genetics professionals that will have access to these tests that don't provide that service that need to be coached or need to be educated so that they can mirror the practices we already have. [Round 2, Group 3; our italics]

There was no consensus among participants that genetic professionals were well prepared for the coming of WGSTs and with it a shifting work landscape. Some drew clear boundaries while others were less sure there should be strict boundaries. Still others re-

presented themselves in this landscape in transformation with NGS, reinforcing the idea of their suitability for any changing environment. In this section, we attempted to illustrate with these examples how some translational genetic professionals manage the ‘outsider’ expectations about WGS in the clinic and how these intersect with their own expectations.

Managing ‘futuristic’ promissory tools: re-envisioning their place in the present

While participants viewed WGSTs as ‘novel technology,’ they showed some ambivalence about how new they were, questioning the ‘*revolution*’ and revolutionary expectation WGSTs in the clinic, as some participants described. While they pointed out that some things were new, most articulated that they did not view WGST as particularly revolutionary. In so doing, they situated genomic tests and WGST within an experiential framework – comparing WGST with other novel technologies introduced within clinical environments. They talked about how genetic professionals are experienced at introducing novel technologies into practice (example #1 below), compared WGSTs to other tools developed in medicine and the rise of genetics in the 20th century (example #2); and described genomic testing as something that was already being done in some areas (example #3):

Ex. 1 Novel tests

P: I think with any novel test, it, it will be a second-tier test until more experience is gained....it’s a complement to the screen that has already been done. And moving forward in the diagnostic process...

P2: I actually think that this is going to be a period that people will move through where I truly believe it will be a second-tier test at first <at first>. I envision a future in which there will be a period of time where everyone will know what their genomes are and they will know them presymptomatically and therefore it will part of your medical history in a sense, uh, as to know what your genome is...and then, physicians of the future will be able to correlate diseases with what’s already known. Right now, we have to think strategically about what the disease might be because we only have certain things we can test for and we only have, in some cases a clinical diagnosis rather than a genetic testing diagnosis. [Round 1, Group 3; our italics]

In the exchange above, these participants classify WGST as a new or novel test but in so doing they situate these tests in the context of how they use clinical diagnostics tests. In the example above, it is a second tier test, that is, triangulating or, ‘complementing’ the more standard test in this case, screening. For them, these tools – similarly to other new tools – are integrated into practice in more evolutionary fashion rather than revolutionary. At the same time, the second participant above enrolls the future in this discussion, especially in our italicized portion. In an SE framework, this can be read as an effort to connect the more futuristic narrative of WGST to the present use, making its ambivalent/questionable status as a test today, perhaps, more meaningful to the participant. In the following example, participants compare WGST to other tests, in this case MRI and body scans:

Ex. 2 Comparison to other tests

P: it makes me think, well if you can say no, you want your MRI, but you know what, the MRI isn't going to show you at all what you need, go ahead and try and find the one person that's happy to let you pay for it or get you. Why can't you say, 'This is really not going to show you any of the information you need.'

P2: But can you say that? What if there is, what if they do have it? I'm not saying it's common.... P: Well, but can you say that about an MRI? Really? ... the people that are doing the fully body scans, right? {right. right}. They come ...to you and they say, 'I want a full body scan,' You could say, 'Well, the truth is we could see something, who knows what it is we'll see since we don't do – you know, we don't have baseline data, we don't do full body scans on everyone. We could see interesting anomalies but they could be nothing, but we could...information.' So it's the same thing like.... [Round 1, Group 3]

In this case, the participant does not enroll the future but compares WGST to a current technology that also has cultural significance in contemporary society: the full body-scan, and in so doing starts a conversation that again highlights an insider, or informed, understanding of novel technologies versus the outsider simple view of biomedical technologies. WGSTs like 'full body scan' are technologies that conjure up in public imagination, technology's ability to see everything about our bodies and by extension everything – about us.

Lastly, in this third example, WGST is presented as a narrative about the diffusion of technology and, specifically, offers that there is a trickling effect. That is to these participants, they may be developed, used, or happening in some areas before they get to other areas of medicine.

Ex. 3 Happening in some areas of medicine

P: I think the development will be to specific pediatric...at least my understanding of where they're moving is metabolic, pediatric, adult onset, even cancer...so that you wouldn't be doing that type –I mean, I could be wrong –maybe in the future, you're right, the whole thing.

P2: I – my thought is...it's being done now.

P: Hmm (agreement).

P: well, some of it was, some of it was not. Some people are offering – said they are offering whole genome...others are doing oligos, others doing BACs...I –it's already –the horse is out of the barn. [Round 1, Group 3]

The main points that we make with these examples are the following: (1) participants tone down the highly expectational narrative that they claim is the public narrative of WGS and WGST; (2) in these articulations participants imagined WGST in situated contexts temporally and spatially; and (3) mobilized, negotiated, and/or resisted strongly expectational discourses. In the first instance, for example, participants articulated a WGST as a novel technology but one that within today's clinical sphere will remain secondary (paraphrasing the participant above 'as most novel technologies in medicine do') until the future. In the second example, a WGST was viewed as analogous to other technologies

today, like a body scan and thus located within a similar hyper-market space. In the third, participants suggested that WGST may currently be located in some clinical-research arenas of medicine, such as pediatrics or cancer. WGST in clinical arenas may develop, first (or primarily) within any one or all of these contexts. In this case perhaps the future is now – they seem to suggest – but not everywhere and at once.

In presenting these examples framed through SE, we argue that expectational narratives were not written off as simply marketing hype or as futuristic visions lacking in content. Rather, expectations were re-narrated, re-articulated by genetic professionals, they appear to perform a different function, namely, to assist in situating themselves within a complex array of social forces, simultaneously helping to bring these new technologies into existence while preserving core elements of the professional identities of future users of emerging technologies. It is for this reason that it is critical to examine the specific expectational narratives being used—for what purposes and by whom.

Managing some negative expectations: professional issues and identity

Participants generally agreed that many patients and other clinicians would buy into the promissory expectations of WG/ES tests – some patients because they would buy into the promises of better health and others (e.g. PCPs) because they would buy into the idea that it was cheaper. Many participants articulated a situation where there would be some changes in their environment with a *'flood of patients'* – patients who *'don't belong in the clinic'* changes in workload, especially the *'amount of work'* because of *'bigger tests'*; and growing need by new professional actors – PCPs and other specialist *'clinicians [who] can't interpret the results so they refer'* to them. Many maintained that they did not want to have their core identity (e.g. the *'medical geneticist'* as diagnostician) to change nor did they think it would. Nor did they think their jobs would be radically different just *'with a little bit more complexity'* as one participant stated. At the same time, however, many participants were concerned about their lack of control over how they believe a WGST will be ordered and how it will enter their practice, as articulated by this participant:

P: I think there will be plenty of work for us but the reality is I don't know that we can control the way...these tests are ordered...you just can't. [Round 4, Group 5]

For some of our participants, the more promissory expectation of NGS in the clinic was simultaneously an expectation of dread for them in the work place. Furthermore, as we describe below, they were concerned about issues related to accountability and promissory expectations about NGS and their WGSTs, which they saw as driving these new technologies and that they themselves might be contributing.

Views of clinical inevitability and future uses of WGST in patient care

As we showed above, participants were concerned that a number of different groups, especially PCPs may potentially flood their clinics with patients, but they did not present them as *the driving factor* for using WGST in patient care. Within these discussions, participants articulated larger forces as driving non-genetic clinicians and themselves towards whole genome testing. These include DTC genomics and biomedicine's thought leaders' largely promotional stance on personalized genomic medicine (PGM). In so doing,

participants often articulated both the clinical inevitability of ‘whole genome’ assessments as clinical tool and their ambivalence about WGS as a tool in patient care, as in this exchange:

P: ...you know, with the development...of the technology for genome sequencing we are soon gonna be able to sequence the entire genome in a whole bunch of people and it will be a huge push for that –for a personalized medicine and not only are all of these diseases going to be unveiled there....

P2: Thousands more.

P:...but every single – every single disease that has ever been implicated is gonna be...

P2: It kind of makes you wonder, you know, when is – sort of like this is kind of at the cusp of being harmful but at what point is it not harmful and you just kind of have to start doing it to be able to develop the methods to be able to do it well. And I don’t know when – it’s hard for me to gauge what point that becomes, you know?

P: It seems like it’s now. You can’t stop a moving train then, you know, that DTC is happening. [Round 2, Group 5]

While not surprising participants tended to voice worries about the ‘*moving train*’ of genomics, many participants also attributed the clinical inevitability of WGST to the science and growth of knowledge of WGS research. In other words, these participants suggested that it is the confluence of DTC genomics as well as techno-scientific advancement that are the primary drivers of clinical genomics. Alongside these views about inevitability, participants also indicated that there would be significant challenges in preparing for these changes.

Clinical applications of NGS and other genomic technologies, for the majority of the participants, were not viewed as simply, futuristic possibilities that will arrive *far off* in the future. Instead, for many of these professionals, genomic tools reside at the boundaries of future and emerging. Participants articulated that WGSTs have crossed the boundary from research into the clinic in some ways but at the same time ‘whole genome sequencing’ test was not a stable concept in that it remained debatable and contentious as to what it was in concept, material test platform, and application. In later focus groups, especially, participants articulated different visions of WGST in the clinic from those visions/versions they believed were offered from the broader public, direct-to-consumer, and designers of genomic test platforms. In particular, participants negotiated or re-envisioned the ‘whole genome test’ as no longer about everything but re-imagined a targeted version of WGST:

P:...using the technology is different from what you do and interpret so you do the sequence.

F: I’m sorry, yes?

P: If the sequence is costing \$500 these days, why would you spend \$1,000 for a single gene test? F: But looking for something specific, yeah.

P: You do them but you apply the filters and look for only these things, those things. [...]

P2: For sure it's cheaper.

P: ...if it's cheaper, sure but don't even pretend that anyone knows what to do with the rest of it.... [Round 4, Group 2]

Many participants' discussions of WGST included efforts of re-conceptualization as reflected above. By this we mean that they re-presented a tool, concept, and/or endeavor, and did so by anchoring it in some way to their understanding of diagnostic tools, their disciplinary and professional cultures, and current clinical medical environments. In so doing, they sometimes re-envisioned the WGST *as well as* their professional practices.

Many participants articulated that they believed WGST would emerge as a clinical tool in the near future but stated they would not use these tools if they had the choice. Many participants across the sites considered simply using WGSTs, when it arrived in their clinic (WGST as a non-specific test), but would turn it into a targeted test – a test of specificity and one they could manage, interpret, and make meaningful for their patient. Our participants viewed this filtering as well as interpreting as both their *new and extended* role within their then current understanding of WGST for clinical practice. *Interpretive flexibility*, that is, as Akrich (1992) describes, the *description*, of WGST seemed rather limited. Despite their attempts to hold their understanding of WGST as separate from the more promotional and commercial vision about genomic test, their articulations, in complex case scenarios, showed repeated boundary crossing. In other words, their articulations about WGST and its future as well as their professional futures remained constrained by the promissory discourse of genomic medicine and its vision, articulated by them as the public understanding of genomics and genomic tests.

Discussion and Conclusion

This paper took as its point of departure the promissory narrative around NGS and the contest to it. In this paper, we showed how some translational genetic professionals managed promissory rhetoric about WGS testing in the clinical environment in the United States. The primary aims of the FG study were to elicit more practical information from participants about utility, ethical and legal implications, and challenges to the interpretation and communication of results of multiplex genetic and genomic platforms. Yet in analyzing the data we also saw participants' attempts to construct meaning of the emerging WGSTs in complex accounts. In presenting this data, we sought to show some specific narrative resources that these professionals used in addition to the outsider/insider frame: a boundary framework of research versus clinical environments, history of medical tools frame, and identity construction in the relationship between tools and profession. As well, we saw this as an opportunity not only to explore their articulations on the subject of WGSTs but to discuss the expectational language in this area further, our analysis informed, especially, by the sociology of expectations that considers how different groups manage expectations (Tutton *et al.* 2008, Wainwright *et al.* 2006, Webster 2009).

In the industrial world, and especially in the US, we are accustomed to the phrase, 'the future is now.' It's often left to audience members to unpack how authors use this expression. However, while there has been/is widespread rhetoric that genomic knowledge

will/is transforming biomedicine, there has been/is also skepticism from many sides. Bioethicists, media, and other commentators on genomic medicine and other new biomedical technologies increasingly frame the issue of emerging technosciences as a question of hype or hope. Hype seeming to suggest something so fantastical it most likely will never come to fruition, at least in our lifetime; hope seeming to suggest it may be realistic, perhaps even on the horizon. In this way, though, commentators, researchers, and readers often attempt to get at either the intentionality of the speaker, hoping to elicit the ‘truth’ of the statement, but recent research, from SE and others, show this isn’t the only framework and may not be the most productive to understand such rhetoric. SE researchers show that scientists construct complex accounts of expectations about emerging technologies (Brown *et al.* 2000).

Medical researchers concerned with translational genomic efforts often frame the problem as the challenges of translating basic science into clinical practice. In biomedical research, translational efforts are often viewed as stymied by both clinical professionals’ lack of scientific understanding of laboratory science and bench scientists’ lack of understanding of research with people (Mancoff 2004; Hörig *et al.* 2005). The discursive dimensions of translation as well as the new often become lost in this frame. SE provides a framework for highlighting the diversity of expectations, expectations in translation, and their contours but also puts more focus back on the discursive dimensions. In these FGs, it doesn’t seem as if the role of extreme promissory expectations was vastly different in participants’ (most were at least partly skeptical) accounts, but it seems that this type of expectation and their recognition of its hyperbole did help these diverse professionals unite themselves as a group of translational experts who were neither the core set nor outsiders. In that sense, there is a material account here.

Using SE as a framework on stakeholder views also helps highlight the role of the researchers here. Reflexively, we acknowledge that our focus group design to some extent contributed to the persistence of the expectational narrative in that we prompted some discussions by raising events, narratives, and situations that contribute to what may be regarded as hyperbole, hype, or promissory language in this domain. As Brown writes, “The dilemma is one in which we use our experience to interrogate expectations whilst also recognizing that we cannot place ourselves outside the world of expectations as if we were objectively disinterested observers. Futures are contingent; they are imagined, fought for, resisted and embraced in the present – in order to draw an imagined future into the real-time now. But it would be impossible to fully disentangle present hype from future reality” (Brown 2003: 17). Despite this we argue that our focus group data provides us a window in which to explore the situatedness of expectations both temporally (that is, their relationship to past, present, and future) and spatially (role, meaning, functions through the assemblage of designers/users, technology/tool, environment, and social worlds). They help us to explore the efforts that have to be made by some ‘stakeholders’ to manage them.

Participants were not only co-constructing expectations and visions of professional identity, they showed that they were simultaneously concerned with managing accountability as these new tools made their way into the clinic. For many, the responsibilities of filtering and interpreting results themselves were not new. These are duties of their profession already,

but they did see whole genome as somewhat new – especially in terms of scale and scope – and so filtering and interpretation at these new levels were new – to them. In articulating these as re-newed duties, then, they also described the need for new social and cultural arrangements that included more collaboration among professionals but also possibly with patients. Participants also re-inserted/asserted translational genetics professionals’ (especially clinical genetics specialists’) value and expertise in this arena, but in articulating these, they often questioned who will be responsible for the outcomes of these tests, especially because the majority of the results will, in the near-term, not be interpretable and therefore remain uncertain and unknown. Some participants in envisioning future scenarios re-distributed responsibility to other professionals as well to patients themselves. In stating this, we do not intend to criticize these professionals. Rather it is to highlight that whole genome sequencing in the clinic will create new uncertainties for all its stakeholders – including clinical professionals.

Many participants were concerned about language and discourse, “I think, words have meanings or mis-meanings and boy, you say, ‘genetics’ and ‘DNA’ and stuff and that means one thing to one person and completely different meaning to another person...[R1 G4].” Many were aware of this even in themselves. Language is part of the politics, interpretation, and ethics of emerging technologies. Language is especially important to attend to in areas that we might call ‘public’ science – that is, sciences that are highly visible across multiple spheres of our society, as genomic medicine is, especially when framed as personalized or individualized medicine. This is an area of emerging medicine, an unstable domain, in terms of discourse and practices, in which different groups and individuals are vying for representational privilege and yet not all come to the table equally, including (potential) users, even medical professionals.

They viewed WGST in clinical practice as on the horizon, but saw little capability on their part in controlling their ‘flood’ into the clinic. These professionals, in the clinical translational space, perhaps not surprisingly, felt that they were best suited as gatekeepers of this emerging/future technology. While many participants were clear WGSTs were not yet ready for clinical practice many participants did not write it off completely. Many participants articulated future benefits from genomic science for medicine that could be read as part of the highly promissory, expectational (outsider/public) representations of WGST but in the FG discussions they also attempted to situate them, for example, historically. By bringing the views of these (potential) users in dialogue with SE, our approach permits what sociologist of science Adam Hedgecoe has described as a process that allows those of us outside the “expectation-generation process to ask questions of commentators’ authority, to suggest that they might benefit from discussing their ideas with specialists in particular disease areas, [and, we would include, others] to root their claims in clinical practice.” (Hedgecoe 2004: 180).

Further, while SE is often associated with anticipatory policy or technology assessment concerns, we suggest that it is also useful for those concerned with participatory research and public understanding of science. On a broader level of public dialogue, we suggest that researchers, public policymakers, media, and stakeholders who are concerned with the ethical, legal, and social aspects, should be more attentive to the diversities of expectations

about WGSTs. We can't argue from this data that participants' visions and scenarios are performative in the sense, e.g., that they work towards the direction of enacting WGSTs sooner into the clinical environment. However, our data and analysis suggest that participants may work to stabilize these promissory expectations in some specific ways, often compelled by their view of its inevitability. While they saw this 'moving train' metaphor as linked to outsiders and promoters and viewed it as hype, their accounts seem to make the hype version into something more realistic. Answering how much their efforts may actually work towards performance in their work places or policy dimensions requires ethnographic engagement. Still in this paper, by bringing attention to some ways in which some professionals try to make sense of WGSTs and expectational language about them, we suggest that this is more than merely rhetoric or a matter of hype or hope. As more groups are enrolled or appealed into translating emerging technologies sooner, examining their efforts to navigate and manage expectational language will be crucial to better public dialogue and participation as well as to the roles of researchers interested in them. We hope that the present paper, by engaging empirical data with this conceptual sociological framework on expectations and in context of NGS literature throws light on the importance of and encourages more interdisciplinary social science perspectives on discourse to the growing medical literature on translational medicine especially in the United States.

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