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"Out of the Labs": The role for ethnography in guiding clinical trials

YOSHA GARGEYA and MADS HOLME
ReD Associates

Ethnography and clinical research appear fundamentally disparate, even conflicting. Their very objectives are dichotomous – the latter moves molecules 'from the lab to consumer market' in controlled environments, while the former studies the uncontrolled environment of everyday life. However, with the new reality of pharmaceutical research and development, companies are urged to look into new ways of delivering impact and value to payers, prescribers, and users. This paper explores how ethnographic research can fill that role in early stages of pharmaceutical clinical trials, challenging current paradigms of method as well as parameters for success – and how bridging methodologies can open new avenues for ethnographic practice in business.

INTRODUCTION: TWO CONFLICTING WORLDS

From the advent of penicillin to anti-cholesterol treatments, history has witnessed major developments in medicine and therapeutic offerings. At the same time, however, the prevalence of both lifestyle and chronic diseases continues to rise (Brok-Kristensen 2007). Coupled with the increasingly competitive reality of pharmaceutical research and development, pharmaceutical companies must look into new ways of delivering impact and value to payers, prescribers, and users of medicine alike.

As clinical trials and ethnography have traditionally stood apart in practice, both because of their methodologies as well as their world-views, ethnography stands as an unlikely candidate to deliver this change. Within clinical trials, the development of medicines takes place by moving a molecule from the lab and testing its efficacy on patients – a long process governed by a highly regulated and controlled system.

In contrast, ethnographic methods have provided us with the means towards studying the real world and real people in uncontrolled, everyday environments. Ethnography has a long tradition for understanding people's well-being, the perception of purity and normality as well as stigma in different social and cultural contexts (Goffman 1956, Butler 1990). However, little emphasis has been put on how we apply these methods to the world of product development in an industry that has become central to modern-day well-being. Using a past project as an example, this paper focuses on how the use of ethnographic insights can inform the early stages of clinical trials and is challenging the current lab-based paradigm both in terms of method as well as the industry's parameters for success.

In our discussion we seek to address the following questions: How can ethnography provide insights into how best to test early drug development in clinical trials? How does this open a space for growth in ethnographic praxis in even the controlled and de-contextualized setting of the lab? How can an integrated approach lead to better patient outcomes and more efficient treatments?

THE NEED FOR DIFFERENTIATION: REALITIES OF THE PHARMACEUTICAL INDUSTRY

The emerging pharmaceutical industry

While the pharmaceutical industry was once best described by its never-ending sequence of blockbusters, the reality it faces today harshly contrasts with the "era of abundance" it once enjoyed (Hewitt *et al.* 2011). Today's world is measured by a rise in regulation and competition, as well as diminishing profits.

The pharmaceutical marketplace has slowly become saturated due to the attraction of past blockbuster successes. While new drugs twenty or even ten years ago often created a new therapeutic class, today's are adding to an already saturated field in rapidly crowding pipelines – leading to drugs that struggle to differentiate themselves from their established predecessors. This growing competition can best be measured by diminishing industry ROI – from 1996 until 2004, drug companies produced an average of 275m USD in fifth-year sales for every 1b USD they spend on R&D. In just the next five years, this fell by over 70%. Only 75m USD in fifth-year sales were generated for every 1b USD spent on R&D from 2005-2010 (Hewitt *et al.* 2011). This pressure on pharmaceuticals comes not only from competing branded therapies, but also from the 'threat of generics'; the patents of drugs amounting to 120b USD in annual revenue will be expiring in the next few years, creating an opening for generics (Kandybin *et al.* 2012). In this climate of competition, pharmaceuticals seek meaningful routes for differentiation in their product pipeline.

This pressure is matched by pushes from payers and governments alike for healthcare reform, which in many instances moderates the frequency, pricing, and reimbursement of prescriptions. The end result is a system squeezed through competition and regulation alike, seeking ways to survive – whether by means of a steadfast pursuit of new blockbusters, a move to generics, or an expansion into diagnostics or other adjacent spheres. Within this context, ethnography can offer a unique tool to pharmaceuticals in the realm of R&D and early commercial development: a meaningful avenue for direction, differentiation, and parameters through which to better patient outcomes and investment ratio success.

Limitations and potential: The structure of the clinical trial process

While ethnography provides vast support to pharmaceuticals seeking to grow through the discovery of new treatments, the clinical trials process even in the 'era of abundance' was no easy task. Regardless of growth potential within the industry, the clinical trial process itself is protracted, expensive, and heavily regulated – one European estimate places trials as 58% of total pharmaceutical R&D costs (EFPIA). Clinical trials are defined to commence with the testing of a therapy on humans – and as such sit after the extensive process of testing on non-humans and of gauging the market potential: only 0.1% of compounds tested in pre-clinical phases subsequently progress to clinical trials (Tufts).

Prior to beginning clinical trials, the sponsor is faced with a number of potential indications and value propositions that they could explore: the process of moving from a molecule to value proposition. These can then be narrowed and combined in order to maximize commercial attractiveness as well as feasibility.

Clinical trials themselves serve many purposes, from being a safe and validated means to test a compound and its indications to demonstrating to payers that a drug has been approved for coverage for certain conditions and populations. It also serves as a period during which prescribers can familiarize themselves with new treatments and their protocols and promise. The process is divided into a series of phases: Phase I – IV. While Phase I tests on a small and healthy sample size primarily to ensure safety, later phases grow to samples in the hundreds and thousands which focus more on efficacy, dosing, and indications. However, even if a drug is suitably safe and efficacious as measured by governing bodies, there is no guarantee that it will be successful in garnering scripts, patient outcomes, or ideally both in conjunction. We will argue that by using ethnography as demonstrated in the following case, developers will be able to increase the probability of this success in the market. Furthermore, by challenging the current paradigm of drug development by moving from a value proposition to a new therapy through the use of ethnography (rather than from a molecule and analysis to a resulting proposition), we argue that developers can better channel and maximize their investments through garnering cross-divisional focus on an over-arching disease strategy.

Though clinical trials are by no means new to ethnography, such studies often focus on the social relations and interconnection of governing systems upon which the research process depends (Petryna 2009). In contrast, our research stood much closer to medical anthropology endeavouring to understand diseases in context (Lock 1995, Cohen 1998, Brok-Kristensen 2007). Its approach to understanding the context and realities of the studied disease was modelled after prior medical anthropology – however, although its analysis and application vastly diverged. As such this paper will focus not on our ethnographic method, but rather on how our project applied our deep understanding of the underlying needs to a set of metrics that could be tested in clinical trials. Through this new approach of creating a design brief for the clinical trials process, our client could measure their compound's success not only in the eyes of regulatory bodies such as the FDA, but also in those of patients and doctors.

CASE STUDY: ETHNOGRAPHY AS A GUIDE FOR EARLY CLINICAL TRIALS

Study background

In the fall of 2012, our firm conducted a consulting project for a major pharmaceutical company in order to better understand current treatments and to inform our client's perspective for developing offerings for a chronic degenerative disease. The project's overall goal was to understand success criteria for a late entrant into a highly lucrative but also rapidly saturating therapeutic class. However, because of our client's unique position at the time – having molecules in Phase II and Phase III clinical trials but no existing portfolio for

this disease area, what began was not a campaign to better market an existing drug. It was rather an exercise in providing an in-depth understanding of the potential of the drug in development and a means for differentiating it by first understanding what 'successful treatment' would mean from a doctor or patient's perspective, as well as how doctors build therapy knowledge and skill in this field. The project found its success in translating and structuring these insights into guiding principles on how to approach the disease as well as recommendations (or 'design briefs for the clinical trials process') and differentiating hypotheses that our client could test in clinical trials.

The study was conducted in the US as well as two European markets, studying patients, doctors, and nurses who were subject to and subjects of this disease. The research was designed so that respondents formed a true ecology. We followed multiple sets of doctors, nurses, and patients of the same clinic, and in so doing made clear the various perspectives of the disease and the criteria for living well with it, treating it well, and effectively slowing its progression.

One finding was that the defining characteristics of the disease varied broadly among stakeholders – a factor common to many disease areas such as diabetes (Schoenberg *et al.* 2005, Brok-Kristensen 2007). Doctors, nurses, and patients simply did not agree on what ought to be included as the components and symptoms of the disease. Patients included many secondary conditions and manifestations of the disease that doctors viewed as tangential or derivative, whilst doctors focused upon the root causes of the disease – which were often neither felt nor noticed by patients. This resulted in having two disparate standards of success for treatment. For a doctor, treating the cause and stymying disease progression was all important but for patients this was insufficient unless matched with relief for the day-to-day symptoms related to the disease that current medicine only indirectly addressed. That is, while governing bodies and our doctors first measured success in a percentage decrease in disease progression, our patients rarely thought in terms of these long-term consequences. Successfully living with the disease was being able to walk their children to the bus stop, or keeping appointments with friends that they had scheduled weeks in advance.

While these results were hardly surprising, when coupled with the current FDA standards for approval or success within treatment, this divide became more poignant. The FDA's success criteria in this therapeutic class met health care professional (HCP) expectations with regards to safety, but its measure of efficacy was far below the standard of HCPs both in stringency and in scope. This became a key issue for to a large degree, portions of clinical trials are run, and variables are measured, so as to prove success in the FDA's (or other governing bodies') terms – neither necessarily in the terms of HCPs, who at the end of the day choose which drug to prescribe, nor patients, the final end-user with the ultimate prescription veto.

This case made it clear that these variations in success criteria were neither semantic nor reducible to marketing campaigns. Rather, HCPs in our studied disease area faced a marketplace of drugs that gave decent results to the average patient, as mandated by regulating bodies. Yet, they faced a wide spectrum of indistinguishable drugs at the individual patient level: they were at a loss for what gave great results for specific patients – the scenario with which they faced in reality. Despite having quite a few drugs on the market

from which to choose, they had little understanding of which would be best for the patients they treated. To complicate this further, this therapeutic class bordered being on prohibitively expensive and had trial periods for success that spanned many months – meaning patients and payers would spend exorbitant amounts of money for 6 months to 1 year before even being able to evaluate if the chosen drug was efficacious. As a medical professional, this amount of uncertainty and inability to clearly procure the best treatment proved to be a great struggle – challenging their self-perception as medical experts.

Furthermore, while HCP and FDA perceptions of efficacy were mostly congruous for this therapeutic class – patients' views of successfully living with the disease stood in stark contrast with the accepted idea of successfully treating the disease. As secondary conditions were central to their perception of the disease but no current drug was specifically aimed towards or tested along these parameters, patients struggled to understand the worth of this exorbitantly expensive therapeutic class.

Given the benefit of an ethnographic approach and the deep understanding of the realities of living with and treating this disease that it allowed, it became clear that the route to ensure success and differentiation for our client would also be one previously unfamiliar to ethnographic studies. What began was the slow process of challenging our client's perspective towards clinical trials, as well as the structure and parameters within it that they would employ. Our joint task was to consider how best to redesign clinical trials not only to demonstrate success in the eyes of the FDA but also to go a step further and include success for both patients and HCPs as foundational criteria.

Setting a direction for early clinical development

Understanding how drugs function and malfunction in the context of their users – understanding how drugs exist outside of the labs – gave us a unique opportunity to provide strategic direction for how drugs should be considered within the labs.

For example, the therapeutic class that we had been studying had been labelled at first by doctors and pharmaceuticals alike as the 'miracle treatments' primarily due to its chemical composition. It was assumed that it would revolutionize life for patients – and in some instances it did. However, for the majority of cases, and with all but one of our respondents, the supposed 'miracle drug' failed them, in part because it was termed a 'miracle drug'. While in the context of the lab, the drug's chemical composition was deemed a miraculous scientific breakthrough, it did not account for the realities of living with the disease or success from the user's perspective.

The discourse around the therapeutic class combined with its prohibitive price led patients to assume this drug would significantly diminish the effects of the disease. However, patients severely discounted the drug's effect on long-term disease progression (what the drug-class targeted), as it was something they could neither feel nor measure. Instead because the short-term and day-to-day effects of the disease were their primary concern (something the drug was never directly intended to combat) patients then felt they had been cheated or misled by pharmaceuticals and their physicians alike. If today they could not braid their daughter's hair or rely on being able to get out of bed and go to work, it did not matter to them that in ten years their disease would not be worse.

This misalignment between how patients experience the disease and how doctors and pharmaceuticals think about the disease was just one finding we were able to translate into the realm of clinical trials. Working alongside different departments within our client's organization, we were able to map out the 'foundational' needs for a drug – the basics for success outside the context of the lab – as well as a number of 'differentiating' needs – areas where no existing drugs yet provided for but would greatly improve either how patients perceive living with the disease or the assurances doctors look for when prescribing this class of drug. Both these foundational and differentiating needs went a step beyond the current drug offerings in that they accounted for the context of the drug in the world of the disease. Thanks to our client's expertise in medical research, we were then together able to propose practical solutions for how to measure success against these new set of needs in clinical trials. These proposals ranged from testing outcomes earlier and more frequently to including and focusing on demographic factors that physicians thought in terms of but which were not currently measured. Translating this knowledge back into something testable and demonstrable in clinical trials allowed our clients to begin to prove to patients and doctors alike that their solution was different – it understood the disease outside of the laboratory.

Translating insights and unmet needs to impact and early differentiation

Our client faced a considerable hurdle – they sought to enter a disease area, which had been populated for over a decade with a half-dozen drugs, as late entrants. They had the foresight to see that these current offerings, while good, did not sufficiently treat the disease. They also realized that each of these drugs ran clinical trials similar to the previous ones, "copy-cat" clinical studies, as our client described them. This means that clinical trials in this therapeutic class run the risk of being demonstrably efficacious only to regulatory standards. Ethnographic insight into the disease allowed us to challenge this – to strive for efficacy to the standard of living well and to translate what efficacy means in a real world perspective, not just as a pharmaceutical term.

In order to make this translation from insight to impact within the tightly defined scope of clinical trials, our team focused first on aligning our internal team, our client's project team, and the various departments with which they worked on a basic value proposition – a guiding principle that encompassed our understanding of success criteria, how key players understood and struggled with the disease. This brought a sense of clarity and a shared language around what it means to create success in the market place, not just in the lab.

This fairly abstract concept or "guiding direction" was then grounded by being applied to each of the foundational and differentiating needs found through our research, which together formed the "key unmet needs". Pairing these components gave the client team direction and strategic fuel: e.g. how do you create a drug provides added value and that stands out in the market? Working together with the client-team, we were then able to consider how we could test for success from the user's perspective within clinical trials.

This model, of moving from a value proposition to a drug, fundamentally contrasted with how clinical trials in our experience were typically run: from a molecule to a set of value

propositions that were narrowed down through further molecular and market analysis. The original model had succeeded for decades – in many instances because drugs at the time were creating a new therapeutic class. There was not the same need for differentiation. In therapy areas that still have openings for significant improvement, translating ethnographic insight into metrics that can be assessed in clinical trials provides one means for differentiation – treating the disease with new and deeper meaning.

THE ROLE FOR ETHNOGRAPHY IN CLINICAL TRIALS

While clinical trials may benefit from ethnographic insights in a multitude of instances, the authors find two areas to have the greatest mutual potential by providing avenues for ethnography to further the practice of running clinical trials, developing treatments with a greater degree of success, and bettering patient outcomes. These junctures are at the onset of clinical trials, and then again in very early stages. In the former ethnography can benefit pharmaceutical development by providing a unified disease strategy and in the latter a treatment value proposition – both of which can be translated into defined metrics for testing in clinical trials.

Defining a unified disease strategy

The status quo in development is to move from a molecule to a value proposition – which makes economic sense: starting with a broad pool of potential uses before narrowing down based on efficacy and market potential. However, in light of the push for differentiation, and ethnography's benefit of moving development from the constraints of the labs, the authors propose moving from a unified disease strategy to development.

A unified disease strategy or a broad cross-departmental approach to treating a disease area can provide a number of benefits. It is the foundation to any broad portfolio development: having a clear perspective on how a disease ought to be treated. Ethnography can provide guidance towards a disease strategy by understanding the underlying phenomena related to the disease in pre-clinical phases. This helps not only to guide innovation around therapeutic classes and to unify broader counter-disease measures, but also to develop cross-departmental synergies in our client organization.

Having an overarching disease strategy means clients can then allocate resources from a variety of departments and through a spectrum of methods (drug development, foundations, services, sales, device development, marketing, etc.) to serve one vision for changing or ameliorating a disease. Given a drug-launch may be years if not over a decade away, having a unified strategy allows for organization-wide efficiency in planning a maximally impactful launch. And, as doctors and patients hardly think of pharmaceuticals as a number of free-standing wings, having a clearly defined disease strategy enables all departments to work towards a single goal in a cohesive manner. Using ethnography to help define this goal ensures that it will reflect the reality of living with and treating a disease today. Not only does ethnography allow for users to be brought to the core of clinical development, it also allows for developers to be able to harness shifts in societal perceptions of diseases in order to innovate – to question constantly: how do we develop drugs for a new reality?

Using treatment value propositions to guide clinical trials

As trials commence, and particularly in their first and second phases, another opportunity opens up to consider development from a perspective outside of the labs. Here, ethnographic insights are not translated into a strategic direction for a disease area, but rather for a specific treatment. At this level, studies can be recalibrated given the additional understanding of success from the patients' and prescribers' perspectives. This lies at the core of running non-"copy-cat" trials: using an understanding of how the disease is lived with and treated in order to form an over-arching value proposition, and then applying that proposition across a number of stakeholder needs. Given this perspective on how to deliver upon these needs, we can then translate these goals into criteria that will be tested in clinical trials.

But, using a treatment value proposition, our client found one way in which they could simultaneously test towards the needs of their users, and aim for a differentiated treatment. In the disease area we were studying, for instance, it is difficult to isolate which drug will be best for which patient; however, we can now begin to test on indicators that will help prescribers identify the best drug for the individual – rather than the current paradigm of having a good drug for the average. By adding in a number of other similar measures to the trials, our clients can begin to reduce the barriers to entry of a new drug from a prescriber's perspective by actively helping them build a skill around how best and on what occasions to use the drug. From a patient perspective, we worked towards adding indicators that measure many related issues that patients consider central to their disease but doctors and pharmaceutical companies have traditionally overlooked as tangential. This higher bar of success (from both the patient and doctor's perspective) is a step towards ensuring accurate use and retention. Finally, while the alignment of departments in disease strategy can provide a unified approach to a disease, having an underlying treatment value proposition means departments can work together towards a more targeted, and perhaps more streamlined, process of drug development.

CONCLUSION

The use of ethnography in clinical trials, it seems, is a space of great opportunity for the practitioners of ethnography, their pharmaceutical clients, and those who treat, pay for, and suffer from diseases. Differentiation is key for emerging treatments and ethnography serves as one potential means to achieve this. It further allows for a shared understanding of the unmet needs of patients and practitioners across departments, which helps align development and can streamline the development process from the earliest stages.

Though many other methods may be successful in helping guide pharmaceutical development towards this outcome, ethnography holds the additional benefit of demonstrating the use and ideal use of treatments in the context of the everyday. Whether this means developing drugs so that they are tested in accordance with the mental models physicians use to treat their patients, or such that physicians can more easily build a skill around – ethnography helps inject inspiration for development from outside of the lab.

In order to do so, however, one must accept the necessity to combine the everyday life reality with the very structured system of clinical trials. In the presented case, some of the needs we found could not be tested for in clinical trials without cannibalizing the potential of the drug (e.g. testing focused on the most ill patients which would lead to poor results) or being unfeasible (e.g. high-frequency monitoring). This lead to a prioritization of our own, understanding the needs most fundamental to the disease in conjunction with how they could best be tested. Without being tailored to sit within the structure of clinical trials, our findings, while interesting would have lost all value to our client.

Furthermore, engaging our client across many departments proved to be a great help both to bolster the methodology as well as the findings, as development is a large organization-wide endeavour. Having a basic value proposition that could serve as strategic guidance and inspiration for all departments and then more granular findings relevant to each individual department allowed for a unity in purpose early in the clinical trials process as well specific recommendations within departments. Despite these cautions, in bridging the methodologies of ethnography and clinical trials, not only can we work towards a new form of drug development, but also a growing area of ethnographic praxis.

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